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### Asymmetric Cyclic Phosphorothionamides Containing Substituted Pyridine

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## Asymmetric Cyclic Phosphorothionamides Containing Substituted Pyridine

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*In order to find high-activity and low-toxicity pesticidal lead compounds, a type of novel, asymmetric cyclic phosphorothionamides containing substituted pyridine were synthesized via the condensation reactions of 2-chloro-4-substitutedphenyl-5,5-dimethyl-1,3,2-dioxaphosphinane 2-sulfide with 3-aminomethylpyridine. The cis and trans isomers of the products were isolated by column chromatography on silica gel. The structures of the products were characterized by  $^1\text{H}$  NMR,  $^{31}\text{P}$  NMR, MS, and elemental analyses. The configuration of **3a** was determined by X-ray diffraction analysis. The results of the preliminary bioassay showed that the new compounds possess potential fungicidal activities.*

**Keywords** Cyclic phosphorothionamide; fungicidal activity; substituted pyridine; X-ray diffraction

## INTRODUCTION

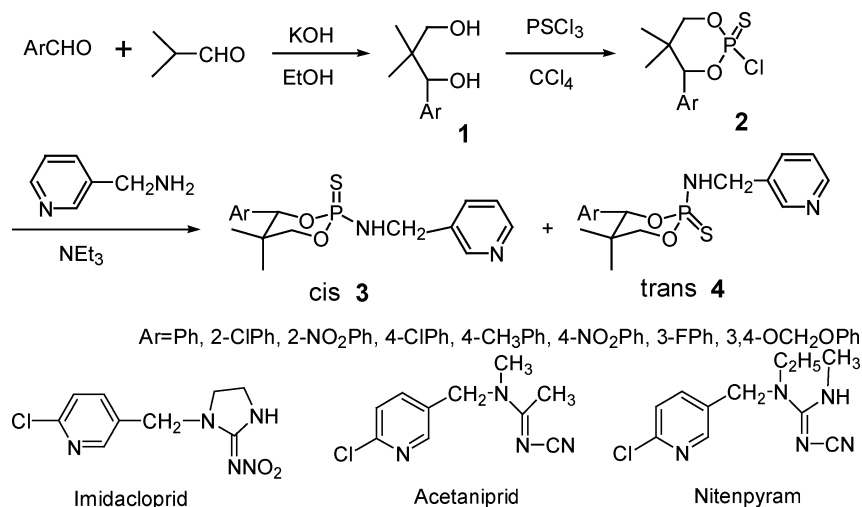
Neonicotinoid insecticides as nicotinic acetylcholine receptor inhibitors have attracted increasing attention because of their safety, low toxicity, wide and high activities.<sup>1,2</sup> A lot of new insecticides such as imidacloprid, acetaniprid, and nitenpyram have been commercialized. It was found that most of the biologically active nicotinic compounds contain the 3-aminomethylpyridine moiety.<sup>3</sup> Due to their wide biological activities, phosphorus heterocyclic compounds play an important role in pesticide science; 1,3,2-dioxaphosphinane compounds appear

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to be very important for their wide biological activities and their stereochemistry.<sup>4–8</sup> 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 type of novel asymmetric cyclic phosphorothionamides containing substituted pyridine **3** and **4**. The synthetic route is shown in Scheme 1. The structures of the products were characterized by <sup>1</sup>H NMR, <sup>31</sup>P NMR, MS, and elemental analyses. The configuration of **3a** was determined by X-ray diffraction analysis. The results of preliminary bioassay showed that the new compounds possess potential fungicidal activities.



**SCHEME 1**

## RESULTS AND DISCUSSION

### Preparation of the Title Compounds

Title compounds **3** and **4** were synthesized by the multistep route outlined in Scheme 1. 1-aryl-2,2-dimethyl-1,3-propanediols **1** are prepared by an aldol condensation followed by a cross Cannizzaro reaction in which two equivalents of isobutyraldehyde and a substituted benzaldehyde are allowed to react in basic alcoholic solution. Diols **1** react with PSCl<sub>3</sub> in a CCl<sub>4</sub> solvent to yield cyclic phosphorochloridate **2**; the ratios of cis and trans isomers of compounds **2** are 1:1 approximately;<sup>9</sup> 3-aminomethylpyridine then reacts with compound **2** in the presence of triethylamine to give products **3** and **4**.

All products were purified by flash column chromatography on silica gel using a mixture of ethyl acetate and petroleum ether as the eluent;

first, the *trans* isomers and then the *cis* isomers were eluted. In most cases, the *cis* isomer is the major product. Moreover, when an *ortho*-substituted group was attached to the aromatic rings, only *cis* isomer products were obtained. However, the reason is not very clear; it maybe due to the thermodynamic favored process.<sup>10</sup>

## Structures of Title Compounds

Structures of compounds **3** and **4** were confirmed by <sup>1</sup>H NMR, <sup>31</sup>P NMR, MS, and elemental analyses. *Cis* isomer **3a** was identified by X-ray diffraction.

