JOC Article

Stereoselective Synthesis of 1,2-Disubstituted β-Amino Alcohols by Nucleophilic Addition to *N*-*tert*-Butanesulfinyl α-Alkoxyaldimines

Jared W. Evans and Jonathan A. Ellman*

Center for New Directions for Organic Synthesis, Department of Chemistry, University of California, Berkeley, California 94720

jellman@uclink.berkeley.edu

Received August 20, 2003

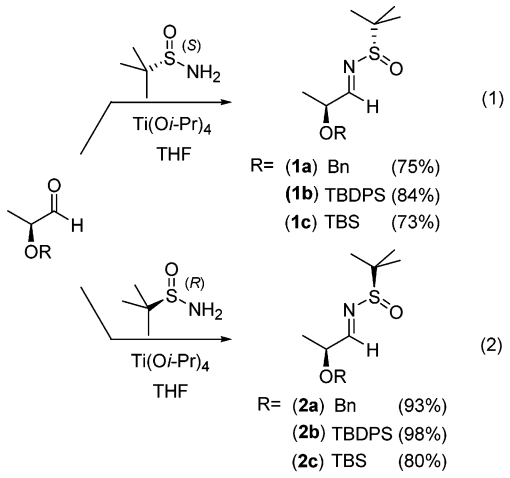
N-*tert*-Butanesulfinyl α-alkoxyaldimines are readily prepared from protected (*S*)-lactals without epimerization at the α-stereocenter. Addition of ethyl and phenyl Grignard reagents, as well as the titanium enolate of methyl acetate, to the *N*-*tert*-butanesulfinyl aldimines provides 1,2-disubstituted β-amino alcohols in good yields (73−98%) and with high diastereoselectivities. Either *syn*- or *anti*-amino alcohol products can be obtained by the appropriate choice of alcohol protecting groups and/or reaction conditions. Finally, deprotection of the addition products provides straightforward access to either *syn*- or *anti*-1,2-amino alcohols.

Introduction

β-Amino alcohols are important structural motifs in natural products, pharmacologically active compounds, chiral auxiliaries, and ligands.[1,2] Many methods for the asymmetric synthesis of 1,2-disubstituted β-amino alcohols, such as the enantioselective aminohydroxylation of alkenes or the reduction of protected α-amino ketones,[3,4] rely on functional group interconversion.[5] A more convergent approach is the well-studied diastereoselective addition of nucleophiles to protected, chiral amino aldehydes.[6] In contrast, only a few reports have appeared on the alternative convergent approach of nucleophilic addition to α-alkoxy imines.[7] Recently, we have reported, as have others, on the diastereoselective addition of nucleophiles to *N*-*tert*-butanesulfinyl-α-alkoxyacetaldimines for the expedient asymmetric synthesis of β-amino alcohols.[8] Here we describe the application of this methodology to the synthesis of both *syn*- and *anti*-1,2-disubstituted β-amino alcohols by the addition of nucleophiles to *N*-*tert*-butanesulfinyl aldimines prepared from hydroxyl protected (*S*)-lactals.

Results and Discussion

Preparation of the *N*-Sulfinyl Imines. The *N*-sulfinyl aldimines **1a**−**c** (eq 1) and **2a**−**c** (eq 2) were



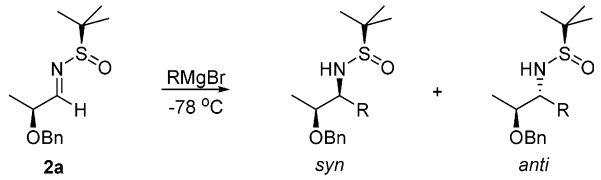
prepared by the titanium-mediated condensation of the corresponding protected (*S*)-lactals with either (S_S)- or (R_S)-*tert*-butanesulfinamide, respectively.[9] Both diastereomers of the protected *N*-sulfinyl aldimines were synthesized to probe the steric and electronic factors involved in the addition reactions. Each enantiomer of *tert*-butanesulfinamide condensed in good yields and with comparable rates regardless of the hydroxyl protecting group. While racemization has previously been reported for the condensation of α-substituted aldehydes with amines,[10] no epimerization of the α-stereocenter of **1a**−**c** or **2a**−**c** was detected by chiral HPLC analysis.[11]

Addition of nucleophiles to *N*-Sulfinyl Imines. We initially explored the addition of phenyl and ethyl Grig-

(1) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835−875.
(2) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds. *Comprehensive Asymmetric Catalysis*, 1st ed.; Springer: Berlin, Germany, 1999.
(3) Andersson, M. A.; Epple, R.; Folkin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 472−475. Demko, Z. P.; Bartsch, M.; Sharpless, K. B. *Org. Lett.* **2000**, *2*, 2221−2223.
(4) Hoffman, R. V.; Maslouh, N.; Cervantes-Lee, F. *J. Org. Chem.* **2002**, *67*, 1045−1056.
(5) For a recent review of asymmetric synthesis of vicinal amino alcohols see: Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561−2576.
(6) Reetz, M. *Chem. Rev.* **1999**, *99*, 1121−1162.
(7) (a) Ishimaru, K.; Tsuru, K.; Yabuta, K.; Wada, M.; Yamamoto, Y.; Akiba, K. *Tetrahedron* **1996**, *52*, 13137−13144. (b) Cianelli, G.; Giacomini, D.; Panunzio, M.; Zarantonello, P. *Tetrahedron Lett.* **1992**, *33*, 7783. (c) Zietlow, A.; Steckhan, E. *J. Org. Chem.* **1994**, *59*, 5658−5661.
(8) (a) Barrow, J. C.; Ngo, P. L.; Pellicore, J. M.; Selnick, H. G.; Nantermet, P. G. *Tetrahedron Lett.* **2001**, *42*, 2051−2054. (b) Tang, T. P.; Volkman S. K.; Ellman, J. A. *J. Org. Chem.* **2001**, *66*, 8772−8778.
(9) Lui, G.; Cogan, D. A.; Owens, T. D.; Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 1278−1284.

10.1021/jo035224p CCC: $25.00
Published on Web 11/22/2003

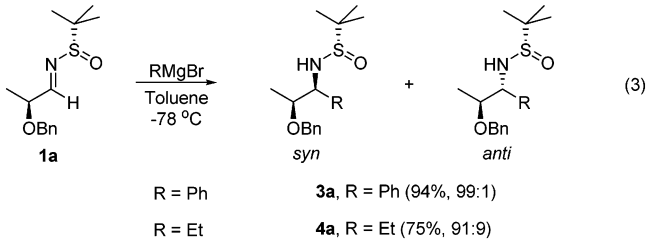
TABLE 1. Organometallic Additions to (R_S,2*S*) Benzyloxysulfinyl Aldimine



entry	product	RM	solvent	yield[a] (%)	dr[b] (syn:anti)
1	**5a**	PhMgBr	toluene	98	23:77
2		PhMgBr	toluene/$AlMe_3$[c]	74	25:75
3		PhMgBr	THF		22:78
4		PhMgBr	THF/TMEDA[d]	80	5:95
5	**6a**	EtMgBr	toluene	93	14:86
6		EtMgBr	THF	93	10:90
7		EtMgBr	THF/TMEDA[d]	86	2:98

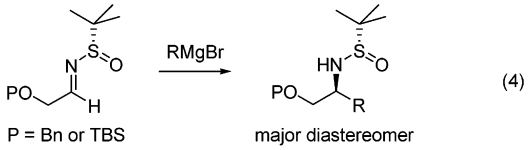
[a] Yields were determined by mass balance of purified material. [b] Ratios were determined by HPLC-MS analysis of crude reaction mixtures after workup. [c] 1.1 equiv of $AlMe_3$ was used. [d] 2.1 equiv of TMEDA was added to the Grignard reagent prior to the addition to the aldimine.

nard reagents as solutions in ether to the *N*-sulfinyl aldimine (S_S,2*S*)-**1a** (eq 3). The syn products were obtained in high yields and with high stereoselectivities for both Grignard reagents. Significantly, no epimerization of the α-stereocenter occurred under the reaction conditions as determined by HPLC analysis.



(3)

The observed syn selectivity for the addition of these nucleophiles to **1a** is consistent with the Cram chelate model for nucleophilic additions into α-alkoxyaldehydes,[12] as well as the sense of induction previously observed for additions to ether protected *N*-*tert*-butanesulfinyl α-hydroxyacetaldimines (eq 4).[8b]



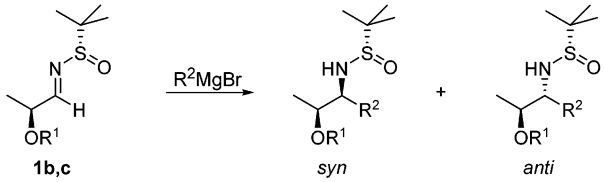
(4)

The addition of the phenyl and ethyl Grignard reagents to *N*-sulfinyl aldimine (R_S,2S)-**2a** proceeded with only modest diastereofacial selectivities in toluene (Table 1, entries 1 and 5). We have previously observed that precomplexation of *N*-sulfinyl imines with the Lewis acid $AlMe_3$ can increase yields and diastereoselectivities for the addition of organometallic reagents.[8b] However, addition of PhMgBr to sulfinyl imine **2a** in the presence of 1.1 equiv of $AlMe_3$ did not enhance selectivities in this case (entry 2). Interestingly, greatly increased anti selectivity (95:5) was observed for the addition of PhMgBr in the presence of the Lewis base *N*,*N*,*N*,*N*-tetramethylethylenediamine (TMEDA) in THF (entry 4). Use of these improved conditions for the addition of EtMgBr to **2a** also led to a higher level of selectivity (98:2) over additions run in THF alone (entry 6 vs 7).

It is interesting to note that anti selectivity was observed, which suggests that the diastereofacial selectivity afforded by the *N*-sulfinyl group overrides the selectivity predicted by the Cram chelate model (eq 4).[12] The increased anti selectivity observed in the presence of TMEDA could be rationalized if TMEDA disrupts the chelate predicted by Cram's model.[13]

To determine the effect of the alcohol protecting group on the diastereofacial selectivity of the nucleophilic additions, we examined the addition of the Grignard reagents to silyl ether protected aldimines (*S*S,2*S*)-**1b** and (*S*S,2*S*)-**1c** (Table 2). Phenyl Grignard reagent added to the TBDPS protected imine **1b** with high anti selectivities when either CH_2Cl_2 or toluene was used as the solvent (entries 1 and 2). In contrast, poor selectivities were observed for the addition of PhMgBr to TBS protected imine **1c** regardless of whether CH_2Cl_2 or toluene was employed (Table 2, entries 3 and 4). Addition of ethyl Grignard reagent gave high anti selectivity for the TBDPS protected imine **1b** (Table 2, entries 5 and 6), while high syn selectivity was observed for the TBS protected imine **1c** (Table 2, entry 7).[14] A similarly dramatic effect of the silyl protecting group (TBS vs TIPS)

TABLE 2. Organometallic Additions to (S_S,2*S*) Silyloxysulfinyl Aldimine



entry	product	R^2MgBr	R^1	temp (°C)	solvent	yield[a] (%)	dr[b] (syn:anti)
1	**3b**	PhMgBr	TBDPS	−48	CH_2Cl_2	80[c]	6:94
2		PhMgBr	TBDPS	−48	toluene	86[c]	7:93
3	**3c**	PhMgBr	TBS	−78	CH_2Cl_2	95	75:25
4		PhMgBr	TBS	−78	toluene	89	40:60
5	**4b**	EtMgBr	TBDPS	−48	CH_2Cl_2	73	10:90
6		EtMgBr	TBDPS	−48	toluene	90	17:83
7	**4c**	EtMgBr	TBS	−78	toluene	94	92:8

[a] Yields were determined by mass balance of purified material. [b] Ratios were determined by ^{1}H NMR analysis of crude reaction mixtures after workup. [c] Yield of major diastereomer was determined by mass balance of purified material.

