Stereoselective Synthesis and Biological Activities of Diethyl (*E*)-{[4-Cyano-5-[[(disubstitutedamino)methylene]amino]-3-(methylthio)-1*H*-pyrazol-1-yl]substituted phenylmethyl}phosphonates

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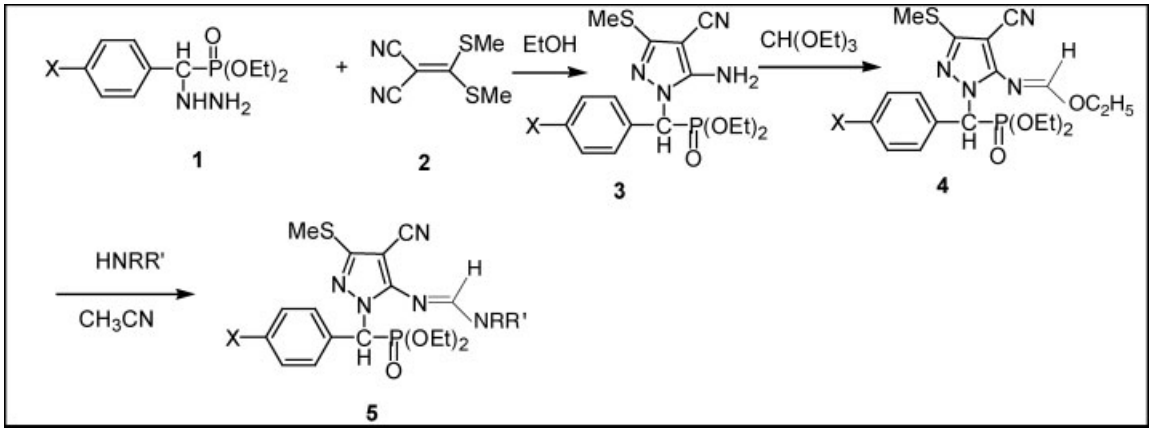

Diethyl {[5-amino-4-cyano-3-(methylthio)-1*H*-pyrazol-1-yl]substitutedphenylmethyl}phosphonates **3** were efficiently synthesized *via* the condensation of [(1-hydrazino)substitutedphenylmethyl]phosphonates **1** with 2-[bis(methylthio)methylene]malononitrile **2**. **3** reacted with triethyl orthoformate to afford diethyl (*E*)-{[4-cyano-5-[(ethoxymethylene)amino]-3-(methylthio)-1*H*-pyrazol-1-yl]substitutedphenylmethyl}phosphonates **4**, which reacted with various secondary amines at room temperature to provide the target compounds **5** in good yields. Their structures were confirmed by ir, ^{1}H and ^{31}P NMR, mass spectroscopy, and elemental analyses. The results of preliminary bioassay indicated that compounds **5** possess potent herbicidal activity against the roots of dicotyledonous (oil rape) plants at the dosage of 100 mg/L, and compounds **5c** and **5g** exhibit 80.8% and 76.7% inhibitory activity against *Colletotrichum gossypi* at the concentration of 50 mg/L, respectively. Abstract end data:

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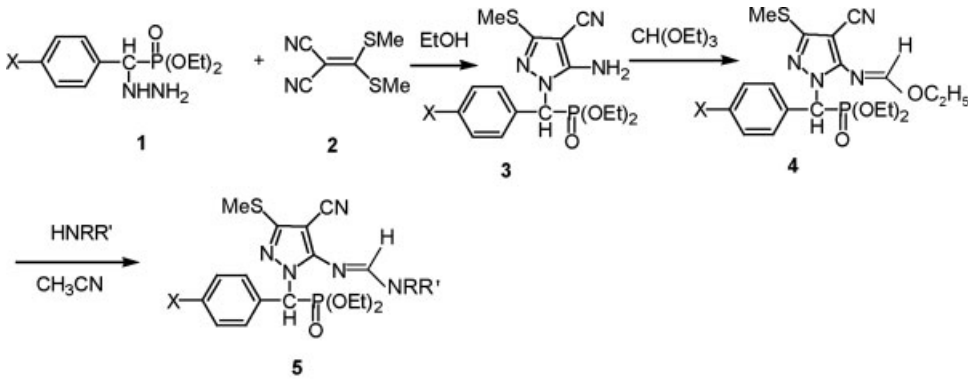
INTRODUCTION

