JOC Article

Asymmetric Synthesis of Aziridine 2-Phosphonates from Enantiopure Sulfinimines (*N*-Sulfinyl Imines). Synthesis of α-Amino Phosphonates

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Received November 21, 2002

An aza-Darzens reaction, involving the addition of chloromethylphosphonate anions to enantiopure sulfinimines, has been developed for the asymmetric synthesis of aziridine 2-phosphonates. Best results involve cyclization of the syn and anti diastereomerically pure α-chloro-*β*-amino phosphonates to *cis*- and *trans*-*N*-sulfinyl aziridine 2-phosphonates, respectively, with *n*-BuLi. A transition-state hypothesis is proposed wherein the chloromethylphosphonate anion adds to the C−N bond on the side that is opposite the bulky *p*-tolyl sulfinyl group. The *N*-sulfinyl group is easily removed by treatment with MeMgBr or TFA/MeOH, which affords the NH-aziridines in good yield. Using transfer hydrogenation conditions, the NH-aziridines were regioselectively opened to the corresponding enantiopure α-amino phosphonates without N-activation and in excellent yield.

Chiral aziridines have found widespread use in organic synthesis.[1] The highly strained three-membered ring readily opens with excellent stereo- and regiocontrol to afford a wide variety of more stable ring-opened or ring-expanded chiral amines (Scheme 1). Consequently, aziridine 2-phosphonates **1** are expected to be important sources of diversely substituted amino phosphonates. Amino phosphonates have found general use as surrogates for amino acids and as such exhibit potent biological activities.[2] Activation of the aziridine nitrogen by an electron-withdrawing group (acyl, sulfonyl), by protonation, or by Lewis acids promotes either C-2 attack to give *β*-amino phosphonates or C-3 attack to give α-amino phosphonates (Scheme 1). The stereo- and regioselectivity is determined by the ring substituents and the reaction conditions, with the majority of nucleophiles expected to react at C-3.

Realizing the potential of aziridine 2-phosphonates **1** for the asymmetric synthesis of structurally diverse α- and *β*-amino phosphonates requires practical and efficient methods for their preparation. Racemic aziridine phosphonates have been synthesized by the reaction of vinyl phosphonates with ethyl *N*-{[(4-nitrobenzene)-sulfonyl]oxy}carbamate,[3] copper-catalyzed aziridination with [*N*-(*p*-toluenesulfonyl)imino]phenyliodonane,[4] cyclization of 1-bromo-2-aminoethyl phosphonic acid,[5] and the Darzens-type addition of chloromethylphosphonate anions to imines.[6] The first asymmetric synthesis of aziridine 2-phosphonates, a highly diastereoselective addition of an enantiopure bicyclic chloromethylphosphonamide anion to imines, was described by Hanessian and co-workers.[7] More recently, enantiopure and optically enriched **1** have been prepared by cyclization of α-hydroxy *β*-amino phosphonates[8] and reduction of 2*H*-azirine-2-phosphonates.[9] However, with the exception of the latter method, wherein the azirine was formed in less than 24% ee, it was not possible to remove the N-substituent to give the NH-aziridine without ring opening.

In preliminary communications we reported the synthesis of enantiopure *N*-sulfinylaziridine 2-phosphonates, which were utilized as polyfunctionalized chiral building blocks in highly stereoselective asymmetric syntheses of α-amino phosphonates[10] and α-methyl α-aminophosphonates.[11] The derived NH-aziridine 2-phosphonates were employed in the first asymmetric syntheses of the smallest of the unsaturated nitrogen heterocycles 2*H*-azirine 2-phosphonaes, and 2*H*-aziridine 3-phosphonates.[11] The latter azirines represent a new class of chiral imino

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(2) For reviews see: (a) Kafarski, P.; Lejczak, B. *Phosphorus, Sulfur, Silicon* **1991**, *63*, 193. (b) Seto, H.; Kuzuyama, T. *Nat. Prod. Rep.* **1999**, *16*, 589. (c) *Aminophosphonic and Aminophosphinic Acids. Chemistry and Biological Activity*; Kukhar, V. P., Hudson, H. R., Eds.; Wiley: Chichester, UK, 2000.

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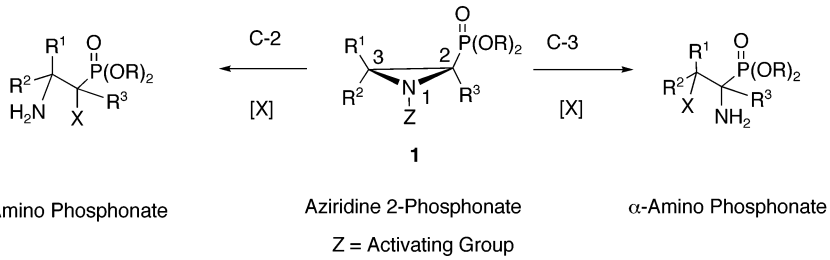
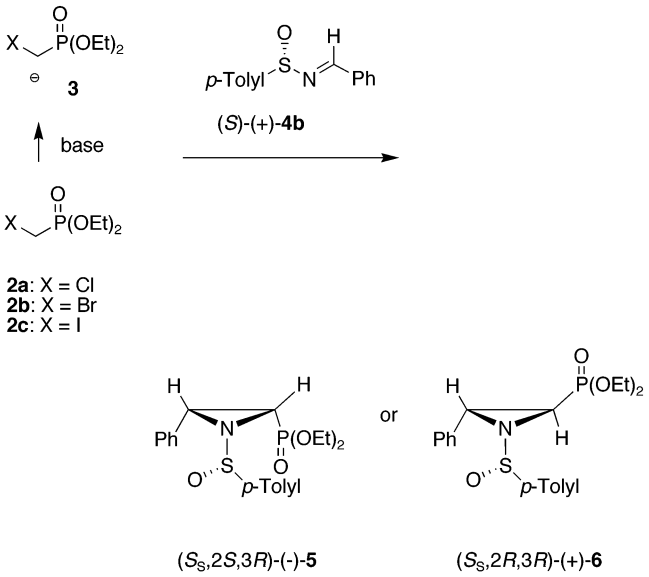
10.1021/jo020707z CCC: $25.00
Published on Web 02/22/2003

SCHEME 1



SCHEME 2



dienophiles and were used in the first enantioselective synthesis of quaternary piperidine phosphonates.[12] In this paper we give a full account of our asymmetric synthesis of *N*-sulfinylaziridine 2-phosphonates from sulfinimines (*N*-sulfinyl imines).

Results and Discussion

Synthesis of Aziridines. Previously we described a one-pot aza-Darzens synthesis of *N*-sulfinyl aziridine 2-carboxylates from sulfinimines and α-bromoenolates.[13] This methodology appears to be particularly useful in terms of its simplicity and ease of incorporating diverse ring and nitrogen substituents. A similar protocol was explored for the synthesis of *N*-sulfinyl aziridine 2-phosphonates **5** and **6** and involves the addition of (*S*)-(+)-*N*-(benzylidene)-*p*-toluenesulfinamide (**4b**) to the anion of diethyl α-halomethyl-phosphonates **2**, at −78 °C and warming to room temperature (Scheme 2). These conditions afforded the cis and trans aziridines **5** and **6** in one pot with isomer ratios varying from 44:56 to 81:19 (Table 1). Unfortunately, it proved to be exceedingly tedious to separate the aziridine isomers and necessitated repetitive chromatography, at least three times, which resulted in poor product yields (Table 1, entry 6).

We found a more practical route to aziridine 2-phosphonates targets was to stop at the intermediate α-chloro-

TABLE 1. Addition of Lithium Diethyl α-Halomethylphosphonates to (*S*)−(+)-4b in THF at −78 °C

entry	**2**, X =	conditions equiv **4b**:**2**:base, temp (time)	% yield[a]	**5**:**6**[b]
1	Cl	1:2:2, *n*-BuLi, −78 °C to rt (2 h)[c]	<10	44:56
2		1:3:3, *n*-BuLi, −78 °C to rt (8 h)	17	78:32
3	Br	1:3:3, *n*-BuLi, −78 to −20 °C (8 h)	38	59:41
4	I	1:3:3, *n*-BuLi, −78 to −45 °C (8 h)	48	69:31
5		1:2:2, LiHMDS, −78 to −40 °C (1 h)	71	81:19
6		1:1.1:1.1, NaHMDS, −78 to −40 °C (3 h)	(46)[d]	78:22

[a] Combined isolated yield of **5** and **6**. [b] Ratio of **5**:**6** determined by proton NMR. [c] See ref 14. [d] Isolated yield of **5** after repetitive chromatography.

β-amino adducts, which can be more easily separated, and then cyclize them to the corresponding aziridines. Optimal reaction conditions involved treating 2 equiv of the chloromethylphosphonate **2a** or **7** and 1 equiv of the sulfinimine **4** with the appropriate base at −78 °C (Scheme 3). The reaction mixture was quenched at this temperature with aqueous sat. NH_4Cl and warmed to room temperature. Under these conditions the aziridine adducts were not detected, thus the difficulty in separating the aziridine isomers was avoided. The major β-amino α-chlorophosphonates **8**/**9** and **10**/**11** were separated by flash chromatography. Also detected in the crude reaction mixture were products believed to be isomer adducts **12**, but these were difficult to isolate and appeared to be unstable to chromatography. These results are summarized in Table 2.

Complicating the separation of the β-amino-α-chlorophosphonates is the presence of excess chloromethylphosphonates **2a** and **7**. To avoid this problem the following separation protocol was devised. First, a rough flash chromatography separated the chloromethylphosphonate and minor isomers **12** from the major syn and anti adducts **8**/**9** and **10**/**11**. On concentration the major syn adducts **8** and **10** solidified. The minor products, **9** and **11**, were viscous oils and could be separated by washing the mixture with a few milliliters of ether−hexane. The *n*-BuLi base gave the best results with this protocol. Interestingly, a variation in the rate of addition of this base to dimethyl chloromethylphosphonate (**7**) resulted in the formation of the β-amino-α-chloro phosphonate monoester **13**. Dropwise addition of *n*-BuLi to the reaction mixture over 15 min produced up to 30% of **13** (Table 2, entry 3). This side product was not detected when all the base was added in one portion (see below).

