Pergamon

Tetrahedron 55 (1999) 8883–8904

TETRAHEDRON

Asymmetric Synthesis of Chiral Amines by Highly Diastereoselective 1,2-Additions of Organometallic Reagents to *N-tert*-Butanesulfinyl Imines

Derek A. Cogan, Guangcheng Liu,† and Jonathan Ellman*

University of California at Berkeley, Department of Chemistry, Berkeley, CA 94720

Received 4 February 1999; accepted 22 April 1999

Abstract: High yielding and highly diastereoselective methods for 1,2-additions of organometallic reagents to *N-tert*-butanesulfinyl aldimines (**2**) and *N-tert*-butanesulfinyl ketimines (**3**) are described. The additions of alkyl, aryl, alkenyl, and allyl carbanions to a diverse set of imines with different steric and electronic properties are demonstrated. Acidic methanolysis of the sulfinamide products (**4** and **6**) delivers highly enantioenriched α-branched and α,α-dibranched amines. Since a broad range of sulfinyl imines are easily accessible from aldehydes and ketones, a wide variety of enantioentriched amines may be prepared.

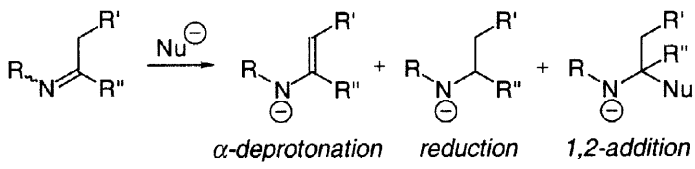
Keywords: Amines; Asymmetric reactions; Diastereoselection; Imines; Sulfinamides.

INTRODUCTION

The amine functionality is incorporated into greater than 75% of all drugs and drug candidates[1] and is also prevalent in natural products, materials, and catalysts. It is therefore surprising that there are few general methods for the asymmetric synthesis of amines bearing an α-stereocenter.[2] Two of the most powerful routes to α-branched chiral amines are the asymmetric reduction of ketimines or their enamine tautomers,[3] and the asymmetric 1,2-addition of carbanions to aldimines.[2b,c] The asymmetric synthesis of α,α-dibranched amines is even more challenging and has only directly been achieved by the 1,2-additions of carbanions to ketimines. However, this approach has been limited only to allylations[4] and the addition of Grignard reagents to α-pyridyl ketimines.[5]

Although imines are versatile intermediates for the synthesis of chiral α-branched amines largely due to the ready availability of a wide range of aldehyde and ketone starting materials, they are not without problems. For the vast majority of aldehyde and ketone precursors, *N*-substitution on the imine is required to prevent oligomerization. Many imines are also hydrolytically unstable, depending both upon the steric and electronic properties of the aldehyde or ketone precursor, and upon the nitrogen substituent. In addition, imines are poor electrophiles and, upon treatment with basic carbanion nucleophiles, are prone to competitive α-deprotonation, resulting in azaenolate formation (Scheme 1). To address these issues, inexpensive *N*-substituents are desired

Scheme 1



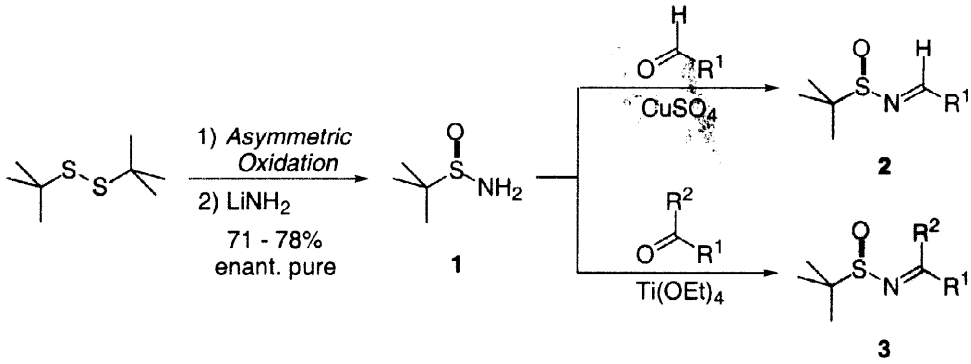
PII: S0040-4020(99)00451-2

that enable straightforward synthesis of stable imines, provide activation for nucleophilic addition, serve as chiral directing groups, and finally, are straightforward to remove under mild conditions. Unfortunately, *N*-substituents have not yet been identified that meet all of these requirements.

The toluenesulfinyl imines pioneered by Davis have many favorable characteristics.[6,7] In particular, the toluenesulfinyl group can provide high diastereofacial selectivity, while both inhibiting imine hydrolysis as well as activating the imine for reductions,[8] additions of enolates and other stabilized nucleophiles,[7,9] and cycloadditions.[10] Significantly, the sulfinyl group is easily cleaved under mildly acidic conditions. Unfortunately, the 1,2-addition of alkyl or aryl carbanions to sulfinyl imines has not been fully developed. The addition of BnMgBr to *N*-*p*-toluenesulfinyl α-arylimines has been reported to proceed with only modest diastereoselectivies (60 - 74%). More ominously, MeMgBr is reported to add exclusively at sulfur to provide *p*-tolyl methyl sulfoxide.[11,12]

In preliminary communications we reported that *tert*-butanesulfinyl imines are extremely effective substrates for the 1,2-addition of strongly basic non-stabilized alkyl and aryl carbanions.[13] Not only do the addition reactions proceed with high yields and diastereoselectivities, but a broad range of *tert*-butanesulfinyl aldimines **2** and ketimines **3** can be rapidly and easily prepared in high yields by direct condensation of *tert*-butanesulfinamide (**1**)[14] with aldehydes or ketones (Scheme 2).[15] Furthermore, the chiral ammonia synthon **1**

Scheme 2



is a crystalline, stable solid that is straightforward to prepare in enantiomerically pure form on large scale in just two steps from the inexpensive *tert*-butyl disulfide. Thus, the 1,2-addition of organometallic reagents to **2** and **3** represents a general method for the rapid preparation of a broad range of enantioenriched α-branched and α,α-dibranched amines.

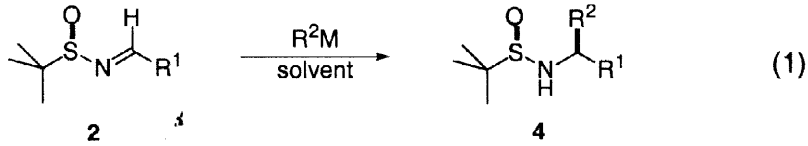
In this article, we further establish the scope and generality of the 1,2-addition of organometallic reagents to *tert*-butanesulfinyl imines **2** and **3**. The effects of different organometallic reagents, solvents, and additives are compared. As well, 1,2-additions to an expanded set of imines with different steric and electronic properties are demonstrated. Finally, transition-state models are presented that consistently predict diastereofacial selectivity for each type of transformation.

RESULTS AND DISCUSSION

Asymmetric synthesis of α-branched amines. The *tert*-butanesulfinyl aldimines (**2**) are prepared by a simple $CuSO_4$ mediated condensation of *tert*-butanesulfinamide **1** with aldehydes.[14] This sequence provides access to a wide array of sulfinyl imines quickly and cheaply. The sulfinyl aldimines **2** chosen for this study incorporate the R^1 substituents ethyl, isopropyl, phenyl, 4-methoxyphenyl, and benzyl, representing *n*-alkyl, branched alkyl, and aryl (including electron rich aryl), and highly enolizable derivatives. Notably, condensation of **1** and phenylacetaldehyde provides the sulfinyl aldimine rather than the enamine, which is the favored tautomeric form of the analogous *p*-toluenesulfinyl aldimine.[6] 1,2-Additions to this aldimine are a particular challenge since competitive α-deprotonation is generally problematic for 1,2-additions to imines prepared from phenylacetaldehyde derivatives.

In order to develop general and straightforward methods for the 1,2-addition of organometallic reagents to **2**, a focus was placed upon the use of commercially or readily available reagents. Experiments were performed by the slow addition of a solution of organometallic reagent to a 0.2 M solution of **2** at –48 °C (eq 1). Additions of MeMgBr to *tert*-butanesulfinyl aldimines **2a**, **2b**, and **2c** in THF at -48 °C provided the desired sulfinamides **4a**, **4b**, and **4c** in high yields and with very promising diastereoselectivities (entries 1-3

Table 1. Solvent Effect on 1,2-Additions of Organometallic Reagents to **2**.[a]



2 **4** (1)

	sulfinyl aldimine **2**				sulfinamide **4**		
entry	compound	R^1	R^2M	solvent	compound	yield(%)[b]	(R_S,*S*)-**4**:(R_S,*R*)-**4**[c]
1	(R_S)-**2a**	*i*-Pr	MeMgBr	THF	**4a**	91	95:5[d]
2	(R_S)-**2b**	Et	MeMgBr	THF	**4b**	78	90:10[d]
3	(R_S)-**2c**	Ph	MeMgBr	THF	**4c**	98	93:7[d]
4	(R_S)-**2a**	*i*-Pr	EtMgBr	THF	**4d**	90	80:20[d]
5	(R_S)-**2c**	Ph	EtMgBr	THF	**4e**	91	50:50[d]
6	(R_S)-**2a**	*i*-Pr	EtMgBr	Et_2O	**4d**	90	85:15[d]
7	(R_S)-**2c**	Ph	EtMgBr	Et_2O	**4e**	87	62:38[d]
8	(R_S)-**2b**	Et	MeMgBr	CH_2Cl_2	**4b**	96	97:3[e]
9	(R_S)-**2c**	Ph	EtMgBr	CH_2Cl_2	**4e**	98	92:8[e]
10	(R_S)-**2b**	Et	MeLi	THF	**4b**	87	75:28[e]
11	(R_S)-**2b**	Et	MeLi	Et_2O	**4b**	86	54:46[e]
12	(R_S)-**2b**	Et	$CeCl_3$/MeLi	THF	**4b**	89	78:22[e]

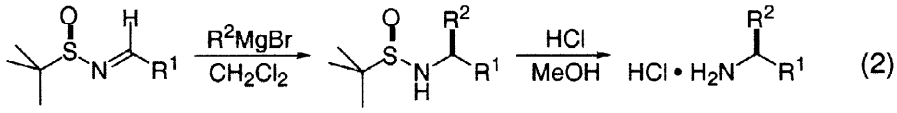
[a] Reactions were performed by the slow addition of a 3.0 M solution of Grignard reagent in Et_2O to a 0.2 M solution of **2** at –48 °C. [b] Isolated yields of analytically pure material. [c] Configurations were determined by correlation with known compounds. See Experimental Section for details. [d] Diastereomeric ratios determined by ^1H NMR analysis of unpurified **4**. [e] Diastereomeric ratios were determined by GC analysis of the MTPA derivatives prepared from the crude amine **5** (*vide infra*).

in Table 1). However, when EtMgBr was tested, the results were disappointing (entries 4 and 5). Changing the solventfrom THF to Et_2O resulted in only a moderate improvement in the diastereoselectivity (entries 6 and 7).

Non-coordinating solvents, such as toluene and CH_2Cl_2, have been shown to improve the diastereoselectivities for Grignard additions to *p*-toluenesulfinyl imines.[11] While the use of toluene as solvent failed to improve the diastereoselectivity, CH_2Cl_2 resulted in a dramatic improvement (entries 8 and 9). In contrast to the Grignard reagents, organolithium and organocerium reagents provided much lower diastereoselectivities (entries 10-12).

