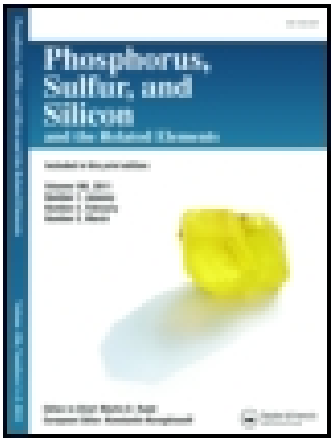

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A Convenient Synthesis and Herbicidal Activity of N-phosphonoalkylpyrazolo[4,3-e][1,2,4]-triazolo[1,5-d]pyrimidines

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A Convenient Synthesis and Herbicidal Activity of *N*-phosphonoalkylpyrazolo[4,3-*e*][1,2,4]-triazolo[1,5-*d*]pyrimidines

Lin-Xia Xiao, Ke Li, and De-Qing Shi
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*An important building block, diethyl [(5-amino-4-cyano-3-methylsulfanyl-pyrazol-1-yl)–(4-fluorophenyl)methyl] phosphonate (**3**) was efficiently synthesized via the condensation of 1-hydrazino-1-(4-fluorophenyl)methyl phosphonate (**1**) with 2-[bis(methylthio)methylene]malononitrile (**2**). **3** reacted with triethyl orthoformate to afford diethyl [(4-cyano-5-ethoxymethyleneamino-3-methylsulfanyl-pyrazol-1-yl)-(4-fluorophenyl)methyl] phosphonate (**4**), which reacted with various acyl hydrazines in refluxing 2-methoxyethanol to provide the target compounds (**5**) in good yields directly. The results of preliminary bioassay indicated that compounds **5** possess potent herbicidal activity against the roots of monocotyledonous (barnyard grass) and dicotyledonous (oil rape) plants, and could be further developed as potential herbicides.*

Keywords 1-Aminoalkyl phosphonate analog; herbicidal activity; pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*d*]pyrimidine; synthesis

INTRODUCTION

In recent years, 1-aminoalkyl phosphonate analogs, as the phosphorus analogs of natural amino acids received an increasing attention in medicinal chemistry and pesticide science[1,2] due to their wide biological activities such as enzyme inhibitors,[3] antibiotics,[4] catalytic antibodies,[5] antifungal agents, herbicides, plant growth regulators and plant virucides.[6] Recently, triazolopyrimidines such as Penoxsulam and Florasulam were commercialized as herbicides[7,8]; and pyrazolo[4,3-*e*]-1,2,4-triazolo-[1,5-*d*]pyrimidine derivatives such as 8FB-PTP, were

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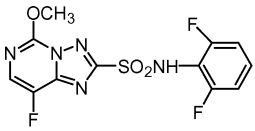
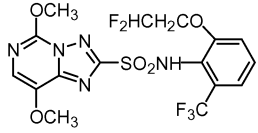
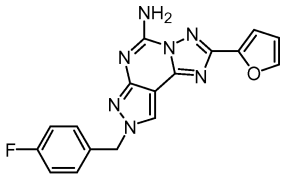
found to be potent adenosine A_{2A} antagonists.[9,10] As part of our ongoing project aimed at investigating novel *N*-phosphonoalkylheterocycles with herbicidal activity, we synthesized a series of novel 1-aminoalkyl phosphonate analogs, *N*-phosphonoalkylpyrazolo[4,3-*e*]-1,2,4-triazolo-[1,5-*d*]pyrimidines using diethyl [(5-amino-4-cyano-3-methylsulfanyl-pyrazol-1-yl)-(4-fluorophenyl)methyl] phosphonate as building block. Herein, we would like to describe the cyclization reaction (Scheme 1) to synthesize the title compounds **5**. The results of bioassay indicated that **5** possess potent herbicidal activity against the roots of oil rape and barnyard grass and can be further developed as potential herbicides.



