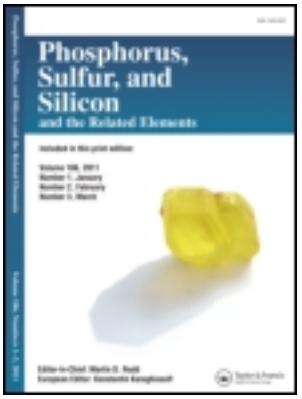

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New Routes to β-Iminophosphonates, Phosphineoxides, and Sulfides

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NEW ROUTES TO β-IMINOPHOSPHONATES, PHOSPHINEOXIDES, AND SULFIDES

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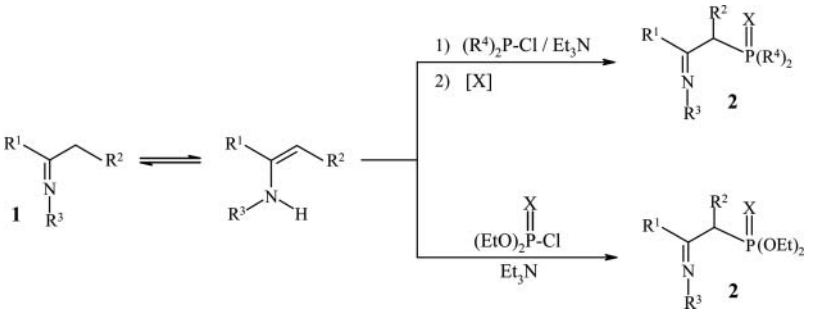
GRAPHICAL ABSTRACT



Abstract *Two synthetic methods leading to β-iminophosphonates, phosphineoxides, and sulfides* ***2*** *are reported. The first method involves the reaction of imines with chlorophosphines and phosphites followed by oxidation or sulfurization. The second one utilizes the reaction of imines with diethylchlorophosphate and thiophosphate. The stereochemistry of the obtained products is discussed, and their structure is confirmed by NMR (^{1}H, ^{31}P, ^{13}C) and IR spectroscopies, and by mass spectrometry.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Imines; β-iminophosphineoxides; β-iminophosphinesulfides; β-iminophosphonates

INTRODUCTION

An increasing interest has been paid for several years to the synthesis of β-iminophosphonates.[1–6] Such interest has been stimulated by their utility as key intermediates

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in the synthesis of β-aminophosphonates,[1–5,7] which are known for their interesting biological activities as antibacterial agents,[8] enzyme inhibitors,[9] haptens for catalytic antibodies,[10] and anti-HIV agents.[11]

β-Iminophosphonates are commonly obtained by the reaction of amines with β-ketophosphonates, which are difficult to synthesize.[4,6,12] Another approach,[13–17] but leading to β-iminophosphines, involves the reaction of lithium salts of imines with chlorophosphines. The phosphorus(III) derivatives obtained are unstable and cannot be widely used in further syntheses. Also, the reaction is limited by a competitive N-phosphorylation process affording N-phosphorus-substituted enamines.

This prompted us to develop new, simple, one-pot methodologies for the synthesis of β-iminophosphonates, phosphineoxides, and sulfides, which use easily made imines directly, instead of their lithium salts, and commercially available chlorophosphines, phosphites, or phosphates as starting materials. These new syntheses have the advantages of good yields, stable products, and mild reaction conditions; besides no competitive N-phosphorylation process was observed in all cases.

RESULTS AND DISCUSSION

For the synthesis of β-iminophosphonates, phosphineoxides, and sulfides **2**, we have used two different approches. The first one (Method A) involves the reaction of imines with chlorophosphines and phosphites followed by oxidation or sulfurization. The second method (Method B) utilizes the reaction of imines with diethylchlorophosphate and thiophosphate.

