Conversion of Thio- and Selenophosphoryl into Phosphoryl Group by Perfluoro *cis*-2,3-Dialkyloxaziridines

Alberto Arnone,† Barbara Novo,† Massimo Pregnolato,*,‡ Giuseppe Resnati,*,† and Marco Terreni‡

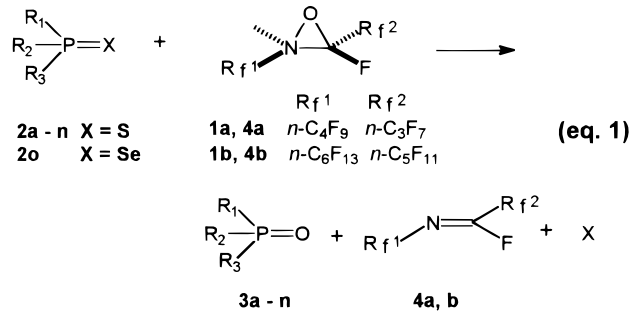
Dipartimento di Chimica Farmaceutica, Università degli Studi, 12 via Taramelli, I-27100 Pavia, Italy, and C.N.R.-Centro di Studio sulle Sostanze Organiche Naturali, Dipartimento di Chimica, Politecnico, 7 via Mancinelli, I-20131 Milano, Italy

Received March 31, 1997

Compounds containing the thiophosphoryl moiety (P═S) have found diversified applications in chemistry. They have been employed as chiral auxiliary agents in extraordinarily diastereoselective alkylation reactions,[1] in the resolution of racemic phenols[2] and in the determination of the optical purity of alcohols and amines.[3] Thiophosphoryl derivatives also proved useful in a vast number of biological investigations. They are effective tools for the study of enzyme-catalyzed reactions,[4] potent inhibitors of metalloproteases,[5] and promising candidates for use in oligonucleotide therapeutics.[6] All of these properties are obviously shared by the substances possessing the phosphoryl group (P═O).[1−6] An easy transformation of the thiophosphoryl into phosphoryl compounds would provide a much greater flexibility in preparing and studying chemical and biological properties of both classes of tetracoordinated phosphorus compounds.

In the course of a study on the oxidation of some organophosphorus agrochemicals by perfluoro *cis*-2,3-dialkyloxaziridines **1a**,**b**,[7] we noticed that these oxaziridines were able to transform phosphorothioates into corresponding phosphates. The noteworthy effectiveness of the observed reaction prompted us to test the conversion of the thiophosphoryl into phosphoryl group on other structurally different phosphorus(V) derivatives, and here we describe the generality of the process.

When trialkyl- and triarylphosphine sulfides **2a**−**d** were reacted with equimolar amounts of the oxaziridine **1a** in an halogenated solvent at room temperature, high yields of the corresponding oxides **3a**−**d** were formed (eq 1). Reactions were complete in less than 5 min, and the only observed coproducts were the azaalkene **4a**, as shown by ^{19}F NMR of crude reaction mixtures, and elemental sulfur, as proven by microanalyses and exact mass of the formed yellowish solid. Similarly, triphenylphosphine selenide (**2o**) afforded quantitatively



the corresponding oxide **3c** and elemental selenium in few minutes at −40 °C.

High yields of phosphoryl products were obtained also when alkoxy and amido residues were bound to the phosphorus atom. Under the usual reaction conditions alkylthiophosphonates and (difluoromethylene)thiophosphonates, **2e** and **2f**, respectively, afforded nearly quantitative yields of the corresponding phosphonate **3e**,**f**. Some commonly employed agrochemicals[8] and their metabolites such as Parathion (**2g**) and its *O*-methyl analogue (**2h**), Fenitrothion (**2i**), Bromophos (**2j**), the sulfinyl derivatives of demethon-*O* (**2l**), and demethon-*O*-methyl (**2k**) all have a dialkyl aryl or trialkyl phosphorothioate moiety which is oxidatively desulfurized cleanly to give corresponding phosphate products **3h**−**l**. At room temperature the reaction occurs very rapidly also on these substrates, but best yields are obtained performing the desulfurization in the cold for longer reaction times (Table). Side reactions are thus avoided (partial hydrolyses of labile *p*-nitrophenoxy residue in **2g**−**i** or sulfinyl to sulfonyl oxidation in **2k**,**l**).

