Asymmetric Synthesis of Protected 1,2-Amino Alcohols Using *tert*-Butanesulfinyl Aldimines and Ketimines

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tert-Butanesulfinyl aldimines and ketimines bearing an α-benzyloxy or α-silyloxy substituent serve as precursors in the synthesis of protected 1,2-amino alcohols in high yields and diastereoselectivities. General protocols are described for the addition of unbranched alkyl, branched alkyl, and aryl organometallic reagents to *N*-sulfinyl aldimines **1** and **2** and ketimines **5** and **6**. Furthermore, the selective *N*- or *O*-deprotection of sulfinamide products **3**, **4**, **7**, and **8** is described, enabling further synthetic transformations of the reaction products.

Introduction

Enantiopure β-amino alcohols are commonly utilized as building blocks for biologically active compounds, chiral auxiliaries, and ligands for asymmetric catalysis.[1,2] Although several methods exist for the construction of this structural motif, including the reduction of α-amino acids,[3] asymmetric aminohydroxylation,[4] and catalytic asymmetric ring opening of epoxides,[2] highly stereoselective methods that enable the incorporation of diverse substituents are still needed.

Previously, we have reported the utility of *tert*-butanesulfinyl imines for the synthesis of α-branched and α,α-dibranched amines,[5,6] β-amino acids,[7] and α,α-disubstituted α-amino acids.[8] Prompted by a recent publication by Barrow et al.,[9] we now report our own efforts toward the highly diastereoselective synthesis of β-amino alcohols utilizing the *tert*-butanesulfinyl chiral directing group.

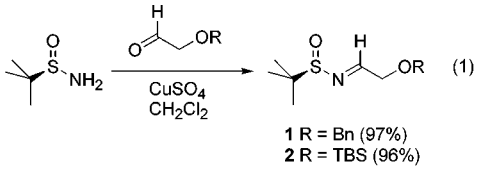
Results and Discussion

We envisioned the synthesis of β-amino alcohols via nucleophilic additions to *tert*-butanesulfinyl imines (**1** and **2**) bearing an α-alkoxy or α-silyloxy substitutent. Under standard $CuSO_4$-mediated conditions,[10] the condensation of *tert*-butanesulfinamide[11] with benzyloxyacetaldehyde and (*tert*-butyldimethylsilyloxy)acetaldehyde afforded *N*-sulfinyl imines **1** and **2** in 97 and 96% yields, respectively (eq 1).[9]

Table 1. Optimization of Reaction Conditions for the Addition of *t*-BuMgCl to Aldimine 1

entry	*T* (°C)	solvent	additive	yield[a] (%)	dr[b,c]
1	−48	CH_2Cl_2	−	95	80:20
2	−78	CH_2Cl_2	−	90	90:10
3	−78	toluene	−	84	97:3
4	−78	toluene	$MgBr_2$	86	87:13
5	−78	CH_2Cl_2	$BF_3{\cdot}OEt_2$	77	97:3
6	−78	toluene	$BF_3{\cdot}OEt_2$	23	99:1
7	−78	CH_2Cl_2	$AlMe_3$	75	98:2
8	−78	toluene	$AlMe_3$	98	99:1

[a] Yields determined by mass balance of purified material. [b] Ratios determined by HPLC-MS of crude reaction mixtures after workup. [c] Absolute configuration determined by deprotection and comparison of optical rotation to literature values.



Addition of *tert*-butylmagnesium chloride to **1** was initially examined using our previously reported conditions (Table 1, entry 1), which resulted in high conversion but uncharacteristically low diastereoselectivity.[11] However, upon lowering the temperature from −48 to −78 °C and using toluene as the reaction solvent, increased selectivities were observed. We have previously observed that Lewis acid additives increased the yields and selectivities for additions to alkyl and aryl *N*-sulfinyl ketimines.[12] Evaluation of Lewis acid additives for additions to **1** (eq 2) revealed that the highest yields and

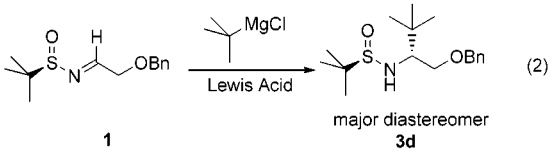


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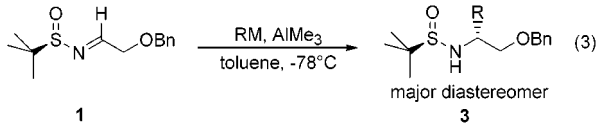
Table 2. Addition of Various Organometallic Reagents to Aldimines 1 in Toluene

entry	compd	RM	additive	yield[a] (%)	dr[b]
1	**3a**[c]	EtMgBr		85	90:10
2		EtMgBr	$AlMe_3$	81	90:10
3	**3b**[c]	*n*-BuMgCl		80	90:10
4		*n*-BuMgCl	$AlMe_3$	84	90:10
5		*n*-BuLi		81	75:25
6		*n*-BuLi	$AlMe_3$	87	97:3
7	**3c**	*i*-PrMgCl		88	90:10
8		*i*-PrMgCl	$AlMe_3$	85	99:1
9	**3d**[c]	*t*-BuMgCl		84	97:3
10		*t*-BuMgCl	$AlMe_3$	98	99:1
11	**3e**[c]	PhMgBr		99	93:7 (75:25)[d]
12		PhMgBr	$AlMe_3$	95	98:2
13		PhLi		92	80:20 (81:19)[e]
14		PhLi	$AlMe_3$	96	96:4

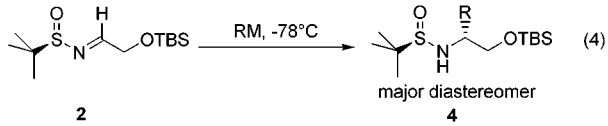
[a] Yields determined by mass balance of purified material. [b] Ratios determined by HPLC-MS of crude reaction mixtures after workup. [c] Absolute configuration determined by deprotection and comparison of optical rotation to literature values. [d] Performed by Barrow et al. with CH_2Cl_2 as solvent.[9] [e] Performed by Barrow et al. with hexane as solvent.[9]

diastereoselectivites were obtained in the presence of $AlMe_3$ (Table 1, entry 8). The scope and generality of organometallic additions to **1** was then examined with toluene as solvent, with or without $AlMe_3$.

The addition of various Grignard reagents to 1 (Table 2, entries 1, 3, 7, 9, and 11) proceeded in high yields and diastereoselectivities (90:10 to 99:1), with modest or no effect observed when the additions were performed in the presence of $AlMe_3$ (Table 2, entries 2, 4, 8, 10, and 12). Organolithiums could also be added to imine **1** (Table 2, entries 5 and 13); however, $AlMe_3$ was required to achieve high diastereoselectivities (Table 2, entries 6 and 14; eq 3). Barrow et al. also examined the additions of PhMgBr and PhLi to **1**. In their studies, CH_2Cl_2 provided the highest diastereoselectivity for PhMgBr addition to **1** (75:25) and hexane provided the highest diastereoselectivity for PhLi addition (81:19).[9] Notably, Barrow et al. did not examine toluene as a solvent.