In recent years, 1-aminoalkyl phosphonate analogs, as the phosphorus analogs of natural amino acids are of increasing interest in medicinal chemistry and pesticide science [1,2] because of their wide biological activities such as enzyme inhibitors [3], antibiotics [4], and haptens of catalytic antibodies [5], antifungal agents, herbicides, plant growth regulators, and plant virucides [6]. Recently, pyrazole compounds play an important role in pesticide science, and some pyrazole derivatives have been developed as herbicides [7,8], insecticides (such as Regent and MK-239) [9,10], and fungicides (Furametpyr, Pyraclostrobin) [11]; to the best of our knowledge, some pyrazole derivatives containing phosphorus have shown good biological activities, for example, pyraclofos and flupyrazofos have been developed as good insecticides [12,13]. As a continuation of our search for new biologically active organic phosphorus heterocyclic compounds, we designed and synthesized a series of novel title compounds.

RESULTS AND DISCUSSION

The versatile intermediates, [(1-hydrazino)substitutedphenylmethyl]phosphonates **1** have been reported by several methods [14]. We synthesized it by a modified procedure of Yuan's report [14a]. For converting substituted benzaldehydes to [(1-hydroxy)substitutedphenylmethyl]-phosphonates, an excess of solid catalyst (potassium fluoride, four times) caused difficulty in stirring and incomplete reactivity. Instead, we used one molecular catalyst triethylamine in methylene chloride to avoid these shortcomings and obtained [(1-hydroxy)substitutedphenylmethyl]phosphonates in better yields. Compounds **1** can be obtained in moderate yields by the reaction of diethyl [(1-hydroxy)substitutedphenylmethyl]phosphonates with mesyl

Scheme 1. Synthetic route to compounds **5**.



1a, **3a**, **4a:** X = H; **1b**, **3b**, **4b:** X = F; **5a:** X = H, NRR' = diethylamino; **5b:** X = H, NRR' = piperidin-1-yl; **5c:** X = F, NRR' = diethylamino; **5d:** X = F, NRR' = dipropylamino; **5e:** X = F, NRR' = dibutylamino; **5f:** X = F, NRR' = piperidin-1-yl; **5g:** X = F, NRR' = morpholin-3-yl

chloride, followed by the nucleophilic substitution with hydrazine in a one-pot reaction. Cyclization of compounds **1** with 2-[bis(methylthio)methylene]malononitrile **2** in a mild condition gave diethyl {[5-amino-4-cyano-3-(methylthio) -1*H*-pyrazol-1-yl]substitutedphenylmethyl}phosphonates **3**, which could easily convert to the corresponding imidates **4** in excess triethyl orthoformate. Compounds **4** reacted with various secondary amines such as diethylamine, piperidine, diisopropylamine, dibutylamine, and morpholine to yield the corresponding target compounds **5a**–**5g** conveniently at room temperature (Scheme 1).

The structures of compounds **5a**–**5g** were deduced from their spectral data (ir, ^{1}H and ^{31}P NMR), ms, and elemental analyses. In the ^{1}H NMR spectra of compounds **5**, the methylthio protons display as a singlet at δ 2.6; the CH proton linking with the phosphonyl group appears as a doublet due to coupling with P atom with the coupling constant of 23 Hz, whereas the N=CH proton in compounds **5** appears as a singlet at δ 8.3. The ir spectra of compounds **5** showed normal stretching absorption bands indicating the existence of the CN, Ar group, P=O, and P—O—C moieties. The EI mass spectra of compounds **5** revealed the existence of their molecular ion peaks and main fragmentation peaks. Because of the existence of a C=N bond, it probably existed in *E* and *Z* isomers in compound **4a**–**4b** and target molecules **5a**–**5g**. In ^{1}H NMR spectra, the N=CH proton in compounds **4** and **5** appears as a singlet at δ 8.4 and 8.3, respectively. Due to probably intramolecular hydrogen bonding between the hydrogen of N=CH— moiety with the nitrogen of the CN group and thermodynamic stable isomer, we deduced the stereoconfigurations in compounds **4** and **5** are all in E-configuration, which was also consisted with the configuration of substituted formamides [15] and that of its C=N analog, which was confirmed by single crystal X-ray diffraction [16].