Penoxsulam



Florasulam

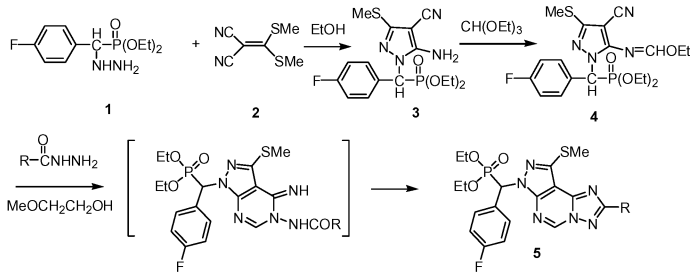


8FB PTP

RESULTS AND DISCUSSION

Synthesis

The versatile intermediate, 1-hydrazino-1-(4-fluorophenyl)methyl phosphonate (**1**) has been reported by several methods.[11] We synthesized it by a modified procedure of Yuan's report.[11*a*] For converting 4-fluoro-benzaldehyde to1-hydroxy-1-(4-fluorophenyl)methyl phosphonate, an excess of solid catalyst (KF, four times) caused difficulty in stirring and incomplete reactivity. Instead, we used one molecular catalyst (Et_3N) in CH_2Cl_2 to avoid these shortcomings and obtained 1-hydroxy-1-(4-fluorophenyl)methyl phosphonate in a better yield (85%). **1** can be obtained in a moderate yield (76%) by the reaction of diethyl 1-hydroxyl-1-(4-fluorophenyl)methyl phosphonate with mesyl chloride, followed by the nucleophilic substitution with hydrazine in a one-pot reaction. Cyclization of **1** with 2-[bis(methylthio)methylene]malononitrile (**2**) in a mild condition gave diethyl [(5-amino-4-cyano-3-methylsulfanyl-pyrazol-1-yl)-(4-fluorophenyl)methyl] phosphonate (**3**), which could easily convert to the corresponding imidate (**4**) (89%) in refluxing triethyl orthoformate. **4** reacted with various acyl hydrazines to yield the corresponding tricyclic target compounds **5a**∼**5h** conveniently in refluxing 2-methoxyethanol in one step (Scheme 1), without the isolation of 5-acylamino-4-imino-4,5-dihydropyrazolo[3, 4-*d*]pyrimidines,



R= 4-totyl; 4-methoxyphenyl; phenoxymethyl; 4-chlorophenoxymethyl; 3-chlorophenoxymethyl; 2,4-dichlorophenoxymethyl; 4-(*t*-butyl)phenoxymethyl; 3-(trifluoromethyl)phenoxymethyl

SCHEME 1 Synthetic route of title compounds **5**.

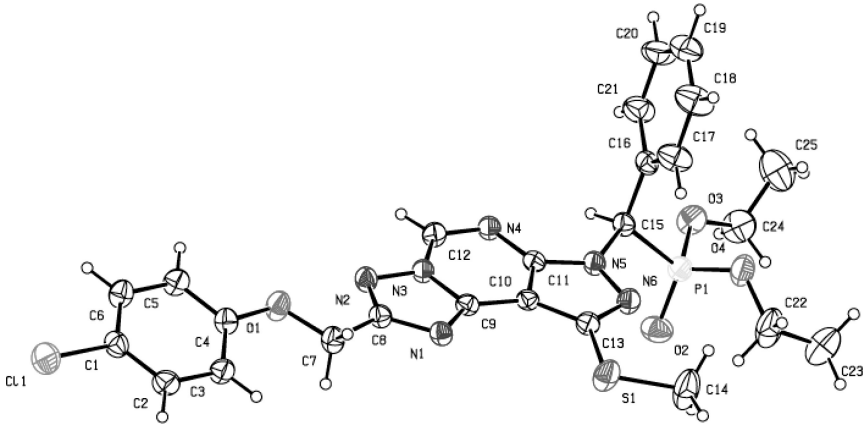


FIGURE 1 X-ray crystal structure of unfluorinated analog **5**.

opposite to the report by Baraldi et al.[12] In Baraldi's report, analogous imidates reacted with various acyl hydrazines in refluxing 2-methoxyethanol to give 5-acylamino-4-imino-4,5-dihydropyrazolo[3, 4-*d*]pyrimidines. While the ring closure to the corresponding pyrazolo[4,3-*e*]-1,2,4-triazolo-[1,5-*d*]pyrimidines thermally needed a higher boiling point solvent (260°C) like diphenyl ether.