To determine the effect of the alcohol protecting group on yield and diastereoselectivity, organometallic additions to *tert*-butyldimethylsilyl (TBS) protected imines **2** were examined (Table 3; eq 4). Additions of Grignard



reagents to **2** (Table 3, entries 1−3 and 5−8) proceeded in high yields (88−96%) and generally high diastereoselectivities (83:17 to 96:4). A significant improvement in diastereoselectivity was observed for **4b** (entry 4) using BuLi with $AlMe_3$ as an additive. $AlMe_3$ was also examined for other organolithium and Grignard additions to **2**; however, no significant enhancement in yields or

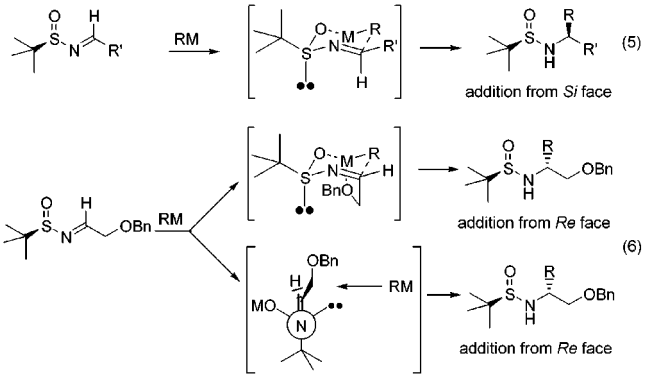
Table 3. Organometallic Additions to *N*-Sulfinyl Imine 2

entry	compd	RM	yield[a] (%)	dr[b]
1	**4a**	EtMgCl	96	88:12
2		EtMgBr	91	91:9
3	**4b**	*n*-BuMgCl	85	83:17 (91:9)[d]
4		*n*-BuLi/$AlMe_3$	89	91:9
5	**4c**	*i*-PrMgCl	88	96:4
6	**4d**[c]	*t*-BuMgCl	90	96:4
7	**4e**	Ph-≡-MgBr	92	90:10 (77:23)[d]
8	**4f**[c]	PhMgBr	95	96:4 (91:9)[e]

[a] Yields determined by mass balance of purified material. [b] Ratios determined by HPLC-MS of crude reaction mixtures after workup. [c] Absolute configuration determined by deprotection and comparison of optical rotation with literature values. [d] Performed by Barrow et al.[9] with Et_2O as solvent. [e] Performed by Barrow et al.[9] with CH_2Cl_2 as solvent.

diastereoselectivities was observed. Barrow et al. examined similar Grignard additions (parenthetical references in entry 3, 7, and 8) using Et_2O and CH_2Cl_2 as reaction solvents, resulting in comparable drs.[9]

Conversion of products **3a**,[13] **3b**,[14] **3d, 3e**,[15] **4d**,[14] and **4f**[9] to the respective 1,2-amino alcohols or *O*-benzyl 1,2-amino alcohols and comparison to literature optical rotation values revealed that the sense of induction for additions to α-benzyloxy or α-silyloxy *N*-sulfinyl aldimines is opposite from that previously observed for additions to alkyl and aryl substituted *N*-sulfinyl imines.[5] This reversal of selectivity for *N*-sulfinyl aldimines bearing an α-coordinating group has ample precedent.[9,16] For Grignard additions to alkyl and aryl *N*-sulfinyl aldimines, attack occurs exclusively from the *Si* face of the imine (eq 5), where the reaction is postulated to occur through a six-membered transition state resulting from the coordination of the *E*-imine with the incoming nucleophile.[5] To explain the reversal in selectivity, Barrow et al. proposed a transition state in which the *Z*-imine is stabilized via coordination of the α-chelating group with the metal of the incoming nucleophile, which correctly translates to the observed diastereoselectivity (eq 6, top). Alternatively, Davis proposed an open transition state where the six-membered chelate is disrupted by chelation of the incoming nucleophiles to the α-coordinating group. The Cram product correctly translates to the observed diastereoselectivity (eq 6, bottom). Although these two



mnemonics accurately predict the stereochemistry of additions to *N*-sulfinyl aldimines **1** and **2**, the actual

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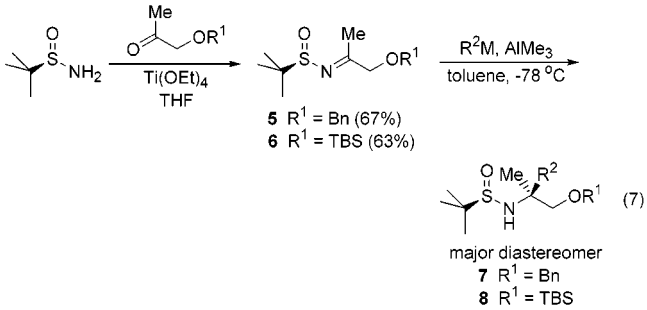
Table 4. Organometallic Additions to *N*-Sulfinyl Ketimine 5

entry	compd	R^1	R^2M	yield[a] (%)	dr
1	**7a**	Bn	*n*-BuLi	52	85:15[b]
2		Bn	*n*-BuMgCl	50	82:18[b]
3	**7b**[d]	Bn	PhLi	42	72:28[c]
4		Bn	PhMgBr	46	85:15[c]

[a] Yields determined by mass balance of purified material. [b] Ratios determined by ^{1}H NMR integration of crude reaction products after workup. [c] Ratios determined by HPLC-MS of crude reaction products after workup. [d] Absolute configuration determined by deprotection and comparison of optical rotation with literature values.

origin of the stereochemical bias cannot at this point be ascertained.

The direct synthesis of β,β-disubstituted β-amino alcohols could also be achieved by additions to *N*-sulfinyl ketimines bearing an α-alkoxy or α-silyloxy substituent. Standard $Ti(OEt)_4$ mediated condensation of *tert*-butanesulfinamide[11] with benzyloxyacetone and ((*tert*-butyldimethylsilyl)oxy)acetone afforded *N*-sulfinyl ketimines **5** and **6** in 67 and 63% yield, respectively (eq 7).[10]



(7)

Previously described organolithium additions to *N*-sulfinyl ketimines required the use of $AlMe_3$ to activate the imine toward addition and minimize side reactions.[12] Under these conditions, organometallic additions to *O*-benzyl imine **5** afforded disubstituted products **7** in moderate yields and diastereoselectivities (Table 4).

Additions to TBS-protected imine **6** resulted in an overall increase in diastereoselectivities in the formation of disubstituted products **8** (Table 5). Unbranched alkyl Grignard additions to imine **6** proceeded in high yields and diastereoselectivities with no Lewis acid additives (Table 5, entries 1 and 4). For aromatic and more sterically hindered organometallic reagents, however, activation with a Lewis acid additive was required (Table 5, entries 8 and 13). For aliphatic organolithium reagents, high diastereoselectivity was observed using $AlMe_3$ activation (Table 5, entries 6 and 11).

The lower isolated yields for additions to *N*-sulfinyl ketimines can be attributed to two competing side reactions. First, α-deprotonation and self-condensation is prevalent for the more hindered nucleophiles (*i*-PrMgCl and *t*-BuMgCl). Second, a competitive methyl transfer from the $AlMe_3$ additive to give **8** (R^2 = Me) occurs in reactions that proceed with low isolated yield of desired product (Table 5, entries 3, 5, 8, 10). Despite the moderate to low yields for these substrates, it is significant to note

