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# Vinylaluminum Addition to Sulfinimines (*N*-Sulfinyl Imines). Asymmetric Synthesis of *anti*-α-Alkyl *β*-Amino Esters

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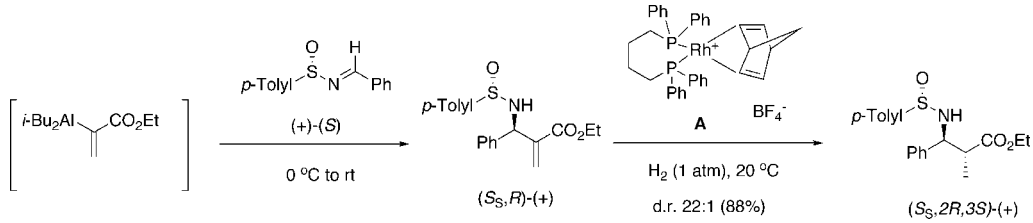
*Received January 23, 2009*




Addition of vinylaluminum NMO reagents to *N*-(*p*-toluenesufinyl)- and *N*-(2-methypropanesulfinyl)-derived sulfinimines gives *N*-sulfinyl aza-Morita−Baylis−Hillman products (dr = 7:1 to 12:1) that result from addition of the reagent from the least hindered direction. Hydrogenation of the aza-MBH adducts with a Rh(I) catalyst affords *anti*-α-substituted *N*-sulfinyl-*β*-amino esters in good yield and high dr (10:1 to 21:1).

## Introduction

The development of new and improved methodologies for the asymmetric synthesis of *β*-amino acids continues to be an important objective because of their valuable biological properties and their utility as chiral building blocks and as precursors of *β*-lactams.[1,2] Substitution of *β*-amino acids for α-amino acids results in *β*-peptides with novel activity and increased enzyme stability.[3] For these reasons, many methods have been devised for the synthesis of *β*-amino acids,[1,2] including the diastereoselective addition of enolates to enantiopure sulfinimines (*N*-sulfinyl imines).[4] However, only a few methods have been reported for the enantioselective synthesis of acyclic α-substituted *β*-amino acids.[1,5]

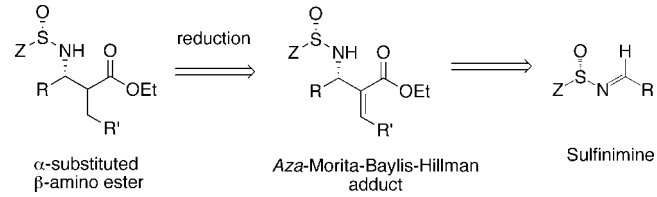



**FIGURE 1.** Retrosynthetic approach to α-substituted *N*-sulfinyl *β*-amino esters.

As part of a program aimed at the asymmetric synthesis of *N*-sulfinyl α-substituted *β*-amino esters and ketones, we have been exploring the addition of prochiral Weinreb amide enolates to sulfinimines.[5a] Another way to access these compounds is the stereoselective reduction of sulfinimine-derived α-(aminoalkyl)acrylates (aza-Morita−Baylis−Hillman) adducts (Figure 1).[6] However, sulfinimines have rarely been employed in the aza-Morita−Baylis−Hillman (aza-MBH) reaction.[7] Aggarwal et al. reported the 7 day reaction of methyl acrylate with sulfinimines to give aza-MBH adducts with modest diastereoselectivity and yield.[8] In the presence of $PhPMe_2$, cyclopent-2-eneone reacts with aromatic aldehyde-derived sulfinimines to give aza-MBH adducts with poor to good diastereoselectivity.[9]

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(6) For a review on the Morita−Baylis−Hillman reaction, see: Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811.
(7) Thermal elimination of benzenesulfenic acid from α-phenylsulfinylmethyl-*β*-(*N*-sulfinylamino) esters is reported to give α-methylene-*β*-(*N*-sulfinyamino) esters. See: Kamimura, A.; Okawa, H.; Morisaki, Y.; Ishikawa, S.; Undo, H. *J. Org. Chem.* **2007**, *72*, 3569.
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10.1021/jo9001504 CCC: $40.75 
Published on Web 03/09/2009

**SCHEME 1**

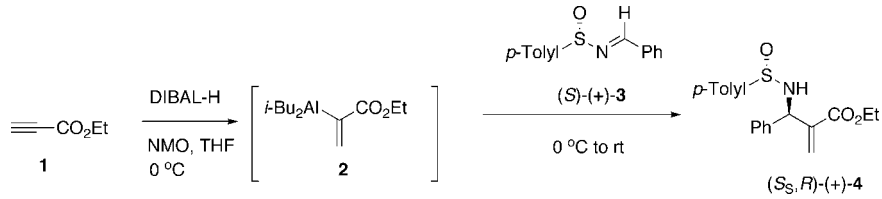


**TABLE 1. Reaction of (*S*)-(+)-3 with [α-(Ethoxycarbonyl)vinyl]-diisobutylaluminum (2) at 0 °C in THF for 6 h**

| entry | conditions (equiv)[a] **1**/ DIBAL-H/NMO | dr[b] | (+)-**4** % isolated yield[c] |
|---|---|---|---|
| 1 | 1:1.5:2.0 | 9:1 | 17 |
| 2 | 3.0:4.5:6.0 | 7:1 | 65 |
| 3 | 3.0:4.5:6.0 [3 $Zn(OTf)_2$] | 8:1 | 63 |

[a] Equivalents based on sulfinamide (+)-**3**. [b] Determined by $^1$H NMR on the crude reaction mixture. [c] Isolated yield of major diastereoisomer.