(10) Reetz, M. T.; Drewes, M. W.; Schmitz, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1141−1143.

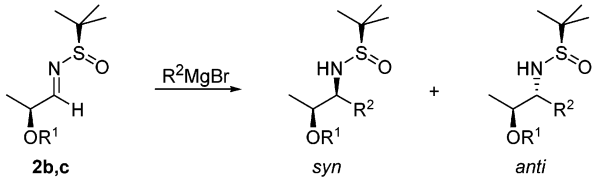
(11) For additions to α-aminosulfinyl aldimine see: Prakash, G. K. S.; Mandal, M. *J. Am. Chem. Soc.* **2002**, *124*, 6538−6539. For an addition to α-alkoxysulfinyl aldimine see: Jung, P. M. J.; Beaudegnies, R.; De Mesmaeker, A.; Wendeborn, S. *Tetrahedron Lett.* **2003**, *44*, 293−297.

(12) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. Stocker, J. H.; Benjamin, B. M.; Collins, C. J. *J. Am. Chem. Soc.* **1960**, *82*, 3913.

(13) Rutherford, J. L.; Hoffmann, D.; Collum, D. B. *J. Am. Chem. Soc.* **2002**, *124*, 264−271.

(14) Addition of ethyl Grignard to (S_S,2*S*) silyloxysulfinyl aldimines **1b** and **1c** in the presence of 2 equiv of TMEDA in THF reversed diastereoselectivities of **5b** from 90:10 (Table 2, entry 5) to 11:89 (anti:syn), and in the case of **5c** decreased selectivities from 92:8 (Table 2, entry 7) to 69:31.

TABLE 3. Organometallic Additions to (R_S,2*S*) Silyloxysulfinyl Aldimine



entry	product	R^2MgBr	R^1	temp (°C)	solvent	yield[a] (%)	dr[b] (syn:anti)
1	**5b**	PhMgBr	TBDPS	−48	toluene	88	21:79
2		PhMgBr	TBDPS	−78	THF		35:65
3		PhMgBr	TBDPS	−78	THF/TMEDA[e]	72[c]	12:88
4	**5c**	PhMgBr	TBS	−78	toluene	90	7:93
5		PhMgBr	TBS	−78	THF/TMEDA[e]	78[c]	2:98[d]
6	**6b**	EtMgBr	TBDPS	−48	toluene	75	65:35
7		EtMgBr	TBDPS	−78	THF/TMEDA[e]	93[c]	2:98[d]
8	**6c**	EtMgBr	TBS	−78	toluene	77	20:80
9		EtMgBr	TBS	−78	THF/TMEDA[e]	81[c]	2:98[d]

[a] Yields were determined by mass balance of purified material. [b] Ratios were determined by ^{1}H NMR analysis of crude reaction mixtures after workup. [c] Yield of major diastereomer was determined by mass balance of purified material. [d] Ratios were determined by HPLC-MS analysis of crude reaction mixtures after workup. [e] 2.1 equiv of TMEDA was added to the Grignard reagent prior to the addition to the aldimine.

upon the diastereoselectivity for the addition of organometallic reagents to α-alkoxyimines, previously reported by Cainelli, was attributed to differential entropies of activation.[15]

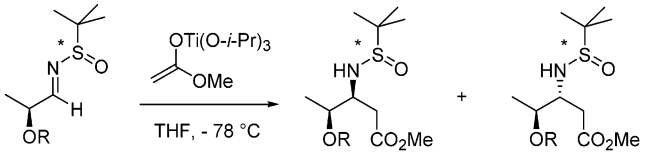
The anti selectivity that is observed, except for the special cases of EtMgBr and PhMgBr additions to the TBS protected lactal **1c** (Table 2, entries 2, 3, and 7), is consistent with both the Felkin Ahn[16] and Conforth[17] models for nucleophilic additions into α-alkoxy ketones and aldehydes, and is opposite to the inherent selectivity provided by the sulfinyl group (eq 4).[8b]

Under optimized reaction conditions high anti selectivities could also be achieved for the addition of nucleophiles to *N*-sulfinyl imines (R_S,2*S*)-**2b** and (R_S,2*S*)-**2c** (Table 3). Addition of PhMgBr to the TBDPS protected aldimine **2b** provided only modest selectivities regardless of the solvent employed (entries 1 and 2). However, addition of PhMgBr in the presence of the TMEDA in THF resulted in a significant improvement in diastereoselectivity to 88:12 (entry 3). Addition of PhMgBr to the TBS protected aldimine **2c** proceeded with high levels of diastereoselectivity when toluene was used as solvent (entry 4), and performing the addition reaction with TMEDA in THF resulted in an even higher diastereoselectivity of 98:2 (entry 5). The addition of EtMgBr to the TBPDS and TBS protected aldimines **2b** and **2c**, respectively, proceeded with excellent selectivity (98:2) with TMEDA in THF (entries 7 and 9), but with only modest selectivities when toluene was employed as the solvent (entries 6 and 8).

The anti selectivity observed for the addition of nucleophiles to **2b** and **2c** is consistent with both Felkin Ahn[16] and Cornforth[17] models, as well as the inherent selectivity previously observed for nucleophilic additions to *N*-sulfinyl α-silyloxyacetaldimines (eq 4).[8b,18] The increased diastereomeric ratios in the presence of TMEDA suggests that the modest selectivities observed in the absence of a Lewis base result from chelation to the silyl ether.

The addition of the titanium enolate of methyl acetate to the benzyl protected sulfinyl imines **1a** and **2a** and the silyl-protected imines **1b**−**c** and **2b**−**c** was also

TABLE 4. Enolate Additions to Sulfinyl Aldimines 1 and 2



entry	product	imine	R	yield[a] (%)	dr[b] (syn:anti)
1	**7a**	**1a**	Bn	96	12:88
2	**7b**	**1b**	TBDPS	74	9:91
3	**7c**	**1c**	TBS	87[c]	5:95
4	**8a**	**2a**	Bn	89	26:74
5	**8b**	**2b**	TBDPS	78	90:10
6	**8c**	**2c**	TBS	51[c]	57:43

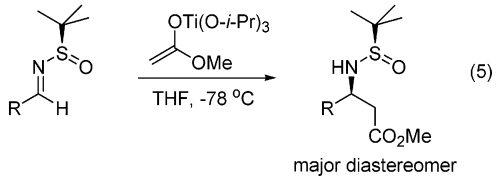
[a] Yields were determined by mass balance of purified material. [b] Ratios were determined by ^{1}H NMR analysis of crude reaction mixtures after workup. [c] Yield of major diastereomer was determined by mass balance of purified material.

evaluated (Table 4). Previous studies had clearly indicated that the titanium counterion provides the highest diastereoselectivities for additions to *N*-*tert*-butanesulfinyl imines.[19] As shown in Table 4, high anti stereoselectivity was observed for the addition to imines (S_S,2*S*)-**1a**−**c**. In contrast, more modest anti selectivity (Table 4, entry 4) or even syn selectivity (entries 5 and 6) was observed for addition to (R_S,2*S*)-**2a**−**c** depending on the alcohol protecting group.

Anti stereoselectivity observed for the titanium enolate additions to imines **1a**−**c** is consistent with the inherent selectivity previously observed for enolate additions to

(15) Cianelli, G.; Giacomini, D.; Galletti, P. *Eur. J. Org. Chem.* **1999**, 61−65.
(16) Ahn, N. T. *Top. Curr. Chem.* **1980**, *88*, 145.
(17) Evans, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 1761−1765.
(18) Addition of EtMgBr to *N*-*tert*-butanesulfinyl-α-*tert*-butyldimethylsilyloxyacetaldimine in the presence of 2 equiv of TMEDA in THF proceeded with 90:10 diastereoselectivity (88:12 diastereoselectivity was reported for the same reaction in toluene).[8b]
(19) Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 12−13.

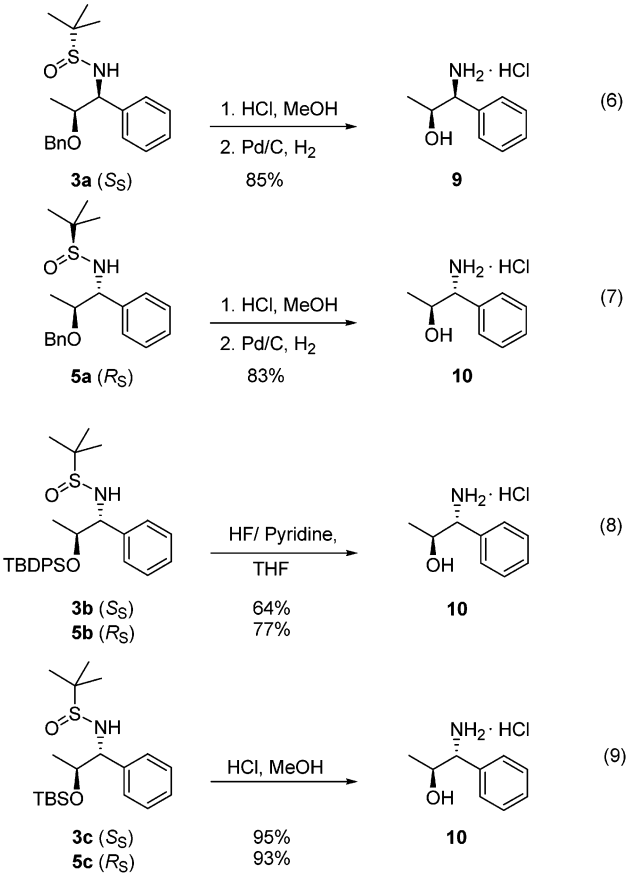
α-alkoxy aldehydes,[20] as well as enolate additions to *N-tert*-butanesulfinyl imines (eq 5).[21] For the titanium



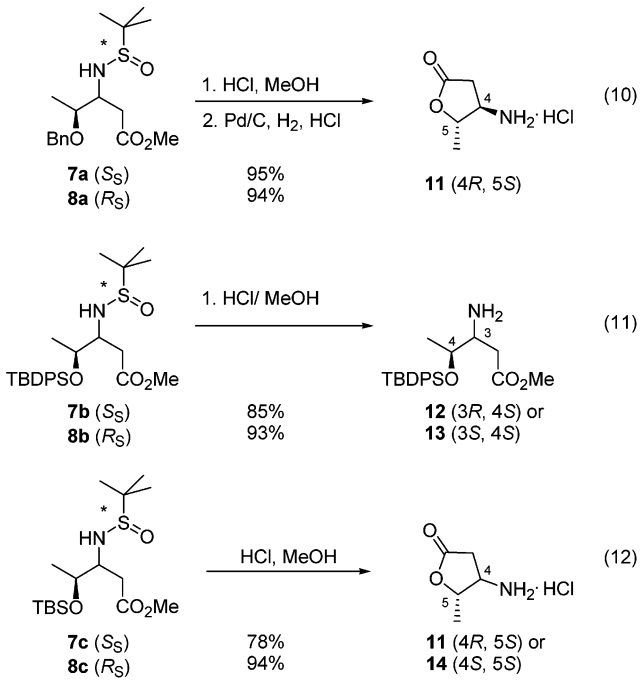
(5)

enolate additions to sulfinyl imines **2a**−**c**, the inherent selectivity provided by the sulfinyl group opposes the selectivity provided by the Felkin Ahn[16] and Conforth[17] models, which explains the poor selectivity for **2a** and **2c** and the syn selectivity for **2b**.

