Synthesis and Reactions of *exo*-Camphorylsulfonyloxaziridine

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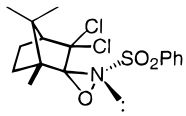
The first example of an *exo*-camphorylsulfonyloxaziridine **4a** was prepared by *m*-CPBA oxidation of camphor imine **9**. This surprising result is due to the conformation of the imine which apparently prevents attack of the peracid from the endo direction. Similar oxidations of all other camphorsulfonylimines result in the *endo*-oxaziridine exclusively. Asymmetric oxidation of sulfides to sulfoxides and the α-hydroxylation of enolates by **4** can be interpreted in terms of open transition states where nonbonded interactions are minimized. These results support earlier conclusions and predictions of the stereoselectivity and mechanisms of molecular recognition by the *N*-sulfonyloxaziridine class of oxidizing reagents.

The enantiopure *N*-sulfonyloxaziridines **1** and **2**, derived from camphor, are important asymmetric oxidants for the reagent-controlled asymmetric synthesis of sulfoxides,[1] selenoxides,[2] and the α-hydroxy carbonyl compounds.[3,4] The latter moiety is a key functional group widely distributed in nature and in pharmacologically active compounds. Not only do the enantiomeric excesses often exceed 95%, but the product stereochemistry is predictable. The mechanism of oxygen transfer from *N*-sulfonyloxaziridines to nucleophiles is thought to involve an S_N2 type mechanism and is supported by both theoretical[5,6] and experimental[7] studies. For the oxidation of sulfides to sulfoxides and sulfones, the molecular recognition is largely steric in origin dictated by the substituents on the oxaziridine and the substrate.[5,7] For the hydroxylation of enolates by oxaziridines, the molecular recognition was also interpreted in terms of the S_N2 mechanism where nonbonded interactions are minimized in an "open" or "nonchelated" transition state.[8,9] While molecular orbital calculations by Bach and co-workers support the S_N2 type mechanism for enolate hydroxylations, a "closed" or chelated transition state was proposed.[6] It was thought that *endo*-camphorysulfonyloxaziridine **3** may provide additional details of the mechanism of oxygen transfer for oxaziridines as well as being a more effective reagent with enhanced asymmetric induction. In *endo*-oxaziridine **3** the sterically demanding elements near the active site oxygen are reversed compared to **2** and, therefore, the opposite stereochemistry is predicted for the product. In this paper we report our attempts to prepare **3** which ultimately resulted in the synthesis of the first *exo*-camphorylsulfonyloxaziridine **4**.



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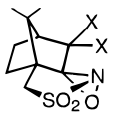
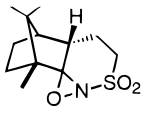


2a, X = H
b, X = Cl
c, X = OMe



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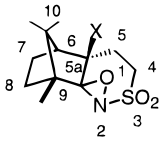

(+)-**4a**, X = H
b, X = Cl

Results and Discussion

Synthesis of Oxaziridines. The strategy employed for the synthesis of (+)-**4a** involves the crucial Michael reaction of the enolate generated from (+)-camphor (**5**) and *N*,*N*-bis[(4-methoxyphenyl)methyl]ethenesulfonamide (**6**)[10] followed by cyclization and oxidation (Scheme 1). Initial attempts to effect the Michael addition of **6** to **5** using LDA produced only ca. 5% of the desired product (Table 1, entry 1). The major side product appeared to be a dimer where 2 equiv of **6** had added to the enolate as evidenced by NMR and HRMS. Use of LiHMDS or NaHMDS offered similar or only slightly improved yields (Table 1, entries 2 and 3). However, addition of CuI to the lithium enolate of camphor, generated using LiHMDS, followed by addition of ethenesulfonamide **6** at −78 °C and stirring the mixture at −20 °C gave **7** in 82% isolated yield as a thick gum. Sulfonamide **7** was obtained as an 80:20 endo/exo mixture of isomers (see below). Interestingly, the use of KHMDS gave **7** in 44% yield with the isomeric ratio reversed (Table 1, entry 4). It has been reported that enolates of camphor react with alkylating agent to give exo products under kinetic control and endo products under thermodynamic con-

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Scheme 1

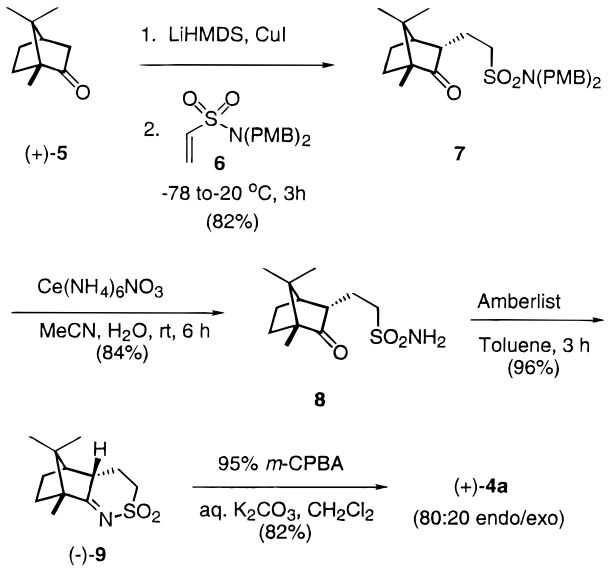

Table 1. Reaction of the Enolate of (+)-Camphor (5) with *N*,*N*-Bis[(4-methoxyphenyl)methyl]-ethenesulfonamide (6)

entry	base[a]	temp (°C)/ time (h)	isolated yield (%)	endo/exo
1	LDA	−78 to 0/3.0	mostly dimer	
2	LiHMDS	−78 to 0/3.5	7	
3	NaHMDS	−78 to 0/3.0	15	
4	KHMDS	−78 to 0/3.5	44	11:89
5	LiHMDS−CuI[b]	−78 to −20/3.0	82	80:20