Table 5. Organometallic Additions to *N*-Sulfinyl Ketimine 6

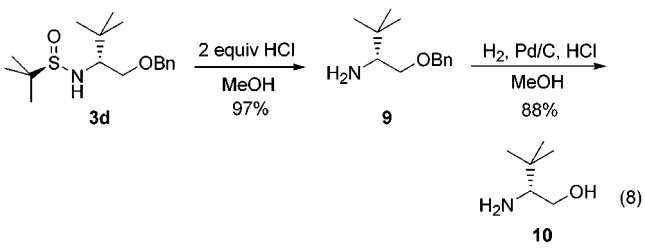
entry	compd	LA	R^1	R^2M	yield[a] (%)	dr
1	**8a**[d]		TBS	EtMgCl	83	91:9[c]
2		$AlMe_3$	TBS	EtMgCl	70	88:12[c]
3		$AlMe_3$	TBS	EtMgBr	40	68:32[c]
4	**8b**		TBS	*n*-BuMgCl	85	88:12[c]
5		$AlMe_3$	TBS	*n*-BuMgCl	54	98:2[c]
6		$AlMe_3$	TBS	*n*-BuLi	89	95:5[c]
7	**8c**		TBS	*i*-PrMgCl		
8		$AlMe_3$	TBS	*i*-PrMgCl	20	96:4[c]
9	**8d**		TBS	*t*-BuMgCl		
10		$AlMe_3$	TBS	*t*-BuMgCl		
11		$AlMe_3$	TBS	*t*-BuLi	36	88:12[c]
12	**8e**[d]		TBS	PhMgBr	40	60:40[b]
13		$AlMe_3$	TBS	PhMgBr	93	96:4[b]
14		$AlMe_3$	TBS	PhLi	76	78:22[b,e]

[a] Yields determined by mass balance of purified material. [b] Ratios determined by ^{1}H NMR integration of crude reaction products after workup. [c] Ratios determined by HPLC-MS of crude reaction products after workup. [d] Absolute configuration determined by deprotection and comparison of optical rotation with literature values. [e] PhLi is only available as a solution in cyclohexane/Et_2O; the presence of Et_2O may affect diastereoselectivities.

the difficulty in synthesizing these highly substituted and hindered amino alcohol derivatives with current methods. To our knowledge, there has been only one other report of nuclephilic additions to ketimines to afford β,β-disubstituted amino alcohols, and in this study, additions of unstabilized Grignard reagents were not reported.[17]

Conversion of products **7b**,[17] **8a**,[18] and **8e**[17] to their respective amino alcohols and comparison to literature optical rotation values revealed that the sense of induction for additions to α-benzyloxy or α-silyloxy *N*-sulfinyl ketimines is the same as previously observed for additions to alkyl and aryl *N*-sulfinyl ketimines.[12] Interestingly, the presence of α-chelating groups does not reverse the face selectivity of additions to *N*-sulfinyl ketimines, as was observed with *N*-sulfinyl aldimines possessing α-chelating groups (vide supra).

The *N*-*tert*-butanesulfinyl group is orthogonal to the benzyl ether and TBS ether. Therefore, sulfinamides **3**, **4**, **7**, and **8** can be selectively deprotected at the nitrogen or oxygen for subsequent organic transformations. For addition products **3** and **7**, the *O*-benzyl amino alcohol may be readily accessed by treatment with HCl in MeOH. For example, treatment of **3d** with HCl in MeOH resulted in the quantitative cleavage of the *N*-sulfinyl group, affording *O*-benzylamine **9** in 97% yield. Deprotection of the *O*-benzyl group was achieved via hydrogenolysis, affording the fully deprotected amino alcohol **10** in 88% yield (eq 8).



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Conversely, the TBS group of sulfinamides **4** and **8** can be selectively removed by treatment with HF in pyridine

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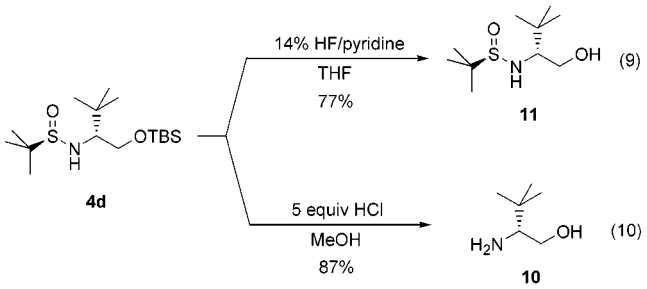
with no *N*-sulfinyl cleavage. For example, treatment of TBS-protected sulfinamide **4d** with 14% HF/pyridine in THF afforded the *N*-sulfinyl *β*-amino alcohol **11** in 77% yield (eq 9).

Furthermore, the simultaneous removal of both the nitrogen and oxygen protecting groups for sulfinamides **4** and **8** can be readily accomplished. Treatment of TBS-protected sulfinamide **4d** with HCl in MeOH resulted in the conversion to amino alcohol **10** in 87% yield (eq 10).



Conclusion

We have demonstrated the use of *N*-*tert*-butanesulfinyl imines bearing an α-benzyloxy or α-silyloxy substituent toward the synthesis of protected mono- and disubstituted 1,2-amino alcohols. Excellent yields and diastereoselectivities for a wide range of nucleophiles were observed. These products can be enriched to diastereomeric purity with standard chromatography and selectively deprotected for use in subsequent organic transformations.

Experimental Section

General Procedure. Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. A solution of 1.0 M $AlMe_3$ in toluene was prepared from neat $AlMe_3$, obtained from Aldrich Chemical Co. Grignard reagents were obtained as solutions in ether, *n*-BuLi in hexanes, PhLi in cyclohexane/Et_2O, and *t*-BuLi in pentane. A 14% solution of HF in pyridine was prepared from 70% HF in pyridine, obtained from Aldrich. $CuSO_4$ was obtained from Aldrich and flame-dried in vacuo before use. $Ti(OEt)_4$ was obtained from Strem and distilled before use. (R_S)-*tert*-Butanesulfinamide was prepared according to previously published protocols.[11] All solvents were distilled under N_2 from the following drying agents immediately before use: tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl, and dichloromethane (CH_2Cl_2) and toluene were distilled from CaH_2. Unless otherwise noted, all reactions were carried out in flame-dried glassware under an inert N_2 atmosphere. Chromatography was carried out using Merck 60 Å 230−400 mesh silica gel. Reaction progress was monitored with thin-layer chromatography on Merck 60 F_{254} 0.25 μm silica plates. Unless otherwise noted, all organic layers were dried over anhydrous $MgSO_4$, and all solvents were removed with a rotary evaporator equipped with a KNF Neuberger dry vacuum pump. IR spectra of liquids were recorded as thin films on NaCl plates, and IR spectra of solids were recorded as KBr pellets; only partial data are listed. Unless otherwise noted, NMR spectra were obtained in $CDCl_3$ at room temperature with either a Bruker AM-400 or Bruker DRX-500. Chemical shifts in NMR spectra are expressed in parts per million, and all coupling constants expressed in hertz. Unless otherwise noted, diastereoselectivity was determined via HPLC-MS with an Agilent 1100 LC-MS equipped with a C8 Zorbax 2.1 μm × 150 mm column, monitored at 210 and 220 nm. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed by the University of California, Berkeley Microanalytical Laboratory and MHW Laboratories (Phoenix, AZ).

General Procedure for the Condensation of Aldehydes with (R_S)-*tert*-Butanesulfinamide. To a 0.500 M solution of (R_S)-*tert*-butanesulfinamide (1.10 equiv) in CH_2Cl_2 was added 2.50 equiv of anhydrous $CuSO_4$ and the aldehyde (1.00 equiv). The mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through a pad of Celite, and the filter cake was washed with CH_2Cl_2 and the filtrate concentrated.

(R_S)-Benzyloxyethylidene-*N*-*tert*-butanesulfinamide (1). The general procedure was followed using (R_S)-*tert*-butanesulfinamide (2.66 g, 22.0 mmol, 1.10 equiv), $CuSO_4$ (7.98 g, 50.0 mmol), and benzyloxyacetaldehyde (3.00 g, 20.0 mmol, 1.00 equiv). Pure **1** was obtained (4.92 g, 97.0%) as a clear, colorless oil after chromatography of the residue (20% EtOAc/Hex to 50% EtOAc/Hex): $[\alpha]^{23}D = -212$ ($c = 1.00$, $CHCl_3$); IR 1736, 1632, 1084 cm^{-1}; ^1H NMR (400 MHz) δ 1.23 (s, 9H), 4.39 (dd, 1H, $J = 16.3, 3.3$), 4.44 (dd, 1H, $J = 16.3, 3.2$), 4.65 (s, 2H), 7.32−7.37 (m, 5H), 8.14 (t, 1H, $J = 3.2$); ^{13}C NMR (100 MHz) δ 22.31, 56.87, 71.18, 73.20, 127.78, 127.96, 128.47, 137.47, 166.61. Anal. Calcd for $C_{13}H_{19}NO_2S$: C, 61.63; H, 7.56; N, 5.53. Found: C, 61.48; H, 7.53; N, 5.30.

