Chemistry of Oxaziridines. 8.[1,2] Asymmetric Oxidation of Nonfunctionalized Sulfides to Sulfoxides with High Enantioselectivity by 2-Sulfamyloxaziridines. The Influence of the Oxaziridine C-Aryl Group on the Asymmetric Induction

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Abstract: Chiral sulfamyloxaziridines **6** and **7**, prepared by biphasic oxidation of the corresponding sulfamylimines **5**, afford high asymmetric induction for the oxidation of a series of nonfunctionalized sulfides to sulfoxides (53–91% ee). The enantioselectivities exhibited by these reagents are comparable to, or in some cases better than, the modified Sharpless reagent reported by Kagan. Steric factors are primarily responsible for the chiral recognition. Planar transition state geometry, where the sulfur lone pairs share a common plane with the oxaziridine ring, is consistent with the stereochemistry of the oxidation. The success of these new asymmetric oxidizing reagents is attributed to the fact that the active site oxygen is incorporated in a rigid three-membered ring and the close proximity of the oxaziridine substituents to the active site oxygen.

A characteristic common to many asymmetric transformations that occur with high enantio- or diastereoselectivity is the ability of the reactants to form highly ordered rigid transition-state geometries that exhibit a large bias for reaction at one of the enantio- or diastereotopic faces of the substrate.[3] These effects minimize the number of possible transition states for the stereoselection. Most often transition-state rigidity is achieved by metal coordination of appropriate functional groups in the chiral auxiliary and/or substrate. Steric effects are generally responsible for the reaction bias at one of the enantio- or diastereotopic faces of the substrate. When the chiral auxiliary and substrate are coordinated together in the transition state, steric requirements for high stereoselectivity are much less than for attack of a substrate on an external chiral auxiliary. An example of the former is the Sharpless epoxidation which is able to accommodate allylic alcohols with very different steric demands.[4]

For the reasons discussed above, the development of reagents for the asymmetric oxidation of *nonfunctionalized* substrates with high enantioselectivities represents a formidable synthetic challenge. Microorganisms, in ways which are not fully understood, are able to epoxidize alkenes (70–100% ee) and oxidize sulfides to sulfoxides (3–100% ee) with high levels of asymmetric induction.[5] However, these enzymatic oxidations are not general, being substrate specific.

The asymmetric oxidation of sulfides to sulfoxides are the most studied nonfunctionalized substrates. Optically active peracids give very low enantioselectivities for the oxidation of sulfides to sulfoxides (1–10% ee).[6] This is understandable because optically active peracids lack conformational rigidity, and the active site is several bonds removed from the chiral center. Somewhat better results, for specific cases, are reported for oxidizing reagents (peracids and $NaIO_4$) in chiral media (up to 80% ee)[7] and electrochemical oxidations with use of a poly(L-valine)-coated platinum electrode (93% ee).[8]

The Sharpless reagent, modified with water, reported by Kagan et al., is the most general asymmetric oxidizing reagent yet discovered for the oxidation of sulfides to sulfoxides (7–93% ee).[9] However, this reagent is also substrate specific, giving lower enantioselectivities, for example, with *n*-butyl and benzyl *p*-tolyl sulfides, 20 and 7% ee, respectively (Table I: entry 1). Although the mechanism of asymmetric induction for this reagent is not fully understood, it appears to be steric in origin. Similar results have been reported for the anhydrous Sharpless reagent by Modena and co-workers.[10]

As part of our interest in developing new reagents for the asymmetric oxidation of nonfunctionalized substrates we are exploring the oxygen-transfer reactions of optically active 2-sulfonyloxaziridines **1** and **2**.[11,12] These compounds are important reagents for the asymmetric synthesis of epoxides,[13] sulfoxides,[11,14] thiosulfinates,[11] and selenoxides.[15] The application of chiral sulfonyloxaziridines in the asymmetric oxidation of enolates to optically active α-hydroxy carbonyl compounds (RR'C(OH)C(O)Z; Z = R, OR, NR_2) in high optical purity (50–95% ee) has recently been described.[16]

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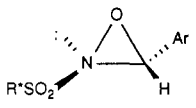
Table I. Effect of Aryl Substitution on the Asymmetric Oxidation of Sulfides to Sulfoxides by 2-Sulfamyloxaziridines **6** and **7** in $CHCl_3$

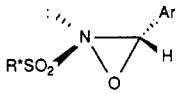
			sulfoxide % ee (configuration)[a]				
			p-tol-S-R		9-anthryl-S-R		
entry	oxaziridine **6** and **7** Ar	temp, °C	R = *n*-Bu	R = *i*-Pr	R = Me	R = *i*-Pr	R = *n*-Bu
1	$Ti(O\text{-}i\text{-}Pr)_4((R,R)\text{-DET})(TBHP)$[b]	−22	20.0 (R)	63.0 (R)	89.0 (R)		
2	(−)-(*S,S*)-**2a**[c]	25	18.9 (S)	23.0 (S)	44.8 (S)	61.2 (S)	48.4 (S)
3	(+)-(*R,R*)-**6a** 4-NO_2Ph	25		11.0 (R)	18.7 (R)		
4	(−)-(*S,S*)-**7a**	25		16.5 (S)	23.2 (S)		
5	(+)-(*R,R*)-**6b** 3-NO_2Ph	25	13.2 (R)	21.0 (R)	29.0 (R)	44.7 (R)	33.1 (R)
6		−20		33.0 (R)	48.0 (R)	53.2 (R)	42.6 (R)
7		−42		48.0 (R)			
8	(+)-(*R,R*)-**6c** 2-NO_2Ph	25		2.8 (S)	5.9 (R)		
9	(−)-(*S,S*)-**7c** 2-NO_2Ph	25			27.0 (S)		
10	(+)-(*R,R*)-**6d** 2-ClPh	25	4.0 (R)	18.9 (R)	15.9 (R)	35.8 (R)	16.7 (R)
11	(+)-(*R,R*)-**6e** 2-Cl, 5-NO_2Ph	25	31.0 (R)	38.1 (R)	53.0 (R)	72.3 (R)	57.5 (R)
12		−22	40.0 (R)	48.5 (R)	68.4 (R)	76.2 (R)	68.4 (R)
13		−42	43.5 (R)	65.0 (R)	*d*	*d*	*d*
14	(−)-(*S,S*)-**7e**	25	31.2 (S)	37.6 (S)	53.0 (S)	72.0 (S)	
15		−22	40.1 (S)	48.4 (S)	68.1 (S)	76.3 (S)	
16		−42		65.0 (S)	*d*	*d*	
17	(+)-(*R,R*)-**6f** 3,5-di-NO_2Ph	25	26.4 (R)	37.0 (R)	69.9 (R)	71.4 (R)	
18		−22	42.5 (R)	52.3 (R)	83.9 (R)	81.7 (R)	
19	(−)-(*S,S*)-**7f**	25	17.8 (S)	30.0 (S)	64.9 (S)	68.0 (S)	
20	(+)-(*R,R*)-**6g** C_6F_5	25	34.6 (R)	34.6 (R)	50.3 (R)	56.6 (R)	
21		−22	36.4 (R)	43.1 (R)	66.9 (R)	67.7 (R)	
22	(−)-(*S,S*)-**7g**	25	30.7 (S)	36.6 (S)	50.0 (S)	59.9 (S)	
23		−42	36.7 (S)	52.2 (S)	77.4 (S)	78.0 (S)	
24		−78	53.3 (S)	60.3 (S)	90.6 (S)	79.9 (S)	

[a] Sulfoxide enantiomers were separated on a Regis Pirkle covalent phenyl glycine HPLC column (ref 17). [b] Data taken from ref 9a and 9b. [c] Data taken from ref 11. [d] No reaction.

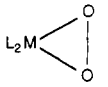
Oxaziridines like the Sharpless reagents and the metal peroxides **3** are members of the same class of oxidizing agents that have their active site oxygen as part of a three-membered ring. We believe that these reagents as well as peracids transfer oxygen by a similar S_N2 type substitution mechanism.[2] If we are correct in this hypothesis, then it should be possible to design chiral oxaziridines that give results comparable to the modified Sharpless reagent for the asymmetric oxidation of sulfides to sulfoxides.



(+)-(R,R)-1



(-)-(S,S)-2



3

a) R*= (+)-10 camphor b) R*= (-)-3-bromocamphor

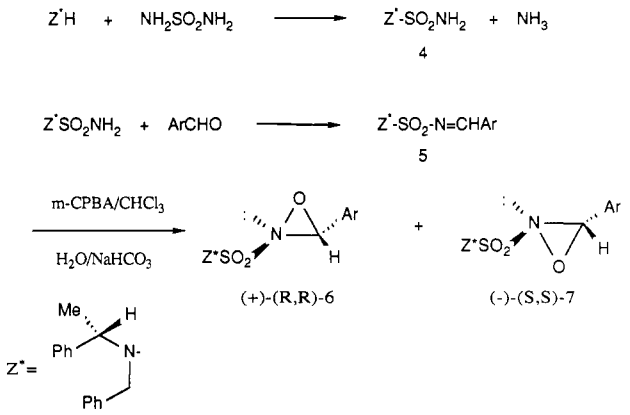
Ar= 2-chloro-5-nitrophenyl

In this paper we describe results of a detailed study of oxaziridine structure on the asymmetric oxidation of sulfides to sulfoxides. These studies have resulted in the preparation of oxaziridines that afford stereoselectivities for the oxidation of nonfunctionalized sulfides to sulfoxides (40–91% ee) which are comparable and in some cases better than the modified Sharpless reagent. From a consideration of the structure reactivity trends it was possible, for the first time, to define the transition-state geometry for the oxidation of sulfides to sulfoxides. The steric factors, primarily responsible for the asymmetric induction, have been identified.