The structures of compounds **5a**∼**5h** were deduced from their spectra data (IR, ^{1}H NMR, ^{31}P NMR, MS and elemental analyses). One of its unfluorinated analogs was determined by X-ray diffraction crystallography as an example (Figure 1). For more detail information, please see Xiao and Shi.[13]

Biological Activities

The herbicidal activity of title compounds **5** against *Brassica napus* (rape) and *Echinochloa crus-galli* (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. Compounds **5** not only show stronger inhibitory activity against oil rape than barnyard, but also those roots than stalks. The herbicidal activity decreases with the decrease of the dosage of compounds **5**. From Table I, we noticed that the substituent R had some effect on the herbicidal activity. For example, the 2,4-dichlorophenoxymethyl substituted compound have the best activity, while the 4-(*t*-butyl)-phenoxymethyl substituted one have the lowest activity. Moreover, compounds containing halogen atoms in R group have better activities than that of no halogen ones. The QSAR studies of **5** are under investigation.

EXPERIMENTAL

Melting points were determined with a WRS-1B digital melting point apparatus and are uncorrected. ^{1}H and ^{31}P NMR spectra were recorded on Varian MERCURY-PLUS400 (400 MHz) spectrometer with $CDCl_3$ as the solvent and TMS and 85% H_3PO4 as the internal and external

TABLE I The Herbicidal Activity of Compounds 5 (inhibitory rate%)

		Relative inhibition (root%/stalk%)			
		Rape		Barnyard grass	
Compd.	R	100 mg/L	10 mg/L	100 mg/L	10 mg/L
5a	4-totyl	51.1/29.2	25.0/29.2	75.7/40.0	18.9/17.1
5b	4-methoxyphenyl	85.2/50.0	33.4/8.3	59.5/17.1	29.7/17.1
5c	phenoxymethyl	85.5/57.9	48.7/35.2	79.4/42.1	34.3/28.6
5d	4-chlorophenoxymethyl	82.4/45.8	54.3/42.1	79.4/60.0	42.9/28.0
5e	3-chlorophenoxymethyl	79.5/58.3	29.5/41.7	81.1/51.4	48.6/22.9
5f	2,4-dichlorophenoxymethyl	96.8/73.6	53.2/47.0	88.2/57.1	58.8/28.6
5g	4-(*t*-butyl)phenoxymethyl	51.0/42.7	37.5/30.8	47.6/32.5	42.8/29.0
5h	3-(trifluoromethyl)phenoxymethyl	70.5/66.7	27.3/41.7	86.5/45.7	78.4/45.7
2,4-D		99.0/91.5	98.2/91.2	97.5/33.5	97.5/31.2

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 EL III CHNSO elementary analyzer. All of the solvents and materials were reagent grade and purified as required. 1-Hydrazino-1-(4-fluorophenyl)methyl phosphonate (**1**),[11a] 2-[bis(methylthio)methylene]malononitrile (**2**),[14] and acyl hydrazines,[15] were prepared according to the literature procedures.

Preparation of Diethyl [(5-Amino-4-cyano-3-methylsulfanyl-pyrazol-1-yl)-(4-fluorophenyl)methyl] Phosphonate (3) 16

A mixture of **1** (6.71 g, 24.3 mmol), **2** (3.89 g, 22.9 mmol) and ethanol (30 mL) was refluxed for 5 h. After cooling, the reaction mixture was concentrated in vacuo and recrystallized from ethyl acetate and petroleum (1:1, *v*/*v*) to give white crystals (6.50 g, 71% yield). m.p. 158–159°C. ^{1}H NMR ($CDCl_3$, 400 MHz)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 (m, 4H, Ar-H); 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.

Preparation of Diethyl [(4-Cyano-5-ethoxymethyleneamino-3-methylsulfanyl-pyrazol-1-yl)- (4-fluorophenyl)-methyl] Phosphonate (4)

5-Amino-4-cyano-pyrazole **3** (2.39 g, 6 mmol) were 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 (EtOAc-light petroleum ether, 1:5, *v*/*v*) to afford **4** as a white solid (2.42 g, 89%). m.p. 77–78°C. ^{1}H NMR ($CDCl_3$, 400 MHz) 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 (t, J = 8.4 Hz, 2H, Ar-H), 7.54 (q, J = 5.2 Hz, J = 8.4 Hz, 2H, Ar-H), 8.41 (s, 1H, N=CH); 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.