More recently, Scheidt and co-workers described the addition of lithium allenolates, in the presence of HMPA, to sulfinimines affording β-substituted aza-MBH products in good yield and high selectivity.[10]

In a series of papers, Li and co-workers explored the addition of vinylcuprates, prepared by Michael addition of $R_2CuLi$ to α-acetylenic esters, to sulfinimines at −23 °C to give novel branched aza-MBH adducts.[11] For the addition to occur, stoichiometric amounts of $Et_2AlCl$ or 40 mol % of $Yb(OTf)_3$ were required. Careful control of the reaction conditions was also necessary for good yields.[11] These workers also reported that vinylaluminum reagents were unreactive.[11c] Ramachandran and co-workers described a new procedure for the synthesis of vinylaluminum reagents from DIBAL-H, α-acetylenic esters, and 4-methylmorpholine *N*-oxide (NMO).[12] These workers demonstrated that their vinylaluminum reagents gave good yields of MBH adducts on reaction with aldehydes and ketones. Inspired by these studies, we describe the application of this protocol to the asymmetric syntheses of *N*-sulfinyl α-(aminoalkyl)acrylates (aza-Morita−Baylis−Hillman products) and their stereoselective reduction to *N*-sulfinyl-α-substituted β-amino esters.

## Results and Discussion

Following the Ramachandran procedure, an NMO (2.0 equiv) THF solution was added to a THF solution of DIBAL-H (1.5 equiv) at 0 °C to give a clear solution. After 1 h, to this solution were added 1.0 equiv of ethyl propiolate (**1**) and 1.0 equiv of (*S*)-(+)-*N*-(benzylidene)-*p*-toluenesufinamide (**3**) (Scheme 1). ($S_S$,*R*)-(−)-Ethyl-2-[phenyl-(*p*-toluenesulfinylamino)methyl]acrylate (**4**) was formed as a 9:1 mixture of diastereoisomers, but the isolated yield of the major diastereoisomer was low (Table 1, entry 1). When the amount of the vinylaluminum reagent **2** was increased 3-fold the yield of (+)-**4** improved to 65%. Use of $Zn(OTf)_2$ in these reactions had little or no effect on the yield or diastereoselectivity. These results are summarized in Table 1.

In the sulfinimine-mediated aza-MBH reaction,[8,9] *Re* face addition of the vinyl anion species to (*S*)-(+)-**3** gave the aza-MBH product having the *S*-configuration at the new C−N stereogenic center.[8,9,11] However, the $^1$H NMR of these products and (+)-**4** were significantly different, suggesting that they were different compounds. For example, the vinyl protons in (+)-**4** appear at δ 6.02 and 6.48 ppm, whereas in the ($S_S$,*S*) aza-MBH adduct reported by Aggrawal, these protons appear at δ 5.8 and 6.4 ppm, respectively.[8]

Because (+)-**4** is an oil, it was not possible to determine its absolute configuration by X-ray analysis, and therefore, it was necessary to convert it into products of known absolute stereochemistry. This requires the stereoselective reduction of the α-methylene group in (+)-**4** to a methyl group. The homogeneous hydrogenation of Baylis−Hillman adducts has been reported and generally gives *anti* products.[6,13] Hydrogenation of *N*-acyl β-amino-α-methylene esters using Rh(II) and Rh(I) catalysts at high pressure (30 atm) gives the corresponding *anti*-α-substituted β-amino esters.[14] However, there are no reports of the reduction of *N*-sulfinyl β-amino-α-methylene esters.

Hydrogenation of (+)-**4** at rt using 7.5 mol % of cationic rhodium complex **A** for 48 h gave a 22:1 mixture of diastereoisomers with isolation of the major diastereoisomer ($S_S$,2*R*,3*S*)-(+)-**5** in 88% yield (Scheme 2). Oxidation with *m*-CPBA gave (2*R*,3*S*)-(−)-**7**, and hydrolysis afforded the known acid (2*R*,3*S*)-(−)-**8** in 87% yield.[15] To further confirm the *trans* stereochemistry, the acid was treated with DCC/4-pyrrolidinopyridine to give β-lactam (3*R*,4*S*)-(−)-**9**, also a known compound (Scheme 2).[15a] In (−)-**9**, the $J_{3,4}$ coupling constant was 3.2 Hz and similar to the reported value of 3.0 Hz ($cis = J_{3,4} = 6$ Hz).[15a] These results indicate that the vinylaluminum reagent adds to the *Si* face in sulfinimine (*S*)-(+)-**3**. Formation of the *anti* product (+)-**5** is consistent with coordination of the Rh catalyst **A** with the sulfinyl nitrogen atom and addition of hydrogen from the more hindered face of the C−C double bond.[1314]

Structures resulting from the addition of organometallic reagents to the C−N double bond of sulfinimines can generally be predicted by assuming chelated, chairlike transition states resulting from coordination of the metal ion with the sulfinyl oxygen. The sulfinimine-mediated aza-MBH reaction[9] and the addition of vinylcuprates[11] to sulfinimines are in agreement with this transition state hypothesis. However, there are exceptions where the organometallic reagent adds to the C−N double bond from the least hindered direction, away from the bulky sulfinyl

