JOC*Article*

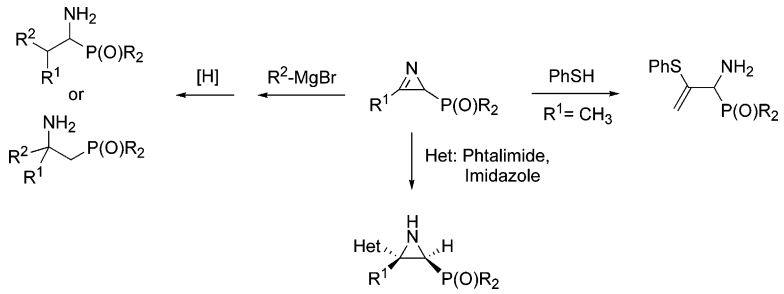
Reaction of 2*H*-Azirine Phosphine Oxide and -Phosphonates with Nucleophiles. Stereoselective Synthesis of Functionalized Aziridines and α- and *β*-Aminophosphorus Derivatives†

Francisco Palacios,* Ana M. Ochoa de Retana, and José M. Alonso

Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco, Apartado 450, 01080 - Vitoria, Spain

francisco.palacios@ehu.es

Received July 7, 2005



A simple and efficient stereoselective synthesis of aziridine-2-phosphonate **3**, and -phosphine oxide **5** by diastereoselective addition of Grignard reagents to 2*H*-azirine phosphonate **1** and -phosphine oxide **4** is reported. Similarly, the addition of heterocyclic amines and benzenethiol to aziridines **1** and **4** yielded functionalized aziridines **10**, **11**, and **18**. These aziridines are used as intermediates for the regioselective synthesis of *β*-aminophosphine oxides **6** and *β*-aminophosphonates **7**, as well as α- aminophosphonates **8**. Phenylsulfenyl-substituted α-aminophosphorus derivatives **15** and **19** are obtained directly from benzenethiol and 2*H*-azirine phosphonates **1** and -phosphine oxides **4**.

Introduction

2*H*-Azirine ring systems represent an important class of compounds because of their high reactivity.[1] They can be used as key intermediates in organic synthesis in the preparation of heterocycles[2a−e] and acyclic functionalized amino derivatives,[2f,g] since all three bonds of the azirine ring can be cleaved, depending on the experimental conditions used. In particular, 2*H*-azirines containing a carboxylic ester group **I** (Scheme 1) are constituents of naturally occurring antibiotics[1d] and are excellent reagents for the preparation of functionalized aziridines[1,2b,c,3] and α-[2c,3b,4a−c] and *β*-amino acid derivatives.[2c,3b,4d,e] 2*H*-Azirine phosphine oxides **IIa** and -phosphonates **IIb** (Scheme 1) may represent an important tool in organic synthesis because these small strained heterocycles are expected to play a role similar to that of their isosteric analogues **I** and therefore could be used as starting materials for the preparation of phosphorus-substituted aziridines and α- or *β*-aminophosphorus derivatives. α-Aminophosphonates[5] can be considered as surrogates

* Corresponding author. Phone: (+34) 945-013103. Fax: (+34) 945-013049.

† Dedicated to Prof. José Barluenga on the occasion of his 65th birthday.

(1) For recent reviews on azirines, see: (a) Pinho e Melo, T. M. V. D.; d'A Rocha Gonsalves, A. M. *Curr. Org. Synth*. **2004**, *1*, 275−292. (b) Palacios, F.; Ochoa de Retana, A. M.; Martínez de Marigorta, E.; de los Santos, J. M. *Org. Prep. Proced. Int.* **2002**, *34*, 219−269. (c) Gilchrist, T. L. *Aldrichimica Acta* **2001**, *34*, 51−55. (d) Palacios, F.; Ochoa de Retana, A. M.; Martínez de Marigorta, E.; de los Santos, J. M. *Eur. J. Org. Chem.* **2001**, 2401−2414.

(2) For recent contributions, see: (a) Padwa, A.; Stengel, T. *Tetrahedron Lett.* **2004**, *45*, 5991−5993. (b) Moneen, K.; Laureyn, I.; Stevens, C. V. *Chem. Rev.* **2004**, *104*, 6177−6215. (c) Zhou, P.; Chen, B.-C.; Davis, F. A. *Tetrahedron* **2004**, *60*, 8003−8030. (d) Pinho e Melo, T. M. V. D.; Cardoso, A. L.; d'A Rocha Gonsalves, A. M. *Tetrahedron* **2003**, *59*, 2345−2351. (e) Timen, S.; Somfai, P. *J. Org. Chem.* **2003**, *68*, 9958−9963. (f) Hilty, F. M.; Brun, K. A.; Heimgartner, H. *Helv. Chim. Acta* **2004**, *87*, 2539−2548. (g) Stamm, S.; Heimgartner, H. *Eur. J. Org. Chem.* **2004**, 3820−3827.

(3) (a) Osborn, H. M. I.; Sweeney, J. B. *Tetrahedron: Asymmetry* **1997**, *8*, 1693−1715. (b) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599−619.

(4) (a) Xiong, C.; Wang, W.; Cai, C.; Hruby, V. J. *J. Org. Chem*. **2002**, *67*, 1399−1402. (b) Filigheddu, S. N.; Taddei, M. *Tetrahedron Lett.* **1998**, *39*, 3857−3860. (c) Zwanenburg, B.; Thijs, L. *Pure Appl. Chem.* **1996**, *68*, 735−738. (d) Righi, G.; D'Achielle, R. *Tetrahedron Lett.* **1996**, *37*, 6893−6896. (e) Lim, Y.; Lee, W. K. *Tetrahedron Lett.* **1995**, *36*, 8431−8434.

(5) For reviews, see: (a) Kafarski, P.; Lejczak, B. *Curr. Med. Chem.*: *Anti-Cancer Agents* **2001**, *1*, 301−312. (b) *Aminophosphonic and Aminophosphinic Acids. Chemistry and Biological Activity*; Kukhar, V. P., Hudson, H. R., Eds.; Wiley: Chichester, 2000.

10.1021/jo051404i CCC: $30.25
Published on Web 09/29/2005

SCHEME 1

for α-amino acids[6a] and have been used as haptens for the generation of catalytic antibodies[6b,c] or biologically active compounds,[6c−f] whereas *β*-aminophosphonate derivatives[7] have been used for the preparation of enzyme inhibitors, agrochemicals, or pharmaceuticals.

