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

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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 enantioenriched amines may be prepared. © 1999 Elsevier Science Ltd. All rights reserved.

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

INTRODUCTION

The amine functionality is incorporated into greater than 75% of all drugs and drug candidates¹ 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 allylations⁴ 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



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 CuSO₄ 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 R¹ 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 addimines 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



	sulfinyl alo	limine 2	·····			sulfinam	ide 4
entry	compound	R ¹	R ² M	solvent	compound	yield(%) ^b	$(R_S,S)-4:(R_S,R)-4^c$
1	(R _S)-2a	<i>i</i> -Pr	MeMgBr	THF	4a	91	95:5 ^d
2	(<i>R</i> _S)-2b	Et	MeMgBr	THF	4 b	78	90:10 ^d
3	(<i>R</i> _S)-2c	Ph	MeMgBr	THF	4 c	98	93:7 ^d
4	(<i>R</i> _S)-2a	i-Pr	EtMgBr	THF	4d	90	$80:20^{d}$
5	(<i>R</i> _S)-2c	Ph	EtMgBr	THF	4e	91	50:50 ^d
6	(R _S)-2a	i-Pr	EtMgBr	Et ₂ O	4d	90	85:15 ^d
7	(<i>R</i> _S)-2c	Ph	EtMgBr	Et ₂ O	4 e	87	62:38 ^d
8	(<i>R</i> _S)-2b	Et	MeMgBr	CH ₂ Cl ₂	4 b	96	97:3 ^e
9	(<i>R</i> _S)-2c	Ph	EtMgBr	CH ₂ Cl ₂	4 e	98	92:8 ^e
10	(<i>R_S</i>)- 2b	Et	MeLi	THF	4 в	87	75:28 ^e
11	(<i>R</i> _S)-2b	Et	MeLi	Et ₂ O	4 b	86	54:46 ^e
12	(<i>R</i> _S)- 2b	Et	CeCl ₃ /MeLi	THF	4 b	89	78:22 ^e

^a Reactions were performed by the slow addition of a 3.0 M solution of Grignard reagent in Et₂O 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 CH₂Cl₂ 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 I	Reagents to 2.	and Methanol	vsis of 4 .ª
	,				



	sulfinyl a	Idimine 2		sulfinamide 4		41.	amine 5	
entry	compound	R ¹	R ² M	compound ^b	yield (%) ^c	dr ^d	compound ^b	yield (%) ^c
1	(R _S)-2b	Et	MeMgBr	(<i>R</i> _S , <i>S</i>)-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	(<i>R</i> _S)- 2b	Et	PhMgBr	(<i>R_S</i> , <i>R</i>)- 4e	quant.	96:4	(R)-5e	90
4	(R _S)- 2a	<i>i</i> -Pr	MeMgBr	(R _S ,S)- 4a	97	98:2	(S)- 5a	97
5	(<i>R</i> _S)-2a	i-Pr	EtMgBr	(R_S,S) -4d ^e	quant.	97:3	(S)- 5d ^e	93 (85) ^f
6	(<i>R_S</i>)-2a	<i>i</i> -Pr	PhMgBr	(R _S ,R)- 4f	98	89:11	(R)-5f	91 (76) ^f
7	(<i>R</i> _S)- 2a	<i>i</i> -Pr	vinylMgBr	$(R_S,R)-4\mathbf{g}^e$	90	88:12	(R)-5g ^e	78
8	(<i>R</i> _S)-2c	Ph	MeMgBr	(<i>R_S</i> , <i>S</i>)-4c	96	97:3	(S)- 5c	88
9	(R _S)-2c	Ph	EtMgBr	(R _S ,S)-4e	98	92:8	(S)- 5e	94
10	(<i>R</i> _S)-2c	Ph	i-PrMgBr	(R _S ,S)- 4f	29			_
11	(<i>R</i> _S)-2c	Ph	vinylMgBr	(<i>RS</i> , <i>S</i>)-4h	79	94:6	(S)- 5h	93
12	(R _S)-2d	Bn	MeMgBr	(<i>R</i> _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	(<i>R_S</i>)-2d	Bn	vinylMgBr	(R _S ,R)- 4k	81	91:9	(<i>R</i>)-5k	97
15	(<i>R_S</i>)-2d	Bn	PhMgBr	(R _S ,R)-41	81	95:5	(R)- 5 1	99
16	(<i>R</i> _S)-2e	p-MeOPh	EtMgBr	(R _S ,S)-4m ^e	88	99 :1	(S)- 5m ^e	quant.
17	(<i>R_S</i>)- 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 Et₂O to a 0.2 M CH₂Cl₂ 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 lithiumhalogen 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 MgBr₂ and PhLi in Et₂O 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 $3 (eq 2).^a$	