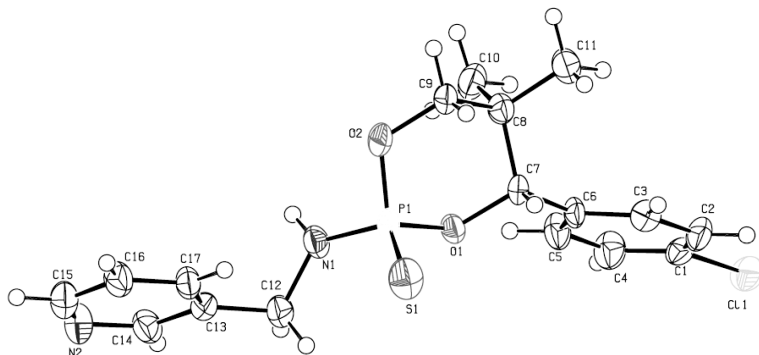
In <sup>1</sup>H NMR spectra, the two methyl protons of 1,3,2-dioxaphosphinane appeared as two singlets, due to the two methyl groups lying in different magnetic environments. The two methylene protons of 1,3,2-dioxaphosphinane displayed a doublet and multiplicity because of their different magnetic surroundings and coupling with each other or with the adjacent phosphorus atom with the coupling constant of 11.6 ppm and 22 ppm, respectively; the 4-position axial proton displayed singlet without coupling with a phosphorus atom. Interestingly, we easily can distinguish *cis* isomers **3** from *trans* isomers **4** by means of <sup>1</sup>H NMR and <sup>31</sup>P NMR. In <sup>1</sup>H NMR spectra, the chemical shift difference between the two methyl groups attached to the 1,3,2-dioxaphosphinane in *trans* **4** are larger than the values in *cis* **3** (0.3–0.4 ppm versus 0.1–0.2 ppm), and in *cis* isomers, 4-position methylene proton in phosphorus heterocycle is shifted downfield relative to that of the *trans* isomers, owing to the unshielded effect of P=O group, and in <sup>31</sup>P NMR spectra, the phosphorus signal of the *cis* isomer is downfield relative to that of the *trans* isomer.<sup>7</sup> The IR spectra of all compounds showed normal stretching absorption bands indicating the existence of the N–H (~3200 cm<sup>-1</sup>), and P=S (~700 cm<sup>-1</sup>), and P–O–C (~1000 cm<sup>-1</sup>) moiety. The EI mass spectra of compounds **3** and **4** revealed the existence of molecular ion peaks and main fragmentation peaks, which were in accordance with the given structures of products.

X-ray diffraction analysis indicated that the single crystal of **3a** is monoclinic; space group P2(1)/n, cell parameters A = 21.753(9), B = 6.879(3), C = 12.219(5) Å, β = 98.980(7), V = 1806.1(1) Å<sup>3</sup>, Z = 4, D<sub>c</sub> = 1.408 g/cm<sup>3</sup>, F(000) = 800, μ = 0.428 mm<sup>-1</sup> and final R = 0.1050, wR = 0.2672 for 2187 reflections (I > 2σ(I)). The selected bond distances and angles are listed in Table I. Figures 1 and 2 are the molecular structure of compound **3a** and packing of the molecules in the unit cell, respectively.

The distorted tetrahedral configuration of the P atom can be attributed to the presence of the dioxaphosphinane ring whose sterical

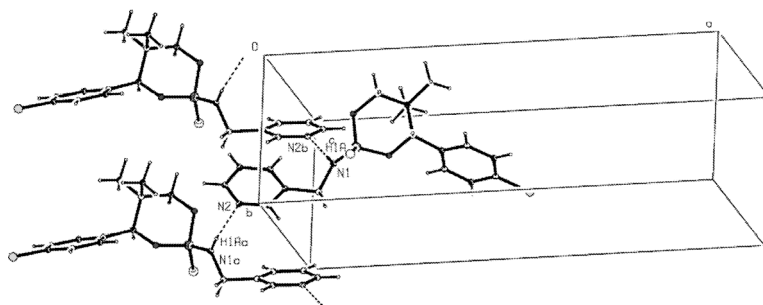
TABLE I Selected Geometric Parameters ( $\text{\AA}$ ,  $^\circ$ )

