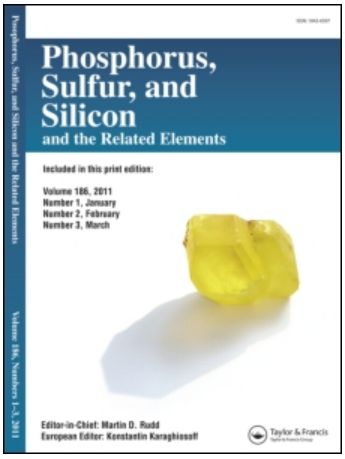

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Synthesis and Biological Activity of Cis 2-(6-Chloropyridine-3-yl)methylamino-4-substitutedphenyl-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxides

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Synthesis and Biological Activity of Cis 2-(6-Chloropyridine-3-yl)methylamino-4-substitutedphenyl-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxides

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A series of novel, asymmetric-cyclic phosphoramides containing substituted pyridine were synthesized via the condensation reactions of trans 2-chloro-4-substitutedphenyl-5, 5-dimethyl-1,3,2-dioxaphosphinane 2-oxide with 2-chloro-5-aminomethylpyridine or 3-aminomethylpyridine. The reactions show good stereoselectivity. Only the cis isomer from configuration inversion was obtained, which is the thermodynamic stable product. The structures of the products were characterized by ^{1}H NMR, ^{31}P NMR, IR, MS, and elemental analysis. The configuration of the product was determined by X-ray diffraction analysis. The results of preliminary bioassay showed that the new compounds possess potential insecticidal and fungicidal activities.

Keywords Biological activities; configuration; cyclic phosphoramide; substituted pyridine; X-ray diffraction

INTRODUCTION

Neonicotinioid insecticides as nicotinic acetylcholine receptor inhibitors have attracted increasing attention because of its safety, low toxicity, and high activities.[1,2] A lot of new insecticides, such as imidacloprid, acetamiprd, and nitenpyram, have been commercialized (Scheme 1).

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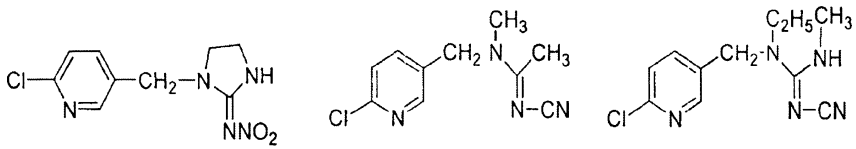
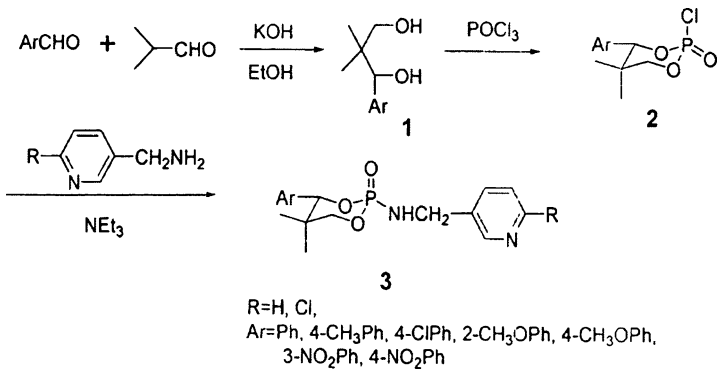


SCHEME 1

It was found that most of the biological active nicotinic compounds contain the 3-aminomethylpyridine moiety.[3] Due to their wide biological activities, organic phosphorus-heterocyclic compounds play an important role in pesticide science; 1,3,2-dioxaphosphinane compounds appear to be very important for their wide biological activities and their stereochemistry.[4–8] As a continuation of our research work, we decided to introduce the structure of 1,3,2-dioxaphosphinane into 3-aminomethylpyridine, and therefore we designed and synthesized a number of novel asymmetric cyclic phosphoramides containing substituted pyridine **3**. The synthetic route is shown in Scheme 2. The structures of the products were characterized by ^{1}H NMR, ^{31}P NMR, IR, MS, and elemental analysis. The X-ray diffraction analysis shows that the configurations of products are cis isomers.