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**SCHEME 2**

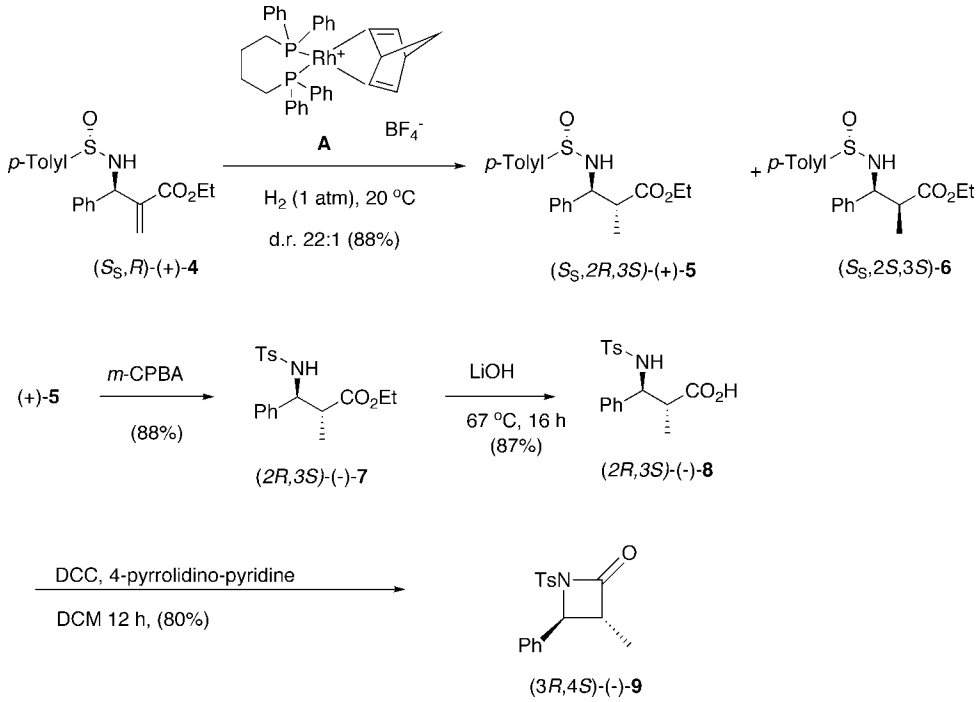


**TABLE 2. Reaction of Propargylic Esters 1, 10, and 11 with Sulfinimines (+)-(*S*)-3 and (−)-(*R*)-12**

| entry | sulfinamide | **1**, **10**, or **11**/DIBAL-H/NMO (equiv) | temp, °C (h) | products, % yield[a] (dr)[b] |
|---|---|---|---|---|
| 1 | (+)-**3** | (**10**: R = Me) 3.0:4.5:6.0 | 25 (16) | **13**, 61 (5:1)[c] |
| 2 | (−)-**12a** (R′ = Ph) | (**1**: R = H) 3.0:4.5:6.0 | 25 (6) | no reaction |
| 3 | | (**1**: R = H) 3.0:4.5:6.0 | 25 (23) | **14a**, 41 (3:1) |
| 4 | | (**1**: R = H) 3.0:4.5:6.0 | 45 (15) | **14a**, 38 (12:1) |
| 5 | | (**1**: R = H) 3.0:4.5:6.0 | 70 (15) | **14a**, 65 (12:1) |
| 6 | | (**10**: R = Me) 3.0:4.5:6.0 | 70 (15) | **14b**, 71 (7:1) |
| 7 | | (**11**: R = Ph) 3.0:4.5:6.0 | 70 (15) | **14c**, 73 (7:1) |
| 8 | (−)-**12b** (R′ = Et) | (**1**: R = H) 3.0:4.5:6.0 | 70 (15) | **14d**, 58 (13:1)[c,d] |
| 9 | | (**10**: R = Me) 3.0:4.5:6.0 | 70 (15) | **14e**, 50 (11:1)[c,d] |
| 10 | | (**11**: R = Ph) 3.0:4.5:6.0 | 70 (15) | **14f**, 35 (6.2:1) |

[a] Isolated yield of major diastereoisomer. [b] Determined by $^1$H NMR on the crude reaction mixture. [c] Inseparable isomers. [d] Determined by $^1$H NMR on the mixture after purification.

group.[16] As previously suggested by us, a Yamamoto-type model **TS-A** (Figure 2), where the vinylaluminum reagent adds to the *Si* face of the C−N double bond, explains our results.[16b] We suggest that the added NMO, which acts as a ligand to aluminum to suppress the tendency of DIBAL-H to reduce C═O and C═N groups,[17] also prevents complexation of aluminum with the sulfinyl group. In the presence of HMPA, lithium allenolates also add to the *Si* face of sulfinimines.[10]

The addition of $\beta$-substituted vinylaluminum reagents to sulfinimines was next examined. Addition of [α-(ethoxycarbonyl)-$\beta$-methylvinyl]diisobutylaluminum, prepared from propargylic ester **10**, afforded **13** as a 5:1 mixture of inseparable diastereoisomers (Table 2, entry 1). In the past, we have solved this separation problem by changing the *N*-sulfinyl auxiliary.[18] However, reaction of **2** with ($R_S$)-(−)-*N*-(benzylidene)-2-methylpropanesulfinamide (**12a**) at rt resulted in no reaction (Table 2, entry 2). When the temperature was increased to 70 °C for 15 h, compound ($R_S$,*S*)-(−)-**14a** was obtained as a 12:1 mixture of diastereoisomers with isolation of the major diastereoisomer in 65% yield (Table 2, entry 5).[19] Under these conditions, addition of [α-(ethoxycarbonyl)-$\beta$-methylvinyl]diisobutylaluminum and [α-(ethoxycarbonyl)-$\beta$-phenylvinyl]diisobutylaluminum to (−)-**12a** gave ($R_S$,*S*)-(−)-**14b** and ($R_S$,*S*)-(−)-**14c**, respectively, as 7:1 mixtures of diastereoisomers. The major diastereoisomers were isolated in 71 and 73% yields (Table 2, entries 6 and 7). Similar results were observed for addition of the $\beta$-substituted vinylaluminum reagents to ($R_S$)-(−)-*N*-(ethylidene)-2-methylpropanesulfinamide (**12b**) to give **14d** (R = H), **14e** (R = Me), and **14f** (R = Ph). However, the diastereoisomers of **14d** (13:1) and **14e** (11:1) could not be separated

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(18) Davis, F. A.; Song, M. *Org. Lett.* **2007**, *9*, 2413.

(19) The absolute stereochemistry of ($R_S$,*S*)-**14a** was established by transforming it into the enantiomer of (2*R*,3*S*)-(−)-**7** isomer (2*S*,3*R*)-(+)-**7** by hydrogenation with catalyst **A** (90%), removal of the sulfinyl group with HCl−$H_2O$, and conversion into the Ts sulfonamide with Ts−Cl, $Et_3N$, and DMAP (79%). See Experimental Section.

