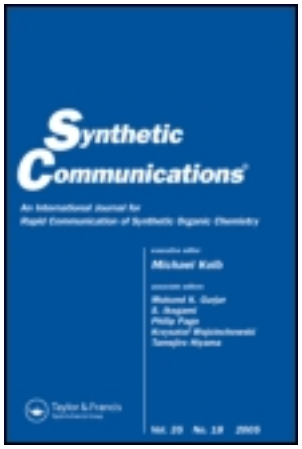

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Synthesis and Biological Activities Evaluation of New 4-(2,4-Difluorophenyl)-N-aryl-5-(1H-1,2,4-triazol-1-yl)thiazol-2-amine

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SYNTHESIS AND BIOLOGICAL ACTIVITIES EVALUATION OF NEW 4-(2,4-DIFLUOROPHENYL)-N-ARYL-5-(1*H*-1,2,4-TRIAZOL-1-YL)THIAZOL-2-AMINE

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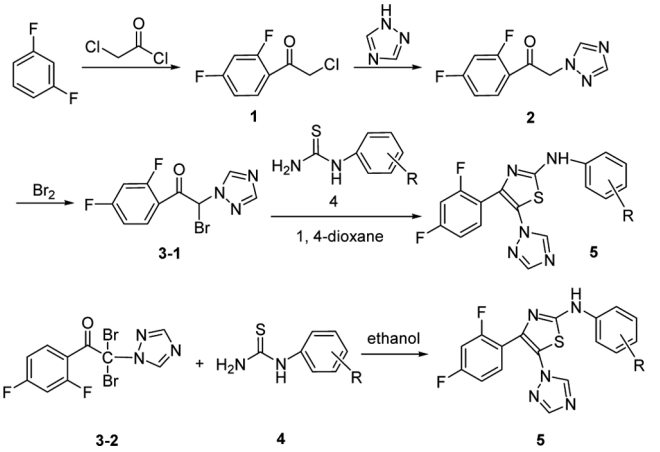
GRAPHICAL ABSTRACT



Abstract *Fifteen new thiazol-2-amine derivatives containing the 2,4-difluorophenyl unit and 1*H*-1,2,4-triazole moiety were synthesized. Their structures of all these new compounds have been confirmed by ^1H NMR spectra and elemental analysis. The antifungal and plant-growth-regulatory activities of the title compounds are discussed.*

Keywords Antifungal activity; plant-growth-regulatory activity; synthesis; thiazol-2-amine

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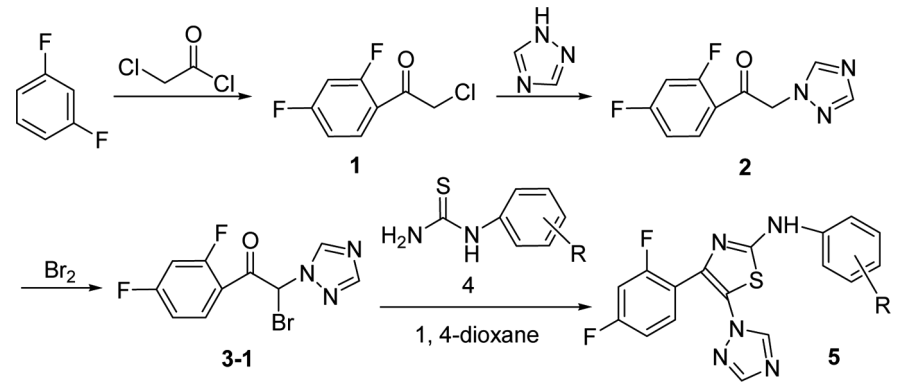
INTRODUCTION

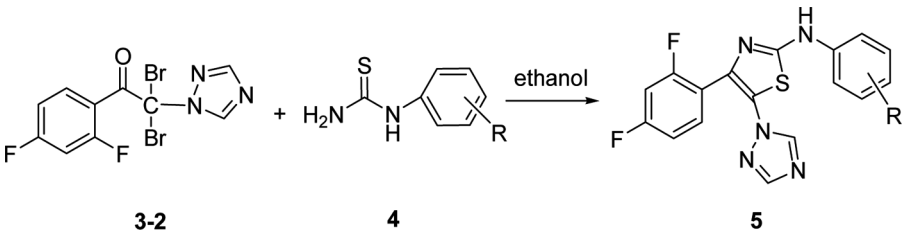
2-Aminothiazole derivatives exhibit a wide spectrum of biological activities, and many of them are well-known antiviral[1] and antifungal agents.[2,3] Some are used widely as agrochemicals, such as pesticides,[4,5] fungicides,[6,7] and herbicides.[8,9] In addition, 1*H*-1,2,4-triazole derivatives not only possess diverse pharmacological properties, such as antifungal,[10] anti-inflammatory,[11] antiviral,[12] antimicrobial,[13] antitumorial,[14] anticonvulsant,[15] analgesic,[16] and antihypotensive activities[17] but also reveal insecticidal, herbicidal, antifungal, and plant-growth-regulatory activities.[18–20] Biochemists have been paid attention to the study of the biological activities of 1*H*-1,2,4-triazole compounds for many years.

Fluorine atoms have many special properties, such as strong electronegativity, small size, and low polarizability of the C-F bond, and they can have considerable impact on the behavior of a molecule in a biological environment.[21] Therefore, fluorinated compounds in general are the focus of much research.[22] In the area of modern crop protection, fluoro agrochemicals are widely employed as herbicides, insecticides, and fungicides.[23,24]

Encouraged by these studies, we synthesized fifteen new thiazol-2-amine derivatives using 2-aminothiazole as the parent compound and introducing aryl, 2,4-difluorophenyl, and 1*H*-1,2,4-triazole-1-yl to the 2, 4, and 5 positions, respectively, (Schemes 1 and 2). The structures have been characterized by ^{1}H NMR spectra



Scheme 1. **5e**: R = 4-F; **5f**: R = 2-Cl; **5g**: R = 3-Cl; **5h**: R = 4-Cl; **5i**: R = 3-Br; **5j**: R = 4-Br; **5k**: R = 3-CF_3; **5l**: R = 4-CF_3; **5m**: R = 3-Cl-4-CH_3: **5n**: R = 2, 4-Cl_2; and **5o**: R = 2, 5-Cl_2.