Bond	Dist.	Angle	( $^\circ$ )	Angle	( $^\circ$ )	Angle	( $^\circ$ )
P(1)–O(1)	1.596(4)	O(2)–P(1)–N(1)	100.4(3)	O(2)–P(1)–S(1)	116.8(2)	C(12)–N(1)–P(1)	126.4(5)
P(1)–O(2)	1.586(5)	O(2)–P(1)–O(1)	101.7(2)	N(1)–P(1)–S(1)	116.3(2)	C(7)–O(1)–P(1)	117.9(4)
P(1)–N(1)	1.598(6)	N(1)–P(1)–O(1)	107.5(3)	O(1)–P(1)–S(1)	112.6(2)	C(9)–O(2)–P(1)	116.8(4)
P(1)–S(1)	1.924(3)						



**Figure 1** The molecular structure of compound **3a**.

and electronic properties influence coordination the values of the  $P1=S1$ ,  $P1\cdots N1$ , and  $P\cdots O$  bonds and the angles  $O\cdots P\cdots O$  and  $O\cdots P\cdots N$  illustrate the irregularities (Table 1). The dioxaphosphinane ring adopts a distorted chair conformation, with the parameters  $Q = 0.571(6)\text{\AA}$ ,  $\theta = 172.8(6)^\circ$  and  $\phi = 329(5)^\circ$ .<sup>11</sup> The length of single bonds of  $P\cdots O$  and  $P1\cdots N1$  are similar to the analogous chemical bonds observed previously [ $1.586(2)\text{\AA}$ ,  $1.572(2)\text{\AA}$ , and  $1.598(6)\text{\AA}$ ]<sup>12</sup> (Table I). The intermolecular  $N1\cdots H1(A)\cdots N2$  interaction joins molecules into a chain along the  $b$  axis (Figure 2). The methylene atom C14 is involved in  $C\cdots H\cdots\pi$  interactions:  $C14\cdots Cg2 = 3.609(8)\text{\AA}$ ,  $H14\cdots Cg2 = 2.80\text{\AA}$ , and  $C14\cdots H14\cdots Cg2 = 146^\circ$ . [Cg2 is the centroid of the pyridine ring of the symmetry-related molecule at  $(-X, -1/2 + Y, 1/2 - Z)$ ]. The interaction of methylene group with the aromatic systems, described by Desiraju,<sup>13</sup> contributes to the crystal packing of *cis* **3a**.



**Figure 2** Packing of the molecules in the unit cell.

**TABLE II The Fungicidal Activities of Compound, 3 and 4 (the Plate Method,<sup>15</sup> C = 50 ppm, Inhibitory Rate: %)**

Fungi kind	<i>Fusarium oxysporium</i>	<i>Rhizoctonia solani</i>	<i>Botrytis cinerea</i>	<i>Gibberella zeae</i>	<i>Botryosphaeria berengeriana</i>	<i>Bopolaris maydis</i>
<b>3a</b>	33.33	44.00	57.14	27.27	65.21	58.82
<b>4a</b>	41.60	42.00	42.86	12.12	30.43	52.94
<b>3b</b>	50.00	84.00	95.24	60.60	78.26	82.35
<b>4b</b>	45.83	85.00	95.23	51.51	78.26	94.12
<b>3c</b>	61.90	80.30	93.33	77.14	83.33	88.46
<b>4c</b>	38.10	27.27	64.44	45.71	50.00	69.23
<b>3d</b>	33.34	39.00	14.29	6.06	30.43	64.71
<b>4d</b>	75.00	84.00	98.81	66.67	82.61	88.24
<b>3e</b>	37.50	62.00	88.10	33.33	60.87	70.59
<b>4e</b>	54.17	85.00	98.91	63.64	82.61	82.35
<b>3f</b>	70.83	92.00	100	81.81	86.96	88.24
<b>4f</b>	45.83	74.00	78.57	42.42	73.91	58.82
<b>3g</b>	37.50	14.00	61.90	15.15	47.83	52.94
<b>3h</b>	58.33	81.00	85.71	51.51	73.91	94.12

## Biological Activities

Preliminary bioassay results show that these title compounds possess weak insecticidal but potential fungicidal activities. The results of fungicidal activities are listed in Table II.

## EXPERIMENTAL

<sup>1</sup>H NMR and <sup>31</sup>P NMR spectra were recorded with a VARIAN MERCURY-PLUS400 spectrometer with TMS and 85% H<sub>3</sub>PO<sub>4</sub> as the internal and external reference, respectively, and CDCl<sub>3</sub> 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 an ELEMENTAR Vario ELIICHNSO elementary analyzer. X-ray diffraction analysis was carried out with an 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. Diols **1** were prepared according to reference.<sup>14</sup>



### The Synthesis of 2-Chloro-4-Substituted Phenyl-5,5-Dimethyl-1,3,2-Dioxaphosphinane 2-Sulfide<sup>9</sup>

0.01 mol of diol **1**, 0.01 mol of thiophosphoryl chloride, and 20 mL of carbon tetrachloride were taken in a 50-mL three-necked reaction flask. The mixture was stirred under reflux for 4 h (monitored by TLC), after removal of the solvent under a reduced pressure, the residue was dissolved in 25 mL of chloroform and washed with sodium bicarbonate solution twice and then by water. The organic layer was dried over sodium sulphate and filtered; after removal of the solvent under a reduced pressure, the crude product was thus obtained and used without further purification. The ratios of the cis and trans isomer of products were determined by <sup>1</sup>H NMR and <sup>31</sup>P NMR, which are listed in Table III.