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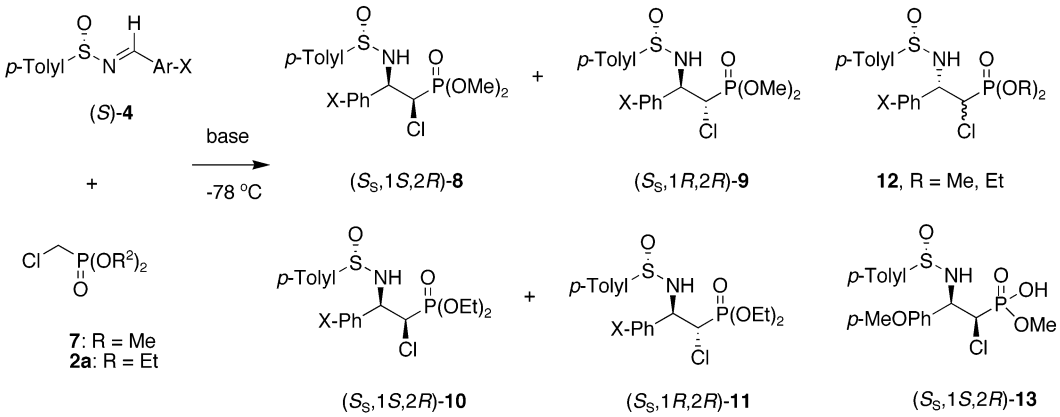
(13) Davis, F. A.; Liu, H.; Zhou, P.; Fang, T.; Reddy, G. V.; Zhang, Y. *J. Org. Chem.* **1999**, *64*, 7559.
(14) Kim, D. Y.; Shu, K. H.; Choi, J. S.; Mang, J. Y.; Chang, S. K. *Synth. Commun.* **2000**, *30*, 87. A 91% yield of **5** was reported by these authors with these reaction conditions.

SCHEME 3



a: X = *p*-MeO; **b**: X = H; **c**: X = *p*-NO_2; **d**: X = *p*-CF_3

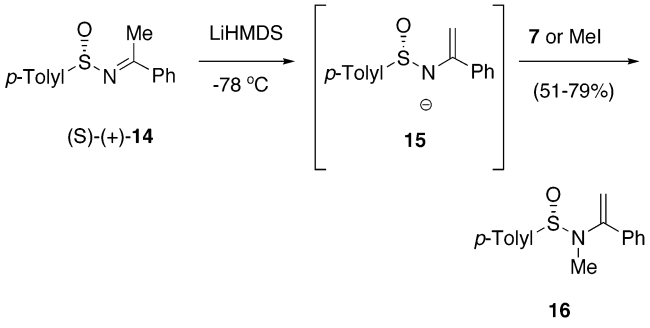
TABLE 2. Reaction of Chloromethylphosphonates with Sulfinimines at −78 °C for 0.5 h

entry	sulfinimine **4** (R^1 =)	phosphonate	base[a]	solvent	**8**:**9**:**12**[b] (% yield)[c] **10**:**11**:**12**	% major[d]	% minor[d]
1	**4a** (*p*-MeOPh)	**7** (Me)	LiHMDS	THF	54:46 (75)	(+)-**8a**, 32	
2			*n*-BuLi	THF	66:34 (75)	(+)-**8a**, 51	
3			*n*-BuLi[e]	THF	66:34 (50)	(+)-**8a**, 24	(+)-**13**, 30
4		**2a** (Et)	LiHMDS	THF	55:30:15 (63)	(+)-**10a**, 25	
5			*n*-BuLi	THF	77:8:15 (72)	(+)-**10a**, 48	
6	**4b** (Ph)	**7** (Me)	LiHMDS	THF	64:22:14 (69)	(+)-**8b**, 58	
7			LiHMDS	Et_2O	65:4:31 (70)		
8			NaHMDS	THF	41:53:6 (73)		
9			KHMDS	THF	38:54:8 (71)		
10			*n*-BuLi	THF	76:8:16 (75)	(+)-**8b**, 56	
11			*n*-BuLi/LiCl	THF	42:50:8 (70)		
12			*n*-BuLi	Et_2O	59:5:36 (70)		
13		**2a** (Et)	LiHMDS	THF	59:41 (98)	(+)-**10b**, 58	(+)-**11b**, 40
14			*n*-BuLi	THF	1:1 (82)		
15	**4c** (*p*-NO_2Ph)	**7** (Me)	LiHMDS	DCM	57:43 (56)	(−)-**8c**, 32	(−)-**9c**, 24
16	**4d** (*p*-CF_3Ph)	**7** (Me)	LiHMDS	THF	53:47 (64)	(+)-**8d**, 41	
17			*n*-BuLi	THF	1:1 (60)	(+)-**8d**, 40	

[a] Base is added all at once to the reaction mixture. [b] Ratio of α-chloro-β-amino isomers determined by ^{1}H NMR on the crude reaction mixture. Compound **12** is estimated to be the combined ratio of the other isomers, but was not isolated. [c] Combined yields of isomers. [d] Isolated yields [e] *n*-BuLi is added to the reaction mixture over 15 min.

The stereochemical assignment of the syn and anti adducts ultimately rests on their conversion to the corresponding aziridines, removal of the *N*-sulfinyl group, and stereoselective ring opening to α-amino phosphonates of known absolute configuration (see blow). The $J_{1,2}$ coupling constants for the C-1 and C-2 protons in the syn adducts (S_S,1*S*,2*R*)-**8** and **10** appear at about 4 Hz while the anti adducts (S_S,1*R*,2*R*)-**9** and **11** have a value of 5−6 Hz. Particularly diagnostic are the ^{31}P and C-2 proton coupling constants where the value for the syn adducts is 18.5 Hz and that for the anti adducts is 12 Hz. The structural assignment for monoester **13** is based on HRMS and proton NMR, which confirms the loss of a methyl group. The proton NMR of **13**, taken in CD_3OD because it was insoluble in most organic solvents, reveals that $J_{1,2}$ is observed at 6.4 Hz and $J_{P,1}$ at 10.8 Hz. The corresponding coupling constants in this solvent for **8** and **10** appear at 5.8−6.1 and 11.8−11.9 Hz, respectively, indicating that **13** also has the syn (S_S,1*S*,2*R*) structure. In the minor anti isomer **9a** (CD_3OD), $J_{1,2}$ appears at 4.0 Hz. We speculate that the monoester **13** arises via attack of *n*-BuLi on the methyl group of the major syn isomer affording *n*-pentane (not detected). Demethylation of dimethylanilinomethylphosphonate by NaOMe has been reported.[15] Additional support for this idea was found in the formation of enamine (+)-**16** in 51% and 79% yield on treatment of aza enolate **15**, derived from sulfinimine (*S*)-(+)-**14**, with dimethyl chloromethylphosphonate (**7**) or iodomethane, respectively (Scheme 4).

SCHEME 4



The results summarized in Table 2 reveal that in all cases mixtures of the α-chloro-β-amino adducts

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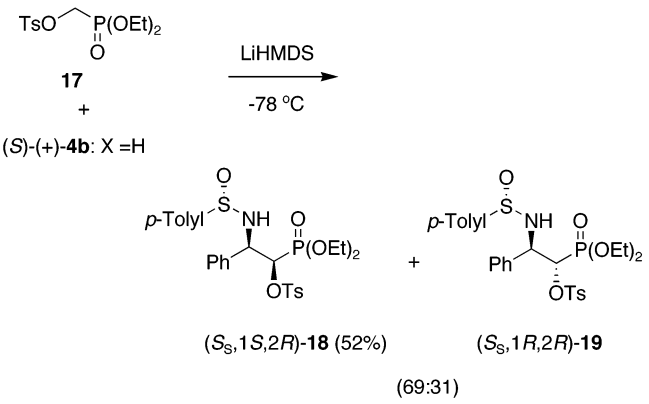
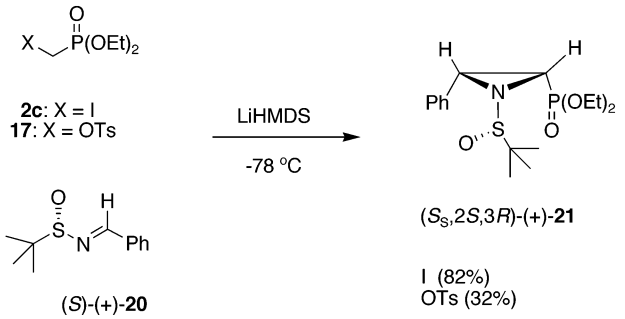
SCHEME 5



SCHEME 6

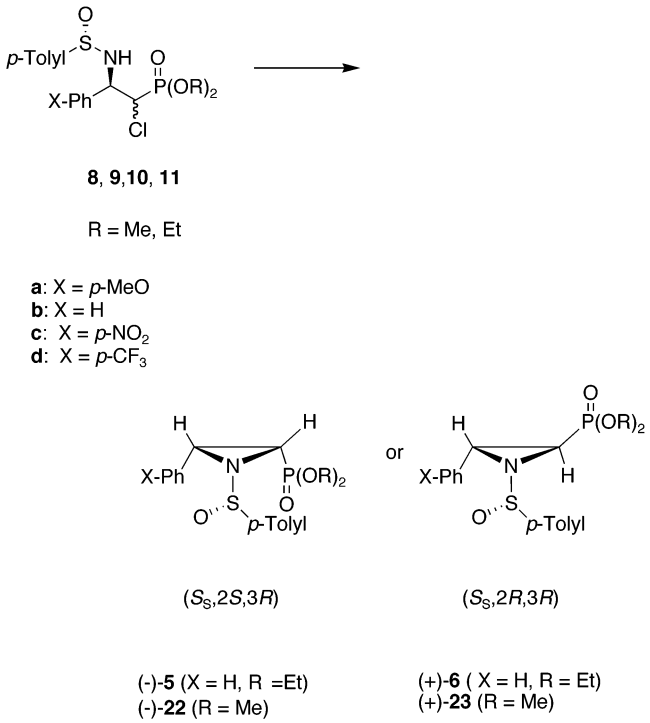


8:**9**/**10**:**11** were obtained. Attempts to improve the isomer ratio by altering the solvent, the base, or the chloromethylphosphonate ester group failed. The aryl substituent X in sulfinimines **4a**−**d** also had little if any effect on the adduct ratio. It has been suggested that aziridine 2-phosphonate formation can result from a reversible equilibration of the α-chloro-*β*-amino adducts on warming.[6] We found no evidence for this in our system. A retained ratio of the aziridine (−)-**5**/(+)-**6** was noted on warming **10b** and **11b** over 3 h to − 5 °C. Our results are consistent with the supposition that halomethylphosphonate anions **3**, unlike enolate ions, have little if any configurational stability and mixtures of products at the α-position are to be expected.[16]

For this reason we next explored the addition of the anion derived from diethylphosphonomethoxytosylate (**17**)[17] to (*S*)-(+)-**4b**. Here it was hoped that a bulkier leaving group and/or intramolecular chelation within the anion might restrict its conformational mobility, resulting in improved adduct ratios. Unfortunately this was not to be the case and mixtures of products **18**:**19**, with ratios similar to those found for the chloromethylphosphonate anions, were observed, i.e., 69:31 (Scheme 5).