Results

Our previous studies have shown that diastereomeric 2-sulfonyloxaziridines **1** and **2** give higher levels of asymmetric induction than chiral peracids for the epoxidation of nonfunctionalized alkenes (13–40% ee)[13] and the asymmetric oxidation of sulfides and disulfides to sulfoxides and thiosulfinates (11–46% ee).[11] Compared to the modified Sharpless reagent, however, the stereoselectivities exhibited by **1** and **2** for the oxidation of sulfides to sulfoxides is considerably lower (Table I: compare entries 1 and 2).

Scheme I



a) Ar = 4-nitrophenyl
b) Ar = 3-nitrophenyl
c) Ar= 2-nitrophenyl
d) Ar = 2-chlorophenyl
e) Ar = 2-chloro-5-nitrophenyl
f) Ar = 3,5-dinitrophenyl
g) Ar = pentafluorophenyl

To increase the efficiencies of chiral 2-sulfonyloxaziridines **1** and **2** as asymmetric oxidizing reagents as well as to understand the mechanism of asymmetric induction it is necessary to vary the groups attached to the oxaziridine N and C atoms in a systematic manner. For all practical purposes chiral sulfonamides ($R^*SO_2NH_2$), necessary for preparing the 2-sulfonyloxaziridines, are restricted to derivatives of camphorsulfonic acid. This limits structural variation of the sulfonyl portion of the oxaziridine. Perhaps of greater importance is the fact that 2-sulfonyloxaziridines are chromatographically unstable. To date **1** and **2** are the only diastereomeric 2-sulfonyloxaziridines that we have been able to separate, optically pure, by crystallization.[11]

Chiral 2-Sulfamyloxaziridines. The structural limitations inherent in the camphorsulfonamides would appear to be absent in the chiral sulfamates ($Z^*SO_2NH_2$, Z* = chiral secondary amine). In principle, a chiral sulfamide can be prepared from any secondary optically active amine by heating with sulfamide ($NH_2SO_2NH_2$) as shown in Scheme I. Indeed heating equivalent

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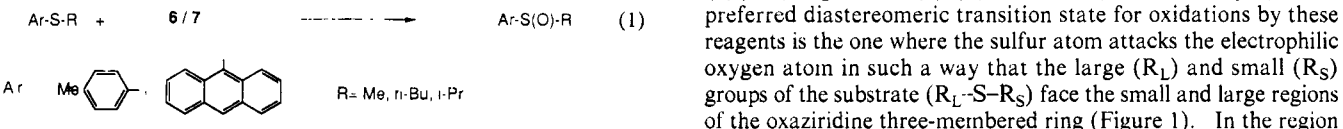
amounts of (−)(*S*)-*N*-(α-methylbenzyl)-*N*-benzylamine with sulfamide in dry dimethoxyethane until the evolution of ammonia has stopped (3–6 days), gives a 78–80% isolated yield of optically active sulfamide **4** (Scheme I).

Earlier we had shown that sulfonimines ($RSO_2N{=}CHAr$) are readily prepared by heating sulfonamides with the diethyl acetals of aromatic aldehydes at 150–180 °C.[11] Attempts to prepare sulfamylimines **5** in a similar manner resulted in rapid decomposition of the reaction mixture due to the thermal instability of the sulfamide. Attempts to lower the temperature of condensation with Lewis acid catalysis ($AlCl_3$, $AlCl_3{\cdot}6H_2O$,$SOCl_2$) were only moderately successful affording low to moderate yields (10–70%) of the desired sulfamylimines **5** as complex mixtures difficult to separate.

Sulfamylimines **5** are prepared in good to excellent yields (70–95%) by heating **4** with an aromatic aldehyde in benzene containing 5-Å powdered molecular sieves and an acid catalyst such as Aerocat Triple A or Amberlyst 15 ion exchange resin (Scheme I). Sulfamylimines **5** are crystalline solids giving satisfactory elemental analyses. These compounds are characterized by a downfield singlet at δ 8.9–9.3 ppm in the proton NMR spectra due to the imino proton and by the infrared C=N stretching band at 1610 cm^{-1}.

Biphasic oxidation of **5** using *m*-CPBA/$NaHCO_3$, as previously described,[11] gives approximately 1:1 mixtures of the two diastereomeric sulfamyloxaziridines **6a–g** and **7a–g** in 80–95% isolated yield. In contrast to the camphorsulfonyloxaziridines **1** and **2** all of the sulfamyloxaziridines are stable to chromatography. Thus the 2-sulfamyloxaziridine diastereoisomers **6** and **7** can be separated, in gram quantities, optically pure by HPLC. 2-Sulfamyloxaziridines (+)-**6** and (−)-**7** were generally crystalline solids, melting with decomposition and, for the most part, giving satisfactory elemental analysis. The proton NMR spectra of these compounds exhibit a characteristic singlet absorption at δ 5.4–6.0 for the oxaziridine 3-proton at the benzylic position.

Asymmetric Oxidation of Sulfides to Sulfoxides. The availability of easily separable diastereomeric 2-sulfamyloxaziridines **6** and **7** made possible a systematic evaluation of the influence of oxaziridine structure on the stereoselectivity of the oxidation of sulfides to sulfoxides. With this goal in mind, we explored the influence of the oxaziridine C-aryl substituent on the asymmetric oxidation of a series of sulfides to sulfoxides as shown in reaction 1. These particular sulfides were chosen because their enantiomeric sulfoxides can be separated on the Pirkle covalent phenyl glycine HPLC column.[17] Thus asymmetric oxidations can be reliably carried out on as little as 5 mg of sulfide.



Asymmetric oxidations were accomplished by dropwise addition of 2-sulfamyloxaziridines **6** and **7** to the sulfide in the desired solvent and at the appropriate temperature. Oxidation of these sulfides was complete and quantitative in less than 10 min at 25 °C, as monitored by NMR, without detectable sulfone formation (eq 1). For oxidations carried out at −22, −42, and −78 °C the reaction mixture was quenched at these temperatures, prior to workup by addition of 1 mL of triethylamine. This was to avoid oxidation at temperatures other than the specified one. Oxaziridines **6e** and **7e** failed to oxidize the 9-anthryl sulfides at −42 °C within 24 h. On the other hand, these sulfides were oxidized quantitatively to the sulfoxides at −78 °C by pentafluorophenyl-2-sulfamyloxaziridines **6g** and **7g** within 1 h. Products were isolated by TLC chromatography in greater than 90% yield when carried out on 0.25 mmolar scale.

The enantiomeric excess (% ee) of the chiral sulfoxides was determined by using the Pirkle chiral HPLC column. Absolute configurations were established by comparison with authentic samples. For all sulfoxides separated to date the first enantiomer eluted had the S-configuration. Similar results were reported by Pirkle and co-workers.[17] These results are summarized in Table I.

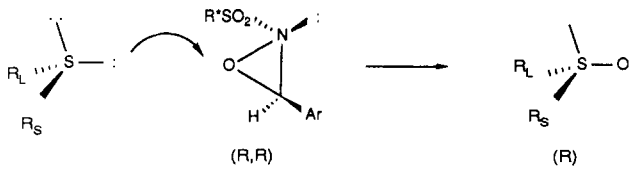
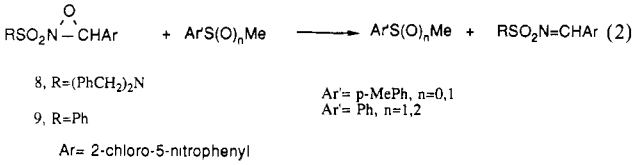


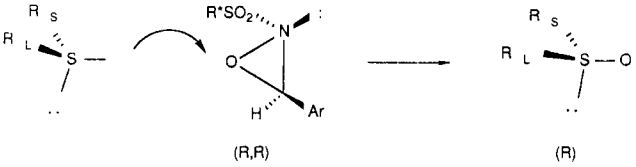
Figure 1. Chiral recognition model for the oxidation of sulfides by (R,*R*)-**1**.

A competitive rate study of the oxidation of methyl *p*-tolyl sulfide and methyl phenyl sulfoxide by oxaziridines **8** and **9** was undertaken to determine the influence of 2-sulfamyl vs. 2-sulfonyl substitution on the rate of sulfide oxidation (eq 2). The rates



of oxidation of sulfide and sulfoxide were 1.7 and 1.4 times slower for the 2-sulfamyloxaziridine **8**. Bulky groups and electron-donating substituents attached to the oxaziridine nitrogen and carbon atoms slow the rate of oxygen transfer by 2-sulfonyloxaziridines.[2] Thus the most likely reasons for the somewhat slower rates of oxidation by **8** are the steric bulk and electron-donating ability of the sulfamyl amino group (Z*) (also see below).