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**SCHEME 3**

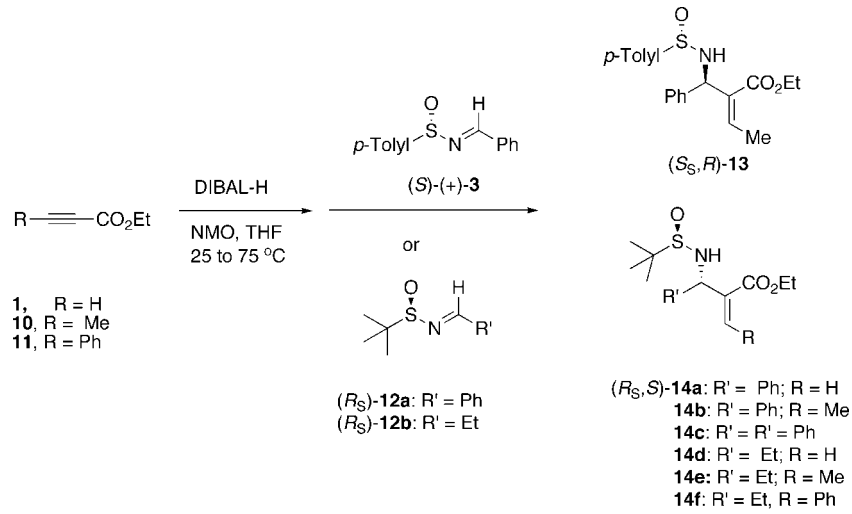



**TABLE 3. Hydrogenation of aza-Morita−Baylis−Hillman Adducts with Catalysts A**

| entry | >**14** (R′, R) | time (h), atm of $H_2$ | >solvent | >**15** dr (% yield)[a] |
|---|---|---|---|---|
| 1 | **14a** (Ph, H) | 48, 1 | $CH_2Cl_2$ | **15a**, 21:1 (83) |
| 2 | **14b** (Ph, Me) | 72, 25 | $ClCH_2CH_2Cl$ | **15b**, 20:1 (81) |
| 3 | **14c** (Ph, Ph) | 72, 25 | $ClCH_2CH_2Cl$ | **15c**, 20:1 (79) |
| 4 | **14d** (Et, H) | 48, 1 | $CH_2Cl_2$ | **15d**, 10:1 (55) |
| 5 | **14e** (Et, Me) | 72, 25 | $ClCH_2CH_2Cl$ | **15e**, decomposition |
| 6 | **14f** (Et, Ph) | 72, 25 | $ClCH_2CH_2Cl$ | **15d**, 17:1 (79) |

[a] Isolated yield of major diastereoisomer.

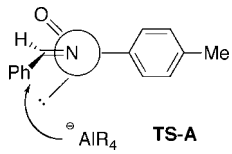


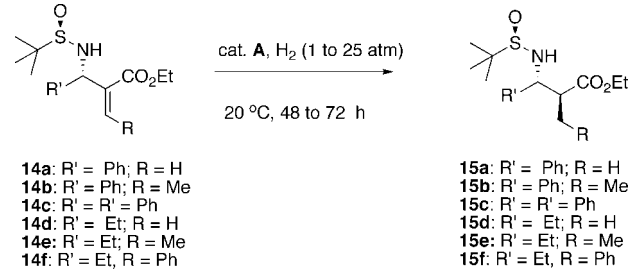

**FIGURE 2.** Model for the addition of vinylaluminum to the *Si* face of (*S*)-(+)-**3**.

(Scheme 3 and Table 2, entries 8−10). On the basis of earlier studies, the stereochemistry **14** is expected to be *Z*.[12,20] Upon irradiation of the C-3 vinyl proton at $\delta$ 6.28 ppm in (−)-**14b**, a positive NOE was observed on the C-2 amine proton at $\delta$ 5.28 (8.3%), consistent with *Z* olefin geometry.

Hydrogenation of **14** as before gave **15** in good yield (Table 3). When R was hydrogen, reduction was complete within 48 h at rt and 1 atm of $H_2$ (Table 3, entries 1 and 4). When R in **14** was Me or Ph, longer times (72 h) and higher pressures of $H_2$ (25 atm) were necessary. $\beta$-Amino ester **15e** was formed as a mixture of inseparable diastereoisomers contaminated with starting material (Scheme 4). Prolonged hydrogenation (>90 h) resulted in decomposition.

In summary, reaction of vinylaluminum NMO reagents with sulfinimines gives *N*-sulfinyl aza-Morita−Baylis−Hillman products that result from addition of the reagent from the least hindered direction via a nonchelation control mechanism. Hydrogenation of the aza-MBH adducts affords *anti*-α-substituted *N*-sulfinyl-$\beta$-amino esters and is a useful new method for their preparation.[21,22]

**SCHEME 4**




## Experimental Section

Sulfinimines (*S*)-(+)-*N*-(benzylidene)-*p*-toluenesulfinamide (**3**),[23] (*R*)-(−)-*N*-(benzylidene)-2-methylpropanesulfinamide (**12a**),[24] and (*R*)-(−)-*N*-(propylidene)-2-methylpropanesulfinamide (**12b**)[24] were prepared as previously described. Catalyst (bicyclo[2.2.1]hepta-2,5-diene)[1,4-bisdiphenylphosphino)butanerhodium(I) tetrafluoroborate **A** was purchased from Aldrich.

**($S_S$,2*R*)-(+)-Ethyl 2-[phenyl(*p*-toluenesulfinylamino)methyl]acrylate (4).** In a 50 mL, dry, single-necked round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed NMO (0.696 g, 5.92 mmol) in THF (8 mL), and the solution was cooled to 0 °C. To the solution was added DIBAL-H (4.48 mL, 1.0 M in THF) at 0 °C, and the mixture was stirred at this temperature for 0.5 h before ethyl propiolate (**1**) (0.304 mL, 2.96 mmol) was added. The mixture was stirred for 1 h at 0 °C, and a solution of (*S*)-(+)-**3** (0.240 g, 0.984 mmol) in THF (8 mL) was added. The mixture was warmed to rt, stirred for 4 h, quenched with Rochelle salt ($NaKC_4H_4O_6 \cdot H_2O$) (10 mL), diluted with EtOAc (15 mL), and vigorously stirred for 30 min. At this time, the solution was extracted with EtOAc (3 × 15 mL), and the combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (50% EtOAc/hexanes) provided 0.220 g (65%) of a colorless oil: $[\alpha]^{20}_D$ +30.0

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(*c* 0.28, $CHCl_3$); IR (neat) 3204, 1711, 1053 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.61 (d, $J = 6.4$ Hz, 2H), 7.24 (m, 7H), 6.47 (s, 1H), 6.03 (d, $J = 0.8$ Hz, 1H), 5.35 (d, $J = 7.2$ Hz, 2H), 4.93 (d, $J = 7.2$ Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.39 (s, 3H), 1.20 (t, $J = 6.8$ Hz, 3H); $^{13}C$ NMR $\delta$ 166.0, 141.8, 141.6, 140.5, 129.9, 128.9, 128.0, 127.4, 127.2, 126.0, 61.3, 58.4, 21.7, 14.5 (one carbon could not be identified due to overlap); HRMS calcd for $C_{19}H_{22}NO_3S$ (M + H) 344.1320, found 344.1327.