(R_S)-2-Methylpropane-2-sulfinic Acid [2-(*tert*-Butyldimethylsilanyloxy)ethylidene]amide (2). The general procedure was followed using (R_S)-*tert*-butanesulfinamide (2.66 g, 22.0 mmol, 1.10 equiv), $CuSO_4$ (7.98 g, 50.0 mmol), and (*tert*-butyldimethylsilyloxy)acetaldehyde (3.00 g, 20.0 mmol, 1.00 equiv). Pure **2** was obtained (4.72 g, 85.0%) as a white solid after chromatography of the residue (10% EtOAc/Hex to 30% EtOAc/Hex): mp 19 °C; $[\alpha]^{23}D = -187$ ($c = 1.00$, $CHCl_3$); IR 1087, 1123, 1702 cm^{-1}; ^1H NMR (400 MHz) δ 0.10 (s, 6H), 0.91 (s, 9H), 1.20 (s, 9H), 4.54 (d, 2H, $J = 3.2$), 8.06 (t, 1H, $J = 3.2$); ^{13}C NMR (100 MHz) δ −5.43, −5.40, 22.25, 25.65, 56.72, 65.47, 110.40, 168.64. Anal. Calcd for $C_{12}H_{27}NO_2SSi$: C, 51.94; H, 9.81; N, 5.05. Found: C, 51.76; H, 9.75; N, 4.91.

General Procedure for the Condensation of Ketones with (R_S)-*tert*-Butanesulfinamide. A 0.5 M solution of $Ti(OEt)_4$ (distilled, 2.5 equiv) and ketone (1.0 equiv) in THF was prepared under a nitrogen atmosphere. To the solution was then added *tert*-butanesulfinamide (1.0 equiv), and the flask was heated to 70 °C. Conversion was followed by TLC, and the mixture cooled upon reaction completion. Once at room temperature, the mixture was poured into an equal volume of brine while being stirred rapidly. The resulting suspension was filtered through a plug of Celite, and the filter cake was washed with EtOAc. The filtrate was transferred to a separatory funnel, where the aqueous layer was extracted (3 × EtOAc). The organic layers were combined, washed with brine, dried, and concentrated.

(R_S)-*N*-(2-(1-Benzyloxy)propylidene-2-methylpropanesulfinamide (5). The general procedure was followed with 665 mg of (R_S)-*tert*-butanesulfinamide (1.00 equiv, 5.48 mmol), 1.00 g of benzyloxyacetone (1.00 equiv, 5.48 mmol) and 2.92 mL of $Ti(OEt)_4$ (2.50 equiv, 13.7 mmol), and 13.0 mL of THF. Pure **5** was obtained (980 mg, 67.0% yield) as a clear, colorless oil after column chromatography (15% EtOAc/Hex to 40% EtOAc/Hex): $[\alpha]^{23}D = -123$ ($c = 1.00$, $CHCl_3$); IR 1077, 1629, 1732 cm^{-1}; ^1H NMR (400 MHz) δ 1.26 (s, 9H), 2.37 (s, 3H), 4.14 (s, 2H), 4.58 (s, 2H), 7.30−7.39 (m, 5H); ^{13}C NMR (100 MHz) δ 19.23, 22.15, 56.65, 72.97, 75.47, 127.67, 127.86, 128.40, 137.30, 181.91. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.73; H, 7.84; N, 5.09.

(R_S)-2-Methylpropane-2-sulfinic Acid [2-(*tert*-Butyldimethylsilanyloxy)-1-methylethylidene]amide (6). The general procedure was followed with 500 mg of (R_S)-*tert*-butanesulfinamide (1.00 equiv, 4.13 mmol), 0.800 mL of (*tert*-butyldimethylsilyloxy)acetone (1.00 equiv, 4.13 mmol), 2.20 mL of $Ti(OEt)_4$ (2.50 equiv, 10.3 mmol), and 9.00 mL of THF. Pure **6** was obtained (770 mg, 63.0% yield) as a brown oil after column chromatography (5% EtOAc/Hex to 35% EtOAc/Hex): $[\alpha]^{23}D = -146$ ($c = 1.00$, $CHCl_3$); IR 1079, 1361, 1631 cm^{-1}; ^1H NMR (400 MHz) δ 0.03 (s, 6H), 0.86 (s, 9H), 1.18 (s, 9H), 2.28 (s, 3H), 4.18 (s, 2H).; ^{13}C NMR (100 MHz) δ −5.56, −5.66, 18.09, 18.71, 22.02, 24.84, 56.40, 69.40, 183.98. Anal. Calcd

for $C_{13}H_{29}NO_2SSi$: C, 53.56; H, 10.03; N, 4.80. Found: C, 53.25; H, 10.10; N, 4.72.

General Procedure for the Grignard/Organolithium Additions to *N*-*tert*-Butanesulfinyl Imines. To a flame-dried flask was added imine **1**, **2**, **5**, or **6** (1.0 equiv) in toluene (0.20 M) and the solution cooled to −78 °C. To this solution was slowly added the organometallic reagent (1.5 equiv) and the solution stirred until the reaction was complete as determined by TLC (1−3 h). Excess organometallic reagent was quenched with a solution of Na_2SO_4 (saturated) The resulting mixture was then warmed to room temperature, dried, filtered through Celite, and concentrated. The residue was purified via flash chromatography to afford sulfinamides **3**, **4**, **7**, or **8** (for yields and diastereoselectivities, see Tables 1−5).

General Procedure for $AlMe_3$-Mediated Organometallic Additions to *N*-*tert*-Butanesulfinyl Imines. To a flame-dried flask was added imine **1**, **2**, **5**, or **6** (1.0 equiv) in toluene (0.50 M) and the solution cooled to −78 °C. To this solution was added a solution of $AlMe_3$ in toluene (1.0 M, 1.1 equiv) and the resulting solution stirred for 30 min. This solution was then slowly transferred over 10 min to a −78 °C solution of the organometallic reagent (1.5 equiv) in toluene (0.50 M). The resulting solution was stirred at −78 °C until the reaction was complete as determined by TLC (1−3 h). A solution of Na_2SO_4 (saturated) was then slowly added until the cessation of gas evolution. The resulting mixture was then warmed to room temperature, dried, filtered through Celite, and concentrated. The residue was purified via flash chromatography to afford sulfinamides **3**, **4**, **7**, or **8** (for yields and diastereoselectivities, see Tables 1−5).

(*R*$_S$, 1*R*)-2-Methylpropane-2-sulfinic Acid (1-(Benzyloxymethyl)propyl)amide (3a). Pure **3a** was obtained as a clear, colorless oil after flash chromatography (50% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 2: HPLC-MS (70−95% MeOH/H_2O over 3 min at 1 mL/min) t_R(major) = 5.01 min, t_R(minor) = 4.78 min; $[\alpha]^{23}D$ = −52.7 (c = 1.00, $CHCl_3$); IR 1069, 1097, 2960 cm^{-1}; ^1H NMR (400 MHz) δ 0.91 (t, 3H, J = 7.41), 1.22 (s, 9H), 1.57−1.64 (m, 2H), 3.31−3.38 (m, 1H), 3.44 (dd, 1H, J = 9.38, 5.14), 3.62−3.65 (m, 2H), 4.48 (d, 1H, J = 11.9), 4.60 (d, 1H, J = 11.9), 7.27−7.37 (m, 5H); ^{13}C NMR (100 MHz) δ_10.14, 22.57, 25.75, 55.63, 57.01, 72.75, 72.96, 127.55, 127.63, 128.28, 138.03. Anal. Calcd for $C_{15}H_{25}NO_2S$: C, 63.56; H, 8.89; N, 4.94. Found: C, 63.78; H, 8.97; N, 4.73.