### The General Procedure for the Synthesis of 2-(3-Pyridylmethylamino)-4-Substitutedphenyl-5,5-Dimethyl-1, 3, 2-Dioxaphosphinane 2-Sulfides

5 mmol of compound **2**, 5 mmol of 3-aminomethylpyridine, 7.5 mmol of triethylamine, and 10 mL of anhydrous dichloromethane were taken in a 50-mL three-necked reaction flask; the mixture was stirred at r.t. or under reflux until the reaction was complete (monitored by TLC). The solid was filtered; after removal of the solvent, the crude product was purified by flash column chromatography on silica gel with a mixture of ethyl acetate and petroleum ether as the eluent. First the trans isomers and then the cis isomers were eluted.

**3a** (Ar = 4-chlorophenyl, cis): white solid, m.p. 166.6–167.0°C, yield 31.5%; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ = 0.78 (s, 3H, CH<sub>3</sub>), 0.95 (s, 3H, CH<sub>3</sub>), 3.84 (dd, <sup>3</sup>J<sub>H–P</sub> = 23.6 Hz, <sup>2</sup>J<sub>H–H</sub> = 14.8 Hz, 1H, CH<sub>2</sub>OP), 4.45–4.58 (m, 3H, CH<sub>2</sub>OP, NCH<sub>2</sub>), 5.46 (s, 1H, CH–Ar), 7.06–7.41 (m, 5H, Ar–H, β–H on pyridine), 7.91 (d, <sup>3</sup>J<sub>H–H</sub> = 8.0 Hz, 1H, γ–H on pyridine), 8.59 (d, <sup>3</sup>J<sub>H–H</sub> = 4.4 Hz, 1H, α–H on pyridine), 8.67 (s, 1H, α–H on pyridine); <sup>31</sup>P NMR (CDCl<sub>3</sub>) δ = 70.13; IR (KBr) (ν<sub>max</sub>/cm<sup>–1</sup>) 3196 (N–H), 1492 (C=N), 713 (P=S), 1038 and 986 (P–O–C); MS, m/z (%) 382 (M<sup>+</sup>, 4.1), 203 (100), 187.1 (19), 179 (14), 165 (23), 145 (20.3), 107 (44.8), 92 (25.8); anal. calcd.

**TABLE III The Ratios of Different Cyclic Thiophosphoryl Chlorides 2**

Compound	2a	2b	2c	2d	2e	2f	2g	2h
Ar	4-ClPh	Ph	4-NO <sub>2</sub> Ph	3-FPh	4-CH <sub>3</sub> Ph	4-OCH <sub>2</sub> OPh	2-NO <sub>2</sub> Ph	2-ClPh
Cis/trans	46/54	48/52	43/57	52/48	47/53	46/54	43/57	45/55

for  $C_{17}H_{20}ClN_2O_2PS$  (382.5): C, 53.33; H, 5.23; N, 7.32. Found: C, 53.54; H, 5.08; N, 7.01.

**4a** (Ar = 4-chlorophenyl, trans): pale yellow solid, m.p. 177.5–177.8°C, yield 13.5%;  $^1H$  NMR ( $CDCl_3$ ) $\delta$  = 0.76 (s, 3H,  $CH_3$ ), 1.05 (s, 3H,  $CH_3$ ), 3.47 (sb, 1H, NH), 3.90 (dd,  $^3J_{H-P}$  = 23.6 Hz,  $^2J_{H-H}$  = 10.8 Hz, 1H,  $CH_2OP$ ), 4.20–4.26 (m, 3H,  $CH_2OP$ ,  $NCH_2$ ), 5.18 (s, 1H,  $CH-Ar$ ), 7.21–7.34 (m, 5H, Ar-H,  $\beta$ -H on pyridine), 7.81 (d,  $^3J_{H-H}$  = 7.6 Hz, 1H,  $\gamma$ -H on pyridine), 8.47 (d,  $^3J_{H-H}$  = 4.0 Hz, 1H,  $\alpha$ -H on pyridine), 8.68 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}P$  NMR ( $CDCl_3$ ) $\delta$  = 68.83; Anal. calcd. for  $C_{17}H_{20}ClN_2O_2PS$  (382.5): C, 53.33; H, 5.23; N, 7.32. Found: C, 53.70; H, 5.26; N, 7.75.