In this context, we described new methods for the preparation of phosphorus-substituted nitrogen heterocycles[8] from functionalized phosphine oxides and phosphonates and the synthetic uses of aminophosphorus derivatives as starting materials for the synthesis of acyclic compounds[9a] and phosphorus-containing heterocycles.[9b,c] Likewise, we reported the preparation of 2*H*-azirine phosphine oxides **IIa** and -phosphonates **IIb** (Scheme 1) through base-mediated Neber reaction of *β*-ketoxime tosylates and their use for the synthesis of aminophosphorus derivatives[11] and phosphorylated pyrazines[12a] or oxazoles.[12b,c] Continuing with our interest in the chemistry of small strained nitrogen heterocycles, we report here the stereoselective addition of some nucleophilic reagents to phosphorylated azirines and the use of functionalized aziridines as key intermediates for the preparation of new *β*-substituted α- or *β*-aminophosphine oxides and phosphonates in a regioselective fashion.

Results and Discussion

Diastereoselective Addition of Grignard Reagents to 2*H*-Azirines. Due to the strain of the three-membered ring, the electrophilic character of the C−N double bond is higher than that in a normal imine and azirines react with nucleophiles at the N−C3 double bond to produce aziridines.[1] The few reports of the addition of Grignard reagents to 2*H*-azirines reveal that the aziridine product is formed by attack at the least hindered face,[13] in a way similar to that reported for other nucleophiles such as hydrides.[1,10b] However, the presence of carboxylic esters in the azirine ring favors the attack of Grignard reagent to the more hindered face (the same of the carboxylic ester) as a consequence of prechelation of the Grignard reagent with the carboxyl ester group.[14] These reports prompted us to explore whether phosphine oxide and phosphonate group, phosphorus isosteric analogous of the carboxylic group, directly bonded to the azirine ring could produce a similar effect to that observed in the case of carboxylic ester and therefore to explore if the reaction of Grignard reagents with phosphorylated azirines takes place through the more or least hindered face of the azirine ring system.

SCHEME 2

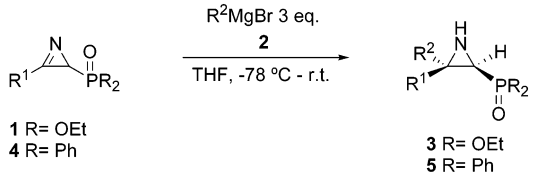


TABLE 1. 3,3-Disubstituted Aziridines 3 and 5 Obtained

entry	compound	R	R^1	R^2	yield (%)[a]
1	**3aa**	OEt	CH_3	C_2H_5	60
2	**3ab**	OEt	CH_3	CH_2−Ph	66
3	**3bc**	OEt	Ph	CH_2−CH=CH_2	87
4	**5aa**	Ph	CH_3	C_2H_5	57
5	**5ac**	Ph	CH_3	CH_2−CH=CH_2	68
6	**5ad**	Ph	CH_3	2-ethyl-[1,3]-dioxolanyl	65
7	**5bc**	Ph	Ph	CH_2−CH=CH_2	63

[a] Yield of isolated purified compounds **3** and **5**.

Reaction of 2*H*-azirine phosphonate **1a** (R = OEt, R^1 = CH_3) with ethylmagnesium bromide **2a** ($R^2 = C_2H_5$) in THF at −78 °C led exclusively to the formation of diethyl *trans*-3-ethyl-3-methylaziridin-2-yl phosphonate **3aa** (R = OEt, $R^1 = CH_3$, $R^2 = C_2H_5$) (Scheme 2, Table 1, entry 1). No trace of the *cis*-aziridine could be observed by ^{31}P NMR. In the ^{31}P NMR spectrum, the diethyl phosphonate group of this aziridine **3aa** resonated at $\delta_P = 25.5$ ppm, while well-resolved doublets at $\delta_H = 1.66$ ppm ($^2J_{PH}$ = 14.7 Hz) for H2 in the ^1H NMR spectrum as well as at $\delta_C = 34.7$ ppm ($^1J_{PC} = 191.9$ Hz) and at $\delta_C = 41.6$ ppm for C2 and C3 in the ^{13}C NMR spectrum were observed. Spectroscopic data were in agreement with the assigned structure of compound **3aa**, and the stereochemical assigment of derivative **3** was based on NOESY 1D experiments. Irradiating the −C2−**H** proton of the aziridine ring at 1.66 ppm showed an enhancement (1.32%) of the methylene group protons ($CH_3C\mathbf{H_2}$−C3) signal at 1.32 ppm (see Figure 1). On the other hand, the irradiation of methyl protons ($C\mathbf{H_3}$−C3) at 1.43 ppm showed an influence in the ethoxy groups bounded to the phosphorus atom with an enhancement (0.30%) of the −O$\mathbf{CH_2}$−

(6) (a) Smith, A. B.; Yager, K. M.; Taylor, C. M. *J. Am. Chem. Soc.* **1995**, *117*, 10879−10888. (b) Smithrud, D. B.; Benkovic, P. A.; Benkovic, S. J.; Taylor, C. M.; Yager, K. M.; Witherington, J.; Phillips, B. W.; Sprengler, P. A.; Smith, A. B.; Hirschmann, R. *J. Am. Chem. Soc.* **1997**, *119*, 278−282. (c) Steere, J. A.; Sampson, P. B.; Honek, J. F. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 457−460. (d) Cristau, H. J.; Coulombeau, A.; Genevis-Borella, A.; Pirat, J. L. *Tetrahedron Lett.* **2001**, *42*, 4491−4494. (e) Georgiadis, D.; Dive, V.; Yiotakis, A. *J. Org. Chem.* **2001**, *66*, 6604−6610. (f) Christensen, B. G.; Beattie, T. R. Ger. Offen. 2.011.092; *Chem Abstr.* **1971**, *74*, 42491.

(7) For a recent review, see: Palacios, F.; Alonso, C.; de los Santos, J. M. *Chem. Rev.* **2005**, *105*, 899−931.

(8) (a) Palacios, F.; Aparicio, D.; López, Y.; de los Santos, J. M.; Alonso, C. *Eur. J. Org. Chem.* **2005**, 1142−1147. (b) Palacios, F.; Ochoa de Retana, A. M.; Martínez de Marigorta, E.; Rodríguez, M.; Pagalday, J. *Tetrahedron* **2003**, *59*, 2617−2623. (c) Palacios, F.; Ochoa de Retana, A. M.; Pagalday, J. *Eur. J. Org. Chem.* **2003**, 913−919.

(9) (a) Palacios, F.; Ochoa de Retana, A. M.; Pascual, S.; Oyarzábal, J. *J. Org. Chem.* **2004**, *69*, 8767−8774. (b) Palacios, F.; Ochoa de Retana, A. M.; Pascual, S.; López de Munáin, R.; Oyarzábal, J.; Ezpeleta, J. M. *Tetrahedron* **2005**, *61*, 1087−1094. (c) Palacios, F.; Alonso, C.; Rodríguez, M.; Martínez de Marigorta, E.; Rubiales G. *Eur. J. Org. Chem.* **2005**, 1795−1804.

