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Asymmetric Synthesis of β-Amino Carbonyl Compounds with *N*-Sulfinyl β-Amino Weinreb Amides

Franklin A. Davis,* M. Brad Nolt, Yongzhong Wu, Kavirayani R. Prasad,† Danyang Li, Bin Yang, Kerisha Bowen, Seung H. Lee, and John H. Eardley

Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122

fdavis@temple.edu

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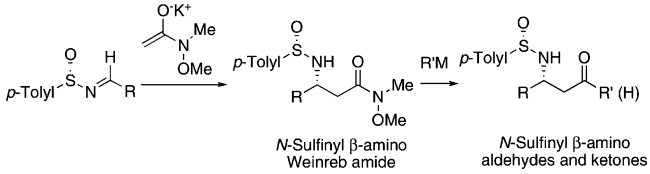

Diverse organometallic reagents readily add to enantiopure *N*-sulfinyl β-amino Weinreb amides providing the corresponding, stable, *N*-sulfinyl β-amino carbonyl compounds in good to excellent yields. This new methodology represents a general solution to the problem of β-amino carbonyl syntheses, which are important chiral building blocks and constituents of natural products. *N*-Sulfinyl β-amino Weinreb amides are prepared by reaction of the potassium enolate of *N*-methoxy *N*-methylacetamide with sulfinimines (*N*-sulfinyl imines) or lithium *N*,*O*-dimethylhydroxylamine with *N*-sulfinyl β-amino esters.

Introduction

Nonracemic β-amino carbonyl compounds are valuable chiral building blocks for the asymmetric syntheses of biorelevant nitrogen-containing molecules.[1,2] For example, β-amino carbonyls are precursors of β-amino acids[3] and 1,3-amino alcohols[4−6] and are also found in natural products[3] and other pharmacologically active compounds. Mannich-type reactions, the aminoalkylation of CH-acidic compounds, represent the most direct method for the preparation of β-amino carbonyl compounds;[2,7] however, to date this methodology has found limited success in the asymmetric synthesis of diversely substituted β-amino aldehydes and ketones.[8] The reason is β-amino aldehydes and ketones, unless suitably *N*-protected, are unstable and undergo self-condensation or β-elimination of the amino group.[9] Indeed there are only a few methods for the asymmetric synthesis of stable β-amino aldehydes and ketones and most of these procedures are target specific.[6,8−11] In this paper we report full details of a general method for the asymmetric synthesis of diverse β-amino aldehydes and ketones from sulfinimine-derived *N*-sulfinyl β-amino Weinreb amides.[6]

Results and Discussion

β-Amino Weinreb Amides from Sulfinimines. Weinreb amides, introduced by Nahm and Weinreb in 1981,[12]

† Present address: Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India.

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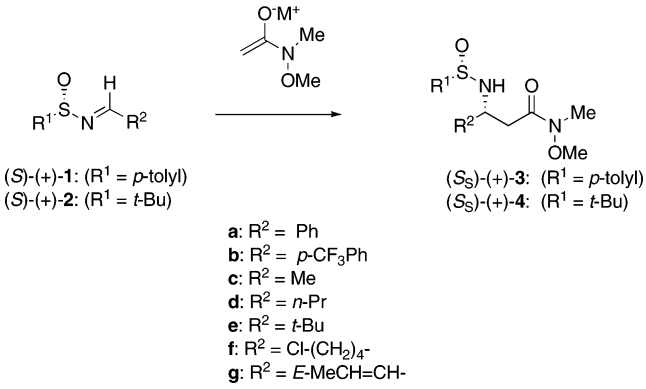
TABLE 1. Synthesis of β-Amino Weinreb Amides 3 and 4 from Sulfinimines and *N*-Methoxy-*N*-methylacetamide at −78 °C

		sulfinimine					
entry		R^1	R^2	base (solvent)	Weinreb amide	dr (% de)[a]	% yield[c]
1	**1a**	*p*-tolyl	Ph	LiHMDS (THF)	(+)-**3a**	79:21 (58)[b]	
2				NaHMDS (THF)		82:18 (64)	
3				KHMDS (THF)		85:15 (70)	65[d]
4				KHMDS (PhMe)		51:49 (2)	
5				KHMDS (Et_2O)		54:46 (8)	
6	**1b**	*p*-tolyl	*p*-CF_3Ph	KHMDS (THF)	(+)-**3b**	77:23 (54)[e]	
7	**1c**	*p*-tolyl	Me	KHMDS (THF)	(+)-**3c**	92:8 (84)	52
8	**1d**	*p*-tolyl	*n*-Pr	KHMDS (THF)	(+)-**3d**	99:1 (98)	68
9	**1e**	*p*-tolyl	*t*-Bu	KHMDS (THF)	(+)-**3e**	99:1 (98)	68
10	**1f**	*p*-tolyl	Cl−$(CH_2)_4$-	KHMDS (THF)	(+)-**3f**	99:1 (98)	76
11	**1g**	*p*-tolyl	*E*-MeCH=CH−	KHMDS (THF)	(+)-**3g**	99:1 (98)	82
12	**2a**	*t*-Bu	Ph	KHMDS (THF)	(+)-**4a**	52:48 (4)[e]	
13	**2d**	*t*-Bu	*n*-Pr	KHMDS (THF)	(+)-**4d**	86:14 (72)[e]	
14	**2e**	*t*-Bu	*t*-Bu	KHMDS (THF)	(+)-**4e**	88:12 (76)[e]	

[a] Determined by ^{1}H NMR of the crude reaction mixture unless otherwise noted. [b] Estimated by isolation of the two diastereoisomers. [c] Isolated yield of major diastereoisomer. [d] Isolated by fractional crystallization. [e] Inseparable mixture of diastereoisomers.

SCHEME 1



are important carbonyl equivalents and have found many applications in the synthesis of carbonyl compounds.[13] While β-amino Weinreb amides have been reported, there are only a few applications that use them, either because of difficult syntheses or problems in the removal of the *N*-substitutents.[14] Here, however, we have found that addition of the enolate of commercially available *N*-methoxy-*N*-methylacetamide to sulfinimines affords the corresponding *N*-sulfinyl β-amino Weinreb amides in good yield and excellent diastereoselectivity (Scheme 1).[15]

The synthesis of the Weinreb amides **3** and **4** was accomplished by addition of sulfinimine (*S*)-(+)-**1** (R^1 = *p*-tolyl) or (*S*)-(+)-**2** (R^1 = *t*-Bu) to 1.5 equiv of the preformed enolate of *N*-methoxy-*N*-methylacetamide at −78 °C (Scheme 1). Workup consisted of quenching at this temperature and isolation by chromatography or crystallization. These results are summarized in Table 1.