Preparation of Diethyl {2-Substituted-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl}substitutedphenylmethyl Phosphonate (5)—General Procedure

A solution of **4** (0.65 g. 1.5 mmol) and acyl hydrazine (1 mmol) in methoxyethanol (20 mL) was stirred under reflux for 3–5 h. After cooling, the solvent was removed under reduced pressure, and the residue was purified on silica gel (acetone and light petroleum,1:6, *v*/*v*) to yield the corresponding target compound **5a–5h**.

Diethyl [2-(4-totyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluorophenyl)methyl Phosphonate (5a)

Colorless crystals: yield 73%; m.p. 145.6–146.7°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18 (t, J = 7.6 Hz, 3H, CH_3), 1.26 (t, J = 7.6 Hz, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.87 (s, 3H, SCH_3), 4.02–4.10 (m, 2H, CH_2O), 4.18–4.22 (m, 2H, CH_2O), 6.42 (d,J = 23 Hz, 1H, PCH), 7.06 (t, J = 8.4 Hz, 2H, Ar-H), 7.31 (t, J = 8.4 Hz, 2H, Ar-H), 7.74 (q, J = 5.2 Hz, J = 7.2 Hz, 2H, Ar-H), 8.23 (d, J = 8.0 Hz, 2H, Ar-H), 9.08 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 15.71; IR(KBr) (cm^{-1}): 2984 (Ar-H), 1452 (Ar-H), 1257 (P=O), 1022 (P-O-C), 752(P-C); EIMS (probe) 70eV, *m*/*z* (rel. int.): 542 (23), 540 (100) $[M]^+$, 405 (11), 403 (75.5), 357 (6.4), 109 (11.2); anal. calcd. for $C_{25}H_{26}FN_6O_3PS$: C 55.55, H 4.85, N 15.55; found C 55.71, H 5.00, N 15.37.

Diethyl [2-(4-Methoxyphenyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluorophenyl)-methyl Phosphonate (5b)

Colorless crystals: yield 85%; m.p. 164.3-165.2°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18 (t, J = 7.2 Hz, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3), 2.86 (s, 3H, SCH_3), 3.89 (s, 3H, OCH_3), 4.02–4.09 (m, 2H, CH_2O), 4.18–4.21 (m, 2H, CH_2O), 6.42 (d,J = 22.8 Hz, 1H, PCH), 7.01–7.08 (m, 4H, Ar-H), 7.74 (q, J = 5.2 Hz, J = 7.2 Hz, 2H, Ar-H), 8.28 (d, J = 8.8 Hz, 2H, Ar-H), 9.06 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 15.78; IR(KBr) (cm^{-1}): 2978 (Ar-H), 1487, 1242 (P=O), 1026(P-O-C), 748 (P-C); anal. calcd. for $C_{25}H_{26}FN_6O_4PS$: C 53.95, H 4.71, N 15.10; found C 53.64, H 4.61, N 14.97.

Diethyl[2-(Phenoxymethyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluoro-phenyl)methyl Phosphonate (5c)

Colorless crystals: yield 79%; m.p. 124.0–124.7°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19 (t, $J = 7.2$ Hz, 3H, CH_3), 1.26 (t, $J = 7.2$ Hz, 3H, CH_3), 2.82 (s, 3H, SCH_3), 4.01–4.08 (m, 2H, CH_2O), 4.10–4.20 (m, 2H, CH_2O), 5.42 (s, 2H, CH_2O), 6.45 (d,$J = 22.8$ Hz, 1H, PCH), 6.97–7.06 (m, 5H, Ar-H), 7.24–7.32 (m, 2H, Ar-H), 7.73 (s, 2H, Ar-H), 9.08 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 15.52; IR(KBr) (cm^{-1}): 2990 (Ar-H), 1252 (P=O), 1030 (P-O-C), 758 (P-C); EIMS (probe) 70eV, *m/z* (rel. int.): 556 $[M]^+$ (18), 419 (100), 326 (16), 279 (12), 109 (11); anal. calcd. for $C_{25}H_{26}FN_6O_4PS$: C 53.95, H 4.71, N 15.10; found C 54.13, H 4.54, N 14.88.