The diethylthiophosphoramidate **2m** and the 1,3,2-oxazaphospholidine 2-sulfide **2n**, bearing one and two amido residues at phosphorus, both gave desired products **3m**,**n** in good yields. Once again, lower reaction temperatures allowed higher yields to be obtained starting from the thiophosphoramidate **2m** having two labile *p*-nitrophenoxy residues, and it is interesting to observe that desulfurization of oxazaphospholidine sulfide **2n** occurred with complete stereoselectivity (>98%) and inversion of configuration at phosphorus (eq 2).[9] The stereochemical course of the thiophosphoryl into phosphoryl transformation has been described for various reagents,[11] and it was shown to depend on the substituent at phosphorus,[11i] the employed oxidizing agent,[10a,11n] and the reaction conditions.[10c,11d,i] It is noteworthy that all

† C.N.R., Milano; e-mail: resnati@dept.chem.polimi.it.
‡ University of Pavia.

(1) (a) Kranz, M.; Denmark, S. E.; Swiss, K. A.; Wilson, S. R. *J. Org. Chem.* **1996**, *61*, 8551. (b) Denmark, S. E.; Chen, C.-T. *J. Am. Chem. Soc.* **1995**, *117*, 11879.
(2) Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem.* **1993**, *58*, 1748.
(3) (a) Alexakis, A.; Frutos, J. C.; Mangeney, P.; Meyers, A. I.; Moorlag, H. *Tetrahedron Lett.* **1994**, *35*, 5125. (b) Johnson, C. R.; Elliot, R. C.; Penning, T. D. *J. Am. Chem. Soc.* **1984**, *106*, 5019.
(4) (a) Eckstein, F.; Gish, G. *Trends Biol. Sci.* **1989**, *14*, 97. (b) Frey, P. A. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1989**, *62*, 119.
(5) Hill, J. M.; Lowe, G. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2001.
(6) (a) Wagner, R. W. *Nature* **1994**, *372*, 333. (b) Marshall, W. S.; Caruthers, M. H. *Science* **1993**, *259*, 1564. (c) De Mesmaeker, A.; Haner, R.; Martin, P.; Moser, H. E. *Acc. Chem. Res.* **1995**, *28*, 366.
(7) Terreni, M.; Pregnolato, M.; Resnati, G.; Benfenati, E. *Tetrahedron* **1995**, *51*, 7981.
(8) Worthing, C. R. *The Pesticide Manual*, 7th ed.; A World Compendium; British Crop Protection Council: Croydon, U.K., 1993.

(9) The (2*S*,4*R*,5*S*) configuration was assigned to the product **3n** obtained by oxidizing (2*S*,4*R*,5*S*)-**2n** with oxaziridines **1a**,**b** as no NOE was observed in this diastereoisomer between the methyl on C-4 and the methylene and aromatic protons of the benzylamido residue. This observation suggested that the two groups are *trans*. In order to confirm this assignment, (2*S*,4*R*,5*S*)-**2n** was oxidized with MCPBA. This reagent is known to perform the oxidative desulfurization reaction with retention of chirality on 2-(methylthio)-1,3,2-oxazaphospholidine 2-sulfides (ref 10a), phosphonamidothioates (ref 10b), phosphinothioates (ref 10c), and phosphorothioates (ref 10d) and in fact a different 1,3,2-oxazaphospholidine 2-oxide **3n** was formed which showed positive NOE effects between the above described residues (see the Experimental Section). These residues were thus in a *cis* relationship, and the (2*R*,4*R*,5*S*) configuration could be assigned unequivocally to this product.

