

# Synthesis and Fungicidal Activity of Novel $\alpha$ -Substituted Aminomethylphosphonates

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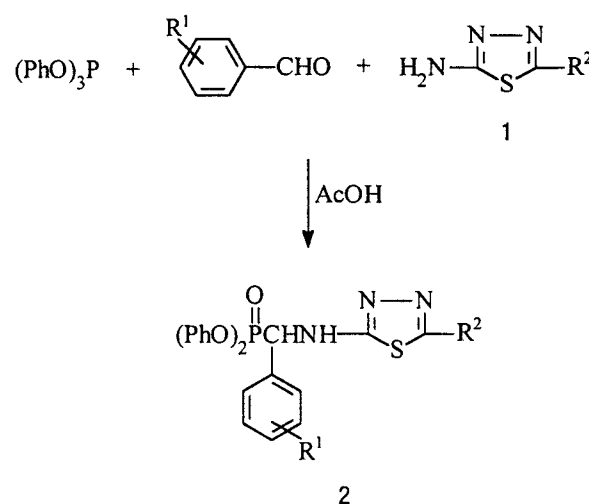
**ABSTRACT:** A series of *O,O*-diphenyl 1-(5-alkyl-1,3,4-thiadiazol-2-yl)aminoarylmethylphosphonates was synthesized by the three-component condensation reactions of 2-amino-5-alkyl-1,3,4-thiadiazoles with triphenyl phosphite and aromatic aldehydes in acetic acid. The reaction conditions were discussed. The structures of products were confirmed by <sup>1</sup>H-NMR, IR, MS, and elemental analyses. The results of preliminary bioassay showed that the new compounds possess fungicidal activity. © 2000 John Wiley & Sons, Inc. *Heteroatom Chem* 11:317–322, 2000

## INTRODUCTION

$\alpha$ -Aminophosphonic acids and their derivatives represent an important class of organophosphorus compounds that continue to attract considerable attention due to their biological importance and extensive application in organic chemistry. A large number of studies on their synthesis and biological activities has been reported during the last two decades [1–6]. On the other hand, 1,3,4-thiadiazole and -oxadiazole derivatives are of fundamental significance as raw materials for medicinal and agricultural chemicals. They are found in a variety of biologically active molecules that have been shown to exhibit bacteriostatic, hypoglycemic, insecticidal, herbicidal, and fungicidal properties [7–11]. However, little atten-

tion has been paid to the synthesis of  $\alpha$ -aminophosphonates bearing these *N*-heterocycles. To the best of our knowledge, only one example of the preparation of such compounds has appeared in the literature. Hafez et al. have described that 1,3,4-oxadiazolyl-containing  $\alpha$ -aminophosphonates can be synthesized by condensation of 2-amino-5-aryl-1,3,4-oxadiazoles with aromatic aldehydes and subsequent addition of a dialkyl phosphite to the resulting Schiff bases [12].

In view of the aforementioned observations and our interest in organophosphorus chemistry and biologically active compounds [13–16], shown in scheme 1, we herein wish to report a convenient and efficient one-pot synthesis of *O,O*-diphenyl 1-(5-alkyl-1,3,4-thiadiazol-2-yl) aminoarylmethylphos-



**SCHEME 1**

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**TABLE 1** Synthesis of  $\alpha$ -Substituted Aminomethylphosphonates **2**