The influence of the sulfinyl auxiliary on the diastereoselectivity of *β*-amino phosphonates was investigated next (Scheme 6). Here the diethyl iodo- or tosylphosphonates **2c** or **17** and sulfinimine (*S*)-(+)-**20**,[18] derived from

SCHEME 7



(*S*)-(+)-*N*-*tert*-butanesulfinamide and benzaldehyde, were treated with LiHMDS at −78 °C (Scheme 6). Importantly, the aziridine (+)-**21** formed directly, as a single isomer, in 82 and 32% isolated yields, respectively. Unfortunately, all attempts to remove the *tert*-butanesulfinyl auxiliary without concomitant ring opening failed (see below).

Structure and Formation of Aziridines. With the *β*-amino-α-chloro adducts in hand (Table 2), cyclization to the corresponding aziridines was readily accomplished by treatment with NaH at room temperature or *n*-BuLi in THF at −78 °C (Table 3, Scheme 7). The stereochemical assignments for the aziridines are based on the large ring proton coupling constants observed for *cis*-(*S*S,2*S*,3*R*) and *trans*-(*S*S,2*R*,3*R*) of 7.5−8.0 and 4.5−5.0 Hz, respectively.[19] Similar values for the coupling constants are observed for the related *N*-sulfinyl aziridine 2-carboxylates.[13] The absolute stereochemistry of (−)-**5** and (+)-**6** was established by selective removal of the *N*-sulfinyl group and ring opening to give the known (*S*)- and (*R*)-diethyl-1-amino-2-phenylethyl phosphonates (+)-**27** and (−)-**28**, respectively (see below). By analogy, and on the basis of similar coupling constants, the major aziridine isomers **22** and **5** are assumed to have the cis geometry.

Removal of the *N*-Sulfinyl Group and Syntheses of α-Amino Phosphonates. An important advantage of using the *N*-sulfinyl group in aziridine 2-carboxylate syntheses is that it can be removed under such conditions that ring opening does not occur.[13] This affords enantiopure 1*H*-aziridines that are valuable precursors of N-substituted aziridines and can be elaborated to 2*H*-azirines.[20] Earlier syntheses of aziridine phosphonates

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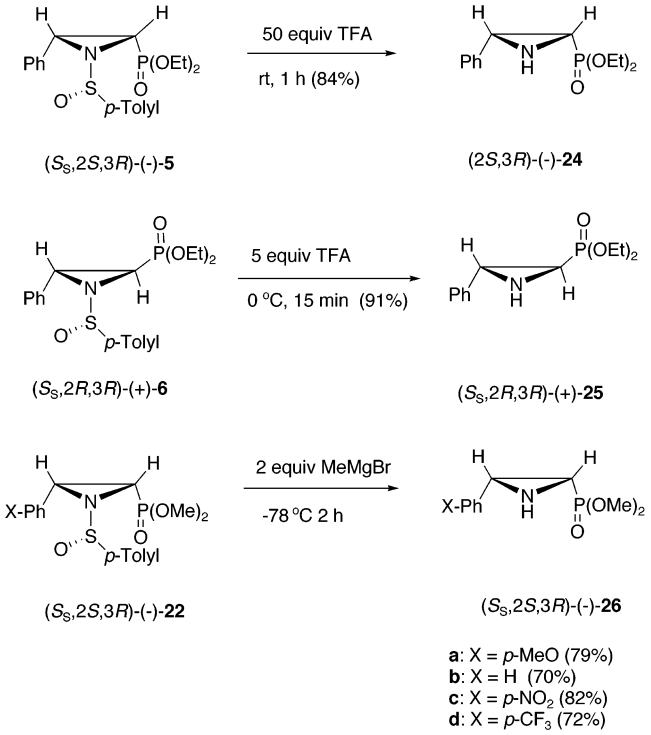
TABLE 3. Formation of Aziridines via Cyclization of α-Chloro *β*-Amino Adducts.

entry	chloro amino adduct	base/h/°C	aziridine (% isolated yield).
1	**8a** (X = *p*-MeO, R = Me)	*n*-BuLi/1/−78 to rt	(*S*S,2*S*,3*R*)-(−)-**22a** (82)
2	**8b** (X = H, R = Me)	NaH/0.5/rt	(*S*S,2*S*,3*R*)-(−)-**22b** (73)
3	**8b** (X = H, R = Me)	*n*-BuLi/1/−78 to rt	(*S*S,2*S*,3*R*)-(−)-**22b** (85)
4	**10b** (X = H, R = Et)	NaH/1/−78 to rt	(*S*S,2*S*,3*R*)-(−)-**5** (76)
5	**11b** (X = H, R = Et)	NaH/1/−78 to rt	(*S*S,2*R*,3*R*)-(+)-**6** (75)
6	**8c** (X = *p*-NO_2, R = Me)	NaH/1/rt	(*S*S,2*S*,3*R*)-(−)-**22c** (80)
7	**9c** (X = *p*-NO_2, R = Me)	NaH/1/rt	(*S*S,2*R*,3*R*)-(+)-**23c** (64)
8	**8d** (X = *p*-CF_3, R = Me)	*n*-BuLi/1/−78 to rt	(*S*S,2*S*,3*R*)-(−)-**22d** (78)

SCHEME 8

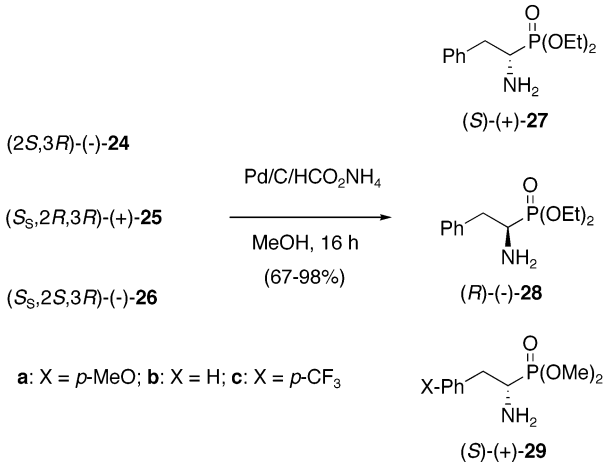


had N-substituents that could not be removed without aziridine ring opening.

Treatment of *N*-sulfinyl aziridine *cis*-(−)-**5** with 50 equiv of trifluoroacetic acid (TFA) at room temperature afforded aziridine (2*S*,3*R*)-(−)-**24** in 84% isolated yield (Scheme 8). However, these conditions with *trans*-(+)-**6** furnished (+)-**25** in less than 22% yield with extensive ring opening and decomposition. The higher reactivity of the trans aziridine probably reflects unfavorable steric interactions between the *N*-sulfinyl group and aziridine ring substituents that are absent in the cis analogues. By performing the desulfinylation process reaction at 0 °C for 15 min with only 5 equiv of TFA the *trans*-(2*R*,3*R*)-(+)-**25** could be isolated in 91% yield. However, even with these milder conditions aziridine (−)-**22a**, which contains the ring-activating 3-(*p*-methoxyphenyl) group, afforded only ring-opening and decomposition products. We found that the best method for removing the *N*-sulfinyl group is treatment of the aziridine phosphonate **22** with 2 equiv of MeMgBr at −78 °C. The corresponding N−H aziridines **26** were obtained in 70−82% yield (Scheme 8). Unfortunately all attempts to remove the *tert*-butanesulfinyl group in (+)-**21** with use of acid or MeMgBr resulted in complex mixtures of decomposition products.

It is generally thought that N-activation is necessary for aziridine ring opening.[1,21] Importantly, we have found

SCHEME 9



that transfer hydrogenation of unactivated N−H-aziridines **24**, **25**, and **26** proceeds at the benzylic position with conservation of the stereochemistry α to the phosphorus to give 1-amino-2-arylethyl phosphonates **27**−**29** (Scheme 9). The lowest yield was for (−)-**26c** (X = *p*-CF_3) furnishing the amino phosphonate (*S*)-(+)-**29** in 67% yield. The other amino acids were isolated in 80−98%. The fact that ring opening occurs without activation at nitrogen means that a deprotection step is not required to give the amino phosphonates. Because amino phosphonates (*S*)-(+)-**27**[22] and (*R*)-(−)-**28**[23] have been described earlier, we can establish the absolute configuration of the corresponding aziridines and the *β*-amino chlorophosphonates (see above).

The structures resulting from the addition of organometallic reagents to the C−N bond of sulfinimines can generally be predicted by assuming chelated, chairlike transition states resulting from the coordination of the metal and the sulfinyl oxygen.[24] By contrast the exclusive (*R*)-absolute configuration at C-2 in **8**/**9** and **10**/**11** is opposite to that found in the analogous aza-Darzens reactions of the bromo enolates that furnish aziridine carboxylates.[13] Thus the addition of halomethylphosphonate anions to sulfinimines is under steric control and the anion adds to the C−N bond on the side that is opposite to the bulky *p*-tolylsulfinyl group, i.e., **TS-1**. We

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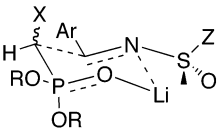
speculate that this difference reflects the much larger size of the halomethylphosphonate anion compared to an enolate as well as the anion's tetrahedral structure. It is worth mentioning that addition of methyl phosphonate anions to sulfinimines to give *β*-amino phosphonates exhibits a similar reversal in stereochemistry.[25]



TS-1

In summary, practical methodology involving an aza-Darzens-type addition of chloromethylphosphonate anions to sulfinimines has been developed for the asymmetric synthesis of *cis*-*N*-sulfinyl aziridine 2-phosphonates. Removal of the *N*-sulfinyl group to give the corresponding N−H-aziridines was readily accomplished, without ring opening, by treatment with excess methylmagnesium bromide.