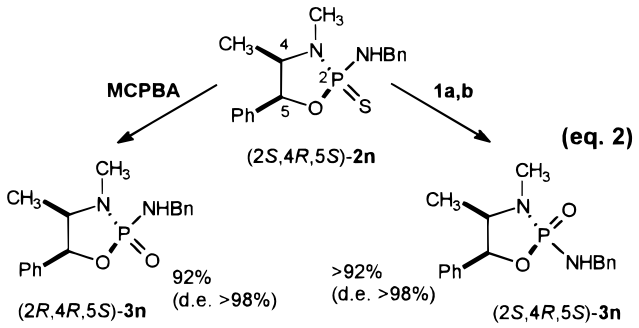
(10) (a) Jackson, J. A.; Berkman, C. E.; Thompson, C. M. *Tetrahedron Lett.* **1992**, *33*, 6061. (b) Hall, C. R.; Inch, T. D.; Williams, N. E. *J. Chem. Soc., Perkin Trans. 1* **1985**, 233. (c) Herriot, A. W. *J. Am. Chem. Soc.* **1971**, *93*, 3304. (d) Cullis, P. M. *J. Chem. Soc., Chem. Commun.* **1984**, 1510.

S0022-3263(97)00572-0 CCC: $14.00

Table 1. Oxidation of Thio- and Selenophosphoryl Substrates 2a−o with Oxaziridines 1a,b

Substrate[a]	R^1	R^2	R^3	Reagent	Yield (%)[b]
2a	Et	Et	Et	**1a**	93
2b	*i*-Bu	*i*-Bu	*i*-Bu	**1a**	95
				1b	92
2c	Ph	Ph	Ph	**1a**	95
				1b	95
2d	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**1a**	97
2e	EtO	EtO	Me	**1a**	93
2f	EtO	EtO	CF_2Br	**1a**	94
				1b	96
2g	MeO	MeO	4-NO_2-C_6H_4O	**1a**	82 (94)
2h	EtO	EtO	4-NO_2-C_6H_4O	**1a**	84 (90)
2i	MeO	MeO	3-CH_3-4-NO_2-C_6H_3O	**1a**	80 (91)
2j	MeO	MeO	2,5-Cl_2-4-Br-C_6H_2O	**1a**	90
2k	MeO	MeO	$EtS(O)CH_2CH_2O$	**1a**	93 (97)
2l	EtO	EtO	$EtS(O)CH_2CH_2O$	**1a**	84 (90)
2m	Et_2N	4-NO_2-C_6H_4O	4-NO_2-C_6H_4O	**1a**	80 (88)
(2*S*,4*R*,5*S*)-2n			C_6H_5-CH_2-NH	**1a**	94[c]
				1b	92[c]
				MCPBA	92[d]
2o	Ph	Ph	Ph	**1a**	97[e]
				1b	97[e]

[a]Compounds **2a-n** are sulfide derivatives and compound **2o** is a selenide derivative (X = S and Se, respectively, in equation 1). [b]Reported yields are referred to products **3** isolated from reactions performed at room temperature for 5 minutes. Yields in parentheses are referred to reactions performed at -30 °C for 6 h. [c]Reaction occurred with complete inversion of configuration at phosphorus stereocentre and (2*S*,4*R*,5*S*)-**3n** was formed. [d] Reaction occurred with complete retention of configuration at phosphorus stereocentre and (2*R*,4*R*,5*S*)-**3n** was formed. [e]Reactions performed at -40 °C, 5 min.



reagents but dimethyl sulfoxide[11] are reported to give retention of configuration when the phosphorus atom is inserted in a cyclic moiety so that the stereochemical behavior of oxaziridines **1** is quite unusual.

The perfluoro-*cis*-2-hexyl-3-pentyloxaziridine **1b** showed a reactivity quite similar to that of the 2-butyl-3-propyl analogue **1a** since yields, reaction times, and diastereoselection for the oxidative desulfurization and deselenization of substrates **2b**,**c**,**f**,**n**,**o** were nearly the same for the two reagents (Table 1).

In general, reaction conditions are milder than those required by other reagents which perform the same reactions. For instance, high temperatures (Me_2SO,[11d,f] chloral,[11p] H_2O_2[11i]), long reaction times (trifluoroacetic anhydride[11s]), or great excess of the reagent (Me_2SO,[11d,f] ethylene oxide,[11o] chloral[11p]) are often required. The reaction workup is notably simple since filtration of the crude reaction mixtures (to remove sulfur) and rotary evaporation (to eliminate excess oxaziridine **1a**, if any, and azaalkene **4a** both of which are quite volatile compounds) often afford desired products **3** in nearly pure form.