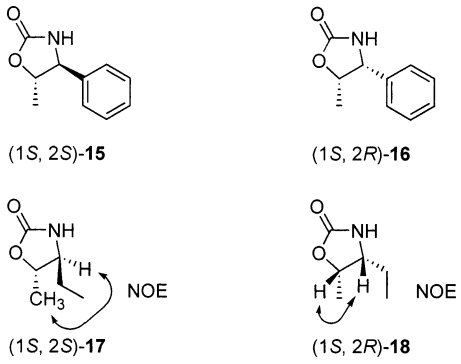
Deprotection of the *N*-Sulfinyl Imine Addition Products. The *N*-sulfinyl imine addition products were deprotected to provide the β-amino alcohols in good to excellent yields. Treatment of the benzyloxy-protected amino alcohols **3a** and **5a** with HCl/MeOH resulted in removal of the sulfinyl groups, and after hydrogenolysis of the benzyloxy ethers, the amine hydrochlorides of amino alcohols **9** and **10** were isolated in 85% and 83% yields, respectively (eqs 6 and 7).[8b] Treatment of the TBDPS ethers **3b** and **5b** with 70% HF/pyridine effectively cleaved both the silyl and sulfinyl groups with comparable rates (eq 8). In contrast, global deprotection of the TBS ethers **3c** and **5c** could be accomplished in high yields (95 and 93%) simply by employing HCl/MeOH (eq 9).



The methyl acetate addition products **7a** and **8a** were readily deprotected to afford lactone **11** in 95% and 94% yields, respectively, by treatment with HCl/MeOH and subsequent hydrogenolysis (eq 10). Unfortunately, attempts to concomitantly cleave both the sulfinyl group and the TBPDS groups from **7b** and **8b** with HF/pyridine were unsuccessful. However, selective cleavage of the sulfinyl group with acidic methanolysis could be accomplished to afford amines **12** and **13** in high yields (eq 11). Concomitant removal of the sulfinyl and TBS groups from methyl acetate addition product **7c** and **8c** could be accomplished with HCl/MeOH to afford lactones **11** and **14,** respectively, also in high yields (eq 12).

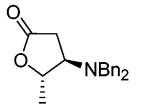


Determination of Relative Stereochemistry of the Addition Products. Stereochemical analysis was performed on addition products **3a**−**c**, **4a**−**c**, **5a**−**c**, and **6a**−**c** to establish the relative stereochemistry. The *N*-sulfinyl and alcohol protecting groups were removed as previously described, and treatment of the resulting free amino alcohols with triphosgene in the presence of *N*,*N*-diisopropylethylamine cleanly provided oxazolidinones **15**−**18**.[22] Stereochemical assignments of **15** and **16** were made by correlation with known literature compounds,[7c] while the assignments of **17** and **18** were determined by NMR based upon the observation of the indicated NOE measurements.

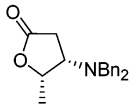


The relative stereochemistries of the methyl acetate addition products **7a**−**c** and **8a**−**c** were established by

converting the addition products into the previously reported lactones **19** and **20**.[23] Specifically, methyl acetate addition products **7a**, **7c**, **8a**, and **8c** were transformed to **11** and **14**, as described previously, followed by *N*,*N*-dibenzylation to afford **19** and **20**. The methyl acetate addition products **7b** and **8b** were transformed to **19** and **20**, respectively, by cleavage of the sulfinyl group with HCl/MeOH to afford **12** and **13**. *N*,*N*-Dibenzylation, subsequent deprotection of the TBDPS group with HF/pyridine, and final cyclization produced lactones **19** and **20,** respectively.



19



20

Conclusion

N-*tert*-Butanesulfinyl aldimines **1a**−**c** and **2a**−**c** have been prepared from protected (*S*)-lactals without epimerization at the α-stereocenter. Grignard reagents and enolates have been added to these *N*-*tert*-butanesulfinyl aldimines in good yields and with high diastereoselectivities. Either the syn or anti addition products can be obtained by the appropriate choice of alcohol protecting groups and/or reaction conditions. Finally, the addition products were readily deprotected in high yields to provide straightforward access to either *syn*- or *anti*-1,2-amino alcohols.

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. $ClTi(Oi\text{-}Pr)_3$ was fractionally distilled and stored under N_2 as a neat liquid, which solidified upon standing. BnBr was filtered through a plug of basic alumina (Brockman activity I, 60−325 mesh) prior to use. *N*,*N*,*N*,*N*-Tetramethylethylenediamine (TMEDA) was distilled under N_2 from either *n*-BuLi or CaH_2. *tert*-Butanesulfinamide was prepared according to previously published protocols.[24] 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), methanol (MeOH), 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 with use of 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 Na_2SO_4, and all solvents were removed with a rotary evaporator. 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. Chemical shifts in NMR spectra are expressed in parts per million, and all coupling constants are expressed in hertz. Unless otherwise noted, all chemical correlations to known compounds were performed on the major diastereomer. Diastereoselectivity was determined by HPLC-MS with an Agilent 1100 LC-MS equipped with a C_{18} Zorbax 2.1 mm × 150 mm column, monitored at 210 and 254 nm, and by electronic ionization. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter.

General Procedure for the Condensation of Aldehydes with *N*-*tert*-Butanesulfinamide. A 0.5 M solution of $Ti(OEt)_4$ (2.5 equiv) and aldehyde (1.0 equiv) in THF was prepared under a nitrogen atmosphere. To the solution was added *tert*-butanesulfinamide (1.1 equiv), and conversion was followed by TLC. Upon reaction completion, 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 with EtOAc (3×). The organic layers were combined, washed with brine, dried, and concentrated to afford the crude product.

(S_S,2*S*)-2-Methyl-propane-2-sulfinic Acid (2-Benzyloxy-propylidene)-amide (1a). The general procedure was followed with use of 0.51 g (3.1 mmol) of (*S*)-2-benzyloxy propanal for 3 h. Pure **1a** (0.61 g, 75%) was obtained as a clear oil after chromatography (35% EtOAc/hexanes). HPLC (Diacel Chiralpak OD column, 99:01 hexanes/IPA; 1.0 mL/min; 254 nm) t_R[(S_S,2*R*)-**1a**] = 8.8 min, t_R[(S_S,2*S*)-**1a**] = 12.8 min; $[\alpha]^{21}_D$ +10.53 (*c* 0.70, CH_2Cl_2); IR 3063, 1626, 1087 cm^{-1}; ^1H NMR (400 MHz) δ 1.21 (s, 9H), 1.38 (d, 3H, J = 6.8), 4.31 (dq, 1H, J = 4.8, 6.8), 4.48 (d, 1H, J = 11.6), 4.63 (d, 1H, J = 11.6), 7.24−7.34 (m, 5H), 8.06 (d, 1H, J = 4.8); ^{13}C NMR (100 MHz) δ 18.4, 22.3, 56.7, 71.4, 77.5, 127.6, 127.8, 128.4, 137.6, 170.3. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.90; H, 8.23; N, 5.35.

(R_S,2*S*)-2-Methyl-propane-2-sulfinic Acid (2-Benzyloxy-propylidene)-amide (2a). The general procedure was followed with use of 0.51 g (3.1 mmol) of (*S*)-2-benzyloxy propanal for 3 h. Pure **2a** (0.77 g, 93%) was obtained as a clear oil after chromatography (35% EtOAc/hexanes). HPLC (Diacel Chiralpak OD column, 99:01 hexanes/IPA; 1.0 mL/min; 280 nm) t_R[(R_S,2*R*)-**2a**] = 8.7 min, t_R[(R_S,2*S*)-**2a**] = 12.2 min; $[\alpha]^{21}_D$ −185.51 (*c* 0.60, CH_2Cl_2); IR 3061, 1620, 1084 cm^{-1}; ^1H NMR (400 MHz) δ 1.21 (s, 9H), 1.39 (d, 3H, J = 6.8), 4.35 (dq, 1H, J = 4.4, 6.8), 4.53 (d, 1H, J = 12.0), 4.65 (d, 1H, J = 12.0), 7.26−7.39 (m, 5H), 8.06 (d, 1H, J = 4.4); ^{13}C NMR (100 MHz) δ 18.6, 22.4, 56.8, 71.5, 76.2, 127.7, 127.8, 129.3, 137.5, 175.2. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.70; H, 8.15; N, 5.00.

(S_S,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-diphenyl-silanyloxy)-propylidene]-amide (1b). The general procedure was followed with use of 2.1 g (6.6 mmol) of (*S*)-2-*tert*-butyl-diphenyl-silanyloxy propanal for 28 h. Pure **1b** (2.3 g, 84%) was obtained as a clear oil after chromatography (25% EtOAc/hexanes). HPLC (Diacel Chiralpak OD column, 99:01 hexanes/IPA; 1.0 mL/min; 280 nm) t_R[(S_S,2*R*)-**1b**] = 5.1 min, t_R[(S_S,2*S*)-**1b**] = 5.7 min; $[\alpha]^{21}_D$ +38.71 (*c* 1.00, CH_2Cl_2); IR 3071, 1625, 1598, 1481, 1111, 1089 cm^{-1}; ^1H NMR (400 MHz) δ 1.08 (s, 9H), 1.19 (s, 9H), 1.28 (d, 3H, J = 6.4), 4.60 (dq, 1H, J = 4.0, 6.4), 7.33−7.44 (m, 6H), 7.64−7.69 (m, 4H), 8.30 (d, 1H, J = 4.0); ^{13}C NMR (100 MHz) δ 19.3, 21.6, 22.4, 26.9, 56.7, 71.3, 127.7, 128.0, 129.87, 129.89, 133.2, 133.7, 135.8, 171.3. Anal. Calcd for $C_{23}H_{33}NO_2SSi$: C, 66.46; H, 8.00; N, 3.37. Found: C, 66.67; H, 8.24; N, 3.17.

(R_S,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-diphenyl-silanyloxy)-propylidene]-amide (2b). The general procedure was followed with use of 0.48 g (1.5 mmol) of (*S*)-2-*tert*-butyl-diphenyl-silanyloxy propanal for 20 h. Pure **2b** (0.63 g, 98%) was obtained as a clear oil after chromatog-

(20) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556−569. Reetz, M. T.; Kesseler, K.; Schmidtberger, S.; Wenderoth, B.; Steinbach, R. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 989−990.
(21) Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **2002**, *67*, 7819−7832.
(22) Andres, J. M.; de Elena, N.; Pedrosa, R.; Perez-Encabo, A. *Tetrahedron* **1999**, *55*, 14137−14144.
(23) Asao, N.; Shimada, T.; Sudo, T.; Tsukada, N.; Yazawa, K.; Gyoung, Y. S.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 6274−6282.
(24) Weix, D. J.; Ellman, J. A. *Org. Lett.* **2003**, *5*, 1317−1320.

raphy (25% EtOAc/hexanes). HPLC (Diacel Chiralpak AS column, 99:01 hexanes/IPA; 1.0 mL/min; 280 nm) t_R[(R_S,2*R*)-**2b**] = 4.8 min, t_R[(R_S,2*S*)-**2b**] = 6.4 min; $[\alpha]^{21}_D$ −296.97 (*c* 1.00, CH_2Cl_2); IR 3071, 1626, 1462, 1111, 1088 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.10 (s, 9H), 1.15 (s, 9H), 1.29 (d, 3H, *J* = 6.4), 4.62 (dq, 1H, *J* = 4.0, 6.4), 7.35−7.46 (m, 6H), 7.65−7.70 (m, 4H), 8.02 (d, 1H, *J* = 4.0); ^{13}C NMR (100 MHz) δ 19.0, 21.5, 22.2, 26.7, 56.5, 71.2, 127.56, 127.61, 129.7, 129.8, 132.9, 133.4, 135.5, 135.7, 171.3. Anal. Calcd for $C_{23}H_{33}NO_2SSi$: C, 66.46; H, 8.00; N, 3.37. Found: C, 66.31; H, 8.15; N, 3.23.