Products	$R^1$	$R^2$	Reaction Time (h)	Yield* (%)	$m.p.$ ( $^{\circ}\text{C}$ )	Elemental Analysis (Found/Calcd.)		
						C	H	N
<b>2a</b>	H	H	3	80.4	170–171	59.42(59.57)	4.19(4.26)	9.79(9.93)
<b>2b</b>	<i>p</i> -Cl	H	3	81.1	201–202	55.20(55.09)	3.64(3.72)	9.06(9.19)
<b>2c</b>	<i>m</i> -Cl	H	5	64.3	149–150	55.22(55.09)	3.61(3.72)	9.11(9.19)
<b>2d</b>	<i>o</i> -Cl	H	5	24.2	221–222	55.10(55.09)	3.68(3.72)	9.14(9.19)
<b>2e</b>	<i>p</i> -Br	H	3	80.0	186–187	50.09(50.21)	3.34(3.39)	8.45(8.37)
<b>2f</b>	<i>p</i> -Me	H	3	80.5	154–155	60.23(60.41)	4.52(4.58)	9.49(9.61)
<b>2g</b>	<i>p</i> -NO <sub>2</sub>	H	3	80.9	177–178	53.65(53.85)	3.58(3.63)	11.79(11.96)
<b>2h</b>	<i>m</i> -NO <sub>2</sub>	H	5	64.2	225–226	53.75(53.85)	3.59(3.63)	11.88(11.96)
<b>2i</b>	<i>o</i> -NO <sub>2</sub>	H	5	25.6	238–239	53.67(53.85)	3.52(3.63)	11.85(11.96)
<b>2j</b>	H	Me	4	78.8	194–195	60.22(60.41)	4.59(4.58)	9.47(9.61)
<b>2k</b>	<i>p</i> -Cl	Me	4	79.2	152–153	55.97(56.00)	3.98(4.03)	8.77(8.92)
<b>2l</b>	<i>m</i> -Cl	Me	5	61.2	173–174	55.91(56.00)	3.95(4.03)	8.85(8.92)
<b>2m</b>	<i>o</i> -Cl	Me	5	23.1	215–216	56.10(56.00)	3.98(4.03)	8.81(8.92)
<b>2n</b>	<i>p</i> -Br	Me	3	78.5	165–166	51.04(51.17)	3.65(3.68)	8.08(8.14)
<b>2o</b>	<i>p</i> -Me	Me	3	79.3	181–182	61.01(61.20)	4.72(4.88)	9.18(9.31)
<b>2p</b>	<i>p</i> -NO <sub>2</sub>	Me	3	80.5	201–202	54.56(54.77)	3.87(3.94)	11.49(11.62)
<b>2q</b>	<i>m</i> -NO <sub>2</sub>	Me	5	62.3	245–246	54.52(54.77)	3.89(3.94)	11.55(11.62)
<b>2r</b>	<i>o</i> -NO <sub>2</sub>	Me	5	24.8	233–234	54.61(54.77)	3.88(3.94)	11.65(11.62)
<b>2s</b>	H	Et	4	76.6	182–183	61.02(61.20)	4.82(4.88)	9.25(9.31)
<b>2t</b>	<i>p</i> -Cl	Et	4	77.2	227–228	56.72(56.85)	4.22(4.33)	8.58(8.66)
<b>2u</b>	<i>p</i> -Br	Et	4	75.5	185–186	51.97(52.08)	3.91(3.96)	8.00(7.93)
<b>2v</b>	<i>p</i> -Me	Et	4	76.8	232–233	61.74(61.94)	5.09(5.16)	8.98(9.03)
<b>2w</b>	<i>p</i> -NO <sub>2</sub>	Et	4	75.4	195–196	55.47(55.64)	4.18(4.23)	11.19(11.29)