As summarized in the table *N*-(*p*-toluenesulfinyl) imines (*S*)-(+)-**1** gave better yields and higher diastereoselectivities than the corresponding *N*-(*tert*-butylsulfinyl) imines (*S*)-(+)-**2** (compare entries 3, 6−11 with 12−14 in Table 1). Indeed the diastereomeric Weinreb amides **4**, derived from the latter sulfinimine, could not be separated by chromatography. For (*S*)-(+)-**1**, the best yields and highest diastereoselectivities of **3** were observed for the potassium enolate of *N*-methoxy-*N*-methylacetamide in THF. With three exceptions, the diastereoselectivities for (S_S,*R*)-**3** were better than 98%. The exceptions were sulfinimines (*S*)-(+)-**1a** (R^2 = Ph), (*S*)-(+)-**1b** (R^2 = *p*-CF_3Ph), and **1c** (R^2 = Me), where the maximum de values for **3a**, **3b**, and **3c** were 70%, 54%, and 84%, respectively (Table 1, entries 3, 6, and 7). Crystallization and chromatography were employed to isolate the pure diastereoisomers (S_S,*R*)-**3a** and (S_S,*R*)-(+)-**3c** in 65% and 52% yields, but the isomers of **3b** were inseparable.

The absolute stereochemistry of the major diastereoisomers for enolate additions to sulfinimines (*S*)-**1** and (*S*)-**2** was determined to be *R* by independent syntheses (see below). The addition of organometallic reagents to the C−N double bond of sulfinimines generally can be predicted by assuming six-membered chairlike transition states where the metal ion, usually Li^+, Na^+, or Zn^{2+}, is coordinated to the sulfinyl oxygen.[15] The results obtained here are in agreement with this chelation-control transition-state hypothesis. However, the fact that the potassium enolate of *N*-methoxy-*N*-methylacetamide gave better diastereoselectivities than either the lithium or sodium enolates was not anticipated (Table 1: entries 1−3) because potassium ions are generally thought to be poorer coordinating ions than lithium or sodium.

β-Amino Weinreb Amides from β-Amino Esters. *N*-Sulfinyl β-amino Weinreb amides **3** can also be prepared in good yield by treating methyl *N*-sulfinyl β-amino carboxylates (S_S,*R*)-**5** with 5 equiv of lithium *N*,*O*-dimethylhydroxyamine (Table 2, Scheme 2). Fewer equivalents of LiN(OMe)Me resulted in incomplete reaction. Because the amino stereocenter in **3** is not affected by this transformation, it serves to establish the absolute stereochemistry of **3** as *R*. The fact that the addition of potassium *N*-methoxy-*N*-methylacetamide to sulfinimine

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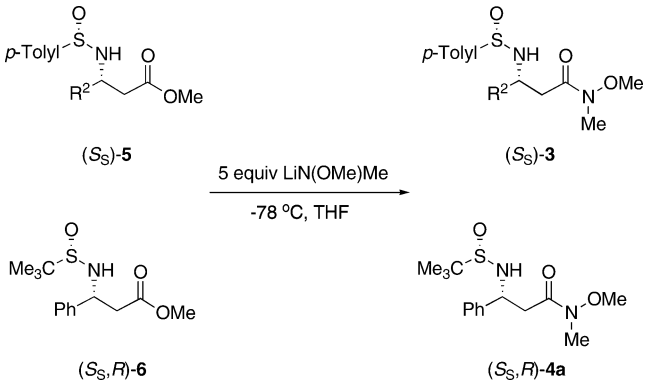
TABLE 2. Synthesis of β-Amino Weinreb Amides from *N*-Sulfinyl β-Amino Methyl Esters and Lithium *N*,*O*-Dimethylhydroxyamine at −78 °C in THF

entry	β-amino ester		equiv of LiN-(OMe)Me	Weinreb amide	% isolated yield
	R¹	R²			
1	**5a** *p*-tolyl	Ph	5	**3a**	78
2			3		61
3	**5b** *p*-tolyl	*p*-CF_3Ph	5	**3b**	54
4	**5c** *p*-tolyl	Me	5	**3c**	66
5	**5e** *p*-tolyl	*t*-Bu	5	**3e**	68
6	**5g** *p*-tolyl	*E*-MeCH=CH−	5	**3g**	82
7	**6** *t*-Bu	Ph	5	**4a**	79

SCHEME 2



(*S*)-(+)-**1a** (R = Ph) affords the *R* isomer provides additional support for our chelation control-transition state model for addition of organometallic reagents to sulfinimines.[15] Similar results were observed for the addition of LiN(OMe)Me to the (S_S*R*)-(+)-methyl-*N*-(*tert*-butylsulfinyl)-3-amino-3-phenyl propanoate (**6**), which afforded (S_S,*R*)-**4a** in 79% isolated yield (Table 2). The β-amino esters were prepared as previously described by addition of the sodium enolate of methyl acetate in ether to the sulfinimine.[17]

***N*-Sulfinyl β-Amino Aldehydes and Ketones.** *N*-Sulfinyl β-amino Weinreb amides **3** react with various organometallic reagents to give good-to-excellent yields of the corresponding *N*-sulfinyl β-amino aldehydes and ketones (Figure 1, Table 3).[16] Usually 5 equiv of the organometallic reagents was found to be best for yields and reaction times. Excess organometallic reagent may be required because of the acidity of the sulfinyl NH proton, which is undoubtedly first removed. With DIBAL-H, **3a** and **3e** gave aldehydes **7a** and **7b** in 84% and 70%, respectively (Table 3, entries 1 and 15). Methylmagnesium bromide with **3a**, **3b**, and **3f** afforded the corresponding methyl ketones **8a**−**c**, respectively, in good yield (Table 3, entries 2, 14, and 17). The reaction of the *N*-(*tert*-butylsulfinyl) imine Weinreb amide (S_S,*R*)-**4a** reacts similarly with methylmagnesium bromide to give ketone **16** in 81% yield (Figure 1). Phenylmagnesium bromide with **3a** and **3e** gives the phenyl ketones **10a** and **10b** in 84% and 88% yields (Table 3, entries 5 and 16). Generally Grignard reagents gave better yields than lithium reagents although *n*-butyllithium with **3a** afforded *n*-butyl ketone **9** in 88% yield (Table 3: entry 7). Reagent additions were usually complete within 1−2 h,