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-dimethyl-silanyloxy)-propylidene]-amide (1c). The general procedure was followed with use of 0.85 g (4.5 mmol) of (*S*)-2-*tert*-butyl-dimethyl-silanyloxy propanal for 13 h. Pure **1c** (0.91 g, 70%) was obtained as a clear oil after chromatography (35% EtOAc/hexanes). HPLC (Diacel Chiralpak AD column, 99:01 hexanes/IPA; 1.0 mL/min; 280 nm) t_R[(S_S,2*S*)-**1c**] = 5.2 min, t_R[(S_S,2*R*)-**1c**] = 5.8 min; $[\alpha]^{21}_D$ +25.38 (*c* 2.13, CH_2Cl_2); IR 1640, 1089 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.08 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.19 (s, 9H), 1.35 (d, 3H, *J* = 6.4), 4.56 (dq, 1H, *J* = 4.0, 6.4), 7.95 (d, 1H, *J* = 4.0); ^{13}C NMR (100 MHz) δ −4.8, −4.7, 18.0, 21.4, 22.3, 25.7, 56.7, 70.5, 171.5; HRMS calcd for $C_{13}H_{30}NO_2SSi$ 292.176654, found 292.176655.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-dimethyl-silanyloxy)-propylidene]-amide (2c). The general procedure was followed with use of 1.3 g (6.9 mmol) of (*S*)-2-*tert*-butyl-dimethyl-silanyloxy propanal for 13 h. Pure **2c** (1.6 g, 80%) was obtained as a clear oil after chromatography (35% EtOAc/hexanes). HPLC (Diacel Chiralpak AD column, 99:01 hexanes/IPA; 1.0 mL/min; 280 nm) t_R[(R_S,2S)-**2c**] = 5.3 min, t_R[(R_S,2*R*)-**2c**] = 5.9 min; $[\alpha]^{21}_D$ −210.60 (*c* 10.00, CH_2Cl_2); IR 1626, 1092 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.08 (s, 3H), 0.09 (s, 3H), 0.93 (s, 9H), 1.20 (s, 9H), 1.35 (d, 3H, *J* = 6.4), 4.60 (dq, 1H, *J* = 3.6, 6.4), 7.98 (d, 1H, *J* = 3.6); ^{13}C NMR (100 MHz) δ −4.8, −4.7, 18.2, 21.7, 22.4, 25.7, 56.7, 70.7, 171.8. Anal. Calcd for $C_{13}H_{29}NO_2SSi$: C, 53.56; H, 10.03; N, 4.80. Found: C, 53.58; H, 10.30; N, 4.84.

General Procedure for the Grignard Additions to *N*-*tert*-Butanesulfinyl Imines. To a flame-dried flask was added the aldimine (1.0 equiv, 0.10 g) in appropriate solvent (Tables 1−4, 0.20 M), and the solution was cooled. The Grignard reagent (2.0 equiv, 3.0 M in ether) was added dropwise to the solution and conversion was followed by TLC. Upon reaction completion, excess organometallic reagent was quenched with NH_4Cl (saturated), and the mixture was warmed to room temperature. The resulting suspension was diluted with an equal portion of brine and extracted with EtOAc (3×). The organic layers were combined, washed with brine, dried, and concentrated to afford the crude product (for yields and diastereoselectivities, see Tables 1−3).

General Procedure for the Grignard Additions to *N*-*tert*-Butanesulfinyl Imines with TMEDA. To a flame-dried flask was added the aldimine (1.00 equiv, 0.10 g) in THF (0.24 M), and the solution was cooled to −78 °C. In another flask was added the Grignard reagent (2.0 equiv, 3.0 M in ether) to a solution of TMEDA (2.05 equiv) in THF (2.0 M), and this mixture was transferred dropwise via cannula to the cooled aldimine solution. Upon reaction completion as determined by TLC, excess organometallic reagent was quenched with NH_4Cl (saturated), and the mixture was warmed to room temperature. The resulting suspension was diluted with an equal portion of brine and extracted with EtOAc (3×). The organic layers were combined, washed with brine, dried, and concentrated to afford the crude product (for yields and diastereoselectivities, see Tables 1 and 3).

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid (2-Benzyloxy-1-phenyl-propyl)-amide (3a). The general procedure was followed with use of 0.081 g (0.30 mmol) of **1a**. A mixture of *syn*- and *anti*-**3a** (0.095 g, 94% yield) was obtained as a clear oil after chromatography (40% EtOAc/hexanes to 55% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*syn*-**3a**) = 9.2 min, t_R(*anti*-**3a**) = 8.5 min. *syn*-**3a**: IR 3269, 3063, 1603, 1495, 1068 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.04 (d, 3H, *J* = 6.2), 1.13 (s, 9H), 3.66 (dq, 1H, *J* = 6.2, 8.6), 4.29 (d, 1H, *J* = 8.6), 4.42 (d, 1H, *J* = 12.0), 4.52 (s, 1H), 4.71 (d, 1H, *J* = 12.0), 7.27−7.37 (m, 10H); ^{13}C NMR (100 MHz) δ 15.8, 22.6, 55.1, 63.0, 70.2, 78.6, 127.7, 127.8, 128.0, 128.36, 128.41, 128.7, 138.0, 138.8. Anal. Calcd for $C_{20}H_{27}NO_2S$: C, 69.53; H, 7.88; N, 4.05. Found: C, 69.46; H, 7.94; N, 3.85.

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-diphenyl-silanyloxy)-1-phenyl-propyl]-amide (3b). The general procedure was followed with use of 0.089 g (0.21 mmol) of **2a**. Pure *anti*-**3b** (0.091 g, 86%) was obtained as a clear oil after chromatography (35% EtOAc/hexanes to 45% EtOAc/hexanes). *syn*-**3b**: ^{1}H NMR (400 MHz) δ 0.82 (d, 3H, *J* = 6.0), 1.09 (s, 9H), 1.17 (s, 9H), 4.09 (apparent pent, 1H, *J* = 6.0), 4.35 (m, 1H), 4.52 (s, 1H), 7.24−7.30 (m, 3H), 7.36−7.46 (m, 8H), 7.65−7.76 (m, 4H); ^{13}C NMR (100 MHz) δ 19.3, 20.5, 22.7, 27.1, 55.3, 65.3, 74.3, 125.4, 127.6, 127.8, 127.9, 128.3, 128.5, 128.8, 129.0, 129.78, 129.81, 135.8, 136.0. *anti*-**3b**: $[\alpha]^{21}_D$ +23.80 (*c* 0.72, CH_2Cl_2); IR 3070, 1593, 1470, 1071 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.94 (d, 3H, *J* = 6.0), 1.09 (s, 9H), 1.23 (s, 9H), 4.07 (d, 1H, *J* = 7.2), 4.21 (dq, 1H, *J* = 4.0, 6.0), 4.29 (dd, 1H, *J* = 4.0, 7.2), 7.27−7.40 (m, 7H), 7.40−7.49 (m, 4H), 7.63 (d, 2H, *J* = 6.6), 7.73 (d, 2H, *J* = 6.6); ^{13}C NMR (100 MHz) δ 19.2, 19.3, 22.5, 26.9, 56.2, 65.1, 73.0, 127.4, 127.5, 127.7, 128.1, 128.2, 129.6, 129.8, 133.2, 133.9, 135.77, 135.81, 139.4. Anal. Calcd for $C_{29}H_{39}NO_2SSi$: C, 70.54; H, 7.96; N, 2.84. Found: C, 70.25; H, 8.18; N, 2.86.

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-dimethyl-silanyloxy)-1-phenyl-propyl]-amide (3c). The general procedure was followed with use of 0.10 g (0.36 mmol) of **1c**. A mixture of *syn*- and *anti*-**3c** (0.13 g, 95% yield) was obtained as a clear oil after chromatography (30% EtOAc/hexanes to 40% EtOAc/hexanes). *anti*-**3c**: $[\alpha]^{21}_D$ +20.61 (*c* 4.67, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 0.05 (s, 3H), 0.07 (s, 3H), 0.92 (s, 9H), 1.33 (d, 3H, *J* = 6.0), 1.19 (s, 9H), 3.87 (dq, 1H, *J* = 6.0, 7.2), 4.18 (d, 1H, *J* = 7.6), 4.69 (s, 1H), 7.27−7.36 (m, 5H); ^{13}C NMR (100 MHz) δ −4.8, −4.2, 17.8, 20.6, 22.6, 25.7, 55.1, 64.8, 73.0, 127.8, 128.3, 128.6, 139.4. *syn*-**3c**: $[\alpha]^{21}_D$ +142.82 (*c* 3.11, CH_2Cl_2); IR 3200, 1603, 1462, 1062 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.02 (s, 3H), 0.03 (s, 3H), 0.75 (s, 9H), 1.01 (d, 3H, *J* = 6.0), 1.20 (s, 9H), 3.99 (d, 1H, *J* = 7.2), 4.12−4.20 (m, 2H), 7.25−7.32 (m, 5H); ^{13}C NMR (100 MHz) δ −4.9, −4.3, 17.9, 20.1, 22.5, 25.7, 56.2, 64.8, 71.7, 127.5, 128.0, 128.4, 139.4; HRMS calcd for $C_{19}H_{36}NO_2SSi$ 370.223604, found 370.223605.

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid (2-Benzyloxy-1-ethyl-propyl)-amide (4a). The general procedure was followed with use of 0.094 g (0.35 mmol) of **1a**. A mixture of *syn*- and *anti*-**4a** (0.079 g, 75% yield) was obtained as a clear oil after chromatography (40% EtOAc/hexanes to 55% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*anti*-**4a**) = 8.5 min, t_R(*syn*-**4a**) = 9.2 min. *anti*-**4a**: ^{1}H NMR (400 MHz) δ 1.03 (t, 3H, *J* = 7.4), 1.18−1.20 (m, 12H), 1.52−1.55 (m, 1H), 1.62−1.71 (m, 1H), 3.17 (d, 1H, *J* = 9.2), 3.21−3.30 (m, 1H), 3.55 (dq, 1H, *J* = 4.0, 6.4), 4.48 (d, 1H, *J* = 11.6), 4.58 (d, 1H, *J* = 11.6), 7.27−7.35 (m, 5H). *syn*-**4a**: $[\alpha]^{21}_D$ +32.00 (*c* 0.10, CH_2Cl_2); IR 1062 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.87 (t, 3H, *J* = 7.2), 1.20 (s, 9H), 1.28 (d, 3H, *J* = 6.4), 1.50−1.53 (m, 1H), 1.71−174 (m, 1H), 3.11−3.15 (m, 1H), 3.59−3.65 (m, 1H), 3.77 (d, 1H, *J* = 6.0), 4.40 (d, 1H, *J* = 11.6), 4.65 (d, 1H, *J* = 11.6), 7.26−7.35 (m, 5H); ^{13}C NMR (100 MHz) δ 9.6, 15.8, 22.7, 25.0, 55.7, 61.2, 70.3, 75.5, 127.5, 127.6, 128.3, 138.4. Anal. Calcd for $C_{16}H_{27}NO_2S$: C, 64.61; H, 9.15; N, 4.71. Found: C, 64.57; H, 9.24; N, 4.85.

