Asymmetric Synthesis and Properties of Sulfinimines (Thiooxime *S*-Oxides)

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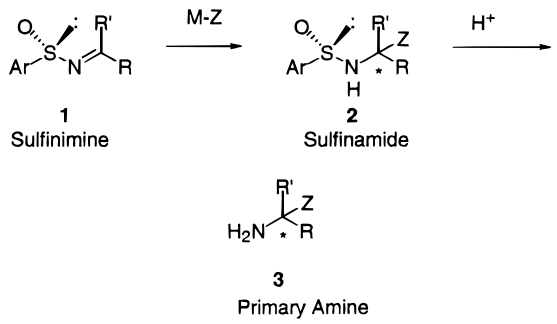
Enantiomerically pure sulfinimines (thiooxime *S*-oxides **10**), important building blocks in the asymmetric synthesis of amine derivatives, are prepared in good to excellent yields in one step from aromatic, heteroaromatic, and aliphatic aldehydes. This protocol involves treating commercially available (*R*)- or (*S*)-menthyl *p*-toluenesufinate (Andersen reagent **4**) with LiHMDS, followed by the aldehyde, affording (*E*)-**10** exclusively. The sulfinimines **10** are formed via a Peterson-type olefination reaction of silylsulfinamide anion **13** with the aldehyde. Anion **13** is generated by reaction of lithium menthoxide (**12a**) with bis(trimethylsilyl)sulfinamide **11**, which is formed in the reaction of **4** with LiHMDS. The other product formed is *O*-(trimethylsilyl)menthol (**12c**), which is isolated in >80% yield for recycling. Two other less efficient methods for the asymmetric synthesis of **10** are discussed: (i) the asymmetric oxidation of sulfenimines **6** with chiral nonracemic oxaziridines and (ii) the reaction of metal aldimines, prepared from nitriles, with **4**. All of these protocols fail with ketones.

The significance of enantiopure primary amine derivatives in nature and in pharmacologically active compounds and their utility as chiral building blocks underlies the importance of developing new and efficient methods for their synthesis as single enantiomers. An attractive route to chiral amine derivatives is the diastereoselective addition of organometallic regents to the C−N double bond of imines.[1] With most chiral nonracemic imines, however, this approach is limited because of their low reactivity (electrophilicity). This results in either no reaction and/or competitive reduction and coupling reactions with organometallic reagents. Other problems include enolization of aliphatic imines, poor diastereoselectivities because imines can exist as syn/anti mixtures, and moisture sensitivity, which results in moderate or low yields. When primary amines are the objective, removing the N-auxiliary is often difficult without epimerizing or destroying the product.

Recent studies in our laboratory have demonstrated that these limitations are avoided using enantiopure sulfinimines (thiooxime *S*-oxides) **1**. Sulfinimines **1** are chiral ammonia imine building blocks because addition of organometallic reagents (M−Z) across the C−N bond affords a sulfinamide **2**, which upon hydrolytic cleavage furnishes primary amine **3** containing a new stereogenic center (Scheme 1). The application of **1**, derived from aliphatic and aromatic aldehydes and ketones, in highly diastereoselective asymmetric syntheses of amines[2−4]

Scheme 1



α-amino acids,[5a] *β*-amino acids,[3,6,7] *β*-aminophosphonic acids,[7e] the taxol C-13 side chain[6] and its fluorinated analog,[7f] 2-arylpyrrolines,[8] *N*-sulfinyl-*cis*-aziridine-2-carboxylic acids,[9] and *β*-hydroxy α-amino acids,[9e] has re-

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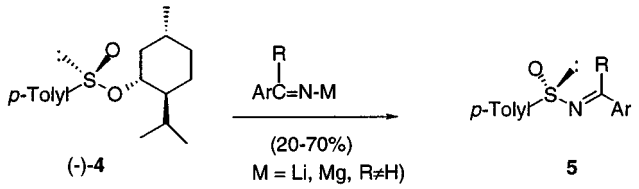
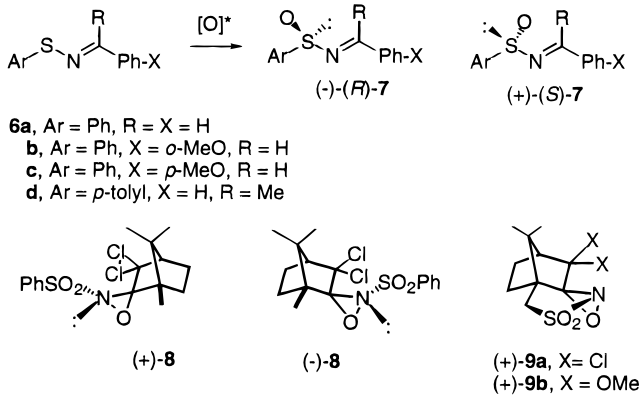
Scheme 2



(-)-**4** **5**

Scheme 3



cently been reported by us and others. In these transformations our work has shown that the *N*-sulfinyl auxiliary in **1** not only activates the C−N bond to such an extent that most nucleophiles are readily added but also avoids competitive enolization with aliphatic examples. Since the *N*-sulfinyl group is a powerful stereodirecting group, high de's result. Because easily separable diastereoisomers are produced in these "chiral auxiliary"-based asymmetric syntheses, mild acid- or base-catalyzed hydrolysis affords the enantiomerically pure product. Importantly, epimerization of the product is not detected in the hydrolysis processes.

The utility of sulfinimines **1** as chiral imine building blocks for the asymmetric synthesis of amine derivatives (Scheme 1) is dependent upon concise methods of preparation. These methods need to be highly efficient and of wide generality. In this paper, we report new information on mechanism, general scope, and efficiency of the asymmetric synthesis of sulfinimines **1** (R′ = H) from aliphatic and aromatic aldehydes in addition to full experimental details.[10]

Introduction. The first examples of sulfinimines **1** were prepared in racemic form by oxidation of sulfenimines ($ArSN{=}CR_2$) with *m*-CPBA.[11,12] Enantiomerically pure sulfinimines **5** were originally obtained by Cinquini et al., in modest yield, by reaction of metal ketimines with the Andersen reagent, (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (**4**) (Scheme 2).[2] The Andersen reagent is the most widely used building block for the asymmetric introduction of the *p*-toluenesulfinyl group, a key auxiliary and stereodirecting group in asymmetric synthesis.[13] It is commercially available in both enantiomeric forms and can be prepared on multigram and kilogram scales from (+)- and (−)-menthol.[14] In a related procedure, Wills et al. prepared a derivative of **5** from an enantiopure sulfinamide, a recoverable precursor.[4a] These Andersen-type syntheses are, however, limited in scope because the metal ketimines (ArC(R)═NM) are generated by reaction of organolithium or Grignard reagents with an aromatic nitrile; e.g., R ≠ H and Ar ≠ alkyl.[2−4] This means that the more versatile aliphatic and aromatic aldehyde-derived sulfinimines **5** (R = H, Ar = alkyl) cannot be prepared by these procedures.

Asymmetric Oxidation of Sulfenimines. A more general route to sulfinimines, in both enantiomeric forms, is the asymmetric oxidation of sulfenimines (Scheme 3).[6] Oxidations were carried out by addition of 1.0 equiv of the chiral oxidant to the sulfinimine at rt in CCl_4. After the reaction was complete, the sulfinimines **7** were isolated by preparative TLC in excellent yield. The ee's were determined using the chiral shift reagent $Eu(hfc)_3$, and the absolute configurations were assigned by comparison with literature values. For **6d** the enantiomeric purity and absolute configuration were determined by conversion into the known β-amino acids.[6] As can be seen from the results summarized in Table 1, only the (+)- and (−)-*N*-(phenylsulfonyl)-1-(3,3-dichlorocamphoryl)oxaziridine (**8**) gives synthetically useful ee's of **7**. Crystallization of these sulfinimines upgrades their enantiomeric purity to >97% ee (Table 1, entries 1−3, 6, 8, and 9). Note that (+)-**8** affords (*S*)-**7** while (−)-**8** gives (*R*)-**7** (Table 1, compare entries 2 and 3). This oxaziridine has previously been shown to give the highest asymmetric induction for the oxidation of sulfides to sulfoxides[15] and selenides to selenoxides.[16] The absolute configuration of **7** is predictable using the sulfide active site model where nonbonded interactions in the transition state are minimized.[15] The (camphorylsulfonyl)imine byproduct can be isolated in high yield (>90%) for recycling.