SCHEME 2

The results of preliminary bioassay showed that the new compounds displayed potential insecticidal and fungicidal activities.

RESULTS AND DISCUSSION

Preparation of the Title Compounds 3

The title compounds **3** were synthesized by the multistep route outlined in Scheme 2. 1-Aryl-2, 2-dimethyl-1, 3-propanediols **1** are prepared by an aldol condensation followed by a cross Cannizzaro reaction when two equivalents of isobutyraldehyde and a substituted benzaldehyde are allowed to react in basic alcoholic solution. Diols **1** react with $POCl_3$ in the presence of dichloromethane as solvent to obtain trans cyclic phosphorochloridate **2**; 3-aminomethylpyridine then attacks trans compound **2** behind the chlorine atom to obtain cis isomer product **3**, which was confirmed by X-ray diffraction.

The Structures of the Title Compounds 3

All the products **3** were purified by flash column chromatography on silica gel with a mixture of ethyl acetate and petroleum ether as the eluent. The structures of compounds **3** were confirmed by ^{1}H NMR, ^{31}P NMR, and IR spectra, and MS and elemental analysis.

For ^{1}H NMR spectra, the protons of the methyl groups at the 5-position in phosphorus heterocycle appear as two single peaks, due to the two methyl groups being in different magnetic environments. The two protons of the 6-position methylene moiety exhibited two sets of multiple peaks because of the coupling with the phosphorus atom with the coupling constant of 11.6 ppm and lying in different magnetic environments, while the 4-position proton was displayed as a set of doublet peaks with the coupling constant of 11.2 ppm. For ^{31}P NMR spectra, the phosphorus atom of all compounds appeared as a single peak with the chemical shifts in the range of 6.0–6.8. The IR spectra of all compounds showed normal stretching absorption bands indicating the existence of the N–H ($\sim$3200 cm^{-1}), C=N (1560–1590 cm^{-1}), P=O ($\sim$1230 cm^{-1}), and P–O–C ($\sim$1000 cm^{-1}) moiety. The EI mass spectra of compound **3** revealed the existence of the molecular ion peaks and the main fragmentation peaks, which were in accordance with the given structures of products **3**.

X-ray diffraction analysis indicated that the single crystal of **3a** is monoclinic, with a space group P2(1)/n, cell parameter A = 6.1648(6), B = 19.943(2), C = 15.2676(16) Å, $\alpha = 90$, $\beta = 99.220(2)$, $\gamma = 90$, V = 1852.8(3) Å^3, Z = 4, Dc = 1.297 g/cm^3, F (000) = 748, $\mu = 0.309$ mm^{-1} and final R = 0.0660, ωR = 0.1675 for 4436 reflections ($I > 2\sigma(I)$). X-ray analysis revealed that the product is the cis isomer, which is the thermodynamic stable configuration. The selected bond distances and

TABLE I Selected Bond Lengths [Å]

Bond	Dist.	Bond	Dist.	Bond	Dist.	Bond	Dist.
P(1)-O(1)	1.468(2)	C(1)-C(2)	1.300(5)	C(5)-N(1)	1.404(5)	C(12)-C(13)	1.393(5)
P(1)-O(3)	1.572(2)	C(1)-N(1)	1.381(5)	C(7)-C(12)	1.498(4)	C(13)-C(14)	1.382(5)
P(1)-O(2)	1.587(2)	C(1)-Cl(1)	1.742(4)	C(7)-C(8)	1.542(4)	C(14)-C(15)	1.384(6)
P(1)-N(2)	1.605(3)	C(2)-C(3)	1.319(5)	C(8)-C(11)	1.519(5)	C(15)-C(16)	1.367(5)
O(2)-C(7)	1.468(4)	C(3)-C(4)	1.377(5)	C(8)-C(10)	1.534(4)	C(15)-Cl(2)	1.736(4)
O(3)-C(11)	1.456(4)	C(4)-C(5)	1.383(5)	C(8)-C(9)	1.535(5)	C(16)-C(17)	1.374(5)
N(2)-C(6)	1.457(4)	C(4)-C(6)	1.503(5)	C(12)-C(17)	1.391(5)		

angles are listed in Tables I and II. Figures 1 and 2 are the molecular structure of compound **3a** and packing of the molecules in the unit cell, respectively.