To investigate generality, nearly all combinations of the five structurally distinct *tert*-butanesulfinyl aldimines **2a-e** and a range of Grignard reagents were tested (Table 2). These reactions were performed at –48 °C for 4-6 h with CH_2Cl_2 as solvent and using ether solutions of organomagnesium bromides (eq 2). In all cases, the addition of Grignard reagents to **2** proceeded from the same face with high levels of diastereocontrol. The selectivities were routinely higher than 9:1 with the highest diastereoselectivity (99:1) observed for the 1,2-

Table 2. 1,2-Additions of Grignard Reagents to **2**, and Methanolysis of **4**.[a]



2 **4** **5**

	sulfinyl aldimine **2**			sulfinamide **4**			amine **5**	
entry	compound	R^1	R^2M	compound[b]	yield (%)[c]	dr[d]	compound[b]	yield (%)[c]
1	(R_S)-**2b**	Et	MeMgBr	(R_S,*S*)-**4b**	96	93:7	(*S*)-**5b**	97
2	(R_S)-**2b**	Et	*i*-PrMgBr	(R_S,*R*)-**4d**[e]	97	98:2	(*S*)-**5d**[e]	92
3	(R_S)-**2b**	Et	PhMgBr	(R_S,*R*)-**4e**	quant.	96:4	(*R*)-**5e**	90
4	(R_S)-**2a**	*i*-Pr	MeMgBr	(R_S,*S*)-**4a**	97	98:2	(*S*)-**5a**	97
5	(R_S)-**2a**	*i*-Pr	EtMgBr	(R_S,*S*)-**4d**[e]	quant.	97:3	(*S*)-**5d**[e]	93 (85)[f]
6	(R_S)-**2a**	*i*-Pr	PhMgBr	(R_S,*R*)-**4f**	98	89:11	(*R*)-**5f**	91 (76)[f]
7	(R_S)-**2a**	*i*-Pr	vinylMgBr	(R_S,*R*)-**4g**[e]	90	88:12	(*R*)-**5g**[e]	78
8	(R_S)-**2c**	Ph	MeMgBr	(R_S,*S*)-**4c**	96	97:3	(*S*)-**5c**	88
9	(R_S)-**2c**	Ph	EtMgBr	(R_S,*S*)-**4e**	98	92:8	(S)-**5e**	94
10	(R_S)-**2c**	Ph	*i*-PrMgBr	(R_S,*S*)-**4f**	29	—	—	—
11	(R_S)-**2c**	Ph	vinylMgBr	(R_S,*S*)-**4h**	79	94:6	(*S*)-**5h**	93
12	(R_S)-**2d**	Bn	MeMgBr	(R_S,*S*)-**4i**	89	95:5	(*S*)-**5i**	95
13	(R_S)-**2d**	Bn	EtMgBr	(R_S,*S*)-**4j**	85	92:8	(*S*)-**5j**	98
14	(R_S)-**2d**	Bn	vinylMgBr	(R_S,*R*)-**4k**	81	91:9	(*R*)-**5k**	97
15	(R_S)-**2d**	Bn	PhMgBr	(R_S,*R*)-**4l**	81	95:5	(*R*)-**5l**	99
16	(R_S)-**2e**	*p*-MeOPh	EtMgBr	(R_S,*S*)-**4m**[e]	88	99:1	(*S*)-**5m**[e]	quant.
17	(R_S)-**2b**	Et	$PhLi/MgBr_2$	(R_S,*R*)-**4e**	88	94:6	—	—

[a] Reactions were performed by the slow addition of a 3.0 M solution of Grignard reagent in Et_2O to a 0.2 M CH_2Cl_2 solution of **2** at –48 °C. [b] Configurations were determined by correlation with known compounds. See Experimental Section for details. [c] Isolated yields of analytically pure material. [d] Diastereomeric ratios were determined by GC analysis of the MTPA derivatives prepared from the crude amine **5**. [e] Configurations were assigned from the transition state model. [f] Yield of enantiomerically pure material after a single recrystallization.

addition of EtMgBr to **2e**, derived from anisaldehyde (entry 16 in Table 2). The lowest diastereoselectivity, which is observed for the addition of vinyl Grignard to **2g**, derived from isobutyraldehyde, was 88:12 (entry 17). Organomagnesium chlorides provide comparable diastereoselectivities to their bromide analogs. However, when solutions of Grignard reagents in THF were employed, substantially lower diastereoselectivites were observed.

Methyl, ethyl, phenyl and vinyl additions to the highly enolizable phenylethylidene derivative **2d** also proceeded without competitive α-deprotonation (entries 12-15). Of the 16 addition reactions performed, only the addition of *i*-PrMgBr to **2c** afforded the desired sulfinamide **4f** in an unsatisfactory yield (29%; entry 10). In this case only, the reduction product of **2c**, *N*-benzyl *tert*-butanesulfinamide, was isolated in 61% yield. However, (R_S,*R*)-**4f** can be obtained in 98% yield by the addition of PhMgBr to **2a** (entry 6).

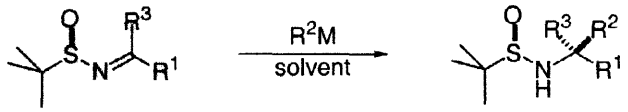
The 1,2-additions of organolithiums to aldimines **2** were not diastereoselective (entries 10-12 in Table 1). Because a wide range of organolithiums are available from directed lithiations of sp^2-carbons or via lithium-halogen exchange, a procedure that effectively applies organolithiums to the synthesis of chiral amines would be useful. For this reason, Li-Mg metathesis reactions were investigated. Satisfyingly, PhMgBr prepared by metathesis of $MgBr_2$ and PhLi in Et_2O was nearly as effective as commercial PhMgBr (entry 17 in Table 2).

Acidic alcoholysis and hydrolysis of sulfinamides has long been known to be a facile process.[16] The *tert*-butanesulfinyl group was readily removed from sulfinamides **4** with a 1:1 mixture of two equivalents of commercially available 4 M HCl in dioxane and MeOH (eq 2). The reactions were usually complete within minutes at room temperature, although the reactions were typically carried out for thirty minutes to ensure complete methanolysis for all sulfinamides. Analytically pure amine hydrochlorides **5** were obtained in all cases after simple precipitation. As shown in Table 2, products **5** are isolated in excellent yields, and due to their crystalline nature, enantiomerically pure amine hydrochlorides can be readily obtained by a single crystallization (entries 5 and 6 in Table 2). For 10 of the 13 derivatives of **5** prepared in this study, the stereochemical configurations were correlated with known compounds. Based upon the product stereochemistry of these derivatives, a consistent and predictable diastereofacial preference for 1,2-addition is observed for 12 transformations. The stereochemistries of the remaining products (**4** and **5d**, **g**, and **m**) have been assigned by analogy.

Asymmetric synthesis of α,α-dibranched amines. Investigations of 1,2-additions of organometallic reagents to *tert*-butanesulfinyl ketimines (**3**) were also performed. The sulfinyl ketimines **3** used in this study were prepared by $Ti(OEt)_4$ mediated condensations of sulfinamide **1** with ketones (acetophenone, methyl naphthyl ketone, butyl phenyl ketone, methyl isopropyl ketone, butyl isopropyl ketone, methyl isobutyl ketone, and methyl butyl ketone) representing *n*-alkyl aryl, *n*-alkyl branched-alkyl, and methyl *n*-alkyl substitution.[14] In cases where the branching about the imine is dissimilar, only the *E* isomer is observed. The remaining sulfinyl imines, derived from methyl isobutyl ketone and methyl butyl ketone, are isolated as mixtures of *E* and *Z* isomers (5:1 and 6:1, respectively). These isomers are presumably in equilibrium, and cannot be separated.[17]

Since allylations of *N*-*p*-toluenesulfinyl ketimines are precedented,[8b,18] 1,2-additions of allylmagnesium bromide to *tert*-butanesulfinyl ketimines **3a** and **3c** were first investigated (eq 3; entries 1 and 2 in Table 3). The reactions were complete within a few hours at 0 °C and sulfinamides **6a** and **6b** were isolated as single diastereomers in 85% and 93% yields respectively. The α,α–dialkylamines **7a** and **7b** were obtained from

Table 3. 1,2-Additions of Organometallic Reagents to **3** (eq 2).[a]



(3)

3 **6**

	sulfinyl ketimine **3**					sulfinamide **6**		
entry	compound	R^1	R^3	R^2M	solvent	compound	yield (%)[b]	dr[c]
1[d]	(R_S)-**3c**	Me	Ph	allylMgBr	CH_2Cl_2	(R_S,*S*)-**6a**	85	>99.9:0.1
2[d]	(R_S)-**3a**	Me	*i*-Pr	allylMgBr	CH_2Cl_2	(R_S,*S*)-**6b**	93	>95:5[e]
3	(R_S)-**3a**	Me	*i*-Pr	PhMgBr	CH_2Cl_2	(R_S,*S*)-**6c**	21	69:31
4	(R_S)-**3a**	Me	*i*-Pr	PhLi	toluene	(R_S,*R*)-**6c**	65	94:6
5	(R_S)-**3b**	Bu	*i*-Pr	PhLi	toluene	(R_S,*R*)-**6d**	54	82:18
6	(R_S)-**3b**	Bu	*i*-Pr	MeLi	toluene	(R_S,*R*)-**6e**	54	82:18
7	(R_S)-**3c**	Me	Ph	BuLi	toluene	(R_S,*S*)-**6f**	26	99:1
8	(R_S)-**3d**[f]	Me	Bu	PhLi	toluene	(R_S,*R*)-**6f**	67	63:37

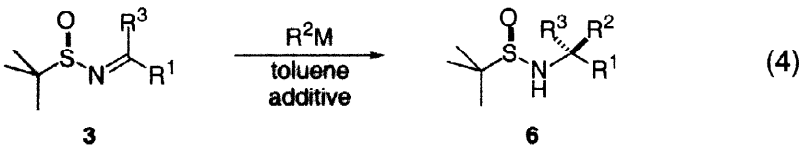
[a] Reactions were performed by the slow addition of an 0.4 M solution of **3** at -78 °C to a 0.4 M solution of organometallic at –78 °C. [b] Isolated yields of analytically pure material. [c] Diastereomeric ratios were determined from GC or HPLC assays. See Experimental Section for details. [d] Reactions were performed using 1.0 M allylMgBr and a 0.2 M solution of **3**. [e] Minor diastereomer not detected by ^{1}H NMR. [f] Sulfinyl ketimine **3d** exists as a 5:1 mixture of *E* and *Z* isomers.

sulfinamides **6a** and **6b** by the same acidic methanolysis procedure described for α-branched sulfinamides **4**, with the analytically pure α,α-disubstituted amine hydrochlorides again isolated by a precipitation procedure. Because a wide range of *tert*-butanesulfinyl ketimines are easily accessible by the direct condensation of sulfinamide **1** with ketones, this method provides rapid access to α,α-dibranched homoallylamines, where the alkene can be elaborated to other functionality.[8b,18]

The addition of other Grignard reagents, such as PhMgBr proceeded poorly (entry 3). In addition, the diastereofacial selectivity was opposite of that observed for the allylations of **3**, as well as the 1,2-additions to aldimines **2**. Other organometallic reagents were also investigated, but organoceriums and cuprates derived from Grignard reagents provided no reaction with *tert*-butanesulfinyl ketimines at 0 °C in CH_2Cl_2. The 1,2-additions of organolithiums were far more promising. With toluene as solvent, the additions of organolithiums to sulfinyl ketimines **3a-3d** proceeded rapidly at –78 °C with both encouraging yields and diastereoselectivities (entries 4-8). Only the 1,2-addition to the more acidic imine **3c** proceeded with a poor yield, and the only diastereoselectivity worse than 5:1 was observed for the addition to imine **3d** (*E*:*Z* = 5).

To improve both yields and selectivities, the effects of Lewis acidic additives or more Lewis acidic organometallic reagents were investigated (eq 4; Table 4). Organoceriums and zincates prepared from organolithiums did not react with **3a** (entries 1-2). Although lithium tetraalkylaluminates were also ineffective as alkyl transfer reagents, when trialkylaluminums were reacted first with the sulfinyl imines **3** in toluene before addition of the resulting mixture to a solution of organolithium at –78 °C, both yields and selectivities were substantially improved (entries 3-9). Varying the trialkylaluminum species among Et_2AlPh, *i*-Bu_3Al, and Me_3Al had no appreciable effect on the diastereocontrol of the addition of PhLi to **3a** (entries 4-6). However,

Table 4. Effects of Lewis Acids on 1,2-Additions of Organometallic Reagents to **3** (eq 2).[a]



3 **6** (4)

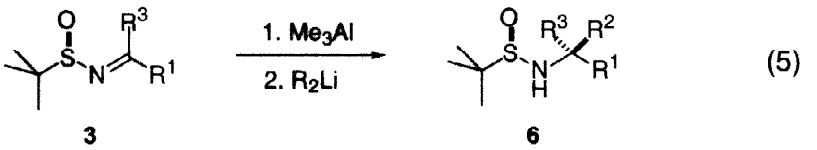
	sulfinyl ketimine **3**					sulfinamide **6**		
entry	compound	R^1	R^3	R^2M	additive	compound	yield (%)[b]	dr[c]
1	(R_S)-**3a**	Me	*i*-Pr	$PhLi/CeCl_3$		—	NR	—
2	(R_S)-**3a**	Me	*i*-Pr	$LiEt_2ZnPh$		—	NR	—
3	(R_S)-**3a**	Me	*i*-Pr	$LiEt_2AlPh_2$		—	NR	—
4	(R_S)-**3a**	Me	*i*-Pr	PhLi	Et_2AlPh	(R_S,*R*)-**6c**	57	98:2
5	(R_S)-**3a**	Me	*i*-Pr	PhLi	*i*-Bu_3Al	(R_S,*R*)-**6c**	76	97:3
6	(R_S)-**3a**	Me	*i*-Pr	PhLi	Me_3Al	(R_S,*R*)-**6c**	93	97:3
7	(R_S)-**3b**	Bu	*i*-Pr	PhLi	Me_3Al	(R_S,*R*)-**6d**	82	91:9
8	(R_S)-**3b**	Bu	*i*-Pr	PhLi	Et_2AlPh	(R_S,*R*)-**6d**	75	81:19
9	(R_S)-**3b**	Bu	*i*-Pr	PhLi	Et_2Al*t*-Bu	(R_S,*R*)-**6d**	34	84:16
10	(R_S)-**3a**	Me	*i*-Pr	PhMgBr	Et_2AlPh	(R_S,*S*)-**6c**	19	69:31
11	(R_S)-**3b**	Bu	*i*-Pr	PhLi	Et_2Zn	(R_S,*R*)-**6d**	16	86:14
12	(R_S)-**3b**	Bu	*i*-Pr	PhLi	BF_3-OEt_2	(R_S,*R*)-**6d**	44	76:24
13	(R_S)-**3b**	Bu	*i*-Pr	PhLi	$ZnCl_2$	(R_S,*R*)-**6d**	26	59:41
14	(R_S)-**3b**	Bu	*i*-Pr	PhLi	$MgBr_2$	(R_S,*R*)-**6d**	38	72:28

[a] Reactions were performed by the slow addition of a toluene solution of **3** and additive (1.1 equiv) to a solution of R^2M at -78 °C in toluene. [b] Isolated yields of analytically pure material. [c] Diastereomeric ratios were determined from GC or HPLC assays. See Experimental Section for details.

for the 1,2-addition of PhLi to **3b**, Me_3Al provided higher levels of diastereocontrol than other trialkylaluminums (entries 7-9). In addition, Me_3Al consistently afforded higher yields than the other trialkylaluminums for the phenyl additions to both **3a** and **3b**. Lewis acids other than trialkylaluminums were also investigated. Zinc, boron, and magnesium salts were inferior to Me_3Al, resulting in less desirable selectivities and yields for the phenyl transfer to **3b** than were observed for the phenyl additions performed in the absence of additives (entries 11-14). Trialkylaluminums had no effect on the 1,2-addition PhMgBr to **3a** (entry 10 in Table 4, and entry 3 in Table 3).