<b>2x</b>	<i>m</i> -NO <sub>2</sub>	Et	5	60.8	235–236	55.45(55.64)	4.17(4.23)	11.15(11.29)
<b>2y</b>	H	Pr	4	74.5	218–219	61.75(61.94)	5.09(5.16)	8.94(9.03)
<b>2z</b>	<i>p</i> -Cl	Pr	4	74.8	185–186	57.56(57.66)	4.52(4.61)	8.27(8.42)
<b>2a'</b>	<i>p</i> -Br	Pr	4	73.7	191–192	52.80(52.95)	4.21(4.23)	7.79(7.72)
<b>2b'</b>	<i>p</i> -Me	Pr	4	74.5	208–209	62.45(62.63)	5.41(5.43)	8.69(8.77)
<b>2c'</b>	<i>p</i> -NO <sub>2</sub>	Pr	4	75.6	204–205	56.27(56.47)	4.43(4.51)	10.86(10.98)
<b>2d'</b>	<i>m</i> -NO <sub>2</sub>	Pr	5	61.3	198–199	56.31(56.47)	4.48(4.51)	10.82(10.98)
<b>2e'</b>	H	<i>i</i> -Pr	4	72.2	157–158	61.80(61.94)	5.07(5.16)	8.98(9.03)
<b>2f'</b>	<i>p</i> -Cl	<i>i</i> -Pr	4	71.5	218–219	57.56(57.66)	4.57(4.61)	8.37(8.42)
<b>2g'</b>	<i>p</i> -Br	<i>i</i> -Pr	5	70.4	205–206	52.85(52.95)	4.19(4.23)	7.80(7.72)
<b>2h'</b>	<i>p</i> -Me	<i>i</i> -Pr	4	72.5	178–179	62.51(62.63)	5.40(5.43)	8.72(8.77)
<b>2i'</b>	<i>p</i> -NO <sub>2</sub>	<i>i</i> -Pr	4	73.6	185–186	56.25(56.47)	4.42(4.51)	10.86(10.98)
<b>2j'</b>	<i>m</i> -NO <sub>2</sub>	<i>i</i> -Pr	5	59.8	212–213	56.44(56.47)	4.43(4.51)	10.99(10.98)
<b>2k'</b>	H	CF <sub>3</sub>	3	87.1	188–189	53.65(53.77)	3.40(3.46)	8.42(8.55)
<b>2l'</b>	<i>p</i> -Cl	CF <sub>3</sub>	3	88.4	159–160	50.17(50.24)	3.11(3.05)	7.89(8.00)
<b>2m'</b>	<i>m</i> -Cl	CF <sub>3</sub>	3	72.5	171–172	50.10(50.24)	3.08(3.05)	7.92(8.00)
<b>2n'</b>	<i>o</i> -Cl	CF <sub>3</sub>	4	50.8	197–198	50.08(50.24)	3.00(3.05)	7.89(8.00)
<b>2o'</b>	<i>p</i> -Br	CF <sub>3</sub>	3	85.8	161–162	46.21(46.32)	2.78(2.81)	7.42(7.37)
<b>2p'</b>	<i>p</i> -Me	CF <sub>3</sub>	3	87.5	185–186	54.48(54.65)	3.71(3.76)	8.39(8.32)
<b>2q'</b>	<i>p</i> -NO <sub>2</sub>	CF <sub>3</sub>	3	85.2	179–180	49.11(49.25)	2.92(2.98)	10.33(10.45)
<b>2r'</b>	<i>m</i> -NO <sub>2</sub>	CF <sub>3</sub>	3	70.2	158–159	49.14(49.25)	2.95(2.98)	10.35(10.45)
<b>2s'</b>	<i>o</i> -NO <sub>2</sub>	CF <sub>3</sub>	4	52.5	210–211	49.08(49.25)	2.93(2.98)	10.38(10.45)

