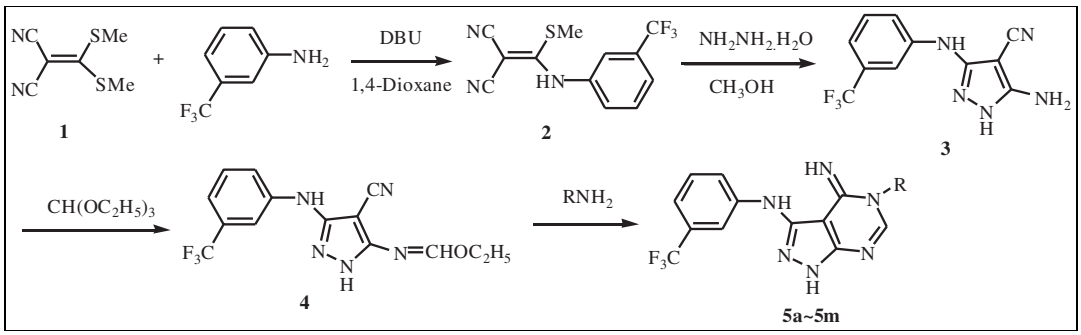
Hai-Bo Li and De-Qing Shi*

Key Laboratory of Pesticide & Chemical Biology of Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, People's Republic of China
*E-mail: chshidq@mail.ccnu.edu.cn

Received June 24, 2011
DOI 10.1002/jhet.1501
Published online 2 December 2013 in Wiley Online Library (wileyonlinelibrary.com).



A series of novel 5-alkyl(aryl)-3-[(3-trifluoromethyl)anilino]-4,5-dihydro-1H-pyrazolo[4,3-d]pyrimidin-4-imines were designed and synthesized by the multistep reactions. **1** reacted with 3-(trifluoromethyl)aniline to obtain *N*, *S*-acetals **2** in the presence of 10 mol% DBU. **2** reacted with hydrazine to form 5-amino-3-[(3-trifluoromethyl) anilino]-1H-pyrazol-4- nitrile **3**, the target compounds **5a ~ 5m** were obtained by the reaction of **3** with triethyl orthoformate followed by the cyclization of **4** with various amines. Their structures were confirmed by IR, ^{1}H NMR, EI-MS, and elemental analyses. The preliminary bioassay indicated that some of them displayed moderate herbicidal activity against dicotyledonous weed *Brassica campestris L* at the concentration of 100 mg/L. For example, compounds **5f**, **5g**, **5h**, and **5j** possessed 60.1%, 63.4%, 67.1%, and 61.3% inhibition against *Brassica campestris L* at the concentration of 100 mg/L.

J. Heterocyclic Chem., **51**, 656 (2014).

INTRODUCTION

Phytoene desaturase (PDS) is a key enzyme for photosynthetic apparatus of green plants. A lack of carotenoid synthesis, when PDS is inhibited by its inhibitor, may lead to typical bleaching symptoms in plants. So, the PDS inhibitors are developed as important bleaching herbicides in plant protection. Among them, Norflurazon, Fluridone Fluorochloridone, Diflufenican, and Picolinafen are commercially PDS herbicides (Fig. 1). PDS inhibitors possess a central five-membered or six-membered heterocycle containing one or two substituted phenyl rings in which a 3-trifluoromethylphenyl group is a common structure in all compounds [1–5]. On the other hand, pyrazolo[4,3-d] pyrimidine derivatives possessed a wide range of pharmaceutical activities, which can be used as PDE1 and PDE5 cGMP phosphodiesterase inhibitors [6], adenosine A_3 receptor antagonists [7], EGF-R tyrosine kinase inhibitors [8], antiviral/antitumor activities [9], some of them exhibited good fungicidal, and herbicidal activities [10–12]. In order to find novel lead compound with good herbicidal activity, we designed and synthesized a series of novel pyrazolo[4,3-d]pyrimidin-4-imine derivatives **5** by introducing 3-trifluoromethylphenyl moiety into the pyrazolo[4,3-d]pyrimidine molecular skeleton. Herein, we would like to report the synthesis and herbicidal activities of the title compounds **5** in this paper (Scheme 1).