Method A: Reaction of Imines with Chlorophosphines and Phosphites

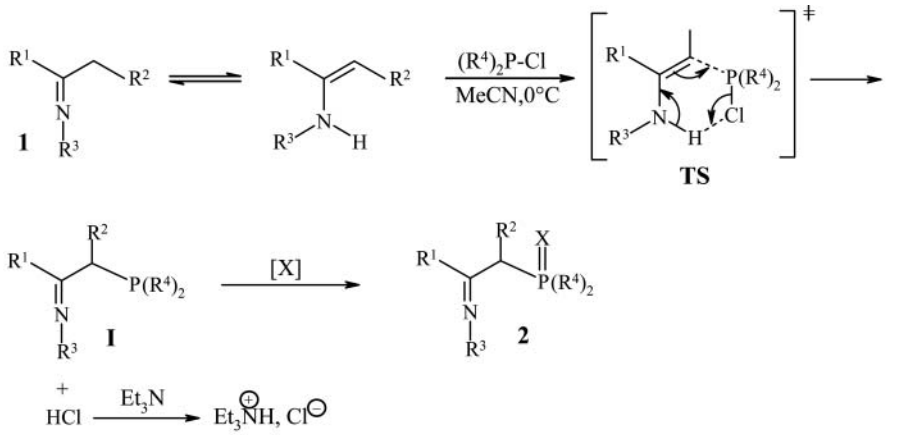
Treatment of imines **1** with chlorophosphines and phosphites, performed in acetonitrile at 0°C in the presence of an equimolar amount of triethylamine, led to the formation of the phosphine intermediate **I** (Scheme 1). A subsequent oxidation or sulfurization carried out, in a one-pot reaction, by treating respectively with dimethylsulfoxide (DMSO) under reflux or with elemental sulfur at 40°C, furnished the β-iminophosphonates, phosphineoxides, and sulfides **2** in good yields.

Based on some data in the literature[18] concerning the reactivity of imines with electrophilic agents, we can propose the reaction mechanism of Scheme 1, which involves a six-membered cyclic transition state **TS**. This allows the hydrogen on the nitrogen atom to be transferred concertedly and avoids the formation of charged intermediates that are high in energy.

In order to obtain a better perspective on the reaction mechanism, we carried out a theoretical *ab initio* SCF/6-31G calculation, which established that the reaction proceeds through a six-membered cyclic transition state having a compact structure stabilized by MO interactions (Figure 1).

Method B: Reaction of Imines with Diethylchlorophosphate and Thiophosphate

Similar to the reaction of chlorophosphines and phosphites, we found that chlorophosphates and thiophosphates can also react with imines **1** in the presence of



	2a	2b	2c	2d	2e	2f
R^1	Ph	Ph	Ph	Et	Et	$(CH_2)_3$
R^2	H	H	H	H	H	
R^3	CH_2-Ph	Ph	CH_2-Ph	CH_2-Ph	CH_2-Ph	CH_2-Ph
R^4	Ph	EtO	EtO	Ph	Ph	EtO
X	O	O	S	S	O	S
Yield(%)	78	72	80	68	71	76

	2g	2h	2i	2j	2k
R^1 R^2	$(CH_2)_3$	$(CH_2)_4$	$(CH_2)_4$	$(CH_2)_4$	$(CH_2)_4$
R^3	CH_2-Ph	CH_2-Ph	iPr	CH_2-Ph	CH_2-Ph
R^4	EtO	Ph	EtO	EtO	Ph
X	O	S	S	O	O
Yield(%)	85	80	82	91	73

Scheme 1

an equimolar amount of triethylamine and using diethylether as solvent to afford the β-iminophosphonates and phosphinesulfides **2** in good yields (Scheme 2).

It is important to note that all compounds **2**, synthesized by methods A and B, are obtained exclusively in their imine form. Indeed, the reaction did not afford any identifiable enamine tautomer for compounds **2**, as evidenced by spectroscopic data.

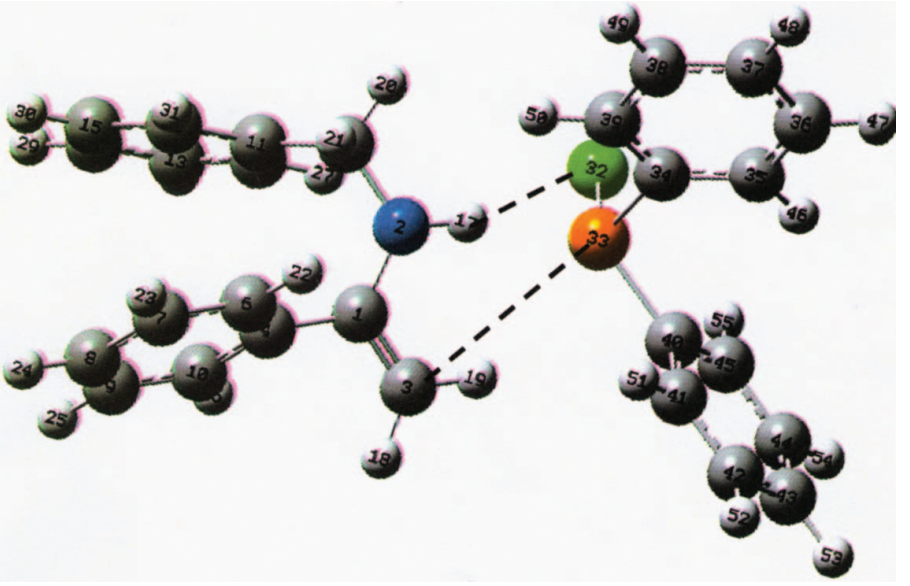


Figure 1 Calculated transition state **TS** in the formation of compound **2a**.