Herbicidal activity. The herbicidal activity of title compounds **5** against *Brassica campestris* L (oil rape) and *Echinochloa crusgalli* (barnyard grass) has been investigated at the dosages of 100 mg/L and 10 mg/L compared with distilled water and the commercially available herbicide, 2,4-dichlorophenoxy acetic acid (**2,4-D**) according to the method described in the experimental section. The preliminary results of bioassay showed that some of compounds **5** possess potent and selective herbicidal activities against dicotyledonous weeds such as oil rape at the dosage of 100 mg/L. For example, compounds **5b**, **5f**, and **5g** exhibit 84.4%, 91.4%, and 96.0% inhibitory activity against the root of rape, respectively. It is also found that compounds **5** exhibit a stronger inhibitory effect against the root of rape than the stem (Table 1). Moreover, the herbicidal activity decreases with the decrease of the dosage of compounds **5**. The QSAR studies of **5** are under investigation.

Fungicidal activities. The preliminary fungicidal activity of the target compounds **5** were evaluated by the classic plate method at a concentration of 50 mg/L. The six fungi used as follows, *Fusarium oxysporium*, *Rhizoctonia solani*, *Botrytis cinereapers*, *Gibberella zeae*, *Dothiorella gregaria*, and *Colletotrichum gossypi*, belong to the group of field fungi and were isolated from corresponding crops. The activity data were also listed in Table 1. The results indicated that most of compounds **5** exhibit moderate to weak inhibitory activities against the above six fungi. For example, compounds **5c** and **5g** exhibit 80.8% and 76.7% inhibitory activity against *Colletotrichum gossypi*, respectively.

In conclusion, we developed an efficient synthesis of diethyl (*E*)-{[4-cyano-5-[[(disubstitutedamino)methylene]amino]-3-(methylthio)-1*H*-pyrazol-1-yl] substituitedphenylmethyl}phosphonates *via* a multistep reaction.

The preliminary bioassays showed that these compounds possess potent herbicidal activity against the roots of dicotyledonous (oil rape) plants at the dosage of 100 mg/L, and some of them displayed moderate fungicidal activity at the concentration of 50 mg/L.

EXPERIMENTAL

Melting points were determined with a WRS-1B digital melting point apparatus and were uncorrected. ^{1}H and ^{31}P NMR spectra were recorded on a Varian MERCURY-PLUS400 (400 MHz) spectrometer with deuteriochloroform as the solvent and TMS and 85% phosphoric acid as the internal and external references, respectively. 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 ELIII CHNSO elementary analyzer. All of the solvents and materials were reagent grade and purified as required. [(1-Hydrazino)substitutedphenylmethyl]-phosphonates **1** [14a], 2-[bis(methylthio)methylene]malononitrile **2** [17] were prepared according to the literature procedures.

General procedure for the preparation of compounds 1. A mixture of substituted benzaldehyde (0.1 moles), diethyl phosphite (13.8 g, 0.1 moles), and triethylamine (5.1 g, 0.05 moles) was heated at 75°C for 0.5 h until the reaction completed (monitored by tlc). After cooling, mesyl chloride (12.5 g, 0.11 moles) in anhydrous methylene chloride (100 mL) was added dropwise at 0°C. After the addition completed, the mixture was stirred at room temperature for 2 h. The solid was removed by filtration, the filtrate was washed by distilled water (30 mL × 3), dried over anhydrous sodium sulphate, and then concentrated *in vacuo* to give [(1-mesyl oxy)-substitutedphenylmethyl]phosphonate as a light yellow liquid, yield: 87–91%, which can be used without further purification.

To the mixture of [(1-mesyl oxy)substitutedphenylmethyl]-phosphonate (0.1 moles) in ethanol (40 mL) was added drop wise 85% hydrazine (26.4 g, 0.4 moles) at 0°C, after the addition finished, the mixture was stirred for 6–8 h at 45–50°C. The workup involved stripping of the solvent followed by an addition of water (100 mL) and extraction of the product into anhydrous ethyl ether (50 mL × 3), after phase separation, drying over anhydrous sodium sulphate, filtration and evaporation, a crude product 1 was yielded as a yellow liquid, yield 40–45%, which can be used without further purification.

General procedure for the preparation of compounds 3. A mixture of 1 (24.3 mmoles), 2 (3.89 g, 22.9 mmoles), and anhydous ethanol (30 mL) was refluxed for 5 h [18]. After cooling, the reaction mixture was concentrated *in vacuo* and recrystallized from ethyl acetate and petroleum ether (1;1, *v*/*v*) to give white crystals.

