Catalytic Asymmetric Oxidation of Sulfides to Sulfoxides Mediated by Chiral 3-Substituted-1,2-benzisothiazole 1,1-Dioxides

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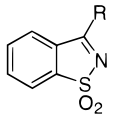
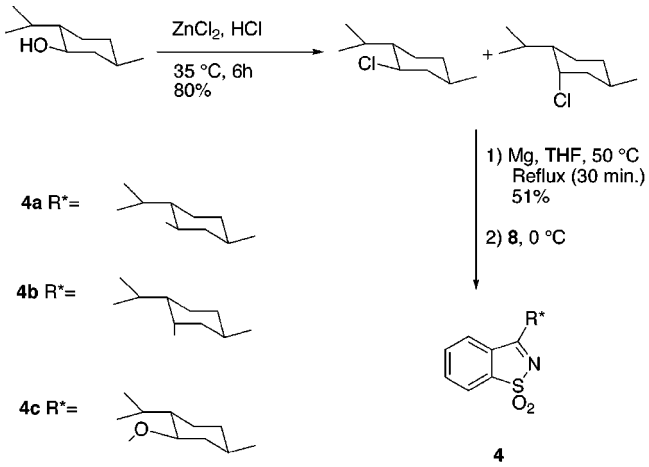
Optically active sulfoxides are useful chiral synthons[1] and auxiliaries[2] in asymmetric synthesis. We have reported the use of a number of mediators for sulfur oxidation, including several based upon 3-substituted-1,2-benzisothiazole 1,1-dioxides, using hydrogen peroxide as the oxidant.[3] Study of the 3-*n*-butyl [**1**], (±)-3-*sec*-butyl [**2**], and 3-*tert*-butyl [**3**] compounds in dichloromethane, in the presence of a 4-fold excess of hydrogen peroxide and base over the sulfide substrates, showed that oxidation to the sulfoxides occurred in good yield, the *tert*-butyl compound being particularly active in promoting oxygen transfer. In this paper are described the syntheses, reactions, and enantioselective oxidations mediated by chiral nonracemic 3-substituted-1,2-benzisothiazole 1,1-dioxides [**4**−**6**] using hydrogen peroxide as the primary oxidant.



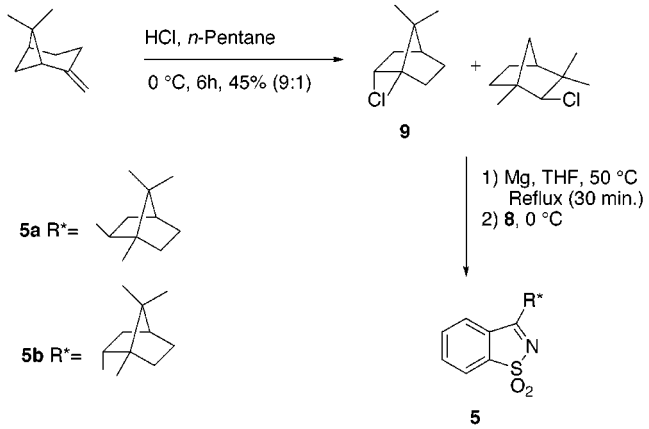
1, R = *n*-Bu
2, R = *sec*-Bu
3, R = *tert*-Bu
7, R = OEt
8, R = Cl

The chiral nonracemic 3-substituted-1,2-benzisothiazole 1,1-dioxides [**4**−**6**] were synthesized by treatment of the corresponding chiral organometallic compounds with ethoxy [**7**] or chloro [**8**] saccharin derivatives (Scheme 1). Menthyl chloride, synthesized by the method of Smith and Wright,[4] was converted into menthylmagnesium chloride using a method previously documented.[5] Treatment of the Grignard reagent with **8** in dry THF afforded a mixture of the diastereoisomeric sulfonylimines [**4a/b**] in moderate yield (Scheme 1), consisting of (−)-3-[(1′*R*)-1′-menthyl]-1,2-benzisothiazole 1,1-dioxide [**4a**] and (+)-3-[(1′*S*)-1′-menthyl]-1,2-benzisothiazole 1,1-dioxide [**4b**], together with a third compound. The diastereoisomer ratio **4a**:**4b**, determined by integration of the signals in the ^{1}H NMR spectrum corresponding to the methine protons adjacent to the heterocyclic ring, which appear at 3.1 and 3.7 ppm, respectively, was 3:1. Separation of these compounds was carried out by column chromatography using dichloromethane/hexane (2:1). The structure of the unknown third compound was shown on the basis of elemental analysis, NMR spectroscopy and X-ray crystallography to be 3-menthoxy-1,2-benzisothiazole 1,1-dioxide [**4c**]. Single-crystal X-ray structures of imines **4a** and **4b** were also determined.

Scheme 1



Scheme 2



An approach similar to that shown in Scheme 1, but starting with bornyl chloride [**9**], synthesized in 45% yield from *β*-pinene as previously reported,[6] was used to prepare the bornyl pseudosaccharin derivative [**5**] (Scheme 2). The diastereoisomeric ratio (54:46) of product **5** was determined from the ^{1}H NMR spectrum by integration of triplet signals due to the methine groups adjacent to the heterocyclic ring, which appear at 3.20 and 3.55 ppm, respectively. All attempts to separate the diastereoisomers by column chromatography or crystallization using different solvent mixtures proved fruitless.