Absolute Configuration of 2-Sulfamyloxaziridine. Studies of the oxidation of sulfides to sulfoxides by 2-sulfonyloxaziridines **1** and **2** revealed that the configuration of the oxaziridine three-membered ring controls the sulfoxide stereochemistry, with steric factors being responsible for the chiral recognition.[11] Thus, (+)(*R*,*R*)-**1** gave, in every case, the (+)-(*R*)-sulfoxide, while



(−)(*S*,*S*)-**2** gave the (−)-(*S*)-sulfoxide (Table I, entry 2). The preferred diastereomeric transition state for oxidations by these reagents is the one where the sulfur atom attacks the electrophilic 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 1). In the region of the oxaziridine three-membered ring the R^*SO_2- was considered to be larger than the C-aryl.

The configuration of the oxaziridine three-membered ring in **6** and **7** also determines the stereochemistry of the product; i.e., (+)-**6** gave the (+)-(*R*)-sulfoxides while (−)-**7** gave the (−)-(*S*)-sulfoxides (Table I). Since the mechanisms of oxygen transfer by **1** and **2** and **6** and **7** are likely to be similar, if not identical, the chiral recognition model shown in Figure 1 can be used to assign the configurations of the oxaziridine three-membered ring to **6** and **7**. This model predicts that the diastereomeric 2-sulfamyloxaziridine that affords the *R*-sulfoxide has the R,R configuration while the S,S-configuration is assigned to those oxaziridines that give *S*-sulfoxides. An X-ray crystal structure of (+)-(*R*,*R*)-2-sulfamyloxaziridine **6b** confirmed these configurational assignments.

Structure of 2-Sulfamyloxaziridines. Figure 2 shows the computer generated structures of 2-sulfamyloxaziridines (+)-**6b** and **8**. The structure of (+)-**6b** establishes that the absolute configuration of the oxaziridine three-membered ring is R,R, in agreement with predictions made based on the chiral recognition model (Figure 1).

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

entry	oxaziridine Ar =	solvent	sulfoxides % ee (configuration)	
			p-X-Ph-S-*i*-Pr	9-anthryl-S-Me
1	(*R*,*R*)-**6b** 3-NO_2Ph	$CHCl_3$	21.0 (R) (X = Me)	30.0 (R)
2		H_2O	26.0 (R)	38.0 (R)
3		4.8 M LiCl, H_2O		38.0 (R)
4		0.2 M LiCl, H_2O		38.4 (R)
5		PhMe		32.8 (R)
6		MeCN		37.4 (R)
7		EtOH		33.6 (R)
8		CH_2Cl_2		34.1 (R)
9	(*S*,*S*)-**7e** 2-Cl, 5-NO_2Ph	$CHCl_3$	37.6 (S) (X = Me)	50.0 (S)
10		PhMe	39.0 (S)	48.0 (S)
11		H_2O		53.0 (S)
12	(*R*,*R*)-**6f** 3,5-di-NO_2	$CHCl_3$	37.4 (R) (X = Me)	69.0 (R)
13		$CHCl_3$	37.6 (R) (X = OMe)	
14		PhMe		74.4 (R)
15	(*R*,*R*)-**6g** C_6F_5	$CHCl_3$	44.6 (R) (X = Me)	50.3 (R)
16		$CHCl_3$	39.0 (R) (X = OMe)	
17		PhMe	31.7 (R) (X = Me)	57.3 (R)

The structures of the oxaziridine three-membered rings in (−)-(*S*,*S*)-**2b**, (+)-(*R*,*R*)-**6b**, and **8** are not significantly different, having similar bond angles and bond lengths. The C–N bonds lengths are, however, statistically different being 1.410 Å in **2b**, 1.461 Å in **6b**, and 1.430 Å in **8**. In the region of the active site oxygen the most significant differences are found in the relationship of the oxaziridine C-aryl group to the three-membered ring. In **2b** the 2-chloro-5-nitrophenyl group is coplanar with the C–N bond of the oxaziridine ring while in **6b** and **8** the aryl groups are approximately coplanar with the oxaziridine C–O bond. The oxaziridine nitrogen atoms in (−)-(*S*,*S*)-**2b**, (+)-(*R*,*R*)-**6b**, and **8** are tetrahedral, sp^3 hybridized.[11,19] The sulfamylamine nitrogen atoms (N(5)) in **6b** and **8** are almost trigonal planar (sp^2 hybridized) suggesting some electron donation (p–d π-bonding) from N(5) to the sulfonyl group. This is in agreement with the slower rate of oxidation observed for 2-sulfamyloxaziridine **8** vs. 2-sulfonyloxaziridine **9** (vide supra). Attempts to obtain suitable crystals for X-ray analysis of **6e** and **7e** were unsuccessful, but the relationship of the C-aryl group to the active site oxygen should be similar to that found in **8**.

Discussion

Inspection of Table I reveals a number of important trends. As observed in many asymmetric transformations, as the temperature of oxidation is lowered from 25 to −78 °C the asymmetric induction increases.[3] This effect is probably related to increased rigidity of the substrate and oxaziridine in the transition state. This hypothesis is supported by the observation that the percent change in enantiomeric excess on lowering the temperature is generally larger for the *p*-tolyl sulfides than for the 9-anthryl sulfides which have fewer conformational degrees of freedom.

The optical purities (% ee) for the oxidation of *p*-tolyl *n*-butyl sulfide by **6e–f** and **7e–f** at −22 °C are approximately twice that observed for the modified Sharpless reagent (Table I; compare entries 1 with 12, 15, and 18). At −78 °C the asymmetric induction for oxidation of this sulfide by (−)-**7g** is approximately 3 times that of the modified Sharpless reagent (53.3 vs. 20.0 ee; Table I: compare entries 1 and 23). While the oxidation of isopropyl *p*-tolyl sulfide and methyl 9-anthryl sulfide by **7e**, **6f**, and **6g** at −22 °C is somewhat poorer than that reported by Kagan et al., comparable results are obtained at −78 °C for oxaziridines **6g** and **7g** (Table I: compare entries 1 with 24).

The enantioselectivities for asymmetric oxidation of the anthryl sulfides were also 2–3 times greater than for the *p*-tolyl sulfides. We attribute this result to the Group Size Difference (GSD) effect previously proposed, i.e., as the size difference of the groups attached to the substrate increases, the enantioselectivity increases.[11] It is interesting to note that there is apparently little difference in the enantioselectivities for the oxidation of methyl and *n*-butyl 9-anthryl sulfides (Table I: entries 2, 5, 6, 10–12). While not directly comparable, the % ee for the asymmetric oxidation of methyl and *n*-butyl *p*-tolyl sulfides was significantly different for the modified Sharpless reagent, 90 vs. 20 % ee, respectively.[9a]

The source of the enantioselectivity for asymmetric oxidations by **6** and **7** appears to be largely steric in origin. If polar (π-acid–π-base, dipole) or hydrophobic effects had a significant role in defining the transition geometry, then large solvent effects on the asymmetric induction would be observed. Solvent effects were found to be negligible as shown in Table II. Furthermore, the asymmetric oxidation of 4-methoxyphenyl isopropyl sulfide, a good π-base by (+)-(*R*,*R*)-**6e** or (+)-(*R*,*R*)-**6f** good π-acids, is virtually identical with that observed for *p*-tolyl isopropyl sulfide (Table II: compare entries 12 and 13 and 15 and 16). Large solvent effects have been observed for the asymmetric epoxidation of nonfunctionalized alkenes by pentafluorophenyl oxaziridines **6g** and **7g** (19–65% ee).[19]

The structure of the oxaziridine C-aryl group has a dramatic effect on the asymmetric induction (Table I). The asymmetric induction observed for **6** and **7**, where the oxaziridine C-aryl group is monosubstituted (2-Cl, 2-NO_2, 3-NO_2, 4-NO_2), is 2–3 times lower than that where the C-aryl group is multisubstituted. Significantly, the asymmetric induction observed for **6** and **7** where the aryl group is a 2-chloro-5-nitro-, 3,5-dinitro-, or pentafluorophenyl gave some of the highest enantioselectivities observed to date for the asymmetric oxidation of sulfides to sulfoxides.

Stereochemistry of Asymmetric Oxidation of Sulfides to Sulfoxides. In light of these results the chiral recognition model shown in Figure 1 needs to be modified. In this steric approach model the chiral recognition is determined by the S_N2 attack of the sulfur atom on the oxaziridine oxygen atom from the least hindered direction (Figure 1). This model predicts that as the difference in size of the groups attached to the sulfide (R_L–S–R_S) or oxaziridine three-membered ring increases the asymmetric induction should increase, i.e., the GSD effect. While this effect does appear to be operational for the sulfides, it does not fully explain the effect of substitution in the oxaziridine C-aryl group. Clearly the size of a 3- or 4-nitrophenyl group is expected to be smaller than a 2-chloro-5-nitro- and 3,5-dinitrophenyl groups.