(10) (a) Palacios, F.; Aparicio, D.; Ochoa de Retana, A. M.; de los Santos, J. M.; Gil, J. I.; Alonso, J. M. *J. Org. Chem.* **2002**, *67*, 7283−7288. (b) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; Ezpeleta, J. M. *J. Org. Chem.* **2000**, *65*, 3213−3217.

(11) Palacios, F.; Aparicio, D.; Ochoa de Retana, A. M.; de los Santos, J. M.; Gil, J. I.; López de Munáin, R. *Tetrahedron: Asymmetry* **2003**, *14*, 689−700.

(12) (a) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; López de Munáin, R. *Org. Lett.* **2002**, *4*, 2405−2408. (b) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; Alonso, J. M. *Tetrahedron: Asymmetry* **2002**, *13*, 2525−2541. (c) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; Alonso, J. M. *Tetrahedron* **2004**, *60*, 8937−8947.

(13) Carlson, R. M.; Lee, S. Y. *Tetrahedron Lett.* **1969**, *10*, 4001−4004.

(14) (a) Davis, F. A.; Liang, C.-H.; Liu, H. *J. Org. Chem.* **1997**, *62*, 3796−3797. (b) Davis, F. A.; Deng, J.; Zhang, Y.; Haltiwanger, R. C. *Tetrahedron* **2002**, *58*, 7135−7143.

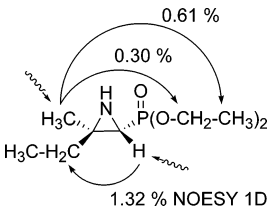


FIGURE 1.

proton signal at 4.10 ppm as well as an enhancement (0.61%) of the $-OCH_2\mathbf{CH_3}$ proton signal at 1.30 ppm. The exclusive formation of *trans*-aziridine **3aa** suggests that the approach of the ethylmagnesium bromide **2a** to cyclic compound from the position opposite the phosphine oxide group is more favorable, due to the high exocyclic dihedral angle of the saturated carbon and to the presence of the bulky phosphorus group, in a way similar to that observed in the case of other nuchelophiles such as hydride.[10b] The scope of the reaction was not limited to ethylmagnesium bromide **2a** ($R^2 = C_2H_5$), but also Grignard reagents containing benzyl substituent **2b** ($R^2 = CH_2-Ph$) as well as olefine groups **2c** ($R^2 = CH_2-CH=CH_2$) reacted with azirines **1a** (R = OEt, $R^1 = CH_3$) and **1b** (R = OEt, R^1 = Ph) to give functionalized *trans*-aziridine phosphonates **3ab** and **3bc** (Scheme 2, Table 1, entries 2 and 3) in a regioselective fashion. Aziridine phosphonates have been also obtained by reaction of α-lithiated halomethylphosphonates[15a,b] with imines, by addition of diethyl phosphite anion to 1-nitro-2,2-diphenylethylene[15c] and by cyclization of α-mesyl β-aminophosphonates.[15d] However, our strategy describes, as far as we know, the first addition of Grignard reagents to 2*H*-azirine-phosphonates, and aziridine derivatives **3** (R = OEt) are formed diastereoselectively by attack of the Grignard reagents at the least hindered face.

This process could also be extended to 2*H*-azirines derived from diphenylphosphine oxide **4**. Treatment of 3-methyl **4a** (R = Ph, $R^1 = CH_3$) and 3-phenyl-2*H*-azirine **4b** (R = Ph, R^1 = Ph) with ethylmagnesium bromide **2a** ($R^2 = C_2H_5$), allylmagnesium bromide **2c** ($R^2 = CH_2-CH=CH_2$), and 2-ethyl-[1,3]-dioxolanylmagnesium bromide **2d** gave diastereoselectively 3,3-disubstituted aziridines **5aa**, **5ac**, **5ad**, and **5bc** (Scheme 2, Table 1, entries 4−7).

Ring Opening of Aziridines. Synthesis of α- and β-Aminophosphorus Derivatives. Aminophosphorus derivatives[5,7] have acquired increased interest in recent years because of their application in organic and medicinal chemistry. For this reason we tried to study if phosphorylated aziridines obtained above by nucleophilic attack of Grignard reagents to azirines could be used for the preparation of α- and β-aminophosphorus derivatives. Catalytic hydrogenation of N-substituted and non-N-substituted aziridines bearing phosphorus functional groups produces the corresponding aminophosphorus derivatives with highly controlled regioselectivity.[15a,16]

(15) (a) Davis, F. A.; Wu, Y.; Yan, H.; McCoull, W.; Prasad, K. R. *J. Org. Chem.* **2003**, *68*, 2410−2419. (b) Coutrot, P.; Abdelaziz, E.; Grison C. *Heterocycles* **1989**, *28*, 1179−1192. (c) Russell, G. A.; Yao, C.-F.; Tashtoush, H. I.; Russell, J. E.; Dedolph, D. F. *J. Org. Chem.* **1991**, *56*, 663−669. (d) Thomas, A. D.; Sharpless, K. B. *J. Org. Chem.* **1999**, *64*, 8379−8385.

(16) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I. *Tetrahedron Lett.* **2000**, *41*, 5363−5366.

SCHEME 3

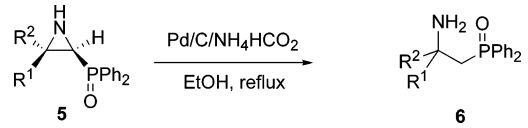
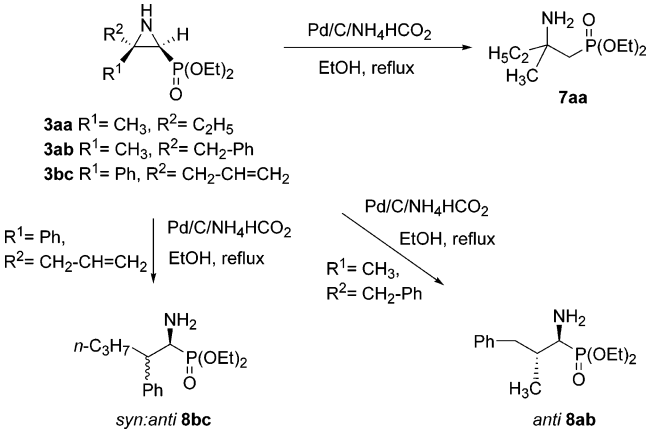


TABLE 2. α- and β-Aminophosphorus Derivatives 6−8 Obtained

entry	starting material	compound	R^1	R^2	yield (%)[a]
1	**5aa**	**6aa**	CH_3	C_2H_5	67
2	**5ac**	**6ac**	CH_3	n-C_3H_7	58
3	**5bc**	**6bc**	Ph	n-C_3H_7	65
4	**3aa**	**7aa**	CH_3	C_2H_5	58
5	**3ab**	**8ab**	CH_3	CH_2-Ph	73
6	**3bc**	**8bc**	Ph	n-C_3H_7	54

[a] Yield of isolated purified compounds **6**, **7**, and **8**.