Experimental Section

General Procedures. Column chromatography was performed on silica gel, Merck grade 60 (230−400 mesh). TLC plates were visualized with UV, in an iodine chamber, or with phosphomolybdic acid, unless otherwise noted. ^{1}H NMR and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively.

THF and Et_2O were freshly distilled under argon from a purple solution of sodium and benzophenone. Unless stated otherwise, all the reagents were purchased from commercial sources and used without additional purification.

Diethyl 2-chloro- and 2-iodomethylphosphonates **2a** and **2c** were purchased from commercial sources. Diethyl 2-bromomethylphosphonate (**2b**)[26] and diethylphosphonomethoxytosylate (**17**)[17] were prepared by literature procedures. Sulfinimines (*S*)-**4** and (*S*)-**14** were prepared by condensation of commercially available (*S*)-(+)-*p*-toluenesulfinamide with the appropriate aldehyde or ketone as previously described.[27] Sulfinimine (*S*)-(+)-**20** was prepared by a literature procedure.[18]

Dimethyl Chloromethylphosphonate (7). In a 500-mL, single-necked, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed chloromethylphosphoric dichloride (20.0 g, 120 mmol) and anhydrous methanol (23.1 g, 29.2 mL, 720 mmol) in Et_2O (150 mL). The stirred solution was cooled to 0 °C and triethylamine (33 mL, 240 mmol) was slowly added. The reaction mixture was stirred for 18 h at room temperature, filtered, and concentrated. Kugelrohr vaccum distillation (80 °C at 1 mmHg) afforded 16.4 g (88%) of a colorless oil; ^{1}H NMR ($CDCl_3$) δ 3.56 (d, $^2J_{PH}$ = 10.0 Hz, 2 H), 3.84 (d, $^3J_{PH}$ = 11.0 Hz, 6 H); ^{31}P NMR ($CDCl_3$) δ 21.24.

One-Pot Synthesis of Aziridines 2-Phosphonates. Diethyl (*S*$_S$,2*S*,3*R*)-(−)-*N*-(*p*-Toluenesulfinyl)-3-phenylaziridine-2-phosphonate (5). In a 100-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (*S*)-(+)-**4b** (0.243 g, 1.0 mmol) and diethyl iodomethylphosphonate (**2c**) (0.834 g, 3.0 mmol) in THF (40 mL). The stirred solution was cooled to −78 °C and *n*-BuLi (1.5 mL, 2.0 M in cyclohexane, 3.0 mmol) was added dropwise via syringe. The reaction mixture was slowly warmed to −45 °C and kept at that temperature for 8 h. At this time the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (2 mL) and warmed to room temperature. After dilution with H_2O (5 mL) the solution was extracted with Et_2O (2 × 20 mL) and EtOAc (3 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a yellow oil. Flash chromatography (CH_2Cl_2−EtOAc, 5:1) gave a mixture of (−)-**5** and (+)-**6** (69:31, 0.189 g, 48%) as a colorless oil. An additional two flash chromatography separations afford pure (−)-**5** as a yellow oil; $[\alpha]^{20}_D$ −33.7 (*c* 1.1, $CHCl_3$); IR (neat) 1250, 1026 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14 (t, ^3J = 7.0 Hz, 3 H), 1.15 (t, ^3J = 7.0 Hz, 3 H), 2.38 (s, 3 H), 2.86 (dd, $^2J_{HP}$ = 16.0 Hz, ^3J = 8.0 Hz, 1 H), 3.67−3.73 (m, 1 H), 3.83−3.97 (m, 4 H), 7.04−7.08 (m, 2 H), 7.15−7.17 (m, 3 H), 7.29−7.31 (m, 2 H), 7.67−7.69 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.1, 21.4, 34.1 (d, $^2J_{CP}$ = 4.0 Hz), 34.8 (d, $^1J_{CP}$ = 207.0 Hz), 62.1 (d, $^2J_{CP}$ = 6.0 Hz), 63.1 (d, $^2J_{CP}$ = 6.0 Hz), 124.5, 127.5, 127.6, 127.8, 129.7, 132.9, 140.7, 142.4; ^{31}P NMR ($CDCl_3$) δ 17.76; HRMS calcd for $C_{19}H_{25}NO_4PS$ (M + H) 394.1242, found 394.1234. Anal. Calcd for $C_{19}H_{24}NO_4PS$: C, 58.00; H, 6.15; N, 3.56. Found: C, 57.74; H, 6.27; N, 3.53.

General Procedure for the Synthesis of α-Chloro-β-aminophosphonates. Dimethyl (*S*$_S$,1*S*,2*R*)-(+)-1-Chloro-2-(4-methoxyphenyl)-2-(*p*-toluenesulfinamide)ethylphosphonate (8a). In a 500-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (*S*)-(+)-*N*-(4-methoxybenzylidene)-*p*-toluenesulfinamide (**4a**) (2.07 g, 7.7 mmol) and dimethyl chloromethylphosphonate (**7**) (2.50 g, 15.8 mmol) in THF (300 mL). The solution was stirred and cooled to −78 °C, and after 10 min *n*-BuLi (8.0 mL, 2.0 M in cyclohexane, 16.0 mmol) was quickly added (<10 s) via syringe. After being stirred at −78 °C 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 (50 mL). The solution was extracted with Et_2O (2 × 100 mL) and EtOAc (3 × 50 mL), and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a yellow oil. Purification by flash chromatography (CH_2Cl_2−EtOAc, 5:1) gave the isomeric amino chlorophosphonates that on washing with hexane (10 mL) and diethyl ether (5 mL) afforded 1.63 g (51%) of a white solid, mp 131−133 °C; $[\alpha]^{20}_D$ +8.5 (*c* 1.6, $CHCl_3$); IR (KBr) 3207, 3005, 2952, 1252, 1049 cm^{-1};^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3 H), 3.62 (d, $^3J_{HP}$ = 10.5 Hz, 3 H), 3.82 (d, $^3J_{HP}$ = 10.5 Hz, 3 H), 3.84 (s, 3 H), 4.43 (dd, $^2J_{HP}$ = 11.5 Hz, ^3J = 4.0 Hz, 1 H), 4.84 (ddd, $^3J_{HP}$ = 19.0 Hz, ^3J = 8.5 Hz, ^3J = 4.0 Hz, 1 H), 5.80 (d, ^3J = 8.0 Hz, 1 H), 6.76 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.20 (d, *J* = 9.0 Hz, 2 H), 7.51 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.7, 54.3 (d, $^2J_{CP}$ = 6.8 Hz), 54.6 (d, $^2J_{CP}$ = 6.8 Hz), 55.7, 55.6 (d, $^1J_{CP}$ = 122.0 Hz), 57.2, 113.7, 126.4, 129.4, 129.7, 130.2 (d, *J* = 6.0 Hz), 141.1, 141.6, 159.6; ^{31}P NMR ($CDCl_3$) δ 19.77; HRMS calcd for $C_{18}H_{23}O_5NPSClNa$ (M + Na) 454.0621, found 454.0628. Anal. Calcd for $C_{18}H_{23}O_5NPSCl$: C, 50.06; H, 5.37; N, 3.24. Found: C, 49.97; H, 5.47; N, 2.63.

Dimethyl (*S*$_S$,1*S*,2*R*)-(+)-1-Chloro-2-phenyl-2-(*p*-toluenesufinamide)ethylphosphonate (8b). Yield 58%; mp 124.5−125.5 °C; $[\alpha]^{20}_D$ +27.2 (*c* 1.0, $CHCl_3$); IR (KBr) 3295, 2938, 1250, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 3.61 (d, *J* = 10.7 Hz, 3 H), 3.84 (d, *J* = 11.0 Hz, 3 H), 4.46 (dd, $^2J_{HP}$ = 11.7 Hz, ^3J = 4.0 Hz, 1 H), 4.93 (ddd, $^3J_{HP}$ = 18.7 Hz, ^3J = 4.0 Hz, ^3J = 8.4 Hz, 1 H), 5.85 (d, *J* = 8.4 Hz, 1 H), 7.17 (d, *J* = 8.1 Hz, 2 H), 7.26 (m, 5 H), 7.53 (d, *J* = 8.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.2, 53.8, 54.2, 54.8, 56.7, 56.8, 126.0, 127.1, 127.7, 129.2, 137.6, 140.5, 141.2; ^{31}P NMR ($CDCl_3$) δ 19.66; HRMS calcd for $C_{17}H_{22}NO_4PS^{35}Cl$ (M + H) 402.0695, found 402.0697. Anal. Calcd for $C_{17}H_{21}NO_4PSCl$: C, 50.81; H, 5.27; N, 3.49. Found: C, 51.16; H, 4.85; N, 3.26.

Dimethyl (*S*$_S$,1*S*,2*R*)-(−)-1-Chloro-2-(4-nitrophenyl)-2-(*p*-toluenesulfinamide)ethylphosphonate (8c). Yield 32%; mp 171−172 °C; $[\alpha]^{20}_D$−45.4 (*c* 1.1, $CHCl_3$); IR (KBr) 3264,

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3047, 2854, 1514, 1350, 1243, 1051 cm^{-1};^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3 H), 3.67 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 3.89 (d, $^3J_{HP}$ =11.0 Hz, 3 H), 4.35 (dd, $^2J_{HP}$ = 12.3 Hz, ^3J = 4.0 Hz, 1 H), 4.99 (ddd, $^3J_{HP}$ = 18.9 Hz, ^3J = 7.0 Hz, ^3J = 4.0 Hz, 1 H), 6.18 (d, J = 7.0 Hz, 1 H), 7.06 (d, J = 7.5 Hz, 2 H), 7.37 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 8.01 (d, J = 9.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.6, 54.7 (2 × d, $^2J_{CP}$ = 6.5 Hz), 54.5, 56.0, 123.2, 126.3, 129.5, 129.7, 140.2, 142.2, 145.3, 147.7; ^{31}P NMR ($CDCl_3$) δ 18.92. Anal. Cacld for $C_{17}H_{20}O_6N_2PSCl$: C, 45.69; H, 4.51; N, 6.27. Found: C, 45.91; H, 4.12; N, 6.32%.