**Ethyl ($R_s$,2*S*)-(−)-2-[Phenyl-(2-methylpropanesulfinylamino)-methyl]acrylate (14a).** In a 50 mL, flame-dried, single-necked round-bottomed flask equipped with a magnetic stirring bar, rubber septum, a reflux condenser, and argon balloon was placed NMO (0.606 g, 5.16 mmol) in THF (6 mL). To the solution was added DIBAL-H (3.9 mL, 1.0 M solution in THF) at 0 °C, and the mixture was stirred for 30 min. Ethyl propiolate (**1**) (0.264 mL, 2.59 mmol) was added via syringe, and the mixture was stirred for 1 h at 0 °C, and (*R*)-(−)-**12a** (0.180 g, 0.864 mmol) in anhydrous THF (6 mL) was added. The mixture was heated to 70 °C and stirred for 15 h, cooled to rt, quenched by addition of saturated aqueous Rochelle salt (10 mL), diluted with EtOAc (15 mL), and stirred vigorously for 0.5 h. The organic phase was washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (25% EtOAc/hexanes) provided 0.174 g (65%) of a colorless oil: $[\alpha]^{20}_D$ −1.40 (*c* 0.93, $CHCl_3$); IR (KBr) 3233, 2980, 1717, 1061 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.26 (m, 5H), 6.45 (s, 1H), 5.99 (s, 1H), 5.49 (d, $J = 4.8$ Hz, 1H), 4.12 (m, 2H), 3.76 (d, $J = 4.8$ Hz, 1H), 1.25 (s, 9H), 1.20 (t, $J = 7.2$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 166.0, 141.6, 140.7, 129.1, 128.3, 127.9, 126.8, 61.3, 59.8, 56.5, 23.0, 14.4; HRMS calcd for $C_{16}H_{24}NO_3S$ (M + H) 310.1477, found 310.1472.

**(*Z*)-Ethyl ($R_S$,2*S*)-(−)-2-[Phenyl-(2-methylpropanesulfinylamino)methyl]but-2-enoate (14b). General Procedure.** In a 50 mL, flame-dried, single-necked round-bottomed flask equipped with a magnetic stirring bar, rubber septum, a reflux condenser, and argon balloon was placed NMO (0.606 g, 5.16 mmol) in THF (6 mL). The solution was cooled to 0 °C, DIBAL-H (3.9 mL, 1.0 M solution in THF) was added, and the reaction mixture was stirred for 30 min at which time ethyl but-2-ynoate (**10**) (0.300 mL, 2.59 mmol) was added via syringe. After stirring for 4 h at rt, (*R*)-(−)-**12a** (0.180 g, 0.864 mmol) in THF (6 mL) was added. The reaction mixture was heated to 70 °C, stirred for 15 h, cooled to rt, and quenched by addition of saturated aqueous Rochelle salt (10 mL). The solution was diluted with EtOAc (15 mL), vigorously stirred, and the organic phase was washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (33% EtOAc/hexanes) provided 0.329 g (71%) of a colorless oil: $[\alpha]^{20}_D$ −24.8 (*c* 0.29, $CHCl_3$); IR (KBr) 3214, 3030, 2959, 2869, 1717 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) major isomer $\delta$ 7.25 (m, 5H), 6.35 (q, $J = 7.2$ Hz, 1H), 5.34 (d, $J = 6.4$ Hz, 1H), 4.09 (m, 2H), 3.85 (d, $J = 6.4$ Hz, 1H), 2.05 (dd, $J = 0.8$, 7.2 Hz, 3H), 1.23 (s, 9H), 1.15 (t, $J = 7.0$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 166.7, 141.0, 138.8, 133.8, 128.7, 127.8, 127.4, 61.9, 60.5, 56.2, 22.8, 15.7, 14.2; HRMS calcd for $C_{17}H_{26}NO_3S$ (M + H) 324.1633, found 324.1649.

**(*Z*)-Ethyl ($R_s$,2*R*)-(−)-2-[Phenyl(2-methylpropanesulfinylamino)methyl]-3-phenylacrylate (14c).** Flash chromatography (25% EtOAc/hexanes) provided 73% of a colorless oil: $[\alpha]^{20}_D$ −41.0 (*c* 1.05, $CHCl_3$); IR (KBr) 3211, 1734, 1225 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.46 (m, 2H), 7.36 (m, 3H), 7.28 (m, 5H), 6.94 (s, 1H), 5.45 (d, $J = 6.0$ Hz, 1H), 4.00 (m, 2H), 3.91 (d, $J = 6.0$ Hz, 1H), 1.27 (s, 9H), 0.97 (t, $J = 7.0$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 168.1, 139.9, 135.7, 135.4, 134.9, 128.8, 128.6, 128.5, 128.3, 128.2, 127.7, 62.7, 60.9, 56.4, 22.8 (3C), 13.7; HRMS calcd for $C_{22}H_{28}NO_3S$ (M + H) 386.1790, found 386.1805.

**($R_S$,3*S*)-(−)-Ethyl 3-(1,1-Dimethylethylsulfinamido)-2-methylenepentanoate (14d).** Flash chromatography (40% EtOAc/hexanes) provided 55% of a colorless oil: IR (neat) 3212, 1718 $cm^{-1}$; $[\alpha]^{20}_D$ −39.6 (*c* 1.26, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 6.26 (s, 1H), 5.27 (s, 1H), 4.22 (m, 2H), 4.04 (dt, $J = 6.8$ Hz, 1H), 3.68 (d, $J = 6.8$ Hz, 1H), 1.86 (m, 2H), 1.31 (t, $J = 6.8$ Hz, 3H), 1.19 (s, 9H), 0.93 (t, $J = 7.6$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 166.4, 141.3, 126.3, 61.2, 60.1, 56.1, 29.1, 22.9, 14.5, 11.3; HRMS calcd for $C_{12}H_{24}NO_3S$ (M + H) 262.1477, found 262.1455.