Prior attempts to describe the transition-state geometry for the oxidation of sulfides to sulfoxides by chiral peracids, based on structure reactivity trends, were unsuccessful. The reasons for this include the lack of understanding of the reaction mechanism, the sensitivity of the asymmetric induction to the reaction conditions, the low enantioselectivities (0–10% ee), and insufficient knowledge of the active site structure of the peracid.[6] Moreover, making a description of the transition state even more difficult is the fact, pointed out by Mislow, that any rotameric conformation on the cone of attack of the sulfide at the active site oxygen gives

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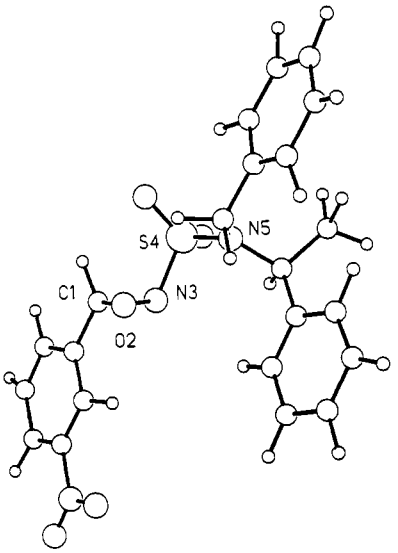


Figure 2. Computer-generated structure of 2-sulfamyloxaziridine (+)-**6b**.

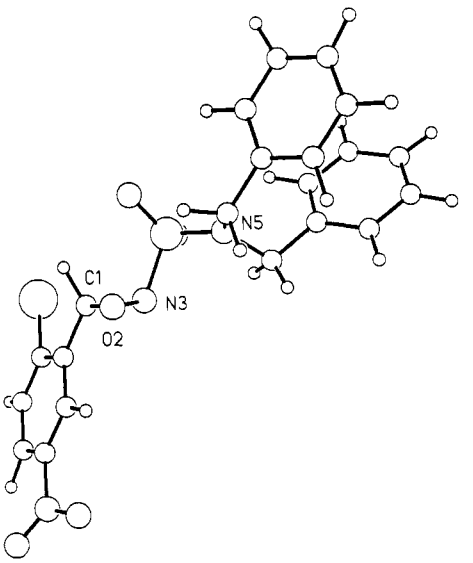
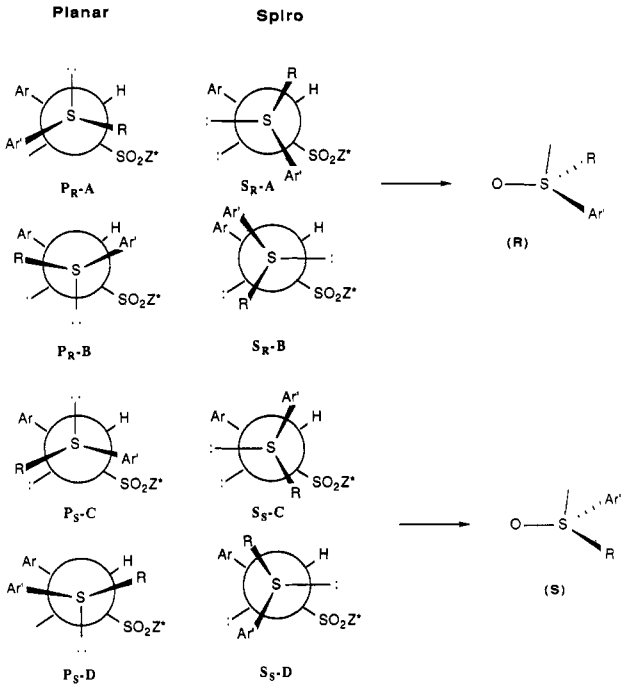


Figure 3. Computer-generated structure of 2-sulfamyloxaziridine **8**.

Scheme II



a sulfoxide of the same absolute configuration.[6b]

Chiral 2-sulfamyloxaziridines **6** and **7** are much better mechanistic probes of the sulfide to sulfoxide transition state because these reagents have a well-defined active site and afford high enantioselectivities for asymmetric oxidations which are insensitive to the reaction conditions. Furthermore, by analogy to our previous studies of the comparable S_N2 transfer of oxygen from oxaziridines to alkenes and sulfoxides, we are able to predict with some confidence, that one of the electron pairs on sulfur will attack the oxygen approximately in the plane of the oxaziridine three-membered ring.[2,20] The two extreme transition states consistent with the formation of the *R*- and *S*-sulfoxides by (+)-(*R*,*R*)-sulfamyloxaziridine **6** are the planar-P and spiro-S geometries shown in Scheme II.

If, in the region of the active site oxygen, the oxaziridine ring is divided into quadrants, then based on the X-ray structures (Figure 2 and 3) and the computer-generated space-filling model representation of oxaziridine **6b** (Figure 4), quadrants A and D are occupied by large groups while B and C are occupied by small

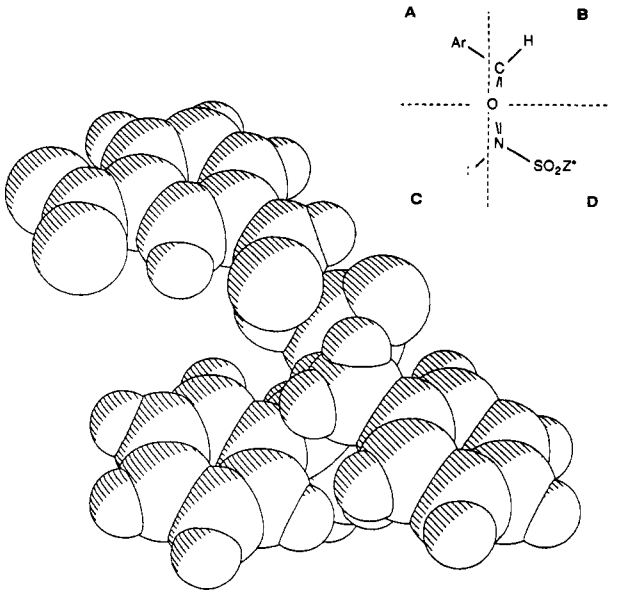


Figure 4. Computer-generated space-filling model of molecule (+)-(*R*,*R*)-**6b**.

groups. Since the stereochemical sense of oxidations by the (*R*,*R*)-2-sulfamyloxaziridines **6** predominantly leads to the *R*-sulfoxides (Table I), it is clear that planar transition states P_r-A and P_r-B have much fewer nonbonded interactions than spiro transition states S_r-A and S_r-B (Scheme II). It is significant to note that a planar transition state geometry is also consistent with the asymmetric epoxidation of alkenes by 2-sulfonyl-[13] and 2-sulfamyloxaziridines[19] as well as by certain conformationally restricted peracids.[21]

On the basis of the requirements for planar transition state geometry (Scheme II) the origins of the stereoselectivities summarized in Table I can be explained in terms of a secondary steric effect which also minimizes the interaction between the sulfide and the oxaziridine C-aryl group. Thus the favored transition state should be the one where there is not only the fewest nonbonded interactions between the Ar′ and Z^*SO_2- groups of the sulfide (Ar–S–R′) and oxaziridine but also the oxaziridine C-aryl group. As the oxaziridine C-aryl group increases in size, that diastereomeric transition state where the Ar group of the sulfide is as far away as possible from both the oxaziridine Z^*SO_2- and C-aryl substituents will be favored, i.e., transition states P_r-A and

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P_r-B are favored while P_s-C and P_s-D are disfavored (Scheme II).

Although the conformation of (+)-(*R*,*R*)-**6b** may differ significantly in solution from that of the solid state, the computer-generated drawings (Figure 2 and 3) indicate that the C–O bond of the oxaziridine and the C-aryl group are coplanar. Thus the effective size of the C-aryl substituent is actually larger than if it were coplanar with the C–N bond of the oxaziridine. We speculate that the higher asymmetric inductions associated with the aryl groups in **6e–f** and **7e–f** may be related to restricted rotation about the C-aryl bond caused by the 2-chloro group in **6e** and **7e** or the C_2-site symmetry of the 3,5-dinitro- and pentafluorophenyl groups in **6f,g** and **7f,g** which reduced the number of possible conformations for the diastereomeric transition states.

Summary and Conclusions

Chiral sulfamyloxaziridines **6** and **7** are some of the most effective reagents discovered to date for the asymmetric oxidation of *nonfunctionalized* sulfides to sulfoxides. Planar transition state geometry, where the sulfur lone pairs share a common plane with the oxaziridine ring, is consistent with the stereochemistry of the asymmetric oxidations. The success of these reagents is attributed to the fact that the active site oxygen is incorporated in a rigid three-membered ring and the close proximity of the oxaziridine substituents to the active site oxygen. Similar structural features in the chiral metal peroxides are, at least in part, responsible for the high enantioselectivities associated with these reagents. Our studies provide further support for the hypothesis that there is a common mechanism of oxygen transfer for the oxaziridines and the metal peroxides, including the Sharpless and modified Sharpless reagents.