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(1) Page, P. C. B., Ed.. *Organosulfur Chemistry,* Vol. 2; Academic Press: London, 1995.
(2) Solladié, G. *Synthesis* **1981**, 185.
(3) Page, P. C. B.; Bethell, D.; Stocks, P. A.; Heer, J. P.; Graham, A. E.; Vahedi, H.; Healy, M.; Collington, E. W.; Andrews, D. M. *Synlett* **1997**, 1355.
(4) Smith, J. G.; Wright, G. F. *J. Org. Chem.* **1952**, *17*, 1116.
(5) Tanaka, M.; Ogata, I. *Bull. Chem. Soc. Jpn.* **1975**, *43*, 1094.
(6) Erickson, G. W.; Fry, J. L. *J. Org. Chem.* **1987**, *52*, 462.

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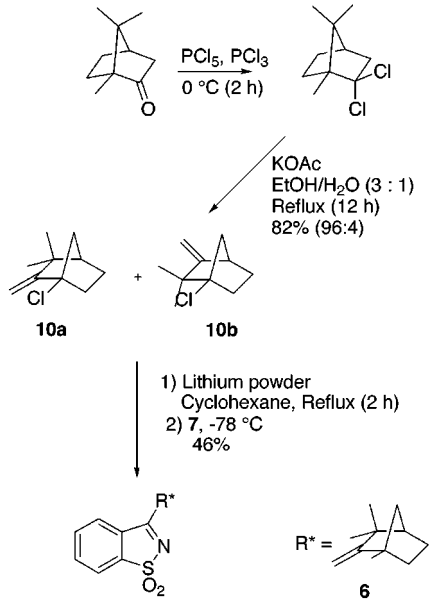
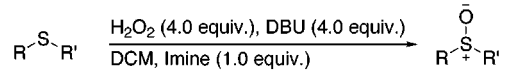
Scheme 3



Scheme 4



Our earlier work[3] had shown that 3-*tert*-alkyl pseudosaccharins are more efficient mediators of sulfur oxidation than are the 3-*n*- and 3-*sec*-alkyl derivatives, probably because of the absence of acidic protons at the α-position in the side chain. Accordingly, a *tert*-alkyl pseudosaccharin derivative [**6**] was prepared: (1*R*,4*R*)-1-chloro-3,3-dimethyl-3-methylenebicyclo[2.2.1]heptane (1-chlorocamphene) [**10a**] was prepared in 80% yield from D-camphor as a 96:4 mixture with its isomer [**10b**] (Scheme 3).[7] By heating the mixture of alkyl halides with lithium powder in dry cyclohexane under an argon atmosphere, the organolithium reagents were prepared and these were then treated with the ethoxy pseudosaccharin derivative [**7**] at −78 °C, allowed to reach room temperature, and stirred overnight (Scheme 3). After column chromatography, 3-[(1′*R*,4′*R*)-1′-(2′,2′-dimethyl-3′-methylenebicyclo[2.2.1]heptane)]-1,2-benzisothiazole 1,1-dioxide [**6**] was obtained as a single, pure compound in 46% yield.

All new sulfonylimines gave a satisfactory elemental analyses, exhibited a signal in the ^{13}C NMR spectrum at 175−180 ppm for the imino carbon, and showed absorption at 1602 cm^{-1} (C═N stretch) in the infrared spectrum.

Asymmetric sulfoxidation reactions mediated by chiral sulfonylimines **4**−**6** were carried out using the method developed by Bulman Page and Bethell by addition of a solution of hydrogen peroxide (30% w/v aqueous solution; 4.0 equiv) to a cooled, stirred dichloromethane solution of DBU (4.0 equiv), followed by the sulfonylimine (1.0 equiv) (Scheme 4).[8] The sulfide substrate (1.0 equiv) was then added, and the reaction progress was monitored by TLC. The results of the oxidation reactions are shown in Table 1. The imine could be recovered by column chromatography and reused; in all of the oxidation reactions in Table 1 the imine was recovered in >90% yield.

Table 1. Oxidation of Sulfides to Sulfoxides Using Imines 4−6[a]

no.	imine	sulfide	temp, °C	time, h	yield, %	ee, %	confign at sulfur
1	**5**	*tert*-butyl methyl	−10	14	63	15	
2	**5**	*p*-tolyl methyl	−10	24	44	21	*S*
3	**4**	2-phenyl-1,3-dithiane	0	40	48	35	*R*
4	**4**	*tert*-butyl methyl	−15	23	29	2	
5	**4**	benzyl methyl	−15	23	28	16	*S*
6	**6**	2-phenyl-1,3-dithiane	−5	14	99[b]	20	*S*
7	**6**	2-phenyl-1,3-dithiane	−15	14	100[b]	34	*S*
8	**6**	2-phenyl-1,3-dithiane	−15	2	31[b]	31	*S*
9	**6**	2-phenyl-1,3-dithiane	−25	14	50[b]	38	*S*
10	**6**	*p*-tolyl methyl	−15	14	61	25	*R*
11	**6**	*tert*-butyl methyl	−5	14	100	8	

[a] The enantiomeric excesses of sulfoxide products were determined by NMR spectroscopy using (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol,[12] and the absolute configurations were established by comparison with those of authentic samples.[8−10] [b] Anti.