Spectrographic Study

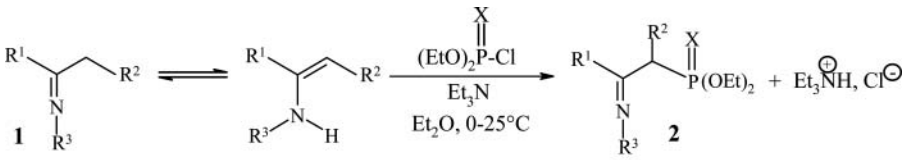
Compounds **2** were characterized on the basis of their ^{31}P, ^{1}H, and ^{13}C NMR data, which indicate that they are obtained, in some cases, as a mixture of Z and E isomers (Scheme 3). Their relative proportions were estimated from the ^{31}P NMR spectra where a singlet for each isomer is present (Table 1).

It is important to note here that the reaction shows considerable diastereoselectivity. Indeed, the less hindered E isomer is the major or the sole one.

The Z and E configurations were attributed on the basis of C_1 chemical shift values (Table 2). Indeed, according to some data in the literature[19–22] concerning the stereochemistry of imines, hydrazones, and oximes, the carbon adjacent to the C=N double bond

Table 1 δ ^{31}P in ppm and% of Z and E isomers for compounds **2**

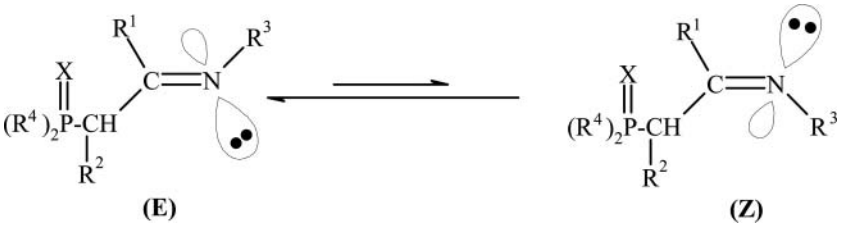
	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**
$\delta^{31}P$(**E**)	21.3	2.6	68.4	60.7	23.5	57.1	10.1
$\delta^{31}P$(**Z**)	—	3.8	70.0	—	—	70.6	—
% **E**	100	81	85	100	100	69	100
% **Z**	—	19	15	—	—	31	—
	2h	**2i**	**2j**	**2k**	**2l**	**2m**	**2n**
$\delta^{31}P$(**E**)	59.6	70.3	8.9	21.3	9.8	9.9	67.6
$\delta^{31}P$(**Z**)	—	—	—	—	—	—	71.6
% **E**	100	100	100	100	100	100	62
% **Z**	—	—	—	—	—	—	38



	2b	2c	2g	2i
R^1	Ph	Ph	$(CH_2)_3$	$(CH_2)_4$
R^2	H	H		
R^3	Ph	CH_2-Ph	CH_2-Ph	iPr
X	O	S	O	S
Yield(%)	83	65	80	71

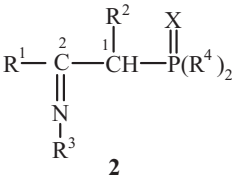
	2j	2l	2m	2n
R^1	$(CH_2)_4$	Et	Ph	$(CH_2)_4$
R^2		H	H	
R^3	CH_2-Ph	CH_2-Ph	CH_2-Ph	CH_2-Ph
X	O	O	O	S
Yield(%)	75	70	67	78

Scheme 2



Scheme 3

Table 2 ^{13}C NMR for compounds **2**: δ in ppm (J_{CP} in Hz)