The generality of the Me_3Al mediated 1,2-addition of organolithiums to *tert*-butanesulfinyl ketimines **5** was next investigated. Sulfinyl imines **3a-g** were treated with Me_3Al before being added slowly to a stirring solution of various organolithiums in toluene at –78 °C (eq 5; Table 5). The Me_3Al mediated 1,2-addition of organolithiums is surprisingly general. Yields are good to excellent, and diastereselectivities for 1,2-additions to sulfinyl ketimines that are isolated as only the *E* isomer (**3a**, **3b**, **3c**, **3f**, and **3g**) are high, ranging from 9:1 to 99:1. Significantly, the diastereoselectivity for the addition of PhLi to **3d**, derived from methyl butyl ketone, which is isolated as an equilibrating mixture of *E* and *Z* isomers, is higher than the initial *E:Z* ratio (entry 6). Moreover, alkyl and aryl lithiums react in good yields and with high levels of diastereocontrol to provide α,α-dibranched sulfinamides **6**. It should be noted that this procedure is not effective for additions of

Table 5. Me_3Al–Mediated 1,2-Additions of Organolithiums to **3**.[a]



3 6 (5)

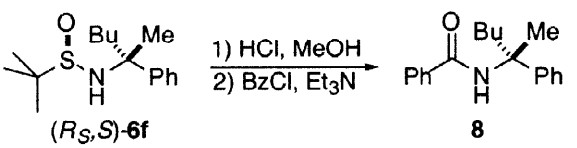
	sulfinyl ketimine **3**				sulfinamide **6**		
entry	compound	R^1	R^3	R^2Li	compound	yield (%)[b]	dr[c]
1	(R_S)-**3a**	Me	*i*-Pr	Bu	(R_S,*S*)-**6e**	61	99:1
2	(R_S)-**3a**	Me	*i*-Pr	Ph	(R_S,*R*)-**6c**	93	97:3
3	(R_S)-**3b**	Bu	*i*-Pr	Me	(R_S,*R*)-**6e**	82	91:9
4	(R_S)-**3b**	Bu	*i*-Pr	Ph	(R_S,*R*)-**6d**[d]	82	91:9
5	(R_S)-**3c**	Me	Ph	Bu	(R_S,*S*)-**6f**	86	98:2
6	(R_S)-**3d**[e]	Me	Bu	Ph	(R_S,*R*)-**6f**	93	89:11
7	(R_S)-**3e**[f]	Me	*i*-Bu	Ph	(R_S,*R*)-**6g**[d]	62	85:15
8	(R_S)-**3f**	Me	2-Npth	Ph	(R_S,*R*)-**6h**[d]	62	99:1
9	(R_S)-**3g**	Bu	Ph	Me	(R_S,*R*)-**6f**	quant.	99:1
10	(R_S)-**2b**	Et	H	Ph	(R_S,*R*)-**3e**	95	67:33

[a] Reactions were performed by the slow addition of a toluene solution of **3** and Me_3Al (1.1 equiv) to a solution of R^2Li at –78 °C in toluene. [b] Isolated yields of analytically pure material. [c] Diastereomeric ratios were determined from GC or HPLC assays. See Experimental Section for details. [d] Configurations assigned from the transition state model. [e] Sulfinyl ketimine **3d** exists as a 5:1 mixture of *E* and *Z* isomers. [f] Sulfinyl ketimine **3e** exists as a 6:1 mixture of *E* and *Z* isomers.

organolithiums to aldimines **2** (entry 10).

The determination of the absolute stereochemistries for the α,α-dibranched amines derived from sulfinamides **6** was complicated by the limited number of alternative methods available to prepare enantiomerically enriched α,α-dibranched amines. For the stereochemical assignment of the amine derived from **6f**, benzamide **8** was prepared by acidic methanolysis of **6f** followed by benzoylation in quantitative yield

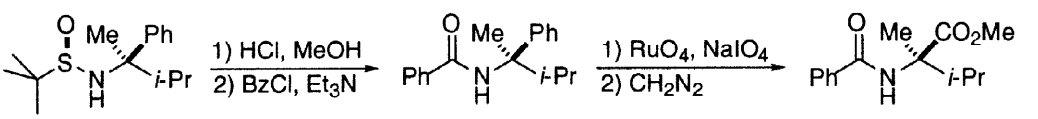
Scheme 3



(R_S,*S*)-**6f** **8**

$[\alpha]_D^{23}$ = +22.0 ° (*c*, 1.0, PhH)

lit. (ref. 19)$[\alpha]_{589}^{18}$ = +3.5 ° (*c*, 1.0, PhH)



(R_S,*S*)-**6c** **9** **10**

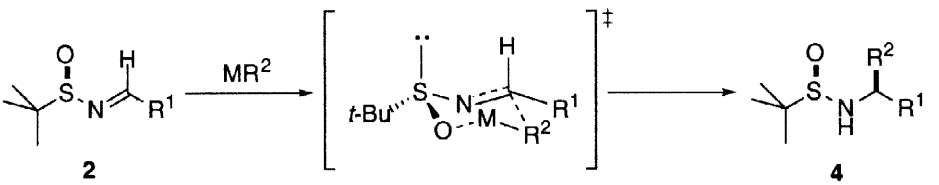
$[\alpha]_D^{23}$ = -21.4 ° (*c*, 1.0, $CHCl_3$)

lit. (ref. 20)$[\alpha]_D^{23}$ = -20.5 ° (*c*, 0.2, $CHCl_3$)

(Scheme 3). The absolute configuration of **8** had previously been determined by Arcus and coworkers, and was corroborated in later work by Hoshi and coworkers by chemical correlation.[19] Similarly, the configuration at the α-site of **6c** was determined by preparation of its benzamide **9** in the same manner as for **6f**. Oxidation of **9** to the benzamido acid followed by methylation afforded the benzamido ester **10**, whose absolute configuration has been determined by X-ray analysis of a dipeptide precursor.[20] The stereochemical configuration of (R_S,R)-**6e** was determined from the X-ray crystal structure of the 4-bromobenzamide derivative prepared after sulfinyl cleavage.

Mechanistic Models that Predict the Stereochemical Outcomes of the 1,2 Addition Reactions. For the additions of Grignard reagents to **2**, a six-membered ring transition state with Mg coordinated to the oxygen of the sulfinyl group can be proposed (Scheme 4) based upon the data in Tables 1

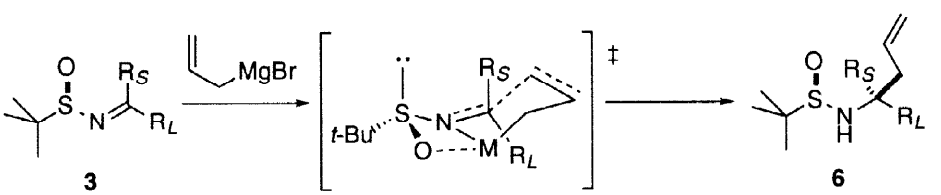
Scheme 4



and 2. In this transition state, the bulky *tert*-butyl group occupies the less hindered equatorial position resulting in preferential attack from the same face for all additions. This transition state is consistent with the observed asymmetric induction for all of the reactions performed and is consistent with the observed solvent effects. The non-coordinating solvent, CH_2Cl_2, provides the highest selectivities, while more strongly coordinating solvents like Et_2O and especially THF likely interfere with the formation of the proposed six-membered ring transition state resulting in reduced selectivities.

Allylations of ketimines have been far more successful than the additions of other alkyl, aryl, or alkenyl carbanions.[4] Indeed, the addition of allylmagnesium bromide to sulfinyl imines is precedented for *p*-toluenesulfinyl imines.[8b,18] The same high levels of diastereocontrol are also observed for allylmagnesium bromide additions to *tert*-butanesulfinyl ketimines **3**. The face selectivity for additions to ketimines **3** is also consistent with the six-membered ring transition state proposed by Hua for allyl additions to toluenesulfinyl imines (Scheme 5). Activation of the imine by coordination of magnesium to the imine nitrogen in this

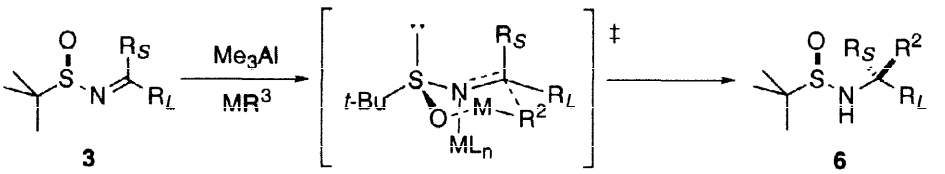
Scheme 5



concerted transition state may explain the higher yields and stereoselectivities that are observed for allyl Grignard additions relative to the additions of other Grignard reagents.

The transition state shown in Scheme 6 is consistent with all of the experimental data for the Me_3Al mediated 1,2-additions of organolithiums to **3**. First, lithium tetraalkylaluminums do not transfer an alkyl group to **3**, therefore the 1,2-additions of organolithiums to **3** in the presence of Me_3Al must occur faster than aluminate formation. Second, the substantial effect of Me_3Al on yield and diastereocontrol supports formation

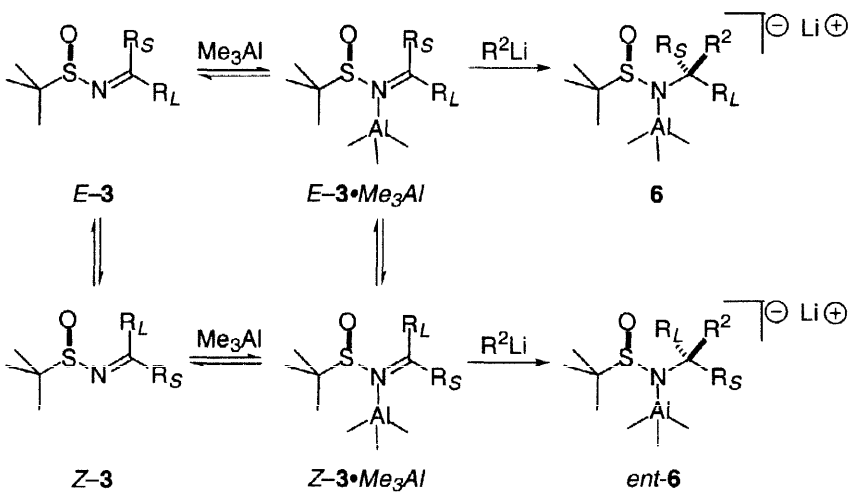
Scheme 6



of a reactive **3**-Me_3Al complex. Third, solvent effects further support a **3**-Me_3Al complex, since coordinating ethereal solvents result in dramatically reduced yields and selectivity. Finally, the six-membered transition state model correctly predicts the product stereochemistry for the five compounds whose configurations could be determined ((*R*$_S$,*R*)-**6c**, (*R*$_S$,*R*)-**6e**, (*R*$_S$,*S*)-**6e**, (*R*$_S$,*R*)-**6f**, and (*R*$_S$,*S*)-**6f**). This constitutes six different 1,2-addition reactions in Table 5 that deliver sulfinamides **6c**, **6e** and **6f**. The remaining products have been tentatively assigned based on this model.