Table 1. Asymmetric Oxidation of Sulfenimines 6 to Sulfinimines 7 at 20 °C in CCl_4

entry	sulfenimine	oxidant (h)	% yield[a] **7**	% ee [*c*] (confign)
1	**6a**	(−)-**8** (5)	95	88 [>97][c] (*R*)
2		(−)-**8** (10)[b]	82	90 [>97][c] (*R*)
3		(+)-**8** (10)[b]	72	88 [>97][c] (*S*)
4		(+)-**9a** (10)	80	13 (*S*)
5		(+)-**9b** (72)	59	13 (S)
6	**6b**	(−)-**8** (4)	89	85 [>97][c] (*R*)
7		Ti(O-*i*-Pr)$_4$, (+)-DET[d] TBHP, CH_2Cl_2, H_2O	80	13 (*S*)
8	**6c**	(−)-**8** (12)	95	89 [>97][c] (*R*)
9	**6d**	(−)-**8** (48)	90	87 [>97][c] (*R*)
10		(+)-**9a** (40)	65	14 (*S*)
11		(+)-**9b** (19)	65	14 (*S*)

[a] Isolated yields. [b] At −20 °C to rt. [c] Enantiomeric purity after crystallization. [d] Modified Sharpless reagent. See ref 17.

As a general route to aromatic and aliphatic aldehyde- and ketone-derived sulfinimines the asymmetric oxidation of sulfenimines by oxaziridine **8** is limited because the asymmetric induction reaches a maximum of 90%

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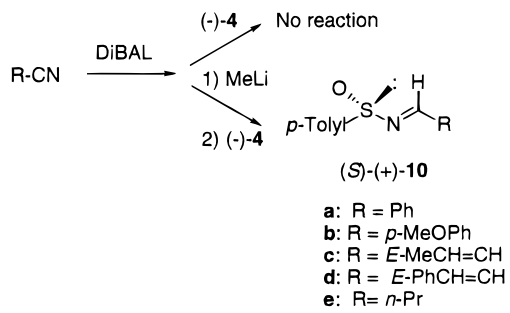
Scheme 4



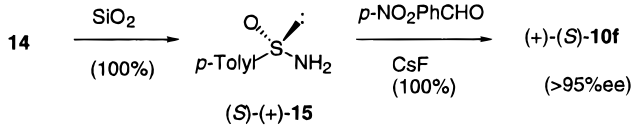
(Table 1). Furthermore, sulfinimines **7** that are noncrystalline, as are many aliphatic examples, cannot be upgraded to enantiomeric purity by crystallization.

Synthesis of Sulfinimines from Nitriles. A potentially attractive route to aldehyde derived sulfinimines **1** (R′ = H) is by the reaction of a metal aldimine (RCH=NM) with **4** (Scheme 4). The reduction of aliphatic and aromatic nitriles by diisobutylaluminum hydride DIBAL-H to aldiminoaluminum compounds (RCH=NAlBu$^i_2$) followed by hydrolysis constitutes an important synthesis of aldehydes.[18] However, treatment of benzonitrile at 0 °C with DIBAL-H followed by addition of (−)-**4** at −78 °C gave none of the desired sulfinimine **10a** under a variety of conditions (Table 2). The fact that hydrolysis gives benzaldehyde in 79% yield means that the aldiminoaluminum species was formed but is apparently not nucleophilic enough to displace the menthyl alkoxide from (−)-**4** (Scheme 4). To circumvent this problem 1 equiv of methyllithium was added to form the *ate* complex [(PhCH=NAl(Me)Bu$^i_2$)$^-$Li$^+$],[19] followed after 2 h by (−)-**4** at −40 °C. (*S*)-(+)-*N*-(Benzylidene)-*p*-toluenesulfinamide (**10a**) was isolated in 36% yield by flash chromatography (Table 2, entry 6). Inversion of configuration occurs on reaction of (−)-**4** with the *ate* complex so that the product has the opposite (*S*)-stereochemistry to that of the starting material. Further optimization of the reaction conditions altering the solvent (Et_2O, THF, hexane, benzene) or temperature did not improve the yields (Table 2, entries 1−6). Using this optimized procedure moderate yields, 33−56%, of the sulfinimines **10a**−**d** were obtained from benzonitrile, 4-methoxybenzonitrile, crotononitrile, and cinnamonitrile, respectively (Table 2, entries 7−9). All attempts to prepare aliphatic sulfinimines using this protocol failed. With butyronitrile none of the desired sulfinimine could be detected by NMR, and with undecanenitrile less than 3% of the sulfinimine was detected. The known ability of MeLi to deprotonate the α-protons of aliphatic aldiminoaluminum species is undoubtedly responsible for the failure to produce aliphatic sulfinimines by this route.[20]

Synthesis of Sulfinimines from Aldehydes. The most efficient method for the asymmetric synthesis of aliphatic and aromatic aldehyde-derived sulfinimines **10** is the "one-pot" protocol outlined in Scheme 5. This procedure builds on the methods developed for the synthesis of *N*-silylimines from aldehydes[22] and the preparation of sulfenimines from *N*,*N*-bis(trimethylsilyl)-sulfenamies.[23] In our procedure, (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (**4**) or (1*S*,2*R*,5*S*)-(+)-menthyl (*R*)-*p*-toluenesulfinate (**4**) in THF is treated at −78 °C with lithium bis(trimethylsilyl)amide (LiHMDS) followed by addition of the aldehyde (Scheme 5).

Addition of LiHMDS to **4** presumably generates *N*,*N*-bis(trimethylsilyl)-*p*-toluenesulfinamide (**11**) and lithium menthoxide **12a**. Sulfinimine **10** is then formed via a Peterson olefination-type reaction involving reaction of silyl sulfinamide anion **13** with the aldehyde (Scheme 5).[24] In our original paper, we thought that it was necessary to generate **13** from **11** using a fluoride ion source.[10] Attempts to isolate **11** were unsuccessful, giving instead (+)-(*S*)-*p*-toluenesulfinamide (**15**). However, quenching the reaction mixture prior to addition of the aldehyde with aqueous NH_4Cl solution, evaporating the solvent, and removing the menthol (**12c**) under high vacuum gave *N*-(trimethylsilyl)-*p*-toluenesulfinamide (**14**) contaminated with **15** (ca. 30%). Attempts to isolate **14** in pure form were unsuccessful because it was quantitatively hydrolyzed on the silica gel column to (*S*)-(+)-**15**. Characteristic absorptions for the trimethylsilyl groups in **14** were observed at δ 0.3 (9 H) in addition to a broad singlet (NH) at δ 3.9 in the ^{1}H NMR.

The enantiomeric purity of **14** was estimated to be >95% by hydrolysis to (+)-**15**, which on treatment with *p*-nitrobenzaldehyde/CsF gave a quantitative yield of (+)-**10f**. Neither **14** nor **15** reacts with *p*-nitrobenzaldehyde in the absence of CsF. All attempts to condense (+)-**15** with other aldehydes such as benzaldehyde failed. (+)-(*S*)-*p*-Toluenesulfinamide (**15**) is the first example of an enantiomerically pure primary sufinamide.[25,26]



The other product of the reaction of LiHMDS and **4** is *O*-(trimethylsilyl)menthol (**12c**), which was isolated along with menthol (**12b**). In a multigram synthesis of (*S*)-(+)-*N*-benzylidene-*p*-toluenesulfinamide (**10a**), where this sulfinimine can be isolated by crystallization, distillation of the mother liquor gave an 80% yield of an 80:20 mixture of **12c**:**12b**. *O*-(Trimethylsilyl)menthol (**12c**) was isolated in 70% yield along with a 25% yield of menthol (**12b**) by flash chromatography on silica gel treated with ammonia. Although a satisfactory elemental analysis for (−)-**12c** could not be obtained, it had spectral properties consistent with its structure. Interestingly, **12c** does not react with CsF in THF but is quantitatively deprotected