Biological Activities

Preliminary bioassays indicate that these title compounds possess potential insecticidal and fungicidal activities. For example, the death ratio of *Aphis glycine Matsumura* by compound **3a**, **3f**, and **3g** is, respectively, 47.2, 18.2, and 35.7% at the concentration of 2.5×10^{-4} while the death ratio of *Tetranychus viennensis zacher* by compound **3f**, **3h**, and **3i** is, respectively, 76.9, 47.1, and 33.3% at the same concentration. The fungicidal activities of some target compounds are listed in Table III. Further studies are under way and will be reported in due course.

TABLE II Selected Bond Angles (°)

Angle	(°)	Angle	(°)	Angle	(°)
O(1)-P(1)-O(3)	115.44(14)	N(1)-C(1)-Cl(1)	118.2(3)	C(12)-C(7)-C(8)	117.0(3)
O(1)-P(1)-O(2)	112.80(14)	C(1)-C(2)-C(3)	117.6(3)	C(11)-C(8)-C(10)	110.5(3)
O(3)-P(1)-O(2)	102.54(13)	C(2)-C(3)-C(4)	124.8(3)	C(11)-C(8)-C(9)	107.4(3)
O(1)-P(1)-N(2)	114.01(15)	C(3)-C(4)-C(5)	116.8(3)	C(10)-C(8)-C(9)	109.8(3)
O(3)-P(1)-N(2)	104.47(14)	C(3)-C(4)-C(6)	123.4(3)	C(11)-C(8)-C(7)	108.6(3)
O(2)-P(1)-N(2)	106.46(13)	C(5)-C(4)-C(6)	119.8(3)	C(10)-C(8)-C(7)	111.9(3)
C(7)-O(2)-P(1)	117.56(18)	C(4)-C(5)-N(1)	119.5(3)	C(9)-C(8)-C(7)	108.5(3)
C(11)-O(3)-P(1)	116.8(2)	C(1)-N(1)-C(5)	116.7(3)	O(3)-C(11)-C(8)	113.6(3)
C(6)-N(2)-P(1)	123.5(2)	N(2)-C(6)-C(4)	114.2(3)	C(17)-C(12)-C(13)	117.9(3)
C(2)-C(1)-N(1)	124.7(4)	O(2)-C(7)-C(12)	106.5(2)	C(17)-C(12)-C(7)	121.5(3)
C(2)-C(1)-Cl(1)	117.1(3)	O(2)-C(7)-C(8)	108.7(3)	C(13)-C(12)-C(7)	120.5(3)
C(14)-C(13)-C(12)	121.3(3)	C(16)-C(15)-C(14)	120.7(3)	C(14)-C(15)-Cl(2)	119.6(3)
C(13)-C(14)-C(15)	119.0(4)	C(16)-C(15)-Cl(2)	119.8(3)	C(15)-C(16)-C(17)	120.2(3)
C(16)-C(17)-C(12)	121.0(3)				

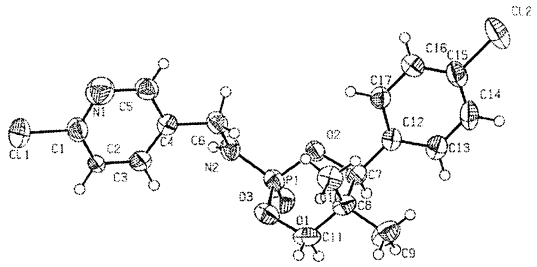


FIGURE 1 Molecular structure of compound **3a**.