\*Isolated yield based on triphenyl phosphite

phosphonates based on the three-component condensation reactions of 2-amino-5-alkyl-1,3,4-thiadiazoles with triphenyl phosphite and aromatic aldehydes in acetic acid, as well as the advantages of mild conditions, simple operation, and satisfactory yields.

## RESULTS AND DISCUSSION

### Synthesis of Products **2**

In order to optimize the reaction conditions, the condensation reactions were carried out under several

TABLE 2 IR, MS, and  $^1\text{H-NMR}$  Data of 2

Products	IR( $\text{cm}^{-1}$ )	MS( $m/z$ )	$^1\text{H-NMR}(\text{CDCl}_3, \delta)$
2a	3344, 1600, 1552, 1480, 1266, 1175, 1050, 930	423( $\text{M}^+$ ), 233, 188, 140, 104, 94	6.02(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.59$ Hz), 6.80–7.57 (m, 16H, $3 \times \text{C}_6\text{H}_5 + \text{NH}$ ), 8.30(s, 1H, CH=N)
2b	3304, 1610, 1563, 1480, 1250, 1165, 1110, 950	459, 457( $\text{M}^+$ , 1:3), 233, 222, 140, 138, 94	5.98(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.50$ Hz), 6.81–7.54 (m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.31(s, 1H, CH=N)
2c	3360, 1615, 1562, 1475, 1220, 1150, 1080, 945	459, 457( $\text{M}^+$ , 1:3), 233, 222, 140, 138, 94	5.88(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.08$ Hz), 6.85–7.53(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.31(s, 1H, CH=N)
2d	3375, 1620, 1575, 1485, 1225, 1150, 1050, 940	459, 457( $\text{M}^+$ , 1:3), 233, 222, 140, 138, 94	5.74(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.13$ Hz), 6.88–7.54(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.32(s, 1H, CH=N)
2e	3350, 1615, 1560, 1475, 1233, 1185, 1070, 940	503, 501( $\text{M}^+$ , 1:1), 266, 233, 182, 140, 94	5.84(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.58$ Hz), 6.80–7.55(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.30(s, 1H, CH=N)
2f	3400, 1620, 1585, 1491, 1235, 1170, 1095, 945	437( $\text{M}^+$ ), 233, 202, 140, 118, 94	2.25(s, 3H, $\text{CH}_3$ ), 6.12(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.03$ Hz), 6.92–7.48(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.30(s, 1H, CH=N)
2g	3380, 1625, 1550, 1470, 1240, 1180, 1090, 935	468( $\text{M}^+$ ), 233, 219, 149, 140, 94	6.12(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.98$ Hz), 6.82–8.05(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.36(s, 1H, CH=N)
2h	3350, 1620, 1563, 1475, 1240, 1190, 1075, 940	468( $\text{M}^+$ ), 233, 219, 149, 140, 94	6.04(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.15$ Hz), 6.89–8.01(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.35(s, 1H, CH=N)
2i	3380, 1610, 1565, 1480, 1240, 1185, 1060, 925	468( $\text{M}^+$ ), 233, 219, 149, 140, 94	5.98(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.88$ Hz), 6.91–7.98(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ ), 8.34(s, 1H, CH=N)
2j	3350, 1620, 1580, 1450, 1240, 1190, 1075, 930	437( $\text{M}^+$ ), 233, 202, 140, 104, 94	2.48(s, 3H, $\text{CH}_3$ ), 6.13(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.15$ Hz), 6.84–7.63(m, 16H, $3 \times \text{C}_6\text{H}_5 + \text{NH}$ )
2k	3405, 1610, 1575, 1475, 1250, 1180, 1060, 945	473, 471( $\text{M}^+$ , 1:3), 236, 233, 140, 138, 94	2.45(s, 3H, $\text{CH}_3$ ), 6.04(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.98$ Hz), 6.87–7.42(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2l	3380, 1620, 1565, 1480, 1245, 1185, 1070, 940	473, 471( $\text{M}^+$ , 1:3), 236, 233, 140, 138, 94	2.44(s, 3H, $\text{CH}_3$ ), 6.15(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.86$ Hz), 6.80–7.43(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2m	3400, 1615, 1570, 1480, 1240, 1150, 1050, 934	473, 471( $\text{M}^+$ , 1:3), 236, 233, 140, 138, 94	2.42(s, 3H, $\text{CH}_3$ ), 6.10(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.05$ Hz), 6.85–7.54(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2n	3365, 1610, 1565, 1460, 1250, 1175, 1065, 940	517, 515( $\text{M}^+$ , 1:1), 280, 233, 182, 140, 94	2.45(s, 3H, $\text{CH}_3$ ), 6.15(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.95$ Hz), 6.90–7.45(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2o	3405, 1610, 1580, 1485, 1235, 1190, 1085, 945	451( $\text{M}^+$ ), 233, 216, 140, 118, 94	2.25(s, 3H, Ph- $\text{CH}_3$ ), 2.49(s, 3H, $\text{CH}_3$ ), 6.14(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.76$ Hz), 7.05–7.62(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2p	3380, 1600, 1575, 1450, 1240, 1185, 1075, 930	482( $\text{M}^+$ ), 247, 233, 149, 140, 94	2.46(s, 3H, $\text{CH}_3$ ), 6.12(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.05$ Hz), 6.92–8.01(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2q	3410, 1610, 1580, 1475, 1250, 1175, 1045, 935	482( $\text{M}^+$ ), 247, 233, 149, 140, 94	2.44(s, 3H, $\text{CH}_3$ ), 6.12(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.85$ Hz), 6.88–8.01(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2r	3380, 1620, 1575, 1485, 1240, 1160, 1080, 940	482( $\text{M}^+$ ), 247, 233, 149, 140, 94	2.45(s, 3H, $\text{CH}_3$ ), 6.15(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.90$ Hz), 6.90–7.95(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2s	3390, 1610, 1585, 1475, 1250, 1150, 1050, 940	451( $\text{M}^+$ ), 233, 216, 140, 104, 94	1.22(t, 3H, $\text{CH}_3$ ), 2.79(q, 2H, $\text{CH}_2$ ), 5.70(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.05$ Hz), 6.79–7.50(m, 16H, $3 \times \text{C}_6\text{H}_5 + \text{NH}$ )
2t	3405, 1600, 1560, 1465, 1240, 1160, 1075, 945	487, 485( $\text{M}^+$ , 1:3), 250, 233, 140, 94	1.24(t, 3H, $\text{CH}_3$ ), 2.78(q, 2H, $\text{CH}_2$ ), 5.72(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.13$ Hz), 6.89–7.52(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2u	3350, 1610, 1585, 1460, 1235, 1150, 1050, 935	531, 529( $\text{M}^+$ , 1:1), 294, 233, 182, 140, 94	1.21(t, 3H, $\text{CH}_3$ ), 2.76(q, 2H, $\text{CH}_2$ ), 5.75(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.05$ Hz), 6.89–7.48(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )

TABLE 2 (Continued) IR, MS, and <sup>1</sup>H-NMR Data of 2

Products	IR(cm <sup>-1</sup> )	MS(m/z)	<sup>1</sup> H-NMR(CDCl <sub>3</sub> , δ)
2v	3380, 1620, 1575, 1475, 1250, 1178, 1070, 940	465(M <sup>+</sup> ), 233, 230, 148, 118, 94	1.24(t, 3H, CH <sub>3</sub> ), 2.25(s, 3H, Ph-CH <sub>3</sub> ), 2.77(q, 2H, CH <sub>2</sub> ), 5.66 (d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.05Hz), 6.85–7.45(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2w	3405, 1610, 1575, 1450, 1240, 1165, 1060, 945	496(M <sup>+</sup> ), 261, 233, 149, 140, 94	1.25(t, 3H, CH <sub>3</sub> ), 2.81(q, 2H, CH <sub>2</sub> ), 5.75(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.21Hz), 6.84–8.03(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2x	3365, 1600, 1565, 1485, 1250, 1180, 1075, 945	496(M <sup>+</sup> ), 261, 233, 149, 140, 94	1.23(t, 3H, CH <sub>3</sub> ), 2.77(q, 2H, CH <sub>2</sub> ), 5.69(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.16Hz), 6.91–7.94(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2y	3405, 1605, 1575, 1490, 1250, 1178, 1055, 950	465(M <sup>+</sup> ), 233, 230, 140, 104, 94	0.92(t, 3H, CH <sub>3</sub> ), 1.60(m, 2H, CH <sub>2</sub> ), 2.92(t, 2H, CH <sub>2</sub> ), 5.00(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.56 Hz), 6.92–7.45(m, 16H, 3 × C <sub>6</sub> H <sub>5</sub> + NH)
2z	3400, 1610, 1570, 1488, 1250, 1180, 1060, 950	501, 499(M <sup>+</sup> , 1:3), 264, 233, 140, 138, 94	0.91(t, 3H, CH <sub>3</sub> ), 1.57(m, 2H, CH <sub>2</sub> ), 2.94(t, 2H, CH <sub>2</sub> ), 5.74(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.05 Hz), 6.87–7.55(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2a'	3390, 1620, 1585, 1480, 1250, 1165, 1075, 940	545, 543(M <sup>+</sup> , 1:1), 308, 233, 182, 140, 94	0.92(t, 3H, CH <sub>3</sub> ), 1.55(m, 2H, CH <sub>2</sub> ), 2.90(t, 2H, CH <sub>2</sub> ), 5.67d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.95 Hz), 6.81–7.53(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2b'	3405, 1610, 1565, 1475, 1235, 1175, 1050, 935	479(M <sup>+</sup> ), 244, 233, 140, 118, 94	0.94(t, 3H, CH <sub>3</sub> ), 1.59(m, 2H, CH <sub>2</sub> ), 2.25(s, 3H, Ph-CH <sub>3</sub> ), 2.87 (t, 2H, CH <sub>2</sub> ), 5.88(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.93 Hz), 6.78–7.42(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2c'	3390, 1618, 1570, 1475, 1255, 1180, 1085, 940	510(M <sup>+</sup> ), 275, 233, 149, 140, 94	0.89(t, 3H, CH <sub>3</sub> ), 1.62(m, 2H, CH <sub>2</sub> ), 2.95(t, 2H, CH <sub>2</sub> ), 5.64(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.89 Hz), 6.94–8.04(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2d'	3325, 1610, 1554, 1495, 1220, 1155, 1050, 936	510(M <sup>+</sup> ), 275, 233, 149, 140, 94	0.95(t, 3H, CH <sub>3</sub> ), 1.64(m, 2H, CH <sub>2</sub> ), 2.91(t, 2H, CH <sub>2</sub> ), 5.69(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.80 Hz), 6.94–8.04(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2e'	3348, 1600, 1568, 1480, 1250, 1150, 1075, 945	465(M <sup>+</sup> ), 233, 230, 140, 104, 94	1.25(m, 6H, 2 × CH <sub>3</sub> ), 3.04(m, 1H, CH), 5.69(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.06Hz), 6.84–7.52(m, 16H, 3 × C <sub>6</sub> H <sub>5</sub> + NH)