**3b** (Ar = phenyl, cis): yellow solid, m.p. 190.2–190.7°C, yield 40.0%;  $^1H$  NMR ( $CDCl_3$ ) $\delta$  = 0.81 (s, 3H,  $CH_3$ ), 0.97 (s, 3H,  $CH_3$ ), 3.86 (dd,  $^3J_{H-P}$  = 26.0 Hz,  $^2J_{H-H}$  = 11.4 Hz, 1H,  $CH_2OP$ ), 4.43–4.59 (m, 3H,  $CH_2OP$ ,  $NCH_2$ ), 5.49 (s, 1H,  $CH-Ar$ ), 7.13–7.33 (m, 6H, Ar-H,  $\beta$ -H on pyridine), 7.86 (d,  $^3J_{H-H}$  = 8.0 Hz, 1H,  $\gamma$ -H on pyridine), 8.57 (d,  $^3J_{H-H}$  = 4.0 Hz, 1H,  $\alpha$ -H on pyridine), 8.63 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}P$  NMR ( $CDCl_3$ ) $\delta$  = 69.68; IR (KBr) ( $\nu_{max}/cm^{-1}$ ) 3193 (N–H), 695 (P=S), 1040 and 991 (P–O–C); MS,  $m/z$  (%) 348 ( $M^+$ , 37.2), 205 (30.6), 203 (97.4), 187 (53.7), 145 (88.7), 128 (85.7), 117 (64.4), 91 (90.3), 79 (33.1), 77 (48.9), 65 (46.5); anal. calcd. for  $C_{17}H_{21}N_2O_2PS$  (348.0): C, 58.62; H, 6.03; N, 8.05. Found: C, 58.84; H, 6.06; N, 8.26.

**4b** (Ar = phenyl, trans): white solid, m.p. 207.2–208.6°C, yield 16.6%;  $^1H$  NMR ( $CDCl_3$ ) $\delta$  = 0.77 (s, 3H,  $CH_3$ ), 1.08 (s, 3H,  $CH_3$ ), 3.20 (d, 1H, NH,  $^3J_{H-H}$  = 5.2 Hz), 3.90 (dd,  $^3J_{H-P}$  = 23.6 Hz,  $^2J_{H-H}$  = 10.8 Hz, 1H,  $CH_2OP$ ), 4.17–4.27 (m, 3H,  $CH_2OP$ ,  $NCH_2$ ), 5.20 (s, 1H,  $CH-Ar$ ), 7.26–7.34 (m, 6H, Ar-H,  $\beta$ -H on pyridine), 7.79 (d,  $^3J_{H-H}$  = 7.6 Hz, 1H,  $\gamma$ -H on pyridine), 8.48 (d,  $^3J_{H-H}$  = 4.2 Hz, 1H,  $\alpha$ -H on pyridine), 8.66 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}P$  NMR ( $CDCl_3$ ) $\delta$  = 68.92; anal. calcd. for  $C_{17}H_{21}N_2O_2PS$  (348.0): C, 58.62; H, 6.03; N, 8.05. Found: C, 53.77; H, 5.78; N, 7.98.

**3c** (Ar = 4-nitrophenyl, cis): pale yellow solid, m.p. 243.9–244.5°C, yield 36%;  $^1H$  NMR ( $CDCl_3$ ) $\delta$  = 0.77 (s, 3H,  $CH_3$ ), 0.86 (s, 3H,  $CH_3$ ), 3.34 (s, 1H, NH), 3.95 (dd,  $^3J_{H-P}$  = 24.0 Hz,  $^2J_{H-H}$  = 11.2 Hz, 1H,  $CH_2OP$ ), 4.31–4.40 (m, 3H,  $CH_2OP$ ,  $NCH_2$ ), 5.58 (s, 1H,  $CH-Ar$ ), 7.36–7.44 (m, 3H, Ar-H,  $\beta$ -H on pyridine), 7.81 (d,  $^3J_{H-H}$  = 7.6 Hz, 1H,  $\gamma$ -H on pyridine), 8.21 (d,  $^3J_{H-H}$  = 4.4 Hz, 2H, Ar-H), 8.53 (d,  $^3J_{H-H}$  = 4.8 Hz, 1H,  $\alpha$ -H on pyridine), 8.67 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}P$  NMR ( $CDCl_3$ ) $\delta$  = 70.46; MS,  $m/z$  (%) 393 ( $M^+$ , 0.5), 103 (5.24), 92 (10), 90 (100), 76 (29.1), 64 (25.8); anal. calcd. for  $C_{17}H_{20}N_3O_4PS$  (393.0): C, 51.91; H, 5.09; N, 10.69. Found: C, 51.44; H, 5.23; N, 10.63.