Diethyl [2-(4-Chlorophenoxymethyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluoro-phenyl)methyl Phosphonate (5d)

Colorless crystals: yield 81%; m.p. 127.7–129.0°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19 (t, $J = 7.2$ Hz, 3H, CH_3), 1.26 (t, $J = 7.2$ Hz, 3H, CH_3), 2.82 (s, 3H, SCH_3), 4.02–4.09 (m, 2H, CH_2O), 4.17–4.21 (m, 2H, CH_2O), 5.38 (s, 2H, CH_2O), 6.41 (d,$J = 22.8$ Hz, 1H, PCH), 6.98 (d, $J = 8.8$ Hz, 2H, Ar-H), 7.06 (t, $J = 8.8$ Hz, 2H, Ar-H), 7.25 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.74 (q, $J = 5.2$ Hz, $J = 7.2$ Hz, 2H, Ar-H), 9.07 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 15.91; IR (KBr) (cm^{-1}): 2985 (Ar-H), 1502 (Ar-H), 1246 (P=O), 1026 (P-O-C), 748 (P-C); EIMS (probe) 70eV, *m/z* (rel. int.): 590 $[M]^+$ (19), 453 (100), 326 (16), 280 (22), 109 (20); anal. calcd. for $C_{25}H_{25}ClFN_6O_4PS$: C 50.81, H 4.26, N 14.22; found C 51.05, H 4.07, N 14.43.

Diethyl [2-(3-Chlorophenoxymethyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluorophenyl)methyl Phosphonate (5e)

Colorless crystals: yield 76%; m.p. 112.1–113.5°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19 (t, $J = 7.2$ Hz, 3H, CH_3), 1.27 (t, $J = 7.2$ Hz, 3H, CH_3), 2.81 (s, 3H, SCH_3), 4.04–4.07 (m, 2H, CH_2O), 4.17–4.21 (m, 2H, CH_2O), 5.39 (s, 2H, CH_2O), 6.41 (d,$J = 22.4$ Hz, 1H, PCH), 6.93–6.98 (m, 2H, Ar-H), 7.03–7.07 (m, 3H, Ar-H), 7.21 (t, $J = 8.4$ Hz, 1H, Ar-H), 7.72 (q, $J = 5.2$ Hz, $J = 7.6$ Hz, 2H, Ar-H), 9.07 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 15.86; IR (KBr) (cm^{-1}): 2978 (Ar-H), 1649, 1593, 1480, 1457 (Ar-H), 1266, 1228 (P=O), 1163, 1059 (P-O-C), 773 (P-C)**;** EIMS (probe) 70eV, *m/z* (rel. int.): 593 (6.0), 592 (8.0), 590 (23.9)

$[M]^+$, 542 (19.4), 540 (100), 456 (21.2), 453 (85.5), 405 (8.5), 404 (52.7), 357(7.0), 109 (19.5); anal. calcd. for $C_{25}H_{25}ClFN_6O_4PS$: C 50.81, H 4.26, N 14.22; found C 51.10, H 4.37, N 14.32.

Diethyl [2-(2,4-Dichlorophenoxymethyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluorophenyl)methyl Phosphonate (5f)

Colorless crystals: yield 88%; m.p. 155.2–157.0°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19 (t, $J = 6.8$ Hz, 3H, CH_3), 1.26 (t, $J = 6.8$ Hz, 3H, CH_3), 2.82 (s, 3H, SCH_3), 4.04–4.07 (m, 2H, CH_2O), 4.18–4.21 (m, 2H, CH_2O), 5.45 (s, 2H, CH_2O), 6.41 (d,$J = 22.4$ Hz, 1H, PCH), 7.02–7.08 (m, 3H, Ar-H), 7.16 (d, $J = 6.4$ Hz, 1H, Ar-H), 7.38 (s, 1H, Ar-H), 7.73 (q, $J = 5.2$ Hz, $J = 7.2$ Hz, 2H, Ar-H), 9.07 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 16.05; IR (KBr) (cm^{-1}): 2984 (Ar-H), 1252 (P=O), 1024 (P-O-C), 756 (P-C); anal. calcd. for $C_{25}H_{24}Cl_2FN_6O_4PS$: C 48.01, H 3.87, N 13.44; found C 47.86, H 3.95, N 13.27.