2f'	3380, 1620, 1580, 1485, 1240, 1185, 1065, 940	501, 499(M <sup>+</sup> , 1:3), 264, 233, 140, 138, 94	1.22(m, 6H, 2 × CH <sub>3</sub> ), 3.11(m, 1H, CH), 5.71(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.03 Hz), 6.92–7.55(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2g'	3405, 1615, 1565, 1480, 1250, 1165, 1050, 945	545, 543(M <sup>+</sup> , 1:1), 308, 233, 182, 140, 94	1.25(m, 6H, 2 × CH <sub>3</sub> ), 3.08(m, 1H, CH), 5.75(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.85 Hz), 6.90–7.51(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2h'	3390, 1620, 1570, 1485, 1245, 1180, 1075, 935	479(M <sup>+</sup> ), 244, 233, 140, 118, 94	1.21(m, 6H, 2 × CH <sub>3</sub> ), 2.25(s, 3H, Ph-CH <sub>3</sub> ), 3.10(m, 1H, CH), 5.70(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.05Hz), 6.94–7.58(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2i'	3400, 1600, 1575, 1480, 1250, 1155, 1070, 945	510(M <sup>+</sup> ), 275, 233, 149, 140, 94	1.24(m, 6H, 2 × CH <sub>3</sub> ), 3.09(m, 1H, CH), 5.78(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.08 Hz), 6.98–8.05(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2j'	3350, 1610, 1563, 1480, 1250, 1150, 1050, 930	510(M <sup>+</sup> ), 275, 233, 149, 140, 94	1.25(m, 6H, 2 × CH <sub>3</sub> ), 3.15(m, 1H, CH), 5.69(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.11Hz), 6.92–7.88(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2k'	3400, 1610, 1570, 1490, 1250, 1155, 1060, 940	491(M <sup>+</sup> ), 256, 233, 140, 104, 94	5.60(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.18 Hz), 6.94–7.42(m, 16H, 3 × C <sub>6</sub> H <sub>5</sub> + NH)
2l'	3350, 1600, 1570, 1490, 1250, 1180, 1050, 945	527, 525(M <sup>+</sup> , 1:3), 290, 233, 140, 138, 94	5.71(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.85 Hz), 6.91–7.53(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2m'	3400, 1620, 1585, 1470, 1250, 1180, 1070, 930	527, 525(M <sup>+</sup> , 1:3), 290, 233, 140, 138, 94	5.75(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 22.05 Hz), 6.90–7.45(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2n'	3350, 1600, 1560, 1485, 1245, 1160, 1080, 945	527, 525(M <sup>+</sup> , 1:3), 290, 233, 140, 138, 94	5.70(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.95 Hz), 6.95–7.55(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2o'	3405, 1610, 1585, 1470, 1240, 1150, 1050, 940	571, 569(M <sup>+</sup> , 1:1), 334, 233, 182, 140, 94	5.68(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.88 Hz), 6.90–7.45(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)
2p'	3385, 1620, 1570, 1475, 1250, 1180, 1075, 945	505(M <sup>+</sup> ), 270, 233, 140, 118, 94	2.25(s, 3H, CH <sub>3</sub> ), 5.72(d, 1H, P(O)CH, <sup>2</sup> J <sub>P-H</sub> = 21.60 Hz), 6.93–7.54(m, 15H, 2 × C <sub>6</sub> H <sub>5</sub> + C <sub>6</sub> H <sub>4</sub> + NH)