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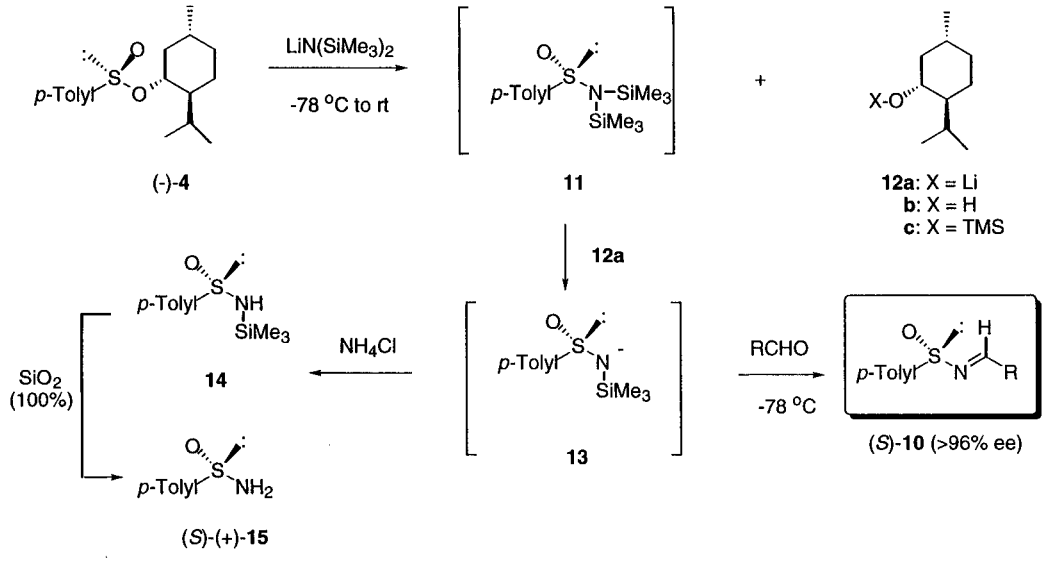
Table 2. Asymmetric Synthesis of Sulfinimines 12 from Nitriles and 4

entry	nitrile	conditions hydride/solvent/RLi	sulfinimine **10** (% yield)[a]
1	PhCN	DIBAH/THF	**10a** (0), PhCHO (79)
2		DIBAH/THF/MeLi	**10a** (11)
3		DIBAH/benzene/MeLi	**10a** (12)
4		DIBAH/ether/MeLi	**10a** (3)[b]
5		DIBAH/*n*-hexane/MeLi	**10a** (6)[b]
6		DIBAH/*n*-pentane/MeLi	**10a** (36)
7	*p*-MeOPhCN	DIBAH/*n*-pentane/MeLi	**10b** (44−56)
8	*E*-MeCH=CHCN	DIBAH/*n*-pentane/MeLi	**10c** (33)
9	*E*-PhCH=CHCN	DIBAH/*n*-pentane/MeLi	**10d** (42−55)
10	*n*-Pr-CN	DIBAH/*n*-pentane/MeLi	**10e** (0)

[a] Isolated yields unless otherwise noted. [b] Estimated by NMR.

Scheme 5



a: R = Ph
b: R = *p*-MeOPh
c: R = E-MeCH=CH-
d: R = E-PhCH=CH-
e: R = *n*-Pr
f: R = *p*-NO_2-Ph
g: R = *o*-MeOPh
h: R = *p*-MeSPh
i: R = *p*-F-Ph
j: R = 3-pyridyl
k: R = 2-furyl
l: R = 2-thienyl
m: R = CH_2=CH-
n: R = *i*-PrCH_2-
o: R = *i*-Pr
p: R = *t*-Bu
q: R = PhCH_2-
r: R = Ph_3C-

on treatment with tetrabutylammonium fluoride (TBAF) for 3 h or with aqueous HCl.

Since less than a 10% yield of **12c** is formed on refluxing **12b** with hexamethyldisilazane the most likely source of menthol *O*-(trimethylsilyl) ether (**12c**) is the reaction of lithium menthoxide (**12a**) with **11** (Scheme 5). This also results in the generation of silylsulfinamide anion **13** and means that a fluoride ion source is not necessary for formation of the sulfinimine **10**. Indeed, the presence or absence of a fluoride ion source had no effect on the enantiomeric purity of sulfinimine **10** and little influence on the yield (vide infra). Consistent with this proposition is the fact that treatment of **14** with benzaldehyde gave none of the sulfinimine **10a**, but better than 82% was obtained on addition of CsF.

In the many reactions where menthol (**12b**) has been used as a chiral auxiliary it is generally not recycled because its high volatility makes it very difficult to isolate.[13] The fact that *O*-(trimethylsilyl)menthol (**14c**) is generated in the synthesis of sulfinimines (Scheme 5) and is readily isolated in good yield means that it can be easily recycled. This is particularly important for the more expensive (1*S*,2*R*,5*S*)-(+)-**12a** isomer.

Optimization studies for the synthesis of (*S*)-(+)-*N*-benzylidene-*p*-toluenesulfinamide (**10a**) are summarized in Table 2. These results reveal that treatment of (−)-**4** at −78 °C with 1.4 equiv of LiHMDS gives the best yields of **10a** (Table 3, entry 7). Racemization occurs on use of sodium bis(trimethylsilyl)amide (NaHMDS) (Table 3, entry 1). Addition of cesium fluoride (CsF) and potassium fluoride (KF) had little, if any, effect on the yields of (+)-**10a** (Table 3, compare entries 1 and 7 with 3 and 8). However, tetrabutylammonium fluoride results in lower yields, presumably because water present in this reagent quenches **13** or hydrolyzes **14** (Table 3, entry 2). Lower yields are also noted on addition of KCl and LiCl (Table 3, entries 10 and 11). Initially, a two-step procedure was used to prepare **10a** because it was thought that better yields might result if the lithium menthoxide (**12a**) and excess LiHMDS were removed. This involved isolation of crude **14** by quickly extracting it into EtOAc and drying prior to treating it with CsF and benzaldehyde. However, as can be seen from Table 3, the yields for the two-step and one-step ("one-pot") processes were similar, e.g., 76−82% (Table 3, compare entry 5 with 7 and 8). Whether the temperature was kept at rt or cooled to −78 °C prior to addition of benzaldehyde also had no effect on the yields. The

Table 3. Asymmetric Synthesis of (*S*)-(+)-*N*-Benzylidene-*p*-toluenesulfinamide (10a) from Benzaldehyde and (−)-4

entry	solvent	base (equiv)[a]	additive	T[c] (°C)[c]	method	% yield[d] (% ee)[e]
1	THF	NaHMDS (1.4)	none	−78 to rt	"one pot"	75 (66)
2		NaHMDS (1.5)	*n*-Bu_4NF (0.5 h)	0 to rt		13
3	Et_2O	NaHMDS (1.5)	CsF			55 (30)
4	THF	LiHMDS (1.2)	$BF_3{\cdot}OEt_2$			13
5		LiHMDS (1.4)	CsF	−78 to rt	"two step"[f]	80 (>95)
6		LiHMDS (1.4)		−78 to rt		0
7		LiHMDS (1.4)	none	−78 to rt, −78	"one pot"	76 (>95)
8		LiHMDS (1.4)	CsF			76−82 (>95)
9		LiHMDS (1.4)	KF			71 (>95)
10		LiHMDS (1.4)	KCl			54 (>95)
11		LiHMDS (1.4)	LiCl			41

[a] NaHMDS or LiHMDS was added to **4** at −78 °C and the reaction mixture warmed to rt for 5 h. [b] Two equiv of the fluoride ion source was added with the aldehyde. [c] Temperature at which the aldehyde and fluoride ion source added. [d] Isolated yields. [e] Determined using the $Eu(hfc)_3$. [f] Two-step procedure involves isolation of crude **14** and then treatment with F^- and the aldehyde.