	sulfinyl ketimine 3				sulfinamide 6			
entry	compound	R ¹	R ³	R ² M	solvent	compound	yield (%) ^b	dr ^c
1d	(<i>R_S</i>)-3c	Me	Ph	allylMgBr	CH ₂ Cl ₂	(R _S ,S)-6a	85	>99.9:0.1
2^d	(R _S)- 3a	Me	<i>i</i> -Pr	allylMgBr	CH_2Cl_2	(R _S ,S)- 6b	93	>95:5 ^e
3	(Rs)-3a	Me	<i>i</i> -Pr	PhMgBr	CH ₂ Cl ₂	(R _S ,S)-6c	21	69:31
4	(R _S)- 3a	Me	<i>i</i> -Pr	PhLi	toluene	(<i>R_S</i> , <i>R</i>)- 6 c	65	94:6
5	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	toluene	(<i>R_S</i> , <i>R</i>)-6d	54	82:18
6	(R _S)- 3b	Bu	<i>i</i> -Pr	MeLi	toluene	(R _S ,R)-6e	54	82:18
7	(<i>R</i> _S)-3c	Me	Ph	BuLi	toluene	(R _S ,S)-6f	26	99 :1
8	(R_S) -3d ^f	Me	Bu	PhLi	toluene	(<i>R_S</i> , <i>R</i>)-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. '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 ¹H 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 CH₂Cl₂. 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 Et₂AlPh, *i*-Bu₃Al, and Me₃Al had no appreciable effect on the diastereocontrol of the addition of PhLi to **3a** (entries 4-6). However,

$\frac{1}{3}$	toluene additive	(4)
. Carl Ladaria 7		
		 summamide 6

 $P_{R^3}R^2$

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

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	sulfir	ıyl ketimin	e 3			S	ulfinamide 6	
entry	compound	R1	R ³	R ² M	additive	compound	yield (%) ^b	drc
1	(R _S)-3a	Me	i-Pr	PhLi/CeCl ₃		_	NR	_
2	(<i>R</i> _S)-3a	Me	i-Pr	LiEt ₂ ZnPh			NR	_
3	(R _S)-3a	Me	<i>i</i> -Pr	LiEt2AlPh2			NR	—
4	(R _S)-3a	Me	<i>i</i> -Pr	PhLi	Et ₂ AlPh	(<i>R_S</i> , <i>R</i>)-6c	57	98:2
5	(<i>R</i> _S)-3a	Me	<i>i</i> -Pr	PhLi	i-Bu ₃ Al	(<i>R_S</i> , <i>R</i>)-6c	76	97:3
6	(<i>R</i> _S)-3a	Me	<i>i</i> -Pr	PhLi	Me ₃ Al	(<i>R_S</i> , <i>R</i>)-6c	93	97:3
7	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	Me ₃ Al	(<i>R</i> _S , <i>R</i>)-6d	82	91:9
8	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	Et ₂ AlPh	(<i>R_S</i> , <i>R</i>)-6d	75	81:19
9	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	Et ₂ Alt-Bu	(<i>R</i> _S , <i>R</i>)-6d	34	84:16
10	(<i>R</i> _S)-3a	Me	<i>i-</i> Pr	PhMgBr	Et ₂ AlPh	(R_{S},S) -6c	19	69:31
11	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	Et ₂ Zn	(<i>R_S</i> , <i>R</i>)-6d	16	86:14
12	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	BF3-OEt2	(<i>R_S</i> , <i>R</i>)-6d	44	76:24
13	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	PhLi	ZnCl ₂	(R _S ,R)-6d	26	59:41
14	(<i>R_S</i>)- 3b	Bu	<i>i</i> -Pr	PhLi	MgBr ₂	(<i>Rs</i> , <i>R</i>)- 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. ^bIsolated 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, Me₃Al provided higher levels of diastereocontrol than other trialkylaluminums (entries 7-9). In addition, Me₃Al 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 Me₃Al, 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 Me₃Al mediated 1,2-addition of organolithiums to *tert*-butanesulfinyl ketimines **5** was next investigated. Sulfinyl imines **3a-g** were treated with Me₃Al before being added slowly to a stirring solution of various organolithiums in toluene at -78 °C (eq 5; Table 5). The Me₃Al 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 diastereselectivity 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

