

Improved Asymmetric Synthesis of Aziridine 2-Phosphonates Using (S)-(+)-2,4,6-Trimethylphenylsulfonamide

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Received April 24, 2003

The aza-Darzens reaction of lithium diethyl iodomethylphosphonate with enantiopure *N*-(2,4,6-trimethylphenylsulfinyl)imines affords a single diastereomeric *N*-sulfinylaziridine 2-phosphonate which, on treatment with MeMgBr, gives the corresponding NH-aziridine 2-phosphonate chiral building blocks. An improved asymmetric synthesis of (S)-(+)-2,4,6-trimethylphenylsulfonamide is also given.

Aziridine 2-phosphonates are valuable polyfunctionalized chiral building blocks for the asymmetric synthesis of amino phosphonates because of their ability to undergo highly regio- and stereospecific ring-opening reactions.^{1–6} Oxidation of NH-aziridine 2-phosphonates provides 2*H*-azirine 2-phosphonates and 2*H*-azirine 3-phosphonates.^{4,7} The latter azirines are a new class of chiral imino dienophiles that undergo Diels–Alder reactions to produce bicyclic aziridines that can be transformed into the first examples of quaternary piperidine phosphonates.⁷ Chiral nonracemic amino phosphonic acids are important amino acid analogues because many exhibit antibacterial, anticancer, and antiviral activity as well as pesticidal, insecticidal, and herbicidal properties.⁸

Recently, we described a new methodology for the asymmetric synthesis of aziridine 2-phosphonates that involves the addition of the anion of halomethylphosphonates **1** to enantiopure *N-p*-toluenesulfinylimines (S)-(+)-**2**.² In this aza-Darzens reaction, the aziridines were formed as cis and trans mixtures of **3/4** that were difficult to separate (Scheme 1). To circumvent this problem, the intermediate α -chloro β -amino phosphonates **5** and **6** were isolated and cyclized with *n*-butyllithium to give the enantiopure aziridines (*S*,2*S*,3*R*)-**3** and (*S*,2*R*,3*R*)-**4**. However, it was noted in one case that if the bulky *N-tert*-

butanesulfinylimine (S)-(+)-**7** was used, the aziridine (+)-**8** was formed in good yield as a single diastereoisomer. Unfortunately, all attempts, under acid or base conditions, to remove the *N-tert*-butanesulfinyl auxiliary without aziridine ring opening failed.

The advantage of the *N-tert*-butanesulfinyl versus the *N-p*-toluenesulfinyl group is that Grignard reagents add to the C–N bond to give amines in the former, while with the latter auxiliary, attack at the sulfinyl sulfur produces sulfoxides.⁹ This difference in reactivity was employed in a highly selective method to deprotect *N-p*-toluenesulfinylaziridines by treating them with methylmagnesium bromide.^{2,10} This protocol affords the valuable NH-aziridines, in excellent yield, without ring-opening, even with highly activated examples. What we required was an *N*-sulfinyl auxiliary that is large enough to produce high diastereoselectivities in the aza-Darzens reaction while permitting selective deprotection using our Grignard protocol. The *N*-(2,4,6-trimethylphenylsulfinyl) auxiliary meets these requirements, as described herein.

Results and Discussion

Senanayake and co-workers recently introduced methodology for the asymmetric synthesis of diversely substituted sulfonamides (RS(O)NH₂), which are the precursors of sulfonimines (*N*-sulfinyl imines).¹¹ This procedure involves reacting Grignard reagents, such as 2,4,6-trimethylphenylmagnesium bromide, with *endo*-(-)-1,2,3-oxathiazolidine-2-oxide **9** to give the corresponding sulfinate ester (-)-**10** (Scheme 2). It was reported that on treatment of **10** with sodium bis(trimethylsilyl)amide (NaHMDS), (S)-(+)-2,4,6-trimethylphenylsulfonamide (**11**)