Table 4. Asymmetric Synthesis of Sulfinimines 10 from Aldehydes and (−)-4 at −78 °C in THF

entry	aldehyde (R =)	fluoride ion source[a]	sulfinimine **10**	% yield[b] (confign)
1	Ph	none	(+)-**10a**	76 (*S*)
2		CsF		76−82 (*S*)
3		none	(−)-**10a**[c]	74 (*R*)
4	*p*-MeOPh	none	(+)-**10b**	89 (*S*)
5		CsF		90 (*S*)
6	*p*-NO_2Ph	none	(+)-**10f**	74 (*S*)
7		CsF		93 (*S*)
8	*o*-MeOPh	KF	(+)-**10g**	91 (*S*)
9	*p*-MeSPh	CsF	(−)-**10h**	80 (*S*)
10	*p*-F-Ph	none	(+)-**10i**	90 (*S*)
11		CsF		84 (*S*)
12	3-pyridyl	none	(+)-**10j**	64 (*S*)
13		CsF[d]	(−)-**10j**[c,d]	70 (*R*)
14	2-furyl	none	(+)-**10k**	68 (*S*)
15	2-thienyl	none	(−)-**10l**	69 (*S*)
16	(*E*)-MeCH=CH	none	(+)-**10c**	60 (*S*)
17		KF		65−77 (*S*)
18	(*E*)-PhCH=CH	CsF	(+)-**10d**	80 (*S*)
19	CH_2=CH	none	(+)-**10m**	64 (*S*)
20		KF		69 (*S*)
21	*n*-Pr	none	(+)-**10e**	65 (*S*)
22		CsF		64 (*S*)
23	*i*-$PrCH_2$−	none	(+)-**10n**	
24		KF		68 (*S*)
25	*i*-Pr−	KF	(+)-**10o**	60 (*S*)
26	*t*-Bu−	none[e]	(+)-**10p**	61 (*S*)
27		KF[e]		68 (*S*)
28	$PhCH_2$−	KF	(+)-**10q**	ca 40
29	Ph_3C−	none[e]	(+) **10r**	40 (*S*)
30		CsF[e]		50 (*S*)
31	acetophenone	none	no reaction	
32		CsF	no reaction	

[a] Two equiv added. [b] Isolated yields unless otherwise noted. [c] (+)-**4** used. [d] Run at 0 °C to rt, ref 7c. [e] Warmed to rt and allowed to react for 14−20 h. [f] Estimated from the NMR.

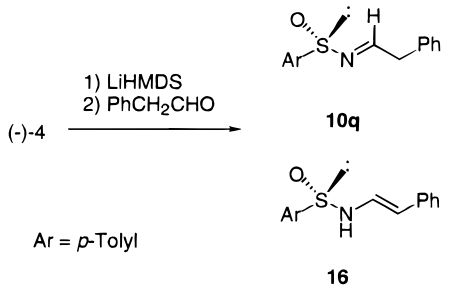
reaction is monitored by TLC (ca. 2 h) and quenched with water, and (+)-**10a** was isolated by flash chromatography in 76−82% yield, along with 20−40% of menthol (**12b**) and 60% of **12c**. On a 10 g scale, (+)-**10a** was isolated by crystallization from *n*-pentane in better than 75% yield.

Many of the conditions that gave good yields of **10a** (Table 3) failed when they were applied to aliphatic aldehydes. For example, in the one-pot procedure when *n*-butyraldehyde was treated according to the protocol in the presence or absence of CsF, less than 10% of (*S*)-(+)-*N*-butylidene-*p*-toluenesulfinamide (**12e**) was detected. Undoubtedly, the poor yields result from aldol reactions of the aldehyde caused by excess LiHMDS or the generated lithium menthoxide (**12a**). This hypothesis is supported by the fact that in the one-pot procedure quenching with TFA to neutralize excess base prior to addition of the aldehyde improved the yield of (+)-**10e** to ca. 30%. The two-step method gave (+)-**10e** in 58% yield. Significantly, it was found that for the one-pot procedure, if the reaction mixture is cooled to −78 °C prior to addition of *n*-butyraldehyde and quenched at this temperature, the isolated yield of **10e** is 64−68%. On the basis of these results the optimized "one-pot" protocol for the enantioselective synthesis of aliphatic and aromatic aldehyde derived sulfinimines **10** is summarized in Table 4.

As can be observed from the results summarized in Table 4, the "one-pot" procedure for the asymmetric synthesis of sulfinimines **10** works well for a diverse group of aromatic, heteroaromatic, and aliphatic aldehydes. Aromatic aldehydes generally gave the best yields, and the presence of electron-attracting and -donating groups had little effect on the yields. Likewise, sterically hindered aldehydes worked nearly as well as those that were unhindered, although a longer reaction time of 14−20 h was necessary for 2,2,2-trimethylacetaldehyde and 2,2,2-triphenylacetaldehyde (Table 4, see entries 26 and 29). Both (*R*)- and (*S*)-sulfinimine enantiomers are readily available, starting with (1*S*,2*R*,5*S*)-

(+)-menthyl (*R*)-*p*-toluenesulfinate (**4**) or (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (**4**) (Table 4, entries 3 and 13).

To date, the only aldehyde that has failed to give satisfactory yields is phenylacetaldehyde. Attempted isolation of **10q**, in the usual manner, by silica gel chromatography failed due to its facile isomerization to the tautomeric enamine **16**, which was obtained in ca. 38% yield. The structure of **16**, which could not be isolated in pure form, is supported by ^{1}H NMR absorptions at δ 6.14 (D_2O exchangeable) for the NH proton and doublets at δ 6.02 and 6.75 (J = 14 Hz) for the vinyl protons. By preconditioning the silica gel column with *n*-pentane washed with concd NH_4OH, and using solvents pretreated in a similar way it was possible to isolate crude **10q** (characteristic imino proton absorption at δ 8.3 ppm) in ca. 40% yield (Table 4, entry 28).



While the presence or absence of fluoride ion generally had little effect on the yields of most sulfinimines, somewhat higher yields were noted for *p*-nitrobenzaldehyde (74 vs 93%), 3-pyridinecarboxaldehyde (64 vs 70%), crotonaldehyde (60 vs 65−77%), and triphenylacetaldehyde (40 vs 50%) on addition of CsF. In these cases generation of silyl amide anion **13** from **11** may, for some reason, not be as efficient in the absence of the fluoride ion.

All attempts to use this protocol to prepare sulfinimines from ketones failed (Table 4, entries 31 and 32). The lower reactivity of ketones vs aldehyde may be responsible for this failure.

Properties of Sulfinimines. Aromatic aldehyde-derived sulfinimines are solids, while the aliphatic derivatives tend to be oils. Generally, sulfinimines prepared from aromatic aldehydes can be stored in the refrigerator indefinitely, whereas noticeable decomposition occurs after ca. 3 months for those prepared from aliphatic aldehydes. Aromatic (including heteroaromatic) sulfinimines exhibit a characteristic singlet absorption at δ 8.7−9.0 for the imino proton. For aliphatic sulfinimines this proton is observed somewhat further upfield at δ 8.1−8.2. The imino carbon atoms in the ^{13}C NMR of **10** appear at δ 158−160 ppm for aromatic and heteroaromatic sulfinimines and at δ 167−173 for the aliphatic examples.

The barrier to planar inversion in ketone-derived sulfinimines *N*-(4,4′-dimethylbenzophenylidene)-[27] and *N*-(2-propylidene)arenesulfinimines[11] ($ArS(O)N{=}CR_2$) is 13.1−14.1 and 17.0 kcal/mol, respectively. Thus, unsymmetrical sulfinimines are capable of existing as rapidly equilibrating as *E*/*Z* mixtures at rt. However, all of the sulfinimines **10** prepared from aldehydes exist in a single isomeric form. The X-ray crystal structure of sulfinimine **10a** indicates that it has the *E*-geometry (Figure 1), and

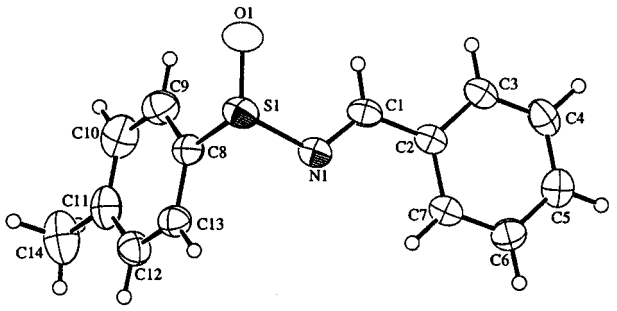
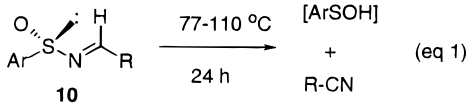


Figure 1. X-ray crystal structure of *N*-benzylidene-*p*-toluenesulfinamide (**10a**).

the reasonable assumption is made that all aldehyde-derived sulfinimines **10** have a similar geometry.[28] Although the imino proton and the sulfinyl oxygen in **10a** are nearly eclipsed in the solid state, the distance between them, 2.376 Å, is too large for there to be any hydrogen-bonding interaction. The preferences for the *E*-geometry may be due to the fact that the bulky R and *p*-tolylsulfinyl groups are in the thermodynamically most stable configuration where there are the fewest nonbonded steric interactions. Alternatively, the high preference for (*E*)-sulfinimines could result from a syn elimination of Me_3SiOLi as is required of the Peterson olefination.[29]

The aromatic and heteroaromatic sulfinimines are more resistant to hydrolysis than the aliphatic sulfinimines, presumably because of conjugative stabilization of the C−N double bond. On heating for 24 h at 77−110 °C, sulfinimines **10** undergo a syn elimination to give the valuable and elusive sulfenic acid (ArSOH) along with the corresponding nitrile (eq 1).[12] Sulfenic acids are key intermediates in many organosulfur reactions, including biological transformations.[30]



In summary, a highly versatile one-step synthesis of enantiomeric sulfinimines **10** from the commercially available (*R*)- and (*S*)-menthyl *p*-toluenesulfinate (**4**) and aromatic and aliphatic aldehydes has been developed. The menthol auxiliary **12b** is isolated in excellent yield for recycling.