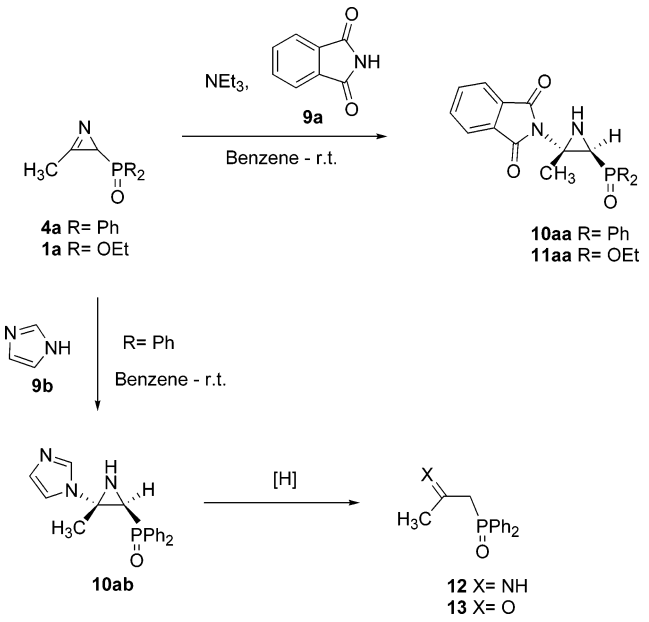
SCHEME 4



Therefore, we explored the regioselective ring opening of aziridines **3** and **5** to obtain N-unprotected α- or β-aminophosphonates or -phosphine oxides. Ring opening of aziridine-2-phosphine oxides **5** was accomplished by catalytic transfer hydrogenation with palladium. Reduction of 3-disubstituted aziridine-2-phosphine oxides **5** with ammonium formate and palladium on carbon in refluxing ethanol gave β-aminophosphine oxides **6** (Scheme 3, Table 2, entries 1−3). The formation of these compounds **6** could be explained by regioselective ring opening of the N−C2 single bond of the ring. Reaction conditions are strong enough to achieve also the hydrogenation of the allyl group ($R^2 = CH_2-CH=CH_2$) to n-propyl substituent ($R^2 = n$-C_3H_7) (Scheme 3, Table 2, entries 2 and 3).

This process could be extended to aziridines derived from phosphonates **3**. Catalytic transfer hydrogenation in the presence of Pd(0)/C and ammonium formate of diethyl 3-ethyl-3-methylaziridin-2-yl phosphonate **3aa** ($R^1 = CH_3$, $R^2 = C_2H_5$) gave β-amino phosphonate **7aa** ($R^1 = CH_3$, $R^2 = C_2H_5$) (Scheme 4, Table 2, entry 4) by regioselective ring opening of the N−C2 single bond of the ring in a way similar to that previously observed for 3-monosubstituted aziridine phosphonates.[16] However, in a manner similar to that reported for aziridine phosphonates with aryl substituents in the 3-position,[11,15a] a different behavior was observed by the hydrogenolysis of diethyl 3-benzyl-3-methylaziridin-2-yl phosphonate **3ab** ($R^1 = CH_3$, $R^2 = CH_2-Ph$) and diethyl 3-allyl-3-

SCHEME 5



phenylaziridin-2-yl phosphonate **3bc** (R^1 = Ph, R^2 = $CH_2-CH=CH_2$), to afford α-amino phosphonate **8ad** (R^1 = CH_3, R^2 = CH_2-Ph) as a single anti isomer[17,18] (Scheme 4, Table 2, entry 5) and **8bb** (R^1 = Ph, R^2 = n-C_3H_7) as a mixture of syn/anti isomers in 50:50 proportion (Scheme 4, Table 2, entry 6). The formation of these compounds could be explained by regioselective ring opening of the N−C3 single bond of the ring as an example of benzylamine-type reduction.[11,19] This strategy allowed us to prepare β-disubstituted β-aminophosphine oxides **6**, α- and β-aminophosphonates **8** and **7** from readily available aziridine phosphonates **3** and aziridine phosphine oxides **5**.

Addition of Phthalimide and Imidazole to 2*H*-Azirines. The behavior of 2*H*-azirine phosphine oxides and -phosphonates toward some nitrogen nucleophiles was also studied. Thus, we explored the behavior of phosphorus-substituted 2*H*-azirines with heterocyclic amines such as phthalimide and imidazole. Treatment of 2*H*-azirine phosphine oxide **4a** (R = Ph) with phthalimide **9a** at room temperature and in the presence of NEt_3 led regioselectively to the formation of *trans*-3-methyl-3-phthalimidylaziridin-2-yldiphenylphosphine oxide **10aa** (R = Ph) as a single product (Scheme 5, Table 3, entry 1). Azirine phosphonates **1** showed a similar behavior: 3-methyl-2*H*-azirine phosphonate **1a** (R = OEt) reacted with phthalimide **9a** to yield exclusively *trans*-aziridinyl phosphonate **11aa** (R = OEt) (Scheme 5, Table 3, entry 3). The stereochemical assigment of aducts **11aa** was based on NOESY 1D experiments,[20] and as before in the case of Grignard reagents, the exclusive formation of *trans*-aziridine **11aa** suggests that the approach of the phthalimide to the 2*H*-azirine ring takes place from the least hindered face.

TABLE 3. Functionalized Aziridine Derivatives 10 and 11

entry	compound	R	yield (%)[a]
1	**10aa**	Ph	87
2	**10ab**	Ph	83
3	**11aa**	OEt	69

[a] Yield of isolated purified compounds **10** and **11**.

Likewise, the reaction of other heterocyclic amine such as imidazole **9b** with 3-methyl-2*H*-azirine phosphine oxide **4a** (R = Ph) at room temperature gave diastereoselectively functionalized *trans*-aziridine phosphine oxide **10ab** (Scheme 5, Table 3, entry 2). Next, we studied the hydrogenolysis of aziridine **10aa** and **11aa**, but unfortunately this gave a complex mixture of products, while hydrogenation of imidazolyl-substituted aziridine phosphine oxide **10ab** led to the formation of 2-oxopropyldiphenylphosphine oxide **13** (X = O). Formation of this β-ketophosphine oxide **13** could be explained by ring opening of the azirine followed by β-elimination of imidazole with formation of imine **12** (X = NH) and hydrolysis of the imine to carbonyl compound **13** (X = O).