**(*Z*)-($R_S$,3*S*)-(−)-Ethyl 3-(1,1-Dimethylethylsulfinamido)-2-ethylidenepentanoate (14e).** Flash chromatography (40% EtOAc/hexanes) provided 50% of a colorless oil: $[\alpha]^{20}_D$ −51.5 (*c* 1.20, $CHCl_3$); IR (neat) 3224, 1714, 1454, $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 6.11 (m, 1H), 4.21 (m, 2H), 3.87 (q, $J = 6.8$ Hz, 1H), 3.58 (d, $J = 6.0$ Hz, 1H), 1.97 (d, $J = 6.8$ Hz, 3H), 1.79 (m, 2H), 1.31 (t, $J = 7.2$ Hz, 3H), 1.17 (s, 9H), 0.90 (t, $J = 7.2$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.5, 137.7, 133.8, 62.6, 60.7, 55.9, 29.4, 22.9, 15.8, 14.6, 11.3; HRMS calcd for $C_{13}H_{26}NO_3S$ (M + H) 276.1633, found 276.1635.

**Ethyl (*Z*)-($R_S$,2*S*)-(−)-2-[Ethyl(2-methylpropanesulfinylamino)methyl]-3-phenylacrylate (14f).** Flash chromatography (50% EtOAc/hexanes) provided 35% of a colorless oil: $[\alpha]^{20}_D$ −36.3 (*c* 0.84, $CHCl_3$); IR (KBr) 3211, 1722, 1225, 1061 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.22 (m, 5H), 6.77 (s, 1H), 4.07 (m, 3H), 3.47 (d, $J = 5.2$ Hz, 1H), 1.98 (m, 1H), 1.83 (m, 1H), 1.20 (s, 9H), 1.06 (t, $J = 7.2$ Hz, 3H), 1.02 (t, $J = 7.6$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 168.7, 135.7, 135.3, 134.8, 128.7, 128.6 128.5, 62.7, 61.1, 56.1, 29.3, 22.9, 14.0, 11.4; HRMS calcd for $C_{18}H_{28}NO_3S$ (M + H) 338.1790, found 338.1781.

**($S_S$,2*R*,3*S*)-(+)-Ethyl 2-Methyl-3-(4-methylphenylsulfinamido)-3-phenylpropanoate (5).** In an oven-dried, 25 mL one-neck round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and a $H_2$ balloon were placed (+)-**4** (0.200 g, 0.585 mmol) and rhodium complex **A** (0.031 g, 0.044 mmol) in anhydrous DCM (5.0 mL). The solution was evacuated and filled with $H_2$, and this sequence was repeated five times. The reaction mixture was stirred for 48 h at rt and concentrated. Flash chromaatography (50% EtOAc/hexanes) afforded 0.180 g (88%) of a colorless oil: $[\alpha]^{20}_D$ +33.6 (*c* 0.65, $CHCl_3$); IR (neat) 3206, 1730, 1090, 1053 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.43 (d, $J = 8.0$ Hz, 2H), 7.21 (m, 3H), 7.11 (m, 4H), 5.06 (d, $J = 7.2$ Hz, 1H), 4.50 (dd, $J = 7.2$, 8.0 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.88 (dq, $J = 6.8$, 8.0 Hz, 1H), 2.32 (s, 3H), 1.21 (t, $J = 7.2$ Hz, 3H), 1.46 (d, $J = 6.8$ Hz, 3H); $^{13}C$ NMR $\delta$ 175.0, 142.0, 141.4, 141.1, 129.5, 129.0, 127.9, 127.3, 126.1, 61.1, 60.4, 46.9, 21.6, 15.8, 14.5; HRMS calcd for $C_{19}H_{23}NO_3SNa$ (M + Na) 368.1296, found 368.1304.

**($R_S$,2*S*,3*R*)-(−)-Ethyl 2-Methyl-3-(4-methylphenylsulfinamido)-3-phenylpropanoate (15a).** Flash chromatograpy (50% EtOAc/hexanes) afforded 83% of a colorless oil: $[\alpha]^{20}_D$ −20.6 (*c* 0.18, $CHCl_3$); IR (neat) 3584, 3256, 1734 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.32 (m, 5H), 4.46 (dd, $J = 8.4$, 8.4 Hz, 1H), 4.12 (q, $J = 7.3$ Hz, 2H), 3.96 (d, $J = 8.4$ Hz, 1H), 2.92 (dq, $J = 7.2$, 8.4 Hz, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.11 (s, 9H), 0.99 (d, $J = 6.8$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.9, 140.4, 128.9, 128.2, 127.4, 63.1, 60.8, 56.4, 46.8, 22.7, 15.2, 14.3; HRMS calcd for $C_{16}H_{26}NO_3S$ (M + H) 312.1633, found 312.1625.

**($R_S$,*S*)-(−)-Ethyl 2-[(*R*)-(1,1-Dimethylethylsulfinamido)(phenyl)methyl]butanoate (15b).** In an oven-dried, 25 mL one-necked, round-bottomed flask equipped with a magnetic stirring bar were placed (−)-**16b** (0.0302 g, 0.093 mmol) and rhodium complex **A** (0.005 g, 0.007 mmol) in 1,2-dichloroethane (4.5 mL). The solution was placed in a high-pressure vessel (Series 4650 2.50 Inch Inside Diameter HP/HT from Parr Instrument Company). The vessel was tightly closed and was filled with $H_2$ until the inner pressure reached 25 atm at which time it was evacuated and refilled with $H_2$ to 25 atm. This sequence was repeated three times. The reaction mixture was stirred at 25 atm of $H_2$ for 72 h at rt, at which time the solution was concentrated. Preparative TLC (50% EtOAc/hexanes) afforded 0.0241 g (81%) of a colorless oil: $[\alpha]^{20}_D$ −44.4 (*c* 0.41, $CHCl_3$); IR (neat) 3216, 1732, 1052 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.30 (m, 5H), 4.60 (dd, $J = 7.6$, 7.6 Hz, 1H), 3.95 (q, $J = 7.2$ Hz, 2H), 3.66 (d, $J = 7.6$ Hz, 1H), 2.80 (m, 1H), 1.63 (m, 2H), 1.20 (s, 9H), 1.04 (t, $J = 7.2$ Hz, 3H), 0.92 (t, $J = 7.2$ Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 173.0, 140.6, 128.6, 128.0, 127.3, 61.7, 60.4, 56.5, 54.2, 22.7, 22.1, 14.0, 11.9; HRMS calcd for $C_{17}H_{28}NO_3S$ (M + H) 326.1790, found 326.1782.