Absolute configuration was determined through sulfinyl group cleavage, affording (*R*)-1-(benzyloxymethyl)propylamine: $[\alpha]^{23}D$ = −16.2 (c = 1.00, $CHCl_3$) [lit.: $[\alpha]^{23}D$ = −18.0 (no conditions given)].[13]

(*R*$_S$,1*R*)-2-Methylpropane-2-sulfinic Acid (1-(Benzyloxymethyl)pentyl)amide (3b). Pure **3b** was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex to 70% EtOAc/Hex), with yields and diastereoselectivities given in Table 2: HPLC-MS (70−95% MeOH/H_2O over 3 min at 1 mL/min) t_R(major) = 4.44 min, t_R(minor) = 4.24 min; $[\alpha]^{23}D$ = −44.0 (c = 1.00, $CHCl_3$); IR 1069, 1604 cm^{-1}; ^1H NMR (400 MHz) δ 0.89 (m, 3H), 1.19 (s, 9H), 1.22−1.35 (m, 4H), 1.49−1.61 (m, 2H), 3.30−3.41 (m, 1H), 3.49 (dd, 1H, J = 9.35, 5.01), 3.61 (dd, 1H, J = 9.37, 4.37), 3.66 (d, 1H, J = 7.15), 4.45 (d, 1H, J = 11.88), 4.56 (d, 1H, J = 11.87), 7.24−7.31 (m, 5H); ^{13}C NMR (100 MHz) δ 13.90, 22.40, 22.53, 27.80, 32.48, 55.59, 55.68, 72.94, 73.12, 127.52, 127.62, 128.25, 138.02. Anal. Calcd for $C_{17}H_{29}NO_2S$: C, 65.55; H, 9.38; N, 4.50. Found: C, 65.50; H, 9.23; N, 4.36.

Absolute configuration was determined through sulfinyl group and benzyl group cleavage, affording (*R*)-2-aminohexan-1-ol: $[\alpha]^{23}D$ = −12.0 (c = 1.00, $CHCl_3$) [lit.: $[\alpha]^{23}D$ = −12.3 (c = 1.00, $CHCl_3$)].[14]

(*R*$_S$,1*R*)-2-Methylpropane-2-sulfinic Acid (1-(Benzyloxymethyl)-2-methylpropyl)amide (3c). Pure **3c** was obtained as a clear colorless oil after column chromatography (50% EtOAc/Hex to 70% EtOAc/Hex), with yields and diastereoselectivities given in Table 2: HPLC-MS (70−95% MeOH/H_2O over 3 min at 1 mL/min) t_R(major) = 5.12 min, t_R(minor) = 4.71 min; $[\alpha]^{23}D$ = −43.7 (c = 1.00, $CHCl_3$); IR 1069, 1604 cm^{-1}; ^1H NMR (400 MHz) δ 0.86 (d, 3H, J = 6.82), 0.88 (d, 3H, J = 6.84), 1.19 (s, 9H), 1.91−1.96 (m, 1H), 3.09−3.13 (m, 1H), 3.57−3.62 (m, 2H), 3.65 (d, 1H, J = 7.97), 4.43 (d, 1H, J = 11.82), 4.55 (d, 1H, J = 11.80), 7.22−7.39 (m, 5H); ^{13}C NMR (100 MHz) δ 18.55, 18.97, 22.64, 29.89, 55.90, 61.37, 70.83, 72.97, 127.53, 127.63, 128.25, 137.99. Anal. Calcd for $C_{16}H_{27}NO_2S$: C, 64.60; H, 9.15; N, 4.71. Found: C, 64.43; H, 9.22; N, 4.65.

(*R*$_S$,1*R*)-2-Methylpropane-2-sulfinic Acid (1-(Benzyloxymethyl)-2,2-dimethylpropyl)amide (3d). Pure **3d** was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex to 70% EtOAc/Hex), with yields and diastereoselectivities given in Tables 1 and 2: HPLC-MS (70−95% MeOH/H_2O over 3 min at 1 mL/min) t_R(major) = 5.06 min, t_R(minor) = 4.61 min; $[\alpha]^{23}D$ = −47.3 (c = 1.00, $CHCl_3$); IR 1072, 1604 cm^{-1}; ^1H NMR (400 MHz) δ 0.95 (s, 9H), 1.26 (s, 9H), 3.01−3.05 (m, 1H), 3.67 (dd, 1H, J = 9.93, 4.24), 3.81 (dd, 1H, J = 9.89, 3.24), 3.97 (d, 1H, J = 8.52), 4.45 (d, 1H, J = 11.82), 4.61 (d, 1H, J = 11.81), 7.31−7.35 (m, 5H); ^{13}C NMR (100 MHz) δ 22.80, 27.21, 35.08, 56.16, 64.27, 70.93, 73.09, 127.40, 127.53, 128.21, 138.20. Anal. Calcd for $C_{17}H_{29}NO_2S$: C, 65.55; H, 9.38; N, 4.50. Found: C, 65.70; H, 9.49; N, 4.37.

Determination of Absolute Configuration through Comparison with (*S*)-*tert*-Leucinol Benzyl Ether. (*S*)-*tert*-Leucinol (1.00 equiv, 168 mg) was added to a slurry of NaH (1.10 equiv, 63.2 mg) in 7.00 mL of THF (0.200 M). After cessation of gas evolution, the solution was transferred via filter cannula to a flask containing BnBr (0.175 mL, 1.00 equiv) in 7.00 mL of THF (0.200 M) and the solution stirred for 6 h. Concentration and chromatography afforded (*S*)-*tert*-leucinol benzyl ether in 78% yield after column chromatography (CH_2Cl_2 to 10% MeOH/CH_2Cl_2): $[\alpha]^{23}D$ = −14.0 (c = 1.00, $CHCl_3$). Refer to procedure for **9** for sulfinyl cleavage of **3d**: $[\alpha]^{23}D$ = +17.0 (c = 1.00, $CHCl_3$).

(*R*$_S$,1*R*)-2-Methylpropane-2-sulfinic Acid (2-Benzyloxy-1-phenylethyl)amide (3e). Pure **3e** was obtained as a clear, colorless solid after column chromatography (50% EtOAc/Hex to 70% EtOAc/Hex), with yields and diastereoselectivities given in Table 2: mp 73 °C; HPLC-MS (70−95% MeOH/H_2O over 3 min at 1 mL/min) t_R(major) = 4.43 min, t_R(minor) = 4.24 min; $[\alpha]^{23}D$ = −124 (c = 1.00, $CHCl_3$); IR 1071, 1603 cm^{-1}; ^1H NMR (400 MHz) δ 1.24 (s, 9H), 3.58−3.68 (m, 2H), 4.25 (s, 1H), 4.53 (d, 1H, J = 11.95), 4.64 (d, 1H, J = 11.94), 4.71−4.75 (m, 1H), 7.29−7.40 (m, 10 H); ^{13}C NMR (100 MHz) δ 22.50, 55.40, 57.21, 72.62, 74.01, 127.79, 127.77, 127.89, 128.00, 128.40, 128.42, 137.55, 138.48. Anal. Calcd for $C_{19}H_{25}NO_2S$: C, 68.85; H, 7.60, N, 4.23. Found: C, 68.80; H, 7.67; N, 4.07.