Addition of Benzenethiol to 2*H*-Azirines. Reaction of sulfur nucleophiles to 2*H*-azirines was also studied to test if these nucleophiles could give a new entry to functionalized aminophosphorus derivatives. For this reason, we explored the reaction of 2*H*-azirine phosphine oxides **4** and -phosphonates **1** with benzenethiol **14**. Treatment of 3-methyl-2*H*-azirin-2-yldiphenylphosphine oxide **4a** (R = Ph, R^1 = CH_3) with benzenethiol **14** at room temperature led exclusively to the formation of 1-amine-2-phenylsulfanylprop-2-en-1-yldiphenylphosphine oxide **15** (R = Ph) (Scheme 6, Table 4, entry 1), instead of the expected functionalized aziridine intermediate **16**. Spectroscopic data were in agreement with the assigned structure of compound **15** (R = Ph). In the ^{31}P NMR spectrum, the phosphine oxide group of this acyclic α-aminophosphorus derivative resonated at δ_P = 30.5 ppm, while well-resolved doublets at δ_H = 4.16 ppm ($^2J_{PH}$ = 6.1 Hz) for H−C1 as well as at δ_H = 5.02 ppm ($^2J_{HHgem}$ = 3.4 Hz) and at δ_H = 5.65 ppm ($^2J_{HHgem}$ = 3.4 Hz) for vinylic protons (=CH_2) were observed in the ^1H NMR spectrum. The ^{13}C NMR spectrum showed doublets at δ_C = 56.1 ppm ($^1J_{PC}$ = 72.1 Hz) for C1 and at δ_C = 116.8 ppm ($^3J_{PC}$ = 6.6 Hz) for C3. The formation of derivative **15** (R = Ph) could be explained by addition of benzenethiol **14** to the imine bond, followed by formation of the carbon−carbon double bond and ring opening of the aziridine intermediate **16** (Scheme 6). The instability of compound **15** (R = Ph) forced us to convert it into the α-aminophosphine oxide hydrochloride **17** (R = Ph) with hydrogen chloride in CH_2Cl_2 (Table 4, entry 2). To verify the reaction mechanism, we accomplished the addition of benzenethiol **14** to 3-phenyl-2*H*-azirin-2-yldiphenylphosphine oxide **4b** (R = Ph, R^1 = Ph) to trap the aziridine intermediate and to avoid the formation of the carbon−carbon double bond. Effectively, the reaction of 3-phenyl-2*H*-azirin-2-yldiphenylphosphine oxide **4b** (R = Ph, R^1

(17) Determination of anti configuration was established according to vicinal $^3J_{HH}$ = 9.7 Hz coupling constant between **H**−C1 and **H**−C2,[18] as well as by comparison with α-aminoesters ($^3J_{HH}$ = 7.5 Hz) obtained by ring opening of aziridine esters.[14a]

(18) (a) Gaudemar, A.; Golfrer, M.; Mandelbaum, A.; Parthasarathy, R. *Determination of Configuration by Spectroscopic Methods*; Kagan, H. B., Ed.; G. Thieme: Stuttgart, 1977; Vol. 1.

(19) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701−2743.

(20) Irradiating $-CH_2-$ protons of diethyl phosphonate moiety at 4.25 ppm showed an enhancement (1.14%) of the CH_3-C3 proton signal at 1.96 ppm, while irradiating H−C2 proton at 2.35 ppm showed no enhancement of the CH_3-C3 proton signal at 1.96 ppm

SCHEME 6

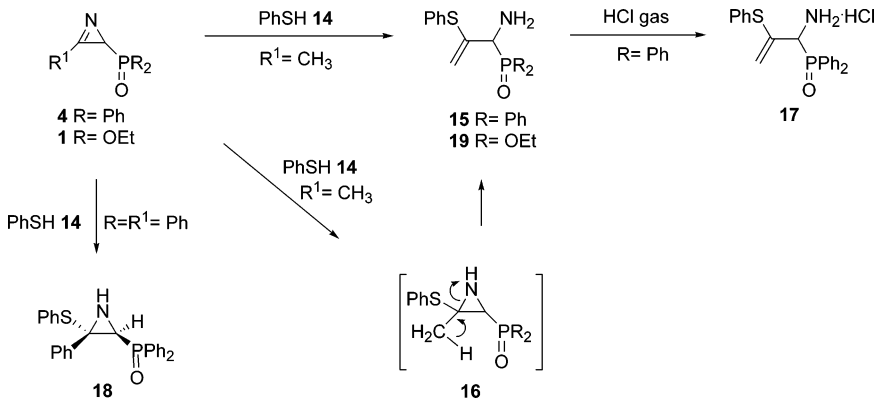


TABLE 4. Sulfur-Containing Aminophosphorus Derivatives 15, 17, 18, and 19

entry	compound	R	yield (%)[a]
1	**15**	Ph	74
2	**17**	Ph	56
3	**18**	Ph	58
4	**19**	OEt	58

[a] Yield of isolated purified compounds **15**, **17**, **18**, and **19**.

= Ph) with benzenethiol **14** at room temperature followed by purification of the crude reaction allowed us to obtain the *trans*-aziridine phosphine oxide **18** (R = Ph, R^1 = Ph) as a single product (Scheme 6, Table 4, entry 3) in a stereoselective fashion. 3-Methyl-2*H*-azirine phosphonate **1a** (R = OEt, R^1 = CH_3) also reacted with benzenethiol **14** to afford regioselectively diethyl 1-amine-2-phenylsulfanylprop-2-en-1-ylphosphonate **19** (R = OEt) (Scheme 6, Table 4, entry 4). This process describes, as far as we know, the first addition of sulfur nucleophiles to phosphorylated 2*H*-azirines and the synthesis of novel sulfur-containing α-aminophosphine oxides and -phosphonates.

Conclusion

In conclusion, this account describes a simple, mild, and convenient strategy for the stereoselective addition of Grignard reagents, phthalimide, imidazole, and benzenethiol to 2*H*-azirines phosphonates **1** and -phosphine oxides **4** to give *trans*-functionalized aziridine phosphonates **3**, **11**, and -phosphine oxides **5**, **10**, **18**. *β*-Aminophosphine oxides **6** and α- and *β*-aminophosphonates **8** and **7** were obtained by catalytic hydrogenation of aziridines **5** and **3**, while reaction of azirine phosphine oxides **4** and -phosphonates **1** with benzenethiol allowed us to obtain sulfur-substituted aziridine **18** as well as α-aminophosphine oxides **15**, **17**, and α-aminophosphonate **19** with a thioolefine in *β*-position. Substituted aziridines as well as α- and *β*-aminophosphorus derivatives are important building blocks in organic synthesis[3,5−7] and in the preparation of biologically active compounds of interest in medicinal chemistry.[5−7]

Experimental Section

General Procedure for the Preparation of Aziridines 3 and 5. To a solution of 2*H*-azirine **1** or **4** (5 mmol) in THF (15 mL) cooled to −78 °C, was added a solution of Grignard reagent **2** (15 mmol) in diethyl ether under nitrogen atmosphere. The mixture was stirred for 1 h at −78 °C and then was allowed to warm to room temperature (15 h). After the reaction was complete, the mixture was quenched with a saturated NH_4Cl solution (15 mL). The crude reaction was extracted three times with CH_2Cl_2 (3 × 15 mL). Organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated under vacuum. The crude residue was then purified by flash cromatography (silica gel, AcOEt), affording derivatives **5** as white solids and derivatives **3** as pale yellow oils.