**($R_S$,2*S*,3*R*)-(−)-Ethyl 2-Benzyl-3-(1,1-dimethylethylsulfinamido)-3-phenylpropanoate (15c).** Preparative TLC (50% EtOAc/hexanes) afforded 79% of a colorless oil: $[\alpha]^{20}_D$ −19.5 (*c* 0.57, $CHCl_3$); IR (neat) 3221, 1730, 1052 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.30 (m, 10H), 4.66 (dd, $J$ = 7.2, 7.2 Hz, 1H), 3.81 (m, 3H), 3.20 (m, 1H), 3.06 (m, 1H), 2.92 (m, 1H), 1.23 (s, 9H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 172.3, 140.0, 138.8, 128.8, 128.6, 128.4, 128.1, 127.3, 126.4, 61.9, 60.3, 56.5, 54.6, 35.0, 22.6, 13.7; HRMS calcd for $C_{22}H_{29}NO_3SNa$ (M + Na) 410.1765, found 410.1766.

**($R_S$,2*S*,3*S*)-(−)-Ethyl-2-methyl-3-(*tert*-butylsulfinylamino)pentanoate (15d).** In a 50 mL, dry, single-necked round-bottom flask equipped with a magnetic stirring bar, rubber septum, and a $H_2$ balloon were placed (−)-**14d** (0.05 g, 0.17 mmol) and rhodium complex **A** (0.009 g, 0.013 mmol) in anhydrous DCM (5 mL). The solution was evacuated and filled with $H_2$, and this sequence was repeated five times. The reaction mixture was stirred at rt for 48 h. Preparative TLC (50% EtOAc/hexane) afforded 0.0255 g (55%) of a colorless oil: $[\alpha]^{20}_D$ −31.46 (*c* 0.06, $CHCl_3$); IR (neat) 3280, 1732, 1462, $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.06 (m, 2H), 3.62 (d, $J$ = 12 Hz, 1H), 3.29 (m, 1H), 2.69 (m, 1H), 1.72 (m, 1H), 1.26 (t, $J$ = 7.2 Hz, 3H) 1.23 (s, 9H), 1.19 (d, $J$ = 7.2 Hz, 3H), 0.99 (t, $J$ = 7.6 Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.9, 61.3, 60.4, 56.2, 43.4, 27.37, 22.7, 14.7, 14.2, 10.0; HRMS calcd for $C_{12}H_{26}NO_3S$ (M + H) 264.1633, found 264.1613.

**($R_S$,2*S*,3*S*)-(−)-Ethyl 2-Benzyl-3-(1,1-dimethylethylsulfinamido-)pentanoate (15f).** Preparative TLC (50% EtOAc/hexanes) afforded 77% of a colorless oil: $[\alpha]^{20}_D$ −27.7 (*c* 0.51, $CHCl_3$); IR (neat) 3228, 1731, 1053 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) major isomer $\delta$ 7.19 (m, 5H), 4.00 (q, $J$ = 7.6 Hz, 2H), 3.66 (m, 1H), 3.23 (d, $J$ = 7.6 Hz, 1H), 2.96 (m, 2H), 2.85 (m, 1H), 1.77 (m, 1H), 1.62 (m, 1H), 1.20 (s, 9H), 1.10 (t, $J$ = 8.1 Hz, 3H), 0.97 (t, $J$ = 7.6 Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 173.2, 139.2, 128.8, 128.5, 126.4, 60.4, 59.8, 56.2, 52.0, 34.1, 26.8, 22.9, 14.1, 10.4; HRMS calcd for $C_{18}H_{29}NO_3SNa$ (M + Na) 362.1766, found 362.1761.

**(2*R*,3*S*)-(−)-Ethyl 2-Methyl-3-(4-methylphenylsulfonamido)-3-phenylpropanoate (7) from (+)-5.** In an oven-dried, 10 mL one-neck, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (+)-**5** (0.168 g, 0.486 mmol) in DCM (18.0 mL). The solution was cooled to 0 °C, *m*-CPBA (0.336 g, 1.458 mmol, 75 wt %) was added in one portion, and the reaction mixture was warmed to rt, stirred for 1.5 h, and quenched by addition of saturated $Na_2S_2O_3$ solution (10 mL). The solution was extracted with DCM (2 × 5 mL), and the combined organic phases were washed with saturated $NaHCO_3$ solution (2 × 5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (50% EtOAc/hexanes) afforded 0.145 g (88%) of a colorless oil: $[\alpha]^{20}_D$ −43.0 (*c* 1.09, $CHCl_3$); IR (neat) 3279, 1733, 1161 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.48 (d, $J$ = 8.0 Hz, 2H), 7.12 (m, 3H), 7.05 (d, $J$ = 8.4 Hz, 2H), 7.00 (m, 2H), 5.96 (d, $J$ = 8.8 Hz, 1H), 4.50 (dd, $J$ = 6.0, 8.4 Hz, 1H), 4.01 (q, $J$ = 7.2 Hz, 2H), 2.79 (quint, $J$ = 6.4 Hz, 1H), 2.31 (s, 3H), 1.13 (m, 6H); $^{13}C$ NMR $\delta$ 174.9, 143.1, 139.4, 138.4, 129.5, 128.6, 127.7, 127.3, 126.9, 61.2, 60.5, 46.3, 21.7, 15.8, 14.3. Spectral properties were consistent with literature values.[25]