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-diphenyl-silanyloxy)-1-ethyl-propyl]-amide (4b). The general procedure was followed with use of 0.11 g (0.26 mmol) of **1b**. A mixture of *syn*- and *anti*-**4b** (0.10 g, 90% yield) was obtained as a clear oil after chromatography (35% EtOAc/hexanes to 45% EtOAc/hexanes). *syn*-**4b**: $[\alpha]^{21}_D$ +31.23 (*c* 1.29, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 0.78 (t, 3H, *J* = 7.6), 1.07 (s, 9H), 1.16 (d, 3H, *J* = 6.0), 1.26 (s, 9H), 1.44−1.50 (m, 1H), 1.51−1.60 (m, 1H), 2.90−2.95 (m, 1H), 3.94−3.98 (m, 2H),

7.36−7.45 (m, 6H), 7.76−7.70 (m, 4H); ^{13}C NMR (100 MHz) δ 10.4, 19.4, 20.5, 22.9, 26.5, 27.0, 55.8, 63.3, 77.8, 127.5, 127.7, 129.6, 129.8, 133.4, 134.0, 135.87, 135.91. *anti*-**4b**: $[\alpha]^{21}_D$ +2.75 (*c* 4.14, CH_2Cl_2); IR 3041, 1591, 1469, 1108, 1055 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.92 (t, 3H, *J* = 7.2), 1.02 (d, 3H, *J* = 6.4), 1.06 (s, 9H), 1.20 (s, 9H), 1.50−1.61 (m, 2H), 3.11−3.16 (m, 2H), 3.83 (dq, 1H, *J* = 2.8, 6.4), 7.24−7.45 (m, 6H), 7.66−7.70 (m, 4H); ^{13}C NMR (100 MHz) δ 10.7, 18.3, 19.2, 22.7, 25.0, 27.0, 55.9, 64.3, 72.0, 127.4, 127.6, 129.6, 129.7, 133.7, 134.2, 135.8, 135.9. Anal. Calcd for $C_{25}H_{39}NO_2SSi$: C, 67.36; H, 8.82; N, 3.14. Found: C, 67.17; H, 9.05; N, 3.06.

(*S*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-dimethyl-silanyloxy)-1-ethyl-propyl]-amide (4c). The general procedure was followed with use of 0.12 g (0.42 mmol) of **1c**. A mixture of *syn*- and *anti*-**4c** (0.13 g, 94% yield) was obtained as a clear oil after chromatography (30% EtOAc/hexanes to 40% EtOAc/hexanes). *syn*-**4c**: $[\alpha]^{21}_D$ +32.98 (*c* 4.85, CH_2Cl_2); IR 1074, 1053 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.86−0.89 (m, 12H), 1.19−1.20 (m, 12H), 1.39−1.46 (m, 1H), 1.54−1.61 (m, 1H), 2.91−2.93 (m, 1H), 3.83−3.87 (m, 2H); ^{13}C NMR (100 MHz) δ −4.2, −3.3, 10.3, 17.8, 20.7, 22.8, 25.7, 26.5, 55.7, 63.0, 69.5. Anal. Calcd for $C_{15}H_{35}NO_2SSi$: C, 56.02; H, 10.97; N, 4.36. Found: C, 56.09; H, 11.17; N, 4.42.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid (2-Benzyloxy-1-phenyl-propyl)-amide (5a). The general procedure with TMEDA was followed with use of 0.020 g (0.075 mmol) of **2a** and 0.024 mL (0.16 mmol, 2.1 equiv) of TMEDA. Pure *anti*-**5a** (0.021 g, 80% yield) was obtained as a clear oil after chromatography (40% EtOAc/hexanes to 55% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*syn*-**5a**) = 10.3 min, t_R(*anti*-**5a**) = 11.3 min. *anti*-**5a**: $[\alpha]^{21}_D$ −125.23 (*c* 2.30, CH_2Cl_2); IR 3278, 3031, 1603, 1494, 1068 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.05 (d, 3H, *J* = 6.4), 1.27 (s, 9H), 3.86 (dq, 1H, *J* = 4.0, 6.4), 4.11 (d, 1H, *J* = 2.0), 4.59 (d, 1H, *J* = 11.6), 4.72 (d, 1H, *J* = 11.6), 4.77 (dd, 1H, *J* = 2.0, 4.0), 7.27−7.41 (m, 10H); ^{13}C NMR (100 MHz) δ 14.6, 22.6, 55.6, 59.3, 70.4, 77.7, 127.5, 127.7, 127.9, 128.1, 128.3, 128.4, 138.0, 138.3. Anal. Calcd for $C_{20}H_{27}NO_2S$: C, 69.53; H, 7.88; N, 4.05. Found: C, 69.69; H, 8.04; N, 4.07.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-diphenyl-silanyloxy)-1-phenyl-propyl]-amide (5b). The general procedure with TMEDA was followed with use of 0.061 g (0.15 mmol) of **2b** and 0.045 mL (0.30 mmol, 2.1 equiv) of TMEDA. Pure *anti*-**5b** (0.052 g, 72% yield) was obtained as a clear oil after chromatography (20% EtOAc/hexanes). *syn*-**5b**: $[\alpha]^{21}_D$ −1.55 (*c* 1.80, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 0.97−0.98 (m, 12H), 1.24 (s, 9H), 4.22 (dq, 1H, *J* = 2.8, 6.0), 4.32−4.33 (m, 2H), 7.25−7.43 (m, 13H), 7.61 (d, 2H, *J* = 8.0). *anti*-**5b**: $[\alpha]^{21}_D$ −90.82 (*c* 5.10, CH_2Cl_2); IR 3281, 3060, 1589, 1472, 1110, 1084 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.92 (d, 3H, *J* = 6.4), 1.12 (s, 9H), 1.31 (s, 9H), 4.05 (dq, 1H, *J* = 4.0, 6.4), 4.24 (s, 1H), 4.46−4.50 (m, 1H), 7.16 (d, 2H, *J* = 7.6), 7.22−7.27 (m, 3H), 7.36−7.49 (m, 6H), 7.66 (d, 2H, *J* = 6.6), 7.70 (d, 2H, *J* = 6.6); ^{13}C NMR (100 MHz) δ 16.9, 19.2, 22.7, 27.0, 55.5, 62.2, 72.9, 127.5, 127.6, 127.8, 128.0, 128.5, 129.7, 130.0, 133.0, 133.8, 135.8, 136.1, 138.1; HRMS calcd for $C_{29}H_{40}NO_2SSi$ 494.254904, found 494.254905.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-dimethyl-silanyloxy)-1-phenyl-propyl]-amide (5c). The general procedure with TMEDA was followed with use of 0.011 g (0.038 mmol) of **2c** and 0.012 mL (0.077 mmol, 2.1 equiv) of TMEDA. Pure *anti*-**5c** (0.011 g, 78% yield) was obtained as a clear oil after chromatography (30% EtOAc/hexanes to 40% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 30 min at 0.4 mL/min), t_R(*syn*-**5c**) = 22.7 min, t_R(*anti*-**5c**) = 23.3 min. *anti*-**5c**: $[\alpha]^{21}_D$ −82.56 (*c* 6.21, CH_2Cl_2); IR 3129, 1583, 1471, 1071 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.09 (s, 3H), 0.14 (s, 3H), 0.88 (s, 9H), 1.02 (d, 3H, *J* = 6.0), 1.25 (s, 9H), 4.10 (dq, 1H, *J* = 4.0, 6.0), 4.13 (d, 1H, *J* = 3.6), 4.45 (dd, 1H, *J* = 3.6, 4.0), 7.25−7.33 (m, 5H); ^{13}C NMR (100 MHz) δ −4.9, −4.5, 18.0, 22.6, 25.8, 55.6, 63.0, 71.9, 127.5, 128.1, 128.6, 138.4. Anal. Calcd for $C_{19}H_{35}NO_2SSi$: C, 61.74; H, 9.54; N, 3.79. Found: C, 61.56; H, 9.90; N, 3.77.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid (2-Benzyloxy-1-ethyl-propyl)-amide (6a). The general procedure with TMEDA was followed with use of 0.030 g (0.11 mmol) of **2a** and 0.035 mL (0.23 mmol, 2.1 eq) of TMEDA. Pure *anti*-**6a** (0.029 g, 86% yield) was obtained as a clear oil after chromatography (40% EtOAc/hexanes to 55% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*anti*-**6a**) = 6.5 min, t_R(*syn*-**6a**) = 8.2 min. *syn*-**6a**: ^{1}H NMR (400 MHz) δ 0.94 (t, 3H, *J* = 7.4), 1.20 (d, 3H, *J* = 6.4), 1.21 (s, 9H), 1.73−1.79 (m, 2H), 2.97−3.05 (m, 1H), 4.47 (d, 1H, *J* = 10.0), 3.65 (dq, 1H, *J* = 4.0, 6.4), 4.45 (d, 1H, *J* = 11.2), 4.61 (d, 1H, *J* = 11.6), 7.27−7.35 (m, 5H). *anti*-**6a**: IR 3035, 1555, 1472, 1066 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.92 (t, 3H, *J* = 7.2), 1.17 (d, 3H, *J* = 7.2), 1.22 (s, 9H), 1.56 (apparent pent, 2H, *J* = 7.2), 3.18 (dq, 1H, *J* = 3.2, 7.2), 3.78 (d, 1H, *J* = 7.2), 3.90−3.95 (m, 1H), 4.52 (d, 1H, *J* = 11.4), 4.56 (d, 1H, *J* = 11.4), 7.26−7.35 (m, 5H); ^{13}C NMR (100 MHz) δ 10.7, 15.4, 22.3, 22.6, 55.8, 61.1, 70.9, 77.4, 127.4, 127.8, 128.3, 138.6. Anal. Calcd for $C_{16}H_{27}NO_2S$: C, 64.60; H, 9.15; N, 4.71. Found: C, 64.39; H, 9.32; N, 4.65.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-diphenyl-silanyloxy)-1-ethyl-propyl]-amide (6b). The general procedure with TMEDA was followed with use of 0.10 g (0. 24 mmol) of **2b** and 0.075 mL (0.50 mmol, 2.1 equiv) of TMEDA. Pure *anti*-**6b** (0.10 g, 93% yield) was obtained as a clear oil after chromatography (25% EtOAc/hexanes to 35% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 20 min at 0.4 mL/min) t_R(*anti*-**6b**) = 19.8 min, t_R(*syn*-**6b**) = 20.5 min. *anti*-**6b**: $[\alpha]^{21}_D$ −53.38 (*c* 2.64, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 0.79 (t, 3H, *J* = 7.6), 0.95 (d, 3H, *J* = 6.4), 1.06 (s, 9H), 1.24 (s, 9H), 1.37−1.44 (m, 1H), 1.66−1.75 (m, 1H), 3.07−3.15 (m, 1H), 3.91 (d, 1H, *J* = 4.8), 4.13 (dq, 1H, *J* = 3.2, 6.4), 7.35−7.44 (m, 6H), 7.68−7.70 (m, 4H); ^{13}C NMR (100 MHz) δ 10.3, 17.6, 19.2, 22.7, 27.0, 33.6, 55.5, 61.5, 71.3, 127.5, 127.6, 129.6, 129.7, 133.2, 134.0, 135.76, 135.84. *syn*-**6b**: $[\alpha]^{21}_D$ −16.91 (*c* 5.21, CH_2Cl_2); IR 3070, 1589, 1472, 1110, 1053 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.86 (t, 3H, *J* = 7.4), 1.05 (d, 3H, *J* = 6.4), 1.17 (s, 9H), 1.20 (s, 9H), 1.61−1.68 (m, 1H), 1.77−1.85 (m, 1H), 2.86−2.88 (m, 1H), 3.26 (d, 1H, *J* = 8.4), 3.89 (dq, 1H, *J* = 2.4, 6.4), 7.34−7.44 (m, 6H), 7.64−7.67 (m, 4H); ^{13}C NMR (100 MHz) δ 10.8, 19.3, 19.8, 22.7, 26.0, 27.0, 56.1, 64.4, 70.2, 127.4, 127.7, 129.6, 129.8, 133.2, 134.4, 135.7, 135.8; HRMS calcd for $C_{29}H_{40}NO_2SSi$ 494.254904, found 494.254905.