One of the most intriguing characteristics of the 1,2-additions to **3** is that diastereoselectivities that exceed the initial *E*:*Z* ratio of the imine **3** can be obtained. It has been established that *p*-toluenesulfinyl ketimines are in rapid equilibrium between *E* and *Z* isomers ($\Delta G^{\ddagger}$ = 13–17 kcal/mol).[17] Assuming the formation of complexes *E*- and *Z*-**3**–Me_3Al in Scheme 7, rapid isomerization may result in a ratio of E-to Z **3**-Me_3Al that

Scheme 7



differs from the initial E- to Z ratio of the uncomplexed imine. Potentially, the product ratio could reflect the *E*- to *Z*-**3**–Me_3Al ratio. Analysis of ^1H NMR spectra of sulfinyl imine **5d**-Me_3Al recorded in toluene-d^8 indicates that there is no change in the *E*:*Z* ratio from the parent imine **5d** (derived from methyl butyl ketone; *E*:*Z* = 5) at

either 22 °C or -78 °C. The selectivity therefore likely arises from a difference in reaction rates between the two Me_3Al imine isomers that are in rapid equilibrium under the reaction conditions.

CONCLUSION

High yielding and highly diastereoselective methods for 1,2-additions of organometallic reagents to *N-tert*-butanesulfinyl aldimines (**2**) and *N-tert*-butanesulfinyl ketimines (**3**) are described. The effects of different organometallic reagents, solvents, and additives are compared, and the additions to a diverse set of imines with different steric and electronic properties are demonstrated. Transition-state models are presented that consistently predict diastereofacial selectivity for each type of transformation. Acidic methanolysis of the sulfinamide products (**4** and **6**) delivers highly enantioenriched α-branched and α,α-dibranched amines. Since a broad range of sulfinyl imines are easily accessible by condensation of aldehydes and ketones and the inexpensive reagent *tert*-butanesulfinamide (**1**), a broad range of enantioentriched amines with α-stereocenters may be prepared.

ACKNOWLEDGEMENTS

The support of the NSF, Abbott laboratories, and Berlex Biosciences is gratefully acknowledged. D. A. C. and G. L. thank Pharmacia & Upjohn for graduate fellowships.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl and toluene was distilled from sodium immediately before use. All reactions were carried out in flame or oven dried glassware under a nitrogen atmosphere. Chromatography was carried out using Merck 60 230-400 mesh silica gel. IR spectra of liquids were recorded as thin films on NaCl plates and IR spectra of solids were recorded as KBr pellets. Chemical shifts in NMR spectra are expressed in ppm. Unless otherwise noted, NMR spectra were obtained in $CDCl_3$ with TMS as an internal standard at room temperature. *tert*-Butanesulfinamide **1**[13a,14] and *tert*-butanesulfinyl imines **2** and **3**[15] were prepared as previously described. Methods for the determination of the absolute stereochemistry of compounds **6c** and **6f** have been previously described.[13b]

General procedure for addition of Grignard reagents to *N-tert*-butanesulfinyl aldimines 2. To a solution of (R_S)-**2** in CH_2Cl_2 at –48 °C was added Grignard reagent in Et_2O. The mixture was stirred at –48 °C for 4-6 h and then was warmed to rt with stirring overnight. When complete, the reaction mixture was quenched by the addition of sat'd aq. NH_4Cl and diluted with EtOAc. The organic layer was removed, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4. Unless otherwise noted, extractive isolation provided analytically pure material.

Unpurified amines (1-2 mg) prepared by treatment of **5** with HCl in MeOH were derivatized with an excess of (*R*)- and (*S*)-α–methoxy-α–(trifluoromethyl)phenylacetyl (MTPA) chloride according to Mosher's procedure.[21] Ratios of the MTPA amide diastereomers were determined by gas chromatography (GC) analysis.

Product Characterization

***N*-(1,2-Dimethyl-propyl)-2-methylpropylsulfinamide (4a).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5a** (HP Ultra II column, 100-250 °C, 2 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5a** t_R = 32.8 min, (*S*)-**5a** t_R = 33.8 min).

(R_S,*S*)-4a. ^{1}H NMR (300 MHz) δ 0.87 (d, *J* = 4.1, 3H), 0.90 (d, *J* = 4.1, 3H), 1.21 (s, 9H), 1.21 (d, *J* = 6.7, 3H), 1.70-1.77 (m, 1H), 2.81 (d, *J* = 7.0, 1H), 3.15-3.25 (m, 1H). Anal. Calcd for $C_9H_{21}NOS$: C, 56.50; H, 11.06; N, 7.32. Found: C, 56.24; H, 10.89; N, 7.46.

***N*-(1-Methylpropyl)-2-methylpropylsulfinamide (4b).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5b** (HP Ultra II column, 100-250 °C, 2 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5b** t_R = 29.6 min, (*S*)-**5b** t_R = 30.2 min).

(R_S,*S*)-4b. ^{1}H NMR (300 MHz) δ 0.91 (t, *J* = 7.4, 3H), 1.19 (s, 9H), 1.24 (d, *J* = 5.3, 3H), 1.44-1.55 (m, 2H), 2.85 (d, *J* = 6.2, 1H), 3.21-3.32 (m, 1H). Anal. Calcd for $C_8H_{19}NOS$: C, 54.19; H, 10.80; N, 7.90. Found: C, 53.87; H, 10.75; N, 8.17.

***N*-(1-Phenylethyl)-2-methylpropylsulfinamide (4c).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5c** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5c** t_R = 16.3 min, (*S*)-**5c** t_R = 16.7 min).

(R_S,*S*)-4c. ^{1}H NMR (300 MHz) δ 1.27 (s, 9H), 1.47 (d, *J* = 10.3, 3H), 3.32 (b, 1H), 4.56-4.58 (m, 1H), 7.25-7.33 (m, 5H). Anal. Calcd for $C_{12}H_{19}NOS$: C, 63.96; H, 8.50; N, 6.22. Found: C, 64.07; H, 8.18; N, 6.27.

***N*-(1-Ethyl-2-methylpropyl)-2-methylpropylsulfinamide (4d).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5d** (HP Ultra II column, 100-250 °C, 2 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5d** t_R = 37.2 min, (*S*)-**5d** t_R = 37.7 min).

(R_S,*S*)-4d. ^{1}H NMR (300 MHz), δ 0.84 (d, *J* = 6.8, 3H), 0.89 (d, *J* = 6.8, 3H), 0.93 (t, *J* = 7.5, 3H), 1.22 (s, 9H), 1.53-1.63 (m, 2H), 1.77-1.86 (m, 1H), 2.84 (d, *J* = 7.2, 1H), 2.93-2.99 (m, 1H). Anal. Calcd for $C_{10}H_{23}NOS$: C, 58.49; H, 11.29; N, 6.82. Found: C, 58.34; H, 11.02; N, 6.82.

(R_S,*R*)-4d. ^{1}H NMR (300 MHz) δ 0.89-0.98 (m, 9H), 1.22 (s, 9H), 1.37-1.47 (m, 1H), 1.51-1.59 (m, 1H), 1.89-2.00 (m, 1), 2.92-3.00 (m, 1H), 3.06 (d, *J* = 7.0, 1H). Anal. Calcd for $C_{10}H_{23}NOS$: C, 58.49; H, 11.29; N, 6.82. Found: C, 58.27; H, 11.22; N, 7.09.

***N*-(1-Phenylpropyl)-2-methylpropylsulfinamide (4e).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5e** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5e** t_R = 17.6 min, (*S*)-**5e** t_R = 18.0 min).

(R_S,*S*)-4e. ^{1}H NMR (300 MHz) δ 0.84 (t, *J* = 7.4, 3H), 1.18 (s, 9H), 1.78-1.90 (m, 2H), 3.39 (br, 1H), 4.26-4.31 (m, 1H), 7.23-7.41 (m, 5H). Anal. Calcd for $C_{13}H_{21}NOS$: C, 65.23; H, 8.84; N, 5.85. Found: C, 65.38; H, 9.05; N, 6.16.

(R_S,*R*)-4e. ^{1}H NMR (300 MHz) δ 0.79 (t, *J* = 7.4, 3H), 1.22 (s, 9H), 1.73-1.83 (m, 1H), 1.96-2.12 (m, 1H), 3.38 (d, *J* = 2.6, 1H), 4.25-4.30 (m, 1H). Anal. Calcd for $C_{13}H_{21}NOS$: C, 65.23; H, 8.84; N, 5.85. Found: C, 65.44; H, 8.85; N, 5.86.

***N*-(2-Methy-1-phenylpropyl)-2-methylpropylsulfinamide (4f).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5f** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5f** t_R = 18.3 min, (*S*)-**5f** t_R = 18.6 min).

(R_S,*S*)-4f. ^{1}H NMR (300 MHz) δ 0.80 (d, *J* = 6.8, 3H), 0.98 (d, *J* = 6.7, 3H), 1.19 (s, 9H), 2.04-2.23 (m, 1H), 3.47 (br, 1H), 4.15 (d, *J* = 5.4 Hz, 1H), 7.23-7.34 (m, 5H). Anal. Calcd for $C_{14}H_{23}NOS$: C, 66.36; H, 9.15; N, 5.53. Found: C, 66.58; H, 8.90; N, 5.13.

(R_S,*R*)-4f. ^{1}H NMR (300 MHz) δ 0.80 (d, *J* = 6.7, 3H), 0.92 (d, *J* = 6.8, 3H), 1.24 (s, 9H), 2.16-2.27 (m, 1H), 3.45 (br, 1H), 4.15 (t, *J* = 5.5, 1H), 7.24-7.61 (m, 5H). Anal. Calcd for $C_{14}H_{23}NOS$: C, 66.36; H, 9.15; N, 5.53. Found: C, 66.47; H, 9.40; N, 5.74.

***N*-(1-(2-propyl)allyl)-2-methylpropylsulfinamide (4g).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5g** (HP Ultra II column, 100-250 °C, 2 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5g** t_R = 35.8 min, (*S*)-**5g** t_R = 36.1 min).

(R_S,*S*)-4g. ^{1}H NMR (300 MHz) δ 0.87 (d, *J* = 6.8, 3H), 0.90 (d, *J* = 6.8, 3H), 1.22 (s, 9H), 1.83-1.95 (m, 1H), 3.08 (d, *J* = 6.4, 1H), 3.54-3.61 (m, 1H), 5.19-5.29 (m, 2H), 5.75-5.86 (m, 1H). Anal. Calcd for $C_{10}H_{21}NOS$: C, 59.07; H, 10.41; N, 6.89. Found: C, 59.10; H, 10.25; N, 6.57.

***N*-(1-Phenylallyl)-2-methylpropylsulfinamide (4h).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5h** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5h** t_R = 17.2 min, (*S*)-**5h** t_R = 17.6 min).

(R_S,*S*)-4h. ^{1}H NMR (300 MHz) δ 1.21 (s, 9H), 4.96 (d, *J* = 6.8, 1H), 5.18-5.32 (m, 2H), 5.99-6.10 (m, 1H), 7.26-7.49 (m, 5H). Anal. Calcd. for $C_{13}H_{19}NOS$: C, 65.78; H, 8.07; N, 5.90. Found: C, 66.03; H, 8.49; N, 5.85.

***N*-(1-Methyl-2-phenylethyl)-2-methylpropylsulfinamide (4i).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5i** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5i** t_R = 18.2 min, (*S*)-**5i** t_R = 18.7 min).

(R_S,*S*)-4i. ^{1}H NMR (500 MHz) δ 1.12 (s, 9H), 1.23 (d, *J* = 6.5, 3H), 2.71 (dd, *J* = 13.5, 6.5, 1H), 2.85 (dd, *J* = 13.5, 6.5, 1H), 3.00 (d, *J* = 6.0, 1H), 3.60-3.64 (m, 1H), 7.17-7.30 (m, 5H). Anal. Calcd for $C_{13}H_{21}NOS$: C, 65.23; H, 8.84; N, 5.85. Found: C, 64.92; H, 9.03; N, 5.79.

***N*-(1-Benzylpropyl)-2-methylpropylsulfinamide (4j).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5j** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5j** t_R = 19.7 min, (*S*)-**5j** t_R = 20.0 min).

(R_S,*S*)-4j. ^{1}H NMR (500 MHz) δ 1.01 (t, *J* = 7.5, 3H), 1.09 (s, 9H), 1.65-1.72 (m, 2H), 2.77-2.84 (m, 2H), 3.05 (d, *J* = 6.0, 1H), 3.39-3.43 (m, 1H), 7.19-7.29 (m, 5H). Anal. Calcd for $C_{14}H_{23}NOS$: C, 66.36; H, 9.15; N, 5.53. Found: C, 66.41; H, 9.06; N, 5.52.

***N*-(1-1-Benzylallyl)-2-methylpropylsulfinamide (4k).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5k** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5k** t_R = 19.1 min, (*S*)-**5k** t_R = 19.4 min).

(R_S,*R*)-4k. ^{1}H NMR (500 MHz) δ 1.10 (s, 9H), 2.83-2.96 (m, 2H), 3.21 (b, 1H), 4.00-4.10 (m, 1H), 5.14-5.32 (m, 2H), 5.85-5.97 (m, 1H), 7.16-7.33 (m, 5H). Anal. Calcd. for $C_{14}H_{21}NOS$: C, 66.89; H, 8.42; N, 5.57. Found: C, 66.93; H, 8.52; N, 5.37.