3a: yield: 64%, mp 161–163°C; ^{1}H NMR: δ 1.19–1.27 (m, 6H, $2CH_3$), 2.53 (s, 3H, SCH_3), 4.01–4.16 (m, 4H, $2CH_2$), 5.54 (s, 2H, NH_2), 5.75 (d, J = 24 Hz, 1H, PCH), 7.27–7.52 ppm (m, 5H, Ar—H); ir: NH_2 3358, Ar—H 2995, CN 2215, P=O 1265, P—O—C 1048, P—C 978 cm^{-1}; ms: *m*/*z* 380 (M^+, 65), 333 (16), 227 (48), 153 (100); Anal. Calcd for $C_{16}H_{21}N_4O_3PS$: C, 50.52; H, 5.56; N, 14.73. Found: C, 50.69; H, 5.48; N, 14.89.

3b: yield: 71%, mp158–159°C. ^{1}H NMR: δ 1.19–1.27 (m, 6H, $2CH_3$), 2.53 (s, 3H, SCH_3), 4.01–4.16 (m, 4H, $2CH_2$), 5.56 (s, 2H, NH_2), 5.72 (d, J = 24 Hz, 1H, PCH), 7.28–7.50 ppm (m, 4H, Ar—H); ir: NH_2 3342, Ar—H 2992, CN 2210, P=O 1256, P—O—C 1045, P—C 975 cm^{-1}; ms: *m*/*z* 398 (M^+, 81), 261 (50), 109 (100); Anal. Calcd for $C_{16}H_{20}FN_4O_3PS$: C, 48.24; H, 5.06; N, 14.06. Found: C, 48.39; H, 4.81; N, 14.14.

General procedure for the preparation of compounds 4. 3 (6 mmoles) was dissolved in triethyl orthoformate (4 mL), and the mixture was refluxed for 2 h. After cooling, the solvent was removed under a reduced pressure, and the residue was purified on silica gel (ethyl acetate-light petroleum ether, 1:5, *v*/*v*) to afford 4 as a white solid.

4a. yield: 95%, mp 64–66°C. ^{1}H NMR: δ 1.18–1.27 (m, 6H, $2CH_3$), 1.40 (t, J = 7 Hz, 3H, CH_3), 2.62 (s, 3H, SCH_3), 4.01–4.20 (m, 4H, $2CH_2$), 4.39 (t, J = 6.6 Hz, 2H, CH_2), 5.90 (d, J = 22.8 Hz, 1H, PCH), 7.33–7.55 (m, 5H, Ar—H), 8.39 ppm (s, 1H, N=CH); ir: Ar—H 2976, CN 2222, C=N— 1608, P=O 1266, P—O—C 1058, P—C 969 cm^{-1}; ms: *m*/*z* 436 (M^+, 65), 391 (79), 389 (52), 109 (100); Anal. Calcd for $C_{19}H_{25}N_4O_4PS$: C, 52.28; H, 5.77; N, 12.84. Found: C, 52.41; H, 5.54; N, 12.72.

4b. yield: 89%, mp 77–78°C. ^{1}H NMR: δ 1.19–1.31 (m, 6H, $2CH_3$), 1.42 (t, J = 7.2 Hz, 3H, CH_3), 2.61 (s, 3H, SCH_3), 4.02–4.05 (m, 2H, CH_2), 4.14–4.18 (m, 2H, CH_2), 4.38–4.41 (m, 2H, CH_2), 5.87 (d, J = 22.4 Hz, 1H, PCH), 7.04 (dd, J = 8.4 Hz, J = 8.4 Hz, 2H, Ar—H), 7.54 (dd, J = 5.2 Hz, J = 8.4 Hz, 2H, Ar—H), 8.41 ppm (s, 1H, N=CH); ir: Ar—H 2972, CN 2210, C=N— 1616, P=O 1248, P—O—C 1042, P—C 970 cm^{-1}; ms: *m*/*z* 456 (16), 454 (M^+, 45), 411 (36), 409 (57), 109 (100); Anal. Calcd for $C_{19}H_{24}FN_4O_4PS$: C 50.21, H 5.32, N 12.33; found C 50.03, H 5.15, N 12.18.