(*R*$_S$,2*S*)-2-Methyl-propane-2-sulfinic Acid [2-(*tert*-Butyl-dimethyl-silanyloxy)-1-ethyl-propyl]-amide (6c). The general procedure with TMEDA was followed with use of 0.15 g (0.52 mmol) of **2c** and 0.16 mL (1.1 mmol, 2.1 equiv) of TMEDA. Pure *anti*-**6c** (0.13 g, 81%) was obtained as a clear oil after chromatography (30% EtOAc/hexanes to 40% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 25 min at 0.4 mL/min) t_R(*syn*-**6c**) = 19.5 min, t_R(*anti*-**6c**) = 20.4 min. *syn*-**6c**: ^{1}H NMR (400 MHz) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.85 (s, 9H), 1.03 (t, 3H, *J* = 6.0), 1.12 (d, 3H, *J* = 6.0), 1.21 (s, 9H), 1.65−169 (m, 1H), 2.94−3.03 (m, 1H), 3.32 (d, 1H, *J* = 7.2), 3.92 (dq, 1H, *J* = 4.4, 6.0); ^{13}C NMR (100 MHz) δ −4.9, −4.2, 10.9, 17.9, 20.7, 22.8, 25.8, 26.6, 56.3, 64.4, 68.7. *anti*-**6c**: $[\alpha]^{21}_D$ −35.92 (*c* 0.65, CH_2Cl_2); IR 1075 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.08 (s, 3H), 0.13 (s, 3H), 0.87 (s, 9H), 0.92 (t, 3H, *J* = 7.2), 1.09 (d, 3H, *J* = 6.4), 1.20 (s, 9H), 1.41−1.56 (br m, 2H), 3.02−3.04 (m, 1H), 3.70 (d, 1H, *J* = 7.2), 4.16 (dq, 1H, *J* = 3.2, 6.4); ^{13}C NMR (100 MHz) δ −4.7, −4.3, 10.7, 17.9, 19.2, 22.0, 22.8, 25.8, 55.8, 63.1, 70.8. Anal. Calcd for $C_{15}H_{35}NO_2SSi$: C, 56.02; H, 10.97; N, 4.36. Found: C, 55.89; H, 10.79; N, 4.48.

General Procedure for the Ti Enolate Addition to *N*-*tert*-Butanesulfinyl Aldimines. A solution of *i*-Pr_2NH (2.20 equiv) in THF (0.70 M) was cooled to 0 °C. *n*-Butyllithium (*n*-BuLi) (2.25 M, 2.10 equiv) was added via syringe and the solution was stirred for 30 min. The solution was then cooled to −78 °C and methyl acetate (2.00 equiv) was added via syringe and the reaction solution was stirred for 30 min. To

this solution was added $ClTi(Oi\text{-}Pr)_3$ (4.20 equiv) in THF (5.00 M) and the orange-colored enolate solution was stirred for 30 min. A solution of the *N*-sulfinyl imine (1.00 equiv) in THF (1.2 M) was slowly added via syringe and the solution was stirred at −78 °C. Upon reaction completion, as determined by TLC, a saturated aqueous solution of NH_4Cl (10 equiv) was added and the suspension was warmed to room temperature. The mixture was diluted with H_2O and vigorously stirred to dissolve the Ti precipitate. The mixture was then decanted into a separatory funnel, and the remaining solid was diluted with equal parts of H_2O and EtOAc and vigorously stirred for 15 min. The mixture was then added to the separatory funnel and the organic layer was collected. The aqueous layer was then extracted with EtOAc (3×). The combined organic layers were washed with brine, dried, and concentrated to afford the crude amino ester product.

(*S*S,4*S*)-4-Benzyloxy-3-(2-methyl-propane-2-sulfinylamino)-pentanoic Acid Methyl Ester (7a). Reaction of 0.10 g (0.37 mmol) of sulfinylimine **1a** according to the general procedure yielded a mixture of *syn*- and *anti*-**7a** (0.12 g, 96% yield) as a clear oil after chromatography (60% EtOAc/hexanes to 70% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*syn*-**7a**) = 4.1 min, t_R(*anti*-**7a**) = 5.0 min. *syn*-**7a**: ^{1}H NMR (400 MHz) δ 1.18 (s, 9H), 1.33 (d, 3H, J = 6.4), 2.58 (d, 2H, J = 6.4), 3.64 (s, 3H), 3.65−3.79 (m, 3H), 4.42 (d, 1H, J = 11.6), 4.65 (d, 1H, J = 11.6), 7.27−7.36 (m, 5H). *anti*-**7a**: $[\alpha]^{21}_D$ +87.37 (*c* 0.64, CH_2Cl_2); IR 3032, 1728, 1071 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.17 (s, 9H), 1.25 (d, 3H, J = 6.4), 2.80 (dd, 1H, J = 5.0, 16.4), 2.88 (dd, 1H, J = 5.0, 16.4), 3.47−3.53 (m, 1H), 3.58−3.67 (m, 4H), 4.35−4.38 (m, 2H), 4.60 (d, 1H, J = 11.6), 7.26−7.36 (m, 5H); ^{13}C NMR (100 MHz) δ 16.6, 22.6, 35.8, 51.5, 55.9, 58.7, 70.9, 76.3, 127.6, 127.7, 128.3, 138.0, 172.1. Anal. Calcd for $C_{17}H_{27}NO_4S$: C, 59.80; H, 7.97; N, 4.10. Found: C, 59.77; H, 8.16; N, 4.13.

(*S*S,4*S*)-4-(*tert*-Butyl-diphenyl-silanyloxy)-3-(2-methyl-propane-2-sulfinylamino)-pentanoic Acid Methyl Ester (7b). Reaction of 0.10 g (0.24 mmol) of sulfinylimine **1b** according to the general procedure yielded a mixture of *syn*- and *anti*-**7b** (0.087 g, 74% yield) as a clear oil after chromatography (50% EtOAc/hexanes). *syn*-**7b**: $[\alpha]^{21}_D$ +6.31 (*c* 0.54, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 1.08 (s, 9H), 1.16, 1.19 (m, 12H), 2.46 (dd, 1H, J = 5.6, 15.2), 2.52 (dd, 1H, J = 15.2, 8.4), 3.60−3.62 (m, 4H), 3.94−3.96 (m, 2H), 7.37−7.46 (m, 6H), 7.64−7.69 (m, 4H); ^{13}C NMR (100 MHz) δ 19.3, 20.1, 22.6, 27.0, 38.9, 51.5, 55.8, 59.1, 70.9, 127.5, 127.7, 129.7, 129.9, 132.9, 134.6, 135.77, 135.80, 171.6. *anti*-**7b**: $[\alpha]^{21}_D$ +18.75 (*c* 5.42, CH_2Cl_2); IR 3071, 1738, 1589, 1478, 1110, 1074 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.02 (d, 3H, J = 7.6), 1.04 (s, 9H), 1.15 (s, 9H), 2.85 (dd, 1H, J = 5.2, 16.8), 2.90 (dd, 1H, J = 5.2, 16.8), 3.49−3.51 (m, 1H), 3.63 (s, 3H), 3.93−3.94 (m, 1H), 4.27 (d, 1H, J = 9.6), 7.36−7.46 (m, 6H), 7.65−7.68 (m, 4H); ^{13}C NMR (100 MHz) δ 19.2, 20.5, 22.5, 26.9, 35.7, 51.6, 55.8, 60.1, 72.1, 127.4, 127.7, 129.6, 129.7, 133.2, 134.0, 135.7, 135.8, 172.6. Anal. Calcd for $C_{26}H_{39}NO_4SSi$: C, 63.76; H, 8.03; N, 2.86. Found: C, 63.77; H, 7.79; N, 2.91.

(*S*S,4*S*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-3-(2-methyl-propane-2-sulfinylamino)-pentanoic Acid Methyl Ester (7c). Reaction of 0.10 g (0.34 mmol) of sulfinylimine **1c** according to the general procedure yielded pure *anti*-**7c** (0.11 g, 87%) as a clear oil after chromatography (45% EtOAc/hexanes to 55% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*syn*-**7c**) = 11.0 min, t_R(*anti*-**7c**) = 13.1 min. *anti*-**7c**: $[\alpha]^{21}_D$ +145.6 (*c* 0.61, CH_2Cl_2); IR 1740, 1076 cm^{-1}; ^{1}H NMR (400 MHz) δ −0.04 (s, 3H), −0.01 (s, 3H), 0.81 (s, 9H), 1.12 (d, 3H, J = 7.2), 1.16 (s, 9H), 2.74 (d, 2H, J = 4.8), 3.30−3.32 (m, 1H), 3.62 (s, 3H), 3.84 (apparent pent, 1H, J = 6.2), 4.32 (d, 1H, J = 9.6); ^{13}C NMR (100 MHz) δ −5.1, −4.2, 17.9, 21.1, 22.7, 25.7, 35.4, 51.6, 55.9, 60.3, 70.5, 173.0. Anal. Calcd for $C_{16}H_{35}NO_4SSi$: C, 52.56; H, 9.65; N, 3.83. Found: C, 52.42; H, 9.98; N, 3.88.

(*R*S,4*S*)-4-Benzyloxy-3-(2-methyl-propane-2-sulfinylamino)-pentanoic Acid Methyl Ester (8a). Reaction of 0.12 g (0.45 mmol) of sulfinylimine **2a** according to the general procedure yielded a mixture of *syn*- and *anti*-**8a** (0.14 g, 89%) as a clear oil after chromatography (60% EtOAc/hexanes to 70% EtOAc/hexanes). HPLC-MS (60−95% MeOH/H_2O over 15 min at 0.5 mL/min) t_R(*syn*-**8a**) = 5.5 min, t_R(*anti*-**8a**) = 6.4 min. *syn*-**8a**: ^{1}H NMR (400 MHz) δ 1.17 (s, 9H), 1.22 (d, 3H, J = 6.0), 2.56 (d, 2H, J = 7.2), 3.64 (s, 3H), 3.65−3.78 (m, 1H), 3.95−4.04 (m, 2H), 4.47 (d, 1H, J = 11.2), 4.60 (d, 1H, J = 11.2), 7.27−7.36 (m, 5H). *anti*-**8a**: $[\alpha]^{21}_D$ +16.87 (*c* 1.00, CH_2Cl_2); IR 3070, 1738, 1069 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.21−1.23 (m, 12H), 2.79 (d, 2H, J = 6.0), 3.62 (s, 3H), 3.62−3.68 (m, 2H), 3.86 (d, 1H, J = 9.6), 4.40 (d, 1H, J = 11.6), 4.60 (d, 1H, J = 11.6), 7.26−7.37 (m, 5H); ^{13}C NMR (100 MHz) δ 16.0, 22.6, 37.9, 51.6, 56.3, 58.0, 70.9, 75.7, 127.6, 127.7, 128.3, 138.1, 172.2. Anal. Calcd for $C_{17}H_{27}NO_4S$: C, 59.80; H, 7.97; N, 4.10. Found: C, 59.59; H, 8.22; N, 3.93.