One final comment concerns the effect of Z* in **6** and **7** on the enantioselectivity. One might expect that Z* would have considerably less influence on the asymmetric induction than the oxaziridine C-aryl group because of its distance from the active site oxygen. Note however that the asymmetric induction for **2e**, where Z* is a camphor group, is about half that of **6e** and **7e** where Z* is a (+)-(*S*)-(*N*-benzyl)-1-phenethylamine group (Table I: compare entries 2 and 11). Studies currently in progress are exploring the effect of Z* in **6** and **7** on the asymmetric oxidation of nonfunctionalized substrates.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^{1}H NMR spectra were measured on a JOEL FX 90Q (90-MHz) NMR spectrometer by using Me_4Si as the internal reference. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Analytical HPLC separations were carried out on a Varian 5000 liquid chromatograph by using a UV detector (254-nm). Preparative HPLC separations were carried out on a Varian 5000 liquid chromatograph or a Rainin HPX liquid chromatograph by using UV (254-nm) detectors. Dimethoxyethane was distilled from sodium–benzophenone prior to use, and all other solvents were purified by standard methods. Sulfamide, diphenylamine, Amberlyst ion exchange resin, and the aromatic aldehydes were purchased from Aldrich Chemical Co. 3,5-Dinitrobenzaldehyde was prepared by reduction of 3,5-dinitrobenzoyl chloride with lithium aluminum tri-*tert*-butoxyhydride.[22] *n*-Butyl *p*-tolyl sulfide,[23] isopropyl *p*-tolyl sulfide,[23] isopropyl *p*-methoxyphenyl sulfide,[24] and methyl 9-anthryl sulfide[25] were prepared by reaction of the metal thiolate with the alkyl bromide or dimethyl sulfate. (−)-(*S*)-*N*-(α-methylbenzyl)amine was purchased from Hexcel Chemical Products and was determined to be >98% optically pure by using the Johnson Reagent[26] and ^{31}P NMR. Aerocat Triple A was obtained from the American Cyanamide Company. The 5 Å molecular sieves were purchased from the Union Carbide Company, dried at 450 °C for 1 h, and stored in a vacuum desiccator.

(*S*)-(−)-*N*-(α-Methylbenzyl)-*N*-benzylamine. In a 500-mL, single-necked flask equipped with a magnetic stirring bar, Dean Stark trap, condenser, and nitrogen bubbler was placed 20.0 g (0.165 mol) of (*S*)-(−)-(α-methylbenzyl)amine and 17.5 g (0.165 mol) of freshly distilled benzaldehyde in 300 mL of dry benzene. The reaction mixture was refluxed overnight and cooled, and the solvent was concentrated on the rotary evaporator to give an oil. If a small amount of white solid was observed on solvent removal, the oil was diluted with *n*-pentane and filtered. Distillation of the oil from barium oxide gave 28.61 g (83%) of (*S*)-(−)-*N*-benzylidene-*N*-(α-methylbenzyl)amine as a clear oil: bp 110–115 °C; 0.5 mm (lit.[27] bp 119–120 °C, 0.8 mm); IR (thin film) 1605 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.51–1.58 (d, 3 H, CH_3, *J* = 7.0 Hz), 4.35–4.56 (q, 1 H, CH, *J* = 7.0 Hz), 7.28–7.35 (m, 8 H, Ar), 7.69 (s, 2 H, Ar), 8.25 (s, 1 H, N=CH).

(*S*)-(−)-*N*-benzylidene-*N*-(α-methylbenzyl)amine was reduced by using sodium borohydride according to the procedure reported by Anderson and Santi.[28] From 28.61 g (0.137 mol) of the imine was obtained 26.1 g (90%) of the (*S*)-(−)-*N*-(α-methylbenzyl)-*N*-benzylamine: bp 110–115 °C, 0.5 mm (lit.[28] bp 118–120 °C 1 mm) $[\alpha]_D$ −39.5° (neat); IR (thin film) 3410–3260 (NH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27–1.46 (d, 3 H, CH_3, *J* = 7.0 Hz), 1.54 (s, 1 H, NH), 3.53 (s, 2 H, CH_2), 3.55–3.96 (q, 1 H, CH, *J* = 7.0 Hz), 7.12–7.34 (m, 10 H, Ar).

Preparation of (*S*)-(−)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamide (4). In a 500-mL, single-necked flask equipped with a magnetic stir bar, condenser, and argon bubbler was placed 26.1 g (0.124 mol) of (*S*)-(−)-*N*-(α-methylbenzyl)-*N*-benzylamine and 11.9 g (0.124 mol) of sulfamide (Aldrich) in 350 mL of freshly distilled 1,2-dimethoxyethane. The reaction mixture was refluxed for 3–6 days under argon until the evolution of ammonia could no longer be detected by damp pH indicator paper. At this time the DME solvent was concentrated on the rotary evaporator, and the residue was dissolved in 300 mL of ether and transferred to a 1-L separatory funnel. The solution was washed with 15% aqueous HCl solution until acidic, the aqueous layer washed with ether (2 × 100 mL), and the combined ether extractions were dried over anhydrous $MgSO_4$. Removal of the solvent gave a viscous oil which, on treatment with *n*-pentane, solidified. Crystallization of the crude solid from methylene chloride/*n*-pentane afforded 28.0 g (78%) of sulfamide **4**: mp 89–90 °C dec; $[\alpha]_D$ −22.0 (*c* 2.28, $CHCl_3$); IR (KBr) 3390 and 3280 (NH_2), 1335 and 1145 (SO_2) cm^{-1}; ^{1}H ($CDCl_3$) δ 1.48–1.56 (d, 3 H, Me, *J* = 7.0 Hz), 3.98–4.40 (ab quartet, 2 H, CH_2, *J* = 16 Hz), 4.30 (s, 2 H, NH_2), 5.02–5.26 (q, 1 H, CH, *J* = 7.0 Hz), 7.16–7.39 (m, 10 H, Ar). Anal. Calcd for $C_{15}H_{19}N_2O_2S$: C, 62.04; H, 6.25. Found: C, 62.25; H, 6.52.

***N*,*N*-Dibenzylsulfamide**: yield 80%; mp 115 °C (methylene chloride/*n*-pentane); IR (KBr) 3400 and 3280 (NH_2), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.30 (s, 4 H, CH_2), 4.44 (s, 2 H, NH_2), 7.33 (s, 10 H, Ar). Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.84; H, 5.84. Found: C, 60.91; H, 5.80.

General Synthesis of Sulfamylimines 5. In a 300-mL, round-bottomed flask equipped with a reflux condenser, magnetic stir bar, argon inlet, and Dean Stark trap were placed 2.04 g (7.03 mmol) of sulfamide **4**, an equivalent amount of the appropriate aldehyde, 10 g of 5 Å powdered molecular sieves, 500 mg of Aerocat Triple A silica catalyst, or 500 mg of Amberlyst 15 ion exchange resin in 150 mL of dry benzene. The mixture was refluxed under an argon atmosphere for 18 h at which time the mixture was cooled and filtered. The residue in the filter funnel was washed with chloroform (2 × 50 mL), the combined solvent was concentrated on a rotary evaporator to give a thick oil which was dissolved in a minimum amount of methylene chloride, and *n*-pentane was added to precipitate the sulfamylimine **5**. The sulfamylimines were purified by crystallization from *n*-pentane/methylene chloride.

(*S*)-*N*-(4-Nitrobenzylidene)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5a): yield 94%; mp 156–158 °C; $[\alpha]_D$ −93.0° (*c* 2.45, $CHCl_3$); IR (KBr) 1590 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59–1.66 (d, 3 H, CH_3, *J* = 7.0 Hz) 4.13–4.58 (ab quartet, 2 H, CH_2, *J* = 16 Hz), 5.22–546 (q, 1 H, CH, *J* = 7.0 Hz), 7.21–7.37 (m, 10 H, Ar), 7.92–8.40 (m, 4 H, Ar), 8.57 (s, 1 H, C=N). Anal. Calcd for $C_{22}H_{21}N_3O_4S$: C, 62.39; H, 4.99. Found: C, 62.22; H, 5.10.

(*S*)-*N*-(3-Nitrobenzylidene)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5b): yield 77%; mp 97–99 °C; $[\alpha]_D$ −96.3° (*c* 2.10, $CHCl_3$); IR (KBr) 1605 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60–1.68 (d, 3 H, CH_3, *J* = 8.0 Hz), 4.15–4.62 (ab quartet, 2 H, CH_2, *J* = 16.0 Hz), 5.22–5.46 (q, 1 H, CH, *J* = 7.0 Hz), 7.23–7.41 (m, 10 H, Ar), 8.62 (s, 1 H, C=N). Anal. Calcd for $C_{22}H_{21}N_3O_4S$: C, 62.39; H, 4.99. Found: C, 62.52; H, 4.92.