2

R^1: $^{11}C_6H_5$, $^{3}CH_2$-$^{4}CH_3$, $^{3}CH_2$-$^{4}CH_2$-$^{5}CH_2$-$^{6}CH_2$, $^{3}CH_2$-$^{4}CH_2$-$^{5}CH_2$

R^2: H

R^3: $^{11}C_6H_5$, $^{7}CH_2$-$^{11}C_6H_5$, $^{7}CH(^{8}CH_3)_2$

R^4: $^{10}CH_3$-$^{9}CH_2$-O, $^{11}C_6H_5$

	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**
C_1	26.1 (71.6)	20.8 (52.1;**Z**) 45.5 (67.9;**E**)	39.8 (44.3;**Z**) 46.5 (70.9;**E**)	44.4 (71.0)	30,7 (38.6)	63.3 (99.6;**Z**) 63.4 (98.9;**E**)	42.3 (109.4)
C_2	141.1	151.3 (**Z**) 154.7 (**E**)	150.7 (**Z**) 157.8 (**E**)	145.0	142.7	162.8 (**Z**) 160.2 (**E**)	157.4
C_3	—	—	—	45.3	45.0	33.7 (**Z**) 32.7 (**E**)	36.3 (18.1)
C_4	—	—	—	8.1	7.8	22.7 (**Z**) 23.1 (**E**)	19.4
C_5	—	—	—	—	—	30.3 (**Z**) 28.6 (**E**)	23.4
C_6	—	—	—	—	—	—	—
C_7	42.8	—	39.4 (**Z**) 42.6 (**E**)	42.5	42.4	45.5	43.4
C_8	—	—	—	—	—	—	—
C_9	—	65.0 (3.0;**Z**) 62.4 (4.5;**E**)	62,9 (4.5;**Z**) 66.2 (3.8;**E**)	—	—	62.6 (4.5; **Z**) 61.5 (6.0; **E**)	60.3 (6.0)
C_{10}	—	15.5 (8.3;**Z**) 15.9 (7.5;**E**)	16.0 (8.3;**Z**) 15.7 (7.5;**E**)	—	—	15.7 (7.5; **Z**) 16.2 (8.3; **E**)	14.3 (6.8)
C_{11}	127.7–137.8*	117.4–133.0	117.3–137.5	127.0–137.6	127.1–136.6	125.1–135.1	124.0–131.9

	2h	**2i**	**2j**	**2k**	**2l**	**2m**	**2n**
C_1	51.6 (92.1)	44.2 (126.0)	54.6 (184.0)	73.9 (81.7)	33.5 (123.8)	43.9 (67.2)	41.0 (125.7;**Z**) 57.0 (172.7;**E**)
C_2	143.8	136.6	140.4	136.4	168.6	155.9	158.0 (**Z**) 152.6 (**E**)
C_3	42.2 (18.0)	42.6 (14.3)	41.2 (18.1)	30.9 (4.7)	46.0	—	41.5 (15.8;**Z**) 29.0 (9.8;**E**)
C_4	23.9	24.3	24.5	25.0	8.5	—	23.7 (**Z**) 24.4 (**E**)
C_5	36.1 (15.5)	24.1 (14.3)	25.7 (18.1)	20.1 (9.7)	—	—	26.1 (6.8)
C_6	27.2	25.0	25.6	27.0	—	—	27.6 (**Z**) 27.3 (**E**)
C_7	45.1	40.9	44.7	42.0	44.8	41.6	45.1 (**Z**) 45.7 (**E**)
C_8	—	26.0	—	—	—	—	—
C_9	—	61.5 (5.3)	61.2 (6.0)	—	61.8 (5.3)	60.4 (5.3)	62.1 (5.3;**Z**) 65.7 (6.8;**E**)
C_{10}	—	14.9 (6.8)	15.7 (7.5)	—	15.7 (8.3)	14.4 (9.8)	15.5 (8.3;**Z**) 15.2 (8.0;**E**)
C_{11}	127.5–134.4	—	126.0–129.1	127.5–132.6	123.4–129.8	124.2–131.7	124.8–131.1

*For aromatic ^{13}C NMR individual signals, see the Experimental section.

resonates at a higher field when it is in syn position to the group on nitrogen atom (R^3 in our case).

EXPERIMENTAL

^1H, ^{31}P, and ^{13}C NMR spectra were recorded with $CDCl_3$ as solvent on a Bruker-300 spectrometer. The chemical shifts are reported in ppm relative to TMS (internal reference) for ^1H and ^{13}C NMR and relative to 85% H_3PO_4 (external reference) for ^{31}P NMR. The coupling constants are reported in Hz. For the ^1H NMR, the multiplicities of signals are indicated by the following abbreviations: s: singlet, d: doublet, t: triplet, q: quartet, qp: quintet, m: multiplet.

Mass spectra were determined on a Micromass Quatro-ultima Pt (triple quadrupole) spectrometer under electrospray ionization (ESI) conditions, or on a GCMSD 5975B (Agilent technologies) spectrometer under electronic impact ionization (EI) conditions.