**4c** (Ar = 4-nitrophenyl, trans): white solid, m.p. 220.9–221.7°C, yield 8.4%;  $^1H$  NMR ( $CDCl_3$ ) $\delta$  = 0.75 (s, 3H,  $CH_3$ ), 0.90 (s, 3H,  $CH_3$ ), 3.34 (d,  $^3J_{H-H}$  = 8.0 Hz, 1H, NH), 3.91 (dd,  $^3J_{H-P}$  = 24.8 Hz,  $^2J_{H-H}$  = 12.0

Hz, 1H, CH<sub>2</sub>OP), 4.08–4.33(m, 3H, CH<sub>2</sub>OP, NCH<sub>2</sub>), 5.20 (s, 1H, CH-Ar), 7.30–7.33 (m, 4H, Ar-H), 7.56 (d, <sup>3</sup>J<sub>H-H</sub> = 8.4 Hz, 1H, β-H on pyridine), 7.80 (d, <sup>3</sup>J<sub>H-H</sub> = 8.0 Hz, 1H, γ-H on pyridine), 8.42 (d, <sup>3</sup>J<sub>H-H</sub> = 3.2 Hz, 1H, α-H on pyridine), 8.56 (s, 1H, α-H on pyridine); <sup>31</sup>P NMR (CDCl<sub>3</sub>) δ = 70.18; anal. calcd. for C<sub>17</sub>H<sub>20</sub>N<sub>3</sub>O<sub>4</sub>PS (393.0): C, 51.91; H, 5.09; N, 10.69. Found: C, 52.16; H, 5.45; N, 10.73.

**3d** (Ar = 3-fluorophenyl, cis): white crystal, m.p. 188.5–189.0°C, yield 32%; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ = 0.83 (s, 3H, CH<sub>3</sub>), 0.96 (s, 3H, CH<sub>3</sub>), 3.86 (dd, <sup>3</sup>J<sub>H-P</sub> = 24.0 Hz, <sup>2</sup>J<sub>H-H</sub> = 11.2 Hz, 1H, CH<sub>2</sub>OP), 4.43–4.59 (m, 3H, CH<sub>2</sub>OP, NCH<sub>2</sub>), 5.48 (s, 1H, CH-Ar), 6.83–7.36 (m, 5H, Ar-H, β-H on pyridine), 7.85 (d, <sup>3</sup>J<sub>H-H</sub> = 8.0 Hz, 1H, γ-H on pyridine), 8.58 (d, <sup>3</sup>J<sub>H-H</sub> = 3.6 Hz, 1H, α-H on pyridine), 8.64 (s, 1H, α-H on pyridine); <sup>31</sup>P NMR (CDCl<sub>3</sub>) δ = 70.06; MS, m/z (%) 367 (M+1, 18.3), 366 (M<sup>+</sup>, 25), 203 (37.3), 135 (39.9), 133 (35.9), 109 (76.9), 92 (100), 65 (54.6), 56 (49.2); anal. calcd. for C<sub>17</sub>H<sub>20</sub>FN<sub>2</sub>O<sub>2</sub>PS (366): C, 55.74; H, 5.46; N, 7.65. Found: C, 56.13; H, 5.39; N, 7.84.

**4d** (Ar = 3-fluorophenyl, trans): white crystal, m.p. 211.0–211.5°C, yield 7%; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ = 0.79 (s, 3H, CH<sub>3</sub>), 1.26 (s, 3H, CH<sub>3</sub>), 3.14(sb, 1H, NH), 3.90 (dd, <sup>3</sup>J<sub>H-P</sub> = 23.6 Hz, <sup>2</sup>J<sub>H-H</sub> = 10.8 Hz, 1H, CH<sub>2</sub>OP), 4.18–4.25 (m, 3H, CH<sub>2</sub>OP, NCH<sub>2</sub>), 5.15 (s, 1H, CH-Ar), 7.23–7.33 (m, 5H, Ar-H, β-H on pyridine), 7.77 (d, <sup>3</sup>J<sub>H-H</sub> = 7.6 Hz, 1H, γ-H on pyridine), 8.50 (s, 1H, α-H on pyridine), 8.65 (s, 1H, α-H on pyridine); <sup>31</sup>P NMR (CDCl<sub>3</sub>) δ = 68.91; anal. calcd. for C<sub>17</sub>H<sub>20</sub>FN<sub>2</sub>O<sub>2</sub>PS (366): C, 55.74; H, 5.46; N, 7.65. Found: C, 55.50; H, 5.61; N, 7.97.