Diethyl *trans*-3-Ethyl-3-methylaziridin-2-ylphosphonate 3aa. The general procedure was followed using 2*H*-azirine-2-phosphonate **1a** (0.96 g, 5 mmol) and ethylmagnesium bromide 3 M **2a** (5 mL, 15 mmol). Chromatographic purification eluting with AcOEt afforded 0.66 g, (60%) of compound **3aa** as a pale yellow oil: R_f 0.61 (AcOEt/MeOH 5/1); ^{1}H NMR ($CDCl_3$) δ 4.17 (m, 4H), 1.66 (d, $^2J_{PH}$ = 14.7 Hz, 1H), 1.55 (m, 2H), 1.50 (s, 3H), 1.36 (m, 7H), 0.98 (t, $^3J_{HH}$ = 7.5 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 62.0 (d, $^2J_{PC}$ = 6.0 Hz), 61.9 (d, $^2J_{PC}$ = 7.0 Hz), 41.6, 34.7 (d, $^1J_{PC}$ = 191.9 Hz), 31.2, 17.5 (d, $^3J_{PC}$ = 2.0 Hz), 16.4, 16.3, 9.8 ppm; ^{31}P NMR ($CDCl_3$) δ 25.5 ppm; IR (NaCl) 3244, 1679, 1454, 1394, 1248 cm^{-1}; MS (EI) *m/z* 221 (M^+, 7), 84 (M^+ − P(O)(OEt)$_2$, 100); Anal. Calcd for $C_9H_{20}NO_3P$: C, 48.86; H, 9.11; N, 6.33. Found: C, 48.97; H, 9.13; N, 6.31.

***trans*-3-Ethyl-3-methylaziridin-2-yldiphenylphosphine Oxide 5aa.** The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **4a** (1.28 g, 5 mmol) and ethylmagnesium bromide 3 M **2a** (5 mL, 15 mmol). Chromatographic purification eluting with AcOEt afforded 0.82 g (57%) of compound **4aa** as a white solid: mp 119−118 °C; ^{1}H NMR ($CDCl_3$) δ 7.83−7.41 (m, 10), 2.11 (d, $^2J_{PH}$ = 23.2 Hz, 1H), 1.80 (s, 1H), 1.59 (m, 1H), 1.42 (s, 3H), 1.38 (m, 1H), 0.92 (t, $^3J_{HH}$ = 7.5 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 134.2−128.6 (m), 42.9 (d, $^2J_{PC}$ = 1.3 Hz), 38.1 (d, $^1J_{PC}$ = 95.4 Hz), 33.6, 17.1 (d, $^3J_{PC}$ = 2.1 Hz), 10.1 ppm; ^{31}P NMR ($CDCl_3$) δ 28.2 ppm; IR (KBr) 3224, 3051, 1434, 1374, 1188 cm^{-1}; MS (EI) *m/z* 285 (M^+, 12), 84 (M^+ − P(O)Ph_2, 100); Anal. Calcd for $C_{17}H_{20}NOP$: C, 71.56; H, 7.07; N, 4.91. Found: C, 71.74; H, 7.08; N, 4.89.

General Procedure for Hydrogenation Ring Opening of Aziridines 3 and 5. To a solution of aziridine **3** or **5** (5 mmol) in EtOH (15 mL) was added under nitrogen atmosphere Pd/C (20%) and then ammonium formate (75 mmol). The mixture was kept at reflux for 8 h. Then, NH_4OH solution (25%) was added until pH 8, and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was evaporated. The crude mixture was purified by flash column chromathography to afford amino phosphorus derivatives **6**, **7**, or **8** as white solids or colorless oils.

2-Amino-2-methylbuthyldiphenylphosphine Oxide 6aa. The general procedure was followed using aziridine-2-diphenylphoshine oxide **5aa** (1.43 g, 5 mmol). Chromatographic purification eluting with AcOEt afforded 0.96 g (67%) of compound **6aa** as a colorless oil: R_f 0.15 (AcOEt/MeOH 5/1); ^{1}H NMR ($CDCl_3$) δ 7.82−7.26 (m, 10H), 2.73 (s, 2H), 2.53 (d,

$^2J_{PH}$ = 10.4 Hz, 2H), 1.57 (q, $^3J_{HH}$ = 7.3 Hz, 2H), 1.15 (s, 3H), 0.82 (t, $^3J_{HH}$ = 7.3 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 135.3−128.6 (m), 54.0 (d, $^2J_{PC}$ = 5.0 Hz), 40.1 (d, $^1J_{PC}$ = 70.4 Hz), 37.0 (d, $^3J_{PC}$ = 8.6 Hz), 28.2 (d, $^3J_{PC}$ = 6.6 Hz), 8.2 ppm; ^{31}P NMR ($CDCl_3$) δ 29.5 ppm; IR (NaCl) 3434, 3045, 1583, 1434, 1180 cm^{-1}; MS (EI) *m/z* 288 (M^+ + 1, 90), 271 (M^+ − NH_2, 100); Anal. Calcd for $C_{17}H_{22}NOP$: C, 71.06; H, 7.72; N, 4.87. Found: C, 71.15; H, 7.74; N, 4.86.