Dimethyl (S_S,1*S*,2*R*)-(+)-1-Chloro-2-(4-trifluoromethylphenyl)-2-(*p*-toluenesulfinamide)ethylphosphonate (8d). Yield 40%; white solid, mp 158−159 °C; $[\alpha]^{20}_D$ 15.8 (*c* 0.5, $CHCl_3$); IR (KBr) 3262, 2953, 2854, 1240, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3 H), 3.82 (d, $^3J_{HP}$ = 10.8 Hz, 3 H), 4.04 (d, $^3J_{HP}$ = 10.8 Hz, 3 H), 4.49 (dd, ^3J = 12.0 Hz, ^3J = 3.6 Hz, 1 H), 5.14 (ddd, J = 6.7 Hz, J = 3.5 Hz, J = 17.4 Hz, 1 H), 6.19 (d, J = 6.9 Hz, 1 H), 7.20 (d, J = 8.0 Hz, 2 H), 7.56−7.59 (m, 4 H), 7.47 (d, J = 8.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.5, 54.7 (d, $^1J_{CP}$ = 34.6 Hz), 55.0 (d, $^2J_{CP}$ = 6.0 Hz), 55.4 (d, $^2J_{CP}$ = 6.0 Hz), 56.6, 125.0 (d, J = 3.5 Hz), 126.2, 128.8, 129.1, 129.6, 140.2, 141.9, 142.1, 142.2; ^{31}P NMR ($CDCl_3$) δ 19.25; ^{19}F NMR ($CDCl_3$) δ −63.073; HRMS calcd for $C_{18}H_{20}ClF_3NO_4PSNa$ (M + Na) 492.0389, found 492.0375.

Dimethyl (S_S,1*R*,2*R*)-(−)-1-Chloro-2-(4-nitrophenyl)-2-(*p*-toluenesulfinamide)ethylphosphonate (9c). Yield 24%; mp 120−122°C; $[\alpha]_D^{20}$ −43.1 (*c* 0.61, $CHCl_3$); IR (KBr) 3199, 3004, 2958, 2856, 1606, 1521, 1348, 1257, 1048 cm^{-1};^{1} H NMR-($CDCl_3$) δ 2.31 (s, 3 H), 3.64 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 3.72 (d, $^3J_{HP}$ = 10.5 Hz, 3 H), 4.43 (dd, $^2J_{HP}$ = 12.5 Hz, ^3J = 5.5 Hz, 1 H), 5.02 (m, 1 H), 5.86 (d, J = 8.5 Hz, 1 H), 7.09 (d, J = 8.0 Hz, 2 H), 7.33 (d, J = 8.5 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 8.03 (d, J = 9.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.6, 54.1 (2 × d, $^2J_{CP}$ = 6.7 Hz), 55.3 (d, $^1J_{CP}$ = 24.8 Hz), 56.5, 123.3, 126.2, 129.70, 129.75, 140.3, 142.2, 145.4, 147.7; ^{31}P NMR ($CDCl_3$) δ 18.07. Anal. Calcd for $C_{17}H_{20}O_6N_2PSCl$: C, 45.69; H, 4.51; N, 6.27. Found: C, 45.97; H, 4.28; N, 6.31.

Diethyl (S_S,1*S*,2*R*)-(+)-1-Chloro-2-phenyl-2-(*p*-toluenesulfinamide)ethylphosphonate (10b), Diethyl (S_S,1*R*,2*R*)-(+)-1-Chloro-2-phenyl-2-(*p*-toluenesulfinamide)ethylphosphonate (11b). In a 500-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (*S*)-(+)-*N*-(benzylidene)-*p*-toluenesulfinamide (**4b**) (1.83 g, 7.52 mmol) and diethyl chloromethylphosphonate (3.18 g, 17.0 mmol) in THF (200 mL). The solution was cooled to −78 °C and LiHMDS (17.0 mL, 1 M in THF, 17.0 mmol) was added dropwise via syringe. After being stirred at −78 °C for 30 min, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (3 mL) and warmed to room temperature. The reaction mixture was diluted with H_2O (50 mL) and the solution was extracted with Et_2O (250 mL) and CH_2Cl_2 (3 × 100 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give an orange oil. Flash chromatography (CH_2Cl_2−EtOAc, 5:1) afforded 1.86 g (58%) of (+)-**10b** and 1.29 g (40%) of (+)-**11b** as colorless oils that solidified on storage at 5 °C.

(+)-10b: mp 96−97 °C; $[\alpha]^{20}_D$ +30.8 (*c* 3.2, $CHCl_3$); IR (KBr) 3226, 1254, 1026 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.12 (t, ^3J = 7.0 Hz, 3 H), 1.37 (t, ^3J = 7.0 Hz, 3 H), 2.34 (s, 3 H), 3.92−3.97 (m, 1 H), 4.02−4.97 (m, 1 H), 4.18−4.27 (m, 2 H), 4.42 (dd, $^2J_{HP}$ = 11.5 Hz, ^3J = 4.0 Hz, 1 H), 4.94 (ddd, $^3J_{HP}$ = 18.5 Hz, ^3J = 8.5 Hz, ^3J = 4.0 Hz, 1 H), 5.90 (d, ^3J = 8.5 Hz, 1 H), 7.14−7.16 (m, 2 H), 7.22−7.31 (m, 5 H), 7.53−7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $^3J_{CP}$ = 6.0 Hz), 16.4 (d, $^3J_{CP}$ = 6.0 Hz), 21.3, 56.4 (d, $^1J_{CP}$ = 153.0 Hz), 56.9, 63.7 (d, $^2J_{CP}$ = 6.0 Hz), 64.7 (d, $^2J_{CP}$ = 6.0 Hz), 126.2, 127.9, 129.4, 137.9 (d, $^3J_{CP}$ = 8.0 Hz), 140.8, 141.3; ^{31}P NMR ($CDCl_3$) δ 18.28. Anal. Calcd for $C_{19}H_{25}NO_4PSCl$: C, 53.08; H, 5.86; N, 3.26. Found: C, 53.40; H, 5.94; N, 3.18.

(+)-11b: mp 71−71.5 °C; $[\alpha]^{20}_D$ +28.1 (*c* 2.1, $CHCl_3$); IR (KBr) 3207, 1254, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.12 (t, ^3J = 7.0 Hz, 3 H), 1.18 (t, ^3J = 7.0 Hz, 3 H), 2.36 (s, 3 H), 3.89−4.08 (m, 4 H), 4.56 (dd, $^2J_{HP}$ = 12.5 Hz, ^3J = 5.0 Hz, 1 H), 4.98 (ddd, $^3J_{HP}$ = 12.0 Hz, ^3J = 7.5 Hz, ^3J = 5.0 Hz, 1 H), 5.59 (d, ^3J = 7.5 Hz, 1 H), 7.17−7.19 (m, 2 H), 7.22−7.28 (m, 5 H), 7.52−7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.1 (d, $^3J_{CP}$ = 6.0 Hz), 16.3 (d, $^3J_{CP}$ = 6.0 Hz), 21.4, 56.6 (d, $^1J_{CP}$ = 153.0 Hz), 57.6, 63.8 (d, $^2J_{CP}$ = 6.0 Hz), 64.1(d, $^2J_{CP}$ = 6.0 Hz), 126.0, 128.1, 128.3, 129.4, 137.8, 140.8, 141.4; ^{31}P NMR ($CDCl_3$) δ 17.51.

(S_S,1*S*,2*R*)-(+)-[1-Chloro-2-(4-methoxyphenyl)-2-(*p*-toluenesulfinamide)ethyl]phosphonic Acid Monomethyl Ester (13). In a 500-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (*S*)-(+)-**4a** (2.50 g, 9.6 mmol) and dimethyl chloromethylphosphonate (**7**) (2.93 g, 18.52 mmol) in THF (300 mL). The solution was cooled to −78 °C and after stirring for 10 min, *n*-BuLi (9.3 mL, 2.0 M in cyclohexane, 18.60 mmol) was added dropwise over 15 min via syringe. Stirring was continued for an additional 30 min, at which time the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (5 mL) at −78 °C. On warming to room temperature a white cotton-like precipitate formed and was collected by filtration. The white precipitate was washed with EtOAc (2 × 100 mL) and dried under high vacuum to 1.2 g (30%) of (+)-**13** as a white solid. The solution was concentrated and the reaction mixture was worked-up as described earlier to give 0.99 g (24%) of (+)-**8a**.

(+)-13: mp 180−182 °C dec; $[\alpha]^{20}_D$ +8.1 (*c* 0.2, CH_3OH); IR (KBr) 3401, 3192, 3003, 2952, 1244, 1053 cm^{-1}; ^{1}H NMR (CD_3-OD) δ 2.37 (s, 3 H), 3.45 (d, $^3J_{HP}$ = 10.4 Hz, 3 H), 3.79 (s, 3 H), 4.26 (dd, $^2J_{HP}$ = 10.8 Hz, ^3J = 6.4 Hz, 1 H), 4.88 (dd, $^3J_{HP}$ = 9.6 Hz, ^3J = 6.4 Hz, 1 H), 6.74 (d, J = 8.2 Hz, 2 H), 7.21−7.25 (m, 4 H), 7.49 (d, J = 8.2 Hz, 2 H); ^{1}H NMR (d^6-DMSO) δ 2.19 (s, 3 H), 3.24 (d, J = 3.9 Hz, 3 H), 3.61 (s, 3 H), 3.82 (t, J = 8.7 Hz, 1 H), 4.46 (d × t, J = 3.3 Hz, J = 8.6 Hz, 1 H), 6.56 (d, J = 8.6 Hz, 2 H), 7.00 (d, J = 8.7 Hz, 2 H), 7.03 (d, J = 8.2 Hz, 2 H), 7.17 (br s, 1 H, −OH), 7.22 (d, J = 8.0 Hz, 2 H), 8.07 (d, J = 2.8 Hz, 1 H, −NH); ^{13}C NMR (CD_3OD) δ 21.6, 53.6, 56.0, 59.0 (d, $^1J_{CP}$ = 140.2 Hz), 60.0, 114.3, 127.4, 130.7, 131.5, 132.9, 142.3, 142.8, 160.8; ^{31}P NMR ($CDCl_3$) δ 12.85; HRMS calcd for $C_{17}H_{21}ClNO_5PS$ (M) 417.0567, found 417.0571.