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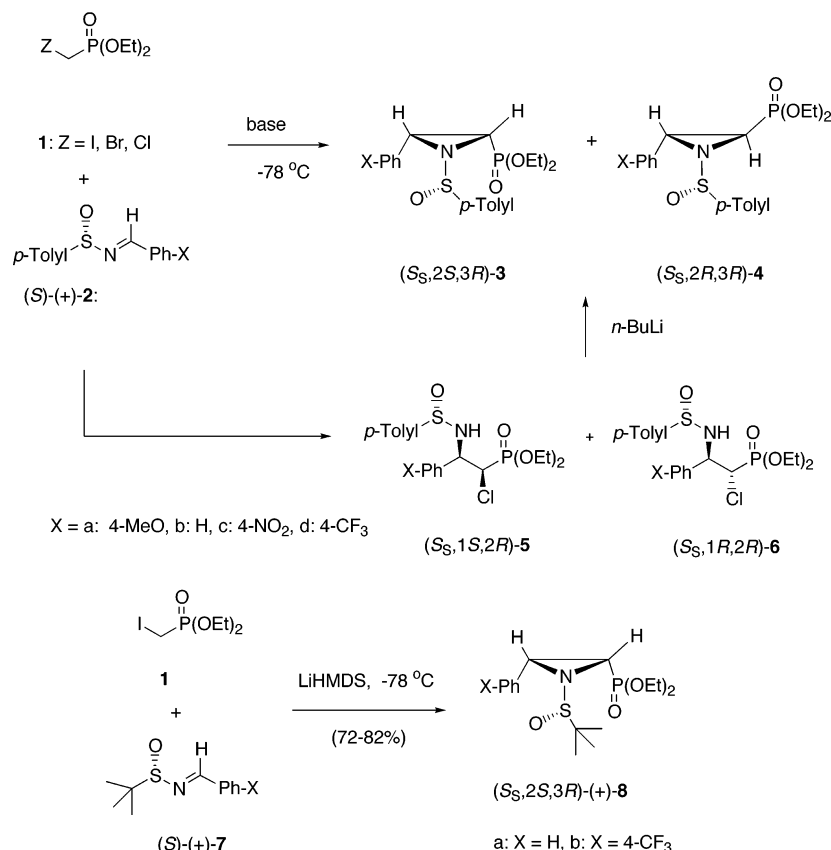
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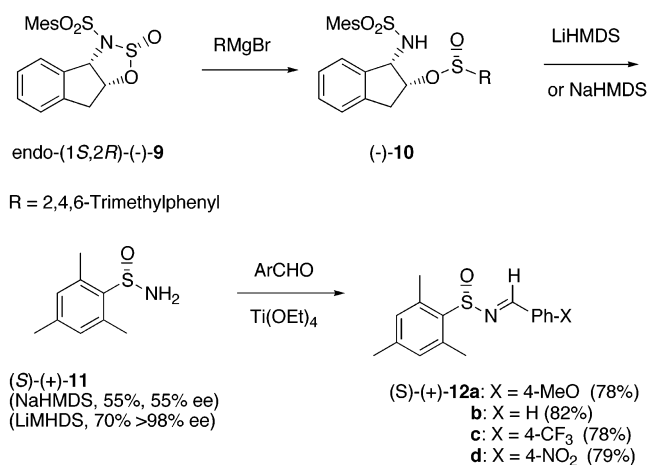
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SCHEME 1



SCHEME 2



was obtained in 80% yield. The enantiomeric purity was judged to be 99% by chiral HPLC analysis.¹¹

However, in our hands, treatment of (-)-10 with NaHMDS at -78 °C to room temperature gave a 55% yield of sulfinamide 11 with a specific rotation of +98.0°. ¹² Chiral HPLC analysis indicated that sulfinamide (S)-(+)-11 was only 55% enantiomerically pure. Attempts to improve the purity by varying the equivalents of base, temperature, and time were without success. In our earlier studies on the one-pot synthesis of enantiopure sulfinimines from the Andersen reagent, (1*R*,2*S*,5*R*)-

(-)-menthyl-(*S*)-*p*-toluenesulfinate, LiHMDS, and aldehydes it was noted that if NaHMDS were used the ee's dropped from >98% to 66% ee.¹³ We attributed this result to racemization of the sulfinimine by the more reactive nucleophile. With this in mind, we treated (-)-10 with 2.2 equiv of LiHMDS at -78 °C to room temperature and obtained a 70% isolated yield of (S)-(+)-11, following chromatography and crystallization. Importantly the specific rotation of the product had increased to +177.8° and chiral HPLC indicated that the enantiomeric purity was >98%.