[a] 3.0 equiv of (+)-camphor was used. [b] 3.0 equiv of CuI was used.

trol.[11] Therefore it is unclear why the potassium enolate of (+)-**5**, which is presumably formed under thermodynamically controlled conditions, preferentially affords the exo product. All attempts to separate the isomers failed. To the best of our knowledge, this is the first report of the Michael addition of a ethenesulfonamide to the lithium cuprate of an enolate.

The removal of *p*-methoxybenzyl groups in **7** was readily accomplished using 6.0 equiv of ceric ammonium nitrate to give sulfonamide **8** in 84% yield. Subsequent cyclization of **8** was achieved by reflux in toluene with a catalytic amount of Amberlyst 15 ion exchange resin for 3 h, affording camphorsulfonimine **9** in 96% yield.[12] That imine **9** exists as a 80:20 endo/exo mixture was indicated by the methyl singlets at δ 1.0 and 0.95 for the major isomer and at δ 0.99 and 0.92 for the minor isomer in the ^{1}H NMR spectra. Interestingly, the same 80:20 endo/exo imine mixture was obtained on cyclization of the sulfonamide derived from the 11:89 endo/exo mixture of **7**.

Because the isomeric sulfonimines **9** could not be easily separated by chromatography, an attempt was made to improve the isomeric ratio by base-catalyzed isomerization (Table 2). Indeed, in all cases, treatment of **9** with base and quenching improved the ratios with NaHMDS, giving an 93:7 endo/exo mixture (Table 2, entry 1). Crystallization gave pure endo imine (−)-**9**.

The mixture of imines **9** was oxidized with 95% *m*-CPBA and saturated K_2CO_3 solution in methylene chloride to give oxaziridine **4** in 82% yield as an 80:20 mixture of endo and exo isomers at C(5a). Oxidation of *endo*-**9** (95:5 endo/exo) gave a nearly identical (82:18) mixture of oxaziridines indicating that base-catalyzed epimerization of the imine at C(5a) occurs prior to oxidation. Crystallization of **4a** from EtOAc/*n*-hexane afforded the pure endo C(5a) oxaziridine (+)-**4a** in 60% yield. All attempts to isolate the minor isomer failed. The endo configuration at C(5a) of oxaziridine (+)-**4a** follows from its X-ray crystal structure (Figure 1), and this result is confirmed by the ^{1}H NMR data. The C(5a) proton appears as a doublet of doublets ($J_{5a,6}$ = 11 Hz, $J_{5a,7}$ = 3.5 Hz) after decoupling of the C(5) proton which is similar to the ^{1}H NMR spectra of the *endo*-(alkylthio) derivatives of camphor.[13]

Table 2. Base-Catalyzed Isomerization of Sulfonimine (−)-9[a]

entry	base (1.5 equiv)	temp (°C)/time (h)	endo/exo
1	NaHMDS	−78/2.0	93:7
2	LiHMDS	−78/2.0	92:8
3	DBU	−78/3.0	89:11
4	KHMDS	−78/2.0	90:10

[a] Yields are quantitative.

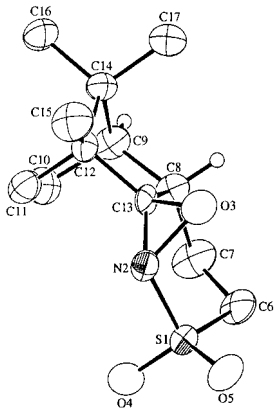

Figure 1. X-ray structure of *exo*-camphorylsulfonyloxaziridine (+)-**4a**.

An important advantage of the camphorylsulfonyloxaziridines is that on oxidation of the corresponding imines they are obtained as single isomers because the exo face of the C−N double bond is blocked by the methyl group of the methylene bridge. In all of the diverse types of camphorylsulfonyloxaziridines prepared to date, only single isomers are produced which have the endo structure exclusively, e.g., **1** and **2**.[1−4,14] Thus the fact that the X-ray structure of (+)-**4a** indicated that it had the exo structure rather than the endo structure **3** was quite unexpected (Figure 1). This must mean that fusion of the 6-membered ring to camphor results in a ring conformation of **9** such that endo attack by the peracid oxidizing reagent is much less favorable than exo attack.