IR spectra were recorded in $CHCl_3$, on a Perkin Elmer Paragon 1000 PC spectrometer. The progress of the reactions was controlled by TLC. Purification of products was performed by column chromatography using silica gel 60 (Fluka).

Synthesis of Imines 1

The starting imines **1** were prepared according to reported procedures.[23–25]

Synthesis of β-Iminophosphonates, Phosphineoxides, and Sulfides 2

Method A. To a mixture of imine **1** (0.01 mol), triethylamine (0.012 mol), and dry MeCN (50 mL), cooled at 0°C and maintained under a nitrogen atmosphere, a solution of chlorophosphine or phosphite (0.01 mol) in dry MeCN (30 mL) was added dropwise with stirring. Stirring at 0°C was continued for 1 h. The reaction mixture was then treated with DMSO or sulfur as follows:

Oxidation. DMSO (0.01 mol) was added, and the mixture was heated under reflux for 2 h. After cooling, $CHCl_3$ (50 mL) was added. The organic phase was washed with water (2 × 25 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue obtained was chromatographed on a silica gel column using ether as eluent.

Sulfurization. Sulfur (0.01 mol) was added, and the mixture was heated at 40°C for 30 min. After cooling, $CHCl_3$ (50 mL) was added. The organic phase was washed with water (2 × 25 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue obtained was chromatographed on a silica gel column using ether as eluent.

Method B. To a mixture of imine **1** (0.01 mol), triethylamine (0.012 mol), and dry Et_2O (50 mL), cooled at 0°C and maintained under a nitrogen atmosphere, a solution of diethylchlorophosphate or thiophosphate (0.01 mol) in dry Et_2O (10 mL) was added dropwise with stirring. Stirring was continued for 24 h at 25°C. The reaction mixture was then extracted with water (2 × 25 mL). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue obtained was chromatographed on a silica gel column using ether as eluent.

2a: mp = 265°C; ^1H NMR: $\delta = 1.79$ (d, 2H, $^2J_{PH} = 13.6$, CH_2-P=O); 3.56 (s, 2H, N-C$\underline{H_2}$-Ph); 7.11-7.97(m, 20H, H arom); IR: $\nu_{C=N} = 1656\ cm^{-1}$; $\nu_{P=O} = 1252\ cm^{-1}$; ^{13}C NMR for arom-C: $\delta = 127.7, 127.9, 128.1, 128.2, 128.3, 128.6, 128.7, 129.0, 130.4, 130.6, 130.8, 131.1, 131.2, 132.5, 136.0, 137.8$; ESI-MS: m/z = 427.552($[M+NH_4]^+$).

2b: Oil; ^{1}H NMR: $\delta = 1.04$ (t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O;**E**); 1.14(t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O;**Z**); 2.12 (d, 2H, $^2J_{PH} = 25.0$, C$\underline{H_2}$-P=O;**Z**); 2.33(d, 2H, $^2J_{PH} = 15.0$, C$\underline{H_2}$-P=O;**Z**); 3.88 (qp, 4H; $^3J_{HH} = {}^3J_{PH} = 6.0$, CH$_3$-C$\underline{H_2}$-O;**E**); 4.04 (qp, 4H, $^3J_{HH} = {}^3J_{PH} = 6.0$, CH$_3$-C$\underline{H_2}$-O;**Z**); 6.50–7.80 (m, 10H, H arom); IR: $\nu_{C=N} = 1642$ cm^{-1}; $\nu_{P=O} = 1266$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 117.4, 119.5, 121.0, 123.7, 127.8, 128.0, 128.1, 128.3, 128.4, 128.7, 129.1, 129.3, 132.4, 133.0$; ESI-MS: m/z = 349.428([M+NH$_4$]$^+$).

2c: Oil; ^{1}H NMR: $\delta = 1.10$ (t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O;**Z**); 1.17 (t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O,**E**); 1.28 (d, 2H, $^2J_{PH} = 9.0$, C$\underline{H_2}$-P = S, **E**); 1.60 (d, 2H, $^2J_{PH} = 9.0$, CH$_2$-P=S,**Z**); 3.92 (qp, 4H, $^3J_{HH} = {}^3J_{PH} = 6.0$, CH$_3$-C$\underline{H_2}$-O,**Z**); 4.06 (qp, 4H, $^3J_{HH} = {}^3J_{PH} = 6.0$, CH$_3$-C$\underline{H_2}$-O,**E**); 6.21 (s, 2H, Ph-C$\underline{H_2}$,**Z**); 6.23 (s, 2H, Ph-C$\underline{H_2}$,**E**); 6.99–7.73 (m, 10H, H arom); IR: $\nu_{C=N} = 1610$ cm^{-1}; $\nu_{P=S} = 1100$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 117.3, 125.5, 125.7, 125.9, 126.0, 126.9, 127.4, 127.6, 128.1, 128.7, 129.2, 130.9, 137.3, 137.5$; EI-MS: m/z = 361(M$^+$, 15%); 345(30%); 332(16%); 270(60%); 91(100%); 77(28%).