***N*-(1,2-Diphenylethyl)-2-methylpropylsulfinamide (4l).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5l** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5l** t_R = 30.3 min, (*S*)-**5l** t_R = 30.7 min).

(R_S,*R*)-4l. ^{1}H NMR (500 MHz) δ 1.15 (s, 9H), 3.01 (dd, *J* = 13.5, 7.5, 1H), 3.29 (dd, *J* = 13.5, 7.0, 1H), 3.55 (d, *J* = 3.5, 1H), 4.57-4.61 (m, 1H), 7.00-7.59 (m, 10H). Anal. Calcd for $C_{18}H_{23}NOS$: C, 71.72; H, 7.69; N, 4.65. Found: C, 71.61; H, 7.49; N, 4.78.

***N*-(1,2-Diphenylethyl)-2-methylpropylsulfinamide (4m).** The diastereomeric ratio was determined by chiral GC analysis of the MTPA derivatives of **5m** (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-**5m** t_R = 22.0 min, (*S*)-**5m** t_R = 22.5 min).

(R_S,*S*)-4m. ^{1}H NMR (500 MHz) δ 0.82 (t, *J* = 7.5, 3H), 1.17 (s, 9H), 1.71-1.85 (m, 2H), 3.37 (d, *J* = 2.0, 1H), 3.79 (s, 3H), 4.10-4.12 (m, 1H), 6.86 (d, *J* = 8.5, 2H), 7.19 (d, *J* = 8.5, 2H). Anal. Calcd for $C_{14}H_{23}NO_2S$: C, 62.42; H, 8.61; N, 5.20. Found: C, 62.17; H, 8.67; N, 5.20.

Specific Experimental Procedures

Addition of MeMgBr to (R_S)-2b (Table 2, entry 1). To a solution of 0.200 g (1.24 mmol) of (R_S)-**2c** in 7.44 mL of CH_2Cl_2 was added 0.83 mL (3.0 M in Et_2O, 2.48 mmol) MeMgBr. Workup provided 0.211 g (97%) of (R_S,*S*)-**4b** as a colorless oil with a 98:2 dr.

Addition of *i*-PrMgBr to (R_S)-2b (Table 2, entry 2). To a solution of 0.200 g (1.24 mmol) of (R_S)-**2c** in 7.44 mL of CH_2Cl_2 was added 0.95 mL (2.6 M in Et_2O, 2.48 mmol) of *i*-PrMgBr. Workup provided 0.246 g (97%) of (R_S,*R*)-**4d** as a colorless oil with a 98:2 dr.

Addition of PhMgBr to (R_S)-2b (Table 2, entry 3). To a solution of 0.200 g (1.24 mmol) of (R_S)-**2b** in 7.44 mL of CH_2Cl_2 was added 0.83 mL (3.0 in Et_2O, 2.48 mmol) of PhMgBr. Workup provided 0.300 g (quantitative yield) of (R_S,*R*)-**4e** as a white solid with a 96:4 dr.

Addition of MeMgBr to (R_S)-2a (Table 2, entry 4). To a solution of 0.200 g (1.14 mmol) of (R_S)-**2a** in 6.84 mL of CH_2Cl_2 was added 0.76 mL (3.0 in Et_2O, 2.28 mmol) of MeMgBr. Workup provided 0.215 g (98%) of (R_S,*S*)-**4a** as a colorless oil with a 98:2 dr.

Addition of EtMgBr to (R_S)-2a (Table 2, entry 5). To a solution of 0.200 g (1.14 mmol) of (R_S)-**2a** in 6.84 mL of CH_2Cl_2 was added 0.76 mL (3.0 in Et_2O, 2.28 mmol) of EtMgBr. Workup provided 0.235 g (quantitative yield) of (R_S,*S*)-**4d** as a colorless oil with a 97:3 dr.

Addition of PhMgBr to (R_S)-2a (Table 2, entry 6). To a solution of 0.100 g (0.570 mmol) of (R_S)-**2a** in 3.42 mL of CH_2Cl_2 was added 0.38 mL (3.0 in Et_2O, 1.14 mmol) of PhMgBr. Chromatography (50:50 EtOAc/hexanes) afforded 0.141 g (98%) of (R_S,*R*)-**4f** as a white solid with a 89:11 dr.

Addition of vinylmagnesium bromide to (R_S)-2a (Table 2, entry 7). To a solution of 0.23 g (1.31 mmol) of (R_S)-**2a** in 6.35 mL of CH_2Cl_2 was added 2.38 mL (1.1 M in Et_2O, 2.62 mmol) of vinylmagnesium bromide. Chromatography (60:40 EtOAc/hexanes) afforded 0.240 g (90%) of (R_S,*S*)-**4g** as a colorless oil with a 88:12 dr.

Addition of MeMgBr to (R_S)-2c (Table 2, entry 8). To a solution of 0.200 g (0.96 mmol) of (R_S)-**2c** in 5.76 mL of CH_2Cl_2 was added 0.64 mL (3.0 in Et_2O, 1.92 mmol) of MeMgBr. Workup provided 0.208 g (96%) of (R_S,*S*)-**4c** as a pale yellow solid with a 97:3 dr.

Addition of EtMgBr to (R_S)-2c (Table 2, entry 9). To a solution of 0.300 g (1.43 mmol) of (R_S)-**2b** in 8.57 mL of CH_2Cl_2 was added 0.96 mL (3.0 in Et_2O, 2.86 mmol) of EtMgBr. Workup provided 0.335 g (98%) of (R_S,*S*)-**4e** as a pale yellow solid with a 92:8 dr.

Addition of *i*-PrMgBr to (R_S)-2c (Table 2, entry 10). To a solution of 0.050 g (0.24 mmol) of (R_S)-**2b** in 1.42 mL of CH_2Cl_2 was added 0.18 mL (2.6 M in Et_2O, 0.48 mmol) of *i*-PrMgBr. Chromatography (40:60 EtOAc/hexanes) afforded 0.018 g (29%) of (R_S,*S*)-**4f** as a white solid with a 97:3 dr, and 0.031 g (61%) of (*R*)-*N*-benzyl-*tert*-butanesulfinamide[14] as the side product.

Addition of vinylmagnesium bromide to (R_S)-2c (Table 2, entry 11). To a solution of 0.250 g (1.20 mmol) of (R_S)-**2b** in 5.82 mL of CH_2Cl_2 was added 2.18 mL (1.1 M in Et_2O, 2.40 mmol) vinylmagnesium bromide. Chromatography (60:40 EtOAc/hexanes) afforded 0.224 g (79%) of (R_S,*S*)-**4h** as a white solid with a 94:6 dr.

Addition of MeMgBr to (R_S)-2d (Table 2, entry 12). To a solution of 0.25 g (1.12 mmol) of (R_S)-**2d** in 7.02 mL of CH_2Cl_2 was added 0.45 mL (3.0 M in Et_2O, 1.34 mmol, 1.2 equiv) MeMgBr. Chromatography (60:40 EtOAc/hexanes) afforded 0.239 g (89%) of (R_S,*S*)-**4i** as a white solid with a 95:5 dr.

Addition of EtMgBr to (R_S)-2d (Table 2, entry 13). To a solution of 0.250 g (1.12 mmol) of (R_S)-**2d** in 7.02 mL of CH_2Cl_2 was added 0.46 mL (2.9 M in Et_2O, 1.33 mmol, 1.2 equiv) EtMgBr. Chromatography (60:40 EtOAc/hexanes) afforded 0.242 g (85%) of (R_S,*S*)-**4j** as a white solid with a 92:8 dr.

Addition of vinylmagnesium bromide to (R_S)-2d (Table 2, entry 14). To a solution of 0.250 g (1.12 mmol) of (R_S)-**2d** in 6.13 mL of CH_2Cl_2 was added 2.04 mL (1.1 M in Et_2O, 2.24 mmol, 2.0 equiv) vinylmagnesium bromide. Chromatography (60:40 EtOAc/hexanes) afforded 0.221 g (81%) of (R_S,*R*)-**4k** as a white solid with a 91:9 dr.

Addition of PhMgBr to (R_S)-2d (Table 2, entry 15). To a solution of 0.25 g (1.12 mmol) of (R_S)-**2d** in 7.02 mL of CH_2Cl_2 was added 0.45 mL (3.0 M in Et_2O, 1.34 mmol, 1.2 equiv) PhMgBr. Chromatography (50:50 EtOAc/hexanes) afforded 0.276 g (81%) of (R_S,*R*)-**4l** as a white solid with a 95:5 dr.

Addition of EtMgBr to (R_S)-2e (Table 2, entry 16). To a solution of 0.400 g (1.67 mmol) of (R_S)-**2e** in 10.5 mL of CH_2Cl_2 was added 0.67 mL (3.0 M in Et_2O, 2.01 mmol, 1.2 equiv) EtMgBr. Chromatography (60:40 EtOAc/hexanes) afforded 0.394 g (88%) of (R_S,*S*)-**4m** as a white solid with a 99:1 dr.

Addition of PhMgBr, derived from PhLi and $MgBr_2$, to (R_S)-2b (Table 2, entry 17). To a mixture of 230 mg (1.25 mmol) of $MgBr_2$ in 250 μL of Et_2O was added 670 μL of PhLi (1.86 M; 1.25 mmol). The resulting slurry was stirred for 30 min at 0 °C before adding slowly to a solution of (*R*)-(–)-**2b** in 6.25 mL of CH_2Cl_2 at -48 °C. Workup provided 0.132 g (88%) of (R_S,*R*)-**4e** as a white solid with a 94:6 dr.

(R_S,*S*)-*N*-(1-Methyl-1-phenylbut-3-enyl)-*tert*-butanesulfinamide 6a. To a solution of 0.030 g (0.13 mmol) of (*R*)-(–)-**3c** in 0.60 mL of CH_2Cl_2 was added 0.26 mL (1.0 M in Et_2O, 0.26 mmol, 2.0 equiv) allylmagnesium bromide solution at 0 °C. The mixture was stirred at 0 °C for 6 h.Chromatography (40:60 EtOAc/hexanes) afforded 0.029 g (85%) of (R_S,*S*)-**6a** as a white solid. Only one diastereomer was observed by GC analysis of the MTPA derivative of **7a** (GC analysis (HP Ultra II column; 110-250 °C, 1 deg/min, 20 psi;(*R*)-MTPA derivative of (*R*)-**7a** (t_R = 90.5 min), (*S*)-**7a** (t_R = 91.0 min)). ^{1}H NMR (500 MHz) δ 1.22 (s, 9H), 1.77 (s, 3H), 2.67-2.69 (m, 2H), 3.77 (b, 1H), 5.11-5.15 (m, 2H), 5.52-5.60 (m, 1H), 7.23-7.44 (m, 5H). Anal. calcd for $C_{15}H_{23}NSO$: C, 67.88; H, 8.73; N, 5.28. Found: C, 68.07; H, 8.90; N, 5.22.

(R_S,*S*)-*N*-(1-Methyl-1-isopropyl-but-3-enyl)-*tert*-butanesulfinamide 6b. To a solution of 0.227 g (1.20 mmol) of (*R*)-(–)-**3a** in 5.60 mL of CH_2Cl_2 was added 2.40 mL (1.0 M in Et_2O, 2.40 mmol, 2.0 equiv) of allylmagnesium bromide solution at 0 °C. The mixture was stirred at 0 °C for 6 h. Chromatography (40:60 EtOAc/hexanes) afforded 0.259 g (93%) of (R_S,*S*)-**6b** as a white solid. ^{1}H NMR (500 MHz) δ 0.82-0.90 (m, 6H), 1.08 (s, 9H), 1.21 (s, 3H), 1.70-1.75 (m, 1H), 2.31-2.38 (m, 2H), 3.25 (b, 1H), 5.10-5.17 (m, 2H), 5.75-5.60 (m, 1H). Anal. calcd for $C_{12}H_{25}NSO$: C, 62.29; H, 10.72; N, 6.05. Found: C, 62.41; H, 10.72; N, 5.89.

For the (*R*)- MTPA amide of the crude material, only one diastereomer was observed by ^{1}H NMR: (500 MHz) δ 0.82 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H), 1.24 (s, 3H), 2.27-2.39 (m, 2H), 2.62-2.76 (m, 1H), 3.41 (s, 3H), 5.08 (m, 2H), 5.68-5.76 (m, 1H), 6.55 (b, 1H), 7.30-7.53 (m, 5H).

General procedure for the synthesis of α-branched amine hydrochlorides 5. To **4** was added 1:1 (v/v) MeOH and HCl dioxane solution (4.0 M, 2.0 equiv). The mixture was stirred at room temperature for 30 minutes and was then concentrated to near dryness. Diethyl ether was added to precipitate the amine hydrochloride. The precipitate was then filtered off and washed with diethyl ether or hexanes to provide analytically pure amine hydrochloride **5**.