An approach similar to that shown in Scheme 1, but starting with (+)-3-chlorocamphor (**10**),[15] was used to prepare (+)-*exo*-5a-chlorocamphorylsulfonyloxaziridine **4b** (Scheme 2). Interestingly attempts to added *N*,*N*-bis-[(4-methoxyphenyl)methyl]ethenesulfonamide (**6**) to the

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Scheme 2

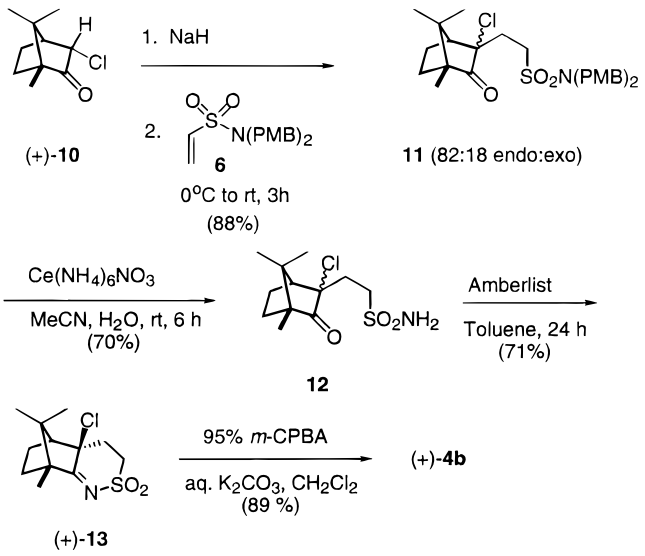


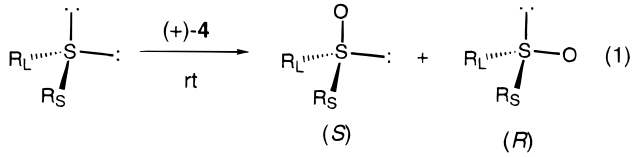
Table 3. Asymmetric Oxidation of Sulfides to Sulfoxides at rt in CCl_4 for 2−4 h[a]

		% ee of sulfoxides (configuration)	
entry	oxaziridine	*p*-tolyl-S(O)-*n*-Bu	$PhCH_2S(O)$-Me
1	(−)-**1**[b]	91 (*S*)	13 (*S*)
2	(+)-**2a**[c]	1 (*S*)	25 (*S*)
3	(+)-**4a**	15 (*S*)	17 (*S*)
4	(+)-**4b**	5 (*S*)	5 (*S*)

[a] Isolated yields 54−70%. [b] Reference 1. [c] Reference 9.

lithium−copper enolate of **10** resulted in decomposition. While potassium carbonate/18-crown-6 in toluene gave a 75:25 endo/exo mixture of **11** (72%), the best conditions employed the sodium enolate of **10**, prepared using NaH, to give **11** in 88% yield as a 82:18 mixture of isomers following flash chromatography (Scheme 2). Removal of the sulfonamide protecting group gave sulfonamide **12** in 70% yield. Cyclization of **12** proved more difficult than **8**, and after reflux in toluene with the Amberlyst catalyst for 24 h, only a 71% yield of **13** could be isolated by flash chromatography. Importantly, only *endo*-(+)-**13** was isolated. Apparently, for steric reasons, *exo*-**12** cannot cyclize to the corresponding imine. Oxidation of (+)-**13** gave (+)-**4b** in 89% isolated yield. The reasonable assumption made is that C(5a)-chloro oxaziridine (+)-**4b** has the same exo structure as (+)-**4a** (vide infra).

Asymmetric Oxidations. The asymmetric oxidation of sulfides to sulfoxides by oxaziridines (+)-**4a** and (+)-**4b** is summarized in Table 3. Values for camphorylsulfonyloxaziridines **1** and **2a** are included for comparison. Oxidations were carried out by treating the sulfide with an equivalent amount of **4** for 2−4 h in CCl_4 at rt (eq 1). Preparative TLC was used to separate the sulfoxides from the imines (+)-**9** and (+)-**13** and the enantiomeric purity determined by NMR using (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol. The absolute configurations were established by comparison with those of authentic samples as previously described.[1]



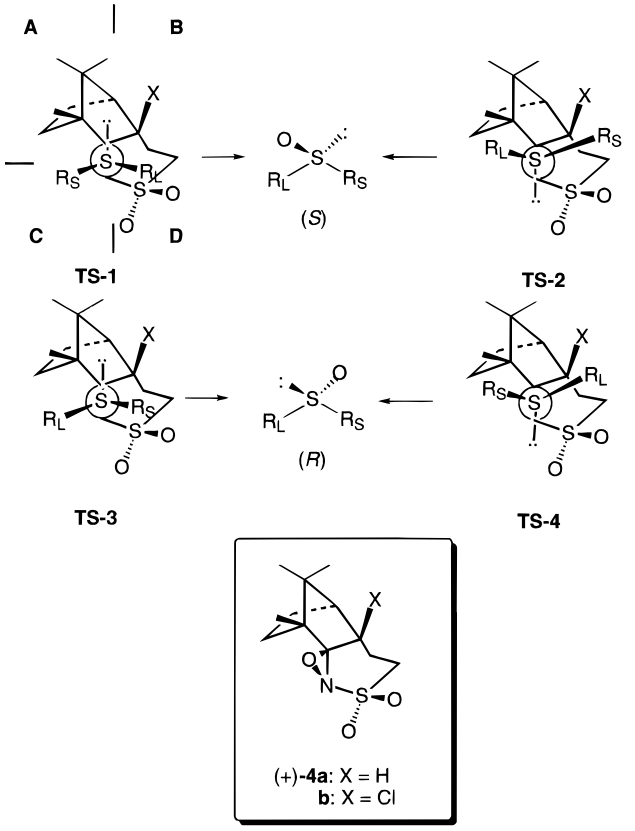


Figure 2. Transition-state structures for the oxidation of sulfides.