Diethyl 2-Amino-2-methylbuthylphosphonate 7aa. The general procedure was followed using aziridine-2-phosphonate **3aa** (1.11 g, 5 mmol). Chromatographic purification eluting with AcOEt afforded 0.65 g (58%) of compound **7aa** as a colorless oil: R_f 0.60 (AcOEt/MeOH 5/1); ^{1}H NMR ($CDCl_3$) δ 4.11 (m, 4H), 1.91 (d, $^2J_{PH}$ = 18.5 Hz, 2H), 1.88 (s, 2H),1.54 (dq, $^3J_{HH}$ = 7.5 Hz, $^2J_{HHgem}$ = 3.7 Hz, 2H), 1.33 (t, $^3J_{HH}$ = 7.2 Hz, 7.0 Hz, 6H), 1.22 (d, $^4J_{PH}$ = 0.8 Hz, 3H), 0.92 (t, $^3J_{HH}$ = 7.5 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 61.3, 61.2, 50.9 (d, $^2J_{PC}$ = 4.5 Hz), 37.9 (d, $^1J_{PC}$ = 136.5 Hz), 37.0 (d, $^3J_{PC}$ = 11.6 Hz), 28.4 (d, $^3J_{PC}$ = 8.6 Hz), 16.4, 16.3, 8.4 ppm; ^{31}P NMR ($CDCl_3$) δ 30.1 ppm; IR (NaCl) 3423, 1633, 1454, 1381, 1241 cm^{-1}; MS (EI) *m/z* 223 (M^+, 10), 222 (M^+ − 1, 100); Anal. Calcd for $C_9H_{22}NO_3P$: C, 48.42; H, 9.93; N, 6.27. Found: C, 48.34; H, 9.91; N, 6.28.

Diethyl 1-Amino-2-methyl-3-phenylpenthylphosphonate 8ab. The general procedure was followed using aziridine-2-phosphonate **3ab** (1.42 g, 5 mmol). Chromatographic purification eluting AcOEt afforded 1.04 g (73%) of compound **8ab** as a colorless oil: R_f 0.26 (AcOEt); ^{1}H NMR ($CDCl_3$) δ 7.23−7.05 (m, 5H), 4.18 (m, 4H), 3.42 (dq, $^3J_{HHanti}$ = 9.5 Hz, 1H), 3.31 (dd, $^3J_{HHanti}$ = 9.5 Hz, $^2J_{PH}$= 10.5 Hz, 1H), 2.40 (s, 2H), 1.70 (s, 2H), 1.21 (m, 9H) ppm; ^{13}C NMR ($CDCl_3$) δ 137.6−125.6 (m), 62.1, 54.3 (d, $^1J_{PC}$ = 153.2 Hz), 36.9, 29.7, 20.0, 16.5 (d, $^5J_{PC}$ = 5.7 Hz) ppm; ^{31}P NMR ($CDCl_3$) δ 28.7 ppm; IR (NaCl) 3384, 1467, 1223, 1064 cm^{-1}; MS (EI) *m/z* 285 (M^+, 7), 148 (M^+ − P(O)(OEt)$_2$, 100); Anal. Calcd for $C_{14}H_{24}NO_3P$: C, 58.93; H, 8.48; N, 4.91. Found: C, 59.08; H, 8.50; N, 4.92.

General Procedure for the Synthesis of Functionalized Aziridines 10 and 11. To a solution of 2*H*-azirine **1** and **4** (5 mmol) in benzene (15 mL) cooled to 0 °C, triethylamine (5.5 mmol) was added slowly under a nitrogen atmosphere and with continuous stirring. Then phthalimide (0.81 g, 5 mmol) was added, and the reaction mixture was stirred at room temperature for 48 h. The crude reaction was then washed three times with H_2O (3 × 5 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated under reduced pressure. Crude reaction was purified by crystallization from diethyl ether/hexane 2:1 for aziridine-2-diphenylphosphine oxide derivatives **10**, while aziridine-2-phosphonate derivatives **11** were purified by column chromatography eluting hexane/AcOEt 2:1.

***trans*-3-Methyl-3-phthalimidylaziridin-2-yldiphenylphosphine Oxide 10aa.** The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **4a** (1.28 g, 5 mmol). Crystallization of the crude from diethyl ether/hexane 2:1 afforded 2.31 g (87%) of compound **10aa** as a white solid: mp 94−93 °C; ^{1}H NMR ($CDCl_3$) δ 8.27−7.42 (m, 14H), 2.92 (d, $^2J_{PH}$ = 21.1 Hz, 1H), 2.37 (s, 1H), 1.80 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 167.1, 134.2−123.2 (m), 48.9, 37.0 (d, $^1J_{PC}$ = 89.6 Hz), 18.4 (d, $^3J_{PC}$ = 1.0 Hz) ppm; ^{31}P NMR ($CDCl_3$) δ 26.8 ppm; IR (KBr) 3429, 3191, 3051, 1719, 1374, 1195 cm^{-1}; MS (CI) *m/z* 403 (M^+ + 1, 60); Anal. Calcd for $C_{23}H_{19}N_2O_3P$: C, 68.75; H, 4.76; N, 6.96. Found: C, 68.89; H, 4.77; N, 6.95.

Diethyl *trans*-3-Methyl-3-phthalimidylaziridin-2-ylphosphonate 11aa. The general procedure was followed using 2*H*-azirine-2-phosphonate **1a** (0.96 g, 5 mmol). Chromatographic purification eluting with hexane/AcOEt 2:1 afforded 1.17 g (69%) of compound **11aa** as a white solid: mp 85−84 °C; ^{1}H NMR ($CDCl_3$) δ 7.86−7.34 (m, 4H), 4.31 (m, 4H), 2.40 (d, $^2J_{PH}$ = 13.8 Hz, 1H), 1.96 (s, 3H), 1.68 (s, 1H), 1.43 (q, $^3J_{HH}$ = 6.9 Hz, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 167.0, 134.3, 123.4, 63.0 (d, $^2J_{PC}$ = 6.0 Hz), 62.6 (d, $^2J_{PC}$ = 5.5 Hz), 47.8, 34.1 (d, $^1J_{PC}$ = 184.8 Hz), 18.9, 16.4, 16.3 ppm; ^{31}P NMR ($CDCl_3$) δ 21.4 ppm; IR (KBr) 3436, 3260, 1725, 1387, 1023 cm^{-1}; MS (CI) *m/z* 339 (M^+ + 1, 92); Anal. Calcd for $C_{15}H_{19}N_2O_5P$: C, 53.26; H, 5.66; N, 8.28. Found: C, 53.39; H, 5.68; N, 8.27.

Procedure for Hydrogenation Ring Opening of Aziridine 10ab. Synthesis of 2-Oxopropyldiphenylphosphine Oxide 13. To a solution of aziridine **10ab** (1.62 g, 5 mmol) in EtOH (15 mL) was added under nitrogen atmosphere Pd/C (20%) and then ammonium formate (75 mmol). The reaction was kept at reflux for 8 h. Then, NH_4OH solution (25%) was added until pH 8, and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was evaporated. The crude mixture was purified by flash column chromathography eluting with AcOEt to afford derivative **13** (0.62 g, 48%) as a white solid: mp 125−126 °C. Spectroscopic data were in agreement with the literature.[21]

Procedure for the Synthesis of Sulfur-Substituted Aminophosphorus Derivatives 15, 18, and 19. Benzenethiol **14** (0.61 g, 5.5 mmol) was added to a solution of 2*H*-azirine **1** or **4** (5 mmol) in CH_2Cl_2 (15 mL) cooled to 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature until TLC indicated the disappearance of azirine (48 h). The crude reaction was washed three times with H_2O (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$ and filtered. Evaporation of solvent under reduced pressure and chromatographic purification by flash column chromatography with hexane/AcOEt 1:1 afforded the corresponding derivatives **15**, **18**, and **19** as pale yellow oils or yellow solids.