As expected, the tertiary alkyl derivative [**6**] is more efficient for the oxidation of sulfides to sulfoxides than are **4** or **5** (Table 1), in agreement with our previous reports.[3] For example, using imine **6**, 2-phenyl-1,3-dithiane was oxidized to give the corresponding sulfoxide in quantitative yield at −15 °C after 14 h (Table 1, entry 7); using imine **4**, with the same substrate at higher temperature and longer reaction time (0 °C, 40 h), the sulfoxide was isolated in only 48% yield (Table 1, entry 3). Lower temperature resulted in improved enantioselectivity (compare entries 6, 8, and 9). Although the conversions in sulfoxidation reactions are high using imine **6**, enantioselectivities are low under our reaction conditions. We excluded the possibility that racemization of the chiral sulfoxide might be occurring under the reaction conditions in reactions carried out over long time periods by showing that, in the oxidation of 2-phenyl-1,3-dithiane, the enantioselectivity after completion of the reaction, 14 h, was almost the same as that in the product of a reaction stopped after just 2 h (Table 1, entries 7 and 8). The implication is that the enantioselectivity is determined kinetically in the O-transfer process.

Table 2. Catalytic Sulfoxidation at Room Temperature Using Imine [6]

sulfide	mol % of imine	time, h	yield, %	ee, %	confign at sulfur
p-tolyl methyl	10	48	100 (16)[a]	14	*R*
phenyl methyl	20	24	95 (9)[a]	14	*R*

[a] Sulfoxide yield in the absence of the imine.

To assess the efficiency as a catalyst for sulfoxidation of imine **6** using substoichiometric quantities, a series of reactions was carried out at room temperature (Table 2)

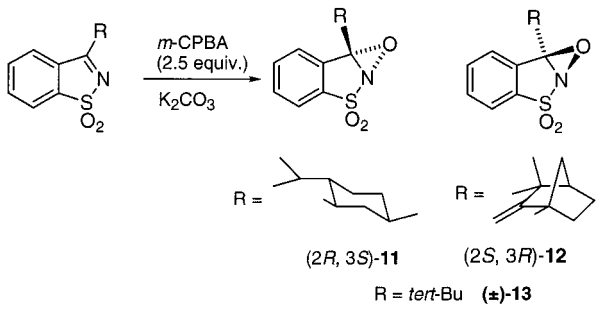
(7) Joshi, G. C.; Warnhoff, E. W. *J. Org. Chem.* **1972**, *37*, 2383.

(8) (a) Page P. C. B.; Graham, A. E.; Bethell, D.; Park, B. K. *Synth. Commun.* **1993**, *23*, 1507. (b) Page P. C. B.; Heer, J. P.; Bethell, D.; Collington, E. W.; Andrews, D. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2911. (c) Page P. C. B.; Heer, J. P.; Bethell, D.; Collington, E. W.; Andrews, D. M. *Tetrahedron Lett.* **1994**, *35*, 9629. (d) Page P. C. B.; Heer, J. P.; Bethell, D.; Collington, E. W.; Andrews, D. M. *Synlett* **1995**, 773.

(9) Page P. C. B.; Wilkes, R. D.; Namwindwa, E. S.; Witty, M. J. *Tetrahedron* **1996**, *52*, 2125; Davis, F. A.; Reddy, R. T.; Han, W.; Carroll, P. J. *J. Am. Chem. Soc.* **1992**, *114*, 1428.

(10) Page P. C. B.; Gareh, M. T.; Porter, R. A. *Tetrahedron: Asymmetry* **1993**, *4*, 2139.

Scheme 5



in which the primary oxidant was potassium percarbonate. Control reactions under similar reaction conditions but in the absence of **6** suggested that direct oxidation can occur for alkyl aryl sulfides, but only very slowly. We were thus able to confirm catalytic turnover in sulfoxidations catalyzed by imine **6**, although the enantiomeric excesses were low.

We have previously argued[8d] that in imine-mediated S-oxidation using hydrogen peroxide there are two pathways for O-transfer to sulfur: (i) via the hydroperoxyamine obtained by addition of the oxidant to the C=N bond of the imine; (ii) via the oxaziridine produced by cyclodehydration of the hydroperoxyamine. To determine the nature of the chiral oxidizing species involved in the present process, we examined the stereochemistry of O-transfer to prochiral sulfides from the oxaziridines derived from imines **4** and **6** (Scheme 5). To oxidize these imines to the corresponding oxaziridines, the procedure used was that previously reported by Davis et al.[11] In each case the reaction afforded the oxaziridine in high yield as a colorless crystalline solid. The C=N bond in imines **4** and **6** possesses diastereotopic faces, so that two diastereoisomeric oxaziridines can in principle be formed in the reactions, each as a single enantiomer. The oxaziridines formed in each case, however, appear to be single enantiomers of single diastereoisomers **11** and **12**, as indicated by their clean ^{13}C and ^{1}H NMR spectra, even, in the case of **12**, in the presence of a chiral shift reagent. Using the known absolute configuration of the menthyl moiety in **11**, and the expected absolute configuration of the 1-camphenyl group in **12**, based on the absolute configuration of the camphor from which it was generated, X-ray crystallography on **11** and **12** permitted assignment of the absolute configurations of the oxaziridine rings as (2*R*,3*S*) and (2*S*,3*R*), respectively, intriguingly having opposite configuration at the oxaziridine carbon atom.