EXPERIMENTAL

^{1}H NMR and ^{31}P NMR spectra were recorded with a VARIAN MERCURY-PLUS400 spectrometer with TMS and an 85% H_3PO_4 as the internal and external reference, respectively, and $CDCl_3$ as the solvent, while mass spectra were obtained with a Finnigan TRACEMS2000 spectrometer using the EI method. IR spectra were measured by a NICOLET NEXUS470 spectrometer. Elemental analyses were performed with a ELEMENTAR Vario ELIIICHNSO elementary analyzer. X-ray diffraction analysis was carried out with a BRUKER SMART APEX CCD X-ray diffraction instrument. Melting points were determined with a WRS-1B digital melting point apparatus and the thermometer was uncorrected.

The reagents and solvents were available commercially and purified according to conventional methods before use. 2-chloro-5-chloromethylpyridine was obtained from the pesticide factory in Shashi in Hubei province, China. Diols **1** and 2-chloro-5-aminomethylpyridine were prepared according to references[9] and[10], respectively.

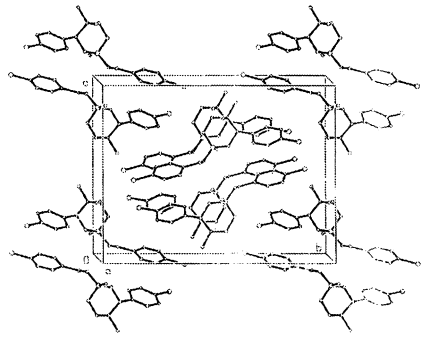


FIGURE 2 Packing of the molecules in the unit cell.

TABLE III The Fungicidal Activities of Compounds 3 (the Plate Method, C = 0.005%, Inhibition%)

Fungi kind	*Fusarium oxysporium*	*Rhizoctonia solani*	*Botrytis cinerea*	*Gibberella zeae*	*Botryosphaeria berengeriana*	*Bopolaris maydis*
3a	33.3	86.5	88.5	51.9	65.0	88.2
3b	47.6	83.3	92.3	48.1	60.0	94.1
3c	66.7	93.8	100	77.8	80.0	94.1
3d	71.4	92.7	96.2	74.1	80.0	94.2
3e	38.1	78.1	92.3	40.7	60.0	82.3
3f	61.9	92.7	98.1	88.9	90.0	94.1
3g	61.9	93.8	96.2	96.3	90.0	97.1
3h	57.1	88.5	98.1	66.7	80.0	88.2
3i	61.9	87.5	92.3	62.9	85	97.1
3j	57.1	90.6	96.2	70.4	85.0	88.2

Synthesis of Trans 2-Chloro-4-substituted Phenyl-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxides

Method A: 0.02 mol of diol **1** in 10 mL of anhydrous CH_2Cl_2 were added to a 50 mL three-necked flask; 0.022 mol of $POCl_3$ was added dropwise at 35°, and the mixture stirred under reflux for 1.5 h. After removing the solvent under a reduced pressure, the crude product was purified by recrystallization with a mixture of CH_2Cl_2/toluene or $CHCl_3$/petroleum ether; a white crystal was obtained in 63–98% yield. Method B: (when 4-methylbenzaldehyde and 4-methoxybenzaldehyde were used): 0.01 mol of diol **1**, 0.02 mol of triethylamine and 20 mL of anhydrous CH_2Cl_2 were added to a 50 mL three-necked flask, the mixture was cooled to 0°C, and 0.01 mol of $POCl_3$ in 5 mL of anhydrous CH_2Cl_2 was added dropwise. The mixture was stirred at 5–10°C for 3 h, the solid was filtered and solvent removed under a reduced pressure. The crude product was purified by recrystallization with a mixture of CH_2Cl_2 and toluene to obtain the product.

General Procedure for the Synthesis of Cis 2-(6-Chloropyridine-3-yl)methylamino-4-substituted Phenyl-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxides

5 mmol of compound **2**, 7.5 mmol of triethylamine, and 10 mL of anhydrous CH_2Cl_2 were added to a 50 mL three-necked reaction flask; the solution of 5 mmol of 2-chloro-5-aminomethylpyridine or 3-aminomethylpyridine in 10 mL of anhydrous CH_2Cl_2 was added dropwise with cooling in an icebath. After the addition was completed, the mixture was stirred at room temperature, or under reflux until the reaction was finished (monitored by TLC). The solid was filtered and

washed with water and the crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 1:2 as the eluent) to obtain compounds **3a–j**.