	1. Me ₃ Al 2. R ₂ Li	$\mathcal{A}_{\mathbf{N}}^{\mathbf{R}^{3}}$	(5)
3		6	

Table 5. Me₃Al-Mediated 1,2-Additions of Organolithiums to 3.^a

	sulfinyl ketimine 3						
entry	compound	R ¹	R ³	R ² Li	compound	yield (%) ^b	drc
1	(<i>R</i> _S)-3a	Me	i-Pr	Bu	(<i>R_S</i> , <i>S</i>)-6e	61	99 :1
2	(R _S)-3a	Me	<i>i</i> -Pr	Ph	(<i>R_S</i> , <i>R</i>)-6c	93	97:3
3	(<i>R</i> _S)- 3b	Bu	<i>i</i> -Pr	Me	(<i>R_S</i> , <i>R</i>)- 6e	82	91:9
4	(<i>R</i> _S)-3b	Bu	<i>i</i> -Pr	Ph	(R_S,R) -6d ^d	82	91:9
5	(<i>R</i> _S)-3c	Me	Ph	Bu	(<i>R_S</i> , <i>S</i>)- 6f	86	98:2
6	(R_S) -3d ^e	Me	Bu	Ph	(R _S ,R)- 6f	93	89:11
7	(R_S) -3 e^f	Me	<i>i</i> -Bu	Ph	(R_S, R) -6g ^d	62	85:15
8	(<i>R</i> _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	(<i>R</i> _S)-2b	Et	Н	Ph	(<i>R_S</i> , <i>R</i>)- 3e	95	67:33

^{*a*} Reactions were performed by the slow addition of a toluene solution of **3** and Me₃Al (1.1 equiv) to a solution of R^2Li at -78 °C in toluene. ^{*b*} Isolated yields of analytically pure material. ^{*c*} Diastereometric 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

(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 Me₃Al 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 Me₃Al must occur faster than aluminate formation. Second, the substantial effect of Me₃Al on yield and diastereocontrol supports formation

Scheme 6



of a reactive 3-Me₃Al complex. Third, solvent effects further support a 3-Me₃Al 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 1,2addition 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-Me₃Al in Scheme 7, rapid isomerization may result in a ratio of E-to Z 3-Me₃Al that

Scheme 7



differs from the initial E- to Z ratio of the uncomplexed imine. Potentially, the product ratio could reflect the Eto Z-3-Me₃Al ratio. Analysis of ¹H NMR spectra of sulfinyl imine 5d-Me₃Al 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 Me₃Al 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.

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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 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 CDCl₃ 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 CH₂Cl₂ at -48 °C was added Grignard reagent in Et₂O. 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. NH₄Cl 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 Na₂SO₄. 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 diastereometric 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).

 $(R_{5,5})$ -4a. ¹H 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 C₉H₂₁NOS: 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 diastereometic 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. ¹H 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 C₈H₁₉NOS: 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 diastereometric 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 $t_R = 16.3 \text{ min}$, (*S*)-5c $t_R = 16.7 \text{ min}$).

 (R_{S},S) -4c. ¹H 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 C₁₂H₁₉NOS: 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 diastereometric 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. ¹H 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 C₁₀H₂₃NOS: C, 58.49; H, 11.29; N, 6.82. Found: C, 58.34; H, 11.02; N, 6.82.

 (R_{S},R) -4d. ¹H 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 C₁₀H₂₃NOS: 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 diastereometic 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. ¹H 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 C₁₃H₂₁NOS: C, 65.23; H, 8.84; N, 5.85. Found: C, 65.38; H, 9.05; N, 6.16.

 (R_{S},R) -4e. ¹H 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 C₁₃H₂₁NOS: 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 diastereometric 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. ¹H 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 C₁₄H₂₃NOS: C, 66.36; H, 9.15; N, 5.53. Found: C, 66.58; H, 8.90; N, 5.13.

 $(\mathbf{R}_{S}, \mathbf{R})$ -4f. ¹H 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 C₁₄H₂₃NOS: 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 diastereometic 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. ¹H 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 C₁₀H₂₁NOS: 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. ¹H 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 C₁₃H₁₉NOS: 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** $t_R = 18.2 \text{ min}$, (*S*)-**5i** $t_R = 18.7 \text{ min}$).

 (R_{S},S) -4i. ¹H 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 C₁₃H₂₁NOS: 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 diastereometric 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_5,S) -4j. ¹H 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 C₁₄H₂₃NOS: 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 diastereometic 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. ¹H 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 C₁₄H₂₁NOS: 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 (41). The diastereometric ratio was determined by chiral GC analysis of the MTPA derivatives of 51 (HP Ultra II column, 150-250 °C, 5 deg/min, 20 psi; (*R*)-MTPA derivative of (*R*)-51 t_R = 30.3 min, (*S*)-51 t_R = 30.7 min).