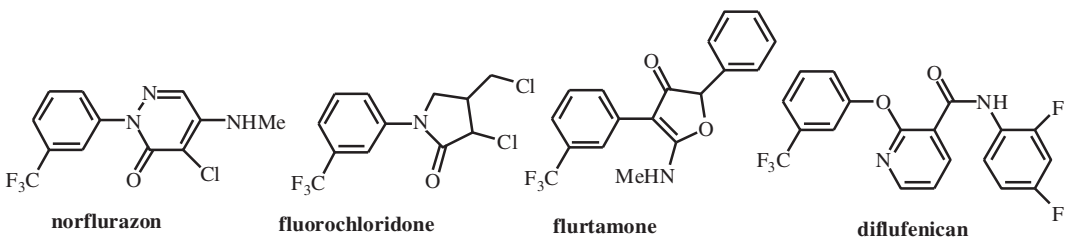
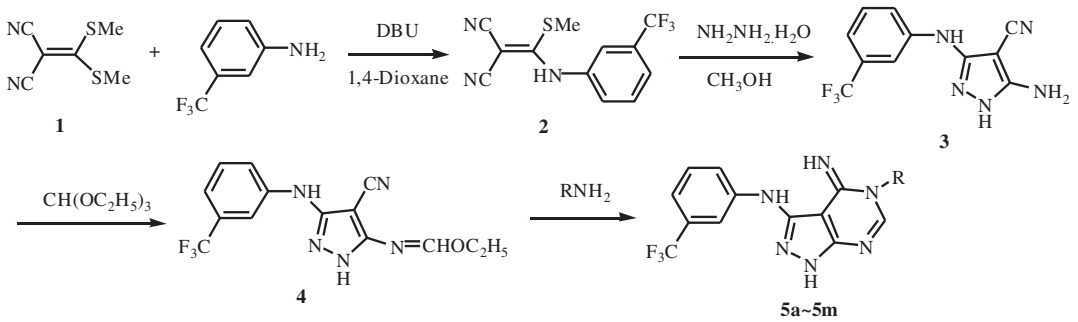


Figure 1. Some commercially PDS inhibitors.

Scheme 1. Synthetic route of target compounds **5a – 5m**.



RESULTS AND DISCUSSION

N,S-acetal **2** was prepared by the substitution of **1** with 3-(trifluoromethyl)aniline in the basic condition. Because of its weak nucleophilicity of 3-(trifluoromethyl)aniline, the substituted reaction is difficult to undergo. We explored the reaction conditions for the synthesis of **2**. Firstly, the yields of **2** are very low without the addition of a base even at higher temperature for a long time (see Table 1, Entries 1, 3, 4, 5). Secondly, when 10 mol% DBU was added and the mixture was refluxed for 36 h, the yield was raised to 43% (Entry 2). Finally, the yield was raised to 65% using 10 mol% DBU under refluxing in 1,4-dioxane for 12 h. **2** reacted with 85% hydrazine hydrate to give 5-amino-3-(3-trifluoromethylanilino)-4-cyano-1H-pyrazole **3** in 90% yield. **3** reacted with excess triethyl orthoformate in the presence of a catalytic amount of acetic anhydride to give corresponding imidate **4**, which cyclized with various amines to obtain the target compounds **5** at room temperature or under reflux in 81–95% yields.

Their structures were deduced from their spectral data (IR, ^{1}H NMR, and EI-MS) and elemental analyses, which were listed in the experimental part. For example, the IR spectra of **5k** revealed OH and NH at 3385 and 3211 cm^{-1}, respectively. The signal 1636 cm^{-1} is attributed to C = N absorption, and 1581 and 1475 cm^{-1} are attributed to C = C absorption bands of aromatic rings. In the ^{1}H NMR spectra of **5h**, the two amino protons showed as two singlets at δ 3.37 and 12.16, respectively, whereas the imino protons displayed as a singlet at δ 8.96; the pyrimidine proton also exhibited as a singlet at δ 8.15. The mass spectrum of **5h** shows strong molecular ion peak at *m/z* 350 with 100% abundance and anticipated fragmentation ion peaks.