The evaluation of the enantioselective efficiencies of these chiral *N*-sulfonyloxaziridines, **11** and **12**, in the asymmetric oxidation of sulfides to sulfoxides is shown in Table 3. These oxidations were carried out by treating the sulfide with an equivalent amount of the oxaziridine in the absence of base in dichloromethane or carbon tetrachloride solution over a range of temperatures from room temperature to as low as −25 °C. The following points should be noted: (i) sulfoxide yields were essentially quantitative in all cases; (ii) **12** gave substantially higher ee values than **11** in the oxidation of

Table 3. Oxidation of Sulfides to Sulfoxides Using Oxaziridines [11] and [12]

no.	oxaziridine	sulfide	temp, C	time, min	yield, %	ee, %	confign at sulfur
1	**11**	2-phenyl-1,3-dithiane	20	60	100[a]	44	*R*
2	**11**	2-phenyl-1,3-dithiane	−14	60	99[a]	54	*R*
3	**11**	2-phenyl-1,3-dithiane	−25	80	100[a]	62	*R*
4	**12**	2-phenyl-1,3-dithiane	0	45	100[a]	82	*S*
5	**12**	2-phenyl-1,3-dithiane	−20	80	100[a]	83	S
6	**12**	2-phenyl-1,3-dithiane	0	30	100[a]	60	*S*
7	**12**	*tert*-butyl methyl	−20	80	100	18	-
8	**12**	*p*-tolyl methyl	−20	120	100	19	*R*

[a] *Anti*. [b] Dichloromethane was used as solvent. [c] Carbon tetrachloride was used as solvent.

2-phenyl-1,3-dithiane; (iii) the major enantiomer in the product obtained using **12** was of opposite configuration to that from reactions using **11**; (iv) the predominant enantiomers were the same as those obtained using hydrogen peroxide and the corresponding imine mediator; (v) enantioselectivities were surprisingly low in the oxidations of *tert*-butyl methyl and *p*-tolyl methyl sulfides.

The identity of the oxidizing species using imines **4** and **6**, hydrogen peroxide, and DBU remains uncertain. The observation that ee values are all lower than those found in reactions in which the related oxaziridines **11** and **12** were the oxidants clearly indicates that the oxaziridines cannot be the sole O-transfer agent in imine-mediated oxidations. Oxygen transfer from the oxaziridine to sulfur is not stereospecific, but it shows higher enantioselectivity than the corresponding imine-mediated reaction. Because **11** and **12** have opposite absolute absolute configurations at their oxaziridine carbon atoms, it is tempting to conclude from the outcome of the oxaziridine reactions that the stereochemistry of O-transfer from the three-membered ring to sulfur is determined largely by the absolute configuration at the oxaziridine carbon atom, the nature of the chiral side chain being of secondary importance, provided that the orientation of the sulfide substrate with respect to the oxaziridine unit is similar for both catalysts.

In the imine-mediated reactions, the O-transfer intermediate could be the α-hydroperoxyamine, from which sulfonylimine is regenerated by elimination of water after oxygen transfer to sulfur. Although we have observed cyclization of α-hydroperoxyamines to yield oxaziridines under certain conditions, such a transformation is unlikely on the time scale of the present experiments in dichloromethane/DBU for the following reasons: (i) hydroxide ion is a poorer leaving group than sulfate or carboxylate, which arise from Oxone- or peracid-mediated oxidations; (ii) even the hindered oxaziridine derived from 3-*tert*-butyl-1,2-benzisothiazole 1,1-dioxide [**13**] reacts completely with DBU after only half an hour at room temperature to regenerate the corresponding imine, making it unlikely that it would transfer oxygen efficiently to the less nucleophilic sulfide in the presence of DBU if formed in the imine-catalyzed process.

The absolute sense of stereochemical induction is the same in imine-mediated oxidations as in the oxaziridine

(11) Davis, F. A.; Reddy, R. E.; Kasu, P. V. N.; Portonovo, P. S.; Carroll, P. J. *J. Org. Chem.* **1997**, *62*, 3625; Davis, F. A.; Reddy, R. T.; McCauley, J. P., Jr.; Przeslawski, R. M.; Harakal, M. E.; Carroll, P. J. *J. Org. Chem.* **1991**, *56*, 809.

(12) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1977**, *42*, 3217.

reactions for every example in this study (Tables 1, 2, and 3). Although this might seem to be expected since the hydroperoxyamine should have the same configuration at the peroxyaminal carbon atom as the corresponding carbon atom in the related oxaziridine, it would only be so if the formation of the α-hydroperoxyamine were stereospecific and if the mechanism and transition state of O-transfer from the α-hydroperoxyamines and oxaziridines were essentially the same, a situation which would require the oxygen atom attached to the peroxyaminal/oxaziridine carbon atom to be transferred in both cases. We have already shown that, in sulfoxidations mediated by camphorsulfonylimine, the major sense of asymmetric induction is opposite to that found in oxidations brought about by the derived oxaziridine.[8d] This difference in behavior between the camphor-derived systems and those based on pseudosaccharin is a continuing puzzle that will require further investigation.