(*R*S,4*S*)-4-(*tert*-Butyl-diphenyl-silanyloxy)-3-(2-methyl-propane-2-sulfinylamino)-pentanoic Acid Methyl Ester (8b). Reaction of 0.11 g (0.27 mmol) of sulfinylimine **2b** according to the general procedure yielded a mixture of *syn*- and *anti*-**8b** (0.10 g, 78%) as a clear oil after chromatography (50% EtOAc/hexanes). *anti*-**8b**: $[\alpha]^{21}_D$ −74.63 (*c* 3.71, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 1.03 (d, 3H, J = 6.4), 1.06 (s, 9H), 1.22 (s, 9H), 2.77 (dd, 1H, J = 6.4, 16.4), 2.82 (dd, 1H, J = 6.4, 16.4), 3.53−3.62 (m, 1H), 3.63 (s, 3H), 3.76 (d, 1H, J = 9.2), 3.95 (dq, 1H, J = 4.0, 6.4), 7.36−7.46 (m, 6H), 7.67−7.69 (m, 4H); ^{13}C NMR (100 MHz) δ 19.2, 19.8, 22.7, 26.9, 37.9, 51.6, 56.2, 58.7, 71.2, 127.4, 127.7, 129.6, 129.9, 132.8, 134.0, 135.7, 171.9. *syn*-**8b**: $[\alpha]^{21}_D$ −11.29 (*c* 2.36, CH_2Cl_2); IR 3070, 1724, 1480, 1130, 1083 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.95 (d, 3H, J = 6.4), 1.07 (s, 9H), 1.16 (s, 9H), 2.58 (dd, 1H, J = 4.4, 15.2), 2.69 (dd, 1H, J = 9.4, 15.2), 3.65 (s, 3H), 3.64−3.75 (m, 1H), 4.00 (d, 1H, J = 8.4), 4.24−4.32 (m, 1H), 7.70−7.72 (m, 6H), 7.40−7.46 (m, 4H); ^{13}C NMR (100 MHz) δ 19.3, 19.8, 22.5, 27.0, 35.3, 51.6, 55.8, 59.5, 72.3, 127.5, 127.7, 129.6, 129.8, 132.8, 133.7, 135.7, 135.8, 172.0; HRMS calcd for $C_{26}H_{40}NO_4SSi$ 490.244734, found 490.244734.

(*R*S,4*S*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-3-(2-methyl-propane-2-sulfinylamino)-pentanoic Acid Methyl Ester (8c). Reaction of 0.091 g (0.31 mmol) of sulfinylimine **2c** according to the general procedure yielded pure *syn*-**8c** (0.058 g, 51%) as a clear oil after chromatography (50% EtOAc/hexanes). HPLC-MS (65−95% MeOH/H_2O over 15 min at 0.4 mL/min) t_R(*anti*-**8c**) = 11.5 min, t_R(*syn*-**8c**) = 12.5 min. *anti*-**8c**: ^{1}H NMR (400 MHz) δ −0.09 (s, 3H), 0.14 (s, 3H), 0.90 (s, 9H), 1.15 (d, 3H, J = 6.3), 1.17 (s, 9H), 2.45−2.55 (m, 2H), 3.55−3.70 (m, 1H), 3.66 (s, 3H), 3.81 (d, 1H, J = 9.2), 4.23 (dq, 1H, J = 3.0, 6.3); ^{13}C NMR (100 MHz) δ −4.7, −4.4, 17.8, 20.5, 22.5, 25.7, 34.6, 51.5, 55.8, 60.1, 71.0, 172.3. *syn*-**8c**: $[\alpha]^{21}_D$ −43.0 (*c* 1.00, CH_2Cl_2); IR 1734, 1078 cm^{-1}; ^{1}H NMR (400 MHz) δ −0.03 (s, 3H), 0.02 (s, 3H), 0.82 (s, 9H), 1.11 (d, 3H, J = 6.3), 1.18 (s, 9H), 2.64 (dd, 1H, J = 7.8, 16.4), 2.76 (dd, 1H, J = 5.9, 16.4), 3.47−3.56 (m, 1H), 3.58−3.72 (m, 1H), 3.66 (s, 3H), 3.91 (dq, 1H, J = 2.0, 6.3); ^{13}C NMR (100 MHz) δ −5.2, −4.5, 17.8, 20.5, 22.5, 25.6, 38.3, 51.5, 56.2, 58.6, 69.5, 172.5. Anal. Calcd for $C_{16}H_{35}NO_4S$: C, 52.56; H, 9.65; N, 3.83. Found: C, 52.67; H, 9.79; N, 3.90.

Representative Procedure for the Sulfinyl Group Cleavage of Sulfinamides (products 1a−c to 8a−c). To a 0.10 M solution of protected amino alcohol **5a** (0.097 g, 0.28 mmol) in MeOH was added 0.35 mL of 4.00 N HCl/dioxane (5.0 equiv, 1.4 mmol). The solution was stirred for 1 h at room temperature and was then concentrated in vacuo. The amine hydrochloride was obtained as a white solid after precipitation from MeOH with ether, and was used without further purification.

Representative Procedure for the Hydrogenation of Benzyl Protected Amino Alcohols (products 3−8a). To a solution of the crude amine hydrochloride resulting from the sulfinyl deprotection of **5a** (ca. 0.060 mmol) in 0.60 mL of MeOH (0.10 M) was added dry Pd/C (0.005 g, 5% Pd/C dry) and then 0.10 mL of 4 N HCl/dioxane (5.0 equiv, 0.35 mmol).

The mixture was purged with a stream of H_2 and stirred overnight under a H_2 atmosphere (balloon). The reaction mixture was filtered through Celite, the cake was washed with MeOH (2×), and the solvent was evaporated. Pure amino alcohol **9** (0.009 g, 83% two steps) was obtained as white solid after precipitation from MeOH with ether.

Representative Procedure for the Deprotection of TBDPS Protected Ethers (products 3−8b). To a polypropylene centrifuge tube containing a solution of **5b** (0.048 g, 0.098 mmol) in THF (0.40 mL) was added 0.20 mL of 70% HF/pyridine dropwise. The solution was stirred at room temperature for 24 h and was then poured into a separatory funnel containing 10 mL of $NaHCO_3$ (saturated) and 10 mL of EtOAc. The separatory funnel was agitated until cessation of gas evolution, and the aqueous layer was extracted with EtOAc (3×). The organic layers were dried and then concentrated. Pure **10** (0.014 g, 77%) was obtained as a white solid after precipitation of the HCl salt from MeOH with ether.

Representative Procedure for the Deprotection of TBS Protected Sulfinamides (products 3−8c). To a solution of **5c** (0.087 mg, 0.24 mmol) in 2.4 mL of MeOH (0.10 M) was added 0.30 mL of 4 N HCl/dioxane (5.0 equiv, 1.2 mmol). The solution was stirred overnight at room temperature and then concentrated in vacuo. The residue was then dissolved in 10 mL of CH_2Cl_2 and washed with 5.0 mL of 2 N NaOH. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic layers were dried and concentrated. Free amino alcohol **10** (0.035 g, 93%) was obtained as a white solid after precipitation of the HCl salt from MeOH with ether.

Representative Procedure for the Formation of Oxazolidinones 15−18. To a solution of amino alcohol **10** (0.052 g, 0.32 mmol) and triphosgene (0.072 g, 0.24 mmol) in 1.6 mL of CH_2Cl_2 was added *N*,*N*-diisopropylethylamine (0.13 mL, 0.71 mmol) dropwise at 0 °C. The mixture was allowed to warm to room temperature over a period of 4 h. The solution was then diluted with CH_2Cl_2 and washed with $NaHCO_3$ (saturated). The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic layers were dried and concentrated to afford **16** (0.040 g, 83%) as a clear oil.

Deprotection and Determination of the Absolute Stereochemistry of 3a. The general procedure for sulfinyl group cleavage was followed with use of 0.070 g (0.21 mmol) of **3a**. After removal of the sulfur impurities in vacuo, the crude HCl salt was hydrogenated by using the general procedure and precipitated from MeOH with ether to afford **9** (0.033 g, 85%) as a white solid. A portion of amino alcohol **9** (0.014 g, 0.072 mmol) was cyclized following the general procedure to afford pure oxazolidone **15** (11 mg, 86%) after column chromatography (90% $CHCl_3$/MeOH). Spectroscopic data are consistent with previously published results.

Amino alcohol **9** (free base): ^{1}H NMR (400 MHz) δ 1.04 (d, 3H, J = 6.0), 3.56 (d, 1H, J = 8.0), 3.76 (dq, 1H, J = 6.0, 8.0), 7.25−7.36 (m, 5H).[25]

Oxazolidone **15**: ^{1}H NMR (400 MHz) δ 1.50 (d, 3H, J = 6.4), 4.43 (dq, 1H, J = 6.4, 8.0), 4.47 (d, 1H, J = 8.0), 5.81 (br, 1H), 7.32−7.41 (m, 5H).[7c]

Deprotection and Determination of the Absolute Stereochemistry of 3b. The general procedure for cleavage of TBDPS protected ethers was followed with use of 0.087 g (0.18 mmol) of **3b**. Pure **10** (0.021 g, 64%) was obtained after trituration of the amine hydrochloride with ether. Amino alcohol **10** (0.051 g, 0.27 mmol) was cyclized following the general procedure to afford oxazolidinone **16** (40 mg, 83%) after column chromatography (90% $CHCl_3$/MeOH). Spectroscopic data are consistent with previously published results.

Amino alcohol **10** (free base): ^{1}H NMR (400 MHz) δ 1.05 (d, 3H, J = 6.0), 3.89 (d, 1H, J = 4.8), 3.93 (dq, 1H, J = 4.8, 6.0), 7.25−7.37 (m, 5H).[25]

Oxazolidinone **16**: ^{1}H NMR (400 MHz) δ 0.92 (d, 3H, J = 6.4), 4.91 (d, 1H, J = 8.0), 5.00 (dq, 1H, J = 6.4, 8.0), 6.52 (br, 1H), 7.32−7.43 (m, 5H).[7c]

Deprotection and Determination of Absolute Stereochemistry of 3c. The general procedure for cleavage of TBS protected ethers was followed with use of 0.055 g (0.15 mmol) of **3c** yielding free amine hydrochloride **10** (27 mg, 95%) as a white solid after precipitation of the HCl salt from MeOH with ether. Spectroscopic data are consistent with previously published results (see deprotection of **3b**).[25]

Deprotection and Determination of the Absolute Stereochemistry of 4a. The general procedure for sulfinyl group cleavage was followed with use of 0.13 g (0.42 mmol) of **4a**. After removal of the sulfur impurities in vacuo, the crude HCl salt was hydrogenated following the general procedure to afford the HCl salt of the free amino alcohol. Cyclization of the crude amino alcohol by using the general procedure yielded oxazolidinone **17** (48 mg, 87%, three steps). Spectroscopic data are consistent with previously published results.[22]

Oxazolidinone **17:** ^{1}H NMR (400 MHz) δ 0.93 (t, 3H, J = 7.5), 1.39 (d, 3H, J = 6.2), 1.48−1.62 (m, 1H), 3.32 (q, 1H, J = 6.2), 4.28 (pent, 1H, 6.2), 6.73, (br, 1H).

Deprotection and Determination of the Absolute Stereochemistry of 4b. To a polypropylene centrifuge tube containing a solution of **4b** (0.095 g, 0.21 mmol) in THF (0.40 mL) was added 0.20 mL of 70% HF/pyridine dropwise. After the solution was stirred at room temperature for 24 h, 0.25 mL of MeOH, and 4 N HCl/dioxane (0.10 mL, 0.40 mmol) was added, and the solution was stirred an additional 1 h. After removal of the solvent and sulfur impurities in vacuo, the free amine hydrochloride was obtained as a mixture with pyridinium hydrochloride (16:1 pyridinium hydrochloride/amino alcohol). Oxazolidinone **18** (0.017 g, 64% two steps) was obtained as a clear oil by using the general cyclization procedure with 20 equiv of *N*,*N*-diisopropylethylamine.