Herbicidal activity. The preliminary herbicidal activities of compounds **5** were evaluated, against two representative targets, oil rape, and barnyard grass, at concentrations of 100 and 10 mg/L according to a literature method [13]. The results are listed in Table 2 and show that these compounds have moderate herbicidal activity against oil rape at the concentration of 100 mg/L. For example, compounds **5f**, **5g**, **5h**, and **5j** possessed 60.1%, 63.4%, 67.1%, and 61.3% inhibition against *Brassica campestris L.* As for the preliminary structure-activity relationships, those compounds when R is ethyl,

Table 1

Optimization of reaction conditions for the synthesis of **2**.

Entry	Solvent	Temp. (°C)	Catalyst	Time (h)	Yield (%)
1	EtOH	70–80	—	36	31
2	EtOH	70–80	DBU (10%)	36	43
3	DMF	80–90	—	12	Trace
4	DMF	120	—	12	41
5	1,4-dioxane	100	—	12	Trace
6	1,4-dioxane	100	DBU (10%)	12	65

Table 2

Herbicide activity of componds **5a – 5m** (growth inhibition rate %).

Compound	*Brassica campestris* root test		*Echinochloa crus-galli* cup test	
	10 μg/mL	100 μg/mL	10 μg/mL	100 μg/mL
5a	7.2	37.8	0	0
5b	0	49.7	0	10.0
5c	0	13.5	0	0
5d	0	9.3	0	10.0
5e	0	6.4	0	15.0
5f	0	60.1	0	5.0
5g	16.4	63.4	5.0	15.0
5h	23.9	67.1	0	0
5i	0	21.8	15.0	20.0
5j	0	61.3	10.0	15.0
5k	0	20.5	5.0	20.0
5l	0	50.5	5.0	15.0
5m	0	53.4	10.0	20.0
Sulcotrione	0	35.0	30.0	35.0

butyl, i-butyl, and allyl exhibited better activity. So, compounds **5** when R is aliphatic substitutes showed better activities than those when R is aromatic group did. Further exploring of structure-activity relationships needs more experimental results to support. Further biological activity (*in vivo*) investigations are on the way.

In conclusion, a series of novel 5-alkyl(aryl)-3-[(3-trifluoromethyl)anilino]-4,5-dihydro-1H-pyrazolo[4,3-d]pyrimidin-4-imines were designed and synthesized by the multistep reactions. Their structures were confirmed by IR, ^{1}H NMR, EI-MS, and elemental analyses. The preliminary bioassay indicated that some of them displayed moderate herbicidal activity against dicotyledonous weed *Brassica campestris L* at the concentration of 100 mg/L.

EXPERIMENTAL

Melting points were determined with a WRS-1B digital melting point apparatus (Wuhan, China) and are uncorrected. ^{1}H NMR spectra was recorded with a Varian Mercury PLUS 600 (600 MHz) spectrometer (USA) with TMS as the internal reference and $CDCl_3$ or DMSO-d6 as the solvent, whereas mass spectra were measured on a Finnigan Trace MS 2000 spectrometer (USA) at 70 eV by using EI method or Applied Biosystems API 2000 LC/MS/MS (ESI-MS) spectrometer (USA). IR spectra were measured by the use of a Nicolet NEXUS470 spectrometer (USA). Elemental analyses were performed with an Elementar Vario ELIII CHNSO elemental analyzer (Germany). **1** can be prepared according to a reported method [14]. All of the solvents and materials were reagent grade (Sinopharm Chemical Reagent Co. Ltd., China, or Acros Organics, Beijing, China) and purified as required.