Experimental Section

General. All moisture-sensitive reactions were carried out in round-bottomed flasks, which were baked at 150 °C for a minimum of 2 h. The flasks were allowed to cool in a desiccator and were purged with nitrogen prior to being sealed with septum caps. Other apparatus such as syringes, needles, cannulas, and magnetic stirrer bars were dried under similar conditions and allowed to cool in a desiccator. Tetrahydrofuran and cyclohexane were freshly distilled under an atmosphere of nitrogen from the sodium benzophenone ketyl radical, and chloroform was distilled from CaH_2 prior to use. Aqueous hydrogen peroxide (30% w/v aqueous solution) and other reagents were used as supplied. Saccharin derivatives, chloro, ethoxy, and *t*-Bu, were synthesized as reported previously.[3]

Flash column chromatography was performed using Merck 9385 Kieselgel 60 silica gel (230−400 mesh); compressed air was used to supply any necessary pressure to the column. Thin-layer chromatography was carried out on aluminum plates coated with a 0.25 mm layer of silica gel containing fluorescence indicator (Merck). UV-inactive compounds were visualized by exposure to iodine mixed with silica gel or by spraying with aqueous potassium permanganate (10 g in 1 L of water containing 5 g of Na_2CO_3) followed by heating.

The chiral shift reagent used to determine enantiomeric excesses from nuclear magnetic resonance (^1H, ^{13}C) spectra was (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[12]

Procedures. (−)-3-[(1′*R*)-1′-Menthyl]-1,2-benzisothiazole 1,1-Dioxide [4a], (+)-3-[(1′*S*)-1′-Menthyl]-1,2-benzisothiazole 1,1-Dioxide [4b], and 3-[(1′*R*)-Menthoxy]-1,2-benzisothiazole 1,1-Dioxide [4c]. In a 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer bar, argon inlet, rubber septum, condenser, and dropping funnel was placed magnesium (340 mg, 13 mmol) and dry tetrahydrofuran (4 mL). The mixture was treated with ethyl bromide (0.4 mL), and after the reaction had progressed for a few minutes, a solution of (−)-menthyl chloride (2.0 mL, 1.87 g, 10 mmol) in tetrahydrofuran (4 mL) was added, portionwise, over a period of 4 h at 50 °C, followed by reflux for 30 min. This solution was added via syringe to a separate 250 mL round-bottom flask equipped with an argon inlet and rubber septum and containing 3-chloro-1,2-benzisothiazole 1,1-dioxide **8** (2.01 g, 10 mmol), in dry tetrahydrofuran (60 mL) cooled to 0 °C. The resulting mixture was stirred overnight and quenched by adding water (50 mL). The solution was diluted with ether (45 mL), and the organic layer was washed with 10% aqueous HCl (35 mL), water (3 × 45 mL), and dried over $MgSO_4$. Removal of the solvent in vacuo gave a mixture of (−)-3-[(1′*R*)-1′-menthyl]-1,2-benzisothiazole 1,1-dioxide **4a** and (+)-3-[(1′*S*)-1′-menthyl]-1,2-benzisothiazole 1,1-dioxide **4b** (3:1) determined by integration from the NMR spectrum, together with a third, unknown compound, **4c**. The crude material was separated by flash column chromatography using *n*-hexane−dichloromethane (1:2) as eluent to give as a colorless solid (−)-3-[(1′*R*)-1′-menthyl]-1,2-benzisothiazole 1,1-dioxide **4a** (1.24 g, 38%): mp 148−149 °C (from EtOH); $[\alpha]_{20}^{D}$ −71.4 (*c* 1.12 in $CHCl_3$) (Found: C, 67.14; H, 7.63; N, 4.56; $C_{17}H_{23}NO_2S$ requires C, 66.85; H, 7.60; N, 4.59%); ν_{max} (Nujol)/cm^{-1} 1606 and 1175; δ_H (300 MHz; $CDCl_3$) 0.75 (3 H, d, J = 7), 0.91 (3 H, d, J = 7), 0.95 (3 H, d, J = 6), 1.1−1.4 (3 H, m), 1.4−1.6 (2 H, s), 1.65−2.1 (5 H, m), 3.1 (1 H, m, J = 5), and 7.6−8.0 (4 H, m); δ_C (75 MHz; $CDCl_3$) 16.3, 21.3, 22.1, 24.3, 28.5, 32.8, 34,4, 40.7, 45.1, 122.8, 123.8, 133.6, 133.8 and 179.8; *m*/*z* (EI) 306 (M^+, 0.78%).