Oxazolidinone **18**: $[\alpha]^{21}_D$ +15.5 (*c* 1.00, CH_2Cl_2); IR 1729, 1074 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.95 (t, 3H, J = 7.2), 1.32 (d, 3H, J = 6.8), 1.41−1.57 (m, 1H), 3.67 (dt, 1H, J = 4.8, 8.4), 4.76 (pent, 1H, 6.8), 6.43, (br, 1H). ^{13}C NMR (100 MHz) δ 10.4, 14.6, 22.9, 57.3, 76.2, 159.8; HRMS calcd for $C_6H_{11}NO_2$ 129.078979, found 129.078979.

Deprotection and Determination of the Absolute Stereochemistry of 4c. The general procedure for cleavage of a TBS protected ether was followed with use of 0.026 g (0.081 mmol) of **4c** yielding the free amine hydrochloride (0.011 g, 97%) as a light yellow oil. Spectroscopic data of the crude amine hydrochloride were consistent with those previously observed for the precursor to oxazolidinone **17** (see deprotection of **4a**).[22]

Deprotection and Determination of the Absolute Stereochemistry of 5a. The general procedure for sulfinyl group cleavage was followed with use of 21 mg (0.060 mmol) of **5a**. After removal of the sulfur impurities in vacuo, the crude HCl salt was hydrogenated and precipitated from MeOH with ether to afford amino alcohol **10** (9.3 mg, 83%). Spectroscopic data were consistent with those previously observed (see deprotection of **3b**).[25]

Deprotection and Determination of the Absolute Stereochemistry of 5b. The general procedure for cleavage of TBDPS protected ethers was followed with use of 48 mg (0.097 mmol) of **5b**. Pure **10** (14 mg, 77%) was obtained after trituration of the amine hydrochloride with ether. Spectroscopic data were consistent with those previously observed (see deprotection of **3b**).[25]

Deprotection and Determination of the Absolute Stereochemistry of 5c. The general procedure for cleavage of TBS protected ethers was followed with use of 74 mg (0.20 mmol) of **5c**. Pure **10** (35 mg, 93%) was obtained after trituration of the amine hydrochloride with ether. Spectroscopic data were consistent with those previously observed (see deprotection of **3b**). [25]

(25) Gelbcke, M.; Baudet, M.; Hoyois, J.; Van deVliedt, G.; Deleers, M. *Nouv. J. Chim.* **1983**, *7*, 41−47.

Deprotection and Determination of the Absolute Stereochemistry of 6a. The general procedure for sulfinyl group cleavage was followed with use of 54 mg (0.18 mmol) of **6a**. After removal of the sulfur impurities in vacuo, the crude material was hydrogenated following the general procedure to afford the HCl salt of the free amino alcohol (23 mg, 92% two steps). Spectroscopic data of the amino alcohol were consistent with those previously observed for the precursor to oxazolidinone **18** (see deprotection of **4b**).

Deprotection and Determination of the Absolute Stereochemistry of 6b. To a polypropylene centrifuge tube containing a solution of the minor diastereomer of **6b** (34 mg, 0.075 mmol) in THF (0.40 mL) was added 0.20 mL of 70% HF/pyridine dropwise. After the solution was stirred at room temperature for 24 h, 0.25 mL of MeOH and 4 N HCl/dioxane (0.10 mL, 0.40 mmol) were added. After an additional 1 h, the solvent and sulfur impurities were removed in vacuo, and the free amine hydrochloride was obtained as a mixture with pyridinium hydrochloride. Spectroscopic data of the mixture were consistent with those previously observed for the precursor to oxazolidinone **18** (see deprotection of **4b**).

Deprotection and Determination of the Absolute Stereochemistry of 6c. The general procedure for cleavage of TBS protected ethers was followed with use of 15 mg (0.046 mmol) of **6c** yielding the free amine hydrochloride (6.2 mg, 96%) as a light yellow oil. Spectroscopic data of the amino alcohol were consistent with those previously observed for the precursor to oxazolidinone **18** (see deprotection of **4b**).

Deprotection and Determination of the Absolute Stereochemistry of 7a. The general procedure for sulfinyl group cleavage was followed with use of 4.5 mg (0.013 mmol) of **7a**. The resulting amine hydrochloride was hydrogenated following the general procedure yielding lactone **11** (1.5 mg, 95%) after column chromatography (9:1:0.1 MeOH/CH_2Cl_2/NH_4OH). Lactone **11** (2.4 mg, 0.025 mmol) was *N*,*N*-dibenzylated by treatment with BnBr (0.11 mL, 0.88 mmol) and K_2CO_3 (0.10 g, 0.76 mmol) in 0.38 mL of CH_3CN at 50 °C. After 16 h, the suspension was cooled, diluted with EtOAc, and washed with brine. The aqueous layer was extracted with EtOAc (3×), and the combined organic layers were dried and concentrated. Pure **19** (3.1 mg, 44%) was obtained after chromatography (20% EtOAc/hexanes) as a clear oil. Spectroscopic data are consistent with previously published results.[23]

Lactone **19**: ^{1}H NMR (400 MHz) δ 1.33 (d, 3H, J = 6.4), 2.59 (dd, 1H, J = 8.4, 18.0), 2.65 (dd, 1H, J = 6.7, 18.0), 3.33−3.38 (m, 1H), 3.50 (d, 2H, J = 13.8), 3.74 (d, 2H, J = 13.8), 4.63 (pent, 1H, J = 6.4), 7.26−7.44 (m, 10H).

Deprotection and Determination of the Absolute Stereochemistry of 7b. The general procedure for sulfinyl group cleavage was followed with use of 0.16 g (0.33 mmol) of **7b**. After evaporation of the solvent, the crude material was diluted with CH_2Cl_2 and washed with $NaHCO_3$ (saturated). The aqueous layer was washed with CH_2Cl_2 (3×), and the combined organic layers were dried and concentrated. Purification of the residue (70% EtOAc/hexanes) yielded free amine **12** (0.11 g, 85%). Amine **12** was added to a mixture of K_2CO_3 (0.10 g, 0.75 mmol) and BnBr (0.090 mL, 0.75 mmol) dissolved in CH_2Cl_2/H_2O (3:1, 0.30 M) at 0 °C. The solution was warmed to room temperature over a period of an hour, and after an additional 16 h the mixture was concentrated in vacuo. Cleavage of the silyl ether by using the general deprotection procedure yielded lactone **19** (18 mg, 22% two steps) after chromatography (20% EtOAc/hexanes). Spectroscopic data were consistent with those previously observed (see deprotection of **7a**).[23]

Amine **12**: IR 3065, 1733, 1111 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.98 (d, 3H, J = 6.4), 1.05 (s, 9H), 2.28 (dd, 1H, J = 10.0, 16.0), 2.45 (dd, 1H, J = 4.0, 16.0), 3.20 (dt, 1H, J = 4.0, 10.0), 3.62 (s, 3H), 3.75−3.84 (m, 1H), 7.35−7.44 (m, 6H), 7.65−7.68 (m, 4H); ^{13}C NMR (100 MHz) δ 18.3, 19.4, 27.0, 37.7, 51.7, 53.9, 72.7, 127.6, 127.7, 129.7, 129.8, 133.6, 134.3, 135.8, 135.9, 173.1; HRMS calcd for $C_{22}H_{32}NO_3Si$ 386.215147, found 386.215148.

Deprotection and Determination of the Absolute Stereochemistry of 7c. The general procedure for cleavage of TBS protected ethers was followed with use of 0.043 g (0.12 mmol) of **7c** yielding lactone **11** (0.014 g, 78%) as a white solid after precipitation of the HCl salt from MeOH with ether. Spectroscopic data of **11** were consistent with those previously observed for the precursor to lactone **19** (see deprotection of **7a**).[23]

Deprotection and Determination of the Absolute Stereochemistry of 8a. The general procedure for sulfinyl group cleavage was followed with use of 82 mg (0.24 mmol) of **8a**. The resulting amine hydrochloride was hydrogenated following the general procedure yielding lactone **11** (26 mg, 94%), which was obtained as a clear, colorless oil after column chromatography (9:1:0.1 MeOH/CH_2Cl_2/NH_4OH). Spectroscopic data of the lactone were consistent with those previously observed for the precursor to lactone **19** (see deprotection of **7a**).[23]

Deprotection and Determination of the Absolute Stereochemistry of 8b. The general procedure for sulfinyl group cleavage was followed with use of 0.68 g (1.4 mmol) of **8b**, and after evacuation of the solvent, the crude material was diluted with CH_2Cl_2 and washed with $NaHCO_3$ (saturated). The aqueous layer was washed with CH_2Cl_2 (3×), and the combined organic layers were dried and concentrated. Free amine **13** (0.50 g, 93%) was obtained as a clear oil after purification (70% EtOAc/hexanes). **13** was added to a mixture of K_2CO_3 (0.40 g, 2.9 mmol) and BnBr (0.34 mL, 2.9 mmol) in CH_2Cl_2/H_2O (3:1, 0.30 M) that had been cooled to 0 °C. The solution was warmed to room temperature over a period of an hour, and after an additional 16 h the mixture was concentrated. Deprotection of the silyl ether by using the general deprotection procedure yielded the free alcohol, which was dissolved in CH_2Cl_2 (0.20 mL) and added to 4 N HCl/dioxane, (1.8 mL). The solution was placed in a sealed tube and after 16 h the solution was concentrated in vacuo to yield a 1:1 mixture of lactone **20** and free alcohol after chromatography (20% EtOAc/hexanes). Spectral data from a pure sample of **20** are consistent with previously published results.[23]

Amine **13**: IR 3071, 1736, 1110 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.01 (d, 3H, J = 6.0), 1.06 (s, 9H), 2.32 (dd, 1H, J = 9.6, 15.6), 2.54 (dd, 1H, J = 4.0, 15.6), 3.12 (dt, 1H, J = 4.0, 9.6), 3.62 (s, 3H), 4.76 (dq, 1H, J = 4.0, 6.0), 7.32−7.41 (m, 6H), 7.67−7.69 (m, 4H); ^{13}C NMR (100 MHz) δ 19.0, 21.2, 26.8, 38.4, 51.2, 53.8, 72.1, 127.2, 127.4, 129.3, 129.5, 133.1, 134.0, 135.52, 135.54, 172.8; HRMS calcd for $C_{22}H_{32}NO_3Si$ 386.215147, found 386.215148.

Lactone **20**: ^{1}H NMR (400 MHz) δ 1.56 (d, 3H, J = 6.4), 2.46 (dd, 1H, J = 8.0, 17.6), 2.71 (dd, 1H, J = 4.8, 17.6), 3.49 (d, 2H, J = 14.0), 3.55−3.60 (m, 1H), 3.73 (d, 2H, J = 14.0), 4.71 (pent, 1H, J = 6.4), 7.24−7.38 (m, 10H).[23]

Deprotection and Determination of the Absolute Stereochemistry of 8c. The general procedure for cleavage of TBS protected ethers was followed with use of 44 mg (0.12 mmol) of **8c** yielding **14** (17 mg, 94%) as a white solid after precipitation of the HCl salt from MeOH with ether. A portion of lactone **14** (3.9 mg, 0.034 mmol) was *N*,*N*-dibenzylated by treatment with BnBr (0.11 mL, 0.88 mmol) and K_2CO_3 (0.10 g, 0.76 mmol) in 0.38 mL of CH_3CN at 50 °C. After 16 h, the suspension was cooled, diluted with EtOAc, and washed with brine. The aqueous layer was extracted with EtOAc (3×), and the combined organic layers were dried and concentrated. Pure **20** (5.9 mg, 59%) was obtained after chromatography (20% EtOAc/hexanes) as a clear oil. Spectroscopic data were consistent with those previously observed (see deprotection of **8b**).[23]

Acknowledgment. This work was supported by the National Science Foundation. The Center for New Directions for Organic Synthesis is supported by Bristol-Myers Squibb as a Sponsoring Member and Novartis Pharma as a Supporting Member.

JO035224P