2d: Oil; ^{1}H NMR: $\delta = 1.19$ (t, 3H, $^3J_{HH} = 7.0$, C$\underline{H_3}$-CH$_2$); 2.05 (d, 2H, $^2J_{PH} = 35.7$, C$\underline{H_2}$-P=S); 3.04 (q, 2H, $^3J_{HH} = 7.0$, CH$_3$-C$\underline{H_2}$); 3.64 (s, 2H, Ph-C$\underline{H_2}$); 6.92–8.16 (m, 15H, H arom). IR: $\nu_{C=N} = 1645$ cm^{-1}; $\nu_{P=S} = 1111$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 127.0, 127.2, 127.3, 127.6, 128.5, 128.7, 130.2, 130.3, 131.2, 132.8, 136.5, 137.6$; EI-MS: m/z = 377(M$^+$, 8%); 286(10%); 217(10%); 160(66%); 91(100%); 77(20%).

2e: Mp = 138°C; ^{1}H NMR: $\delta = 1.28$ (t, 3H, $^3J_{HH} = 6.6$, C$\underline{H_3}$-CH$_2$); 2.22 (d, 2H, $^2J_{PH} = 47.1$, C$\underline{H_2}$-P=O); 3.02 (q, 2H, $^3J_{HH} = 6.6$, CH$_3$-C$\underline{H_2}$); 3.66 (s, 2H, Ph-C$\underline{H_2}$); 7.14–7.54 (m, 15H, H arom). IR: $\nu_{C=N} = 1646$ cm^{-1}; $\nu_{P=O} = 1260$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 127.1, 127.3, 127.6, 127.7, 127.9, 128.1, 128.2, 128.9, 129.7, 131.2, 134.8, 136.6$; EI-MS: m/z = 361(M$^+$, 33%); 270(13%); 201(53%); 160(86%); 91(100%); 77(29%).

2f: Oil; ^{1}H NMR: $\delta = 1.08$ (t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O, **Z**); 1.19 (t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O, **E**); 1.25–3.05 (m, 7H, cyclic H and C$\underline{H}$-P=S); 3.79–4.15 (m, 6H, CH$_3$-C$\underline{H_2}$-O and Ph-C$\underline{H_2}$); 6.94–7.31 (m, 5H, H arom); IR: $\nu_{C=N} = 1616$ cm^{-1}; $\nu_{P=S} = 1096$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 125.1, 125.7, 127.0, 127.7, 128.2, 128.4, 132.9, 135.1$; EI-MS: m/z = 325(M$^+$, 25%); 234(16%); 186(60%); 91(100%).

2g: Oil; ^{1}H NMR: $\delta = 1.22$ (t, 6H, $^3J_{HH} = 6.0$; C$\underline{H_3}$-CH$_2$-O); 1.39–3.20 (m, 7H, cyclic H and C$\underline{H}$-P=O); 3.98–4.30 (m, 6H, CH$_3$-C$\underline{H_2}$-O and Ph-C$\underline{H_2}$); 7.00–7.60 (m, 5H, H arom); IR: $\nu_{C=N} = 1620$ cm^{-1}; $\nu_{P=O} = 1250$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 124.0, 125.2, 126.8, 131.9$; EI-MS: m/z = 309(M$^+$, 33%); 218(20%); 186(67%); 91(100%).

2h: Oil; ^{1}H NMR: $\delta = 1.50$–3.10 (m, 9H, cyclic H and C$\underline{H}$-P=S); 4.10 (s, 2H, Ph-C$\underline{H_2}$); 6.90–8.20 (m, 15H, H arom). IR: $\nu_{C=N} = 1650$ cm^{-1}; $\nu_{P=S} = 1106$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 127.5, 127.6, 128.0, 128.4, 128.5, 128.6, 128.7, 131.5, 131.6, 132.0, 133.1, 134.4$; EI-MS: m/z = 403(M$^+$, 16%); 312(20%); 217(29%); 186(75%); 91(100%); 77(25%).