(S_S)-(+)-*N*-(*p*-Toluenesulfinyl)-*N*-methyl-1-phenylvinylamine (16) Prepared from Dimethyl Chloromethylphosphonate. In a 50-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed sulfinimine (*S*)-(+)-**14** (0.14 g, 0.545 mmol) in THF (15 mL). The solution was cooled to 0 °C, LiHMDS (1 M in THF, 0.60 mL, 0.6 mmol, 1.1 equiv) was added via syringe, and after 10 min, **7** (0.086 g, 0.545 mmol) was added dropwise via syringe. The reaction mixture was stirred for 16 h at which time saturated aqueous NH_4Cl (1 mL) and H_2O (3 mL) were added. The reaction mixture was extracted with Et_2O (10 mL), and EtOAc (3 × 10 mL) and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a brown oil. Flash chromatography (CH_2Cl_2−EtOAc, 4:1) afforded 0.075 g (51%) of a slightly yellow oil; $[\alpha]^{20}_D$ +53.6 (*c* 0.3, $CHCl_3$); IR (neat) 2955, 1253, 1031 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3 H), 2.51 (s, 3 H), 4.67 (d, $^2J_{HH}$ = 0.8 Hz, 1 H), 4.72 (d, $^2J_{HH}$ = 0.96 Hz, 1 H), 7.18−7.52 (m, 11 H); ^{13}C NMR ($CDCl_3$) δ 21.8, 29.9, 99.8, 125.9, 128.3, 128.9, 129.3, 130.1, 138.1, 140.2, 141.9, 151.6; HRMS calcd for $C_{16}H_{17}NOS$ (M) 271.1031, found 271.1037.

From Iodomethane. In a 25-mL, oven-dried, two necked, round-bottom flask fitted with a magnetic stirring bar, a rubber septum, and an argon balloon was placed (*S*)-(+)-**14** (0.11 g, 0.43 mmol) in THF (5 mL). The solution was cooled to 0 °C, and LiHMDS (1 M in THF, 0.5 mL, 0.5 mmol) was added via syringe. After the reaction mixture was stirred for 15 min, iodomethane (0.072 mL, 0.50 mmol) was added, and the solution was stirred for 30 min at 0 °C, warmed to room temperature for 20 min, and cooled to °C. To the reaction mixture was added H_2O (1 mL) and ethyl acetate (5 mL), the organic phase was separated, and the aqueous phase was

extracted with EtOAc (2 × 5 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated to give a brown oil. Flash chromatography (hexanes−EtOAc, 9:1) afforded 0.094 g (79%) of (+)-**16** as a slightly yellow oil.

Diethyl (*S*$_S$,1*S*,2*R*)-(+)-1-(*p*-Toluenesulfonyloxy)-2-phenyl-2-(*p*-toluenesulfinamide)ethylphosphonate (18). In a 100-mL, two-necked, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (*S*)-(+)-**4b** (0.24 g, 1.0 mmol) and diethyl-*p*-toluenesulfonyloxymethyl phosphonate (**17**) (0.62 g, 2.0 mmol) in THF (20 mL). The solution was cooled to −78 °C, and after 10 min, LiHMDS (1 M solution in THF, 2.0 mL, 2.0 mmol) was added via syringe. After stirring at −78 °C for 30 min, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (5 mL) and warmed to room temperature. After dilution with water (20 mL), the reaction mixture was extracted with EtOAc (3 × 25 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated to give a viscous mass. Flash chromatography (hexanes−EtOAc, 50:50) afforded 0.29 g (52%) of a viscous mass; $[\alpha]_D$ +53.2 (*c* 0.5, $CHCl_3$); IR (neat) 3286, 3059, 1373, 1249 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (t, J = 7.1 Hz, 3 H), 0.97 (t, J = 7.1 Hz, 3 H), 2.18 (s, 3 H), 2.31 (s, 3 H), 3.49−3.33 (m, 1 H), 3.56−3.51 (m, 2 H), 3.85−3.79 (m, 1 H), 4.66 (ddd, J = 5.2 Hz, J = 10.2 Hz, J = 30.0 Hz, 1 H), 5.19 (dd, J = 5.2 Hz, J = 10.2 Hz, 1 H), 6.31 (d, J = 10.2 Hz, 1 H), 7.04−6.98 (m, 7 H), 7.21(d, J = 8.2 Hz, 2 H), 7.32 (d, J = 8.2 Hz, 2 H), 7.77 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.22 (d, $^3J_{CP}$ = 6.1 Hz), 16.44 (d, $^3J_{CP}$ = 6.1 Hz), 21.7, 22.1, 54.9, 63.37 (d, $^2J_{CP}$ = 6.2 Hz), 64.35 (d, $^2J_{CP}$ = 7.6 Hz), 76.7 (d, $^1J_{CP}$ = 159.0 Hz), 126.8, 128.0, 128.24, 128.29, 129.1, 130.3, 132.9, 137.15, 137.19, 140.0, 141.5, 145.6; ^{31}PNMR ($CDCl_3$) δ 15.88; HRMS calcd for $C_{26}H_{32}NO_7PS_2Na$ (M + Na) 588.1256, found 588.1276.

Diethyl (S$_S$,2*S*,3*R*)-(+)-*N*-(*tert*-Butanesulfinyl)-3-phenylaziridine-2-phosphonate (21). In a 25-mL, two-neck, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon were placed sulfinimine (+)-**20** (0.13 g, 0.61 mmol) and diethyl iodomethylphosphonate (**2c**) (0.28 g, 1.0 mmol) in THF (10 mL). The solution was cooled to −78 °C, and after 10 min LiHMDS (1 M in THF, 1.0 mL, 1.0 mmol) was added via syringe. After being stirred at −78 °C 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 (25 mL) and the reaction mixture was extracted with EtOAc (2 × 25 mL). The combined organic phases were washed with sat. sodium thiosulfate and brine, dried ($MgSO_4$), and concentrated to give a yellow oil. Flash chromatography (EtOAc−hexane, 1:1) afforded 0.17 g (82%) as a colorless oil; $[\alpha]_D^{20}$ +46.8 (*c* 0.6, $CHCl_3$); IR (neat) 1250, 1027 cm^{-1}; ^{1}H NMR (CD_3Cl) δ 1.05 (t, J = 7.1 Hz, 3 H), 1.14 (t, J = 7.1 Hz, 3 H), 1.19 (s, 9 H), 2.51 (dd, J = 7.4 Hz, 15.9 Hz, 1 H), 3.88−3.76 (m, 5 H), 7.28−7.22 (m, 3 H), 7.44−7.41 (m, 2 H); ^{13}C NMR (CD_3Cl) δ 16.61 (d, $^3J_{CP}$ = 5.8 Hz), 16.69 (d, $^3J_{CP}$ = 6.0 Hz), 23.0, 33.6 (d, $^1J_{CP}$ = 209.1 Hz), 36.2, 57.7, 62.50 (d, $^2J_{CP}$ = 6.0 Hz), 62.70 (d, $^2J_{CP}$ = 5.8 Hz), 128.43, 128.54, 128.9, 133.1; ^{31}P NMR (CD_3Cl) δ 18.40; HRMS calcd for $C_{17}H_{27}NO_4PS$ (M + H) 360.1398, found 360.1392.

Dimethyl (S$_S$,2*S*,3*R*)-(−)-*N*-(*p*-Toluenesulfinyl)-3-(*p*-methoxyphenyl)aziridine-2-phosphonate (22a): Typical Procedure. In a 500-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (+)-**8a** (1.27 g, 2.96 mmol) in THF (150 mL). The stirred solution was cooled to −78 °C and after 10 min *n*-BuLi (1.78 mL, 2.0 M in cyclohexane, 3.56 mmol) was added dropwise via syringe. The solution was slowly warmed to room temperature, stirred for 1 h, and quenched with saturated aqueous NH_4Cl (10 mL). The mixture was extracted with Et_2O (100 mL) and EtOAc (3 × 50 mL) and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a colorless oil. Flash chromatography (CH_2Cl_2-EtOAc, 3:1) afforded 0.97 g (82%) of a colorless oil; $[\alpha]^{20}_D$ −66.0 (*c* 1.9, $CHCl_3$); IR (neat) 3124, 2956, 1250, 1032 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 2.80 (dd, ^3J = 7.5 Hz, $^2J_{HP}$ = 16.5 Hz, 1 H), 3.41 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 3.53 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 3.71 (s, 3 H), 3.90−3.91 (m, 1 H), 6.68 (d, J = 8.5 Hz, 2 H), 6.98 (d, J = 9.0 Hz, 2 H), 7.28 (d, J = 8.5 Hz, 2 H), 7.65 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 22.2, 34.4, 36.1, 53.4 (d, $^2J_{CP}$ = 6.0 Hz), 53.6 (d, $^2J_{CP}$ = 6.0 Hz), 55.8, 113.9, 125.3, 125.6, 129.7, 130.4, 141.5, 143.2, 159.8; ^{31}P NMR ($CDCl_3$) δ 20.37; HRMS calcd for $C_{18}H_{22}O_5NPSClNa$ (M + Na) 418.0854, found 418.0840.

Dimethyl (S$_S$,2*S*,3*R*)-(−)-*N*-(*p*-Toluenesulfinyl)-3-phenylaziridine-2-phosphonate (22b). Yield 85%; $[\alpha]^{20}_D$ −46.1 (*c* 0.9, $CHCl_3$); IR (neat) 2956, 1249, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.39 (s, 3 H), 2.88 (dd, $^2J_{HP}$ = 16.5 Hz, ^3J = 7.3 Hz, 1 H), 3.37 (d, J = 10.7 Hz, 3 H), 3.54 (d, J = 11.0 Hz, 3 H), 3.97 (m, 1 H), 7.06 (m, 2 H), 7.17 (m, 3 H), 7.30 (d, J = 8.0 Hz, 2 H), 7.68 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.4, 33.1, 33.9, 35.9, 52.5, 52.8, 124.5, 127.7, 129.7, 132.9, 140.6, 142.4; ^{31}P NMR ($CDCl_3$) δ 20.14; HRMS calcd for $C_{17}H_{21}NO_4PS$ (M + H) 366.0928, found 366.0930. Anal. Calcd for $C_{17}H_{20}NO_4PS$: C, 55.88; H, 5.52; N, 3.83. Found: C, 55.51; H, 5.23; N, 3.59.