(+)-3-[(1′*S*)-1′-Menthyl]-1,2-benzisothiazole 1,1-dioxide 4b (0.41 g, 13%) was also isolated as a colorless crystalline solid from the product mixture by flash column chromatography using *n*-hexane−dichloromethane (1:2) as eluent: mp 202−204 °C (from EtOH), $[\alpha]_{20}^{D}$ +63.29 (*c* 0.79 in $CHCl_3$) (Found: C, 66.65; H, 7.61; N; 4.55. $C_{17}H_{23}NO_2S$ requires C, 66.85; H, 7.59; N, 4.59%); δ_H (300 MHz; $CDCl_3$) 0.18−0.78 (9 H, m), 1.08−2.04 (9 H, m), 3.70 (1 H, s), and 7.60−8.00 (4 H, m); δ_C (75 MHz; $CDCl_3$) 16.8, 20.6, 21.9, 23.7, 26.7, 31.4, 34.0, 39.9, 47.4, 83.6, 121.9, 123.3, 133.4, 134.0 and 176.8; *m*/*z* (EI) 305 (M^+, 0.2%).

Compound **4c** was isolated from the above reaction mixture by flash column chromatography using *n*-hexane−dichloromethane (1:2) as eluent and shown to be 3-[(1′*R*)-menthoxy]-1,2-benzisothiazole 1,1-dioxide (0.51 g, 15%). Crystallization gave colorless needles: mp 121−122 °C (from EtOH), $[\alpha]_{20}^{D}$ −92.9 (*c* 3.11 in $CHCl_3$) (Found: C, 63.47; H, 7.23; N, 4.34. $C_{17}H_{23}NO_3S$ requires C, 63.52; H, 7.22; N, 4.36%); ν_{max} (Nujol)/cm^{-1} 1614 and 1173; δ_H (300 MHz; $CDCl_3$) 0.8−1.4 (12 H, m), 1.4−2.2 (5 H, m), 2.2−2.6 (1 H, m), 5.0−5.2 (1 H, m) and 7.6−8.0 (4 H, m); δ_C (75 MHz; $CDCl_3$) 16.8, 20.5, 21.8, 23.7, 26.7, 31.4, 34.0, 39.9, 47.4, 83.6, 121.8, 123.3, 133.3, 133.9 and 168.6; *m*/*z* (EI) 321 (M^+, 0.04%).

3-(2-Bornyl)-1,2-benzisothiazole 1,1-Dioxide [5]. 3-(2-Bornyl)-1,2-benzisothiazole 1,1-dioxide **5** was prepared using the same procedure as described for (−)-3-[(1′*R*)-1′-menthyl]-1,2-benzisothiazole 1,1-dioxide **4a** above using (−)-bornyl chloride **9** (2.0 g, 11.5 mmol, 1.0 equiv), magnesium (1.0 g, 41.1 mmol), ethyl bromide (0.05 mL), and 3-chloro-1,2-benzisothiazole 1,1-dioxide **8** (2.3 g, 11.4 mmol). Bornyl chloride was purified before use by sublimation under reduced pressure, followed by recrystallization from methanol and vacuum-drying for several hours. 3-(2-Bornyl)-1,2-benzisothiazole 1,1-dioxide **5** was isolated from the reaction mixture by flash column chromatography using petroleum ether−dichloromethane (1:1) as eluent (0.9 g, 26%). All attempts to prepare diastereoisomerically pure 3-(2-bornyl)-1,2-benzisothiazole 1,1-dioxide by column chromatography or crystallization using different mixtures of solvents proved disappointing. The ^1H NMR spectrum indicated the presence of a 54:46 ratio of 3-[(2′*S*)-2′-bornyl)-1,2-benzisothiazole 1,1-dioxide **5a** and 3-[(2′*R*)-2′-bornyl)]-1,2-benzisothiazole 1,1-dioxide **5b**, determined by integration of the triplets for the methine proton adjacent to the heterocyclic ring and appearing at 3.20 and 3.55 ppm. The isomeric mixture had mp 158−160 °C (from EtOH): $[\alpha]_{20}^{D}$ +49.4 (*c* 0.89 in CH_2Cl_2) (Found: C, 67.05; H, 7.01; N, 4.53. $C_{17}H_{21}NO_2S$ requires C, 67.30; H, 6.98; N, 4.62%); ν_{max} (Nujol)/cm^{-1} 1602 and 1171; δ_H (300 MHz; $CDCl_3$) 0.85−1.17 (6 H, m) 1.20−2.08 (9 H, m), 2.10−2.60 (1 H, m), 3.20 (1 H, t, J = 9), 3.55 (1 H, m, J = 5) and 7.45−8.60 (4 H, m); δ_C (75 MHz; $CDCl_3$) 14.4, 18.8, 20.1, 27.5, 29.2, 34.0, 40.3, 45.3, 48.5, 51.6, 122.4, 124.7, 133.3 and 133.6; *m*/*z* (EI) 305 (M^+, 0.45%).