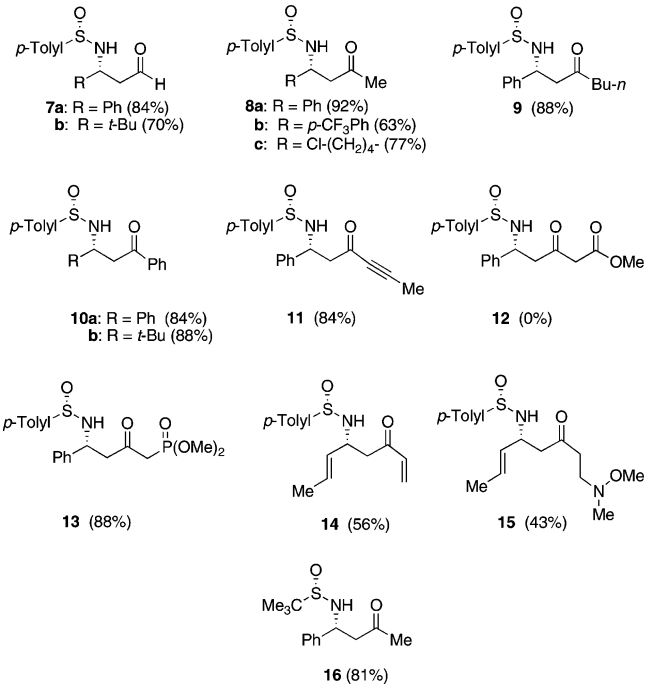


FIGURE 1. Reactions of *N*-sulfinyl Weinreb amides with organometallic reagents.

but 1-propynylmagnesium bromide and **3a** (R¹ = Ph) required more than 12 h and warming to room temperature to give alkynyl ketone **11** in 72% and 95% yield (Table 3, entries 8 and 9). All attempts to treat **3a** with the lithium enolate of methyl acetate to prepare *N*-sulfinyl δ-amino β-ketoester **12**, an important chiral building block for piperidine[18] and pyrrolidine alkaloid synthesis,[19] were unsuccessful (Table 3: entry 11). On the other hand, lithium dimethyl methyl phosphonate with **3a** (R¹ = Ph) gave *N*-sulfinyl δ-amino β-ketophosphonate **13** in 88% yield (Table 3: entry 13).[20] This new sulfinimine-derived chiral building block has been recently employed in the asymmetric syntheses of 4-aminocyclopentenones, valuable intermediates in the asymmetric construction of carbocyclic nucleosides,[20a] and *cis*-5-substituted pyrrolidine phosphonates, proline surrogates.[20b]

The reaction of unsaturated Weinreb amide **3g** with vinylmagnesium bromide warrants special comment. The addition of vinyl Grignard reagents to Weinreb amides generally results in low yields of the vinyl ketone.[21] The reason is that the Michael addition product of the liberated *N*,*O*-dimethylhydroxylamine reacts very rapidly with the desired vinyl ketone product producing a β-(*N*-methoxy-*N*-methyl) aminoethyl ketone. Attempts to mini-

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TABLE 3. Synthesis of *N*-Sulfinyl *β*-Amino Aldehyde and Ketones from *β*-Amino Weinreb Amides and Organometallic Reagents

entry	Weinreb amide (R^2)		R^3 (equiv)	conditions: solvent, h, °C	*β*-amino carbonyl compd	% isolated yield (R^3)
1	Ph	**3a**	DiBAL-H (5)	THF, 1.0, −78	**7a**	84 (H)
2			MeMgBr (5)	THF, 2.5, −78 to rt	**8a**	92 (Me)
3			MeMgBr (3)	THF, 2.5, −78 to rt	**8a**	67 (Me)
4			MeLi (5)		**8a**	60 (Me)
5			PhMgBr (5)	THF, 2.5, −78 to rt	**10a**	84 (Ph)
6			PhLi (5)	THF, 1.0, 78 to rt		49 (Ph)
7			*n*-BuLi (8)	THF, 0.5, −78	**9**	88 (*n*-Bu)
8			MeC≡CMgBr (5.0)	THF, 2.5, −78 to rt	**11**	72 (MeC≡C)
9			MeC≡CMgBr (5.0)	THF, 12, −78 to rt	**11**	95 (MeC≡C)
10			PhC(O)Me	LDA	NR	
11			CH_3CO_2Me	LHMDS	**13**	0
12			$CH_3P(O)(OMe)_2$ (2.0)	LHMDS, THF, 3, −78	NR	
13			− (2.0)	*n*-BuLi, THF, 2, −78	**14**	88 ($CH_2P(O)(OMe)_2$
14	*p*-CF_3Ph	**3b**	MeMgBr (5)	THF, 2.5, −78 to rt	**8b**	63 (Me)
15	*t*-Bu	**3e**	DIBAL-H (5)	THF, 2, −78	**7b**	70 (H)
16			PhMgCl (5)	THF, 2,5 h, −78 to rt	**10b**	88 (Ph)
17	Cl−$(CH_4)_4$−	**3f**	MeMgBr (5)	THF, 0.5, −78 to rt	**8c**	77 (Me)
18	*E*-MeCH=CH−	**3g**	CH_2=CHMgBr (10)	THF, 0.5, 0[a]	**14**	29 (CH_2=CH−)
				THF, 0.5, 0[a]	**15**	43 (CH_2=CH−)
19				THF, 0.5, 0[b]	**14**	56 (CH_2=CH−)
20	Ph	**4a**	MeMgBr (5)	THF, 3, −78 to rt	**16**	81 (Me)

[a] Quenched by addition of aqueous saturated NH_4Cl to the reaction mixture. [b] Quenched by addition of the reaction mixture to 5:1 H_2O:AcOH.

mize this side product have not been successful. Indeed when we used our normal quenching procedure with aqueous saturated NH_4Cl, *β*-amino vinyl ketone **14** was isolated in only 29% yield and the major product was the Michael addition product **15**, which was obtained in 43% yield (Figure 1, Table 3, entry 18). However, quenching with 5:1 H_2O:AcOH resulted in isolation of the vinyl ketone **14** in 56% yield (Table 3, entry 18). The fact that the Michael addition product **15** was not detected when the reaction was quenched with acetic acid likely results from the reduced nucleophilicity of the *N*,*O*-dimethylhydroxylamine under these conditions.[22]

All of the Weinreb amide derived *N*-sulfinyl *β*-amino aldehydes and ketones (Figure 1) were stable compounds and could be stored for long periods of time. These results further confirm the unique nitrogen protecting-group abilities of the sulfinyl group.[15] The *N*-sulfinyl group can be oxidized with *m*-CPBA to the *N*-tosyl nitrogen protecting group[6] or removed with acid and the products used to prepare polysubstituted piperidines and indolizidines.[10]

In conclusion, new and general methodology has been introduced for the asymmetric synthesis of *N*-sulfinyl *β*-amino Weinreb amides by addition of the potassium enolate of *N*-methoxy-*N*-methylacetamide to sulfinimines or by treating *N*-sulfinyl *β*-amino esters with lithium *N*,*O*-dimethylhydroxyamine. In the former reaction, *N*-*p*-toluenesulfinyl imines **1** gave better yields and diastereoselectivities when compared to *N*-*tert*-butylsulfinyl imines **2** with the same substituents. Various organometallic reagents readily react with *N*-sulfinyl *β*-amino Weinreb amides to give good to excellent yields of *β*-amino aldehydes and ketones, which are valuable chiral building blocks for the asymmetric syntheses of biorelevant nitrogen-containing compounds.