2i: Oil; ^{1}H NMR: $\delta = 1.07$ (d, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH-N); 1.22 (t, 6H, $^3J_{HH} = 6.0$, C$\underline{H_3}$-CH$_2$-O); 1.38–2.25 (m, 9H, cyclic H and C$\underline{H}$-P=S); 3.36 (m, 1H, $^3J_{HH} = 6.0$, CH$_3$-C$\underline{H}$-N); 3.88–4.10 (m, 4H, CH$_3$-C$\underline{H_2}$-O); IR: $\nu_{C=N} = 1632$ cm^{-1}; $\nu_{P=S} = 1097$ cm^{-1}; ESI-MS: m/z = 292.474([M+H]$^+$).

2j: Oil; ^{1}H NMR: $\delta = 1.18$ (t, 6H, $^3J_{HH} = 7.2$, C$\underline{H_3}$-CH$_2$-O); 1.53–2.28 (m, 9H, cyclic H and C$\underline{H}$-P=O); 3.80–4.05 (m, 6H, CH$_3$-C$\underline{H_2}$-O and Ph-C$\underline{H_2}$); 7.04–7.30 (m, 5H, H arom); IR: $\nu_{C=N} = 1631$ cm^{-1}; $\nu_{P=O} = 1254$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 126.0, 126.7, 127.8, 129.1$; EI-MS: m/z = 323(M$^+$, 36%); 232(15%); 186(62%); 91(100%).

2k: Mp = 176°C; ^{1}H NMR: $\delta = 1.50$–2.50 (m, 9H, cyclic H and C$\underline{H}$-P=O); 5.52 (m, 2H, Ph-C$\underline{H_2}$); 7.00–8.30 (m, 15H, H arom); IR: $\nu_{C=N} = 1664$ cm^{-1}; $\nu_{P=O} = 1253$ cm^{-1}; ^{13}C NMR for arom-C: $\delta = 127.5, 127.6, 127.9, 128.2, 128.4, 128.8, 129.0, 130.0, 130.8, 131.8,$

132.5, 132.6; EI-MS: m/z = 387(M^+, 19%); 296(71%); 201(63%); 186(90%); 91(100%); 77(28%).

2l: Oil; ^{1}H NMR: δ = 1.15 (t, 3H, $^3J_{HH}$ = 6.0, C$\underline{H_3}$-CH_2-C); 1.25 (t, 6H, $^3J_{HH}$ = 6.0; C$\underline{H_3}$-CH_2-O); 2.18 (d, 2H, $^2J_{PH}$ = 21.0, C$\underline{H_2}$-P=O); 3.02 (q, 2H, $^3J_{HH}$ = 6.0, CH_3-C$\underline{H_2}$-C); 3.84–4.16 (m, 6H, CH_3-C$\underline{H_2}$-O and Ph-C$\underline{H_2}$); 7.00–7.62 (m, 5H, H arom). IR: $\nu_{C=N}$ = 1651 cm^{-1}; $\nu_{P=O}$ = 1265 cm^{-1}; ^{13}C NMR for arom-C: δ = 123.4, 125.2, 128.6, 129.8; EI-MS: m/z = 297(M^+, 14%); 281(34%); 268(16%); 207(67%); 91(100%); 77(17%).

2m: Oil; ^{1}H NMR: δ = 1.24 (t, 6H, $^3J_{HH}$ = 6.0, C$\underline{H_3}$-CH_2-O); 2.35 (d, 2H, $^2J_{PH}$ = 30.0, C$\underline{H_2}$-P=O); 3.85–4.30 (m, 6H, CH_3-C$\underline{H_2}$-O and Ph-C$\underline{H_2}$); 6.80–8.20 (m, 10H, H arom); IR: $\nu_{C=N}$ = 1630 cm^{-1}; $\nu_{P=O}$ = 1274 cm^{-1}; ^{13}C NMR for arom-C: δ = 124.2, 124.6, 125.1, 126.9, 127.4, 127.7, 128.0, 131.5, 131.7; EI-MS: m/z = 345(M^+, 20%); 329(15%); 254(60%); 91(100%); 77(20%).

2n: Oil; ^{1}H NMR: δ = 1.14(t, 6H, $^3J_{HH}$ = 6.0, C$\underline{H_3}$-CH_2-O, **Z**); 1.25 (t, 6H, $^3J_{HH}$ = 6.0, C$\underline{H_3}$-CH_2-O, **E**); 1.45–3.01 (m, 9H, cyclic H and C$\underline{H}$-P=S); 3.84–4.19 (m, 6H, CH_3-C$\underline{H_2}$-O and Ph-C$\underline{H_2}$); 7.00–7.57 (m, 5H, H arom); IR: $\nu_{C=N}$ = 1631 cm^{-1}; $\nu_{P=S}$ = 1096 cm^{-1}; ^{13}C NMR for arom-C: δ = 124.8, 126.3, 126.7, 127.2, 127.9, 128.3, 130.4, 131.1; EI-MS: m/z = 339(M^+, 30%); 248(12%); 186(55%); 91(100%).