Synthesis of 2-[methylthio-(3-trifluoromethylanilino)-methylene]-malononitrile 2. **1** (1.34 g, 20 mmol), DBU (2 mmol), and anhydrous 1,4-dioxane (20 mL) were added to a 50-mL three-necked flask when the mixture was heated to 90°C; the solution of 3-(trifluoromethyl)aniline (2.94 g, 20 mmol) in anhydrous 1,4-dioxane (5 mL) were added dropwise slowly. After the addition of chemicals was finished, the mixtures were allowed to be stirred under reflux for 12 h until the reaction was complete (monitored by TLC). The workup involved stripping of the solvent followed by addition of water (50 mL) and extraction of the product mixture into chloroform (25 mL*3), after phase separation, drying over anhydrous magnesium sulfate, filtration, and evaporation, the solid was filtered and recrystallized by anhydrous methanol to give the target compound **2** as colorless crystals in 65% yield. mp 157~158°C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 2.32 (s, 3H, CH_3), 7.47 (s, 1H, ArH), 7.54 (s, 1H, ArH), 7.58(d, J = 6.8 Hz, 2H, ArH), 8.26 (s, 1H, NH). *Anal*. calcd for $C_{12}H_9F_3N_3S$: C 50.88, H 2.85, N 14.83; found C, 50.72; H, 2.99; N, 14.50.

Synthesis of 5-amino-3-(3-trifluoromethylanilino)-4-cyano-1H-pyrazole 3. **2** (5.66 g, 20 mmol) and anhydrous methanol (20 mL) were added to a 50-mL three-necked flask, 85% hydrazine hydrate (1.0 g, 20 mmol) in anhydrous methanol (5 mL) were added dropwise slowly at room temperature. After the addition of chemicals was finished, the mixtures were allowed to be stirred under reflux for 1 h until the reaction was complete (monitored by TLC). After the solvent was concentrated under vacuum, **3** was obtained as colorless crystals in 90% yield. mp 143~144°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 3.38 (s, 2H, NH_2), 6.38 (s, 1H, NH), 7.09 (d, J = 7.8 Hz, 1H, ArH), 7.40 (t, J = 8.1 Hz, 1H, ArH), 7.69 (d, J = 7.8 Hz, 1H, ArH), 8.01 (s, 1H, ArH); ESI-MS *m/z* (%): 300 (M + Na-1, 10), 268 (M^+, 100). *Anal*. calcd for $C_{11}H_9F_3N_5$: C 49.44, H 3.02, N 26.21; found C, 49.73; H, 3.24; N, 26.07.

Synthesis of 5-(ethoxymethyleneamino)-3-(3-trifluoromethylanilino)-4-cyano-1H-pyrazole 4. **3** (2.67 g, 10 mmol), triethyl orthoformate (10 mL) and several drops of acetic anhydride were added to a 50-mL three-necked flask, and the mixture was refluxed for 2 h while ethanol formed was removed until no ethanol was evaporated; after cooling, excess triethyl orthoformate was removed under a reduced pressure, the crude product was recrystallized from ethanol to give **4** as light yellow crystals in 75% yield. mp 147~148°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 1.33 (t, J = 7.2 Hz, 3H, CH_3), 4.33 (q, J = 7.2 Hz, 2H, CH_2), 7.14 (d, J = 6.6 Hz, 1H, ArH), 7.45 (t, J = 7.2 Hz, 1H, ArH), 7.73 (d, J = 6.0 Hz, 1H, ArH), 8.01 (s, 1H, ArH), 8.44 (s, 1H, N = CH). *Anal*. calcd for $C_{14}H_{12}F_3N_5O$: C 52.01, H 3.74, N 21.66; found C, 52.27; H, 3.97; N, 3.40.

General procedure for the synthesis of 5-alkyl(aryl)-3-[(3-trifluoromethyl)anilino]-4,5-dihydro-1H-pyrazolo[4,3-d]pyrimidin-4-imines 5. **4** (1.0 mmol), aliphatic or aromatic amine (1.0 mmol), and THF (10 mL) were added to a 50-mL three-necked flask, and the mixture was allowed to be stirred at room temperature for 1–3 h (for aliphatic amine) or under refluxed for 3–7 h (for aromatic amine; monitored by TLC). After the solvent was removed under a reduced pressure, the crude product was recrystallized from ethanol to give **5** in 81–95% yields.