Experimental Section

The preparation of sulfinimines (*S*)-(+)-*N*-(benzylidene)-*p*-toluenesulfinamide (**1a**),[23] (*S*)-(+)-*N*-(*p*-trifluoromethylbenzylidene)-*p*-toluenesulfinamide (**1b**),[24] (*S*)-(+)-*N*-(acetylidene)-*p*-toluenesulfinamide (**1c**),[23] (*S*)-(+)-*N*-(butylidene)-*p*-toluenesulfinamide (**1d**),[23] (*S*)-(+)-*N*-(2,2-dimethylpropylidene)-*p*-toluenesulfinamide (**1e**),[23] (*S*)-(+)-*N*-(pentylidine)-5-chloro-*p*-toluenesulfinamide (**1f**),[6] (*S*)-(+)-*N*-(crotonylidene)-*p*-toluenesulfinamide (**1g**),[23] (*S*)-(+)-*N*-(benzylidene)-2-methylpropanesulfinamide (**2a**),[25]and (*S*)-(+)-*N*-(2,2-dimethylpropylidene)-2-methylpropanesulfinamide (**2e**);[25] and Weinreb amides (S_S,3*R*)-(+)-*N*-(*p*-toluenesulfinyl)-3-amino *N*-methoxy-*N*-methyl-3-phenylpropionamide (**3a**)[6] and (S_S,3*S*)-(+)-7-chloro-*N*-(*p*-toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methylheptanoamide (**3f**);[6] *β*-amino esters (S_S,*R*)-(+)-methyl *N*-(*p*-toluenesulfinyl)-3-amino-3-phenylpropanoate (**5a**),[26] (S_S,*R*)-(+)-methyl *N*-(*p*-toluenesulfinyl)-3-amino-3-*tert*-butylpropanoate (**5e**),[19b] (S_S,*R*)-(+)-methyl *N*-(*p*-toluenesulfinyl)-3-amino-3-(*E*)-propenylpropanoate (**5g**),[11a] (S_S,*R*)-(−)-methyl *N*-(2-methylpropanesulfinyl)-3-amino-3-phenylpropanoate (**6**),[27] (S_S,3*R*)-(+)-*N*-(*p*-toluenesulfinyl)-3-amino-3-phenylpropionaldehyde (**7a**),[6] (S_S,3*R*)-(+)-*N*-(*p*-toluenesulfinyl)-3-amino-1-methyl-3-phenylpropan-1-one (**8a**),[6] (S_S,3*R*)-(+)-*N*-(*p*-toluenesulfinyl)-3-amino-1-(*n*-butyl)-3-phenylpropan-1-one (**9**),[10] and (S_S,3*R*)-(+)-*N*-(*p*-toluenesulfinyl)-3-amino-1,3-diphenylpropan-1-one (**10a**)[6] were prepared according to literature procedures.

(*S*)-(+)-*N*-(Butylidene)-2-methylpropanesulfinamide (2d). In a two-neck, 100-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon inlet was

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placed *n*-butylaldehyde (0.22 mL, 2.5 mmol), $Ti(OEt)_4$ (0.63 mL, 3.0 mmol), and (*S*)-(−)-*tert*-butylsulfinamide (0.121 g, 1.00 mmol) in DCM (10 mL). After the reaction mixturewas stirred for 3 h it was cooled to 0 °C, brine (1 mL) was added, and the solution was stirred vigorously for 10 min. At this time the solution was filtered through packed Celite and rinsed with DCM (2 × 10 mL). The filtrate was extracted with Et_2O (3 × 10 mL), washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Chromatography (EtOAc/*n*-hexanes, 1:1) gave 0.191 g (100%) of a clear oil; $[\alpha]^{25}_D$ 122.3 (*c* 0.5, $CHCl_3$); IR 2960; ^1H NMR ($CDCl_3$) δ 8.04 (t, J = 5.0 Hz, 1 H), 2.50−2.46 (m, 2 H), 1.64 (sextet, J = 7.5 Hz, 2 H), 1.17 (s, 9 H), 0.97 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 14.2, 19.4, 22.7, 38.5, 56.9, 170.2. HRMS calcd for $C_8H_{17}NOS$ (M + H) 176.1109, found 176.1106.

General Procedure for the Synthesis of *N*-Methoxy-*N*-methyl Acetamide (*N*-sulfinyl Weinreb amides): (*S*$_S$,3*S*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy- *N*-methylbutanoamide (3c). In an oven-dried, 25-mL, one-neck, round-bottom flask equipped with a magnetic stirring bar and argon balloon was placed KHMDS (0.43 mmol, 0.86 mL of 0.5 M solution in toluene) in ether (5 mL). The solution was cooled to −78 °C and *N*-methoxy-*N*-methyl acetamide (0.043 mL, 0.40 mmol, Aldrich) was added, and the solution was stirred at this temperature for 1 h. At this time a solution of (+)-**1c** (0.049 g, 0.27 mmol) in ether (2 mL) was added and the reaction mixture was stirred for 2 h and then quenched at −78 °C by addition of saturated aqueous NH_4Cl (2 mL). After warming to room temperature the solution was poured into H_2O (2 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were washed with brine (2 mL), dried (Na_2SO_4), and concentrated. Chromatography (EtOAc/*n*-hexanes, 1:1) gave 0.148 g (52%) of a clear, viscous oil. The physical properties are identical with those of (+)-**3c,** prepared from the β-amino ester (+)-**5c** (see below).

(*S*$_S$,3*S*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methylhexanoamide (3d). Chromatography (1:1, EtOAc/*n*-hexanes) gave 68% of a clear viscous oil (96:4 ratio of inseparable diastereomers); $[\alpha]^{20}_D$ 116.7 (*c* 2.6, $CHCl_3$, 92% de); IR (neat) 3231, 2958, 1652; major diastereomer ^1H NMR ($CDCl_3$) δ 0.94 (t, J = 7.5 Hz, 3 H), 1.40−1.44 (m, 1 H), 1.47−1.54 (m, 1 H), 1.58−1.12 (m, 1 H), 1.68−1.73 (m, 1 H), 2.39 (s, 3 H), 2.77 (s, 2 H), 3.15, (s, 3 H), 3.65 (s, 3 H), 3.69−3.72 (m, 1 H), 4.94 (d, J = 8.5 Hz, 1 H), 7.28 (d, J = 8.0 Hz, 2 H), 7.58 (d, J = 7.5 Hz, 2 H); major diastereomer ^{13}C NMR ($CDCl_3$) δ 14.2, 19.9, 21.7, 32.2, 37.9, 38.3, 53.4, 61.6, 125.7, 129.8, 141.4, 143.2, 172.7. HRMS calcd for $C_{15}H_{24}N_2O_3SNa$ (M + Na) 335.1412, found 335.1405.