In conclusion, perfluorooxaziridines **1** have previously been shown to be useful reagents for the oxidation at carbon,[12a−f] nitrogen,[12g,h] sulfur,[12i,j] and silicon[12k] sites. Results here reported show how they are effective also for the high yield and stereoselective transformation of thio- and selenophosphoryl groups into phosphoryl groups under mild reaction conditions in a wide variety of phosphorus(V) derivatives (R^1, R^2, R^3 = alkyl, aryl, *O*-alkyl, *O*-aryl, NH-alkyl, N-$alkyl_2$ in **2** and **3**).

Experimental Section

Oxaziridines **1a**,**b** have been prepared in two steps starting from commercially available perfluoro-tri-*n*-butyl- and -tri-*n*-hexylamine.[13] Dichloropentafluoropropane is a 43:56 mixture of HCFC-225ca and HCFC-225cb ($CF_3CF_2CHCl_2$ and $CClF_2CF_2CHClF$, respectively) purchased from PCR incorporated. Analytical instruments employed and spectral data format are described in refs 7 and 12i. Starting compounds **2a**−**e**,**o** have been purchased from Aldrich, Fluka, Alfa, or Acros; **2g**,**h**,**k**,**l** have been prepared according to ref 7.

Diethyl (1-Bromo-1,1-difluoromethylene)thiophosphonate (2f). A solution of diethyl (1-bromo-1,1-difluoromethylene)-phosphonate (Aldrich, 1.07 g, 4.0 mmol) and 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide (Lawesson's reagent, 1.62 g, 4.0 mmol) in dry toluene (20 mL) was refluxed with stirring under nitrogen for 2 h. The solvent was evaporated under reduced pressure and the residue purified through flash chromatography (*n*-hexane/ethyl acetate, 70:30) to give 736 mg (2.60 mmol, 65% yield) of pure **2f**: ^{1}H NMR ($CDCl_3$) δ 1.40, 4.33; ^{19}F NMR ($CDCl_3$) δ −62.3; ^{31}P NMR ($CDCl_3$) δ 69.5 (69.38).[14]

***O*,*O*-Bis-(4-nitrophenyl) *N*,*N*-diethylthiophosphoramidate (2m).** A suspension of *N*,*N*-diethylthiophosphoramidic dichloride (1.00 g, 4.8 mmol) and sodium *p*-nitrophenate (1.56 g, 9.7 mmol) in EtOH was refluxed with stirring for 2 h. The solvent was evaporated under reduced pressure and the residue purified through flash chromatography (*n*-hexane/ethyl acetate, 80:20) to give 450 mg of **2m** (1.10 mmol, 23% yield): ^{1}H NMR ($CDCl_3$) δ 1.18 (t, 6H, J = 7.2), 3.47 (dq, 4H, $J_{H,H}$ = 7.2, $J_{H,P}$ = 14.5), 7.37 (m, 4H, $J_{H,P}$ = 1.6), 8.27 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 65.7. Anal. Calcd for $C_{16}H_{18}N_3O_6PS$: C, 46.71; H, 3.92; N, 10.21; S, 7.79. Found: C, 46.94; H, 4.18; N, 10.02; S, 7.97.

(2*S*,4*R*,5*S*)-2-(Benzylamino)-1,3,2-oxazaphospholidine 2-Sulfide (2n). To a solution of 2-chloro-1,3,2-oxazaphospholi-