 (R_S, R) -41. ¹H 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 C₁₈H₂₃NOS: 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 diastereometric 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_{5},S) -4m. ¹H 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 C₁₄H₂₃NO₂S: 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 CH₂Cl₂ was added 0.83 mL (3.0 M in Et₂O, 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 CH₂Cl₂ was added 0.95 mL (2.6 M in Et₂O, 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 CH₂Cl₂ was added 0.83 mL (3.0 in Et₂O, 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 CH₂Cl₂ was added 0.76 mL (3.0 in Et₂O, 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 CH₂Cl₂ was added 0.76 mL (3.0 in Et₂O, 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 CH₂Cl₂ was added 0.38 mL (3.0 in Et₂O, 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 CH₂Cl₂ was added 2.38 mL (1.1 M in Et₂O, 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 CH₂Cl₂ was added 0.64 mL (3.0 in Et₂O, 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 CH₂Cl₂ was added 0.96 mL (3.0 in Et₂O, 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 CH₂Cl₂ was added 0.18 mL (2.6 M in Et₂O, 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-butanesulfinamide¹⁴ 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 CH₂Cl₂ was added 2.18 mL (1.1 M in Et₂O, 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 CH₂Cl₂ was added 0.45 mL (3.0 M in Et₂O, 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 CH₂Cl₂ was added 0.46 mL (2.9 M in Et₂O, 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 CH₂Cl₂ was added 2.04 mL (1.1 M in Et₂O, 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 CH₂Cl₂ was added 0.45 mL (3.0 M in Et₂O, 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 CH₂Cl₂ was added 0.67 mL (3.0 M in Et₂O, 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 MgBr₂, to (R_S) -2b (Table 2, entry 17). To a mixture of 230 mg (1.25 mmol) of MgBr₂ in 250 µL of Et₂O 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 CH₂Cl₂ 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 CH₂Cl₂ was added 0.26 mL (1.0 M in Et₂O, 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)). ¹H 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 C₁₅H₂₃NSO: C, 67.88; H, 8.73; N, 5.28. Found: C, 68.07; H, 8.90; N, 5.22.

 (R_{5},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 CH₂Cl₂ was added 2.40 mL (1.0 M in Et₂O, 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_{5},S) -6b as a white solid. ¹H 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 C₁₂H₂₅NSO: 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 ¹H 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)). ¹H NMR (300 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 14.0, 16.1, 17.5, 31.3, 52.7. Anal. Calcd for C₅H₁₄ClN: 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_5, 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). ¹H NMR (300 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) 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)). ¹H NMR (300 MHz, CD₃OD) δ 1.61 (d, J = 6.9 Hz, 3H), 4.43 (q, J = 6.9 Hz, 1H), 7.37-7.45 (m, 5H). ¹³C NMR (125 MHz, CD₃OD) 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). ¹H NMR (300 MHz, CD₃OD) 0.97-1.02 (M, 9H), 1.53-1.76 (M, 2H), 1.89-2.00 (m, 1H), 2.89-2.96 (m, 1). ¹³C NMR (101 MHz, CD₃OD) δ 10.2, 18.2, 18.5, 23.8, 31.0, 60.0. Anal. Calcd for C₆H₁₆ClN: 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_5 ,S)-4e (0.287 g, 1.20 mmol) provided 0.190 g (90%) of scalemic (*R*)-5e. Free amine $[\alpha]_D^{23}+35.1 \circ (c \ 1.0, CHCl_3)$ (lit.²⁵ $[\alpha]_D^{23}$ -36.6 $\circ (c \ 1.0, CHCl_3)$ for (*S*)-1-phenyl-propylamine). ¹H NMR (300 MHz, CD₃OD) $\delta \ 0.87$ (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). ¹³C NMR (125 MHz, CD₃OD) $\delta \ 10.7$, 28.9, 58.5, 128.5, 130.5, 130.5, 138.2. Anal. Calcd for C₉H₁₄NSO: 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, CHCl₃) (lit.²⁶ $[\alpha]_D^{23}$ -36.6 ° (c 1.0, CHCl₃)).

(*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, CHCl₃) (lit.^{12a} $[\alpha]_D^{23}$ -11.5 ° (*c* 1.0, CHCl₃) 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, CHCl₃). ¹H NMR (300 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) 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, CD₃OD). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 17.9, 19.3, 32.2, 61.1, 122.1, 133.5. Anal. Calcd for C₆H₁₄ClN: 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_5 , S)-4h (0.140 g, 0.595 mmol) provided 0.928 g (93%) of scalemic (*R*)-5h. ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 58.4, 120.2, 128.7, 130.4, 130.5, 135.4. Anal. Calcd for C₉H₁₂NCl: 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 Na₂CO₃ to provide (*R*)-1-phenylpropylamine: [α]_D²³-28.2 ° (c 1.1, CHCl₃).