General procedure for the preparation of compounds 5. A solution of 4 (1 mmole) and secondary amine (1.5 mmoles) in anhydrous acetonitrile (15 mL) was stirred at room temperature for 0.5–1 h (monitorede by tlc). After the reaction was complete, the solvent was removed under reduced pressure, and the residue was purified on silica gel (petroleum ether and acetone, 4:1, *v*/*v*) to yield the corresponding target compounds 5a–5g.

5a. Colorless oil, yield: 75%; ^{1}H NMR: δ 1.18–1.29 (m, 12H, $4CH_3$), 2.62 (s, 3H, SCH_3), 3.32 (q, J = 6.8 Hz, 2H, NCH_2), 3.34–3.48 (m, 1H, NCH_2), 3.56–3.61 (m, 1H, NCH_2), 3.99–4.06 (m, 2H, OCH_2), 4.16–4.21 (m, 2H, OCH_2), 6.06 (d, J = 23 Hz, 1H, PCH), 7.27–7.32 (m, 3H, Ar—H), 7.54 (d, 2H, J = 6.4 Hz, Ar—H), 8.26 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 16.79 ppm; ir: Ar—H 2974, CN 2214, C=N— 1617, P=O 1260, P—O—C 1026, P—C 976 cm^{-1}; ms: *m*/*z* 463 (M^+, 35), 326 (100), 279 (18); Anal. Calcd for $C_{21}H_{30}N_5O_3PS$: C, 54.41; H, 6.52; N, 15.11. Found: C, 55.14; H, 6.67; N, 14.98.

5b. Colorless crystals, yield: 95%; mp 87.9–89.6°C; ^{1}H NMR: δ 1.17–1.26 (m, 6H, $2CH_3$), 1.62–1.71 (m, 6H, $CH_2CH_2CH_2$), 2.62 (s, 3H, SCH_3), 3.37 (t, J = 5.2 Hz, 2H, NCH_2), 3.64 (t, J = 5.2 Hz, 2H, NCH_2), 3.98–4.04 (m, 2H, OCH_2), 4.14–4.21 (m, 2H, OCH_2), 6.07 (d, J = 23.2 Hz, 1H, PCH), 7.29–7.35 (m, 3H, Ar—H), 7.56 (d, J = 7.6 Hz, 2H, Ar—H), 8.23 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 16.98 ppm; ir: Ar—H 2985, CN 2212, C=N— 1618, P=O

Table 1

The herbicidal and fungicidal activities of compounds **5** (inhibitory rate %).

Compd.	Herbicidal activity				Fungicidal activity (50 mg/L)					
	Oil rape (root/stem)		Barnyard (root/stem)							
	100 (mg/L)	10 (mg/L)	100 (mg/L)	10 (mg/L)	*Fusarium oxysporium*	*Rhizoctonia solani*	*Botrytis cinereapers*	*Gibberella zeae*	*Dothiorella gregaria*	*Colleto-trichum gossypii*
5a	67.0/60.0	40.7/44.4	56.8/65.6	32.4/15.6	42.9	60.0	33.3	42.9	41.4	50.0
5b	84.4/60.0	33.7/38.9	59.5/37.5	45.9/28.1	42.9	33.3	37.0	63.6	44.8	68.3
5c	74.0/71.1	37.2/50.0	73.0/46.9	48.6/43.7	67.1	63.3	37.0	70.7	65.2	80.8
5d	78.6/60.0	27.9/38.9	27.0/12.5	21.6/3.1	43.3	48.3	25.9	46.4	44.8	60.0
5e	76.3/65.5	16.3/22.2	43.2/25.0	37.8/18.7	19.1	31.7	0.0	17.9	31.0	41.7
5f	91.4/54.4	43.0/33.3	81.1/50.0	43.2/28.1	33.8	36.7	14.8	60.0	44.8	76.7
5g	96.0/65.6	41.9/33.3	75.7/62.5	37.8/21.9	23.8	0.0	18.5	7.1	10.3	33.3
2,4-D	99.0/91.5	98.2/91.2	97.5/33.5	97.5/31.2						

1261, P—O—C 1046, P—C 976 cm^{-1}; ms: *m/z* 475 (M^+, 26), 428 (10.8), 338 (74), 248 (100); Anal. Calcd for $C_{22}H_{30}N_5O_3PS$: C, 55.56; H, 6.36; N, 14.73. Found: C, 55.30; H, 6.15; N, 14.69.