(*S*$_S$,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methyl-3-*tert*-butylpropionamide (3e). Chromatography (EtOAc/*n*-hexanes, 60:40) gave 72% of a white solid; mp 99−101 °C. The physical properties are identical with those of (+)-**3e** prepared from the β-amino ester (+)-**5e** (see below).

(*S*$_S$,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methyl-hex-4-enamide (3g). Chromatography (EtOAc/*n*-hexanes, 1:1) gave 82% of a clear oil: $[\alpha]^{20}_D$ 118.3 (*c* 5.4, $CHCl_3$); IR (neat) 3221 (NH), 1656 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.64 (dd, J = 1.0 Hz, J = 6.4 Hz, 3 H), 2.31 (s, 3 H), 2.57−2.71 (m, 2 H), 3.04 (s, 3 H), 3.56 (s, 3 H), 4.14−4.20 (m, 1 H), 5.10 (d, J = 5.6 Hz, 1 H), 5.45−5.51 (m, 1 H), 5.66−5.75 (m, 1 H), 7.18 (d, J = 8.4 Hz, 2 H), 7.50−7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.1, 21.6, 32.2, 38.6, 53.7, 61.6, 125.8, 129.1, 129.8, 131.1, 141.4, 142.9, 172.2. HRMS calcd for $C_{15}H_{23}N_2O_3S$ (M + H) 311.1429, found 311.1432.

(*S*$_S$,3*R*)-(+)-Methyl *N*-(*p*-Toluenesulfinyl)-3-amino-3-(*p*-trifluoromethylphenyl)propanoate (5b). In an oven-dried, 50-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed NaHMDS (0.34 mmol, 0.34 mL of a 1.0 M solution in THF) in ether (5 mL). The solution was cooled to −78 °C, and anhydrous methyl acetate (0.34 mmol, 0.027 mL) was added via syringe. After the solution was stirred at this temperature for 1 h, (+)-**1b** (0.070 g, 0.22 mmol) in ether (5 mL) was added via cannula. After being stirred at this temperature for 4 h, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution (1 mL) and warmed to room temperature and H_2O (5 mL) was added. The solution was extracted with EtOAc (3 × 10 mL), and the combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated. Flash chromatography (EtOAc/*n*-hexanes, 2:5) afforded 0.060 g (73%) of a slightly yellow oil: $[\alpha]^{20}_D$ 60 (*c* 3.8, $CHCl_3$); IR (neat) 3189, 2955, 1739, 1327; ^1H NMR ($CDCl_3$) δ 2.41 (s, 3 H), 2.85−2.86 (m, 2 H), 3.59 (s, 3 H), 4.91 (dd, J = 12.0, 12.5 Hz, 1 H), 5.26 (d, J = 6.0 Hz, 1 H), 7.29−7.31 (m, 2 H), 7.53−7.63 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 21.4, 41.7, 52.0, 54.2, 76.7, 77.1, 77.5, 125.4, 125.7, 125.80, 125.85, 127.6, 129.7, 141.7, 144.7, 170.9. HRMS calcd for $C_{18}H_{18}NO_3F_3SNa$ (M + Na) 408.0856, found 408.0857.

(*S*$_S$,3*S*)-(+)-Methyl *N*-(*p*-toluenesulfinyl)-3-aminobutanoate (5c). Chromatography (EtOAc/*n*-hexanes, 1:1) gave 0.184 g (72%) of a clear oil which solidified upon standing at −20 °C; $[\alpha]^{25}_D$ 131.3 (*c* 2.4, $CHCl_3$); IR ($CHCl_3$) 3208, 2951, 1733; ^1H NMR ($CDCl_3$) δ 1.37 (d, J = 6.5 Hz, 3 H), 2.40 (s, 3 H), 2.53 (m, 2H), 3.64 (s, 3 H), 3.80−3.75 (m, 1 H), 4.63 (d, J = 7.5 Hz, 1 H), 7.30 (d, J = 5.0 Hz, 2 H), 7.56 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.7, 22.8, 42.5, 47.5, 52.1, 126.1, 129.9, 141.7, 142.2, 172.1. HRMS calcd for $C_{12}H_{17}NO_2SNa$ (M + Na) 278.0827, found 278.0827.

General Procedure for the Synthesis of β-Amino Weinreb Amides from *N*-Sulfinyl β-Amino Esters: (*S*$_S$,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methyl-3-*tert*-butylpropionamide (3e). In an oven-dried, 50-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed *N*,*O*-dimethylhydroxyamine hydrochloride (0.21 g, 2.06 mmol, Aldrich) in THF (4 mL). The solution was stirred and cooled to −78 °C, and *n*-BuLi (2.10 mL, 2.0 M in cyclohexane, 4.11 mmol) was added dropwise via syringe. After the reaction was stirred at this temperature for 5 min, the cooling bath was removed for ca. 15 min, the solution was cooled to −78 °C, and (+)-**5e** (0.122 g, 0.41 mmol) in THF (5 mL) was added via syringe. After being stirred at this temperature for 4 h, the reaction mixture was warmed to −60 °C for 1 h, quenched by addition of saturated NH_4Cl solution (1.5 mL), and warmed to room temperature. Water (3 mL) was added and the solution was extracted with Et_2O (15 mL) and EtOAc (3 × 15 mL). The combined organic phases were washed with brine (3 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc/*n*-hexanes, 60:40) gave 0.091 g (68%) of a white solid: mp 99−101° C; $[\alpha]^{20}_D$ 137.6 (*c* 0.5, $CHCl_3$); IR (neat) cm^{-1} 3226 (NH), 2960, 1659, 1416, 1065; ^1H NMR ($CDCl_3$) δ 0.91 (s, 9 H), 2.32 (s, 3 H), 2.66−2.68 (m, 2 H), 3.15 (s, 3 H), 3.64 (m, 4 H), 4.63 (d, J = 8.8 Hz, 1 H), 7.20 (d, J = 8.0 Hz, 2 H), 7.54 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.7, 27.0, 32.8, 34.4, 36.1, 61.8, 62.6, 63.1, 125.7, 129.9, 141.5, 144.0, 173.1. Anal. Calcd for $C_{16}H_{26}N_2O_3S$: C 58.87, H 8.03, N 8.58. Found: C 59.02, H 8.21, N 8.28.