With enantiopure (S)-(+)-2,4,6-trimethylphenylsulfinamide (11) in hand, we proceeded to condense it in the usual manner with 4-methoxybenzaldehyde, benzaldehyde, 4-trifluoromethylbenzaldehyde, and 4-nitrobenzaldehyde in the presence of excess Ti(OEt)₄.¹⁴ The corresponding sulfinimines (S)-(+)-12a–d were isolated in 78–82% yield (Scheme 2). Next, a solution of (S)-(+)-12 and 2 equiv of diethyl iodomethylphosphonate were treated at -78 °C with 2 equiv of LiHMDS (Scheme 3). Importantly, sulfinimines 12a and 12b, having the 4-methoxyphenyl and phenyl groups, afford aziridines (S_S,2*S*,3*R*)-(-)-13a and (S_S,2*S*,3*R*)-(-)-13b as single diastereoisomers in one pot and in 75–78% isolated yield (Table 1, entries 1 and 3). The cis stereochemistry is supported by the H_{2,3} proton coupling constants of *J* =

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(12) In our work, we prepared and used the enantiomers of the compounds described in ref 11. Specific rotations and melting points were not provided.

SCHEME 3

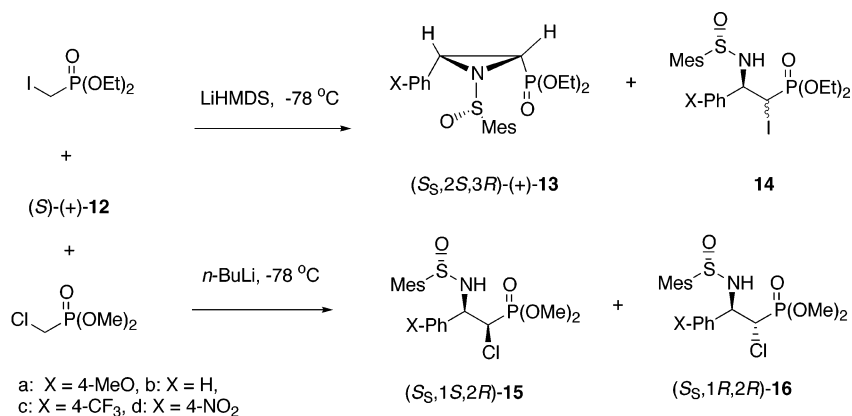


TABLE 1. Addition of Lithium Halomethylphosphonate Anions to Sulfinimines (S)-(+)-12

entry	sulfinimine (X =)	1 (Z =)	aziridine 13 ^a (% yield) ^b	β -amino α -chlorophosphonate 15/16 (% yield) ^b
1	12a (4-MeO)	I	(+)- 13a (75%)	
2		Cl		77:23 (70%) [77:23] ^d
3	12b (H)	I	(+)- 13b (78%)	
4	12c (4-CF ₃)	I		43:57 ^c (82%)
5		Cl		23:77 (70%) [1:1] ^d
6	12d (4-NO ₂)	I		53:47 ^c (78%)
7	7b (4-CF ₃)	I	(+)- 8b (72%)	

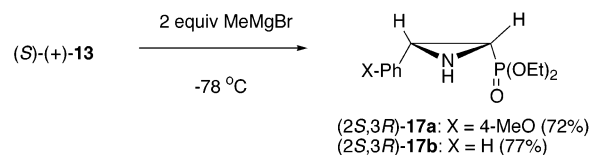
^a Aziridines were >98:2. ^b Isolated yield. ^c Ratio of aziridine diastereoisomers to β -amino α -iodophosphonate mixtures. ^d Ratio of **15/16** using the *p*-toluenesulfinyl auxiliary. See ref 2.

7.6 Hz² and their conversion into known compounds (see below). By contrast, sulfinimines **12c** and **12d**, having the electron-attracting 4-trifluoromethylphenyl and 4-nitrophenyl groups, gave complex mixtures of products consisting of the aziridines diastereomers **13c,d** and isomeric mixtures of the β -amino α -iodophosphonates **14**. All attempts to separate these mixtures proved unsuccessful.