**3e** (Ar = 4-methylphenyl, cis): white solid, m.p. 189.4–189.9°C, yield 29.7%; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ = 0.79 (s, 3H, CH<sub>3</sub>), 0.97 (s, 3H, CH<sub>3</sub>), 2.35 (s, 3H, CH<sub>3</sub>-Ar), 3.86 (dd, <sup>3</sup>J<sub>H-P</sub> = 23.8 Hz, <sup>2</sup>J<sub>H-H</sub> = 11.2 Hz, 1H, CH<sub>2</sub>OP), 4.44–4.58 (m, 3H, CH<sub>2</sub>OP, NCH<sub>2</sub>), 5.46 (s, 1H, CH-Ar), 7.04 (d, <sup>3</sup>J<sub>H-H</sub> = 8.4 Hz, 1H, Ar-H), 7.10 (d, <sup>3</sup>J<sub>H-H</sub> = 8.4 Hz, 1H, Ar-H), 7.26 (s, 1H, Ar-H), 7.34–7.37 (m, 2H, Ar-H, β-H on pyridine), 7.90 (d, <sup>3</sup>J<sub>H-H</sub> = 7.6 Hz, 1H, γ-H on pyridine), 8.59 (d, <sup>3</sup>J<sub>H-H</sub> = 4.4 Hz, 1H, α-H on pyridine), 8.65 (s, 1H, α-H on pyridine); <sup>31</sup>P NMR (CDCl<sub>3</sub>) δ = 69.90; IR (KBr) (ν<sub>max</sub>/cm<sup>-1</sup>) 3082 (N-H), 1517 and 1579 (C=N), 712 and 666 (P=S), 1037 and 1022 (P-O-C); MS, m/z (%) 362 (M<sup>+</sup>, 4.0), 203 (86.25), 187 (46.6), 159 (100), 145 (83.3), 135 (29.4), 119 (34.5), 107 (66.8), 105 (62), 91 (58.1), 77 (36.3), 65 (22.5); anal. calcd. for C<sub>18</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>PS (362): C, 59.67; H, 6.35; N, 7.73. Found: C, 59.51; H, 6.23; N, 7.98.

**4e** (Ar = 4-methylphenyl, trans): white solid, m.p. 170.3–170.8°C, yield 11.5%; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ = 0.75 (s, 3H, CH<sub>3</sub>), 1.08 (s, 3H, CH<sub>3</sub>), 2.38 (s, 3H, CH<sub>3</sub>-Ar), 3.47 (d, 1H, NH, <sup>3</sup>J<sub>H-H</sub> = 6.0 Hz), 3.89 (dd, <sup>3</sup>J<sub>H-P</sub> = 24.0 Hz, <sup>2</sup>J<sub>H-H</sub> = 10.8 Hz, 1H, CH<sub>2</sub>OP), 4.17–4.26 (m, 3H, CH<sub>2</sub>OP, NCH<sub>2</sub>), 5.17 (s, 1H, CH-Ar), 7.14–7.29 (m, 5H, Ar-H, β-H on pyridine), 7.78 (d, <sup>3</sup>J<sub>H-H</sub> = 8.0 Hz, 1H, γ-H on pyridine), 8.50 (d,

$^3J_{\text{H-H}} = 4.4$  Hz, 1H,  $\alpha$ -H on pyridine), 8.64 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ )  $\delta = 68.98$ ; anal. calcd. for  $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_2\text{PS}$  (362): C, 59.67; H, 6.35; N, 7.73. Found: C, 59.90; H, 6.44; N, 7.71.

**3f** (Ar = 3, 4-dioxymethylene, cis): white solid, m.p. 181.8–182.9°C, yield 33.5%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta = 0.79$  (s, 3H,  $\text{CH}_3$ ), 0.98 (s, 3H,  $\text{CH}_3$ ), 3.85 (dd,  $^3J_{\text{H-P}} = 28.4$  Hz,  $^2J_{\text{H-H}} = 11.4$  Hz, 1H,  $\text{CH}_2\text{OP}$ ), 4.45–4.55 (m, 3H,  $\text{CH}_2\text{OP}$ ,  $\text{NCH}_2$ ), 5.40 (s, 1H,  $\text{CH-Ar}$ ), 5.98 (s, 2H,  $\text{OCH}_2\text{OAr}$ ), 6.60–6.76 (m, 3H, Ar-H), 7.26–7.39 (m, 1H,  $\beta$ -H on pyridine), 7.88–7.90 (d,  $^3J_{\text{H-H}} = 8.0$  Hz, 1H,  $\gamma$ -H on pyridine), 8.59 (d,  $^3J_{\text{H-H}} = 4.4$  Hz, 1H,  $\alpha$ -H on pyridine), 8.65 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ )  $\delta = 70.49$ ; MS,  $m/z$  (%) 393 ( $\text{M}+1$ , 16.7), 392 (50.2), 337 (95.78), 239 (19.9), 190 (35.2), 187 (67.9), 165 (78.4), 131 (46.8), 117 (52), 115 (67.6), 92 (100), 91 (72.5), 77 (38.4), 65 (79.7), 51 (45.8); anal. calcd. for  $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_4\text{PS}$  (392): C, 55.10; H, 5.36; N, 7.14. Found: C, 55.23; H, 5.09; N, 7.01.