Diethyl [2-(4-T-butyl phenoxymethyl)-9-(methylsulfanyl)-7H-pyrazolo-[4,3-e]-1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluorophenyl)methyl Phosphonate (5g)

Colorless crystals: yield 70%; m.p. 104.1–105.6°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19 (t, $J = 7.2$ Hz, 3H, CH_3), 1.25 (t, $J = 7.2$ Hz, 3H, CH_3), 1.31 (s, 9H, CH_3), 2.82 (s, 3H, SCH_3), 3.98–4.16 (m, 2H, CH_2O), 4.18–4.21 (m, 2H, CH_2O), 5.40 (s, 2H, CH_2O), 6.42 (d,$J = 22.4$ Hz, 1H, PCH), 6.98–7.08 (m, 4H, Ar-H), 7.31 (d, $J = 6.8$ Hz, 2H, Ar-H), 7.73 (q, $J = 5.6$ Hz, $J = 8.0$ Hz, 2H, Ar-H), 9.08 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 15.47; IR(KBr) (cm^{-1}): 2985 (Ar-H), 1248 (P=O), 1028 (P-O-C), 746 (P-C); EIMS (probe) 70eV, m/z (rel. int.): 614 (9.3), 612 (25.7) $[M]^+$, 475 (100), 459 (6.1), 419 (18.6), 326 (21.4), 279 (13.8), 109 (7.9); anal. calcd. for $C_{29}H_{33}ClFN_6O_4PS$: C 53.83, H 5.14, N 12.99; found C 54.08, H 5.40, N 12.73.

Diethyl [2-(3-Trifluoromethylphenoxymethyl)-9-(methyl-sulfanyl)-7H-pyrazolo-[4,3-e]- 1,2,4-triazolo-[1,5-d]-pyrimidin-7-yl]-(4-fluorophenyl)methyl Phosphonate (5h)

Colorless crystals: yield 71%; m.p. 38–39°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19 (t, $J = 7.2$ Hz, 3H, CH_3), 1.28 (t, $J = 7.2$ Hz, 3H, CH_3), 2.82 (s, 3H, SCH_3), 4.04–4.09 (m, 2H, CH_2O), 4.17–4.21 (m, 2H, CH_2O), 5.45 (s, 2H, CH_2O), 6.41 (d,$J = 22.8$ Hz, 1H, PCH), 7.06 (t, $J = 8.4$ Hz, 2H, Ar-H), 7.22 (d, $J = 8.8$ Hz, 2H, Ar-H), 7.33 (s, 1H, Ar-H), 7.39

(t, $J = 8.4$ Hz, 1H, Ar-H), 7.73 (q, $J = 5.6$ Hz, $J = 7.0$ Hz, 2H, Ar-H), 9.07 (s, 1H, N=CH); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 16.18; IR (KBr) (cm^{-1}): 2992 (Ar-H), 1245 (P=O), 1026 (P-O-C), 758 (P-C), 694, 565; EIMS (probe) 70eV, m/z (rel. int.): 624 $[M]^+$ (17), 487 (100), 326 (17), 280 (21), 109 (21); anal. calcd. for $C_{26}H_{24}ClF_4N_6O_4PS$: C 47.39, H 3.67, N 12.75; found C 47.27, H 3.62, N 12.95.

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 a 9-cm diameter test plate 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 I.

CONCLUSIONS

In conclusion, we have developed an efficient and selective synthesis of *N*-phosphonoalkylpyrazolo[4,3-*e*]-1,2,4-triazolo-[1,5-*d*]pyrimidines, via the direct ring closure of functionalized imidates with various acyl hydrazines. The preliminary biological evaluation showed that these compounds have potent and selective herbicidal activity.

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