Absolute configuration was determined through sulfinyl group cleavage to afford (*R*)-2-benzyloxy-1-phenylethylamine: $[\alpha]^{23}D$ = −24.6 (c = 1.00, $CHCl_3$) [lit.: $[\alpha]^{23}D$ = −28.3° (c = 1.10, $CHCl_3$)].[15]

(*R*$_S$,1*R*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)propyl]amide (4a). The general procedure was followed with 52 mg of **2** (0.19 mmol), 1.0 mL of toluene, and 0.10 mL of EtMgBr (3.0 M solution in Et_2O, 0.29 mmol). Pure **4a** (53 mg, 91%) was obtained as a clear, colorless oil after column chromatography (20% EtOAc/Hex to 60% EtOAc/Hex), with a dr (crude) of 91:9: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 11.85 min, t_R(minor) = 11.44 min; $[\alpha]^{23}D$ = −57.0 (c = 1.00, $CHCl_3$); IR 1056, 1077, 1104, 1472 cm^{-1}; ^1H NMR (400 MHz) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 0.88−0.90 (m, 3H), 1.21 (s, 9H), 1.52−1.59 (m, 2H), 3.19−3.23 (m, 1H), 3.57−3.59 (m, 1H), 3.71−3.77 (m, 2H); ^{13}C NMR (100 MHz) δ −5.61, −5.48, 10.08, 18.09, 22.55, 25.25, 25.73, 55.46, 58.33, 65.58. Anal. Calcd for $C_{14}H_{33}NO_2SSi$: C, 54.67; H, 10.81; N, 4.55. Found: C, 54.38; H, 10.91; N, 4.65.

(*R*$_S$,1*R*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)pentyl]amide (4b). Pure **4b** (53 mg, 85%) was obtained as a clear, colorless oil after column chromatography (20% EtOAc/Hex to 60% EtOAc/Hex), with yields and diastereoselectivities given in Table 3: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 13.25 min, t_R(minor) = 12.90 min; $[\alpha]^{23}D$ = −46.4 (c = 1.00, $CHCl_3$); IR 1057, 1075, 1106 cm^{-1}; ^1H NMR (400 MHz) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.20 (s, 9H), 1.27−1.36 (m,

5H), 1.50−1.64 (m, 2H), 3.19−3.28 (m, 1H), 3.54−3.60 (m, 2H), 3.71−3.74 (m, 2H), 3.75−3.77 (m, 1H); ^{13}C NMR (100 MHz) δ −5.61, −5.48, 13.89, 18.09, 22.50, 22.54, 25.73, 27.73, 32.01, 55.43, 56.91. Anal. Calcd for $C_{16}H_{37}NO_2SSi$: C, 57.26; H, 11.11; N, 4.17. Found: C, 56.99; H, 11.21; N, 4.10.

(R_S,1*R*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-2-methylpropyl]amide (4c). The general procedure was followed with 52 mg of **2** (0.19 mmol), 1.0 mL of toluene, and 0.15 mL of *i*-PrMgCl (2.0 M solution in Et_2O, 0.29 mmol). Pure **4c** (53 mg, 88%) was obtained as a clear, colorless oil after column chromatography (20% EtOAc/Hex to 60% EtOAc/Hex), with a dr (crude) of 96:4: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 12.63 min, t_R(minor) = 12.12 min; $[\alpha]^{23}D = -37.1$ (c = 1.00, $CHCl_3$); IR 1077, 1104, 1472 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 0.87−0.90 (m, 6H), 1.20 (s, 9H), 1.87−1.94 (m, 1H), 2.93−3.01 (m, 1H), 3.69 (d, 1H, J = 7.9), 3.73 (d, 2H, J = 4.5); ^{13}C NMR (100 MHz) δ −5.65, −5.55, 18.02, 18.51, 18.94, 22.62, 25.70, 29.51, 55.69, 62.63, 63.51. Anal. Calcd for $C_{15}H_{35}NO_2SSi$: C, 56.02; H, 10.97; N, 4.36. Found: C, 55.97; H, 10.99; N, 4.29.

(R_S,*R*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethylpropyl]amide (4d). The general procedure was followed with 52 mg of **2** (0.19 mmol), 1.0 mL of toluene, and 0.15 mL of *t*-BuMgCl (2.0 M solution in Et_2O, 0.29 mmol). Pure **4d** (57 mg, 90%) was obtained as a clear, colorless oil after column chromatography (20% EtOAc/Hex to 60% EtOAc/Hex), with a dr (crude) of 96:4: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 13.38 min, t_R(minor) = 12.50 min; $[\alpha]^{23}D = -80.8$ (c = 1.00, $CHCl_3$); IR 1077, 1111, 1472 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 0.92 (s, 9H), 1.23 (s, 9H), 2.84−2.87 (m, 1H), 3.77 (dd, 1H, J = 10.3, 4.2), 3.94 (dd, 1H, J = 10.3, 1.8), 4.10 (d, 1H, J = 7.5); ^{13}C NMR (100 MHz) δ −5.71, −5.67, 17.93, 22.78, 25.70, 27.27, 35.17, 55.91, 63.29, 64.91. Anal. Calcd for $C_{16}H_{37}NO_2SSi$: C, 57.26; H, 11.11; N, 4.17. Found: C, 57.14; H, 11.31; N, 4.09. Refer to details for compound **10** for assignment of absolute configuration.

(R_S,*R*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-3-phenylprop-2-ynyl]amide (4e). Phenylacetylmagnesium bromide was first prepared according to a modified procedure by Poncini:[19] To a 25 mL Schlenk tube with sidearm under a N_2 atmosphere was added a solution of EtMgBr (0.32 mL, 0.97 mmol, 3.0 M) in Et_2O. To this solution was then added phenylacetylene (0.61 mL, 0.54 mmol). The valve was then closed and the tube heated to 60 °C for 6 h. The valve was then opened and the solvent evaporated under a stream of nitrogen for 45 min. To the residue was added 1.5 mL of toluene and the suspension cooled to −78 °C. To this mixture was added a solution of **2** (75 mg, 0.27 mmol) in 1.5 mL of toluene. Pure **4e** (63 mg, 90%) was obtained as a clear, colorless oil after column chromatography (30% EtOAc/Hex to 60% EtOAc/Hex), with a dr (crude) of 90:10: HPLC-MS (70−95% MeOH/H2O over 10 min at 1 mL/min) t_R(major) = 9.982 min, t_R(minor) = 10.87 min; ^{1}H NMR (400 MHz) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.91 (s, 9H), 1.24 (s, 9H), 3.70−3.77 (m, 1H), 3.80−3.87 (m, 2H), 7.27−7.30 (m, 3H), 7.40−7.44 (m, 2H); ^{13}C NMR (100 MHz) δ −5.45, −5.39, 18.19, 22.49, 25.73, 50.03, 56.18, 66.86, 85.61, 86.44, 128.09, 128.14, 128.27, 131.68. Barrow et al. previously prepared this compound.[9]

(R_S,1*R*)-2-Methylpropane-2-sulfinic Acid [2-(*tert*-Butyldimethylsilanyloxy)-1-phenylethyl]amide (4f). The general procedure was followed with 52 mg of **2** (0.19 mmol), 1.0 mL of toluene, and 0.10 mL of PhMgBr (3.0 M solution in Et_2O, 0.29 mmol). Pure **4f** (63 mg, 95%) was obtained as a clear, colorless oil after column chromatography (20% EtOAc/Hex to 60% EtOAc/Hex), with a dr (crude) of 96:4: HPLC-MS (60.0−97.5% MeOH/H_2O over 20 min at 1 mL/min) t_R(major) = 16.70 min, t_R(minor) = 16.45 min; $[\alpha]^{23}D = -111$ (c = 1.00, $CHCl_3$); IR 1069, 1077, 1630 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.05 (s, 3H), 0.07 (s, 3H), 0.91 (s, 9H), 1.23 (s, 9H), 3.59−3.64 (m, 1H), 3.78 (dd, 1H, J = 10.1, 4.1), 4.29 (m, 1H), 4.51−4.55 (m, 1H), 7.28−7.36 (m, 5H); ^{13}C NMR (100 MHz) δ −5.61, −5.42, 18.07, 22.47, 25.72, 55.23, 59.25, 67.76, 110.40, 127.95, 128.32, 138.45. Anal. Calcd for $C_{18}H_{33}NO_2SSi$: C, 60.79; H, 9.35; N, 3.94. Found: C, 60.40; H, 9.58; N, 3.73.