3a (Ar = 4-ClPh, R = Cl): white solid, m.p. 185.3–186.9°C, yield 81.2%; ^{1}H NMR ($CDCl_3$) $\delta = 0.76$ (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 3.60 (m, 1H, CH_2OP), 3.87 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 4.32 (m, 2H, NCH_2), 4.48 (d, 1H, CH—Ar, $^3J_{H-P} = 10.8$ Hz), 5.42 (s, 1H, N—H), 7.02 (d, 2H, Ar—H, $^3J_{H-H} = 7.6$ Hz), 7.26–7.34 (m, 3H, Ar—H, β-H on pyridine), 7.78 (d, 1H, γ-H on pyridine, $^3J_{H-H} = 7.6$ Hz), 8.39 (s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.51$; IR (KBr) (υ_{max}/cm^{-1}) 3199 (N—H), 1568 and 1590 (C=N), 1229 (P=O), 1047 and 990 (P—O—C); MS, m/e (%) 400, 401, 403 (M^+, 6.9), 347 (56.5), 344 (34.0), 205(100), 141 (39.5), 139 (30.6), 125 (20.0), 77 (20.6), 56 (56.6); Anal. Calcd. For $C_{17}H_{19}O_3N_2Cl_2P$ (401): C, 50.87; H, 4.74; N, 6.98. Found: C, 50.56; H, 4.68; N, 7.17.

3b (Ar = Ph, R = Cl): white solid, m.p. 169.2–170.1°C, yield 78.4%; ^{1}H NMR ($CDCl_3$) $\delta = 0.77$ (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 3.82–3.91 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 4.12 (m, 1H, CH_2OP), 4.31 (m, 2H, NCH_2), 4.48 (d, 1H, CH—Ar, $^3J_{H-P} = 10.8$ Hz), 5.42 (d, 1H, N—H), 7.08 (m, 2H, Ar—H), 7.25–7.34 (m, 4H, Ar—H, β-H on pyridine), 7.80 (d, 1H, γ-H on pyridine, $^3J_{H-H} = 6.8$ Hz), 8.39 (s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.50$; IR (KBr) (υ_{max}/cm^{-1}) 3195 (N—H), 1567 and 1587 (C=N), 1233 (P=O), 1045 and 992 (P—O—C); MS, m/e (%) 366 (M^+, 2.1), 310 (11.9), 204 (39.1), 140 (16.4), 128 (13.6), 114 (19.1), 104 (30.2), 90 (42.2), 76 (38.5), 56 (100); Anal. Calcd. For $C_{17}H_{20}O_3N_2ClP$ (366.5): C, 55.66; H, 5.46; N, 7.64. Found: C, 55.81; H, 5.68; N, 7.93.

3c (Ar = 3-NO_2Ph, R = Cl): pale yellow solid, m.p. 210.3–210.7°C, yield 42.5%; ^{1}H NMR ($CDCl_3$) $\delta = 0.84$ (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 3.58 (m, 1H, CH_2OP), 3.86–3.95 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.6$ Hz), 4.36 (m, 2H, NCH_2), 4.54 (d, 1H, CH—Ar, $^3J_{H-P} = 11.2$ Hz), 5.56 (s, 1H, N—H), 7.34–7.57 (m, 3H, Ar—H), 7.80 (d, 1H, β-H on pyridine, $^3J_{H-H} = 8.0$ Hz), 8.09 (s, 1H, Ar—H), 8.22 (d, 1H, γ-H on pyridine, $^3J_{H-H} = 8.0$ Hz), 8.42(s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.32$; IR (KBr) (υ_{max}/cm^{-1}) 3200 (N—H), 1570 and 1585 (C=N), 1230 (P=O), 1045 and 990 (P—O—C); MS, m/e (%) 412 (M^+, 2.9), 356 (12.1), 223 (20.8), 221 (100), 205 (90.9), 141 (21.8), 126 (11.8), 115 (8.5), 91 (4.7), 56 (27.5); Anal. Calcd. For $C_{17}H_{19}O_5N_3ClP$ (411.5): C, 49.57; H, 4.62; N, 10.21. Found: C, 49.32; H, 4.85; N, 10.20.