(*S*)-(*N*-2-Nitrobenzylidene)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5c): yield 84%; mp 75–77 °C; $[\alpha]_D$ −30.8° (*c* 2.00, $CHCl_3$); IR (KBr) 1605 (C=N), 1340 and 1150 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.51–1.59 (d, 3 H, CH_3, *J* = 7.0 Hz), 3.99–4.51 (ab quartet, 2 H, CH_2,

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16 Hz), 5.21–5.50 (q, 1 H, CH, J = 7.0 Hz), 7.17–7.36 (m, 10 H, Ar), 7.46–7.86 (m, 4 H, Ar), 8.65 (s, 1 H, CH=N). Anal. Calcd for $C_{22}H_{21}N_3O_4S$: C, 62.39; H, 4.99. Found: C, 62.22; H, 5.16.

(*S*)-(*N*-2-Chlorobenzylidene)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5d): yield 73%; mp 74–75 °C; $[\alpha]_D$ −57.4 (c 2.10, $CHCl_3$); IR (KBr) 1590 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.55–1.62 (d, 3 H, CH_3, J = 7.0 Hz), 4.05–4.53 (ab quartet, 2 H, CH_2, 16 Hz), 5.22–5.44 (q, 1 H, CH, J = 7.0 Hz), 7.18–745 m, 10 H, Ar), 7.95–815 (m, 4 H, Ar), 9.08 (s, 1 H, CH=N). Anal. Calcd for $C_{22}H_{21}ClN_2O_2S$: C, 63.99; H, 5.13. Found: C, 63.82; H, 5.02.

(*S*)-*N*-(2-Chloro-5-nitrobenzylidene)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5e): yield 95%; mp 97–98 °C; $[\alpha]_D$ −97.6° (c 2.04, $CHCl_3$); IR (KBr) 1605 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H ($CDCl_3$) δ 1.53–1.61 (d, 3 H, CH_3, J = 7.0 Hz), 4.11–4.55 (ab quartet, 2 H, CH_2, 15.8 Hz), 5.17–5.41 (q, 1 H, CH, J = 7.0 Hz), 7.16–7.44 (m, 10 H, Ar), 7.53–8.74 (m, 3 H, Ar), 8.86 (s, 1 H, CH=N). Anal. Calcd for $C_{22}H_{20}ClN_3O_4S$: C, 57.70; H, 4.40. Found: C, 57.56; H, 4.27.

(*S*)-*N*-(3,5-Dinitrophenyl)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5f): yield 80%; mp 112–113 °C; $[\alpha]_D$ −94.8° (c 1.5, $CHCl_3$); IR (film) 1610 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50–1.66 (d, 3 H, CH_3, J = 7.0 Hz), 4.17–4.57 (ab quartet, 2 H, CH_2, J = 15.8 Hz), 5.19–5.43 (q, 1 H, CH, J = 7 Hz), 7.19–7.56 (m, 10 H, Ar), 8.50 (s, 1 H, CH=N), 8.79–8.81 (d, 2 H, Ar, J = 2.0 Hz), 9.15–9.20 (t, 1 H, Ar, J = 2.0 Hz). Anal. Calcd for $C_{22}H_{20}N_4O_6S$; C, 56.40; H, 4.30. Found: C, 56.28; H, 4.02.

(*S*)-*N*-(Pentafluorobenzylidene)-*N'*-(α-methylbenzyl)-*N'*-benzylsulfamide (5g): yield 80%; mp 99–100 °C; $[\alpha]_D$ −58.8° (c 2.0, $CHCl_3$); IR (film) 1610 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.55–1.62 (d, 3 H, CH_3, J = 7.0 Hz), 4.05–4.51 (ab quartet, 2 H, CH_2, J = 15.8 Hz), 5.16–5.40 (q, 1 H, CH, J = 7.0 Hz), 7.04–7.34 (m, 10 H, Ar), 8.56 (s, 1 H, CH=N). Anal. Calcd for $C_{22}H_{17}F_5N_2SO_2$: C, 56.41; H, 3.66. Found: C, 56.49; H, 3.66.

***N*-(2-Chloro-5-nitrobenzylidene)-*N'*,*N'*-dibenzylsulfamide**: yield 79%; mp 122 °C; IR (KBr) 1605 (C=N), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H ($CDCl_3$) δ 4.43 (s, 4 H, CH_2), 7.33 (s, 10 H, Ar), 7.61–7.70 (d, 1 H, Ar, J = 8.01 Hz), 8.27–8.40 (d of d, 1 H, Ar, J = 2.7 Hz), 8.75–8.78 (d, 1 H, Ar, J = 2.7 Hz), 9.18 (s, 1 H, CH=N). Anal. Calcd for $C_{21}H_{18}ClN_3O_4S$: C, 56.82; H, 4.09. Found: C, 57.09; H, 4.29.

***N*-(2-Chloro-5-nitrobenzylidene)benzenesulfonamide**: yield 80%; mp 138–140 °C; IR (KBr) 1610 (C=N), 1350 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.58–8.10 (m, 6 H, Ar), 8.29–8.42 (d of d, J = 2.64 Hz, 1 H, Ar), 8.93–8.97 (d, J = 2.93 Hz, 1 H, Ar), 9.51 (s, 1 H, N=CH). Anal. Calcd for $C_{13}H_9ClN_2O_4S$: C, 48.08; H, 2.79. Found: C, 48.21; H, 2.55.

General Preparation of Optically Active 2-Sulfamyloxaziridines 6 and 7. In a 500-mL, three-necked, Morton flask equipped with a mechanical stirrer and dropping funnel was placed 7.5 mmol of the appropriate 2-sulfamylimine **5** in 100 mL of chloroform and 100 mL of 5% $NaHCO_3$. After having cooled the mixture to 0 °C in an ice bath, 2.9 g (9 mmol) of 85% *m*-chloroperbenzoic acid (*m*-CPBA) in 60 mL of chloroform was added to the stirring reaction mixture over 0.5 h. The reaction mixture was stirred overnight, and the organic phase was washed with 2 × 100 mL each of saturated solutions of Na_2SO_3, $NaHCO_3$, NaCl, and finally with 100 mL of H_2O. For **5d** the oxidation was carried out in the presence of 300 mg of benzyltriethylammonium chloride (BTEAC) at 0 °C for 4 h to prevent hydrolysis. After drying over anhydrous K_2CO_3 and filtering through a plug of silica gel, the solvent was concentrated on the rotary evaporator (bath temperature ≤45 °C) to afford the diastereomeric 2-sulfamyloxaziridines **6** and **7**, which were washed with *n*-pentane until solid. The 2-sulfamyloxaziridine diastereoisomers **6** and **7** were separated by preparative HPLC as described below.

2-[(*S*)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(4-nitrophenyl)oxaziridine (6a and 7a): yield 92% as a diastereomeric mixture eluting in the order R,R:S,S (47.5:52.5) and separated on a Varian MCH-10 reverse-phase C_{18} column (0.8 × 50 cm) eluting with MeOH/H_2O (70/30) at a flow rate of 2.5 mL/min. For pure (*R*,*R*)-**6a**: mp 124–126 °C $[\alpha]_D$ +2.50° (c 2.87, $CHCl_3$); IR (KBr) 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52–1.60 (d, 3 H, CH_3, J = 7.2 Hz), 4.01–4.69 (ab quartet, 2 H, CH_2, 16 Hz), 5.32–5.55 (q, 1 H, CH, J = 7.2 Hz), 5.40 (s, 1 H, oxaziridine-H), 7.22–7.53 (m, 10 H, Ar), 7.65–8.33 (m, 4 H, Ar).

For pure (*S*,*S*)-**7a**: mp 122–124 °C; $[\alpha]_D$ −111° (c 3.54, $CHCl_3$); IR (KBr) 1350 and 1170 (m, SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59–1.67 (d, 3 H, CH_3, J = 7.1 Hz), 4.15–4.62 (ab quartet, 2 H, CH_2, 15.8 Hz), 5.25–5.47 (q, 1 H, CH, J = 7.1 Hz), 5.32 (s, 1 H, oxaziridine-H), 7.08–7.43 (m, 10 H, Ar), 7.53–8.34 (m, 4 H, Ar). Anal. Calcd for $C_{22}H_{21}N_3O_5S$: C, 60.12; H, 4.82. Found: C, 59.87; H, 4.91.

2-[(*S*-)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(3-nitrophenyl)oxaziridine (6b and 7b): yield 81% as a diastereomeric mixture eluting in the order R,R:S,S (47:53) and separated on a Varian MCH-10 reverse-phase C_{18} column (0.8 × 50 cm) eluting with MeOH/H_2O (70/30) at a flow rate of 2.5 mL/min. Pure (*R*,*R*)-**6b** was isolated in 35% yield by crystallization from methanol: mp 137–138 °C; $[\alpha]_D$ +35.7° (c 2.00, $CHCl_3$); IR (KBr) 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52–1.60 (d, 3 H, CH_3, J = 7.0 Hz), 4.03–4.67 (ab quartet, 2 H, CH_2, 16 Hz), 5.31–5.55 (q, 1 H, CH, J = 7.0 Hz), 5.37 (s, 1 H, oxaziridine-H), 7.20–7.39 (m, 10 H, Ar), 7.59–8.25 (m, 4 H, Ar). Anal. Calcd for $C_{22}H_{21}N_3O_5S$: C, 60.12; H, 4.82. Found: C, 60.12; H, 4.70.