**(2*S*,3*R*)-(+)-Ethyl 2-Methyl-3-(4-methylphenylsulfonamido)-3-phenylpropanoate, the Enantiomer of (−)-(7) from ($R_S$,2*S*)-(−)-15a.** In an oven-dried, 50 mL one-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (−)-**15a** (0.110 g, 0.354 mmol) in anhydrous MeOH (13 mL). The solution was cooled to 0 °C, and HCl (0.7 mL, 2.0 M in $Et_2O$) was added dropwise, warmed to rt, stirred for 3 h, and quenched by addition of 1 N NaOH solution adjusting the pH to 9. The solution was extracted with EtOAc (3 × 5 mL), washed with brine (5 mL), dried ($MgSO_4$), and concentrated. The residue was placed in a 15 mL single-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon balloon in DCM (5.2 mL). TsCl (0.067 g, 0.531 mmol) was added, the solution was cooled to 0 °C, and $Et_3N$ (0.1 mL, 0.708 mmol) and DMAP (2.1 mg, 0.0177 mmol) were added. The reaction mixture was warmed to rt, stirred for 12 h, and quenched with $H_2O$ (3 mL). The solution was extracted with DCM (3 × 5 mL), and the combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Chromatography (25% EtOAc/hexanes) afforded 0.101 g (79%) of colorless oil: $[\alpha]^{20}_D$ +45.0 (*c* 0.21, $CHCl_3$), $[\alpha]^{20}_D$ −43.0 (*c* 1.09, $CHCl_3$) for the enantiomer of (−)-**7**; IR (neat) 3279, 1733, 1161 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.48 (d, $J$ = 8.0 Hz, 2H), 7.12 (m, 3H), 7.05 (d, $J$ = 8.4 Hz, 2H), 7.0 (m, 2H), 5.96 (d, $J$ = 8.8 Hz, 1H), 4.50 (dd, $J$ = 6.0, 8.4 Hz, 1H), 4.01 (q, $J$ = 7.2 Hz, 2H), 2.79 (quint, $J$ = 6.4 Hz, 1H), 2.31 (s, 3H), 1.13 (m, 6H); $^{13}C$ NMR $\delta$ 174.9, 143.1, 139.4, 138.4, 129.5, 128.6, 127.7, 127.3, 126.9, 61.2, 60.5, 46.3, 21.7, 15.8, 14.3; HRMS calcd for $C_{19}H_{22}NO_4S$ (M + H) 362.1426, found 362.1419.

**(2*R*,3*S*)-(−)-2-Methyl-3-(4-methylphenylsulfonamido)-3-phenylpropanoic acid (8).** In an oven-dried, 10 mL one-necked, round-bottomed flask equipped with a magnetic stirring bar, reflux condenser, and rubber septum were placed (−)-**7** (0.0435 g, 0.120 mmol) and LiOH monohydrate (0.0435 g, 0.120 mmol) in THF (9 mL) and $H_2O$ (0.33 mL). The reaction mixture was refluxed for 16 h at 67 °C, cooled to rt, and concentrated. The residue was diluted with DCM (10 mL), and 1 N HCl was added until the solution reached pH >2. The solution was stirred for 10 min and extracted with DCM (3 × 5 mL), and the combined organic phases were washed with brine (4 mL), dried ($MgSO_4$), and concentrated. Preparative TLC (50% EtOAc/hexanes) afforded 0.0363 g (91%) of white solid: mp 131−133 °C; [lit[15b] mp 135−136 °C]; $[\alpha]^{20}_D$ −23.6 (*c* 0.49, EtOAc), [lit[15b] $[\alpha]^{20}_D$ −25.6 (*c* 0.06, EtOAc), lit[15a] $[\alpha]^{20}_D$ −28.1 (*c* 1.0, EtOAc)]; IR (neat) 3263, 1712, 1160 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.47 (m, 2H), 7.11 (m, 3H), 7.02 (m, 4H), 6.20 (d, $J$ = 9.2 Hz, 1H), 4.50 (dd, $J$ = 7.2, 8.8 Hz, 1H), 2.87 (quint, $J$ = 6.8 Hz, 1H), 2.29 (s, 3H), 1.17 (d, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR $\delta$ 178.6, 143.3, 138.9, 138.0, 129.5, 128.7, 127.9, 127.3, 127.1, 60.5, 46.1, 21.7, 15.7; HRMS calcd for $C_{17}H_{20}NO_4S$ (M + H) 334.1113, found 334.1126. Spectral properties were consistent with literature values.[15]

**(3*R*,4*S*)-(−)-3-Methyl-4-phenyl-1-tosylazetidin-2-one (9).** In an oven-dried, 10 mL one-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon balloon were placed (−)-**8** (0.0224 g, 0.067 mmol), DCC (0.017 mg, 0.0804 mmol), and 4-pyrrolidinopyridine (3.7 mg) in DCM (2.5 mL). The reaction mixture was stirred for 16 h at rt, filtered through Celite, and the filtrate was washed with water (3.0 mL), 5% aqueous HOAc (3 mL), and water (3 mL). The organic phase was washed with brine (3.5 mL), dried ($MgSO_4$), and concentrated. Preparative TLC (25% EtOAc/hexanes) afforded 0.0165 g (80%) of a white solid: mp 133−135 °C [lit[15a] mp 134−135 °C; $[\alpha]^{20}_D$ −103 (*c* 0.58, EtOAc), lit[15a] $[\alpha]^{20}_D$ −114 (*c* 1.05, EtOAc)]; IR (neat) 1794, 1361, 1168 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.62 (dd, $J$ = 3.2, 6.4 Hz, 2H), 7.26 (m, 7H), 4.60 (d, $J$ = 3.2 Hz, 1H), 3.16 (m, 1H), 2.42 (s, 3H), 1.34 (d, $J$ = 7.6 Hz, 3H); $^{13}C$ NMR $\delta$ 167.9, 145.4, 136.5, 136.1, 130.1, 129.3, 129.2, 127.8, 126.9, 65.4, 55.0, 22.0, 12.8; HRMS calcd for $C_{17}H_{18}NO_3S$ (M + H) 316.1007, found 316.1013. Spectra properties were consistent with literature values.[15]

**Acknowledgment.** We thank Professor Rodrigo Andrade of Temple University for helpful suggestions. This work was supported by a grant from the National Institutes of General Medical Sciences (GM 57870) and Boehringer Ingelheim Pharmaceuticals.

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

JO9001504

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