REFERENCES

1. Palacios, F.; Aparicio, D.; Garcia, J. *Tetrahedron* **1996,** *52*, 9609–9628.
2. Palacios, F.; Aparicio, D.; Garcia, J.; Rodriguez, E. *Eur. J. Org. Chem.* **1998**, 1413–1423.
3. Xiao, J.; Yuan, C. *Heteroat. Chem.* **2000,** *7*, 541–545.
4. Varlet, J. M.; Collignon, N.; Savignac, P. *Tetrahedron* **1981,** *37*, 3713.
5. Srivastava, H. K.; Quntar, A.; Azab, A.; Srebnik, M.; Shurki, A. *Tetrahedron* **2009,** *65*, 4389.
6. Jelaiel, N.; Said, N.; Touil, S.; Efrit, M. L. *Phosphorus, Sulfur Silicon Relat. Elem.* **2010,** *185*, 2382–2392.
7. Palacios, F.; Alonso, C.; de los Santos, J. M. *Chem. Rev.* **2005,** *105*, 899.
8. Allen, J. G.; Arthenton, F. R.; Hall, M. J.; Hassall, C. H.; Holmes, S. W.; Lambert, R. W.; Nisbet, L. J.; Ringrose, P. S. *Nature* **1978,** *272*, 56.
9. (a) Smith, W. W.; Bartlett, P. A. *J. Am. Chem. Soc.* **1998,** *120*, 4622; (b) Allen, M. C.; Fuhrer, W.; Tuck, B.; Wade, R.; Wood, J. M. *J. Med. Chem.* **1989,** *32*, 1652.
10. Hirschmann, R.; Smith, A. B.; Taylor, C. M.; Benkovic, P. A.; Taylor, S. D.; Yager, K. M.; Sprengler, P. A.; Benkovic, S. J. *Science* **1994,** *265*, 234.
11. Alonso, E.; Solis, A.; del Pozo, C. *Synlett* **2000**, 698.
12. Coutrot, P.; Grison, C.; Lachgar, M.; Ghribi, A. *Bull. Soc. Chim. Fr.* **1995,** *132*, 925.
13. Kabachnik, M. M.; Novikova, Z. S.; Chadnaya, I. A.; Borisenko, A. A.; Beletskaya, I. P. *Russ. Chem. Bull.* **1998,** *47*, 332.
14. Novikova, Z. S.; Kabachnik, M. M.; Chadnaya, I. A.; Borisenko, A. A.; Beletskaya, I. P. *Russ. J. Org. Chem.* **1993,** *29*, 385.
15. Chadnaya, I. A.; Kabachnik, M. M.; Borisenko, A. A.; Novikova, Z. S. *J. Gen. Chem. USSR* **1991,** *61*, 1765.
16. Chadnaya, I. A.; Potapova, E. L.; Kabachnik, M. M.; Borisenko, A. A.; Novikova, Z. S. *J. Gen. Chem. USSR*, **1991,** *61*, 1561.
17. Novikova, Z. S.; Kabachnik, M. M.; Chadnaya, I. A.; Borisenko, A. A.; Lutzenko, I. F. *Phosphorus, Sulfur Silicon Relat. Elem.* **1990,** *51*, 268.
18. d'Angelo, J.; Desmaële, D.; Dumas, F.; Guingant, A. *Tetrahedron: Asymmetry* **1992,** *3*, 459.
19. Naulet, N.; Filleux, H. L.; Martin, G. J.; Pornet, J. *Org. Magn. Reson*. **1975,** *7*, 326.

20. Levy, G. C.; Nelson, G. L. *J. Am. Chem. Soc.* **1972,** *94*, 4897.
21. Touil, S.; Zantour, H. *J. Soc. Chim. Tunisie* **1998,** *4*, 159.
22. Ben Akacha, A.; Barkallah, S.; Zantour, H. *Magn. Reson. Chem.* **1999,** *37*, 916.
23. Jewers, K.; McKenna, J. *J. Chem. Soc.* **1958**, 2209.
24. Norton, D. G.; Haury, V. E.; Davis, F. C.; Metchell, L. J.; Ballard, S. A. *J. Org. Chem.* **1954,** *19*, 1054.
25. Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1978,** *43*, 2907.