3d (Ar = 4-CH_3OPh, R = Cl): white solid, m.p. 192.1–192.6°C, yield 28.3%; ^{1}H NMR ($CDCl_3$) $\delta = 0.78$ (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 3.72 (s, 3H, $ArOCH_3$), 3.80–3.92 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.6$ Hz), 4.14 (m, 1H, CH_2OP), 4.30 (m, 2H, NCH_2), 4.50 (d, 1H, CH—Ar, $^3J_{H-P} = 11.4$ Hz), 5.42 (d, 1H, N—H), 6.95–7.20 (dd, 4H, Ar—H, $^3J_{H-H} = 8.0$ Hz), 7.28–7.80 (dd, 2H, β, γ-H on pyridine, $^3J_{H-H} = 8.0$ Hz), 8.40 (s, 1H,

α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.66$; IR (KBr) (υ_{max}/cm^{-1}) 3202 (N—H), 1572 and 1580 (C=N), 1235 (P=O), 1040 and 975 (P—O—C); Anal. Calcd. For $C_{18}H_{22}O_4N_2ClP$ (396.5): C, 54.48; H, 5.55; N, 7.06. Found: C, 54.58; H, 5.34; N, 6.92.

3e (Ar = 2-CH_3OPh, R = Cl): white solid, m.p. 208.1–208.9°C, yield 31.3%; ^{1}H NMR ($CDCl_3$) $\delta = 0.76$ (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 3.78 (s, 3H, $ArOCH_3$), 3.82–3.91 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 4.15 (m, 1H, CH_2OP), 4.33 (m, 2H, NCH_2), 4.50 (d, 1H, CH—Ar, $^3J_{H-P} = 10.8$ Hz), 5.42 (d, 1H, N—H), 6.70–7.25 (dd, 4H, Ar—H, $^3J_{H-H} = 8.2$ Hz), 7.30–7.81 (dd, 2H, β, γ-H on pyridine, $^3J_{H-H} = 8.0$ Hz), 8.45 (s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.84$; IR (KBr) (υ_{max}/cm^{-1}) 3193 (N—H), 1565 and 1580 (C=N), 1230 (P=O), 1045 and 990 (P—O—C); Anal. Calcd. For $C_{18}H_{22}O_4N_2ClP$ (396.5): C, 54.48; H, 5.55; N, 7.06. Found: C, 54.27; H, 5.51; N, 7.39.

3f (Ar = 4-CH_3Ph, R = Cl): white solid, m.p. 180.9–181.8°C, yield 69.9%; ^{1}H NMR ($CDCl_3$) $\delta = 0.76$ (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 2.35 (s, 3H, $ArCH_3$), 3.88 (m, 1H, CH_2OP), 3.82–3.91 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 4.32 (m, 2H, NCH_2), 4.47 (d, 1H, CH—Ar, $^3J_{H-P} = 10.8$ Hz), 5.40 (d, 1H, N—H), 6.97–7.14 (dd, 4H, Ar—H, $^3J_{H-H} = 8.4$ Hz), 7.28–7.81 (dd, 2H, β, γ-H on pyridine, $^3J_{H-H} = 8.0$ Hz), 8.38 (s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.06$; IR (KBr) (υ_{max}/cm^{-1}) 3190 (N—H), 1572 and 1585 (C=N), 1230 (P=O), 1050 and 995 (P—O—C); MS, m/e (%) 380 (M^+, 1.27), 327 (9.2), 325 (38.7), 247 (2.2), 245 (8.4), 221 (14.8), 207 (22.2), 205 (100), 141 (19.3), 128 (24.8), 126 (37.4), 119 (45.5), 105 (27.3), 91 (40.3), 77(16.8); Anal. Calcd. For $C_{18}H_{22}O_3N_2ClP$ (380.5): C, 56.77; H, 5.78; N, 7.36. Found: C, 56.79; H, 5.94; N, 7.21.