Diethyl (S$_S$,2*R*,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-phenylaziridine-2-phosphonate (6). Yield 73%; $[\alpha]^{20}_D$ +147.0 (*c* 0.46, $CHCl_3$); IR (neat) 1254, 1023 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11 (t, ^3J = 7.0 Hz, 3 H), 1.30 (t, ^3J = 7.0 Hz, 3 H), 2.42 (s, 3 H), 3.45 (dd, $^2J_{HP}$ = 15.5 Hz, ^3J = 4.5 Hz, 1 H), 3.58−3.63 (m, 1 H), 3.89−3.94 (m, 1 H), 4.07−4.14 (m, 3 H), 7.20−7.32 (m, 2 H), 7.36−7.44 (m, 5 H), 7.64−7.66 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.8 (d, $^3J_{CP}$ = 6.0 Hz), 17.0 (d, $^3J_{CP}$ = 4.0 Hz), 21.4, 29.7, 44.4 (d, $^2J_{CP}$ = 8.0 Hz), 62.7 (d, $^2J_{CP}$ = 6.0 Hz), 62.9 (d, $^2J_{CP}$ = 6.0 Hz), 125.2, 128.6, 128.9, 129.1, 129.4, 131.8, 141.8, 142.2; ^{31}P NMR ($CDCl_3$) δ 24.03. Anal. Calcd for $C_{19}H_{24}NO_4PS$: C, 58.00; H, 6.15; N, 3.56. Found: C, 58.23; H, 6.15; N, 3.46.

Dimethyl (S$_S$,2*S*,3*R*)-(−)-*N*-(*p*-Toluenesulfinyl)-3-(*p*-nitrophenyl)aziridine-2-phosphonate (22c). Yield 82%; mp 123−124°C; $[\alpha]^{20}_D$ −126.2 (*c* 0.48, $CHCl_3$); IR (KBr) 3031, 2955, 2852, 1520, 1348, 1263, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.84 (dd, $^2J_{HP}$ = 4.0 Hz, ^3J = 7.6 Hz, 1 H), 3.49 (d, $^3J_{HP}$ = 10.96 Hz, 3 H), 3.52 (d, $^3J_{HP}$ = 10.96 Hz, 3 H), 3.87 (t, ^3J = 7.6 Hz, 1 H), 7.13 (d, J = 8.8 Hz, 2 H), 7.26 (d, J = 8.0 Hz, 2 H), 7.58 (d, J = 8.0 Hz, 2 H), 7.95 (d, J = 6.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.9, 33.4 (d, $^2J_{CP}$ = 5.0 Hz), 34.3 (d, $^1J_{CP}$ = 204.8 Hz), 53.3 (2 × d, $^2J_{CP}$ = 6.3 Hz), 123.4, 124.8, 129.2, 130.3, 140.8, 143.4, 147.9; ^{31}P NMR ($CDCl_3$) δ 19.22; MS *m*/*z* 433.1 (100%, M + Na); HRMS calcd for $C_{17}H_{19}N_2O_6PSNa$ (M + Na) 433.0599, found 433.0610.

Dimethyl (S$_S$,2*R*,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl)-3-(*p*-nitrophenyl)aziridine-2-phosphonate (23c). Yield 64%; colorless oil; $[\alpha]^{20}_D$ +147.1 (*c* 0.35, $CHCl_3$); IR (neat) 3049, 2955, 2853, 1521, 1347, 1257, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3 H), 3.32−3.35 (br s, 1 H), 3.43 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 3.73 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 4.13 (dd, $^3J_{HP}$ = 9.0 Hz, ^3J = 5.0 Hz, 1 H), 7.29 (d, J = 8.0 Hz, 2 H), 7.51 (d, J = 8.0 Hz, 2 H), 7.60 (d, J = 8.0 Hz, 2 H), 8.19 (d, J = 8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.8, 33.5, 42.6, 53.7 (2 × d, $^2J_{CP}$ = 6.3 Hz), 124.1, 125.3, 130.1, 130.3, 140.2, 141.9, 142.8, 148.4; ^{31}P NMR ($CDCl_3$) δ 20.81. All attempts to obtain an HRMS of this material were unsuccessful because of its instability.

Dimethyl (S$_S$,2*S*,3*R*)-(−)-*N*-(*p*-Toluenesulfinyl)-3-(*p*-trifluoromethylphenyl)aziridine-2-phosphonate (22d). Yield 78%; colorless oil; $[\alpha]^{20}_D$ −28.4 (*c* 0.28, $CHCl_3$); IR (NaCl) 3070, 2958, 2875, 1326, 1253, 1066 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.81 (dd, ^3J = 7.44 Hz, $^2J_{HP}$ = 16.1 Hz, 1 H), 3.41 (d, $^3J_{HP}$ = 10.9 Hz, 3 H), 3.47 (d, $^3J_{HP}$ = 10.9 Hz, 3 H), 3.89 (m, 1 H), 7.08 (d, J = 8.3 Hz, 2 H), 7.24 (d, J = 8.0 Hz, 2 H), 7.35 (d, J = 8.2 Hz, 2 H), 7.59 (d, J = 8.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.9, 33.8 (d, $^2J_{CP}$ = 5.0 Hz), 34.0 (d, $^1J_{CP}$ = 208.3 Hz), 53.1 (d, $^2J_{CP}$ = 6.3 Hz), 53.4 (d, $^2J_{CP}$ = 6.0 Hz), 124.9, 125.2 (d, J = 3.1 Hz), 128.7, 129.6, 130.3, 137.5, 140.9, 143.2, 145.0; ^{31}P NMR ($CDCl_3$) δ 19.64; ^{19}F NMR ($CDCl_3$) δ −63.05; HRMS calcd for $C_{18}H_{19}F_3NO_4PSNa$ (M + Na) 456.0622, found 456.0614.

Dimethyl (2*S*,3*R*)-(−)-3-Phenylaziridine-2-phosphonate (24). In a 25-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed *N*-sulfinyl aziridine (−)-**5** (0.121 g, 0.308 mmol) dissolved in acetone−H_2O (1:1, 3 mL). To the vigorously stirred solution was added TFA (1.2 mL, 15.6 mmol) via syringe. After being stirred for 1 h, the reaction mixture was diluted with H_2O (10 mL) and aq NH_4OH added until pH 9 was attained. The reaction mixture was extracted with Et_2O (2 × 20 mL) and CH_2Cl_2 (2 × 20 mL), the combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a green oil. Flash chromatography (EtOAc) afforded 0. 066 g (84%) of a colorless oil; $[\alpha]^{20}_D$ −36.5 (*c* 0.85, $CHCl_3$); IR (KBr) 3252, 1239, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11(t, ^3J = 7.0 Hz, 3 H), 1.15 (t, ^3J = 7.0 Hz, 3 H), 1.26 (s, 1 H), 2.39−2.45 (m, 1 H), 3.52−3.63 (m, 2 H), 3.78−3.91 (m, 3 H), 7.25−7.28 (m, 1 H), 7.32−7.35 (m, 2 H), 7.46−7.48 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.0, 16.1, 31.4 (d, $^1J_{CP}$ = 208.0 Hz), 37.5, 61.5 (d, $^2J_{CP}$ = 6.0 Hz), 62.6 (d, $^2J_{CP}$ = 4.0 Hz), 127.3, 127.7, 127.8, 135.5; ^{31}P NMR ($CDCl_3$) δ 22.46; HRMS calcd for $C_{12}H_{19}NO_3P$ (M + H) 256.1103, found 256.1090.

Dimethyl (2*R*,3*R*)-(+)-3-Phenylaziridine-2-phosphonate (25). In a 100-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed sulfinyl aziridine (+)-**6** (0.366 g, 0.93 mmol) dissolved in acetone−H_2O (1:1, 12 mL). To the vigorously stirred solution at 0 °C was added TFA (358 μL, 4.65 mmol) via syringe. After being stirred for 15 min at 0 °C, the reaction mixture was diluted with H_2O (50 mL), aqueous NH_4OH was added until pH 9 was attained, and the solution was extracted with Et_2O (2 × 75 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a colorless oil. Flash chromatography (CH_2Cl_2−EtOAc, 5:1) afforded 0.215 g (91%) of a colorless oil; $[\alpha]^{20}_D$ +38.5 (*c* 0.89, $CHCl_3$); IR (KBr) 3238, 1239, 1023 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, ^3J = 7.0 Hz, 3 H), 1.40 (t, ^3J = 7.0 Hz, 3 H), 1.61 (s, 1 H), 1.92−1.97 (m, 1 H), 3.40−3.44 (m, 1 H), 4.14−4.24 (m, 4 H), 7.24−7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 16.4, 16.5, 33.2 (d, $^1J_{CP}$ = 187.0 Hz), 36.1, 62.6 (d, $^2J_{CP}$ = 6.0 Hz), 62.7 (d, $^2J_{CP}$ = 6.0 Hz), 125.9, 127.7, 128.6, 137.8; ^{31}P NMR ($CDCl_3$) δ 24.59. Anal. Calcd for $C_{12}H_{18}O_3NP$: C, 56.47; H, 7.11; N, 5.49. Found: C, 56.28; H, 7.29; N, 5.35.

Dimethyl (2*S*,3*R*)-(−)-3-(*p*-Methoxyphenyl)aziridine-2-phosphonate (26a): Typical Procedure. In a 250-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed (−)-**22a** (0.954 g, 2.42 mmol) in THF (100 mL). The solution was cooled to −78 °C and after 10 min, MeMgBr (1.61 mL, 3.0 M in Et_2O) was added dropwise via syringe. After being stirred at −78 °C for 2 h, the reaction mixture was quenched by addition of H_2O (5 mL) and warmed to room temperature. Aqueous NH_4-OH was added until pH 10 was attained and the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a colorless oil. Flash chromatography (CH_2Cl_2−EtOAc, 4:1) afforded 0.49 g (79%) of a white solid; mp 50−51 °C; $[\alpha]^{20}_D$ −28.0 (*c* 0.5, $CHCl_3$); IR (KBr) 3433, 3279, 3011, 2980, 1249, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52 (br s, 1 H), 2.50 (br s, 1 H), 3.30∼3.56 (m, 7 H), 3.79 (s, 3 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 7.41 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 31.0 (d, $^1J_{CP}$ = 216.0 Hz), 37.1, 52.9, 53.4, 55.9, 114.0, 129.3, 129.7, 159.7; ^{31}P NMR ($CDCl_3$) δ 24.72; HRMS calcd for $C_{11}H_{16}O_4NPNa$ (M + Na) 280.0715, found 280.0719. Anal. Calcd for $C_{11}H_{16}O_4NP$: C, 51.36; H, 6.27; N, 5.45. Found: C, 51.50; H, 6.37; N, 5.42.