Experimental Section

General Procedure. Column chromatography was performed on silica gel, Merck grade 60 (230−400 mesh). Analytical and preparative thin-layer chromatography was performed on precoated silica gel plates (250 and 1000 microns) purchased from Analtech Inc. TLC plates were visualized with UV, in an iodine chamber or with phosphomolybdic acid unless noted otherwise. Melting points were recorded on a Mel-Temp apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341polarimeter. THF was freshly distilled under nitrogen from a purple solution of sodium and benzophenone. Elemental analyses were performed in the

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(28) The X-ray structure of (+)-[*S*-(*E*)]-*N*-(α-methylbenzylidene)-*p*-toluenesulfinamide has been reported. Robinson, P. D.; Hua, D. H.; Chen, J. S.; Saha, S. *Acta Crystallogr.* **1991**, *C47*, 594.

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(+)- or (−)-*N*-(Phenylsulfonyl)-1-(3,3-dichlorocamphoryl)-oxaziridine (**8**)[15] and (+)-(camphorylsulfonyl)oxaziridine **9a** and **9b**[31] were prepared as previously described, as were the sulfenimines **1**.[32] (1*R*,2*S*,5*R*)-(−)-Menthyl (*S*)-*p*-toluenesulfinate (**4**) and (1*S*,2*R*,5*S*)-(+)-menthyl (*R*)-*p*-toluenesulfinate (**4**) were purchased from Aldrich and/or prepared according to a literature procedure.[14a] Aldehydes and nitriles were purchased from Aldrich and used without additional purification.

The enantiomeric purity of the sulfinimines **10** was determined by monitoring the methyl protons of the *p*-toluenesulfinyl group at δ 2.4 ppm as a function of increasing amounts of the chiral shift reagent Eu(hfc)$_3$ in $CDCl_3$ or C_6D_6 in the ^{1}H NMR.

Typical Procedure for the Asymmetric Oxidation of Sulfenimines 6 to Sulfinimines 7 Using *N*-(Phenylsulfonyl)-1-(3,3-dichlorocamphoryl)oxaziridine (8). In a dry 25 mL two-necked round-bottomed flask equipped with a magnetic stir bar and argon inlet was placed the appropriate sulfenimine **6** (1.1 mmol, 1.1 equiv) in CCl_4 (40 mL), which was then cooled to the appropriate temperature followed by addition of 0.376 g (1.0 mmol) of oxaziridine (+)-**8** or (−)-**8**. The progress of the oxidation was monitored by TLC (20% ethyl acetate/*n*-hexane), noting the absence of the oxaziridine at which time the solvent was removed (below 35 °C) and the sulfinimines **7** isolated by flash (silica gel) chromatography (20% ethyl acetate/*n*-hexane). The (camphorylsulfonyl)imine, the oxaziridine byproduct, was isolated in 80−90% yield and recycled.[15]

(−)-(*R*)-*N*-(Benzylidene)benzenesulfinamide (7a): yield 95%; mp 95−96 °C [lit.[6] mp 78−79 °C]; ee 88%; $[\alpha]^{20}_D$ −112° (*c* 1.18, $CHCl_3$); crystallized from *n*-hexane (74%), ee >95%; $[\alpha]^{20}_D$ −126° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40−7.55 (m, 6H), 7.72−7.80 (m, 2H), 7.80−7.90 (m, 2H), 8.75 (s, 1H, N=CH).

(+)-(*S*)-*N*-(Benzylidene)benzenesulfinamide (7a): yield 72%; mp 95 °C; crystallized from *n*-hexane, ee >95%; $[\alpha]^{20}_D$ +124° (*c* 1.18, $CHCl_3$).

(*R*)-(−)-*N*-(*p*-Methoxybenzylidene)benzenesulfinamide (7c): yield 95%; mp 117.5−119 °C; >97% ee $[\alpha]^{20}_D$ −47.5° (*c* 1.4 $CHCl_3$); IR (KBr) 1593, 1570 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3 H), 6.95 (d, 2 H, J = 8.8 Hz), 7.48−7.52 (m, 3 H), 7.70−7.76 (m, 2 H), 7.80 (d, 2 H, J = 8.8 Hz), 8.68 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.8, 159.4, 144.9, 131.2, 130.7, 128.8, 126.5, 124.4, 114.0, 55.2. Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40; Found: C, 64.46; H, 5.07; N, 5.11.

Typical Procedure for the Synthesis of Sulfinimines from Nitriles: (*S*)-(+)-*N*-(Benzylidene)-*p*-toluenesulfinamide (10a). In a 50 mL single-necked round-bottomed flask equipped with a magnetic stir bar and argon inlet was placed 0.31 g (3.0 mmol) of benzonitrile in 10 mL of *n*-pentane. The solution was cooled to 0 °C, and 3.0 mL of DIBAL-H (3.0 mmol, 1.0 M in hexane) was added dropwise via syringe. After the reaction mixture was stirred for 30 min, 2.2 mL (3.0 mmol, 1.4 M in ethyl ether) of methyllithium was added. After being stirred for 2 h at 0 °C, the reaction mixture was cooled to −40 °C and 0.294 g (1.0 mmol) of (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (**4**) in 10 mL of *n*-pentane was added via syringe. After being warmed to rt and stirred for 8 h, the reaction mixture was quenched with saturated NH_4Cl solution (0.5 mL) at 0 °C, diluted with ethyl acetate (20 mL) and water (10 mL), and filtered through Celite. The aqueous layer was separated and extracted with ethyl acetate (10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated to give a solid that was purified by flash chromatography (5−10% ethyl acetate in *n*-hexane) to afford 0.25 g (36%) of (+)-**10a**: mp 77−78 °C [lit.[7b] mp 77−78 °C]; $[\alpha]^{20}_D$ +117.3° (*c* 1.77 $CHCl_3$) [lit.[7b] $[\alpha]^{20}_D$ +119.3° (*c* 1.77 $CHCl_3$)].

Synthesis of 2,2,2-Triphenylacetaldehyde. In a 100 mL single-necked round-bottomed flask equipped with a magnetic stir bar and argon inlet was placed 0.56 g (15.0 mmol) of $LiAlH_4$ in 20 mL of freshly distilled THF. The slurry was cooled to 0 °C, and a solution of 1.79 g (6.2 mmol) of 2,2,2-triphenylacetic acid in 20 mL of dry THF was added via syringe. The reaction mixture was warmed to rt, stirred for 14 h, cooled to 0 °C, and quenched with 1 N HCl until the solution became clear. The reaction mixture was extracted with diethyl ether (3 × 50 mL), and the combined organic phases were washed with brine (20 mL), dried (Na_2SO_4), and concentrated. Purification by flash chromatography (15% ethyl acetate:*n*-pentane) afforded 1.25 g (74%) of 2,2,2-triphenylethanol: mp 105−106 °C (lit.[33] mp 105−106 °C).

In a 100 mL single-necked round-bottomed flask equipped with a magnetic stir bar and argon inlet were placed 0.70 g (2.55 mmol) of 2,2,2-triphenylethanol, 0.83 g (3.83 mmol) PCC, and 0.83 g of Celite in 25 mL of freshly distilled CH_2Cl_2. The reaction mixture was stirred at rt for 3 h, quenched with ether (50 mL), filtered through Celite, and concentrated. Purification by flash chromatography (5% ethyl acetate:*n*-pentane) afforded 0.58 g (84%) of 2,2,2-triphenylacetaldehyde: mp 104−106 °C (lit.[34] mp 104−105 °C); ^{1}H NMR ($CDCl_3$) δ 7.07 −7.36 (m, 15 H), 10.30 (s, 1H); ^{13}C NMR($CDCl_3$) δ 198.9, 141.1, 131.1, 129.0, 128.1, 70.6.