1-Amino-2-phenylsulfanylpro-2-en-1-yldiphenylphosphine Oxide 15. The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **4a** (1.28 g, 5 mmol). Chromatographic purification eluting with hexane/AcOEt 1:1 afforded 1.29 g (74%) of compound **15** as a pale yellow oil: R_f 0.21 (AcOEt); ^{1}H NMR ($CDCl_3$) δ 8.08−7.18 (m, 15H), 5.65 (d, $^2J_{HHgem}$ = 3.5 Hz, 1H), 5.02 (d, $^2J_{HHgem}$ = 3.4 Hz, 1H), 4.16 (d, $^2J_{PH}$ = 6.1 Hz, 1H), 2.28 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 133.2−128.1 (m), 116.8 (d, $^3J_{PC}$ = 6.6 Hz), 56.1 (d, $^1J_{PC}$ = 72.1 Hz) ppm; ^{31}P NMR ($CDCl_3$) δ 30.5 ppm; IR (NaCl) 3383, 3051, 1725, 1672, 1633, 1434, 1182 cm^{-1}; MS (CI) *m/z* 366 (M^+ + 1, 100); Anal. Calcd for $C_{21}H_{20}NOPS$: C, 69.02; H, 5.52; N, 3.83; S, 8.77. Found: C, 68.91; H, 5.50; N, 3.84; S, 8.76.

Preparation of *trans*-3-Phenyl-3-phenylsulfanylaziridin-2-yldiphenylphosphine Oxide 18. The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **4b** (1.59 g, 5 mmol). Chromatographic purification eluting with hexane/AcOEt 1:1 afforded 1.03 g (58%) of compound **18** as a yellow solid: mp 74−73 °C; ^{1}H NMR ($CDCl_3$) δ 7.95−6.89 (m, 15H), 3.22 (d, $^2J_{PH}$ = 17.1 Hz, 1H), 2.17 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$) δ 134.8−125.3 (m), 51.8, 40.6 (d, $^1J_{PC}$ = 102.7 Hz) ppm; ^{31}P NMR ($CDCl_3$) δ 25.4 ppm; IR (KBr) 3158, 3051, 1626, 1580, 1434, 1175, 1122 cm^{-1}; MS (CI) *m/z* 428 (M^+ + 1, 100); Anal. Calcd for $C_{26}H_{22}NOPS$: C, 73.05; H, 5.19; N, 3.28; S, 7.50. Found: C, 73.18; H, 5.20; N, 3.27; S, 7.48.

Diethyl 1-Amino-2-phenylsulfanylpro-2-en-1-ylphosphonate 19. The general procedure was followed using 2*H*-azirine-2-phosphonate **4a** (0.96 g, 5 mmol). Chromatographic purification eluting with hexane/AcOEt 1:1 afforded 0.88 g (58%) of compound **19** as a pale yellow oil: R_f 0.19 (AcOEt); ^{1}H NMR ($CDCl_3$) δ 7.48−7.20 (m, 5H), 5.65 (d, $^4J_{PH}$ = 4.4 Hz, 1H), 5.15 (d, $^4J_{PH}$ = 4.0 Hz, 1H), 4.19 (m, 4H), 3.76 (d, $^2J_{PH}$ = 19.1 Hz, 1H), 1.90 (s, 2H), 1.35 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 143.3−126.5 (m), 116.3 (d, $^3J_{PC}$ = 8.6 Hz), 62.8 (d, $^2J_{PC}$ = 7.1 Hz), 62.7 (d, $^2J_{PC}$ = 7.1 Hz), 54.1 (d, $^1J_{PC}$ = 151.1 Hz), 16.3, 16.2 ppm; ^{31}P NMR ($CDCl_3$) δ 24.1 ppm; IR (NaCl) 3456, 3376, 3297, 1732, 1606, 1480, 1434, 1241 cm^{-1}; MS (CI) *m/z* 302 (M^+ + 1, 100); Anal. Calcd for $C_{13}H_{20}NO_3PS$: C, 51.81; H, 6.69; N, 4.65; S, 10.64. Found: C, 51.95; H, 6.70; N, 4.64; S, 10.65.

Preparation of 1-Diphenylphosphinyl-2-phenylsulfanylallylammonium Chloride 17. A solution of the sulfur-substituted amino phosphorus derivative **15** (1.83 g, 5 mmol)

(21) Corbel, B. *Synthesis* **1985**, 1048−1051.

in CH_2Cl_2 (15 mL) was saturated with hydrogen chloride, and the mixture was stirred at room temperature under nitrogen atmosphere until the disappearance of the starting material. Evaporation of solvent under reduced pressure and crystallization from diethyl ether afforded 1.12 g (56%) of compound **17** as a yellow solid: mp 74−73 °C; ^{1}H NMR ($CDCl_3$) δ 9.49 (s, 3H), 7.98−7.09 (m, 15H), 5.65 (s, 1H), 5.16 (d, $^4J_{PH}$ = 1.5 Hz, 1H), 5.06 (d, $^2J_{PH}$ = 6.9 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$) δ 137.1−126.4 (m), 117.8 (d, $^3J_{PC}$ = 6.6 Hz), 52.7 (d, $^1J_{PC}$ = 67.0 Hz) ppm; ^{31}P NMR ($CDCl_3$) δ 31.9 ppm; IR (KBr) 3429, 3151, 3058, 1732, 1679, 1586, 1440, 1175 cm^{-1}; MS (CI) *m/z* 402 (M^+ + 1, 7), 203 ($P(O)Ph_2^+$ + 2, 100); Anal. Calcd for $C_{21}H_{21}ClNOPS$: C, 62.76; H, 5.27; N, 3.49; S, 7.98. Found: C, 62.63; H, 5.26; N, 3.49; S, 7.99.

Acknowledgment. We thank the Dirección General de Investigación del Ministerio de Ciencia y Tecnología (MCYT, Madrid DGI, PPQ2003-00910) and the Universidad del País Vasco (UPV, GC/ 2002) for supporting this work. J.M.A. thanks the Ministerio de Educación (Madrid) for a predoctoral fellowship.

Supporting Information Available: Experimental procedures and characterization data (^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR, and elemental analysis) for compounds **3ab**, **3bc**, **5ac**, **5ad**, **5bc**, **6ac**, **6bc**, **8bc**, and **10ab**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO051404I