Dimethyl (2*S*,3*R*)-(−)-3-Phenylaziridine-2-phosphonate (26b). Yield 70%; mp 55−56 °C; $[\alpha]^{20}_D$ −49.0 (*c* 1.0, $CHCl_3$); IR (KBr) 3235, 1266, 1042 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.71 (br, 1 H), 2.45 (m, 1 H), 3.31 (d, *J* = 9.0 Hz, 3 H), 3.50 (d, *J* = 10.6 Hz, 3 H), 3.58 (m, 1 H), 7.27 (m, 1 H), 7.34 (m, 2 H), 7.47 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.9, 32.5, 37.7, 52.8 (d, *J* = 6.1 Hz), 53.2 (d, *J* = 6.1 Hz), 128.0, 128.4, 128.5, 136.4; ^{31}P NMR ($CDCl_3$) δ 24.84; HRMS calcd for $C_{10}H_{15}NO_3P$ (M + H) 228.0789, found 228.0792. Anal. Calcd for $C_{10}H_{15}NO_3P$: C, 52.86; H, 6.21; N, 6.17. Found: C, 52.88; H, 6.09; N, 5.84.

Dimethyl (2*S*,3*R*)-(−)-3-(*p*-Nitrophenyl)aziridine-2-phosphonate (26c). Yield 82%; mp 145−147 °C; $[\alpha]^{20}_D$ −50.0 (*c* 0.25, $CHCl_3$); IR (KBr) 3281, 3241, 3001, 2956, 2863, 1508, 1344, 1027 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70 (br s, 1 H, NH), 2.58−2.61 (br s, 1 H), 3.49 (d, $^3J_{HP}$ = 11.0 Hz, 3 H), 3.56 (d, $^3J_{HP}$ = 10.5 Hz, 3 H), 3.64 (m, 1 H), 7.64 (d, *J* = 9.0 Hz, 2 H), 8.20 (d, *J* = 10.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.9 (d, $^1J_{CP}$ = 213.9 Hz), 37.1, 52.9 (d, $^2J_{CP}$ = 38.5 Hz), 123.5, 129.3, 143.5, 147.8; ^{31}P NMR ($CDCl_3$) δ 23.6059; HRMS calcd for $C_{10}H_{14}N_2O_5P$ (M + H) 273.0640, found 273.0637.

Dimethyl (2*S*,3*R*)-(−)-3-(*p*-Trifluoromethylphenyl)-aziridine-2-phosphonate (26d). Yield 72%; white solid, mp 90−92 °C; $[\alpha]^{20}_D$ −44.8 (*c* 0.65, $CHCl_3$); IR (KBr) 3226, 2995, 2851, 1264, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (br s, 1 H), 2.48−2.57 (m, 1 H), 3.29 (d, $^3J_{HP}$ = 10.8 Hz, 3 H), 3.48 (d, $^3J_{HP}$ = 10.8 Hz, 3 H), 3.53−3.59 (m, 1 H), 7.51−7.56 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 30.7 (d, $^1J_{CP}$ = 216.5 Hz), 36.9 (d, $^2J_{CP}$ =3.1 Hz), 52.7 (d, $^2J_{CP}$ = 5.8 Hz), 53.2 (d, $^2J_{CP}$ = 5.6 Hz), 125.2, 128.8, 129.6, 130.5, 140.3; ^{31}P NMR ($CDCl_3$) δ 23.9; ^{19}F NMR ($CDCl_3$) δ −62.89. Anal. Calcd for $C_{11}H_{13}F_3NO_3P$: C, 44.76; H, 4.44; N, 4.74. Found: C, 44.44; H, 4.54; N, 4.33.

General Procedure for Hydrogenation of Aziridines: Diethyl (*S*)-(+)-1-Amino-2-phenylethylphosphonate (27). In a 10-mL, round-bottom flask equipped with a magnetic stirring bar, rubber septum, and argon balloon was placed aziridine (−)-**24** (0.033 g, 0.129 mmol) and Pd/C (0.035 g, 10% Pd) in MeOH (1 mL). To the stirred solution was added HCO_2-NH_4 (0.070 g, 1.11 mmol) in one portion, and after being stirred for 16 h, the reaction mixture was filtered through Celite and the residue was washed with MeOH (2 × 5 mL) and Et_2O (2 × 5 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give a pale yellow oil. Flash chromatography (EtOAc−MeOH, 19:1) afforded 0.033 g (99%) of a yellow oil; $[\alpha]^{20}_D$ +16.9 (*c* 0.9, $CHCl_3$) [lit.[19] $[\alpha]^{25}_D$ +17.9]; IR (neat) 3376, 3299, 1242, 1026 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (br s, 2 H), 1.37 (t, ^3J = 7.0 Hz, 3 H), 1.38 (t, ^3J = 7.0 Hz, 3 H), 2.65−2.72 (m, 1 H), 3.22−3.32 (m, 2 H), 4.17−4.24 (m, 4 H), 7.25−7.28 (m, 3 H), 7.33−7.36 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.4, 16.5, 37.8, 50.2 (d, $^1J_{cp}$ = 155.0 Hz), 61.2 (d, $^2J_{cp}$ = 6.0 Hz), 62.3 (d, $^2J_{cp}$ = 6.0 Hz), 126.6, 128.5, 129.1, 137.8 (d, $^3J_{cp}$ = 16.0 Hz); ^{31}P NMR ($CDCl_3$) δ 28.07; HRMS calcd for $C_{12}H_{21}$-NO_3P (M + H) 258.1249, found 258.1259. Anal. Calcd for $C_{12}H_{20}NO_3P$: C, 56.02; H, 7.84. Found C, 56.21; H, 7.84. Mosher amide from (+)-Mosher's acid chloride δ_F −69.44 (internal reference $CFCl_3$) indicated that (*S*)-(+)-**27** was >96% ee.

Diethyl (*R*)-(−)-1-Amino-2-phenylethylphosphonate (28). The same procedure as for the preparation of (+)-**27** was applied. Flash chromatography (EtOAc−MeOH, 19:1) afforded (−)-**28** as a colorless oil (83%, 0.108 mmol scale), which exhibited spectroscopic data as for (+)-**27**. $[\alpha]^{20}_D$ −16.5 (*c* 0.9, $CHCl_3$) [lit.[20] $[\alpha]$ −18.1 (*c* 1.66, $CHCl_3$)]. Mosher amide from (+)-Mosher's acid chloride δ_F −69.55 (internal reference $CFCl_3$).

Dimethyl (*S*)-(+)-1-Amino-2-(*p*-methoxyphenyl)ethylphosphonate (29a). Yield 81%; $[\alpha]^{20}_D$ +19.2 (*c* 1.2, $CHCl_3$); IR (neat) 3374, 3301, 3055, 2952, 1246, 1032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (br s, 2 H), 2.57−2.64 (m, 1 H), 3.12−3.17 (m, 1 H), 3.22−3.28 (m, 1 H), 3.78 (s, 3 H), 3.79 (d, $^3J_{HP}$ = 6.0 Hz, 3 H), 3.81 (d, $^3J_{HP}$ = 5.5 Hz, 3 H), 6.84 (d, *J* = 8.5 Hz, 2 H), 7.13 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR($CDCl_3$) δ 37.3, 49.8 (d, $^1J_{CP}$ = 153.3 Hz), 53.4 (2 × d, $^2J_{CP}$ = 9.8 Hz), 55.7, 114.4, 129.8 (d, $^3J_{CP}$ = 16.1 Hz), 130.6, 158.9; ^{31}P NMR ($CDCl_3$) δ 30.47; HRMS calcd for $C_{11}H_{18}NO_4PNa$ (M + Na) 282.0871, found 282.0878.

Dimethyl (*S*)-(+)-1-Amino-2-phenylethylphosphonate (29b). Yield 98%; $[\alpha]^{20}_D$ +25.9 (*c* 0.9, $CHCl_3$); IR (neat) 3377, 3308, 2952, 1244, 1031 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (br s, 2 H), 2.68 (m, 1 H), 3.22 (m, 1 H), 3.32 (m, 1 H), 3.81 (d, *J* = 5.9

Hz, 3 H), 3.83 (d, J = 5.8 Hz, 3 H), 7.25 (m, 3 H), 7.33 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 38.2, 50.4 (d, $^1J_{CP}$ = 155.1 Hz), 53.5 (2 × d, J = 11.1 Hz), 127.2, 129.0, 129.6, 138.1; ^{31}P NMR ($CDCl_3$) δ 30.35; HRMS calcd for $C_{10}H_{16}NO_3PNa$ (M + Na) 252.0762, found 252.0774.

Dimethyl (*S*)-(+)-1-Amino-2-(*p*-trifluoromethylphenyl)ethylphosphonate (29c). Colorless oil; yield 67%; $[\alpha]^{20}_D$ +16.5 (*c* 1.0, $CHCl_3$); IR (neat) 3370, 3305, 1245, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19 (br s, 2 H), 2.64−2.74 (m, 1 H), 3.15−3.19 (m, 1 H), 3.21−3.27 (m, 1 H), 3.73 (d, $^3J_{HP}$ = 4.3 Hz, 3 H), 3.76 (d, $^3J_{HP}$ = 4.3 Hz, 3 H), 7.28 (d, J = 8.0 Hz, 2 H), 7.52 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 38.5, 49.9 (d, $^1J_{CP}$ = 152.7 Hz), 53.9 (2 × d, $^2J_{CP}$ = 6.8 Hz), 126.3, 129.8, 130.4, 130.6, 142.7 (d, $^3J_{CP}$ = 16.7 Hz); ^{31}P NMR ($CDCl_3$) δ 29.72; ^{19}F NMR ($CDCl_3$) δ −62.912; HRMS calcd for $C_{11}H_{15}NO_3F_3PNa$ (M + Na) 320.0639, found 320.0649.

Acknowledgment. We thank Professor Louis D. Quin for stimulating discussions. This work was supported by a grant from the National Institute 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.

JO020707Z