2-[(*S*)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(2-nitrophenyl)oxaziridine (6c and 6c): yield 94% as a diastereomeric mixture eluting in the order R,R:S,S (54.5:45.5) and separated on a Varian MCH-10 reverse-phase C_{18} column (0.8 × 50 cm) eluting with MeOH/H_2O (80/20) at a flow rate of 2.0 mL/min. For pure (*R*,*R*)-**6c**: mp 113–115 °C; $[\alpha]_D$ +22.0° (c 0.64, $CHCl_3$); IR (KBr) 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50–1.59 (d, 3 H, CH_3, J = 7.4 Hz), 4.23–4.70 (ab quartet, 2 H, CH_2, 16 Hz), 5.31–5.55 (q, 1 H, CH, J = 7.4 Hz), 6.04 (s, 1 H, oxaziridine-H), 7.26–7.49 (m, 10 H, Ar), 7.54–8.39 (m, 4 H, Ar).

For pure (*S*,*S*)-**7c**: mp 127–128 °C; $[\alpha]_D$ −22.1 (c 1.29, $CHCl_3$); IR (KBr) 1350 and 1170 (m, SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54–1.63 (d, 3 H, CH_3, J = 7.4 Hz), 4.26–4.73 (ab quartet, 2 H, CH_2, 16 Hz), 5.29–5.54 (q, 1 H, CH, J = 7.4 Hz), 6.01 (s, 1 H, oxaziridine-H), 7.18–7.45 (m, 10 H, Ar), 7.51–8.35 (m, 4 H, Ar). Anal. Calcd for $C_{22}H_{21}N_3O_5S$: C, 60.12; H, 4.82. Found: C, 59.87; H, 5.00.

2-[(*S*)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(2-chlorophenyl)oxaziridine (6d and 7d): yield 78% as a diastereomeric mixture eluting in the order R,R:S,S (48.1:51.9) and separated on a Rainin (21.4 mm × 25 cm) Dynamax silica column eluting with hexane/CH_2Cl_2 (70/30) at a flow rate of 10.0 mL/min. For pure (*R*,*R*)-**6d**: viscous oil; $[\alpha]_D$ +11.1° (c 3.34, $CHCl_3$); IR (KBr) 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50–1.58 (d, 3 H, CH_3, J = 7.0 Hz), 4.09–4.59 (ab quartet, 2 H, CH_2, 16 Hz), 5.35–5.58 (q, 1 H, CH, J = 7.0 Hz), 5.85 (s, 1 H, oxaziridine-H), 7.21–7.40 (m, 10 H, Ar), 7.54–8.07 (m, 4 H, Ar).

For pure (*S*,*S*)-**7d**: mp 91–93 °C; $[\alpha]_D$ −76.9° (c 1.40, $CHCl_3$); IR (KBr) 1360 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54–1.62 (d, 3 H, CH_3, J = 7.0 Hz), 4.12–4.65 (ab quartet, 2 H, CH_2, 16 Hz), 5.38–5.61 (q, 1 H, CH, J = 7.0 Hz), 5.81 (s, 1 H, oxaziridine-H), 7.23–7.42 (m, 10 H, Ar), 7.56–8.11 (m, 4 H, Ar). Anal. Calcd for $C_{22}H_{21}ClN_2O_3S$: C, 61.60; H, 4.93. Found: C, 61.61; H, 4.70.

2-[(*S*)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(2-chloro-5-nitrophenyl)oxaziridine (6e and 7e): yield 92% as a diastereomeric mixture eluting in the order R,R:S,S (53.5:46.5) and separated on a Rainin (21.4 mm × 25 cm) Dynamax silica column eluting with hexane/CH_2Cl_2 (60/40) at a flow rate of 2.5 mL/min. For pure (*R*,*R*)-**6e**: mp 137–118 °C; $[\alpha]_D$ +42.7° (c 1.76, $CHCl_3$); IR (KBr) 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53–1.61 (d, 3 H, CH_3, J = 7.2 Hz), 4.06–4.70 (ab quartet, 2 H, CH_2, 16.2 Hz), 5.30–5.52 (q, 1 H, CH, J = 7.2 Hz), 5.83 (s, 1 H, oxaziridine-H), 7.23–7.40 (m, 10 H, Ar), 7.58–8.34 (m, 3 H, Ar).

For pure (*S*,*S*)-**7e**: mp 121–123 °C; $[\alpha]_D$ −109.0° (c 1.60, $CHCl_3$); IR (KBr) 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.56–1.65 (d, 3 H, CH_3, J = 7.2 Hz), 4.13–4.67 (ab quartet, 2 H, CH_2, 15.5 Hz), 5.29–5.50 (q, 1 H, CH, J = 7.2 Hz), 5.74 (s, 1 H, oxaziridine-H), 7.14–7.39 (m, 10 H, Ar), 7.56–8.29 (m, 3 H, Ar). Anal. Calcd for $C_{22}H_{21}ClN_2O_3S$: C, 55.76; H, 4.25. Found: C, 55.84; H, 4.24.

2-[(*S*)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(3,5-dinitrophenyl)oxaziridine (6f and 7f): yield 78% as a diastereomeric mixture eluting in the order S,S:R,R (48.1:51.9) and separated on a Rainin (21.4 mm × 25 cm) Dynamax reverse phase C-18 column with MeOH/H_2O (80/20) at a flow rate of 10.75 mL/min. For pure (*R*,*R*)-**6f**: viscous oil; $[\alpha]_D$ +17.4° (c 2.1, $CHCl_3$); IR (film) 1380 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.56–1.64 (d, 3 H, CH_3, J = 7.1 Hz), 4.08–4.66 (ab quartet, 2 H, CH_2, J = 16.0 Hz), 5.30–5.54 (q, 1 H, CH, J = 7.1 Hz), 5.42 (s, 1 H, oxaziridine-H), 7.23–7.39 (m, 10 H, Ar), 8.52–8.54 (d, 2 H, Ar, J = 2.0 Hz), 9.10–9.15 (t, 1 H, Ar, J = 2.0 Hz).

For pure (*S*,*S*)-**7f**: viscous oil; $[\alpha]_D$ −106.7° (c 2.4, $CHCl_3$); IR (film) 1390 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.62–1.70 (d, 3 H, CH_3, J = 7.3 Hz), 4.19–4.62 (ab quartet, 2 H, CH_2, J = 16.0 Hz), 5.22–5.46 (q, 1 H, CH, J = 7.3 Hz), 5.29 (s, 1 H, oxaziridine-H), 6.95–7.50 (m, 10 H, Ar), 8.48–8.50 (d, 2 H, Ar, J = 2.0 Hz), 9.09–9.14 (t, 1 H, Ar, J = 2.0 Hz). A satisfactory elemental analysis could not be obtained.

2-[(*S*)-*N*-(α-Methylbenzyl)-*N*-benzylsulfamyl]-3-(pentafluorophenyl)oxaziridine (6g and 7g): yield 90% as a diastereomeric mixture eluting in the order R,R:S,S (48.8:52.2) and separated on a Rainin (21.4 mm × 25 cm) Dynamax silica column eluting with hexane/CH_2Cl_2 (60/40) at a flow rate of 10.75 mL/min. For pure (*R*,*R*)-**6g**: mp 92–93 °C; $[\alpha]_D$ +22.80° (c 1.6, $CHCl_3$); IR (film) 1380 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.46–1.54 (d, 3 H, CH_3, J = 7.2 Hz), 3.91–4.68 (ab quartet, 2 H, CH_2, J = 16.0 Hz), 5.30–5.54 (q, 1 H, CH, J = 7.2 Hz), 5.63 (s, 1 H, oxaziridine-H), 7.22–7.40 (m, 10 H, Ar).

For pure (*S*,*S*)-**7g**: mp 105–106 °C; $[\alpha]_D$ −93.2° (c 1.6, $CHCl_3$); IR (film) 1380 and 1170 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 1.58–1.66 (d, 3

H, CH_3, J = 7.2 Hz), 4.15–4.60 (ab quartet, 2 H, CH_2, J = 16.0 Hz), 5.23–5.47 (q, 1 H, CH, J = 7.2 Hz), 5.54 (s, 1 H, oxaziridine-H), 7.06–7.43 (m, 10 H, Ar). Anal. Calcd for $C_{22}H_{17}F_5N_2SO_3$: C, 54.55; H, 3.53. Found: C, 54.66; H, 3.45.

2-(*N*,*N*-Dibenzylsulfamyl)-3-(2-chloro-5-nitrophenyl)oxaziridine (8): yield 85%; mp 130–132 °C; IR (KBr) 1340 and 1140 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.30–4.71 (ab quartet, 4 H, CH_2), 5.87 (s, 1 H, oxaziridine-H), 7.34 (s, 10 H, Ar). 7.59–7.70 (d, 1 H, Ar, J = 8.3 Hz), 8.15–8.35 (m, 2 H, Ar). Crystals suitable for X-ray analysis were obtained by slow crystallization from ether. Anal. Calcd for $C_{21}H_{18}ClN_3O_5S$: C, 54.84; H, 3.94. Found: C, 55.06; H, 4.06.