(11) Me_2SO-H^+ and Me_2SO-I_2: (a) Luckenbach, R. *Synthesis* **1973**, 307. (b) Luckenbach, R.; Kern, M. *Chem. Ber.* **1975**, *108*, 3533. (c) Mikolajczyk, M.; Luczak, J. *Synthesis* **1975**, 114. (d) Okruszek, A.; Stec, W. J. *Tetrahedron Lett.* **1982**, *23*, 5203. (e) Mikolajczyk, M.; Luczak, J. *Chem. Ind. (London)* **1974**, 701. (f) Guga, P.; Okruszek, A. *Tetrahedron Lett.* **1984**, *25*, 2897. Me_2SeO: (g) Mikolajczyk, M.; Luczak, J. *J. Org. Chem.* **1978**, *43*, 2132. $Me_3SiOOSiMe_3$: (h) Kowalski, J.; Wozniak, L.; Chojnowski, J. *Phosphorus, Sulfur* **1987**, *30*, 125. H_2O_2: (i) Stec, W. J.; Okruszek, A.; Michalski, J. *J. Org. Chem.* **1976**, *41*, 233. Dimethyldioxirane: (j) Sánchez-Baeza, F.; Durand, G.; Barceló, D.; Messeguer, A. *Tetrahedron Lett.* **1990**, *31*, 3359. $KMnO_4$: (k) Horner, L. *Pure Appl. Chem.* **1964**, *9*, 225. (l) Horner, L.; Winkler, H. *Tetrahedron Lett.* **1964**, 175. (m) Stec, W.; Okruszek, A.; Michalski, J. *Angew. Chem., Int. Ed. Engl.* **1971**, *13*, 491. N_2O_4 and HNO_3: (n) Michalski, J.; Okruszek, A.; Stec, W. *J. Chem. Soc., Chem. Commun.* **1970**, 1495. Styrene oxide and chloral: (o) Guga, P.; Stec, W. J. *Tetrahedron Lett.* **1983**, *24*, 3899. (p) Okruszek, A.; Stec, W. J. *J. Chem. Soc., Chem. Commun.* **1984**, 117. (q) Chan, T. H.; Finkenbine, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 2880. MCPBA: refs 10a−d. O_3: (r) Skowronska, A.; Krawczyk, E. *Synthesis* **1983**, 509. Trifluoroacetic anhydride: (s) Helinski, J; Skrzypczynski, Z.; Wasiak, J.; Michalski, J. *Tetrahedron Lett.* **1990**, *31*, 4081.

(12) (a) DesMarteau, D. D.; Petrov, V. A.; Montanari, V.; Pregnolato, M.; Resnati, G. *Tetrahedron Lett.* **1992**, *33*, 7245. (b) DesMarteau, D. D.; Donadelli, A.; Montanari, V.; Petrov, V. A.; Resnati, G. *J. Am. Chem. Soc.* **1993**, *115*, 4897. (c) Arnone, A.; Cavicchioli, M.; Montanari, V.; Resnati, G. *J. Org. Chem.* **1994**, *59*, 5511. (d) Arnone, A.; Bernardi, R.; Cavicchioli, M.; Resnati, G. *J. Org. Chem.* **1995**, *60*, 2314. (e) Cavicchioli, M.; Mele, A.; Montanari, V.; Resnati, G. *J. Chem. Soc., Chem. Commun.* **1995**, 901. (f) Petrov, V. A.; Resnati, G. *Chem. Rev.* **1996**, *96*, 1809. (g) Balsarini, C.; Novo, B.; Resnati, G. *J. Fluorine Chem.* **1996**, 80, 31. (h) Bernardi, R.; Novo, B.; Resnati, G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2517. (i) DesMarteau, D. D.; Petrov, V. A.; Montanari, V.; Pregnolato, M.; Resnati, G. *J. Org. Chem.* **1994**, *59*, 2762. (j) Bégué, J.-P.; M'Bida, A.; Bonnet-Delpon, D.; Novo, B.; Resnati, G. *Synthesis* **1996**, 399. (k) Cavicchioli, M.; Montanari, V.; Resnati, G. *Tetrahedron Lett.* **1994**, *35*, 6329.

(13) Petrov, V. A.; DesMarteau, D. D. *J. Org. Chem.* **1993**, *58*, 4754.

(14) Piettre S. R. *Tetrahedron Lett.* **1996**, *37*, 4707.