(*S*$_S$,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methyl-3-(*p*-trifluoromethylphenyl)propionamide (3b). Chromatography (EtOAc/*n*-hexanes, 1:1) gave 54% of a slightly yellow oil: $[\alpha]^{20}_D$ 43.51 (*c* 0.37, $CHCl_3$); IR (neat) 3229, 2923, 1636, 1326; ^1H NMR ($CDCl_3$) δ 2.36 (s, 3 H), 2.95−2.96 (m, 2 H), 3.05 (s, 3 H), 3.54 (s, 3 H), 4.89 (dd, J = 11.6, 12.0 Hz, 1 H), 5.59 (d, J = 5.6 Hz, 1 H), 7.24−7.26 (m, 2 H), 7.54−7.59 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 21.4, 29.7, 29.7, 31.9, 39.1, 54.7, 61.3, 76.6, 77.0, 77.5, 125.3, 125.71, 125.76, 125.9, 127.7, 129.7, 141.5, 145.3, 171.4. HRMS calcd for $C_{19}H_{21}N_2O_3F_3SNa$ (M + Na) 437.1126, found 437.1123.

(*S*$_S$,3*S*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-*N*-methoxy-*N*-methylbutanoamide (3c). Chromatography (EtOAc/*n*-hexanes, 1:1) gave 66% of a clear, viscous oil: $[\alpha]^{25}_D$ 154.8 (*c* 2.7, $CHCl_3$); IR (neat) 3482, 3220, 2970, 1652; ^1H NMR ($CDCl_3$) δ 1.42 (d, J = 6.6 Hz, 3 H), 2.42 (s, 3 H), 2.67 (d, J = 5.5 Hz, 2 H), 3.16 (s, 3 H), 3.62 (s, 3H), 3.85 (quintet, J = 6.6, 13.9 Hz, 1 H), 5.06 (d, J = 7.6 Hz, 1 H), 7.3 (d, J = 8.4 Hz, 2 H),

7.61 (q, J = 4.9, 8.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.8, 22.7, 40.0., 47.9, 61.6, 126.1, 129.9, 141.5, 142.6, 172.2. HRMS calcd for $C_{13}H_{20}N_2O_3SNa$ (M + Na) 307.1092, found 307.1090.

(S_S,3R)-(+)-*N*-(2-Methylpropanesulfinyl)-3-amino-*N*-methoxy-*N*-methyl-3-phenylpropionamide-(4a). Chromatography (EtOAc/*n*-hexanes, 1:1) gave 79% of a clear viscous oil: $[\alpha]^{20}_D$ 184.1 (c 0.78, $CHCl_3$); IR (neat) cm^{-1} 3236 (NH), 1652; ^{1}H NMR (CDCl3) δ 1.23 (s, 9 H), 2.87−2.90 (dd, J = 9.0 Hz, 7.0 Hz, 1 H), 3.05−3.08 (m, 1 H), 3.16 (s, 3 H), 3.61 (s, 3 H), 4.77−4.80 (m, 1 H), 5.39 (s, 1 H), 7.27−7.31 (m, 2 H), 7.33−7.38 (m, 3 H); ^{13}C NMR ($CHCl_3$) δ 23.1, 32.3, 39.5, 55.9, 56.0, 61.7, 127.7, 128.1, 141.8, 172.4; HRMS calcd for $C_{15}H_{25}N_2O_3S$ (M + H) 313.1586, found 313.1586.

(S_S,3R)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-3-*tert*-butylpropionaldehyde (7b). In an oven-dried, 10-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septa, and argon balloon was placed (+)-**3e** (0.033 g, 0.1 mmol) in THF (2 mL). The solution was cooled to −78 °C and DIBAL-H (0.5 mmol, 0.5 mL of a 1 M solution in CH_2Cl_2) was introduced. After being stirring for 1 h at −78 °C, the reaction mixture was quenched with saturated NH_4Cl (2 mL) solution, filtered through packed Celite, poured into H_2O (5 mL), and extracted with EtOAc (2 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Chromatography (EtOAc/*n*-hexanes, 85:15) gave 0.019 g (70%) of a thick, colorless oil: $[\alpha]^{20}_D$ 123.3 (c 0.33, $CHCl_3$); IR (neat) cm^{-1} 3168, 1724; ^{1}H NMR (CDCl3) δ 0.91 (s, 9 H), 2.34 (s, 3 H), 2.55 (ddd, J = 1.6, 4.8, 17.2 Hz, 1 H), 3.65−3.71 (m, 1 H), 3.86 (d, J = 9.2 Hz, 1 H), 4.77−4.80 (m, 1 H), 5.39 (s, 1 H), 7.19−7.24 (m, 2 H), 7.51−7.53 (m, 2 H), 9.73 (t, J = 1.1 Hz, 1 H); ^{13}C NMR ($CHCl_3$) δ 21.7, 26.9, 35.8, 46.9, 60.2, 125.6, 130.0, 142.0, 143.2, 201.3. HRMS calcd for $C_{14}H_{22}NO_2S$ (M + H) 268.1371, found 268.1378.

(S_S,3R)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-3-phenylpropinoaldehyde (7a). Chromatography (*n*-hexane:EtOAc, 15:85) gave 84% of a thick colorless oil; $[\alpha]^{25}_D$ +175.1 (c 0.41, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.33 (s, 3 H), 2.87 (dd, J = 1.2, 6.4, 2 H), 4.66 (d, J = 5.2, 1 H), 4.90 (q, J = 6.4, 1 H), 7.25−7.21 (m, 3 H), 7.35−7.28 (m, 4 H), 7.50 (d, J = 8.4, 2 H), 9.53 (t, J = 1.6, 1 H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 21.8, 51.3, 53.4, 125.8, 127.7, 128.6, 129.3, 130.0, 140.8, 142.0, 142.3, 200.2. HRMS calcd for $C_{16}H_{17}NO_2SNa$ (M + Na) 310.0878, found 310.0884.