TABLE 2 (Continued) IR, MS, and  $^1\text{H-NMR}$  Data of 2

Products	IR( $\text{cm}^{-1}$ )	MS( $m/z$ )	$^1\text{H-NMR}(\text{CDCl}_3, \delta)$
2q'	3405, 1600, 1565, 1480, 1230, 1160, 1075, 935	536( $\text{M}^+$ ), 301, 233, 149, 140, 94	5.74(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.58$ Hz), 6.94–8.05(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2r'	3360, 1605, 1570, 1490, 1250, 1160, 1075, 945	536( $\text{M}^+$ ), 301, 233, 149, 140, 94	5.66(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 21.77$ Hz), 6.92–7.89(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )
2s'	3400, 1620, 1580, 1485, 1240, 1160, 1070, 940	536( $\text{M}^+$ ), 301, 233, 149, 140, 94	5.70(d, 1H, P(O)CH, $^2J_{\text{P-H}} = 22.01$ Hz), 6.90–7.91(m, 15H, $2 \times \text{C}_6\text{H}_5 + \text{C}_6\text{H}_4 + \text{NH}$ )

conditions. Firstly, the reaction temperature should be maintained between 75 and 85°C. Below 75°C, this type of reaction was very slow and almost no product 2 could be obtained. Conversely, on increasing the reaction temperature to over 85°C, side reactions occurred and the yield of 2 was significantly reduced. In addition, the effect of solvent was studied. It has been reported that the presence of acetyl chloride can accelerate the three-component condensation reaction [17,18]. Moreover, when we used acetyl chloride instead of acetic acid as solvent in the present reaction, no remarkable improvement of the yield of product was observed. Further, we also examined the effects of reaction time and the molar ratio of the substrates on the condensation reaction. The best result was obtained when 2-amino-5-alkyl-1,3,4-thiadiazole 1 was reacted with 1.05 equiv of aromatic aldehyde and 0.95 equiv of triphenyl phosphite in acetic acid at 80°C for 3–5 hours. Under these reaction conditions, the three-component condensation reaction proceeded smoothly, and the results are summarized in Table 1.