In an attempt to fix this problem, as we had done previously, the β -amino α -chlorophosphonates **15c/16c** were prepared from (S)-(+)-**12c** and the lithium anion of dimethyl chloromethylphosphonate (Scheme 3). For comparison, a similar study was carried out with (+)-**12a**, and these results are summarized in Table 1. Unfortunately, chromatographically inseparable mixtures of the corresponding β -amino α -chlorophosphonates **15/16** were produced in both cases (Table 1, entries 2 and 5). This contrasts sharply with the results obtained when the *N-p*-toluenesulfinyl auxiliary was employed and separable mixtures of **15/16** (*p*-tolyl instead of mes) were produced.² This result may reflect the greater lipophilicity of the mes group versus the *p*-tolyl group. It is interesting to note that for **12a** (X = 4-MeO) similar ratios of **15/16** were observed for the *N*-2,4,6-trimethylphenylsulfinyl and *N-p*-tolylsulfinyl auxiliaries (Table 1, entry 2), whereas the ratios for **12c** (X = 4-CF₃) were 23:77 and 1:1, respectively (Table 1, entry 5).

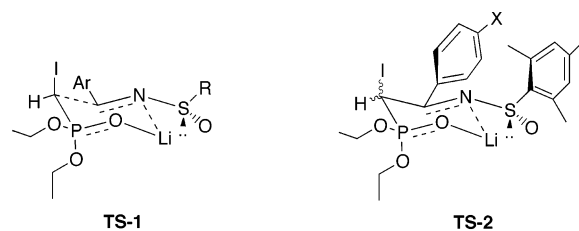
We propose that the greater selectivity observed in the aza-Darzens reaction of lithium iodomethylphosphonate with sulfinimines having bulky *N*-sulfinyl auxiliaries is primarily due to two types of steric interactions in transition state **TS-1**. First, the iodomethylphosphonate anion is highly favored to attack the C–N double opposite

SCHEME 4



to the bulky *N*-sulfinyl group R. However, this alone would not predispose the transition state toward a single diastereomeric aziridine. The transformation also requires that the iodo group occupy the axial position in the transition state. Because halomethylphosphonate anions, unlike enolates, lack configuration stability, we suggest that the reason this position is preferred is that there are fewer gauche interactions between the iodo and ethoxy phosphonate groups when the former is in axial position.

The explanation for the much lower selectivity on addition of the lithium anion of **1** to sulfinimines **12c** and **12d**, which have electron-attracting groups, is less apparent. One possibility is that π -acid π -base interactions (π -stacking) between the 2,4,6-trimethylphenyl group and the imino aryl group as in **TS-2** may sterically alter the equatorial–axial ratio of the iodo group which would result in poorer selectivity. In support of this hypothesis is the fact that sulfinimine **7b** (X = 4-CF₃), having the *N-tert*-butanesulfinyl auxiliary where π -stacking is unlikely, affords a single diastereomeric aziridine (S_S,2S,3R)-(+)-**8b** in 72% yield (Scheme 1).



Removal of the *N*-Sulfinyl Auxiliary. Reaction of aziridines (S)-(+)-**13a** and (S)-(+)-**13b** with 2 equiv of MeMgBr at –78 °C readily removed the 2,4,6-trimethylphenyl-sulfinyl group affording the corresponding NH-aziridines (2S,3R)-(-)-**17a** and (2S,3R)-(-)-**17b** in 72 and 77% isolated yield (Scheme 4). Their physical properties were in agreement with literature values,² which further serves to confirm the cis geometry of these aziridines.

In summary, improved methodology has been introduced for the asymmetric synthesis of NH-aziridine 2-phosphonates, which are valuable polyfunctionalized chiral building blocks for α -amino phosphonates and 2*H*-azirine 3-phosphonate synthesis. This new procedure employs the *N*-(2,4,6-trimethylphenylsulfinyl)imines (*S*)-(+)-**12** and lithium diethyl iodomethylphosphonate. However, aryl sulfinimines containing electron-attracting groups give complex mixtures with this protocol. Although β -amino α -chloro phosphonates were produced with improved diastereomeric ratios compared to the *N*-(*p*-tolylsulfinyl) auxiliary, they were chromatographically inseparable, which may reflect the greater lipophilicity of the former auxiliary. In addition it was found that the use of LiHMDS in place of NaHMDS in the synthesis of (*S*)-(+)-2,4,6-trimethyl-phenylsulfinamide (**11**) results in an enantiomerically pure product.