General Procedure for Addition of Grignard Reagents to *N*-Sulfinyl β-Amino Weinreb Amides: (S_S,3R)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-3-*tert*-butyl-1-phenylpropan-1-one (10b). In an oven-dried, 25 mL, round-bottom flask equipped with a magnetic stirring bar, a rubber septum, and an argon balloon was placed (+)-**3e** (0.033 g, 0.10 mmol) in THF (3 mL). The solution was cooled to −78 °C, phenylmagnesium chloride (0.25 mL of a 2.0 M solution in THF, 0.50 mmol) was added, and the reaction mixture was warmed to room temperature. After being stirred for 3 h, the solution was cooled to −78 °C and quenched by addition of a saturated aqueous NH_4Cl (1 mL) solution. The reaction mixture was poured into H_2O (1 mL) and extracted with EtOAc (3 × 2 mL), and the combined organic phases were washed with brine (1 mL), dried ($MgSO_4$), and concentrated. Chromatography (EtOAc: *n*-hexanes, 1:1) gave 0.031 g (88%) of a white solid: mp 78−80 °C; $[\alpha]^{20}_D$ 153.9 (c 0.46, $CHCl_3$); IR (neat) 1685.7 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 9 H), 2.31 (s, 3 H), 3.21−3.24 (m, 2 H), 3.87−3.89 (m, 1 H), 4.25 (d, J = 8.8 Hz, 1 H), 7.18 (d, J = 7.6 Hz, 2 H), 7.36−7.40 (m, 2 H), 7.46−7.51 (m, 3 H), 7.86−7.88 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 23.6, 29.5, 37.9, 43.4, 63.6, 127.6, 130.4, 130.9, 131.8, 135.4, 139.4, 143.49, 145.5, 200.8. Anal. Calcd for $C_{20}H_{25}NO_2S$: C 69.93, H 7.34, N 4.08. Found: C 70.13, H 7.53, N 3.72.

(S_S,3R)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-1-methyl-3-(*p*-trifluoromethylphenyl)-1-one (8b). Flash chromatography (EtOAc/*n*-hexanes, 7:3) gave 63% of an oil; $[\alpha]^{20}_D$ 40.93 (c 0.43, $CHCl_3$); IR (neat) 3178, 2952, 1716, 1365; ^{1}H NMR ($CDCl_3$) δ 2.09 (s, 3 H), 2.42 (s, 3 H), 3.03−3.04 (m, 2 H), 4.93 (dd, J = 12.0, 12.0 Hz, 1 H), 5.05 (d, J = 5.5 Hz, 1 H), 7.30−7.32 (m, 2 H), 7.53−7.64 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 21.6, 32.2, 51.9, 55.1, 61.6, 77.0, 77.3, 77.7, 125.4, 125.5, 125.6, 126.0, 128.0, 129.9, 141.8, 145.7, 171.7. HRMS calcd for $C_{18}H_{18}NO_2F_3S$ (M + Na) 392.0908, found 392.0916.

(S_S,3R)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-1,3-diphenylpropan-1-one (10a). In an oven-dried, 25-mL, single-neck, round-bottom flask equipped with a magnetic stirring bar, a rubber septum, and an argon balloon was placed (+)-**3a** (0.034 g, 0.1 mmol) in THF (3 mL). The solution was cooled to −78 °C, and PhLi (0.27 mL of a 1.8 M solution in cyclohexanes−ether, 0.5 mmol) was introduced into the flask. The reaction mixture stirred at −78 °C for 0.5 h, warmed to room temperature, and stirred for 20 min, then cooled to −78 °C and cautiously quenched with saturated NH_4Cl (2 mL) solution. The reaction mixture was diluted with water (2 mL) and extracted with EtOAc (3 × 5 mL), and the combined organic phases were washed with brine (2 mL) and dried ($MgSO_4$). Chromatography (*n*-hexane:EtOAc, 30:70) gave 0.030 g (84%) of a white solid, mp 94−96 °C; $[\alpha]^{25}_D$ +80.08 (c 1.25, $CHCl_3$); IR ($CHCl_3$) 3017, 1683, 1464 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.28 (s, 3 H), 3.42 (d, J = 6.5 Hz, 2 H), 5.11 (d, J = 4.9 Hz, 1 H), 5.04 (q, J = 6.0 Hz, 1 H), 7.17 (m, 3 H), 7.29 (m, 4 H), 7.40 (m, 3 H), 7.50 (m, 2 H), 7.73 (d, J = 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.5, 47.0, 55.1, 125.8, 128.0, 128.4, 128.5, 129.0, 129.2, 130.0, 133.9, 136.8, 141.2, 141.7, 142.8, 198.2. HRMS calcd for $C_{22}H_{21}NO_2SNa$ (M + Na) 386.1191, found 386.1198.

(S_S,3R)-(+)-*N*-(*p*-Toluenesulfinyl)-3-amino-3-phenyl-1-propynyl-1-one (11). This reaction required 12 h at room temperature for completion. Chromatography (EtOAc/hexane 70%) gave 95% of a colorless oil: $[\alpha]^{20}_D$ 91.17 (c 0.60, $CHCl_3$); IR (neat) 3191, 2216, 1669 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.97 (s, 3 H), 2.42 (s, 3 H), 3.06 (d, J = 6.5 Hz, 2 H), 4.82 (d, J = 6.5 Hz, 1 H), 4.98 (q, 1 H), 7.28−7.29 (m, 3 H), 7.38 (t, 2 H), 7.42 (d, J = 8.5 Hz, 2 H), 7.57 (d, J = 8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 4.3, 21.6, 52.8, 54.4, 80.3, 92.3, 125.6, 127.7, 128.3, 129.0, 129.8, 140.3, 141.6, 142.3, 184.9. HRMS calcd for $C_{19}H_{19}NO_2SNa$ (M + Na) 348.1034, found 348.1037.

(S_S,R)-(+)-Dimethyl 2-Oxo-4-*N*-(*p*-toluenesulfinylamino)-4-phenylbutylphosphonate (13). In a 25 mL, single-necked, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed dimethyl methylphosphonate (0.394 mL, 3.53 mmol) in THF (5 mL), cooled to −78 °C, and *n*-BuLi (2 M in cyclohexane, 1.77 mL, 3.54 mmol) was added by syringe. After 15 min, the reaction mixture was transferred to a 50-mL, round-bottom flask containing (+)-**3a** (0.153 g, 0.443 mmol) in THF (10 mL) at −78 °C, and the solution was stirred at this temperature for 2 h. At this time the reaction was quenched by addition of saturated aqueous NH_4Cl (2 mL) and the solution was warmed to room temperature. After dilution with H_2O (2 mL) the solution was extracted with Et_2O (10 mL) and EtOAc (2 × 15 mL). The combined organic phases were washed with brine (2 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc) afforded a colorless oil that was subjected to Kugelrohr vacuum distillation (60 °C under 2.5 mmHg), to remove the excess dimethyl methylphosphonate, affording 0.159 g (88%) of a colorless oil; $[\alpha]^{20}_D$ 72.5 (c 1.0, $CHCl_3$); IR (neat) cm^{-1} 3188 (NH), 1717; ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3 H), 2.93 (d, $^2J_{HP}$ = 22.8 Hz, 2 H), 3.12 (d, J = 6.04 Hz, 2 H), 3.61 (d, $^3J_{HP}$ = 11.3 Hz, 6 H), 4.86−4.90 (m, 2 H), 7.29 (m, 7 H), 7.50 (d, J = 8.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.7, 41.8 (d, $^1J_{CP}$ = 127.4 Hz), 51.4, 53.4 (2 × d, $^2J_{CP}$ = 6.3 Hz), 54.7, 125.7, 127.7, 128.3, 129.1, 129.1, 129.9, 140.9, 141.8, 142.7, 200.1 (d, $^2J_{CP}$ = 5.2 Hz); ^{31}P NMR ($CDCl_3$) δ 21.84. HRMS calcd for $C_{19}H_{24}NO_5PNa$ (M + Na) 432.1011, found 432.1016.