3g (Ar = 4-NO_2Ph, R = Cl): pale yellow solid, m.p. 212.9–213.4°C, yield 46.1%; ^{1}H NMR ($CDCl_3$) $\delta = 0.82$ (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 3.80 (m, 1H, CH_2OP), 3.85–3.94 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.6$ Hz), 4.34 (m, 2H, NCH_2), 4.50 (d, 1H, CH—Ar, $^3J_{H-P} = 11.6$ Hz), 5.54 (d, 1H, N—H), 7.28 (d, 2H, Ar—H), 7.35 (d, 1H, β-H on pyridine, $^3J_{H-H} = 8.4$ Hz), 7.79 (d, 1H, γ-H on pyridine), 8.21 (d, 2H, Ar—H, $^3J_{H-H} = 8.8$ Hz), 8.43(s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.31$; IR (KBr) (υ_{max}/cm^{-1}) 3206 (N—H), 1565 and 1587 (C=N), 1225 (P=O), 1040 and 991 (P—O—C); MS, m/e (%) 412 (M^+, 33.8), 356 (12.1), 223 (22.5), 221 (72.2), 205 (100), 191 (18.0), 141 (75.7), 126 (58.4), 115 (48.3), 91 (34.5), 77 (41.0), 56 (100); Anal. Calcd. For $C_{17}H_{19}O_5N_3ClP$ (411.5): C, 49.57; H, 4.62; N, 10.21. Found: C, 49.32; H, 4.85; N, 10.25.

3h (Ar = 4-CH_3Ph, R=H): white solid, m.p. 161.2–161.8°C, yield 70.2%; ^{1}H NMR ($CDCl_3$) $\delta = 0.76$ (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.55 (m, 1H, CH_2OP), 3.82–3.91 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 4.34 (m, 2H, NCH_2), 4.48 (d, 1H, CH—Ar, $^3J_{H-P} = 11.6$ Hz),

5.41 (d, 1H, N—H), 6.98–7.13 (dd, 4H, Ar—H, $^3J_{H-H} = 8.0$ Hz), 7.30(m, 1H, β-H on pyridine), 7.83 (d, 1H, γ-H on pyridine, $^3J_{H-H} = 8.0$ Hz), 8.56 (d, 1H, α-H on pyridine, $^3J_{H-H} = 3.6$ Hz), 8.63 (s, 1H, α-H on Pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.50$; IR (KBr) (υ_{max}/cm^{-1}) 3190 (N—H), 1575 (C=N), 1230 (P=O), 1044 and 988 (P—O—C); MS, m/e (%) 346 (M^+, 4.4), 291 (38.9), 226 (4.7), 209 (7.1), 187 (20.3), 171 (100), 128 (10.6), 119 (41.9), 105 (31.2), 91 (40.9), 56(17.4); Anal. Calcd. For $C_{18}H_{23}O_3N_2P$ (346): C, 62.43; H, 6.65; N, 8.09. Found: C, 62.59; H, 6.70; N, 8.24.

3i (Ar = 4-ClPh, R=H): white solid, m.p. 162.0–162.7°C, yield 84.4%; ^{1}H NMR ($CDCl_3$) $\delta = 0.75$ (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 3.80–3.89 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 4.12 (dd, 1H, CH_2OP), 4.32 (m, 2H, NCH_2), 4.47 (d, 1H, CH—Ar, $^3J_{H-P} = 11.2$ Hz), 5.39 (d, 1H, N—H), 7.00 (d, 2H, Ar—H, $^3J_{H-H} = 8.4$ Hz), 7.28(m, 3H, Ar—H, β-H on pyridine), 7.79 (d, 1H, γ-H on pyridine, $^3J_{H-H} = 7.6$ Hz), 8.53 (d, 1H, α-H on Pyridine, $^3J_{H-H} = 4.4$ Hz), 8.60 (s, 1H, α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.81$; IR (KBr) (υ_{max}/cm^{-1}) 3185 (N—H), 1577 (C=N), 1234 (P=O), 1050 and 990 (P—O—C); MS, m/e (%) 367 (M + 1, 50.7), 311 (41.6), 231 (18.2), 187 (25.7), 171 (100), 141 (54.0), 107 (40.6), 105 (31.2), 92 (57.2), 77 (30.0), 56(66.0); Anal. Calcd. For $C_{17}H_{20}O_3N_2ClP$ (366.5): C, 55.66; H, 5.46; N, 7.64. Found: C, 55.73; H, 5.77; N, 7.47.