Synthesis of (*S*)-(+)-*N*-Benzylidene-*p*-toluenesulfinamide (10a) from Benzaldehyde. In a 500 mL two-necked, round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed 14.0 g (47.5 mmol) of (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (**4**) (Andersen reagent) dissolved in 225 mL of freshly distilled THF and the mixture cooled to −78 °C. A solution of 62.0 mL of LiHMDS (62.0 mmol, 1.0 M solution in THF) was added dropwise via syringe, and the reaction mixture was allowed to warm to rt with stirring. After 5 h, as monitored by TLC for disappearance of Andersen reagent, the reaction mixture was cooled to −78 °C, and 5.0 mL (53.0 mmol) of benzaldehyde was added via syringe. After being stirred for 2 h at −78 °C, the reaction mixture was quenched with water (50 mL), diluted with ethyl ether (500 mL), and warmed to rt. The organic layer was washed with water (2 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated to give an oil that was crystallized from *n*-pentane to give a light yellow solid (6.10 g, 53%) of (+)-**10a.** The mother liquor was concentrated, and a second crop of crystals was obtained. This process was repeated three times to give a total yield of 8.75 g (76%) of (+)-**10a**: mp 77−78 °C; $[\alpha]^{20}_D$ +117.3° (*c* 1.77 $CHCl_3$).

(*R*)-(−)-*N*-Benzylidene-*p*-toluenesulfinamide (10a): mp 77−78 °C; $[\alpha]^{20}_D$ −115.1° (*c* 1.2 $CHCl_3$).

Isolation of *O*-(Trimethylsilyl)menthol (12c) and L-Menthol (12b). The mother liquor from the preceding reaction was concentrated and transferred to a 25 mL single-necked round-bottomed flask equipped with a stir bar and distillation condenser connected to a fraction collector. The distillation was carried out at 210−225 °C (1 atm) to give 9.0 g of a colorless oil consisting of *O*-(trimethylsilyl)menthol (**12c**) and 20% of menthol (**12b**).

Pure *O*-trimethylsilylmenthol (**12c**) was separated from menthol (4:1 of *O*-(trimethylsilyl)menthol and menthol) by flash chromatography, eluting with hexane presaturated with ammonia: oil $[\alpha]^{20}_D$ −63.9 (*c* 1.7, $CHCl_3$); IR (neat) 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 9H), 0.69 (d, J = 6.9 Hz, 3H), 0.75−1.15 (m, 5H), 0.86 (d, J = 7.2 Hz, 6H), 1.25−1.42 (m, 1H), 1.50−1.65 (m, 1H), 1.75−1.85 (m, 1H), 2.07−2.17 (m, 1H), 3.35 (dt, J = 4.5,10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 73.0, 50.6, 46.1, 35.2, 32.3, 25.8, 23.5, 22.9, 21.8, 16.5, 1.1. A satisfactory elemental analysis could not be obtained.

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Desilylation of Menthyl *O*-Trimethylsilyl Ether (12c). In a 250 mL single-necked round-bottomed flask equipped with a magnetic stir bar was placed 9.0 g of **12b**, **12c** (4:1) mixture in 250 mL of ethyl ether. Hydrochloric acid, 1.0 M, 100 mL, was added dropwise and the solution rapidly stirred for 3 h. The reaction was monitored by TLC for the disappearance of **12c**, and the ether layer was separated and washed with 2% Na_2CO_3 (25 mL) and brine (30 mL), dried (Na_2SO_4), and concentrated below 30 °C to afford 5.93 g (80%) of menthol: mp 43−45 °C with spectral properties identical to an authentic sample.

Synthesis of *(S)*-(+)-*N*-Butylidene-*p*-toluenesulfinamide (10e) from *n*-Butyraldehyde. In a 25 mL two-necked, round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed 0.318 g (1.08 mmol) of (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (**4**) dissolved in 6 mL of freshly distilled THF and the mixture cooled to −78 °C. A solution of 1.29 mL of LiHMDS (1.0 M solution in THF) was added dropwise via syringe, and the reaction mixture was allowed to warm to rt with stirring. After 4 h, as monitored by TLC for the disappearance of **4**, the reaction mixture was cooled to −78 °C and 0.11 mL (1.19 mmol) of *n*-butrylaldehyde was added via syringe. Stirring was continued for 45 min at −78 °C, and the reaction mixture was quenched with water (5 mL), diluted with ethyl ether (30 mL), and warmed to rt. The organic layer was washed with water (2 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated. The crude product was purified by flash chromatography (20% ether in *n*-pentane) to give 0.15 g (64%) of **10e** as an oil and 0.125 g (50%) of *O*-(trimethylsilyl)menthol (**12c**). For **10e:** $[\alpha]^{20}_D$ +308° (*c* 1.35, $CHCl_3$); IR (neat) 1732, 1621, 809 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, 3H, J = 7.4 Hz), 1.49−1.59 (m, 2H), 2.42 (s, 3H), 2.42−2.50 (m, 2H), 7.29 (d, 2H, J = 8.15 Hz), 7.55 (d, 2H, J = 8.15 Hz), 8.22 (t, 1H, J = 4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 166.9, 141.6, 141.5, 129.6, 124.4, 37.8, 21.5, 18.9, 13.8. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.01; H, 7.44; N, 6.40.

Asymmetric Synthesis of (*S*)-(+)-*N*-Benzylidene-*p*-toluenesulfinamide (10a) and (*S*)-(+)-*N*-Butylidene-*p*-toluenesulfinamide (10e) Using Fluoride Ion. Two-Step Method. In a 25 mL one-neck round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed 0.294 g (1.0 mmol) of (−)-**4** in 6 mL of ether. The reaction mixture was cooled to −78 °C, and 1.4 mL (1.0 M solution in THF) of LiHMDS was added via syringe. The reaction mixture was warmed to rt, stirred for 5 h, and cooled to −78 °C, and 1.5 mL of saturated NH_4Cl solution was added. An additional 2.0 mL of water was added, and the reaction mixture was immediately extracted with ethyl acetate (40 mL), dried ($MgSO_4$) for 1 min, filtered, and concentrated. The crude material was placed under high vacuum for 10 min, dissolved in THF (6 mL), and cooled to 0 °C. The appropriate aldehyde (2 equiv) was added via syringe, followed by the addition of 0.3 g (2 mmol) of CsF or 0.12 g (2 mmol) of KF fluoride. The reaction mixture was stirred for 8 h, quenched with saturated NH_4Cl (2 mL), extracted with ethyl acetate (2 × 30 mL), washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The sulfinimine was purified by flash chromatography using 5−20% ethyl acetate/*n*-hexane. **One-Pot Procedure.** In a 25 mL one-neck round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed 0.294 g (1.0 mmol) of (−)-**4** in 6 mL of ether or THF. The reaction mixture was cooled to −78 °C, and 1.4 mL (1.0 M solution in THF) of LiHMDS was added via syringe. The reaction mixture was warmed to rt, stirred for 5 h, cooled to −78 °C, and treated with the appropriate aldehyde and fluoride ion source as described above.

***N*-(Trimethylsilyl)-*p*-toluenesulfinamide (14).** In 25 mL one-neck, round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed 0.295 g (1.0 mmol) of (−)-**4** dissolved in 6 mL of Et_2O. The reaction mixture was cooled to −78 °C, and 1.4 mL of LiHMDS (1.0 M solution in THF) was added via syringe. The reaction mixture was warmed to rt and stirred for 5 h, monitoring the disappearance of (−)-**4** by TLC. The reaction mixture was cooled to −78 °C and quenched with 1.5 mL of saturated NH_4Cl, an additional 2.0 mL of water added, and the reaction mixture immediately extracted with ethyl acetate (40 mL). After being dried ($MgSO_4$) for ca. 1 min, the solution was filtered and concentrated. The crude mixture was placed under high vacuum for 12 h to remove **12c**, affording 0.223 g of a 7:3 mixture of **14**:**15** and a trace of **12b**. For **14**: ^1H NMR ($CDCl_3$) δ 0.30 (s, 9 H), 2.40 (s, 3 H), 3.92 (bs, 1H), 7.28 (d, 2 H, J = 8.1 Hz), 7.54 (d, 2 H, J = 8.2 Hz).