(S_S,3R)-(+)-*p*-Toluenesulfinic Acid (3-Oxo-1-propenyl-pent-4-enyl)amide (14). In a 50-mL, single-necked, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (+)-**3g** (0.058 g, 0.187 mmol) in THF (10 mL). The solution was cooled to 0 °C and

vinylmagnesium bromide (1.87 mL, 1 M in THF, 1.87 mmol) was added by syringe. After 30 min, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (2 mL) solution and warmed to room temperature. Water (2 mL) was added and the solution was extracted with Et_2O (10 mL) and EtOAc (3 × 10 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc) afforded 0.015 g (29%) of **14** as a colorless oil; $[\alpha]^{20}_D$ 94.5 (*c* 0.7, $CHCl_3$); IR (neat) 3203 (NH), 1709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (dd, J = 0.8 Hz, J = 6.4 Hz, 3 H), 2.33 (s, 3 H), 2.81−2.82 (m, 2 H), 4.22−4.25 (m, 1 H), 4.62 (d, J = 5.6 Hz, 1 H), 5.43−5.49 (m, 1 H), 5.65−5.72 (m, 1 H), 5.75 (dd, J = 0.8 Hz, J = 10.4 Hz, 1 H), 6.07−6.11 (m, 1 H), 6.17 (dd, J = 10.4 Hz, J = 17.6 Hz, 1 H), 7.20 (d, J = 8.2 Hz, 2 H), 7.50 (d, J = 8.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.7, 19.2, 43.6, 50.8, 123.3, 126.9, 127.0, 127.4, 128.3, 134.4, 139.1, 140.2, 196.5. HRMS calcd for $C_{15}H_{20}NO_2S$ (M + H) 278.1215, found 278.1216.

(*S*S,3*R*)-(+)-*p*-Toluenesulfinic Acid {1-[4-(*N*-Methoxy-*N*-methylamino)-2-oxobutyl]but-2-enyl}amide (15). The second fraction to elute (EtOAc/*n*-hexanes, 1:1) yielded 43% of a clear oil: $[\alpha]^{20}_D$ 82.9 (*c* 0.9, $CHCl_3$); IR (neat) 3203 (NH), 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (dd, J = 0.8 Hz, J = 6.4 Hz, 3 H), 2.33 (s, 3 H), 2.45 (s, 3 H), 2.51 (t, J = 6.8 Hz, 2 H), 2.67 (d, J = 5.6 Hz, 2 H), 2.76 (t, J = 6.8 Hz, 2 H), 3.34 (s, 3 H), 4.17−4.20 (m, 1 H), 4.64 (d, J = 5.6 Hz, 1 H), 5.40−5.46 (m, 1 H), 5.66−5.72 (m, 1 H), 7.20 (d, J = 8.0 Hz, 2 H), 7.49−7.51 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.1, 21.7, 41.6, 45.3, 49.1, 53.2, 55.2, 60.2, 125.8, 129.4, 129.8, 130.8, 141.6, 142.8, 208.3. HRMS calcd for $C_{17}H_{26}N_2O_3NaS$ (M + Na) 361.1562, found 361.1565.

(*S*S,3*R*)-(+)-*p*-Toluenesulfinic Acid (3-Oxo-1-propenyl-pent-4-enyl)amide (14) Using Acid Quench. In a 50-mL, single-necked, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (+)-**3g** (0.060 g, 0.193 mmol) in THF (10 mL), and the reaction was cooled to 0 °C and vinylmagnesium bromide (1.93 mL, 1 M in THF, 1.93 mmol) was added by syringe. After 30 min, the mixture was quenched by transferring it to a mixture of H_2O (5 mL) and acetic acid (1 mL) via cannula. The solution was extracted with Et_2O (20 mL) and EtOAc (3 × 20 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc) afforded 0.033 g (56%) of colorless oil with properties identical with those of (+)-**14** prepared above.

(*S*S,3*R*)-(+)-*N*-(2-Methylpropanesulfinyl)-3-amino-1-methyl-3-phenylpropan-1-one (+)-(16). In an oven-dried, 25-mL, single-neck, round-bottom flask equipped with a magnetic stirring bar, a rubber septum, and argon balloon was placed (+)-**4a** (0.031 g, 0.1 mmol) in THF (3 mL). The solution was cooled to −78 °C and methylmagnesium chloride (0.17 mL of a 3 M solution in THF, 0.5 mmol) was added via syringe. The reaction mixture was stirred at −78 °C for 0.5 h, warmed to room temperature, and stirred for 20 min. At this time the reaction mixture was cooled to −78 °C and quenched by addition of saturated aqueous NH_4Cl solution (2 mL). The solution was diluted with H_2O (2 mL) and extracted with EtOAc (3 × 5 mL), and the combined organic phases were washed with brine (2 mL), dried ($MgSO_4$), and concentrated. Chromatography (EtOAc/*n*-hexanes, 1:1) gave 0.022 g (81%) of a clear oil; $[\alpha]^{20}_D$ 94.6 (*c* 1.54, $CHCl_3$); IR (neat) 3227, 1715; ^1H NMR ($CDCl_3$) δ 1.14 (s, 9 H), 2.07 (s, 3 H), 2.92 (dd, J = 17.2, 7.2 Hz, 1 H), 2.98 (dd, J = 17.2, 5.2 Hz, 1 H), 4.53 (d, J = 4.4 Hz, 1 H), 4.71 (ddd, J = 4.8, 3.6, 2.4 Hz, 1 H), 7.21−7.29 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 23.0, 31.2, 51.0, 55.6, 56.0, 127.7, 128.2, 129.0, 141.2, 207.7. HRMS calcd for $C_{14}H_{22}NO_2S$ (M + H) 268.1371, found 268.1373.

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Supporting Information Available: Spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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