The yield of product 2 is obviously dependent on the position of the substituent on the benzene ring of the aromatic aldehyde. For the same substituent, the yield decreases in the order of *para*, *meta*, and *ortho*. On the other hand, this reaction is also affected by the electronic effect of the substituent on the heterocycle, the presence of an electron-withdrawing substituent results in a better yield.

The structures of all products 2 were confirmed by IR, MS,  $^1\text{H-NMR}$ , and elemental analyses. The spectral data of products 2 are given in Table 2. The IR spectra of products 2 exhibited bands at about 3400  $\text{cm}^{-1}$ , indicating the presence of NH. The signals at 1640–1450  $\text{cm}^{-1}$  were assigned to C=N and C=C vibrations. The strong absorptions of P=O appeared at 1250–1220  $\text{cm}^{-1}$ . A set of peaks at 1200–920  $\text{cm}^{-1}$  was due to C–O, C–N, and P–O vibrations. In  $^1\text{H-NMR}$  spectra, all phenyl protons showed mul-

tiplet peaks at  $\delta$  6.80–8.05. Because of coupling with the phosphorus atom, the proton of P(O)CH exhibited doublet peaks at about  $\delta$  5.80 and their coupling constants are around 21.50–22.20 Hz. The MS spectra revealed that the molecular ion peaks and fragmentation peaks were in accordance with the given structures of products 2.

#### Fungicidal Activity of Products 2

The fungicidal activities of new compounds 2 were evaluated against *Rhizoctonia solani*, *Pellicularia sasakii*, *Gibberella saubinetii*, *Cercospora beticolasacc* and *Cercospora asparagas* by the usual agar plate technique at 50 ppm. The results indicated that all compounds 2 had significant toxicity against five fungi. When R<sup>1</sup> was *p*-chloro, the compounds 2 exhibited a strong fungicidal effect (for 2b: 100% inhibition against *Pellicularia sasakii* and 95% against *Cercospora asparagas*). The activities of compounds 2 bearing the 5-trifluoromethyl group on the heterocycle were higher than for those bearing other substituents. The compounds 2 were more active against *Pellicularia sasakii* than against the other four fungi.

#### EXPERIMENTAL

Melting points were uncorrected. Elemental analyses were carried on a Yanaco CHN Corder MT-3 apparatus IR spectra were recorded on a Shimadzu-435 spectrometer.  $^1\text{H-NMR}$  spectra were measured by using a Bruker AC-200 spectrometer with  $\text{CDCl}_3$  as solvent and TMS as internal standard. MS spectra were performed on a HP 5988A spectrometer. All materials were reagent grade and purified as required. 1a, 1b, 1c, 1d, 1e [19], and 1f [20] were prepared by literature methods.

*General Procedure for the Synthesis of O,O-Diphenyl 1-(5-Alkyl-1,3,4-thiadiazol-2-yl)aminoarylmethylphosphonates 2a-s'*

The mixture of 2-amino-5-alkyl-1,3,4-thiadiazole (10 mmol), aromatic aldehyde (10.5 mmol) and triphenyl phosphite (2.95 g, 9.5 mmol) in glacial acetic acid (10 mL) was heated at 80°C for 3–5 hours. The solvent was removed under reduced pressure, and the oily residue was dissolved in methanol (15 mL) and left for crystallization at –15°C. After 1–3 hours the crystalline solid was collected by filtration and recrystallized from ethanol. A white crystalline material was obtained.

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