Absolute determination was determined through deprotection of **4e**, affording (*R*)-phenylglycinol: $[\alpha]^{23}D = -29.1$ (c = 0.750, 1.00 *N* HCl) [lit.: $[\alpha]^{23}D = -26.7$ (c = 0.075, 1.00 N HCl)].[9]

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid (1-(Benzyloxymethyl)-1-methylpentyl)amide (7a). Pure **7a** was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 4. (Diastereomeric ratio determined through comparison of integration of doublets (major) at 3.26 and 3.40 ppm with doublet at 3.34 ppm: $[\alpha]^{23}D = -57.1$ (c = 1.00, $CHCl_3$); IR 1069 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.90 (t, 3H, J = 6.9), 1.18−1.19 (m, 12H), 1.21−1.34 (m, 4H), 1.68−1.72 (m, 2H), 3.26 (d, 1H, J = 8.9), 3.40 (d, 1H, J = 8.9), 3.61 (s, 1H), 4.50 (d, 1H, J = 12), 4.55 (d, 1H, J = 12), 7.26−7.36 (m, 5H); ^{13}C NMR (100 MHz) δ 13.96, 22.51, 23.04, 23.08, 25.85, 37.80, 55.39, 58.03, 73.10, 76.83, 127.46, 127.49, 128.22, 138.23. Anal. Calcd for $C_{18}H_{31}NO_2S$: C, 66.42; H, 9.60; N, 4.30. Found: C, 66.60; H, 9.49; N, 4.19.

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid (2-Benzyloxy-1-methyl-1-phenylethyl)amide (7b). Pure **7b** was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 4: HPLC-MS (60.0−97.5% MeOH/H_2O over 20 min at 1 mL/min) t_R(major) = 11.36 min, t_R(minor) = 11.69 min; $[\alpha]^{23}D = -30.9$ (c = 1.00, $CHCl_3$); IR 1068, 1602 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.21 (s, 9H), 1.64 (s, 3H), 3.76 (d, 1H, J = 9.0), 3.87 (d, 1H, J = 9.0), 4.09 (d, 1H, J = 2.8), 4.51 (d, 1H, J = 12), 4.59 (d, 1H, J = 12), 7.26−7.43 (m, 8H), 7.49−7.51 (m, 2H); ^{13}C NMR (100 MHz) δ 22.58, 26.54, 55.87, 60.75, 73.20, 77.53, 126.65, 127.22, 127.50, 127.55, 128.12, 128.24, 137.99, 143.48. Anal. Calcd for $C_{20}H_{27}NO_2S$: C, 69.53; H, 7.88; N, 4.05. Found: C, 69.37; H, 7.94; N, 3.89.

Determination of Absolute Configuration of 7b. The representative procedures were followed for conversion of *O*-benzyl sulfinamides **7** to amino alcohols, affording (*S*)-2-amino-2-phenylpropan-1-ol (8.6 mg, 70%): $[\alpha]^{23}D = +7.40$ (c = 0.500, EtOH) [lit.: $[\alpha]^{23}D = +14.3$ (c = 0.980, EtOH)].[17]

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-1-methylpropyl]amide (8a). Pure **8a** was obtained as a clear, colorless oil after column chromatography (30% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 5: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 10.45 min, t_R(minor) = 10.69 min; $[\alpha]^{23}D = -43.6$ (c = 1.00, $CHCl_3$); IR 1077, 1463 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.06 (s, 3H), 0.06 (s, 3H), 0.86−0.94 (m, 3H), 0.90 s, 9H), 1.14 (s, 3H), 1.19 (s, 9H), 1.73 (q, 2H, J = 7.4), 3.32 (d, 1H, J = 9.4), 3.51 (d, 1H, J = 9.4), 3.66 (s, 1H); ^{13}C NMR (100 MHz) δ −5.76, −5.72, 8.32, 18.08, 21.71, 22.52, 25.71, 30.61, 55.35, 58.77, 69.27. Anal. Calcd for $C_{15}H_{35}NO_2SSi$: C, 56.02; H, 10.97; N, 4.36. Found: C, 55.98; H, 10.99; N, 4.30.

Determination of Absolute Configuration of 8a. The general procedure was followed for conversion of TBS protected sulfinamides **8** to amino alcohols, affording (*S*)-2-amino-2-methylbutan-1-ol (9.1 mg, 74%): $[\alpha]^{23}D = -4.40$ (c = 0.500, EtOH) [lit.: (*R*)-enantiomer $[\alpha]^{23}D = +3.40$ (c not reported, EtOH)].[18]

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-1-methylpentyl]amide (8b). Pure **8b** was obtained as a clear, colorless oil after column chromatography (30% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 5: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 11.55 min, t_R(minor) = 11.76 min; $[\alpha]^{23}D = -46.5$ (c = 1.00, $CHCl_3$); IR 1072, 1104, 1471 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 0.90 (m, 3H), 1.19 (s, 9H), 1.24 (s, 3H), 1.29 (m, 2H), 1.66−1.70 (m, 4H), 3.32 (d, 1H, J = 9.4), 3.51 (d, 1H, J = 9.4), 3.68 (s, 1H); ^{13}C NMR (100 MHz) δ

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−5.68, −5.62, 13.99, 18.08, 22.07, 22.52, 23.09, 25.71, 26.16, 37.80, 55.32, 58.53, 69.54. Anal. Calcd for $C_{17}H_{39}NO_2SSi$: C, 58.40; H, 11.24; N, 4.01. Found: C, 58.20; H, 11.13; N, 3.89.

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-1,2-dimethylpropyl]amide (8c). Pure **8c** was obtained as a clear, colorless oil after column chromatography (30% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 5: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 11.02 min, t_R(minor) = 11.57 min; $[\alpha]^{23}D = -29.8$ ($c = 0.500$, $CHCl_3$); IR 1072, 1105 cm^{-1}; ^1H NMR (500 MHz) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 0.94 (d, 3H, $J = 6.9$), 0.98 (d, 3H, $J = 3.9$), 1.10 (s, 3H), 1.19 (s, 9H), 2.02−2.08 (m, 1H), 3.38 (d, 1H, $J = 9.6$), 3.59 (d, 1H, $J = 9.5$), 3.69 (s, 1H); ^{13}C NMR (125 MHz) δ −5.68, −5.63, 17.26, 17.65, 18.09, 19.27, 22.63, 25.76, 33.69, 55.58, 60.98, 68.82. Anal. Calcd for $C_{16}H_{37}NO_2SSi$: C, 57.26; H, 11.11; N, 4.17. Found: C, 57.22; H, 10.98; N, 4.12.