5c. Colorless crystals, yield: 84%; mp 62.9–64.1°C. ^1H NMR: δ 1.18–1.27 (m, 12H, $4CH_3$), 2.62 (s, 3H, SCH_3), 3.34 (q, J = 6.8 Hz, 2H, NCH_2), 3.46–3.50 (m, 1H, NCH_2), 3.57–3.60 (m, 1H, NCH_2), 4.00–4.06 (m, 2H, OCH_2), 4.15–4.19 (m, 2H, OCH_2), 6.04 (d, J = 22.8 Hz, 1H, PCH), 6.99 (dd, J = 8.8 Hz, J = 8.4 Hz, 2H, Ar—H), 7.55 (dd, J = 5.2 Hz, J = 8.4 Hz, 2H, Ar—H), 8.27 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 17.17 ppm; ir: Ar—H 2980, CN 2212, C=N— 1620, P=O 1260, P—O—C 1047, P—C 973 cm^{-1}; ms: *m/z* 483 (4.3), 481 (M^+, 28), 344 (100), 297 (8), 236 (8), 175 (20), 109 (16); Anal. Calcd for $C_{21}H_{29}FN_5O_3PS$: C, 52.38; H, 6.07; N, 14.54. Found: C, 52.43; H, 6.36; N, 14.73.

5d. Colorless crystals, yield: 85%; mp 56.1–56.9°C; ^1H NMR: δ 0.89–0.98 (m, 6H, $2CH_3$), 1.18–1.27 (m, 6H, $2CH_3$), 1.60–1.68 (m, 4H, $2CH_2$), 2.61 (s, 3H, SCH_3), 3.23 (t, J = 7.2 Hz, 2H, NCH_2), 3.32–3.37 (m, 1H, NCH_2), 3.45–3.50 (m, 1H, NCH_2), 4.00–4.06 (m, 2H, OCH_2), 4.14–4.21 (m, 2H, OCH_2), 6.01 (d, J = 22.8 Hz, 1H, PCH), 7.01 (dd, J = 8.8 Hz, J = 8.8 Hz, 2H, Ar—H), 7.52 (dd, J = 5.6 Hz, J = 8.8 Hz, 2H, Ar—H), 8.27 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 17.08 ppm; ir: Ar—H 2970, CN 2210, C=N— 1620, P=O 1255, P—O—C 1045, P—C 977 cm^{-1}; ms: *m/z* 511 (11.9), 509 (M^+, 44), 372 (100), 330 (11), 264 (14), 108 (6), 43 (8); Anal. Calcd for $C_{23}H_{33}FN_5O_3PS$: C, 54.21; H, 6.53; N, 13.74. Found: C, 54.36; H, 6.22; N, 13.57.

5e. Colorless oil, yield: 88%; ^1H NMR: δ 0.92–0.99 (m, 6H, $2CH_3$), 1.18–1.30 (m, 6H, $2CH_3$), 1.32–1.40 (m, 4H, $2CH_2$), 1.54–1.63 (m, 4H, $2CH_2$), 2.61 (s, 3H, SCH_3), 3.26 (t, J = 7.6 Hz, 2H, NCH_2), 3.36–3.41 (m, 1H, NCH_2), 3.48–3.54 (m, 1H, NCH_2), 3.99–4.06 (m, 2H, OCH_2), 4.17–4.19 (m, 2H, OCH_2), 6.02 (d, J = 22.8 Hz, 1H, PCH), 7.00 (dd, J = 8.4 Hz, J = 8.8 Hz, 2H, Ar—H), 7.54 (dd, J = 5.2 Hz, J = 8.8 Hz, 2H, Ar—H), 8.26 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 17.06 ppm; ir: Ar—H 2960, CN 2212, C=N— 1619, P=O 1260, P—O—C 1025, P—C 973 cm^{-1}; ms: *m/z* 539 (23.8), 537 (M^+, 42), 400 (100), 292 (26), 231 (20), 140 (42), 109 (52); Anal. Calcd for $C_{25}H_{37}FN_5O_3PS$: C, 55.85; H, 6.94; N, 13.03. Found: C, 55.74; H, 7.13; N, 12.89.