Experimental Section

Diethyl 2-chloro- and 2-iodomethylphosphonates were purchased from commercial sources. (*S*)-(+)-2-Methyl-*N*-(1*E*)-[4-(trifluoromethyl)phenyl]methylene]-2-propanesulfinamide (**7b**) [$[\alpha]_D^{20}$ 81 (*c* 0.68, CHCl₃)] was prepared in 78% yield as described earlier.^{15,16}

(**1S,2R**)-(-)-*N*-2-Mesitylaminoindanol (**9**) [mp 160–161 °C; $[\alpha]_D^{20}$ -37.4 (*c* 1.0 CHCl₃), IR (neat) 3101, 1574 cm⁻¹] and (**R_S,1S,2R**)-(-)-2,4,6-trimethylbenzenesulfonic acid 1-(2,4,6-trimethylbenzenesulfonylamino)indan-2-yl ester (**10**) [mp 145–146 °C; $[\alpha]_D^{20}$ -55.4 (*c* 1.0 CHCl₃); IR (neat) 3210, 3092 cm⁻¹] were prepared as previously described¹¹ from commercially available (1*S,2R*)-(-)-*cis*-1-amino-2-indanol and had spectral properties consistent with literature values.¹¹

(*S*)-(+)-2,4,6-Trimethylphenylsulfinamide (**11**). In a 100-mL, one-necked, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed 1.0 g (0.0021 mol) of (-)-**10** in THF (15 mL). The solution was cooled to -78 °C, and 4.2 mL (0.0042 mol, 1 M solution) of lithium bis(trimethylsilyl)amide (LiHMDS) was added via syringe. The reaction mixture was slowly warmed to room temperature, stirred for 4 h, and quenched at -78 °C by addition of 30% NH₄Cl (10 mL). The reaction mixture was diluted with water (20 mL) and extracted with EtOAc (2 × 25 mL), and the combined organic phases were dried (Na₂SO₄) and concentrated. Purification by chromatography (EtOAc) and crystallization from EtOAc at -20 °C afforded 0.26 g (70%) of a white solid: mp 125–126 °C; $[\alpha]_D^{20}$ +177.8 (*c* 0.5, CHCl₃); IR (neat) 3205, 3092 cm⁻¹. The ¹H NMR and ¹³C NMR spectra were identical with the enantiomer (+)-**11** previously reported.¹¹ The enantiomeric purity was determined using a Chiralcel OD, 4–6 × 250 mm, 10 μm; 9:1 (hexane/*i*-PrOH), 1.0 mL/min, 250 nm; (*S*)-**10**, retention 17.5 min.

Typical Procedure for the Synthesis of Sulfinimines from Aldehydes Using Titanium(IV) Ethoxide. (*S*)-(+)-*N*-(Benzylidene)-2,4,6-trimethylphenylsulfinamide (**12b**). In a 50-mL, round-bottom flask equipped with a stirring bar and argon balloon was placed 0.10 g (0.546 mmol) of (+)-**11**, 0.055 mL (0.546 mmol) of benzaldehyde, and 0.572 mL (2.73 mmol) of titanium(IV) ethoxide in CH₂Cl₂ (15 mL). After being stirred at room temperature for 4 h (monitoring for completion by TLC), the reaction mixture was quenched by addition of H₂O (10 mL). The turbid solution was filtered through Celite, and the filter cake was washed with CH₂Cl₂ (2 × 10 mL). The mixture was extracted with CH₂Cl₂ (10 mL), and the combined organic phases were dried (Na₂SO₄) and concentrated to give 0.121 g (82%) of a white solid: mp 100–101 °C; $[\alpha]_D^{20}$ 127 (c

0.5, CHCl₃); IR (neat) 3050, 1607, 1576, 1461 cm⁻¹; ¹H NMR (CDCl₃) δ 2.28 (s, 3 H), 2.50 (s, 6 H), 6.88 (s, 2 H), 7.46–7.47 (m, 3 H), 7.84–7.86 (m, 2 H), 8.83 (s, 1H); ¹³C NMR (CDCl₃) δ 19.3, 21.5, 129.3, 129.9, 131.2, 132.9, 134.2, 135.7, 138.8, 142.1, 162.0. Anal. Calcd for C₁₆H₁₇NOS: C, 70.81; H, 6.31; N, 5.16. Found: C, 71.13, H, 6.23, N, 4.97.