In earlier studies we suggested that complementary topological dissymmetry near the active site oxygen in camphorylsulfonyloxaziridines is a fundamental requirement for achieving high asymmetric induction.[1,16] These studies showed that the molecular recognition for the asymmetric oxidation of sulfides to sulfoxides by camphorylsulfonyloxaziridine **1** and **2** was predictable using a simple active-site model.[1,9] In this model the nonbonded steric interactions between the large (R_L) and small (R_S) groups of the sulfide (R_L-S-R_S) and the active-site surface of the oxaziridine were minimized in a planar transition state arrangement. The related planar transition-state structures for the oxidation of sulfides to sulfoxides by **4** are shown in Figure 2. The low enantiomeric excesses (ee's) for the asymmetric oxidation of sulfides to sulfoxides (Table 3) suggests that the regions occupied by the R_L and R_S group of the sulfide have similar steric environments. The fact that (*S*)-sulfoxides are preferentially formed favors **TS-2** and is consistent with the fact that replacement of X by Cl in **4** lowers the ee (Table 3, compare entries 3 and 4).

The asymmetric hydroxylation of the enolate of 2-methyl-1-tetralone (**14**) by oxaziridines (+)-**4a** and (+)-**4b** is summarized in Table 4. Hydroxylations were effected,

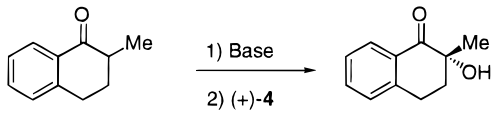


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Table 4. Asymmetric Hydroxylation of the Enolate of 2-Methyl-1-tetralone (14) by *exo*-Camphorylsulfonyloxaziridines 4 at rt

			2-methyl-2-hydroxy-1-tetralone (**15**)	
entry	oxaziridine	base	% isolated yield	% ee[a] (confign)
1	(+)-**2a**[b]	LDA	82	30 (*R*)
2	(X = H)	NaHMDS	90	16 (*R*)
3		KHMDS	76	6 (*R*)
4	(+)-**2b**[c]	LDA	60	>95 (*R*)
5	(X = Cl)	NaHMDS	66	>95 (*R*)
6		KHMDS	61	60 (*R*)
7	(+)-**4a**	LDA	44	racemic
8	(X = H)	NaHMDS	57	58 (*R*)
9		KHMDS	48	racemic
10	(+)-**4b**	LDA	48	racemic
11	(X = Cl)	NaHMDS	67	6 (*R*)
12		KHMDS	53	racemic

[a] Ee's were determined using Eu(hfc)$_3$. [b] At 0 °C, see ref 8. [c] At −78 °C, see ref 9.

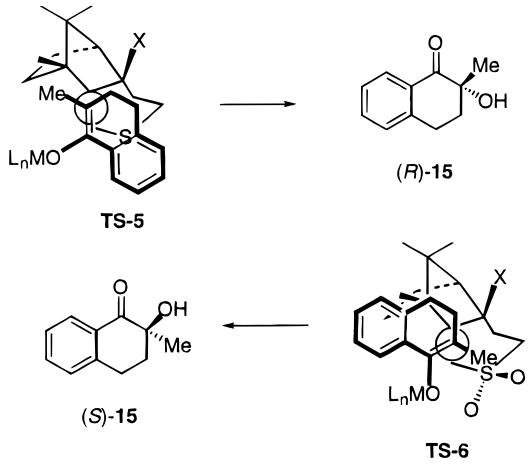

Figure 3. Transition-state structures for the hydroxylation of the enolates of **14**.

as previously described, by addition of 1.0 equiv of the oxaziridine to the preformed enolate at −78 °C.[8,9] The hydroxylations were slow, and it was necessary to warm the reaction to rt for 12 h prior to quenching at −78 °C by addition of NH_4I solution. 2-Hydroxy-2-methyl-1-tetralone (**15**) was isolated by preparative TLC, and the ee's and absolute configurations were determined by comparison with authentic samples.

exo-Camphorylsulfonyloxaziridines **4a** and **4b** are much less reactive than *endo*-oxaziridines **2a** and **2b** as indicated by the fact that it was necessary to carry out the hydroxylation of **14** for 12 h at rt (Figure 3). Importantly, however, even at rt, (+)-**4a** affords a 2-hydroxy-2-methyl-1-tetralone (**15**) in 58% ee having the (*R*)-configuration (Table 4, entry 8). This result is better than that of oxaziridine (+)-**2a** (0 °C, 30% ee), but poorer than that of chloro oxaziridine (+)-**2b** (−78 °C, >95% ee) (Table 4, entries 1 and 5). As previous studies have shown these results can be rationalized in terms of transition-state structures **TS-5** and **TS-6** where nonbonded steric interactions are minimized in an "open" transition state.[3a] In these transition states the reasonable assumption is made that the sterically most demanding group in the vicinity of the enolate C−C bond is the enolate−oxygen metal aggregate.[8,9] This interpretation predicts that increasing the size of X will result in increased steric congestion in **TS-5**, and poorer asymmetric induction is observed, e.g., **4a** (X = H) 58% ee vs **4b** (X = Cl) 6% ee (Table 4, entries 8 and 11).