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid [1-((*tert*-Butyldimethylsilanyloxy)methyl)-1,2,2-trimethylpropyl]amide (8d). Pure **8d** was obtained as a clear, colorless oil after column chromatography (30% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 5: HPLC-MS (70−95% MeOH/H_2O over 10 min at 1 mL/min) t_R(major) = 10.78 min, t_R(minor) = 11.52 min; $[\alpha]^{23}D = -35.2$ ($c = 0.500$, $CHCl_3$); IR 1073, 1432 cm^{-1}; ^1H NMR (400 MHz) d 0.06 (s, 3H), 0.07 (s, 3H), 0.91 (s, 9H), 1.04 (s, 9H), 1.18 (s, 3H), 1.21 (s, 9H), 3.43 (d, 1H, $J = 10$), 3.72 (d, 1H, $J = 10$), 3.77 (m, 1H); ^{13}C NMR (100 MHz) δ −5.76, −5.72, 14.09, 19.02, 22.61, 25.74, 26.50, 37.14, 55.87, 62.46, 69.31. Anal. Calcd for $C_{17}H_{39}NO_2SSi$: C, 58.40; H, 11.24; N, 4.01. Found: C, 58.32; H, 11.25; N, 3.87.

(R_S,1*S*)-2-Methylpropane-2-sulfinic Acid [2-(*tert*-Butyldimethylsilanyloxy)-1-methyl-1-phenylethyl]amide (8e). Pure **8e** was obtained as a clear, colorless oil after column chromatography (30% EtOAc/Hex to 70% EtOAc/Hex) with yields and diastereoselectivities given in Table 5. Diastereomeric ratio determined through comparison of integration of doublets (major) at 3.75 and 3.85 ppm with doublets at 3.47 and 3.80 ppm: $[\alpha]^{23}D = -33.8$ ($c = 1.00$, $CHCl_3$); IR 1071, 1252, 1472 cm^{-1}; ^1H NMR (400 MHz) δ −0.09 (s, 3H), −0.04 (s, 3H), 0.83 (s, 9H), 1.24 (s, 9H), 1.62 (s, 3H), 3.75 (d, 1H, $J = 9.5$), 3.85 (d, 1H, $J = 9.5$), 4.19 (s, 1H), 7.23−7.27 (m, 1H), 7.31−7.33 (m, 2H), 7.49−7.51 (m, 2H); ^{13}C NMR (100 MHz) δ −5.83, −5.77, 18.04, 22.59, 25.64, 56.17, 63.21, 71.46, 110.39, 126.89, 127.91, 144.10. Anal. Calcd for $C_{19}H_{35}NO_2SSi$: C, 61.74; H, 9.54; N, 3.79. Found: C, 61.65; H, 9.49; N, 3.75.

Determination of Absolute Configuration of 8e. The general procedure was followed for conversion of TBS protected sulfinamides **8** to amino alcohols, affording 2-amino-2-phenylpropan-1-ol (9.1 mg, 70%): $[\alpha]^{23}D = +11.6$ ($c = 0.500$, EtOH) [lit.: (*S*)-enantiomer $[\alpha]^{23}D = +14.3$ ($c = 0.980$, EtOH)].[17]

Representative Procedure for the Sulfinyl Group Cleavage for Sulfinamides 7, (*R*)-1-(Benzyloxymethyl)-2,2-dimethylpropylamine (9). To a 0.160 M solution of sulfinamide **3d** (50.0 mg, 0.161 mmol) in MeOH (1.00 mL) was added 0.400 mL of 4.00 N HCl/dioxane (10.0 equiv, 1.61 mmol). The solution was stirred for 30 min at room temperature and then concentrated in vacuo. Pure **9** (32.1 mg, 97%) was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex to elute sulfur-containing impurities then 10% MeOH/CH_2Cl_2): $[\alpha]^{23}D = +17.0$ ($c = 1.00$, $CHCl_3$), IR 1602 cm^{-1}; ^1H NMR (400 MHz) δ 0.90 (s, 9H), 1.59 (s, 2H), 2.74 (dd, 1H, $J = 9.2, 2.9$), 3.25 (t, 2H, $J = 9.1$), 3.64 (dd, 1H, $J = 9.0, 2.9$), 4.51 (d, 1H, $J = 12$), 4.53 (d, 1H, $J = 12$); ^{13}C NMR (100 MHz) δ 26.44, 32.94, 59.49, 72.52, 73.21, 127.53, 127.57, 128.35, 138.36. Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.05; H, 10.23; N, 6.66.

Representative Procedure for the Hydrogenation of Bn Protected Amino Alcohols. (*R*)-*tert*-Leucinol (10). To a solution of **9** (32.1 mg, 0.156 mmol) in MeOH (0.500 M) was added a slurry of dry Pd/C (50.0 mg, 10% Pd) in EtOAc and then 0.400 mL of HCl/dioxane (10.0 equiv, 1.56 mmol). The mixture was briefly purged with a stream of H_2 and then stirred overnight under a H_2 atmosphere (balloon). The reaction mixture was then filtered through Celite and concentrated. The residue was then dissolved in EtOAc and washed with 5.00 mL of 4 N NaOH. The aqueous layer was extracted 3× with EtOAc, and the combined organic layers were dried and evaporated to afford pure **10** (16.0 mg, 88.0%). Spectroscopic data were consistent with those previously observed.[14]

Representative Procedure for the Deprotection of TBS Protected Sulfinamides 4 and 8. (*R*)-*tert*-Leucinol (10). To a solution of **4d** (50.0 mg, 0.143 mmol) in MeOH (0.300 mL) was added 0.360 mL of 4 N HCl/dioxane (1.43 mmol). The solution was stirred for 30 min at room temperature and then concentrated in vacuo. The residue was then dissolved in EtOAc and washed with 5.00 mL of 4 N NaOH. The aqueous layer was extracted 3× with EtOAc, and the combined organic layers were dried and evaporated. Pure **10** (14.6 mg, 87.0%) was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex to elute sulfur-containing impurities then 10% MeOH/CH_2Cl_2). Spectroscopic data was consistent with that previously observed: $[\alpha]^{23}D = -34.0$ ($c = 1.00$, EtOH) [lit.: (*S*)-enantiomer $[\alpha]^{26}D = +37.2$ ($c = 3.00$, EtOH)].[14]

(R_S,*R*)-2-Methylpropane-2-sulfinic Acid (1-(Hydroxymethyl)-2,2-dimethylpropyl)amide (11). In a polypropylene centrifuge tube was added a solution of **4d** (50.0 mg, 0.143 mmol) in THF (0.715 mL) and the solution cooled to 0 °C. To this solution was added 0.715 mL of 14% HF/pyridine. The solution was stirred at room temperature for 24 h and then poured into a separatory funnel containing 10.0 mL of $NaHCO_3$ (saturated) and 10.0 mL of EtOAc. The separatory funnel was agitated until cessation of gas evolution, and then the aqueous layer was extracted 3× with EtOAc. The organic layers were washed with brine (1×), dried, and then concentrated. Pure **11** (24.4 mg, 77.0%) was obtained as a clear, colorless oil after column chromatography (50% EtOAc/Hex): $[\alpha]^{23}D = -30.4$ ($c = 0.500$, $CHCl_3$); IR 1071 cm^{-1}; ^1H NMR (400 MHz) δ 0.95 (s, 9H), 1.29 (s, 9H), 2.98 (m, 1H), 3.43 (m, 1H), 3.94 (m, 1H), 4.59 (m, 1H); ^{13}C NMR (100 MHz) δ 22.80, 26.85, 29.58, 57.07, 64.90, 69.57. Anal. Calcd for $C_{10}H_{23}NO_2S$: C, 54.26; H, 10.47; N, 6.33. Found: C, 54.01; H, 10.44; N, 6.29.

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