dine 2-sulfide (Aldrich, 400 mg, 1.52 mmol) and triethylamine (230 mg, 2.28 mmol) in THF (8 mL) was added benzylamine (163 mg, 1.52 mmol) at rt under stirring. After 2 h the reaction mixture was washed with water and extracted with ether, and the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (*n*-hexane/diethyl ether, 50:50) afforded 425 mg (1.28 mmol, 84% yield) of **2n**: ^{1}H NMR ($CDCl_3$) δ 0.73 (d, 3H, $J_{H,H} = 6.8$), 2.68 (d, 3H, $J_{H,P} = 11.7$), 3.58 (ddq, 1H, $J_{H,H} = 6.8$ and 6.8, $J_{H,P} = 9.1$), 4.23 (dd, 1H, $J_{H,H} = 15.8$, $J_{H,P} = 13.2$), 4.24 (dd, 1H, $J_{H,H} = 15.8$, $J_{H,P} = 12.1$), 5.68 (br d, 1H, $J_{H,H} = 6.8$), 7.1−7.5 (m, 10H); ^{31}P NMR ($CDCl_3$) δ 80.6. Anal. Calcd for $C_{17}H_{21}N_2OPS$: C, 61.43; H, 6.37; N, 8.43; S, 9.65. Found: C, 61.64; H, 6.70; N, 8.70; S, 9.62.

General Procedure for the Oxidative Desulfurization and Deselenization of Compounds 2 with Oxaziridines 1a,b. Synthesis of Triisobutylphosphine Oxide (3b). To a solution of triisobutylphosphine sulfide **2b** (200 mg, 0.85 mmol) in $CHCl_3$ (2 mL) was added a solution of the oxaziridine **1a** (449 mg, 1 mmol) in HCFC-225ca/225cb (5 mL) at rt and under nitrogen. After the reaction mixture was stirred for 5 min, the starting compound had disappeared (TLC analysis). ^{19}F NMR of crude reaction mixture showed that the azaalkene (*Z*)-**4a** was the only coproduct formed. The mixture was filtered, and the exact mass and microanalysis of the separated yellowish solid was that expected for elemental sulfur. Volatiles were removed under reduced pressure to give 166 mg (0.76 mmol, 95% yield) of nearly pure oxide **3b**. An analytically pure sample was obtained through flash chromatography (*n*-hexane/ethyl acetate, 20:80): ^{1}H NMR ($CDCl_3$) δ 1.08 (d, 18H, $J_{H,H} = 6.4$), 1.63 (dd, 6H, $J_{H,H} = 6.4$, $J_{H,P} = 10.9$), 2.09 (m, 3H); ^{31}P NMR ($CDCl_3$) δ 47.7. MS (CI, CH_4) *m*/*z* 219 (M + 1). Anal. Calcd for $C_{12}H_{27}OP$: C, 66.04; H, 12.46; P, 14.18. Found: C, 66.31; H, 12.52; P, 14.08.

Triethylphosphine oxide (**3a**), triphenylphosphine oxide (**3c**), tri-*p*-tolylphosphine oxide (**3d**), diethyl methylphosphonate (**3e**), and diethyl (1-bromo-1,1-difluoromethylene)phosphonate (**3f**) were identified through comparison of isolated products with authentic samples from Alfa and Aldrich. Elemental selenium formed in the oxidation of **2o** was identified through its typical mass spectrum.

O,*O*-Dimethyl *O*-(4-nitrophenyl) phosphate (**3g**),[10a] Paraoxon (**3h**),[11j] *O*,*O*-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphate (**3i**),[11j] and *O*,*O*-dimethyl *O*-(4-bromo-2,5-dichlorophenyl) phosphate (**3j**),[11j] were identified through comparison of their spectral and physical data with those reported in the literature.

***O*,*O*-Dimethyl *O*-[2-(ethylsufinyl)ethyl] phosphate (3k):** oil; ^{1}H NMR ($CDCl_3$) δ 1.37 (t, 3H, $J_{H,H} = 7.5$), 2.80 and 2.81 (m, 2H), 2.93 and 3.07 (m, 2H), 3.81 (d, 6H, $J_{H,P} = 11.2$), 4.48 and 4.51 (m, 2H). Anal. Calcd for $C_6H_{15}O_5PS$: C, 66.04; H, 6.57; P, 13.45. Found: C, 66.27; H, 6.71; P13.28.