2-(Phenylsulfonyl)-3-(2-chloro-5-nitrophenyl)oxaziridine (9): yield 85%; mp 127–129 °C (methanol); IR (KBr) 1340 and 1160 (m, SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.97 (s, 1 H, oxaziridine H), 7.59–8.32 (m, 8 H, Ar). Anal. Calcd for $C_{13}H_9ClN_2O_5S$: C, 45.82; H, 2.66. Found: C, 45.95; H, 2.71.

Competitive Rate Study of the Oxidation Sulfides and Sulfoxides by Oxaziridines 8 and 9. In a 5-mm NMR tube was placed 350 μL of a 0.03817 molar solution of sulfamyloxaziridine **8** (prepared by dissolving 0.1003 g of **8** in 2.0 mL of $CDCl_3$) and 340 μL of a 0.1121 molar solution of 2-sulfonyloxaziridine **9** (prepared by dissolving 0.1146 g of **9** in 3.0 μL of $CDCl_3$). The NMR spectrum indicated that the oxaziridine-3-protons in **8** and **9** occurring at δ 5.87 and 5.97 ppm, respectively, were present in a 1:1 ratio. For, methyl phenyl sulfoxide, 160 μL of a 0.2378 molar solution in $CDCl_3$ was added to the NMR tube reaction mixture, and after 24 h the ratio of **9**:**8** was determined by integration. For methyl *p*-tolyl sulfide, 186 μL of a 0.2055 molar $CDCl_3$ solution was added to the oxaziridine mixture in the NMR tube, and after 30 min the ratio of **8**:**9** was determined by integration. Each oxidation was performed at least 3 times, and the results were averaged. 2-Sulfonyloxaziridine **9** oxidized methyl phenyl sulfoxide and methyl *p*-tolyl sulfide 1.40 and 1.67 times faster, respectively, than did 2-sulfamyloxaziridine **8**.

Isopropyl and *n*-Butyl 9-Anthryl Sulfides. In a dry, 200-mL, three-necked flask equipped with magnetic stirrer, condenser, addition funnel, and argon bubbler was added 0.7 g (17.0 mmol) of a 60% mineral oil dispersion of sodium hydride. The dispersion was washed with *n*-pentane (2 × 30 mL), 75 mL of dry THF was added, and the reaction mixture was cooled in an ice bath. 9-Anthrylthiol,[29] 3.0 g (14.3 mmol) in 30 mL of THF, was added dropwise over 30 min, the reaction mixture was refluxed for 0.5 h and cooled to 0 °C in an ice bath, and a solution of 15.0 mmol of isopropyl bromide or *n*-butyl bromide in 30 mL of THF was added. After refluxing overnight the reaction mixture was cooled in an ice bath and cautiously quenched by addition of 100 mL of saturated brine. The reaction mixture was transferred to a 500-mL separatory funnel, and 100 mL of water and 100 mL of ether were added. The organic layer was washed with 5% NaOH (2 × 100 mL) containing trace (20 mg) of sodium hydrosulfite and water (100 mL) followed by drying over anhydrous Na_2SO_4. Evaporation of the solvent on the rotatory evaporator gave a viscous oil which was triturated with *n*-pentane.

Isopropyl 9-anthryl sulfide:[30] yield 84% of a yellow solid; mp 64–66 °C; ^1H NMR ($CDCl_3$) δ 1.17–1.25 (d, 6 H, CH_3, J = 6.60 Hz), 3.13–3.55 (septet, 1 H, CH, J = 6.60 Hz), 7.44–7.59 (m, 4 H, Ar), 7.93–8.04 (m, 2 H, Ar), 8.45 (s, 1 H, Ar), 8.92–9.02 (m, 2 H, Ar).

***n*-Butyl 9-anthryl sulfide**:[30] yield 97% of an orange-yellow oil.

General Procedure for Asymmetric Oxidations. For Oxidations at 25 °C. Into a 5-mL, round-bottomed flask equipped with magnetic stir bar and nitrogen inlet was placed 0.017 mmol of the appropriate sulfide dissolved in 2 mL of the desired solvent. To this mixture was added an equimolar amount of chiral oxaziridines **6** and **7** dissolved in 1 mL of solvent and allowed to stir for 1 h prior to workup. **For Oxidations at −22 °C.** The sulfide solution was cooled to −78 °C in a dry ice–acetone bath, and an equimolar amount of **6** and **7** in 1 mL of solvent previously cooled to −78 °C was rapidly added. The reaction mixture was placed in a freezer maintained at −22 °C. After 48 h at this temperature the reaction mixture was cooled to −78 °C and quenched by addition of 1 mL of triethylamine. **For Oxidations at −42 °C.** In a 5-mL, round-bottomed flask equipped with a magnetic stir bar, nitrogen inlet, and a jacketed addition funnel was placed the appropriate sulfide dissolved in 2 mL of solvent. The reaction flask and addition funnel were cooled to −42 °C in a dry ice–acetonitrile bath, and an equimolar amount of **6** and **7** in 1 mL of solvent cooled to −42 °C was rapidly added. After the addition was complete, the reaction mixture was placed in a Dewar flask cooled to −42 °C for 48 h and then quenched by addition of 1 mL of triethylamine. **For Oxidations at −78 °C.** The sulfide solution was cooled to −78 °C in a dry ice–acetone bath, and an equimolar amount of the oxaziridine **6g** and **7g** in 1 mL of solvent cooled to −78 °C was rapidly added. The reaction mixture was maintained at this temperature for 2 h and then quenched by addition of 1 mL of triethylamine. After removal of the solvent on the rotatory evaporator, the optically active sulfoxides were isolated by preparative TLC (silica gel G) eluting with ether.

General Procedure for Determining Optical Purities of Sulfoxides. The optical purities (% ee) and absolute configurations of the sulfoxides obtained above were determined by using the Regis Pirkle covalent phenylglycine HPLC column and a UV (254-nm) detector. The alkyl *p*-tolyl sulfoxides were separated by eluting with *n*-hexane/2-propanol (95:5) at a flow rate of 1.0 mL/min. The alkyl 9-anthryl sulfoxides were separated by eluting with *n*-hexane/2-propanol (80:20) at a flow rate of 1.0 mL/min. Absolution configurations were determined by comparison with authentic samples of the sulfoxides. As previously reported by Prikel et al. the *S*-sulfoxides were the first to be eluted.[17]

X-ray Analysis of Sulfamyloxaziridines (+)-6b and 8. All data were collected on a Syntex $P2_1$ diffractometer by using a θ:2θ scan (2θ < 114.7°) with variable scan rate and graphite monochromated Cu K radiation (λ = 1.54189 Å). Lattice parameters were obtained from a least-squares refinement of 15 reflections whose angles were measured by a centering routine associated with a diffractometer system. Crystals of nearly uniform dimensions were used, and equivalent reflections were examined for the effects of absorption. Standard reflections were monitored during data collection. Lorentz and polarization corrections were applied, and the structures were solved by the application of direct methods techniques.[31] Full-matrix least-squares refinements were carried out, and the function $\Sigma\omega(|F_o| - |F_c|)^2$ was minimized where $w = 1/\sigma^2(F_o)$ was derived from counting statistics. Locally written programs were used for data reduction: MULTAN78[31] for direct methods calculations and XRAY76[32] for all others. Atomic scattering factors for C, N, O, S, and Cl were taken from Cromer and Mann[33] while those for hydrogen were taken from Stewart, Davidson, and Simpson.[34] Real and imaginary contributions to the anomalous dispersion were included.

Compound 6b: $C_{22}H_{21}N_3O_5S$, M_r = 439.49, crystal dimensions 0.35 × 0.29 × 0.30 mm, space group $P2_1$ (consistent with extinctions and statistics), a = 12.460 (4) Å, b = 8.111 (2) Å, c = 10.583 (3) Å, β = 94.07 (2)°, V = 1066.8 (5) Å^3, Z = 2, D_c = 1.368 g cm^{-3}, μ = 16.55 cm^{-1}, $F(000)$ = 460, 1594 reflections with $I > 3\sigma(I)$, R = 0.038, R_w = 0.051.

Compound 8: $C_{21}H_{18}ClN_3O_5S$, M_r = 459.9, crystal dimensions 0.38 × 0.42 × 0.32 mm, space group $P\bar{1}$ (consistent with extinctions and statistics), a = 11.092 (4) Å, b = 15.246 (6) Å, c = 6.866 (3) Å, α = 95.88 (3)°, β = 90.75 (3)°, γ = 111.49 (3)°, V = 1073.1 (8) Å^3, Z = 2, D_c = 1.423 g cm^{-3}, μ = 27.91 cm^{-1}, $F(000)$ = 476, 2000 reflections with $I > 3\sigma(I)$, R = 0.049, R_w = 0.064.

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Supplementary Material Available: Tables of atomic positional parameters, thermal parameters, fractional coordinates, and bond distances and bond angles of (+)-**6b** and **8** from X-ray experiments (12 pages). Ordering information is given on any current masthead page.

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