(*S*)-1,2-Dimethylpropylamine hydrochloride (5a). Methanolysis of (R_S,*S*)-**4a** (0.173 g, 0.910 mmol) provided 0.108 g (97%) of scalemic (*S*)-**5a**. $[\alpha]_D^{23}$ -2.80 ° (*c* 4.0, MeOH) (lit.[22] $[\alpha]_D^{23}$ -2.16 ° (*c* 4.0, MeOH)). ^{1}H NMR (300 MHz, CD_3OD) δ 0.98 (t, *J* = 7.5 Hz, 6H), 1.22 (d, *J* = 6.7 Hz, 3H), 1.80-1.91 (m, 1H), 3.05-3.14 (m, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ 14.0, 16.1, 17.5, 31.3, 52.7. Anal. Calcd for $C_5H_{14}ClN$: C, 48.58; H, 11.41; N, 11.33. Found: C, 48.78; H, 11.35; N, 11.32.

(*S*)-2-1-Methylpropylamine hydrochloride (5b). Methanolysis of (R_S,*S*)-**4b** (0.189 g, 1.06 mmol) provided 0.112 g (97%) of scalemic (*S*)-**5b**. $[\alpha]_D^{23}$ -1.50 ° (*c* 4.0, MeOH) (lit.[23] $[\alpha]_D^{23}$ +2.64 ° (*c* 4.0, MeOH) for (*R*)-1-methylpropylamine hydrochloride). ^{1}H NMR (300 MHz, CD_3OD) δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.26 (d, *J* = 6.6 Hz, 3H), 1.48-1.75 (m, 2H), 3.14-3.21 (m, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ 10.3, 18.4, 28.9, 50.5.

(*S*)-1-Phenylethylamine hydrochloride (5c). Methanolysis of (R_S,*S*)-**4c** (0.184 g, 0.818 mmol) provided 0.113 g (88%) of scalemic (*S*)-**5c**. $[\alpha]_D^{23}$ -4.4 ° (*c* 4.0, MeOH) (lit.[24] $[\alpha]_D^{23}$ -4.6 ° (*c* 4.0, MeOH)). ^{1}H NMR (300 MHz, CD_3OD) δ 1.61 (d, *J* = 6.9 Hz, 3H), 4.43 (q, *J* = 6.9 Hz, 1H), 7.37-7.45 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 20.9, 52.5, 127.9, 130.3, 130.5, 139.8.

(*S*)-1-Ethyl-2-methylpropylamine hydrochloride (5d). Methanolysis of (R_S,*S*)-**4d** (0.210 g, 1.02 mmol) provided 0.130 g (93%) of scalemic (*S*)-**5d**. The (*S*) configuration is tentatively assigned. $[\alpha]_D^{23}$ -11.5 ° (*c* 4.0, MeOH). ^{1}H NMR (300 MHz, CD_3OD) 0.97-1.02 (M, 9H), 1.53-1.76 (M, 2H), 1.89-2.00 (m, 1H), 2.89-2.96 (m, 1). ^{13}C NMR (101 MHz, CD_3OD) δ 10.2, 18.2, 18.5, 23.8, 31.0, 60.0. Anal. Calcd for $C_6H_{16}ClN$: C, 52.35; H, 11.72; N, 10.18. Found: C, 52.70; H, 11.80; N, 10.23. Recrystallization from a mixture of *tert*-butyl methyl ether and ethanol provided optically pure amine hydrochloride as determined by GC analysis in 85% yield: $[\alpha]_D^{23}$ -12.0 ° (*c* 4.0, MeOH).

(*R*)-1-Ethyl-2-methylpropylamine hydrochloride (5d). Methanolysis of (R_S,*R*)-**4d** (0.218 g, 1.06 mmol) provided 0.132 g (92%) of scalemic (*R*)-**5d**. $[\alpha]_D^{23}$ +9.30 ° (*c* 4.0, MeOH). The (*R*) configuration is tentatively assigned.

(*R*)-1-Phenylpropylamine hydrochloride (5e). Methanolysis of (R_S,*S*)-**4e** (0.287 g, 1.20 mmol) provided 0.190 g (90%) of scalemic (*R*)-**5e**. Free amine $[\alpha]_D^{23}$+35.1 ° (*c* 1.0, $CHCl_3$) (lit.[25] $[\alpha]_D^{23}$ -36.6 ° (*c* 1.0, $CHCl_3$) for (*S*)-1-phenyl-propylamine). ^{1}H NMR (300 MHz, CD_3OD) δ 0.87 (t, *J* = 7.4 Hz, 3H), 1.88-2.13 (m, 2H), 4.12 (dd, *J* = 9.2, 6.0 Hz, 1H), 7.38-7.47 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 10.7, 28.9, 58.5, 128.5, 130.5, 130.5, 138.2. Anal. Calcd for $C_9H_{14}NSO$: C, 62.97; H, 8.22; N, 8.16. Found: C, 62.78; H, 7.97; N, 8.21.

(*S*)-1-Phenylpropylamine hydrochloride (5e). Methanolysis of (R_S,*S*)-**4e** (0.167 g, 0.698 mmol) provided 0.112 g (94%) of scalemic (*S*)-1-phenyl-propylamine hydrochloride. Amine $[\alpha]_D^{23}$ -30.0 ° (*c* 1.0, $CHCl_3$) (lit.[26] $[\alpha]_D^{23}$ -36.6 ° (*c* 1.0, $CHCl_3$)).

(*R*)-2-Methyl-1-phenylpropylamine hydrochloride (5f). Methanolysis of (R_S,*R*)-**5f** (0.136 g, 0.540 mmol) provided 0.090 g (91%) of scalemic (*R*)-**5f**. Free amine $[\alpha]_D^{23}$ +10.8 ° (*c* 1.0, $CHCl_3$) (lit.[12a] $[\alpha]_D^{23}$ -11.5 ° (*c* 1.0, $CHCl_3$) for (*S*)-2-methyl-1-phenyl-propylamine). Recrystallization from a mixture of *tert*-butane methyl ether and ethanol provided optically pure amine hydrochloride as determined by GC analysis in 76% yield: free amine $[\alpha]_D^{23}$ +11.6 ° (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD) δ 0.78 (d, *J* = 6.7 Hz, 3H), 1.12 (d, *J* = 6.6 Hz, 3H), 2.12-2.24 (m, 1H), 3.90 (d, *J* = 9.2 Hz, 1H), 7.35-7.48 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 19.6, 19.8, 34.1, 63.3, 128.7, 130.4, 130.4, 138.3.

(*S*)-1-Isopropylallylamine hydrochloride (5g). Methanolysis of (R_S,*S*)-**4g** (0.140 g, 0.070 mmol) provided 0.073 g (78%) of scalemic (*S*)-**5g**. The (*S*) configuration is tentatively assigned. $[\alpha]_D^{23}$ -17.6 ° (*c* 1.0, CD_3OD). ^{1}H NMR (500 MHz, CD_3OD) δ 0.99 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 1.91-2.02 (m, 1H), 3.51-3.52 (m, 1H), 5.40-5.52 (m, 2H), 5.81-5.88 (m, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ 17.9, 19.3, 32.2, 61.1, 122.1, 133.5. Anal. Calcd for $C_6H_{14}ClN$: C, 53.13; H, 10.40; N, 10.33. Found: C, 52.94; H, 10.78; N, 10.57.

(*R*)-1-Phenylallylamine hydrochloride (5h). Methanolysis of (R_S,*S*)-**4h** (0.140 g, 0.595 mmol) provided 0.928 g (93%) of scalemic (*R*)-**5h**. ^{1}H NMR (500 MHz, CD_3OD) δ 4.95-4.96 (m, 1H), 5.40-5.48 (m, 2H), 6.12-6.19 (m, 1H), 7.41-7.42 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 58.4, 120.2, 128.7, 130.4, 130.5, 135.4. Anal. Calcd for $C_9H_{12}NCl$: C, 63.72; H, 7.13; N, 8.26. Found: C, 63.87; H, 7.31; N, 8.22. Scalemic (*R*)-**5h** was hydrogenated followed by treatment with Na_2CO_3 to provide (*R*)-1-phenylpropylamine: $[\alpha]_D^{23}$ -28.2 ° (c 1.1, $CHCl_3$).

(*S*)-1-Methyl-2-phenylethylamine hydrochloride (5i). Methanolysis of (R_S,*S*)-**4i** (0.193 g, 0.810 mmol) provided 0.132 g (95%) of scalemic (*S*)-**5i**. $[\alpha]_D^{23}$ +11.1 ° (*c* 1.0, CH_2Cl_2). (lit.[26] $[\alpha]_D^{23}$ +12.5 ° (*c* 2.0, CH_2Cl_2). ^{1}H NMR (500 MHz, CD_3OD) δ 1.25 (d, *J* = 6.5 Hz, 3H), 2.79 (dd, *J* = 13.6, 8.0 Hz, 1H), 3.01 (dd, *J* = 14.0, 6.5 Hz, 1H), 3.49-3.56 (m, 1H), 7.25-7.37 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 18.4, 41.9, 50.4, 128.5, 130.1, 130.5, 137.5. Anal. Calcd for $C_9H_{14}ClN$: C, 62.97; H, 8.22; N, 8.16. Found: C, 63.19; H, 8.44; N, 7.90.

(*S*)-1-Benzyl-propylamine hydrochloride (5j). Methanolysis of (R_S,*S*)-**4j** (0.169 g, 0.670 mmol) provided 0.122 g (98%) of scalemic (*S*)-**5j**. $[\alpha]_D^{23}$ +33.9 ° (*c* 1.0, H_2O). (lit.[12a] $[\alpha]_D^{23}$ +33.16 ° (*c* 2.0, H_2O). ^{1}H NMR (500 MHz, CD_3OD) δ 1.03 (t, *J* = 7.5 Hz, 3H), 1.59-1.72 (m, 2H), 2.89-2.97 (m, 2H), 3.47-3.49 (m, 1H), 7.27-7.37 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 9.9, 26.4, 39.6, 55.7, 128.5, 130.2, 130.6, 137.4. Anal. Calcd for $C_{10}H_{16}ClN$: C, 64.68; H, 8.68; N, 7.54. Found: C, 64.86; H, 8.50; N, 7.63.

(*R*)-1-Benzylallylamine hydrochloride (5k). Methanolysis of (R_S,*R*)-**4k** (0.140 g, 0.560 mmol) provded 0.089 g (87%) of scalemic (*R*)-**4k**. $[\alpha]_D^{23}$ -4.1 ° (*c* 1.0, MeOH). ^{1}H NMR (500 MHz, CD_3OD) δ 2.95 (dd, *J* = 13.5, 8.5 Hz, 1H), 3.06 (dd, *J* = 13.5, 6.0 Hz, 1H), 3.96-4.00 (m, 1H), 5.26 (d, *J* = 17.5 Hz, 1H), 5.33 (d, *J* = 11.0 Hz, 1H), 5.82-5.89 (m, 1H), 7.24-7.36 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 40.6, 56.5, 121.2, 128.5, 130.0, 130.7, 134.8, 136.8. Anal. Calcd for $C_{10}H_{14}ClN$: C, 65.39; H, 7.68; N, 7.63. Found: C, 65.49; H, 7.81; N, 7.61. Scalemic amine was converted to (*R*)-3-*tert*-butoxycarbonylamino-4-phenyl-1-butene: $[\alpha]_D^{23}$ -30.0 ° (*c* 1.6, $CHCl_3$). (lit.[27] [α] +36.7 (c 9.0, $CHCl_3$) for (*S*)-3-*tert*-butoxycarbonylamino-4-phenyl-1-butene.

(*R*)-1, 2-Diphenylethylamine hydrochloride (5l). Methanolysis of (R_S,*R*)-**4l** (0.116 g, 0.385 mmol) provided 0.089 g (99%) of scalemic (*R*)-**5l**. ^{1}H NMR (500 MHz, CD_3OD) δ 3.20 (dd, *J* = 13.5, 9.0 Hz, 1H), 3.32 (dd, *J* = 13.5, 6.5 Hz, 1H), 4.51 (dd, *J* = 9.0, 6.5 Hz, 1H), 7.10-7.38 (m, 10H), 7.10-7.38 (m, 10H). ^{13}C NMR (125 MHz, CD_3OD) δ 42.1, 58.5, 128.4, 128.7, 129.9, 130.3, 130.4, 130.6, 137.0, 137.9. Anal. Calcd for $C_{10}H_{16}ClN$: C, 64.68; H, 8.68; N, 7.54. Found: C, 64.86; H, 8.50; N, 7.63. The amine hydrochloride was converted to the free amine by treatment with sodium carbonate. $[\alpha]_D^{23}$ -14.1 ° (*c* 1.6, $CHCl_3$). (lit.[22] $[\alpha]_D^{23}$ -10.9 ° (*c* 1.6, $CHCl_3$).