***O*,*O*-Diethyl *O*-[2-(ethylsulfinyl)ethyl] phosphate (3l):** oil; ^{1}H NMR ($CDCl_3$) δ 1.36 (dt, 6H, $J_{H,H} = 7.2$, $J_{H,P} = 1.2$), 1.37 (t, 3H, $J_{H,H} = 7.5$), 2.80 and 2.81 (m, 2H), 2.93 and 3.07 (m, 2H), 4.15 (dq, 4H, $J_{H,H} = 7.2$, $J_{H,P} = 8$), 4.46 and 4.50 (m, 2H); ^{31}P NMR ($CDCl_3$) δ −1.0. Anal. Calcd for $C_8H_{19}O_5PS$: C, 37.20; H, 7.41; P, 11.99. Found: C, 37.42; H, 7.70; P, 11.86.

***O*,*O*-Bis(4-nitrophenyl) *N*,*N*-diethylaminophosphate (3m):** oil; ^{1}H NMR ($CDCl_3$) δ 1.13 (t, 6H, $J = 7.1$), 3.29 (dq, 4H, $J_{H,H} = 7.1$, $J_{H,P} = 12.6$), 7.40 (m, 4H, $J_{H,P} = 1.0$), 8.27 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 0.3. Anal. Calcd for $C_{16}H_{18}N_3O_7P$: C, 48.61; H, 4.59; N, 10.63. Found: C, 48.89; H, 4.73; N, 10.91.

(2*S*,4*R*,5*S*)-2-(Benzylamino)-1,3,2-oxazaphospholidine 2-oxide (3n): ^{1}H NMR (acetone-d_6) δ 0.74 (d, 3H, $J_{H,H} = 6.6$), 2.59 (d, 3H, $J_{H,P} = 10.0$), 3.76 (ddq, 1H, $J_{H,H} = 6.6$ and 6.2, $J_{H,P} = 16.7$), 4.20 (d, 2H, $J_{H,P} = 12.3$), 5.57 (dd, 1H, $J_{H,H} = 6.2$, $J_{H,P} = 3.5$), 7.2−7.6 (m, 10H); ^{31}P NMR ($CDCl_3$) δ 24.5; NOE experiments (acetone-d_6), no enhancement (<0.1%) of NCH_2, NCH_2ArH_{ortho} was observed on irradiation of CH_3-4 and the reverse. Anal. Calcd for $C_{17}H_{21}N_2O_2P$: C, 64.55; H, 6.69; N, 8.85. Found: C, 64.71; H, 6.80; N, 8.84.

(2*R*,4*R*,5*S*)-2-(Benzylamino)-1,3,2-oxazaphospholidine 2-Oxide (3n). MCPBA Method. *m*-Chloroperbenzoic acid (57 mg, 0.33 mmol) was added to a solution of (2*S*,4*R*,5*S*)-**2n** (100 mg, 0.30 mmol) in $CHCl_3$. After 15 min the mixture was filtered and the solution washed with dilute aqueous sodium carbonate. Concentration of the organic layer and flash chromatography ($CHCl_3$/acetone, 50:50) of the residue gave (2*R*,4*R*,5*S*)-**3n** (85 mg, 0.27 mmol, 90% yield) in pure form: ^{1}H NMR (acetone-d_6) δ 0.68 (d, 3H, $J_{H,H} = 6.6$), 2.63 (d, 3H, $J_{H,P} = 9.4$), 3.71 (ddq, 1H, $J_{H,H} = 6.6$ and 6.5, $J_{H,P} = 10.9$), 4.17 (dd, 1H, $J_{H,H} = 15.8$, $J_{H,P} = 13.1$), 4.23 (dd, 1H, $J_{H,H} = 15.8$, $J_{H,P} = 14.2$), 5.60 (br d, 1H, $J_{H,H} = 6.5$), 7.20−7.40 (m, 8H), 7.45 (m, 2H); ^{31}P NMR ($CDCl_3$) δ 26.4; NOE experiments (acetone-d_6) irradiation of NCH_2 enhanced CH_3-4 (0.5%) and NCH_2ArH_{ortho} (1%), irradiation of CH_3-4 enhanced H-4 (4.5%), CH_3-3 (1%), NCH_2 (1%), CH_2ArH_{ortho} (0.5%).

Acknowledgment. We gratefully acknowledge the financial support of the European Union (INTAS-93−799-Ext) and MURST (Rome) for 60%. We thank Dr. E. Benfenati (IRF "Mario Negri" Milano, Italy) for a generous gift of Fenitrothion (**2i**) and Bromophos (**2j**).

JO970572A