(1*R*,4*R*)-1-Chloro-3,3-dimethyl-2-methylenebicyclo[2.2.1]-heptane [10]. (1*R*,4*R*)-1-Chloro-3,3-dimethyl-2-methylenebicyclo-[2.2.1]heptane, **10**, was prepared as previously described.[7] In a dry 250 mL round-bottomed flask equipped with a magnetic stirrer was placed D-camphor (15.2 g, 0.10 mol) in dichlomethane (25 mL). The flask was chilled in an ice bath, and phosphorus trichloride (12.8 g) and phosphorus pentachloride (22.2 g) were added in small portions. After 2 h the reaction mixture was allowed to reach room temperature for 10 h. The reaction mixture was poured onto ice and extracted with petroleum ether (2 × 40 mL). The extract was washed with water (2 × 30 mL) and evaporated to leave a clear, colorless liquid (15 g) which was refluxed for 12 h with potassium acetate (20 g) in ethanol−water (100 mL, 75:25). The solution was then poured into water (100 mL) and extracted with petroleum ether (2 × 40 mL). The combined organic extracts were washed with water (2 × 40 mL), dried over $MgSO_4$, and evaporated *in vacuo*. Distillation of the residue under reduced pressure (72−78 °C, 1 mmHg) gave a

colorless oil which partially solidified on standing. This product was further purified by flash column chromatography using petroleum ether as eluent to give a colorless oil (14 g, 82%). ^{1}H NMR spectroscopy indicated the presence of a 96:4 ratio of (1*R*,4*R*)-1-chloro-3,3-dimethyl-2-methylenebicyclo[2.2.1]-heptane **10a** and (1*R*,4*R*)-1-chloro-2,2-dimethyl-3-methylenebicyclo[2.2.1]heptane **10b** as determined by integration of the olefinic protons, $[\alpha]_{20}^{D}$ −9.4 (*c* 2.1 in CH_2Cl_2): ν_{max} (neat)/cm^{-1} 1664; δ_H (300 MHz; $CDCl_3$) 1.07−1.14 (6 H, s), 1.64−2.18 (7 H, m), and 4.95 (2 H, s); *m*/*z* (EI) 171.09378 (M^+, $C_{10}H_{16}Cl$ requires 171.09405).

(+)-3-[(1′*R*,4′*R*)-1′-(3′,3′-Dimethyl-2′-methylenebicyclo-[2.2.1]heptane)]-1,2-benzisothiazole 1,1-Dioxide [6]. In a 100 mL, oven-dried, three-necked, round-bottomed flask equipped with a magnetic stirrer, dropping funnel, reflux condenser, and rubber septum, under argon, was placed lithium powder (0.6 g, 86 mmol), the equipment was purged with dry argon for 2 min, and the atmosphere maintained using an argon-filled balloon. Cyclohexane (12 mL), freshly distilled from sodium and benzophenone, was added to the flask via a cannula, followed dropwise by (1*R*,4*R*)-1-chloro-3,3-dimethyl-2-methylenebicyclo-[2.2.1] heptane **10a** (4.0 g, 23 mmol) in dry cyclohexane (6 mL). The reaction mixture was stirred for 30 min and then held at reflux for 2 h. As the reaction progressed, the initially clear mixture acquired a brown coloration and the lithium took on a black coating and sank to the bottom of the flask. At this point the stirring was stopped and the solids were allowed to settle to the bottom of the flask.

In a separate 250 mL reaction flask was placed pseudosaccharin ethyl ether (3-ethoxy-1,2-benzisothiazole 1,1-dioxide) **7** (1.8 g, 8.52 mmol) in tetrahydrofuran (50 mL), cooled to −78 °C. The 1-lithio-3,3-dimethyl-2-methylenebicyclo[2.2.1]heptane solution, prepared above, was added to the cooled reaction flask containing pseudosaccharin ethyl ether, via a cannula, at −78 °C. The flask containing organolithium compound was washed with cyclohexane (3 × 6 mL), and the contents were transferred to the reaction mixture. The reaction mixture was stirred overnight and was quenched by slow addition of water (40 mL) and diluted with ether (2 × 30 mL). The combined organic phase was washed with water (2 × 40 mL) and dried over $MgSO_4$. The solvent was removed in vacuo and the residue purified by flash column chromatography using dichloromethane−petroleum ether (1:1) as eluent to give (+)-3-[(1′*R*,4′*R*)-1′-(3′,3′-dimethyl-2′-methylenebicyclo[2.2.1]heptane)]-1,2-benzisothiazole 1,1-dioxide **6** (3.25 g, 46%): mp 162−164 °C (from EtOH); $[\alpha]_{20}^{D}$ +61 (*c* 1.0 in $CHCl_3$) (Found: C, 67.61; H, 6.37; N, 4.66. $C_{17}H_{19}NO_2S$ requires C, 67.75; H, 6.35; N, 4.65%); ν_{max} (Nujol)/cm^{-1} 1602, 1175, and 1647; δ_H (300 MHz; $CDCl_3$) 1.23 (3 H, s), 1.33 (3 H, s), 1.50−1.84 (5 H, m), 1.85−1.98 (1 H, m), 2.22 (1 H, s), 2.32−2.56 (2 H, m), 4.50 (1 H, s), 4.80 (1 H, s), and 7.50−8.10 (4 H, m; δ_C (75 MHz; $CDCl_3$) 23.8, 25.9, 29.7, 32.7, 43.1, 44.1, 48.8, 59.2, 104.1, 122.4, 127.1, 130.7, 133.0, 133.3, 140.6, 164.2 and 177.4; *m*/*z* (EI) 301 (M^+, 35%).