(*S*)-(+)-*p*-Toluenesulfinamide (15). As in the preceding section on the synthesis of **14**, after the reaction mixture was quenched with 2 mL of saturated NH_4Cl the reaction mixture was warmed to rt, extracted with ethyl acetate (2 × 30 mL), dried ($MgSO_4$), and concentrated. Purification by flash chromatography (50% EtOAc/*n*-hexane) gave 0.148 g of (+)-**15** (96%): mp 113 °C; $[\alpha]^{20}_D$ +79.2° (*c* 1.0 $CHCl_3$).

Alternatively, after being quenched with saturated NH_4Cl solution, the reaction mixture was vigorously stirred for 0.5 h at rt, extracted with ethyl acetate (2 × 25 mL), dried ($MgSO_4$), and concentrated. The crude material was washed with a few mL of *n*-hexane to remove **12b** to give 0.118 g (76%) of (+)-**15**: mp 110−112 °C (lit.[25a] mp 115 °C); $[\alpha]^{20}_D$ +79.7° (*c* 1.2 $CHCl_3$), IR (KBr) 3200, 3094 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.42 (s, 3 H), 4.33 (s, 2H), 7.32 (d, 2 H, J = 8.1 Hz), 7.64 (d, 2 H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 21.3, 125.3, 129.5, 141.4, 143.4. Anal. Calcd for C_7H_8NOS: C, 54.17; H, 5.84; N, 9.03. Found: C, 54.08; H, 5.89; N, 9.13.

Determination of the Enantiomeric Purity of 15 via Condensation with *p*-Nitrobenzaldehyde To Give (+)-10f. In a 10 mL one-neck round-bottomed flask equipped with a magnetic stir bar were placed 0.06 g (0.39 mmol) of *S*-(+)-*p*-toluenesulfinamide (**15**) and 0.062 g (0.41 mmol) of *p*-nitrobenzaldehyde dissolved in 3 mL of THF. Cesium fluoride, 0.089 g (0.59 mmol), was added, and the reaction mixture was stirred for 12 h, filtered through Celite, concentrated, and purified by flash chromatography (20−40% ethyl acetate/*n*-hexane) to give 0.103 g (92%) of sulfinimine (+)-**10f** with a rotation of $[\alpha]^{20}_D$ +19.7° (*c* 1.1, $CHCl_3$), indicating that it had >96% ee (vide infra).

(*S*)-(+)-*N*-(*p*-Methoxybenzylidene)-*p*-toluenesulfinamide (10b): yield 90%; purification, flash chromatography 20% EtOAc/hexane; mp 135−136.6 °C; $[\alpha]^{20}_D$ +37.9° (*c* 1.49 $CHCl_3$); IR (KBr) 1594 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3 H), 3.89 (s, 3H), 6.94 (d, 2 H, J = 8.8 Hz), 7.29 (d, 2 H, J = 8.1 Hz), 7.63 (d, 2 H, J = 8.2 Hz), 7.79 (d, 2 H, J = 8.8 Hz), 8.67 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.9, 159.6, 142.1, 141.4, 131.4, 129.7, 126.9, 124.7, 114.2, 55.5, 21.5. Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12. Found: C, 65.76; H, 5.68; N, 4.87.

(*S*)-(+)-*N*-(*o*-Methoxybenzylidene)-*p*-toluenesulfinamide (10g): yield 91%; purification, flash chromatography 20% EtOAc/hexane; mp 71−72.5 °C; $[\alpha]^{20}_D$ +363.0° (*c* 1.43 $CHCl_3$); IR (KBr) 1590, 761 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3 H), 3.90 (s, 3H), 6.93−7.00 (m, 2 H), 7.30 (d, 2 H, J = 8.2 Hz), 7.42−7.49 (m, 1 H), 7.64 (d, 2 H, J = 8.2 Hz), 7.97 (dd, 1H, J = 7.7, 1.6 Hz), 9.24 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.5, 156.5, 142.0, 141.3, 134.0, 129.6, 128.3, 124.7, 122.4, 120.5, 111.2, 55.5, 21.5. Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12. Found: C, 65.77; H, 5.54; N, 4.83.

(*S*)-(−)-*N*-[*p*-(Methylthio)benzylidene]-*p*-toluenesulfinamide (10h): yield 80%; purification, flash chromatography 30% EtOAc/hexane; mp 132−134 °C; $[\alpha]^{20}_D$ −40.2° (*c* 1.1 $CHCl_3$); IR (KBr) 1587 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3 H), 2.50 (s, 3 H), 7.25 (d, 2 H, J = 8.3 Hz), 7.30 (d, 2 H, J = 8.3 Hz), 7.62 (d, 2 H, J = 8.3 Hz), 7.72 (d, 2 H, J = 8.3 Hz), 8.68 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.3, 144.9, 141.5, 141.2, 129.8, 129.4, 124.9, 124.4, 21.2, 14.6. Anal. Calcd for $C_{15}H_{15}NOS_2$: C, 62.25; H, 5.22. Found: C, 62.48; H, 5.28.

(*S*)-(+)-*N*-(*p*-Fluorobenzylidene)-*p*-toluenesulfinamide (10i): yield 84%; purification, crystallization 20% EtOAc/pentane; mp 111−3 °C; $[\alpha]^{20}_D$ +105.8° (*c* 2.7 $CHCl_3$); IR (KBr) 1609, 838 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3 H),7.12−7.14 (m, 2 H), 7.31 (d, 2 H, J = 8.2 Hz), 7.62 (d, 2 H, J = 8.2 Hz), 7.85−7.86 (m, 2 H), 8.71 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 116.0 (d, J = 254.3 Hz), 159.9, 142.4 (d, J = 16.3 Hz), 132.5, 132.4, 131.0, 130.5, 125.4, 116.8 (d, J = 22.3 Hz), 22.1. Anal. Calcd

for $C_{14}H_{12}NOS$: C, 64.28; H, 4.59; N, 5.35. Found: C, 64.62; H, 4.89; N, 5.29.

(*S*)-(+)-*N*-(*p*-Nitrobenzylidene)-*p*-toluenesulfinamide (10f): yield 95%; purification, flash chromatography 45% EtOAc/hexane; mp 157−158.5 °C; $[\alpha]^{20}_D$ +19.8° (*c* 1.1 $CHCl_3$); IR (KBr) 1588, 806 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (s, 3 H), 7.34 (d, 2 H, *J* = 8.1 Hz), 7.64 (d, 2 H, *J* = 8.2 Hz), 8.01 (d, 2 H, *J* = 8.8 Hz), 8.30 (d, 2 H, *J* = 8.8 Hz), 8.82 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 158.2, 149.7, 142.0, 140.6, 138.7, 130.1, 129.9, 124.6, 123.9, 21.5. Anal. Calcd for $C_{14}H_{12}N_2O_3S$: C, 58.32; H, 4.20; N, 9.71. Found: C, 58.19; H, 4.48; N, 9.87.

(*R*)-(−)-*N*-(3-Pyridinemethylidene)-*p*-toluenesulfinamide (10j): yield 70%; isolated by flash chromatography using 70% EtOAc/hexane and crystallized from *n*-hexane:EtOAc; mp 77−78 °C (lit.[7c] mp 77−78 °C); $[\alpha]^{20}_D$ −149.8° (*c* 1.17, $CHCl_3$).[7c]

(*S*)-(+)-*N*-(3-Pyridinemethylidene)-*p*-toluenesulfinamide (10j): $[\alpha]^{20}_D$ 147.0° (*c* 1.34, $CHCl_3$).

(*S*)-(+)-*N*-(2-Furylmethylidene)-*p*-toluenesulfinamide (10k): yield 68%; purification, flash chromatography 20% EtOAc/hexane; mp 65 °C; $[\alpha]^{20}_D$ +78.3 (c 0.65 $CHCl_3$); IR (KBr) 1700, 1652, 1216, 770, 669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.32 (s, 3 H), 6.49−6.47 (m, 1H), 6.96 (d, 2 H, *J* = 3.6 Hz), 7.24 (d, 2 H, *J* = 8.1 Hz), 7.56 (d, 2 H, *J* = 8.1 Hz), 8.51 (s,1H); ^{13}C NMR ($CDCl_3$) δ 15.0.3, 147.5, 146.9, 141.7, 141.42, 129.74, 124.5, 119.2, 112.4, 21.2. Anal. Calcd for $C_{12}H_{11}NO_2S$: C, 61.78; H,4.75; N, 6.00. Found: C, 61.72; H, 4.71; N, 5.89.