In summary, studies of the asymmetric oxidation of sulfides to sulfoxides and enolates to α-hydroxy carbonyl compounds by the first *exo*-camphorylsulfonyloxaziridines **4** can be interpreted in terms of "open" transition states where nonbonded steric interactions are minimized. These results provide additional strong support for similar conclusions and predictions for the stereoselectivity and mechanisms of molecular recognition by the *N*-sulfonyloxaziridine class of oxidizing reagents.[1,3a]

Experimental Section

General Procedure. Column chromatography was performed on silica gel, Merck grade 60 (230−400 mesh). Analytical and preparative thin layer chromatography were performed on precoated silica gel plates (250 and 1000 μm) purchased from Analtech Inc. Optical rotations were measured on Perkin-Elmer Model 341 and 241 polarimeters. THF was freshly distilled under nitrogen from a purple solution of sodium and benzophenone. Elemental analyses were performed in the Department of Chemistry, University of Pennsylvania, Philadelphia, PA.

N,*N*-Bis[(4-methoxyphenyl)methyl]ethenesulfonamide (**6**)[10] and 3-chloro-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**10**)[15] were prepared according to literature procedures. *m*-Chloroperbenzoic acid (*m*-CPBA) was obtained free of *m*-chlorobenzoic acid by being washed with commercial *m*-CPBA (57−86%) with buffer at pH 7.4 (NaH_2PO_3−NaOH) as previously described.[17]

***N*,*N*-Bis[(4-methoxyphenyl)methyl]-4,7,7-trimethyl-3-oxobicyclo[2.2.1]heptane-2-ethanesulfonamide (7) (80:20 Endo/Exo Mixture).** In a 50 mL, two-neck, round bottomed flask equipped with a magnetic stir bar, rubber septum, and an argon-filled balloon was placed 1.61 g (10.3 mmol) of (+)-camphor in freshly distilled THF (15 mL). The reaction mixture was cooled to −78 °C, 10.3 mL (10.3 mmol) of LiHMDS was added dropwise, and after 15 min the mixture was warmed to 0 °C and stirred for 20 min. The resulting pale yellow mixture was cooled to −78 °C, and 1.95 g (10.3 mmol) of CuI (98%) was quickly added. After the solution was stirred for 1 h, 1.20 g (3.45 mmol) of *N*,*N*-bis[(4-methoxyphenyl)-methyl]ethenesulfonamide (**6**) in THF (10 mL) at −78 °C was added via a double-ended needle to the gray reaction mixture. The solution was slowly warmed to −20 °C after 30 min, stirred for 3 h, and quenched at −78 °C by addition of 3 mL of saturated NH_4Cl solution. The reaction mixture was warmed to rt, diluted with ethyl acetate (40 mL) and water (10 mL), and filtered through Celite. The aqueous layer was extracted with ethyl acetate (2 × 15 mL), and the combined organic portions were washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The product was purified by flash chromatography (15% EtOAc/*n*-hexane) to afford 1.42 g (82%) of an 80:20 endo/exo mixture of **7** as a thick gum: IR (neat) 2959, 1736, 1611, 1513, 1249, 1142, 1034, 907, 824, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 80/100, 3H), 0.84 (s, 20/100, 3H), 0.89 (s, 3H), 0.92 (s, 80/100, 3H), 0.98 (s, 20/100, 3H), 1.25−2.20 (m, 8H), 2.92−3.05 (m, 1H), 3.1−3.2 (m, 1H), 3.8 (s, 6H), 4.25 (s, 4H), 6.85 (d, 4H, J = 8.60 Hz), 7.18 (d, 4H, J = 8.46 Hz); mass spectrum (*m*/*z*) 499 (M^+), 435, 378, 256, 147, 136, 121; exact mass calcd for $C_{28}H_{37}NSO_5$ 522.2290 (M^++ Na), found 522.2289 (M^+ + Na).

4,7,7-Trimethyl-3-oxobicyclo[2.2.1]heptane-2-ethanesulfonamide (8) (80:20 Endo/Exo Mixture). In a 500 mL, single-neck, round bottom flask fitted with magnetic stir bar was placed 1.42 g (2.84 mmol) of **7**, dissolved in CH_3CN (200 mL), and water (80 mL) followed by the addition of 12.45 g (22.72 mmol) of ceric ammonium nitrate (CAN). The reaction mixture was stirred for 6 h at rt, concentrated, and extracted with ethyl acetate (2 × 40 mL). The combined organic phases

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were washed with brine (15 mL), dried ($MgSO_4$), and concentrated, and the crude product was purified by flash chromatography (40% EtOAc/*n*-hexane) to give 0.62 g (84%) of an 80:20 endo/exo mixture of sulfonamides **8**: IR (KBr) 3350, 3265, 2960, 1729, 1560, 1324, 1150, 913, 786, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (s, 80/100, 3H), 0.87 (s, 20/100, 3H), 0.91 (s, 3H), 0.95 (s, 80/100, 3H), 1.01 (s, 20/100, 3H), 1.3−2.35 (m, 8H), 3.15−3.45 (m, 2H), 4.75 (bs, 2H); mass spectrum (*m*/*z*) 259 (M^+), 231, 151, 135, 108, 95, 83, 69. Anal. Calcd for $C_{12}H_{21}NSO_3$: C, 55.5; H, 8.16; N, 5.40. Found: C, 55.10; H, 8.09; N, 5.55.