General Procedure for Asymmetric Oxidation Mediated by Imines [4−6]. Aqueous hydrogen peroxide (0.15 mL, 4.0 equiv., 30% w/v) was added to a stirred dichloromethane (7 mL) solution of DBU (202 mg, 4.0 equiv), and this was followed by imines **4**−**6** (1.0 equiv). The sulfide substrate (1.0 equiv) was then added and the mixture stirred at the appropriate temperature. The reaction progress was monitored by TLC. Dichloromethane (15 mL) was then added and the mixture transferred to a separating funnel and washed with saturated aqueous sodium sulfite (15 mL) to quench any hydrogen peroxide remaining. The organic layer was washed with brine (2 × 15 mL), dried over $MgSO_4$, and evaporated in vacuo. Separation of the imine and sulfoxide was achieved by column chromatography on silica gel using successively dichloromethane and ethyl acetate as eluents.

(+)-(2*R*,3*S*)-3-[(1′*R*)-1′-Menthyl]-1,2-benzisothiazole 1,1-Dioxide Oxide [11] and (+)-(2*S*,3*R*)-3-[(1′*R*,4′*R*)-1′-(3′,-3′-Dimethyl-2′-methylenebicyclo[2.2.1]heptane)]-1,2-benzisothiazole 1,1-Dioxide Oxide [12]. In a 250 mL, two-necked round-bottomed flask equipped with a magnetic stirrer were placed imines **4** or **6** (3.32 mmol) in dichloromethane (50 mL) and saturated aqueous potassium carbonate (54 mL). The reaction mixture was vigorously stirred while a solution of 85% *m*CPBA (11.4 mmol) in dichloromethane (33 mL) was added dropwise over 30 min. The reaction mixture was stirred overnight. Saturated aqueous sodium sulfite (20 mL) was added, and the reaction mixture was diluted with dichloromethane (25 mL) and water (25 mL). The aqueous layer was extracted with dichloromethane (2 × 20 mL), and the combined organic phases were washed with a saturated sodium hydrogen carbonate solution (20 mL) and brine (2 × 30 mL), and dried over $MgSO_4$. Removal of the solvent in vacuo gave the crude oxaziridines. Recrystallization from absolute ethanol afforded the pure oxaziridines.

(+)-(2*R*,3*S*)-3-[(1′*R*)-1′-Menthyl]-1,2-benzisothiazole 1,1-dioxide oxide, **11**, colorless solid (0.601 g, 95%): mp 133−135 °C (from EtOH); $[\alpha]_{20}^{D}$ +75 (*c* 2.14 in $CHCl_3$) (Found: C, 63.57; H, 7.19; N, 4.34. $C_{17}H_{23}NO_3S$ requires C, 63.52; H, 7.19; N, 4.35%); ν_{max}($CHCl_3$)/cm^{-1} 1184; δ_H (300 MHz; $CDCl_3$) 0.73 (3 H, d, J = 7), 0.82−0.94 (3 H, m), 1.17 (3 H, d, J = 7), 1.45−1.22 (1 H, m), 1.22−1.70 (5 H, m), 1.70−1.94 (3 H, m), 1.94−2.30 (1 H, m) and 7.60−8.00 (4 H, m); δ_C (75 MHz; $CDCl_3$) 15.4, 21.3, 22.1, 24.5, 28.4, 32.3, 34.5, 37.4, 45.4, 88.0, 124.4, 126.6, 132.4 and 133.9; *m*/*z* (EI) 321 (M^+, 0.36%).

(+)-(2*S*,3*R*)-3-[(1′*R*,4′*R*)-1′-(3′,3′-Dimethyl-2′-methylenebicyclo-[2.2.1] heptane)]-1,2-benzisothiazole 1,1-dioxide oxide, **12**, colorless crystals (0.92 g, 87%): mp 152−153 °C (from EtOH); $[\alpha]_{20}^{D}$ +67 (*c* 0.1 in $CHCl_3$) (Found: C, 64.15; H, 6.7; N, 4.34. $C_{17}H_{19}NSO_3$ requires C, 64.33; H, 6.03; N, 4.41%); ν_{max} ($CHCl_3$)/cm^{-1} 1186; δ_H (300 MHz; $CDCl_3$) 1.56 (6 H, s), 1.44−1.74 (3 H, m), 1.76−1.88 (2 H, m), 2.28 (1 H, s), 2.20−2.34 (1 H, m), 4.70 (2 H, d, J = 5) and 7.50−8.00 (4 H, m); δ_C (75 MHz; $CDCl_3$) 23.4, 25.7, 29.4, 30.7, 40.2, 43.6, 47.7, 55.0, 86.6, 103.9, 124.0, 128.3, 132.2, 133.4, 135.1 and 162.1; *m*/*z* (EI) 317 (M^+, 0.76%).

General Procedure for Oxidation of Sulfides to Sulfoxides Using Oxaziridines 11 and 12. Typically, oxaziridine **11** or **12** (0.311 mmol) was added to a precooled solution of sulfide (1.0 equiv) in dichloromethane or carbon tetrachloride (5 mL). The progress of the reaction was monitored by TLC (using ethyl acetate as eluent) until complete sulfoxidation had occurred. Sulfoxide was isolated by column chromatography using ethyl acetate as eluent.

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