(*S*)-(+)-*N*-(*p*-Methoxybenzylidene)-2,4,6-trimethylphenylsulfinamide (**12a**): yield 78%; mp 67–68 °C; $[\alpha]_D^{20}$ 98.8 (*c* 0.5, CHCl₃); IR (neat) 1594, 1072 cm⁻¹; ¹H NMR (CDCl₃) δ 2.28 (s, 3 H), 2.50 (s, 6 H), 3.86 (s, 3 H), 6.85 (s, 2 H), 6.94 (d, *J* = 9 Hz, 2 H), 7.79 (d, *J* = 9 Hz, 2 H), 8.75 (s, 1 H); ¹³C NMR (CDCl₃) δ 17.6, 19.8, 54.2, 113.0, 125.7, 129.5, 130.2, 134.4, 137.1, 140.3, 159.5, 161.8. Anal. Calcd for C₁₇H₁₉N₂O₂S: C, 67.74; H, 6.35; N, 4.65. Found: C, 67.52, H, 6.44, N, 4.06.

(*S*)-(+)-*N*-(4-Trifluoromethylbenzylidene)-2,4,6-trimethylphenylsulfinamide (**12c**): yield 78%; mp 92–93 °C; $[\alpha]_D^{20}$ 104.4 (*c* 0.5, CHCl₃); IR (neat) 1571, 1449 cm⁻¹; ¹H NMR (CDCl₃) δ 2.29 (s, 3 H), 2.49 (s, 6 H), 6.88 (s, 2 H), 7.71 (d, *J* = 8 Hz, 2 H), 7.96 (d, *J* = 8 Hz, 2 H), 8.87 (s, 1 H); ¹³C NMR (CDCl₃) δ 19.3, 21.5, 125.3, 126.3, 130.1, 131.3, 134.3, 135.1, 137.1, 138.9, 142.4, 160.2. Anal. Calcd for C₁₇H₁₆F₃NOS: C, 60.16; H, 4.75; N, 4.13. Found: C, 60.21 H, 4.79; N, 4.02.

(*S*)-(+)-*N*-(4-Nitrobenzylidene)-2,4,6-trimethylphenylsulfinamide (**12d**): yield 79%; mp 141–142 °C; $[\alpha]_D^{20}$ 40.2 (*c* 0.5, CHCl₃); IR (neat) 1583, 1534, 1344, 1105 cm⁻¹; ¹H NMR (CDCl₃) δ 2.28 (s, 3 H), 2.48 (s, 6 H), 6.87 (s, 2 H), 8.0 (d, *J* = 11 Hz, 2 H), 8.29 (d, *J* = 11 Hz, 2 H), 8.89 (s, 1 H); ¹³C NMR (CDCl₃) δ 19.2, 21.5, 124.5, 130.5, 131.4, 134.8, 138.9, 139.2, 142.5, 150.2, 159.6. Anal. Calcd for C₁₆H₁₆N₂O₃S: C, 60.74; H, 5.10; N, 8.85. Found: C, 61.16, H, 5.02, N, 8.37.

Typical One-Pot Synthesis of Aziridine 2-Phosphonates. (*S_S,2S,3R*)-(+)-*N*-(2,4,6-Mesitylsulfinyl)-3-phenylaziridine-2-phosphonate (**13b**). In a 25-mL, two-neck, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon were placed 0.10 g (0.368 mmol) of (+)-**12b** and 0.21 g (0.737 mmol) of diethyl 2-iodomethylphosphonate in THF (10 mL). The solution was cooled to -78 °C, and after 10 min, 0.737 mL (0.737 mmol, 1 M in THF) of LiHMDS was added via syringe. After being stirred at this temperature for 30 min, the solution was quenched by addition of saturated aqueous NH₄Cl (5 mL) and the solution was warmed to room temperature. At this time, the reaction mixture was diluted with water (10 mL) and the solution was extracted with EtOAc (2 × 25 mL). The combined organic phases were washed with saturated sodium thiosulfate (10 mL) and brine (15 mL), dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography (EtOAc–hexane, 6:4) afforded 0.121 g (78%) as a colorless oil: $[\alpha]_D^{20}$ 56.4 (*c* 0.5, CHCl₃); IR (neat) 2976, 2927, 1244, 1103 cm⁻¹; ¹H NMR (CDCl₃) δ 0.97 (t, *J* = 8 Hz, 3 H), 1.06 (t, *J* = 8 Hz, 3 H), 2.22 (s, 3 H), 2.50 (s, 6 H), 2.68 (dd, ²*J*_{HP} = 16.4 Hz, *J* = 7.6 Hz, 1 H), 3.50–3.53 (m, 1 H), 3.71–3.86 (m, 3 H), 4.10 (dd, ³*J*_{CP} = 7.8 Hz, *J* = 7.6 Hz, 1 H), 6.70 (s, 2 H), 7.08–7.15 (m, 5 H); ¹³C NMR (CDCl₃) δ 16.6 (d, ³*J*_{CP} = 5.7 Hz), 19.6, 21.5, 34.1 (d, ¹*J*_{CP} = 229.4 Hz), 38.5, 62.5 (2 x d, ²*J*_{CP} = 6.1 Hz), 128.2, 128.3, 128.4, 131.5, 133.4, 136.1, 138.5, 142.1; ³¹P NMR (CDCl₃) δ 19.0; HRMS calcd for C₂₁H₂₈NO₄PS (M + Na) 444.1374, found 444.1364.