[4a*S*-(4aα,5α,8α)]-4,4a,5,6,7,8-Hexahydro-8,9,9-trimethyl-5,8-methano-3*H*-2,1-benzothiazine 2,2-Dioxide (9). In a 50 mL, one-neck round bottom flask fitted with a Dean−Stark column and a magnetic stir bar were placed 1.23 g (4.7 mmol) of sulfonamide **8** in toluene (17 mL) and 0.21 g of Amberlyst-15 ion exchange resin. The mixture was refluxed for 3 h, cooled, and filtered, and the filtrate was washed with CH_2Cl_2 (25 mL). Concentration of the combined organic phases gave 1.1 g (96%) of an 80:20 endo/exo mixture of isomers. An analytically pure sample of endo imine **9** was obtained as white crystals by crystallization (Et_2O/*n*-hexane): mp 90−91 °C; $[\alpha]^{20}_D$ −37.38° (*c* 0.67, $CHCl_3$); IR (KBr) 2962, 1737, 1639, 1451, 1325, 1155, 1141, 1100, 1015, 921, 869, 832 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 3H), 1.0 (s, 3H), 1.06 (s, 3H), 1.4−1.5 (m, 1H), 1.7−1.9 (m, 2H), 2.0-2.2 (m, 4H), 2.6−2.7 (m, 1H), 3.25−3.35 (m, 1H), 3.5−3.6 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 10.376, 19.258, 20.439, 21.103, 22.915, 35.551, 43.753, 47.944, 48.753, 49.982, 59.107, 200.252; mass spectrum (*m*/*z*) 241 (M^+), 226, 198, 162, 134, 95, 84, 67; exact mass calcd for $C_{12}H_{19}NSO_2$ 242.1214 ($M^+ + H^+$), experimental mass 242.1215 ($M^+ + H^+$). Anal. Calcd for $C_{12}H_{19}NSO_2$: C, 59.72; H, 7.93; N, 5.80. Found: C, 59.79; H, 7.90; N, 5.53.

[5a*S*-(5aα,6α,9α,9a*S)]-(+)-Hexahydro-9,10,10-trimethyl-6,9-methano-4*H*-oxazirino[3,2-*j*][2,1]benzothiazine 3,3-Dioxide (4a).** In a 500 mL, three-neck Morton flask fitted with a overhead mechanical stirrer were placed 1.1 g (4.4 mmol) of imine **9** in CH_2Cl_2 (70 mL) and saturated aqueous K_2CO_3 (69 mL), followed by 3.03 g (17.5 mmol) of *m*-CPBA (95%). The reaction mixture was vigorously stirred for 48 h at which time a sodium sulfite solution (10 mL) was added. The reaction mixture was diluted with $CHCl_3$ (50 mL) and water (25 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 20 mL), and the combined organic phases were washed with a saturated $NaHCO_3$ solution (2 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The product was purified by flash chromatography (20% EtOAc/*n*-hexane) to afford 0.96 g (82%) of oxaziridine **4a** as an 80:20 endo/exo mixture. Crystallization (EtOAc/*n*-hexane) afforded the pure *endo*-oxaziridine as white crystals: mp 115−116 °C; $[\alpha]^{20}_D$ +88.83° (*c* 1.54, $CHCl_3$); IR (KBr) 2966, 1356, 1154, 846, 776, 676, 529 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.65 (s, 3H), 0.95 (s, 3H), 1.00 (s, 3H), 1.5−2.3 (m, 7H), 2.59−2.7 (m, 1H), 3.2−3.3 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 8.051, 19.173, 19.231, 19.465, 20.146, 22.016, 30.823, 38.459, 43.944, 47.205, 50.821, 100.631; mass spectrum (*m*/*z*) 257 (M^+), 214, 176, 161, 150, 107, 91. Anal. Calcd for $C_{12}H_{19}NSO_3$: C, 56.00; H, 7.44; N, 5.44. Found: C, 55.77; H, 7.48; N, 5.11.

Typical Procedure for Isomerization of Sulfonimine 9. In a 25 mL, oven dried, two-necked, round bottom flask fitted with an argon balloon, rubber septum, and a magnetic stir bar was placed 0.030 g (0.12 mmol) of the 80:20 endo/exo mixture of sulfonimine **9** in freshly distilled THF (2 mL). The reaction flask was cooled to −78 °C, and 0.18 mL (0.18 mmol) of 0.1 M solution of the appropriate base was added dropwise. The reaction mixture was stirred for 2 h and quenched with an aqueous NH_4Cl solution or camphorsulfonic acid [0.12 mmol in 1 mL of THF]. After being warmed to rt, the mixture was diluted with ethyl acetate (10 mL), the aqueous phase was extracted with ethyl acetate (2 × 5 mL), the combined organic phases were washed with brine (10 mL) and dried ($MgSO_4$). Concentration afforded sulfonimine **9** enriched in the endo isomer.