(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, CH₂Cl₂). (lit.²⁶ $[\alpha]_D^{23}$ +12.5 ° (c 2.0, CH₂Cl₂). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 18.4, 41.9, 50.4, 128.5, 130.1, 130.5, 137.5. Anal. Calcd for C₉H₁₄ClN: 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, H₂O). (lit.^{12a} $[\alpha]_D^{23}$ +33.16 ° (c 2.0, H₂O). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 9.9, 26.4, 39.6, 55.7, 128.5, 130.2, 130.6, 137.4. Anal. Calcd for C₁₀H₁₆ClN: 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). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 40.6, 56.5, 121.2, 128.5, 130.0, 130.7, 134.8, 136.8. Anal. Calcd for C₁₀H₁₄ClN: 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, CHCl₃). (lit.²⁷ [α] +36.7 (c 9.0, CHCl₃) for (*S*)-3-tert-butoxycarbonylamino-4-phenyl-1-butene.

(*R*)-1, 2-Diphenylethylamine hydrochloride (51). Methanolysis of (R_S , R)-41 (0.116 g, 0.385 mmol) provided 0.089 g (99%) of scalemic (R)-51. ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 42.1, 58.5, 128.4, 128.7, 129.9, 130.3, 130.4, 130.6, 137.0, 137.9. Anal. Calcd for C₁₀H₁₆ClN: 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. [α]_D²³ -14.1 ° (c 1.6, CHCl₃). (lit.²² [α]_D²³ -10.9 ° (c 1.6, CHCl₃).

(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. [α]_D²³ +13.6 ° (*c* 1.0, MeOH). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 10.7, 28.7, 56.0, 58.0, 115.7, 129.9, 129.9, 161.9. Anal. Calcd for C₁₀H₁₆ClN: 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. [α]D²³ -9.8 ° (c 1.0, MeOH). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) δ 25.5, 46.7, 59.8, 121.8, 126.3, 129.7, 130.3, 132.1, 141.6. Anal. Calcd for C₁₁H₁₆ClN: 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: [α]D²³ -44.1 ° (c 0.86, CH₂Cl₂).(lit.¹⁸ [α]D²³ +45.8 ° (c 0.86, CH₂Cl₂) 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). ¹H NMR (500 MHz, CD₃OD) 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). ¹³C NMR (125 MHz, CD₃OD) 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 Me₃Al 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. Na₂SO₄ was added dropwise until gas was no longer evolved upon addition, and solid MgSO₄ 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 N₂ flow. Amines were not purified, but were dissolved in satd NaHSO₄, extracted once with ether, then basified with KOH and extracted with CH₂Cl₂. The resulting solution was dried, filtered, and then treated with excess Et₃N and either benzoyl chloride or (*R*)- and (*S*)-MTPA chloride²¹ for two hours.

Product Characterization

Sulfinamide 6c. The diastereometic 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, $J \approx 6.7, 3$ H), 0.86 (d, $J \approx 6.8, 3$ H), 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). ¹³C 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 C₁₂H₁₇NOS: 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). ¹³C 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 C₁₈H₃₁NOS: C, 69.85; H, 10.10; N, 4.53. Found: C, 70.14; H, 9.73; N, 4.46.

Sulfinamide 6e. The diastereometric 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). ¹³C 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 C₁₂H₁₇NSO: 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). ¹³C 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 C₁₂H₁₇NSO: 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: $[\alpha]_D^{23} + 22.0^\circ$ (*c* 1.0, benzene) (lit.¹⁹ for (*S*)-8: $[\alpha]_{589}^{18} + 3.5^\circ$ (*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). ¹³C 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 C₁₂H₁₇NSO: 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). ¹³C 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 C₁₂H₁₇NSO: C, 68.28; H, 9.67; N, 4.98. Found: C, 68.12; H, 9.56; N, 4.94.

Sulfinamide 6g. The diastereometric 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). ¹³C 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 C₁₆H₂₇NOS: C, 68.28; H, 9.67; N, 4.98. Found: C, 68.41; H 9.48; N, 4.90.

Sulfinamide 6h. The diastereometric 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). ¹³C 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 C₂₂H₂₅NOS: 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 Me₃Al (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 Me₃Al (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 Me₃Al (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 Me₃Al (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 Me₃Al (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 Me₃Al (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 Me₃Al (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 Me₃Al (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 Me₃Al (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.

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