(*S_S,2S,3R*)-(+)-*N*-(2,4,6-Mesitylsulfinyl)-3-(*p*-methoxyphenyl)aziridine-2-phosphonate (**13a**): yield 75%; $[\alpha]_D^{20}$ 37.7 (*c* 1.0, CHCl₃); IR (neat) 2979, 2931, 1612, 1026 cm⁻¹; ¹H NMR (CDCl₃) δ 1.15 (2 x t, *J* = 6.4 Hz, 6 H), 2.32 (s, 3 H), 2.60 (s, 6 H), 2.71 (dd, ²*J*_{HP} = 16.8, *J* = 6.8 Hz, 1 H), 3.69–3.70 (m, 1 H), 3.71 (s, 3 H), 3.88–3.96 (m, 3 H), 4.10–4.15 (m, 1 H), 6.77 (d, *J* = 7.6 Hz, 2 H), 6.87 (s, 2 H), 7.14 (d, *J* = 7.6 Hz, 2 H); ¹³C NMR (CDCl₃) δ 16.7, 19.6, 21.5, 34.2 (d, ¹*J*_{CP} = 208.6 Hz), 38.1, 55.6 (2 x d, ²*J*_{CP} = 6.0 Hz), 113.7, 125.3, 129.6, 131.5, 136.2, 138.5, 142.0, 159.6; ³¹P NMR (CDCl₃) δ 19.2; HRMS calcd for C₂₂H₃₀NO₅PS (M + Na) 474.1480, found 444.1474.

Typical Procedure for the Synthesis of α -Chloro- β -aminophosphonates 15 and 16. In a 50-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum,

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(16) Plobeck, N.; Powell, D. *Tetrahedron: Asymmetry* **2002**, *13*, 303.

and argon balloon were placed 0.05 g (0.166 mmol) of (*S*)-(+)-**12a** and 0.052 g (0.322 mmol) of dimethyl chloromethylphosphonate in THF (20 mL). The mixture was cooled to -78°C , and after 10 min, 0.166 mL (0.322 mmol, 2.0 M in cyclohexane) of *n*-BuLi was added quickly via syringe. After being stirred at this temperature for 30 min, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (5 mL), warmed to room temperature, and diluted with H_2O (10 mL). The solution was extracted with Et_2O (2×10 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated to give a yellow oil. Purification by flash chromatography (EtOAc –hexane, 6:1) gave 0.053 g (70%) of an inseparable mixture of **15a/16a** as an oil in a ratio of 77:23.