2-Chloro-*N*,*N*-bis[(4-methoxyphenyl)methyl]-4,7,7-trimethyl-3-oxobicyclo[2.2.1]heptane-2-ethanesulfonamide (11) (82:18 Endo/Exo Mixture). In a 100 mL, two-neck, round bottom flask equipped with magnetic stir bar, rubber septum, and an argon-filled balloon was placed 2.0 g (10.75 mmol, 2 equiv) of 3-chloro-1,7,7-trimethylbicyclo[2.2.1]-heptane-2-one (**10**) in freshly distilled THF (60 mL). The reaction flask was cooled to 0 °C, 1.04 g (43 mmol) of NaH was added, and after 15 min the mixture was warmed to rt and stirred for 20 min. The resulting suspension was cooled to 0 °C, and 1.72 g (5.38 mmol) of *N*,*N*-bis[(4-methoxyphenyl)-methyl]ethenesulfonamide (**6**) in THF (20 mL) was added via syringe. After 1 h the reaction mixture was warmed to rt and stirring was continued until TLC indicated the absence of starting material (typically 1.5 h). The reaction mixture was quenched at rt by addition of 5 mL of NH_4Cl solution and diluted with EtOAc (40 mL) and water (10 mL). The aqueous phase was extracted with ethyl acetate (2 × 20 mL), and the combined organic phases were washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography (20% EtOAc/hexanes) to afford 2.32 g (88%) of an 82:18 endo/exo mixture of **11** as a thick gum: IR (neat) 2960, 1751, 1611, 1585, 1512, 1303, 1248 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (s, 82/100, 3H), 0.9 (s, 82/100, 3H), 0.95 (s, 18/100, 3H), 1.0 (s, 18/100, 3H), 1.08 (s, 82/100, 3H), 1.1 (s, 18/100, 3H), 1.57−2.7 (m, 7H), 3.3−3.4 (m, 2H), 3.81 (s, 6H), 4.25 (m, 4H), 6.86−6.89 (d, 4H, J = 8.58 Hz), 7.2−7.23 (d, 4H, J = 8.63 Hz); mass spectrum (*m*/*z*) 533 (M^+), 256, 148, 136, 121, 91, 77; mass calcd for $C_{28}H_{36}NSO_3Cl$ 534.094, obsd 533.

2-Chloro-4,7,7-trimethyl-3-oxobicyclo[2.2.1]heptane-2-ethanesulfonamide (12) (82:18 Endo/Exo Mixture). In a 500 mL single-neck, round bottom flask fitted with magnetic stir bar were placed 1.77 g (3.31 mmol, 1 equiv) of chloro adduct **11** in CH_3CN (100 mL) and water (50 mL). To the reaction mixture was added 14.7 g (26.83 mmol) of ceric ammonium nitrate (CAN), and the solution was stirred for 6 h at rt. The solvent was removed, the residue was dissolved in ethyl acetate (2 × 40 mL), and the combined organic extracts were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography (40% EtOAc/*n*-hexane) to give 0.673 g (70%) of an 82:18 endo/exo mixture of **12** as a thick gum: IR (neat) 3350, 3265, 2960, 1729, 1560, 1324, 1150, 913, 786, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (s, 3H), 0.98 (s, 82/100, 3H), 1.04 (s, 18/100, 3H), 1.09 (s, 82/100, 3H), 1.15 (s, 18/100, 3H), 1.65−1.72 (m, 2H), 1.9−2.0 (m, 1H), 2.23−2.3 (m, 2H), 2.46−2.53 (m, 1H), 2.66−2.69 (m, 1H), 3.5−3.56 (m, 1H), 3.63−3.66 (m, 1H), 4.58 (bs, NH); mass spectrum (*m*/*z*) 294 ($M^+ + H^+$), 277, 250, 133, 83, 71. Anal. Cacld for $C_{12}H_{20}NSO_3Cl$: C, 49.06, H, 6.86; N, 4.77. Found: C, 49.08; H, 6.65; N, 4.20.

[4a*R*-(4aα,5α,8α)]-(+)-4a-Chloro-4,4a,5,6,7,8-hexahydro-8,9,9-trimethyl-5,8-methano-3*H*-2,1-benzothiazine 2,2-Dioxide (13). In a 50 mL, one-neck, round bottom flask fitted with a Dean−Stark column and a magnetic stir bar was placed 0.490 g (1.67 mmol) of chloro sulfonamide **12** in toluene (7 mL) with 0.082 g of Amberlyst-15 ion exchange resin. The reaction mixture refluxed for 24 h at which time it was cooled and filtered, and the filtrate was washed with CH_2Cl_2 (10 mL). Concentration gave a solid residue which was purified by flash chromatography to give 0.322 g (71%) of (+)-**13**: mp 152−155 °C; $[\alpha]^{20}_D$ +197.6 (*c* 0.7, $CHCl_3$); IR (KBr) 2962, 1649, 1341, 1326, 1158, 1139, 794 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (m, 3H), 1.059 (m, 3H), 1.15 (s, 3H), 1.76−1.82 (m, 1H), 1.96−2.03 (m, 2H), 2.18 (d, 1H, J = 3.7 Hz), 2.37−2.41 (m, 1H), 2.52−2.56 (m, 1H), 2.79−2.80 (m, 1H), 3.47−3.52 (m, 1H), 4.06−4.13 (td, 1H, $J_{1,3}$ = 13.2 Hz; $J_{1,2}$ = 5.5 Hz); ^{13}C NMR ($CDCl_3$) δ 10.74, 21.26, 22.84, 26.33, 29.06, 35.02, 47.23, 49.08, 53.10, 56.22, 64.26, 188.51; mass calcd for $C_{12}H_{18}NSO_2Cl$ 275, obsd 275. Anal. Calcd for $C_{12}H_{18}NSO_2Cl$: C, 52.26; H, 6.58; N, 5.08. Found: C, 52.20; H, 6.52; N, 4.80.