5a. (R = 4-ClC_6H_4): yellow solid, yield: 89%, mp 218~220°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 7.23 (d, J = 7.8 Hz, 2H, ArH), 7.50 (t, J = 7.8 Hz, 2H, ArH), 7.88 (d, J = 7.8 Hz, 2H, ArH), 8.04 (s, 1H, Pyrimidine-H), 8.17 (s, 2H, ArH), 8.16 (s, 1H, NH), 9.39 (s, 1H, NH), 12.08 (s, 1H, NH); IR (KBr) υ: 3226 (NH), 2961 (ArH), 1645 (C = N), 1580, 1475, 1452 (Ar) cm^{-1}. *Anal*. calcd for $C_{18}H_{12}ClF_3N_6$: C 53.41, H 2.99, N 20.85; found C, 53.23; H, 3.09; N, 20.55.

5b. (R = 3-$CF_3C_6H_4$): white solid, yield: 85%, mp 201~203°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 7.13 (d, J = 7.2 Hz, 2H, ArH), 7.45 (t, J = 8.1 Hz, 2H, ArH), 7.75 (d, J = 7.8 Hz, 2H, ArH), 8.17 (s, 1H, Pyrimidine-H), 8.36 (s, 2H, ArH), 8.96 (s, 1H, NH), 9.12 (s, 1H, NH), 12.56 (s, 1H, NH); IR (KBr) υ: 3231 (NH), 2958 (ArH), 1668 (C = N), 1572, 1486, 1448 (Ar) cm^{-1}. *Anal.* calcd for $C_{19}H_{12}F_6N_6$: C 52.06, H 2.76, N 19.17; found C, 51.93; H, 2.99; N, 19.02.

5c. (R = Bn): colorless solid, yield: 95%, mp 216~218 C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 4.54 (s, 2H, CH_2), 7.10 (d, J = 7.8 Hz, 1H, ArH), 7.29 (d, J = 7.8 Hz, 1H, ArH), 7.36 (t, J = 7.8 Hz, 4H, ArH), 7.42 (t, J = 7.8 Hz, 1H, ArH), 7.70 (d, J = 7.8 Hz, 1H, ArH), 7.99 (s, 1H, ArH), 8.26 (s, 1H, Pyrimidine-H), 8.58 (s, 1H, NH), 8.98 (s, 1H, NH), 12.21 (s, 1H, NH); IR (KBr) υ: 3245 (NH), 2974 (ArH), 1648 (C = N), 1569, 1472, 1456 (Ar) cm^{-1}. *Anal*. calcd for $C_{19}H_{15}F_3N_6$: C 59.37, H 3.93, N 21.87; found C, 59.48; H, 3.84; N, 21.63.

5d. (R = C_6H_5): yellow solid, yield: 94%, mp 224~226°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 6.82 (t, J = 6.9 Hz, 2H, ArH), 7.28 (d, J = 7.2 Hz, 1H, ArH), 7.32 (t, J = 7.5 Hz, 1H, ArH), 7.55

(t, J = 7.8 Hz, 1H, ArH), 7.89 (d, J = 7.8 Hz, 1H, ArH), 8.04 (d, J = 7.2 Hz, 1H, ArH), 8.14 (s, 1H, Pyrimidine-H), 8.37 (s, 1H, ArH), 9.14 (s, 1H, ArH), 9.24 (s, 1H, NH), 9.82 (s, 1H, NH), 12.06 (s, 1H, NH); IR (KBr) υ: 3238 (NH), 2985 (ArH), 1651 (C = N), 1562, 1478, 1458 (Ar) cm^{-1}. *Anal*. calcd for $C_{18}H_{13}F_3N_6$: C 58.38, H 3.54, N 22.69; found C, 58.10; H, 3.79; N, 22.73.