(*S*)-1-*p*-Methoxyphenylpropylamine hydrochloride (5m). Methanolysis of (R_S,*S*)-**4m** (0.231 g, 0.860 mmol) provided 0.173 g (quantitative yield) of (*S*)-**5m**. The (*S*) configuration is tentatively assigned. $[\alpha]_D^{23}$ +13.6 ° (*c* 1.0, MeOH). ^{1}H NMR (500 MHz, CD_3OD) δ 0.87 (t, *J* = 7.5 Hz, 3H), 1.89-2.07 (m, 2H), 3.81 (s, 3H), 4.10 (dd, *J* = 9.5, 5.5 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, H), 7.36 (d, *J* = 9.0 Hz, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ 10.7, 28.7, 56.0, 58.0, 115.7, 129.9, 129.9, 161.9. Anal. Calcd for $C_{10}H_{16}ClN$: C, 59.55; H, 8.00; N, 6.95. Found: C, 59.76; H, 7.89; N, 6.71.

(*S*)-1-Methyl-1-phenyl-3-butenylamine hydrochloride (7a). Methanolysis of (R_S,*S*)-**6a** (0.200 g, 0.750 mmol) was carried out as for α-branched sulfinamides **4**, except that after the reaction mixture was concentrated, 5 mL of toluene was added and the resulting solution was concentrated to near dryness. Hexanes was used for precipitation and washing to provide 0.125 g (85%) of (*S*)-**7a**. $[\alpha]_D^{23}$ -9.8 ° (*c* 1.0, MeOH). ^{1}H NMR (500 MHz, CD_3OD) δ 1.74 (s, 3H), 2.74-2.82 (m, 2H), 5.17-5.23 (m, 2H), 5.50-5.58 (m, 1H), 7.38-7.48 (m, 5H). ^{13}C NMR (125 MHz, CD_3OD) δ 25.5, 46.7, 59.8, 121.8, 126.3, 129.7, 130.3, 132.1, 141.6. Anal. Calcd for $C_{11}H_{16}ClN$: C, 66.83; H, 8.16; N, 7.08. Found: C, 67.02; H, 7.94; N, 7.14. The amine hydrochloride was converted to the free amine: $[\alpha]_D^{23}$ -44.1 ° (*c* 0.86, CH_2Cl_2).(lit.[18] $[\alpha]_D^{23}$ +45.8 ° (*c* 0.86, CH_2Cl_2) for (*R*)-1-methyl-1-phenyl-3-butenylamine.

(*S*)-1-Isopropyl-1-methyl-3-butenylamine hydrochloride (7b). Methanolysis of (R_S,*S*)-**6b** (0.200 g, 0.865 mmol) was carried out as for α-branched sulfinamides **4**, except that after the reaction mixture was concentrated, 5 mL of toluene was added and the resulting solution was concentrated to near dryness. Hexanes was used for precipitation and washing to provide 0.122 g (86%) of (*S*)-**7b**. $[\alpha]_D^{23}$ +9.0 ° (*c* 1.0, MeOH). ^{1}H NMR (500 MHz, CD_3OD) δ 1.01 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 1.25 (s, 3H), 1.92-2.00 (m, 1H), 2.36-2.47 (m, 2H), 5.27-5.30 (m, 2H), 5.83-5.91 (m, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ 17.1, 17.1, 20.8 35.3, 41.8, 60.5, 121.8, 132.1.

General procedure for the addition of organolithiums to *tert*-butanesulfinyl ketimines, 3. To a 1 M solution of sulfinyl imine (1 equiv) in toluene at -78 °C was slowly added a 1 M solution of Me_3Al in toluene (1.1 equiv). The resulting solution was stirred for ca. 5 min before it was added over the course of

20 min to a -78 °C solution of commercial organolithium (2.2 equiv) diluted to ca. 0.5 M with toluene. Stirring was continued at -78 °C for 2-4 h before the mixture was warmed to 0 °C. Saturated aq. Na_2SO_4 was added dropwise until gas was no longer evolved upon addition, and solid $MgSO_4$ was added. The slurry was stirred for 5 min before it was filtered and the filter cake was rinsed with EtOAc. The residue remaining after concentration of the filtrate was chromatographed to afford sulfinamides **6**.

General procedure for sulfinyl cleavage and acylation of sulfinamides, 6. Sulfinamides were dissolved in equal volumes of MeOH and HCl in dioxane (4 M; 2-4 equiv). After stirring for 10 min, the solvent was removed under a steady N_2 flow. Amines were not purified, but were dissolved in satd $NaHSO_4$, extracted once with ether, then basified with KOH and extracted with CH_2Cl_2. The resulting solution was dried, filtered, and then treated with excess Et_3N and either benzoyl chloride or (*R*)- and (*S*)-MTPA chloride[21] for two hours.

Product Characterization

Sulfinamide 6c. The diastereomeric ratio was determined by HPLC analysis (Rainin Microsorb (Si) column; 98:2 hexanes/IPA, 1 mL/min, 264 nm; (R_S,*R*)-**6c** t_R = 14.4 min, (R_S,*S*)-**6c** t_R = 19.8 min.).

(***R*$_S$,*R*)-6c**: IR 1054, 1362, 1386, 1446 cm^{-1}. ^1H NMR (400 MHz) δ 0.79 (d, *J* = 6.7, 3H), 0.86 (d, *J* = 6.8, 3H), 1.26 (s, 3H), 1.66 (s, 9H), 2.25 (m, 1H), 3.59 (s, 1H), 7.21-7.24 (m, 1H), 7.31-7.38 (m, 2H), 7.43-7.49 (m, 2H). ^{13}C NMR (101 MHz) δ 17.3, 17.4, 22.8, 24.2, 38.2, 56.3, 63.7, 126.6, 126.7, 127.9, 145.5. Anal. Calcd for $C_{12}H_{17}NOS$: C, 67.37; H, 9.42; N, 5.24. Found: C, 67.19; H, 9.22; N, 5.21.

Sulfinamide-6d. The diastereomeric ratio was determined by HPLC analysis (Rainin Microsorb (Si) column; 98:2 hexanes/IPA, 1 mL/min, 264 nm; (R_S,*R*)-**6d** t_R = 15.3 min, (R_S,*S*)-**6d** t_R = 19.8 min.).

(*R*$_S$,*R*)-6d: IR: 1468, 1364, 1071 cm^{-1}. ^1H NMR (400 MHz) δ 0.77 (d, *J* = 6.6, 3H), 0.82-1.03 (m, 8H), 1.20-1.49 (m, 2H), 1.33 (s, 9H), 1.93-2.0 (m, 1H), 2.28-2.34 (m, 1H), 2.52 (septet, *J* = 6.6, 1H), 7.22-7.42 (m, 5H). ^{13}C NMR (101 MHz): δ 13.9, 16.9, 17.7, 22.9, 23.1, 25.8, 34.2, 38.3, 56.7, 67.4, 126.6, 127.6, 127.7, 142.4. Anal. Cacd. for $C_{18}H_{31}NOS$: C, 69.85; H, 10.10; N, 4.53. Found: C, 70.14; H, 9.73; N, 4.46.

Sulfinamide 6e. The diastereomeric ratio was determined by HPLC analysis of the MTPA derivatives formed after clevage of the sulfinyl group (Rainin Microsorb (Si) column; 1.5% MTBE in hexanes; 0.8 mL/min, 230 nm; (*R*,*S*)-amide t_R = 20.5 min, (*R*,*R*)-amide t_R = 22.3 min). The stereochemical assignments are tentatively made based upon consistent diastereofacial selectivity observed in the syntheses of sulfinamides **6c** and **6f**.

(*R*$_S$,*S*)-6e: IR 1053, 1363, 1468 cm^{-1}. ^1H NMR (400 MHz) δ 0.76 (d, *J* = 6.8, 3H), 0.79 (d, *J* = 6.8, 3H), 0.79 (t, *J* = 7.1, 3H), 1.05 (s, 3H), 1.09 (s, 9H), 1.10–1.25 (m, 4H), 1.45–1.60 (m, 2H), 1.64 (septet, *J* = 6.8, 1H), 2.97 (s, 1H). ^{13}C NMR (101 MHz) δ 13.9, 16.7, 16.9, 21.8, 22.6, 23.0, 25.2, 35.5, 40.0, 55.7, 60.1. Anal. Calcd for $C_{12}H_{17}NSO$: C, 63.10; H, 11.81; N, 5.66. Found: C, 62.96; H, 11.89; N, 5.39.

(*R*$_S$,*R*)-6e: IR 1055, 1377, 1467 cm^{-1}. ^1H NMR (400 MHz) δ 0.83 (d, *J* = 0.7, 3H), 0.83 (m, 3H), 0.85 (d, *J* = 0.7, 3H), 1.13 (s, 9H), 1.14 (s, 3H), 1.16-1.26 (m, 4H), 1.38-1.47 (m, 2H), 1.80 (septet, *J* = 6.9, 1H), 3.05 (s, 1H). ^{13}C NMR (101 MHz) δ 14.0, 17.0, 16.9, 22.6, 23.1, 23.4, 25.3, 36.1, 37.7, 55.6, 60.1. Anal. Calcd for $C_{12}H_{17}NSO$: C, 63.10; H, 11.81; N, 5.66. Found: C, 63.21; H, 11.63; N, 5.58.

Sulfinamide 6f. The diastereomeric ratio was determined by chiral HPLC analysis of the benzamide **8** (Chiralcel OD column, 97:3 hexanes/IPA; 0.9 mL/min; 254 nm; (*R*)-**8** t_R = 16.1 min, (*S*)-**8** t_R = 18.0 min). Absolute stereochemical determination was made by comparison of the optical rotation of **8** with the the reported value. (*S*)-**8**: $[\alpha]_D^{23}$ +22.0° (*c* 1.0, benzene) (lit.[19] for (*S*)-**8**: $[\alpha]_{589}^{18}$ +3.5° (*c* 1.0, benzene)).

(***R*S,*R*)-6f**: IR 1064, 1446, 1468 cm^{-1}. ^1H NMR (400 MHz) δ 0.80 (t, *J* = 7.3, 3H), 0.96-1.13 (m, 2H), 1.08-1.27 (m, 2H), 1.23 (s, 9H), 1.71 (s, 3H), 1.91-1.98 (m, 2H), 3.46 (s, 1H), 7.21-7.25 (m, 1H), 7.30-7.34 (m, 2H), 7.41-7.46 (m, 2H). ^{13}C NMR (101 MHz) δ 13.9, 22.7, 22.8, 26.2, 26.4, 42.5, 55.9, 60.8, 126.0, 126.9, 128.1, 145.9. Anal. Calcd for $C_{12}H_{17}NSO$: C, 68.28; H, 9.67; N, 4.98. Found: C, 68.44; H, 9.62; N, 4.90.

(***R*S,*S*)-6f**: IR 1057, 1447, 1468 cm^{-1}. ^1H NMR (400 MHz) δ 0.80 (t, *J* = 7.3, 3H), 1.01- 1.16 (m, 2H), 1.18-1.26 (m, 2H), 1.19 (s, 9H), 1.69 (s, 3H), 1.82-1.90 (m, 1H), 1.93-2.03 (m, 1H), 3.50 (s, 1H), 7.20-7.24 (m, 1H), 7.29-7.33 (m, 2H), 7.38-7.40 (m, 2H). ^{13}C NMR (101 MHz) δ 13.8, 22.5, 22.6, 22.8, 26.1, 44.1, 55.9, 60.8, 126.2, 126.8, 128.6, 145.2. Anal. Calcd for $C_{12}H_{17}NSO$: C, 68.28; H, 9.67; N, 4.98. Found: C, 68.12; H, 9.56; N, 4.94.

Sulfinamide 6g. The diastereomeric ratio was determined by HPLC analysis of the benzamide derivative formed after clevage of the sulfinyl group (Chiralcel OD column; 97:3 hexanes/IPA; 1 mL/min, 254 nm; (*R*)-benzamide t_R = 14.5 min, (*S*)-benzamide t_R = 16.9 min). The stereochemical assignments are tentatively made based upon consistent diastereofacial selectivity observed in the syntheses of sulfinamides **6c** and **6f**.

(***R*S,*R*)-6g**: IR 1446, 1363, 1066 cm^{-1}. ^1H NMR (400 MHz) δ 0.68 (d, *J* = 6.7, 3H), 0.74 (d, *J* = 6.7, 3H), 1.26 (s, 9H), 1.23 (s, 9H), 1.48 (d septet, *J* = 5.5, 6.7, 1H), 1.88 (d, *J* = 5.5, 2H), 3.45 (s, 1H), 7.21-7.25 (m, 1H), 7.30-7.37 (m, 2H), 7.43-7.48 (m, 2H). ^{13}C NMR (101 MHz) δ 22.7, 24.1, 24.3, 24.5, 28.4, 51.7, 55.9, 61.1, 126.2, 127.0, 128.1, 146.0. Anal. Calcd. for $C_{16}H_{27}NOS$: C, 68.28; H, 9.67; N, 4.98. Found: C, 68.41; H 9.48; N, 4.90.

Sulfinamide 6h. The diastereomeric ratio was determined by HPLC analysis of the MTPA derivatives formed after cleavage of the sulfinyl group (Rainin Microsorb (Si) column; 2% MTBE in hexanes; 1.2 mL/min, 266 nm; (*S,R*)-amide t_R = 19.5 min, (*R,R*)-amide t_R = 23.5 min). The stereochemical assignments are tentatively made based upon consistent diastereofacial selectivity observed in the syntheses of sulfinamides **6c** and **6f**.