**4f** (Ar = 3, 4-dioxymethylene, trans): white solid, m.p. 190.0–190.3°C, yield 17%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta = 0.76$  (s, 3H,  $\text{CH}_3$ ), 1.09 (s, 3H,  $\text{CH}_3$ ), 3.34 (sb, 1H, NH), 3.88 (dd,  $^3J_{\text{H-P}} = 24$  Hz,  $^2J_{\text{H-H}} = 14.6$  Hz, 1H,  $\text{CH}_2\text{OP}$ ), 4.20–4.24 (m, 3H,  $\text{CH}_2\text{OP}$ ,  $\text{NCH}_2$ ), 5.12 (s, 1H,  $\text{CH-Ar}$ ), 5.98 (s, 2H,  $\text{OCH}_2\text{OAr}$ ), 6.69–6.84 (m, 3H, Ar-H), 7.27–7.32 (m, 1H,  $\beta$ -H on pyridine), 7.80–7.82 (d,  $^3J_{\text{H-H}} = 8$  Hz, 1H,  $\gamma$ -H on pyridine), 8.51 (d,  $^3J_{\text{H-H}} = 4.0$  Hz, 1H,  $\alpha$ -H on pyridine), 8.67 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ )  $\delta = 68.97$ ; anal. calcd. for  $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_4\text{PS}$  (392): C, 55.10; H, 5.36; N, 7.14. Found: C, 54.96; H, 5.41; N, 7.08.

**3g** (Ar = 2-nitrophenyl, cis): pale yellow solid, m.p. 178.3–177.8°C, yield 28%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta = 0.72$  (s, 3H,  $\text{CH}_3$ ), 0.95 (s, 3H,  $\text{CH}_3$ ), 3.84 (dd,  $^3J_{\text{H-P}} = 23.4$  Hz,  $^2J_{\text{H-H}} = 11.4$  Hz, 1H,  $\text{CH}_2\text{OP}$ ), 4.45–4.63 (m, 3H,  $\text{CH}_2\text{OP}$ ,  $\text{NCH}_2$ ), 6.65 (s, 1H,  $\text{CH-Ar}$ ), 7.27–7.58 (m, 5H, Ar-H,  $\beta$ -H on pyridine), 7.85–7.91 (m, 1H,  $\gamma$ -H on pyridine), 8.59 (d,  $^3J_{\text{H-H}} = 4.0$  Hz, 1H,  $\alpha$ -H on pyridine), 8.66 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ )  $\delta = 69.44$ ; MS,  $m/z$  (%) 393 ( $\text{M}^+$ , 0.4), 128 (13.3), 115 (24.4), 105 (24.6), 92 (100), 91 (39.4), 77 (27.9), 65 (41.8), 56 (72.1), 55 (52.5), 41 (58.1); anal. calcd. for  $\text{C}_{17}\text{H}_{20}\text{N}_3\text{O}_4\text{PS}$  (393.0): C, 51.91; H, 5.09; N, 10.69. Found: C, 51.83; H, 5.00; N, 10.76.

**3h** (Ar = 2-chlorophenyl, cis): white solid, m.p. 184.7–185.1°C, yield 53%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta = 0.87$  (s, 3H,  $\text{CH}_3$ ), 1.07 (s, 3H,  $\text{CH}_3$ ), 3.86 (dd,  $^3J_{\text{H-P}} = 22.8$  Hz,  $^2J_{\text{H-H}} = 11.4$  Hz, 1H,  $\text{CH}_2\text{OP}$ ), 4.46–4.66 (m, 3H,  $\text{CH}_2\text{OP}$ ,  $\text{NCH}_2$ ), 6.09 (s, 1H,  $\text{CH-Ar}$ ), 7.17–7.41 (m, 5H, Ar-H,  $\beta$ -H on pyridine), 7.94 (d,  $^3J_{\text{H-H}} = 7.6$  Hz, 1H,  $\gamma$ -H on pyridine), 8.58 (d,  $^3J_{\text{H-H}} = 4.4$  Hz, 1H,  $\alpha$ -H on pyridine), 8.67 (s, 1H,  $\alpha$ -H on pyridine);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ )  $\delta = 69.46$ ; MS,  $m/z$  (%) 383 ( $\text{M}+1$ , 10.9), 202 (56.5), 128 (33.4), 114 (45), 106 (97.5), 91 (100), 76 (33.6), 64 (51), 55 (30.5); anal. calcd. for  $\text{C}_{17}\text{H}_{20}\text{ClN}_2\text{O}_2\text{PS}$  (382.5): C, 53.33; H, 5.23; N, 7.32. Found: C, 53.67; H, 5.41; N, 7.40.

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