5e. (R = 4-$CH_3OC_6H_4$): white solid, yield: 83%, mp 231~233°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 3.76 (s, 3 H, CH_3O), 6.96 (d, J = 8.4 Hz, 2H, ArH), 7.13 (d, J = 7.2 Hz, 1 H, ArH), 7.18 (d,J = 7.8 Hz, 1 H, ArH), 7.44 (t, J = 7.8 Hz, 2 H, ArH), 7.89 (s, 2H, ArH), 8.04 (s, 1H, Pyrimidine-H), 10.14 (s, 1H, NH), 10.61 (s, 1H, NH), 12.44 (s, 1H, NH); IR (KBr) υ: 3242 (NH), 2981 (ArH), 1647 (C = N), 1561, 1473, 1462 (Ar) cm^{-1}; EI-MS(70 eV) *m/z* (%): 400 (M^+, 100), 379 (6), 238 (7), 134 (17), 108 (18). *Anal*. calcd for $C_{19}H_{15}F_3N_6O$: C 57.00, H 3.78, N 20.99; found C, 57.25; H, 3.87; N, 21.06.

5f. (R = C_2H_5): yellow solid, yield: 90%, mp 224~226°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 1.23 (t, J = 7.8 Hz, CH_3), 3.30 (q, J = 7.8 Hz, 2H, CH_2), 7.14 (d, J = 7.2 Hz, 1H, ArH), 7.42 (t, J = 7.2 Hz, 1H, ArH), 7.45 (d, J = 7.8 Hz, 1H, ArH), 7.70 (s, 1H, ArH), 8.01 (s, 1H, Pyrimidine-H), 8.20 (s, 1H, NH), 8.80 (s, 1H, NH), 12.78 (s, 1H, NH); IR (KBr) υ: 3248 (NH), 2988 (ArH), 1652 (C = N), 1560, 1471, 1468 (Ar) cm^{-1}. *Anal*. calcd for $C_{14}H_{13}F_3N_6$: C 52.17, H 4.07, N 26.08; found C, 52.31; H, 3.90; N, 25.87.

5g. (R = Bu): white solid, yield: 95%, mp 214~216 °C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 0.89 (t, J = 7.2 Hz, 3H, CH_3), 1.33–1.37 (m, 2H, CH_2), 1.46–1.55 (m, 2H, CH_2), 3.27 (t, J = 7.2 Hz, 2H, CH_2), 7.11 (d, J = 8.1 Hz, 1H, ArH), 7.42 (t, J = 7.2 Hz, 1H, ArH), 7.70 (d, J = 7.8 Hz, 1H, ArH), 7.88 (s, 1H, NH), 8.00 (s, 1H, ArH), 8.12 (s, 1H, Pyrimidine-H), 9.00 (s, 1H, NH), 12.10 (s, 1H, NH); IR (KBr) υ: 3231 (NH), 2982 (ArH), 1653 (C = N), 1565, 1473, 1466 (Ar) cm^{-1}. *Anal*. calcd for $C_{16}H_{17}F_3N_6$: C 54.85, H 4.89, N 23.99; found C, 54.59; H, 4.70; N, 24.05.

5h. (R = *i*-Bu): yellow solid, yield: 93%, mp 213~215°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 0.88 (d, J = 7.2 Hz, 6H, $2CH_3$), 1.85–1.89 (m, 1H, CH), 2.99 (d, J = 7.2 Hz, 2H, CH_2), 3.37 (s, 1H, NH), 7.10 (d, J = 7.8 Hz, 1H, ArH), 7.42 (t, J = 7.8 Hz, 1H, ArH), 7.70 (d, J = 7.8 Hz, 1H, ArH), 8.00 (s, 1H, ArH), 8.15 (s, 1H, Pyrimidine-H), 8.28 (s, 1H, NH), 8.96 (s, 1H, NH), 12.16 (s, 1H, NH); IR (KBr) υ: 3235 (NH), 2980 (ArH), 1658 (C = N), 1561, 1471, 1469 (Ar) cm^{-1}; EI-MS(70 eV) *m/z* (%): 350 (M^+, 100), 307 (5), 238 (7), 294 (96), 267 (28), 252 (12), 145 (17), 57 (22). *Anal*. calcd for $C_{16}H_{17}F_3N_6$: C 54.85, H 4.89, N 23.99; found C, 54.94; H, 4.98; N, 23.75.