(***R*S,*R*)-6h**: IR: 1042 cm^{-1}. mp. 109-111 °C. ^1H NMR (400 MHz) δ 1.25 (s, 9H), 2.24 (s, 3H), 3.94 (s, 1H), 7.25-7.38 (m, 6H), 7.48-7.50 (m, 2H), 7.49 (d, *J* = 3.8, 1H), 7.71-7.73 (m, 1H), 7.84-7.97 (m, 1H), 8.28 (s, 1H). ^{13}C NMR (101 MHz) δ 22.8, 30.4, 56.4, 64.1, 125.6, 126.2, 126.3, 126.6, 127.1, 127.4, 127.9, 128.4, 128.4, 132.4, 132.8, 142.8, 147.4. Anal. Calcd. for $C_{22}H_{25}NOS$: C, 75.17; H, 7.17; N, 3.98. Found: C, 75.07; H, 7.03; N, 3.92.

Specific Experimental Procedures

Phenyllithium addition to 3a; (*R*S,*R*)-6c (Table 5, entry 2). The general procedure was followed with: 297 mg (1.57 mmol) of **3a** in 1.6 mL of toluene, 1.73 mL of Me_3Al (1.73 mmol), 1.75 mL of PhLi (2.0 M in cyclohexane/ether; 3.45 mmol) in 6.4 mL of toluene. Chromatography (gradient elution; 5:1–3:1 hexanes/EtOAc) afforded 390 mg (93%) of (*R*S,*R*)-**6c** as a colorless semi-solid with a 97:3 dr.

Butyllithium addition to 3a; (R_S,S)-6e (Table 5, entry 1). The general procedure was followed with: 253 mg (1.34 mmol) of **3a** in 1.6 mL of toluene, 1.73 mL of Me_3Al (1.47 mmol), 1.2 mL of BuLi (2.4 M in hexanes; 3.0 mmol) in 8.4 mL of toluene. Chromatography (slow gradient elution; 6:1–3:1 hexanes/EtOAc) afforded 202 mg (61%) of (R_S,S)-**6e** as a pale yellow oil with a 99:1 dr.

Methyllithium addition to 3b; (R_S,R)-6e (Table 5, entry 3). The general procedure was followed with: 378 mg (1.64 mmol) of **3b** in 1.6 mL of toluene, 1.80 mL of Me_3Al (1.80 mmol), 2.58 mL of MeLi (1.4 M in ether; 3.61 mmol) in 6.9 mL of toluene. Chromatography (gradient elution; 6:1–4:1 hexanes/EtOAc) afforded 332 mg (82%) of (R_S,R)-**6e** as a pale yellow oil with a 91:9 dr.

Phenyllithium addition to 3b; (R_S,R)-6d (Table 5, entry 4). The general procedure was followed with: 467 mg (1.76 mmol) of **3b** in 2.0 mL of toluene, 1.94 mL of Me_3Al (1.94 mmol), 1.96 mL of PhLi (2.0 M in ether; 3.87 mmol) in 6.2 mL of toluene. Chromatography (gradient elution; 6:1–3:1 hexanes/EtOAc) afforded 537 mg (99%) of (R_S,R)-**6d** as a pale yellow oil with a 91:9 dr.

Butyllithium addition to 3c; (R_S,S)-6f (Table 5, entry 5). The general procedure was followed with: 420 mg (1.88 mmol) of **3c** in 1.9 mL of toluene, 2.1 mL of Me_3Al (2.1 mmol), 1.73 mL of BuLi (2.4 M in hexanes; 4.14 mmol) in 7.6 mL of toluene. Chromatography (gradient elution; 6:1–3:1 hexanes/EtOAc) afforded 454 mg (86%) of (R_S,S)-**6f** as a pale yellow oil with a 98:2 dr.

Phenyllithium addition to 3d; (R_S,R)-6f (Table 5, entry 6). The general procedure was followed with: 413 mg (2.03 mmol) of **3d** in 2 mL of toluene, 2.23 mL of Me_3Al (2.23 mmol), 2.27 mL of PhLi (2.0 M in cyclohexane/ether; 4.47 mmol) in 8 mL of toluene. Chromatography (gradient elution; 6:1–4:1 hexanes/EtOAc) afforded 527 mg (93%) of (R_S,R)-**6f** as a pale yellow oil with a 89:11 dr.

Phenyllithium addition to 3e; (R_S,R)-6g (Table 5, entry 7). The general procedure was followed with: 68.6 mg (0.338 mmol) of **3e** in 0.8 mL of toluene, 0.19 mL of Me_3Al (0.19 mmol), 0.25 mL of PhLi (2.0 M in cyclohexane/ether; 0.50 mmol) in 0.9 mL of toluene. Chromatography (gradient elution; 6:1–4:1 hexanes/EtOAc) afforded 59 mg (62%) of (R_S,R)-**6g** as a colorless oil with a 85:15 dr.

Phenyllithium addition to 3f; (R_S,R)-6h (Table 5, entry 8). The general procedure was followed with: 75.2 mg (0.275 mmol) of **3f** in 0.7 mL of toluene, 0.15 mL of Me_3Al (0.30 mmol), 0.21 mL of PhLi (2.0 M in cyclohexane/ether; 0.41 mmol) in 0.7 mL of toluene. Chromatography (gradient elution; 5:1–3:1 hexanes/EtOAc) afforded 60.0 mg (62%) of (R_S,R)-**6h** as yellow solid with a 99:1 dr.

Methyllithium addition to 3g; (R_S,R)-6f (Table 5, entry 9). The general procedure was followed with: 265 mg (1.56 mmol) of **3g** in 1.6 mL of toluene, 1.72 mL of Me_3Al (1.72 mmol), 2.45 mL of MeLi (1.4 M in ether; 3.43 mmol) in 6.9 mL of toluene. Chromatography (gradient elution; 6:1–3:1 hexanes/EtOAc) afforded 439 mg (quant.) of (R_S,R)-**6f** as a pale yellow oil with a 99:1 dr.

REFERENCES AND NOTES

† Present address: NTH 2122, Glaxo Wellcome Inc., P. O. Box 13398, Research Triangle Park, NC 27709-3398.
* E-mail: JEllman@uclink.berkeley.edu

1. MDL Drug Data Report, MDL Information Systems, Inc., San Leandro, CA.
2. (a) Johansson, A. *Contemp. Org. Synth.* **1995**, *2*, 393-407. (b) Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, 8, 1895-1946. (c) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407-1438.
3. (a) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952-8965. (b) Verdaguer, X.; Lange, U. E. W.; Buchwald, S. L. *Angew. Chem. Int. Ed. Eng.* **1998**, *37*, 1103-1107. (c) Lee, N. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 5985-5986. (d) Verdaguer, X.; Lange, U. E. W.; Reding, M. T.; Buchwald, S. L. *J. Am.*

Chem. Soc. **1996**, *118*, 6784-6785. (e) Burk, M. J.; Martinez, J. P.; Feaster, J. E.; Cosford, N. *Tetrahedron* **1994**, *50*, 4399-4428. (f) Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142-5143. (g)Uematsu, N.; Fujii, A.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 4916-4917.

4. (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207-2293. (b) Kleinman, E. F.; Volkmann, R. A. in *Comprehensive Organic Synthesis: Additions to C-X π-Bonds, Part 2*; Heathcock, C. H., Ed.; Pergamon: Oxford, 1991; Vol. 2, pp 975-1006.
5. Spero, D. M.; Kapadia, S. R. *J. Org. Chem.* **1997**, *62*, 5537-5541.
6. Davis, F. A.; Reddy, R. E.; Szewczyk, J. M.; Reddy, G. V.; Portonovo, P. S.; Zhang, H.; Fanelli, D.; Reddy, R. T.; Zhou, P.; Carroll, P. J. *J. Org. Chem.* **1997**, *62*, 2555-2563.
7. For reviews on the applications of *p*-toluenesulfinyl imines, see: (a) Davis, F. A.; Zhou, P.; Chen, B.-C. *Chem. Soc. Rev.* **1998**, *27*, 13-18. (b) Davis, F. A.; Portonovo, P. S.; Reddy, R. E.; Reddy, G. V.; Zhou, P. *Phosphorus, Sulfur, and Silicon and the Related Elements* **1997**, *120 & 121*, 291-303.
8. (a) Annunziata, R.; Cinquini, M.; Cozzi, F. *J. Chem. Soc., Perkin Trans. 1* **1982**, 341-343. (b) Hua, D. H.; Lagneau, N.; Wang, H.; Chen, J. *Tetrahedron: Asymmetry* **1995**, *6*, 349-352.
9. (a) Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 12-13. (b) Fujisawa, T.; Kooriyama, Y.; Shimizu, M. *Tetrahedron Lett.* **1996**, *37*, 3881-3884. (c) Lefebvre, I. M.; Evans, S. A., Jr. *J. Org. Chem.* **1997**, *62*, 7532-7533. (d) Mikolajczyk, M.; Lyzwa, P.; Drabowicz, J.; Wieczorek, M. W.; Blaszczyk, J. *J. Chem. Soc. Chem. Commun.* **1996**, 1503-1504.
10. (a) Davis, F. A.; Reddy, G. V.; Liu, H. *J. Am. Chem. Soc.* **1995**, *117*, 3651-3652. (b) Davis, F. A.; Zhou, P. *Tetrahedron Lett.* **1994**, *35*, 7525-7528. (c) Davis, F. A.; Zhou, P.; Reddy, G. V. *J. Org. Chem.* **1994**, *59*, 3243-3245. (d) Davis, F. A.; Liu, H.; Reddy, G. V. *Tetrahedron Lett.* **1996**, *37*, 5473-5476. (e) Ruano, J. L. G.; Fernández, I.; Catalina, M. D.; Cruz, A. A. *Tetrahedron: Asymmetry* **1996**, *7*, 3407-3414. (f) Viso, A.; Fernández, I.; Guerrero-Strachan, C.; Alonso, M.; Martìnez-Ripoll, M.; André, I. *J. Org. Chem.* **1997**, *62*, 2316-2317.
11. Moreau, P.; Essiz, M.; Mérour, J.-Y.; Bouzard, D. *Tetrahedron: Asymmetry* **1997**, *8*, 591-598.
12. There have also been limited reports of 1,2-additions to more synthetically complex sulfinyl imines: (a) Yang, T.-K.; Chen, R.-Y.; Lee, D.-S.; Peng, W.-S.; Jiang, Y.-Z.; Mi, A.-Q.; Jong, T.-T. *J. Org. Chem.* **1994**, *59*, 914-921. (b) Hose, D. R. J.; Mahon, M. F.; Molloy, K. C.; Raynham, T.; Wills, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 691-703.
13. (a) Liu, G.; Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1997**, *119*, 9913-9914. (b) Cogan, D. A.; Liu, G.; Ellman, J. A. *J. Am. Chem. Soc.*, **1999**, *121*, 268-269.
14. Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011-8019.
15. Liu, G.; Cogan, D. A.; Owens, T.; Tang, T. P. *J. Org. Chem.* **1999**, *64*, 1278-1284.
16. Mikolajczyk, M.; Drabowicz, J.; Bujnicki, B. *J. Chem. Soc. Chem. Commun.* **1976**, 568-569.
17. (a) Davis, F. A.; Friedman, A. J.; Kluger, E. W. *J. Am. Chem. Soc.* **1974**, *96*, 5000-5001 (b) Davis, F. A.; Kluger, E. W. *J. Am. Chem. Soc.* **1976**, *98*, 302-303.
18. Hua, D. H.; Miao, S. W.; Chen, J. S.; Iguchi, S. *J. Org. Chem.* **1991**, *56*, 4-6.
19. (a) Arcus, C. L.; Kenyon, J.; Levin, S. *J. Chem. Soc.* **1951**, 407-410. (b) Hosi, N.; Furkukawa, Y.; Hagiwara, H.; Uda, H.; Sato, K. *Chem. Lett.* **1980**, 47-50.
20. Obrecht, D.; Bohdal, U.; Broger, C.; Bur, D.; Lehman, C.; Ruffieux, R.; Schönholzer, P.; Spiegler, C.; Müller, K. *Helv. Chim. Acta* **1995**, *78*, 563-580.
21. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512-519.
22. Wu, M.-J.; Pridgen, L. N. *J. Org. Chem.* **1991**, *56*, 1340-1344.
23. Brown, H. C.; Kim, K.-W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761-6764.
24. Rangaishenvi, M. V.; Singaram, B.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 3286-3294.
25. Mokhallalati, M. K.; Pridgen, L. N. *Syn. Comm.* **1993**, *23*, 2055-2064.
26. Buckley III, T. F., Rappoport, H. *J. Am. Chem. Soc.* **1981**, *103*, 6157-6163.
27. Wei, Z.-Y.; Knaus, E. E. *Synthesis*, **1994**, 1463-1466.