[5a*R*-(5aα,6α,9α,9a*S)]-(+)-5a-Chlorohexahydro-9,10,-10-trimethyl-6,9-methano-4*H*-oxazirino[3,2-*j*][2,1]-benzothiazine 3,3-Dioxide (4b).** In a 250 mL, three-neck Morton flask fitted with an overhead mechanical stirrer were placed 0.241 g (0.88 mmol) of endo chloro imine **13** in CH_2Cl_2 (120 mL), saturated aqueous K_2CO_3 (24 mL), and 0.456 g (2.63 mmol) of *m*-CPBA (95%). The reaction mixture was vigorously stirred for 48 h, at which time a saturated solution of sodium sulfite (5 mL) was added. The solution was diluted

with $CHCl_3$ (50 mL) and water (25 mL), and the aqueous phase was extracted with $CHCl_3$ (2 × 20 mL). The combined organic phases were washed with a saturated $NaHCO_3$ solution (2 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. Crystallization (EtOAc/*n*-hexane) of the residue gave 0.258 g (89%) of *endo*-**4b**: mp 152−153 °C; $[\alpha]^{20}_D$ +63.5° (*c* 1.76, $CHCl_3$); IR (KBr) 2952, 2361, 1734, 1349, 1165, 788, 668 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79 (s, 3H), 1.10 (s, 3H), 1.2 (s, 3H), 1.74−1.81 (m, 1H), 1.89−1.94 (m, 2H), 2.2 (d, 1H, J = 3.7 Hz), 2.39−2.44 (m, 1H), 2.45−2.49 (m, 1H), 2.88−2.94 (m, 1H), 3.24−3.28 (m, 1H), 3.74−3.8 (td, 1H, $J_{1,3}$ = 14.3 Hz; $J_{1,2}$ = 2.6 Hz); ^{13}C NMR ($CDCl_3$) δ 9.361, 20.816, 22.966, 26.189, 28.440, 37.04, 43.97, 47.49, 50.05, 55.59, 73.39, 100.13; mass spectrum (*m*/*z*) 291 (M^+), 256, 192, 174, 105, 91, 77, 69. Anal. Cacld for $C_{12}H_{18}NSO_3Cl$: C, 49.39; H, 6.11; N, 4.8. Found: C, 49.65; H, 6.64; N, 4.69.

Typical Procedure for Asymmetric Oxidation of Sulfides to Sulfoxides. In a 10 mL, oven-dried, two-necked, round bottom flask fitted with an argon-filled balloon, a rubber septum, and a magnetic stir bar was placed 0.25 mmol of the appropriate oxaziridine in CCl_4 (10 mL). The sulfide, 1.1 equiv, in CCl_4 (5 mL) was added to the reaction mixture which was stirred at rt for 2−4 h. After the oxidation was complete, as indicated by TLC, the solvent was removed and the sulfoxide isolated by preparative TLC (silica gel G). The enantiomeric purity and absolute configuration were determined by comparison with authentic samples and literature values.[1]

Typical Procedure for Hydroxylation of 2-Methyl-1-tetralone (14) to 2-Hydroxy-2-methyl-1-tetralone (15). In a 25 mL, oven-dried, two-necked, round bottom flask fitted with an argon-filled balloon, a rubber septum, and a magnetic stir bar was placed 0.024 g (0.15 mmol) of 2-methyl 1-tetralone in freshly distilled THF (2 mL). The reaction flask was cooled to −78 °C, and 0.18 mL (0.18 mmol, 1.2 equiv) of a 1.0 M solution of the appropriate base was added via syringe. After 30 min, the reaction mixture was warmed to 0 °C, stirred for 30 min, and cooled to −78 °C and a solution of 0.056 g (0.25 mmol) of the oxaziridine in THF (1 mL) was added via syringe. The reaction mixture was warmed to rt after 30 min, stirred for 12 h, and quenched at −78 °C by addition of 3 mL of a freshly prepared saturated NH_4I solution. The solution was diluted with ethyl acetate (10 mL), the aqueous phase was extracted with ethyl acetate (2 × 5 mL), and the combined organic phases were washed with a saturated $Na_2S_2O_3$ solution (2 × 15 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by preparative TLC (25% EtOAc/*n*-hexane) to give **15** as an oil with spectral properties identical with an authentic sample: ee 58%; $[\alpha]^{20}_D$ +9.9° (*c* 0.66, MeOH) [lit.[9] $[\alpha]^{20}_D$ +17.3° (*c* 2.0, MeOH)].

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Supporting Information Available: ^1H NMR spectra for endo/exo mixtures of compounds **7** and **11** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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