(*S*)-(+)-*N*-(2-Thienylmethylidene)-*p*-toluenesulfinamide (10l): yield 72%; purification, flash chromatography 20% EtOAc/hexane; mp 82 °C; $[\alpha]^{20}_D$ −96.4 (*c* 0.69 $CHCl_3$); IR (KBr) 1582, 819, 717 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.34 (s, 3 H), 7.07 (t, 1H, *J* = 4.2 Hz), 7.25 (d, 2 H, *J* = 9.0 Hz), 7.50−7.58 (m, 4 H), 8.80 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 153.4, 141.6, 139.8, 134.2, 132.6, 129.7, 128.0, 124.7, 21.3. Anal. Calcd for $C_{12}H_{11}NO_2S_2$: C, 57.83; H, 4.42; N, 5.62. Found: C, 57.71; H, 4.41; N, 5.48.

(*S*)-(+)-*N*-(Crotonylidene)-*p*-toluenesulfinamide (10c): yield 70%; purification, flash chromatography 20% EtOAc/hexane; $[\alpha]^{20}_D$ +617.0° (*c* 1.7, $CHCl_3$); mp 39−40 °C; IR (KBr) 1645, 1572, 967, 813 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.96 (dd, 3H, *J* = 6.6, 1.2 Hz), 2.39 (s, 3H), 6.35−6.66 (m, 2H), 7.30 (d, 2H, *J* = 7.9 Hz), 7.56 (d, 2H, *J* = 8.2 Hz),, 8.34 (d, 1H, *J* = 9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 161.6, 147.1, 141.8, 141.5, 130.0, 129.7, 124.5, 21.5, 19.0. Anal. Calcd. for $C_{11}H_{13}NOS$: C, 63.74; H,6.32; N, 6.76. Found: C, 63.62; H, 6.52; N, 6.66.

(*S*)-(+)-*N*-(Cinnamylidene)-*p*-toluenesulfinamide (10d): yield 80%; crystallized from ether; $[\alpha]^{20}_D$ +337° (*c* 1.49, $CHCl_3$); mp 114−115 °C; IR (KBr) 1627, 1581, 994, 960, 811 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3H), 7.05 (dd, 1H, *J* = 15.8, 9.1 Hz), 7.21−7.52 (m, 8H), 7.59 (d, 2H, *J* = 8.1 Hz), 8.52 (d, 2H, *J* = 9.1Hz); ^{13}CNMR ($CDCl_3$) δ 161.4, 146.7, 141.7, 134.7, 130.2, 129.8, 128.8, 127.8, 125.4, 124.4, 21.6. Anal. Calcd for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.45; H, 5.76; N, 5.22.

(*S*)-(+)-*N*-(Propenylidene)-*p*-toluenesulfinamide (10m): yield 71%; oil; flash chromatography (20% ether in pentane); $[\alpha]^{20}_D$ +729° (*c* 2.2, $CHCl_3$); IR (KBr) 1624, 948, 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3H), 5.89 (s, 1H), 6.04 (d, 1H, *J* = 6.3 Hz), 6.66 (m, 1H), 7.33 (d, 2H, *J* = 8.1 Hz), 7.57 (d, 2H, *J* = 8.3 Hz), 8.37 (d, 1H, *J* = 9.3 Hz); ^{13}CNMR ($CDCl_3$) δ 161.9, 141.8, 141.4, 134.5, 132.1, 129.8, 124.6, 21.4. Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.73; N, 7.24. Found: C, 62.40; H, 6.00; N, 7.60.

***(S)*-(+)-*N*-(3-Methylbutylidene)-*p*-toluenesulfinamide (10n):** yield 68% (thick gum); flash chromatography (20% ether in pentane); $[\alpha]^{20}_D$ +317° (*c* 1.4, $CHCl_3$); IR (neat) 2957, 1621, 1492, 1465, 1142, 1097, 1074, 1017, 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (q, 3H, *J* = 3.6, 6.7 Hz), 2.09−1.98 (m, 3H), 2.4 (s, 1H), 7.27 (d, 1H, *J* = 8.3 Hz), 7.53 (d, 1H, *J* = 8.2 Hz), 8.20 (t, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 166.8, 141.6, 129.8, 124.5, 44.6, 26.2, 22.5, 21.4. Anal. Calcd for $C_{12}H_{17}NOS$: C, 64.57; H, 7.62; N, 6.27. Found: C, 64.33; H, 7.45; N, 5.92.

***(S)*-(+)-*N*-Isobutylidene-*p*-toluenesulfinamide (10o):** yield 60%; oil; flash chromatography (20% ether in pentane); $[\alpha]^{20}_D$ +387.5° (*c* 2.1, $CHCl_3$); IR (neat) 1732, 1619, cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, 3H, *J* = 2.9 Hz), 1.01 (d, 3H, *J* = 2.8Hz), 2.45 (s, 3H), 2.46−2.58 (m, 1H), 7.13 (d, 2H, *J* = 8.1 Hz), 7.40 (d, 2H, *J* = 8.2 Hz), 7.98 (d, 1H, *J* = 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ 170.9, 141.8, 141.3, 129.5, 124.4, 34.6, 21.4, 18.7. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22. Found: C, 62.96; H, 7.23.

(*S*)-(+)-*N*-(2,2-Dimethylpropylidene)-*p*-toluenesulfinamide (10p). The reaction mixture was stirred overnight at rt, quenched at −78 °C, and worked up as usual: yield 68%; crystallization from *n*-pentane; mp 73−75 °C; $[\alpha]^{20}_D$ +371.5° (*c* 1.94, $CHCl_3$);[5a] IR (KBr): 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (s, 9H), 2.40 (s, 3H), 7.30 (d, 2H, *J* = 8.2 Hz), 7.55 (d, 2H, *J* = 8.2 Hz), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 173.4, 142.2, 141.5, 129.7, 124.7, 37.7, 26.5, 21.4. Anal. Calcd for $C_{12}H_{17}NOS$: C, 64.54; H, 7.67; N, 6.20. Found: C, 64.41; H, 7.60; N, 5.88.

***(S)*-(+)-*N*-(2-Phenylethylidene)-*p*-toluenesulfinamide (10q).** To isolate this sulfinimine is was necessary to wash the chromatographic solvents with concd NH_4OH. The solvents were then used to precondition the silica gel column: isolated yield 38%; thick gum; flash chromatography (20% ether in *n*-pentane, saturated with ammonia); $[\alpha]^{20}_D$ +256.1° (*c* 1.0, $CHCl_3$); IR (neat) 3389, 3027, 2916, 1613, 1494, 1453, 1093, 623 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.38 (s, 3H), 3.68−3.83 (m, 2H), 7.15−7.29 (m, 7H), 7.52 (d, *J* = 8.1Hz, 2H), 8.24 (t, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 165.7, 142.5, 130.5, 129.9, 129.6, 129.5, 128.8, 128.7, 127.9, 125.2, 43.0.

(*S*)-(+)-*N*-(*S*)-*p*-Toluenesulfinyl)-β-styrenylenamine (16): yield 40%; thick gum; flash chromatography (20% ether in *n*-pentane); $[\alpha]^{20}_D$ +121.3 (*c* 1.0, $CHCl_3$); IR (KBr) 3362−3100, 3028, 811 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.44 (s, 3H), 6.02 (d, *J* = 13.8 Hz, 1H), 6.14 (d, *J* = 10.8 Hz, 1H), 6.75 (dd, *J* = 11.1, 14.0 Hz, 1H), 7.18−7.37 (m, 7H), 7.65 (d, *J* = 8.1 Hz, 2H).

(*S*)-(+)-*N*-(2,2,2-Triphenylethylidene)-*p*-toluenesulfinamide (10r): yield 50%; flash chromatography (10% EtOAc/pentane); mp 114−115 °C; $[\alpha]^{20}_D$ +126.0° (*c* 0.63, $CHCl_3$); IR (KBr) 1609, 807 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3 H), 7.00−7.02 (m, 6 H), 7.25−7.28 (m, 11 H), 7.48 (d, 2 H, *J* = 8.1 Hz), 8.98 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.3, 143.2, 142.1, 130.9, 130.3, 128.7, 128.5, 127.7, 125.5, 64.4, 22.0. Anal. Calcd for $C_{27}H_{23}NOS$: C, 79.18; H, 5.66; N, 3.42. Found: C, 79.55; H, 5.95; N, 3.31.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of **10q**, **12c**, **14**, **16**, and a mixture of **14** and **15** (7 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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