3j (Ar = Ph, R=H): white solid, m.p. 143.3–144.3°C, yield 79.3%; ^{1}H NMR ($CDCl_3$) $\delta = 0.77$ (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 3.82–3.91 (dd, 1H, CH_2OP, $^3J_{H-P} = 11.2$ Hz), 3.95 (m, 1H, CH_2OP), 4.33 (m, 2H, NCH_2), 4.48 (d, 1H, CH—Ar, $^3J_{H-P} = 11.2$ Hz), 5.43 (d, 1H, N—H), 7.11 (m, 1H, β-H on pyridine), 7.20–7.40 (m, 5H, Ar—H), 7.81 (d, 1H, γ-H on pyridine, $^3J_{H-H} = 7.6$ Hz), 8.53–8.61 (m, 2H, 2α-H on pyridine); ^{31}P NMR ($CDCl_3$) $\delta = 6.66$; IR (KBr) (υ_{max}/cm^{-1}) 3190 (N—H), 1575 (C=N), 1230 (P=O), 1044 and 988 (P—O—C); MS, m/e (%) 332 (M^+, 1.7), 277 (46.3), 197 (9.3), 187 (19.7), 171 (81.9), 170 (73.3), 129 (20.2), 115 (17.1), 107 (46.0), 91 (37.7), 79 (30.4), 77 (24.7), 56(22.6), 40 (100); Anal. Calcd. For $C_{17}H_{21}O_3N_2P$ (332): C, 61.45; H, 6.33; N, 8.43. Found: C, 61.31; H, 6.28; N, 8.35.

REFERENCES

[1] (a) K. Shiokawa, S. Tsubo, S. Kagabu, K. Moriya, Heterocyclic Compounds, *EP*, 192060, (1986), and (b) E. Rudolf and P. Ludwig, Diketones and their use as components of liquid crystal dielectrics, *DE* 2918775, (1980).

[2] M. Tomizawa, *J. Pesticide Sci*., **19,** 335 (1994).

[3] I. Yamamoto, G. Yabita, M. Tomizawa, et al., *J. Pesticide Sci*., **19,** 335 (1994).

[4] C. Meier, *Angew. Chem. Int. Ed. Engl.*, **35,** 70 (1996).

[5] H. Matsumoto, K. Seto, R. Sako, and R. Dakoda, Preparation of 2(hydrazino-1-propenyl) 2-oxo-1,3,2-dioxaphorinanes, *Eur. Pat. Appl. EP*, **485,** 851, (1992).

[6] A. Hirashima, I. Ishaaya, R. Ueno, Y. Ichiyama, S. Y. Wu, and M. Eto, *Agric. Biol. Chem*., **50,** 1831 (1986).
[7] R. L. Shao, M. H. Yang, and C. X. Zhi, *Chem. J. Chinese Univ*., **15,** 1473 (1994).
[8] D. Q. Shi, Z. L. Sheng, X. P. Liu, H. Wu, *Heteroatom Chem*., **14,** 266 (2005).
[9] W. Ten Hoeve and H. Wynberg, *J. Org. Chem*., **50,** 4508 (1985).
[10] X. Liu, R. Q. Huang, M. R. Cheng, Y. G. Zhao, Z. G. Li, *Chem. J. Chinese Univ*., **20,** 1404 (1999).