Typical Deprotection Procedure. Diethyl (2*S*,3*R*)-(–)-3-Phenylaziridine-2-phosphonate (17b). In a 25-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed 0.10 g (0.237 mmol) of (+)-**13b** in THF (10 mL). The solution was cooled to -78°C , and after 10 min, 0.156 mL (0.468 mmol, 3.0 M in Et_2O) of MeMgBr was added dropwise via syringe. After being stirred at this temperature for 2 h, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (5 mL) and the solution was warmed to room temperature. At this time, the solution was extracted with EtOAc (2×25 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated to give a green oil. Flash chromatography (CH_2Cl_2 – EtOAc , 4:1) afforded 0.466 g (77%) of colorless oil: $[\alpha]_{\text{D}}^{20} -36.1$ (*c* 0.80, CHCl_3) [lit.² $[\alpha]_{\text{D}}^{20} -36.5$ (*c* 0.85, CHCl_3)]. Spectral properties were consistent with literature values.²

Diethyl (2*S*,3*R*)-(–)-3-(*p*-methoxyphenyl)aziridine-2-phosphonate (17a): yield 72%; mp 33 – 34°C ; $[\alpha]_{\text{D}}^{20} -25.0$ (*c* 0.65, CHCl_3); IR (KBr) 3237, 1250, 1031 cm^{-1} ; $^1\text{H NMR}(\text{CDCl}_3)$ δ 1.07–1.19 (m, 6 H), 1.50 (brs, 1 H), 2.46 (m, 1 H), 3.30–3.55 (m, 2 H), 3.70–3.95 (m, 6 H), 6.83 (d, $J = 8$ Hz, 2 H), 7.29–7.41 (brs, 2 H); $^{13}\text{C NMR}(\text{CDCl}_3)$ δ 16.9, 31.4(d, $^1J_{\text{CP}} = 218$ Hz), 37.2, 55.9, 62.3 (t, $^2J_{\text{CP}} = 16.2$ Hz), 113.9, 129.4, 129.9, 159.7; $^{31}\text{P NMR}(\text{CDCl}_3)$ δ 22.26. Anal. Calcd. for

$\text{C}_{13}\text{H}_{20}\text{NO}_4\text{P}$: C, 54.73; H, 7.07; N, 4.91. Found: C, 54.86; H, 7.37; N, 4.83.

(*S*,2*S*,3*R*)-(+)-*N*-[1-(2-Methylpropane-2-sulfinyl)-3-(4-trifluoromethylphenyl)aziridin-2-yl]phosphonic Acid Diethyl Ester (8b). In a 25-mL, two-neck, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon were placed 0.1 g (0.365 mmol) of (+)-**7b** and 0.203 g (0.731 mmol) of diethyl 2-iodomethylphosphonate in THF (10 mL). The solution was cooled to -78°C , and after 10 min, 0.731 mL (1 M in THF, 0.731 mmol) of LiHMDS was added via syringe. After being stirred at this temperature for 30 min, the solution was quenched by addition of saturated aqueous NH_4Cl (5 mL) and warmed to room temperature. The solution was diluted with water (10 mL), and the reaction mixture was extracted with EtOAc (2×25 mL). The combined organic phases were washed with saturated sodium thiosulfate (10 mL) and brine (15 mL), dried (Na_2SO_4), and concentrated. Flash chromatography (EtOAc –hexane, 6:4) afforded 0.112 g (72%) as a colorless oil: $[\alpha]_{\text{D}}^{20} 42.4$ (*c* 1.25, CHCl_3); IR (neat) 2989, 1314, 1267, 2273 cm^{-1} ; $^1\text{H NMR}(\text{CDCl}_3)$ δ 1.05 (t, $J = 6.8$ Hz, 3 H), 1.15 (t, $J = 6.8$ Hz, 3 H), 1.18 (s, 9 H), 2.55 (dd, $^2J_{\text{HP}} = 15.2$ Hz, $J = 7.2$ Hz, 1 H), 3.72–3.81 (m, 2 H), 3.85–3.95 (m, 3 H), 7.52–7.57 (m, 4 H); $^{13}\text{C NMR}(\text{CDCl}_3)$ δ 16.6 (2 x d, $^3J_{\text{CP}} = 5.5$ Hz), 23.0, 33.8 (d, $^1J_{\text{CP}} = 209.7$ Hz), 35.7, 57.9, 62.8 (d, $J = 5.5$ Hz), 125.4, 128.8, 129.4, 130.7, 137.4; $^{31}\text{P NMR}(\text{CDCl}_3)$ δ 17.70; HRMS calcd for $\text{C}_{17}\text{H}_{25}\text{F}_3\text{NO}_4\text{PS}$ (*M* + *Na*) 450.1094, found 450.1092

Acknowledgment. This work was supported by the National Institutes of General Medical Sciences (NIGMS 57870).

Supporting Information Available: Spectral data for compounds where only HRMS is available. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO030142M