5i. (R = CH_2CH_2): white solid, yield: 83%, mp 196~198°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 2.80 (s, 2H, CH_2), 3.96 (s, 2H, CH_2), 7.14 (t, J = 7.8 Hz, 2H, ArH), 7.42–7.47 (m, 2H, ArH), 7.70 (d, J = 7.2 Hz, 1H, ArH), 7.79 (d, J = 7.8 Hz, 1H, ArH), 7.93 (s, 1H, ArH), 8.01 (s, 1H, ArH), 8.06 (s, 2 H, NH), 8.19 (s, 2H, Pyrimidine-H), 8.82 (s, 2H, NH), 12.05 (s, 2H, NH); IR (KBr) υ: 3237 (NH), 2981 (ArH), 1672 (C = N), 1564, 1466, 1450 (Ar) cm^{-1}. *Anal*. calcd for $C_{26}H_{20}F_6N_{12}$: C 50.82, H 3.28, N 27.35; found C, 50.94; H, 3.47; N, 27.13.

5j. (R = allyl): yellow solid, yield: 92%, mp 215~217°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 4.61 (d, J = 7.8 Hz, 2H, CH_2), 5.18 (d, J = 7.8 Hz, 2H, =CH_2), 6.0–6.04 (m, 1H, =CH), 7.16 (d, J = 7.8 Hz, 1H, ArH), 7.47 (t, J = 7.2 Hz, 1H, ArH), 7.72 (d, J = 7.8 Hz, 1H, ArH), 7.98 (s, 2H, ArH + Pyrimidine-H), 8.20 (s, 1H, NH), 8.88 (s, 1H, NH), 12.79 (s, 1H, NH); IR (KBr) υ: 3227 (NH), 2984 (ArH), 1650 (C = N), 1549, 1465, 1453 (Ar) cm^{-1}. *Anal*. calcd for $C_{15}H_{13}F_3N_6$: C 53.89, H 3.92, N 25.14; found C, 53.61; H, 4.04; N, 25.27.

5k. (R = CH_2CH_2OH): white solid, yield: 87%, mp 227~228°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 3.69 (s, 2H, CH_2), 4.07 (s, 2H, CH_2), 5.08 (s, 1H, OH), 7.19 (d, J = 7.8 Hz, 1H, ArH), 7.50 (t, J = 7.8 Hz, 1H, ArH), 7.76 (d, J = 7.8 Hz, 1H, ArH), 7.91 (s, 1H, ArH), 8.01 (s, 1H, Pyrimidine-H), 8.06 (s, 1H, NH), 8.90 (s, 1H, NH), 12.71 (s, 1H, NH); IR (KBr) υ: 3385 (OH), 3221 (NH), 2959 (ArH), 1636 (C = N), 1581, 1499, 1475 (Ar) cm^{-1}; EI-MS(70 eV) *m/z* (%): 338 (M^+, 93), 294 (100), 250 (10), 145 (17), 44 (31). *Anal*. calcd for $C_{14}H_{13}F_3N_6O$: C 49.71, H 3.87, N 24.84; found C, 49.92; H, 3.74; N, 24.60.

5l. (R = $CH(CH_3)CH_2OH$): white solid, yield: 81%, mp 208~209°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 1.07 (d, J = 7.2 Hz, 3H, CH_3), 3.61 (d, J = 7.2 Hz, 2H, CH_2), 3.95–3.98 (m, 1H, CH), 5.18 (s, 1H, OH), 7.15 (d, J = 7.2 Hz, 1H, ArH), 7.46 (t, J = 7.2 Hz, 1H, ArH), 7.70 (d, J = 7.2 Hz, 1H, ArH), 7.86 (s, 1H, ArH), 8.03 (s, 1H, Pyrimidine-H), 8.12 (s, 1H, NH), 8.83 (s, 1H, NH), 12.72 (s, 1H, NH); IR (KBr) υ: 3387 (OH), 3224 (NH), 2971 (ArH), 1633 (C = N), 1575, 1481, 1477 (Ar) cm^{-1}. *Anal*. calcd for $C_{15}H_{15}F_3N_6O$: C 51.14, H 4.29, N 23.85; found C, 51.03; H, 4.10; N, 23.67.