5f. Colorless crystals, yield: 83%; mp 115.0–116.4°C; ^1H NMR: δ 1.18–1.26 (m, 6H, $2CH_3$), 1.63–1.73 (m, 6H, $CH_2CH_2CH_2$), 2.59 (s, 3H, SCH_3), 3.38 (t, J = 5.6 Hz, 2H, NCH_2), 3.66 (t, J = 5.6 Hz, 2H, NCH_2), 4.00–4.05 (m, 2H, OCH_2), 4.13–4.19 (m, 2H, OCH_2), 6.04 (d, J = 23.2 Hz, 1H, PCH), 7.01 (dd, J = 8.8 Hz, J = 8.8 Hz, 2H, Ar—H), 7.56 (dd, J = 8.4 Hz, J = 5.2 Hz, 2H, Ar—H), 8.24 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 17.25 ppm; ir: Ar—H 2945, CN 2210, C=N— 1622, P=O 1254, P—O—C 1023, P—C 956 cm^{-1}; ms: *m/z* 495 (13.0), 493 (M^+, 50), 446 (11), 356 (100), 309 (23), 248 (19), 108 (9); Anal. Calcd for $C_{22}H_{29}FN_5O_3PS$: C, 53.54; H, 5.92; N, 14.19. Found: C, 53.31; H, 5.83; N, 14.10.

5g. Colorless crystals, yield: 94%; mp 127.6–129.3°C; ^1H NMR: δ 1.18–1.27 (m, 6H, $2CH_3$), 2.61 (s, 3H, SCH_3), 3.45–3.48 (m, 2H, NCH_2), 3.70–3.78 (m, 6H, NCH_2 + $2OCH_2$), 3.99–4.05 (m, 2H, CH_2O), 4.13–4.21 (m, 2H, CH_2O), 6.00 (d, J = 23.2 Hz, 1H, PCH), 7.02 (dd, J = 8.8 Hz, J = 8.4 Hz, 2H, Ar—H), 7.53 (dd, J = 5.6 Hz, J = 8.4 Hz, 2H, Ar—H),

8.28 ppm (s, 1H, N=CH); ^{31}P NMR (162 MHz): δ 16.60 ppm; ir: Ar—H 2976, CN 2215, C=N— 1621, P=O 1263, P—O—C 1024, P—C 974 cm^{-1}; ms: *m*/*z* 497 (17.8), 495 (M^+, 79), 448 (9), 358 (100), 108 (10), 81 (5); Anal. Calcd for $C_{21}H_{27}FN_5O_4PS$: C, 50.90; H, 5.49; N, 14.13. Found: C, 50.71; H, 5.65; N, 14.32.

Bioassay method

Herbicidal activities testing. Herbicidal testing of the newly synthesized compounds **5** was carried out in a greenhouse, with temperature 23 ± 1°C, relative humidity (RH) 60 ± 5%, light intensity 10 Klux, photoperiod 8 h/day. Twenty seeds of each weed species including oil rape and barnyard grass were chosen for testing. Seedlings were grown in the test plate of 9 cm diameter containing two pieces of filter paper and 9 mL solution of the tested compound (100 mg/L and 10 mg/L, respectively). Distilled water and **2,4-D** were used as the comparison compounds. The herbicidal activity was assessed as the inhibitory rate in comparison with the distilled water. The herbicidal rating score based on visual observation. Range from 0 to 100%, 0% means no effect, 100% means complete killing. The test was run three times, and the results were averaged and given as activity in Table 1.

Fungicidal activity testing. The fungicidal activity measurement method was adapted from the one described by Molina-Torres *et al* [19]. The synthesized target compounds were dissolved in 0.5–1.0 mL of *N*,*N*-dimethylformamide to the concentration of 500 mg/L. The solutions (1 mL) were mixed rapidly with thawed potato glucose agar culture medium (9 mL) under 50°C. The mixtures were poured into petridishes. After the dished were cooled, the solidified plates were incubated with 4 mm mycelium disk, inverted, and incubated at 28°C for 48 h. Distilled water was used as the blank control. Three replicates of each test were carried out. The mycelial elongation radius (mm) of fungi settlements was measured after 48 h of culture. The growth inhibitory rates were calculated with the following equation: $I = [(C - T)/C] * 100\%$. Here, I is the growth inhibitory rate (%), C and T are the mycelial elongation radius (mm) of fungus settlements and that of treatment group, respectively. The results are also given in Table 1.

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