5m. (R = i-Pr): white solid, yield: 89%, mp 196~198°C; ^{1}H NMR (DMSO-d6, 600 MHz) δ: 1.19 (d, J = 6.6 Hz, 6H, $2CH_3$), 4.07–4.11 (m, 1H, CH), 7.11 (d, J = 7.8 Hz, 1H, ArH), 7.43 (t, J = 7.8 Hz, 1H, ArH), 7.72 (d, J = 7.8 Hz, 1H, ArH), 8.02 (s, 1H, ArH), 8.06 (s, 1H, Pyrimidine-H), 8.10 (s, 1H, NH), 9.00 (s, 1H, NH), 12.19 (s, 1H, NH); IR (KBr) υ: 3220 (NH), 2963 (ArH), 1635 (C = N), 1576, 1472, 1452 (Ar) cm^{-1}. *Anal*. calcd for $C_{15}H_{15}F_3N_6$: C 53.57, H 4.50, N 24.99; found C, 53.71; H, 4.34; N, 25.11.

Herbicidal activity testing. The herbicidal activity measurement method was adapted according to a literature method [13].

Acknowledgments. This work was supported by the Natural Science Foundation of China (No. 20872046) and the Natural Science Foundation of Hubei Province (No. 2008CDB086).

REFERENCES AND NOTES

[1] Sandmann, G.; Böger, P. In Herbicide Activity: Toxicology, Biochemistry, and Molecular Biology; Roe, R. M., Burton, J. D., Kuhr, R. J., Eds.; IOS Press: Amsterdam, 1997; pp 1–10.

[2] Sandmann, G. In Herbicidal Classes in Development: Mode of Action, Targets, Genetic Engineering, Chemistry; Böger, P., Wakabayashi, K., Hirai, K., Eds.; Springer: Berlin, 2002; pp 43–55.

[3] Mitchell, G. In Synthesis and Chemistry of Agrochemicals IV, Baker, D. A., Fenyes, J. G., Moberg, W. K., Cross, B., Eds.; ACS Symposium Series, American Chemical Society: Washington, DC, 1995; Vol. 584, pp 161–170.

[4] Sandmann, G.; Kowalczyk-Schroder S.; Taylor, H. M. Pestic Biochem Physiol 1992, 42(1), 1.

[5] Sandmann, G.; Kunert, K. J.; Böger, P. Pestic Biochem Physiol 1981, 15, 28.

[6] Cramp, M. C.; Gilmour, J.; Hatton, L. R. Pestic Sci 1987, 18(1), 15.

[7] Xia, Y.; Samuel, C.; Michael, C.; Hsingan, T.; Henry, V.; Renee, C.; John, C.; Ahmad, F.; Robert, W.; Zhang, H. J Med Chem 1997, 40(26), 4372.

[8] Taliani, S.; La Motta, C.; Mugnaini, L.; Simorini, F.; Salerno, S.; Marini, A. M.; Da Settimo, F.; Cosconati, S.; Cosimelli, B.; Greco, G.; Vittorio, L.; Marinelli, L.; Novellino, E.; Ciampi, O.; Daniele, S.; Trincavelli, M. L.; Martini, C. J Med Chem 2010, 53(10), 3954.

[9] Traxler, P.; Bold, G.; Frei, J.; Lang, M.; Lydon, N.; Mett, H.; Buchdunger, E.; Meyer, T.; Mueller, M.; Furet, P. J Med Chem 1997, 40(22), 3601.

[10] Ugarkar B. G.; Cottam, H. B.; McKernan, P. A.; Robins, R. K.; Revankar, G. R.; J Med Chem 1984, 27(8), 1026.

[11] Liu, T. L.; Xie, J. H.; Yang, Z. H. Chin J Org Chem 2000, 20, 900.

[12] Bell, A. S.; Sandwich, K.; Terrett, N. K. EP 0463756, 1991.

[13] Tang, W.; Shi, D. Q. J Heterocycl Chem 2010, 47, 162.

[14] Zhao, W. G.; Wang, S. H.; Wang, W. Y.; Li, Z. M. Huaxue Shiji 2000, 22, 376.