Scheme 2. **5a**: R=H; **5b**: R = 2-CH_3; **5c**: R = 3-CH_3; and **5d**: R = 4-CH_3.

and elemental analysis. Preliminary bioassay showed in vitro biological activities and plant-growth-regulatory activities.

RESULTS AND DISCUSSION

Synthesis

The preferred method for the formation of 2-aminothiazole derivative is the classical Hantzsch synthesis.[25] Following the Hantzsch protocol, *N*-monosubstituted aryl thioureas containing acceptor groups treated with α-mono-bromo ketones in 1,4-dioxane can form the *N*-substituted 2-aminothiazole derivative **5e–5o** smoothly (Scheme 1). When the aryl thioureas do not contain acceptor groups, they could not react with α -mono-bromo ketones to get the corresponding title compound, such as **5a**–**5d**. To our delight, using α,α-dibromo ketones reacted with *N*-monosubstituted aryl thioureas in ethanol, title compounds **5a**–**5d** could be prepared successfully. To the best of our knowledge, the factors affecting Hantzsch synthesis mainly have electronic and steric effects. The donor electronic effects of the substituents at the phenyl ring of aryl thioureas depressed its reaction activity of NH_2 of aryl thioureas, and it made the reaction of aryl thioureas (R = H, CH_3) with α-mono-bromo ketones difficult. As α,α-dibromo ketones possess greater reaction activity than α-mono-bromo ketones, that make the reaction of α,α-dibromo ketones with *N*-monosubstituted aryl thioureas easy. The resolvent is also an important factor affecting the title reaction. Although the title compounds can be synthesized using these methods, the yields were not encouraging. The steric and electronic effects of the bulky group 1*H*-1,2,4-triazole unit of α-bromo ketones and α,α-dibromo ketones may be the main factors that affect the yields of this reaction.

Biological Activity

The title compounds **5** were screened for their biological activities in vitro against the *G. zeae*, *A. solani*, *C. arachidicola*, *P. piricola*, *P. asparagi*, *C. cucumerinum*, *S. sclerotiorum*, and *P. oryzae* at the concentration of 50 μg/L, and the relative inhibitory ratios (%) against these fungi are listed in Table 1. As shown in Table 1, compounds **5h** and **5n** showed greater fungicidal activities than other title compounds **5**. Of all the selected target fungi, compound **5** exhibited the best fungicidal activity in vitro against *C. cucumerinum*. Although the screening data revealed that all selected compounds **5** showed some antifungal activities, they were not significant compared with known commercial agents. The resolvability and rigidity of the title molecules may be the main factors that influence the biological activities of the title compounds. First, these compounds were insoluble in most organic solvents at room temperature, and this made it difficult to screen the biological activities exactly. Second, as the 2,4-difluorophenyl unit and 1*H*-1,2,4-triazole group connect directly with the 2-aminothiazole cycle, the title molecules were too stiff to contact the target efficiently. To clarify this further, we modified the molecular structure based on the title compounds **5**, and the study will be presented in forthcoming papers.

The plant-growth-regulatory activities of the title compounds were tested by the cucumber cotyledon test at the concentration of 10 μg/L. All of the compounds

Table 1. Fungicidal activity of the title compounds **5**

Compound	Relative inhibitory ratio (%)							
	G. zeae	*A. solani*	*C. ara.*	*P. piri.*	*P. asp.*	*C. cucu.*	*S. scler.*	*P. oryzae*
5a	46.7	32.6	49.1	46.7	68.9	69.3	78.8	27.9
5b	36.7	37.8	46.9	54.7	55.5	57.9	58.2	66.4
5c	23.9	19.7	37.5	47.6	19.1	23.0	65.3	78.6
5d	46.9	59.3	57.3	49.6	55.0	67.2	76.9	34.1
5e	40.9	59.8	36.7	38.8	69.6	60.7	59.7	49.9
5f	55.9	37.6	21.9	67.8	25.8	56.7	66.8	46.7
5g	58.6	66.2	50.5	58.8	55.5	68.1	64.9	65.5
5h	46.8	75.9	45.9	79.7	75.4	69.5	55.8	67.3
5i	57.5	47.9	26.8	32.2	37.5	87.6	55.3	76.8
5j	37.8	78.0	47.5	39.9	57.1	65.8	57.2	59.9
5k	47.8	39.8	37.7	47.8	57.6	76.7	60.0	59.9
5l	43.1	29.8	46.5	49.6	39.1	33.0	65.8	78.6
5m	65.0	47.9	59.2	38.9	57.0	78.7	69.5	45.8
5n	67.8	56.9	21.6	69.7	79.8	67.9	79.5	78.5
5o	47.8	44.3	33.9	57.1	66.3	56.0	52.9	58.7
[a]	95.6	100	99.5	100	100	99.8	100	100

[a]Triadimenol, 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1, 2,4-triazol-1-yl)butan-2-ol.

exhibited some activities on the growth of cucumber cotylendon, and the inhibitory ratio is 1.3–50.0%.

SUMMARY

In this study, 15 new thiazol-2-amine derivatives containing the 2,4-difluorophenyl unit and 1*H*-1,2,4-triazole moiety were synthesized using the Hantzsch method. Replacement of α-mono-bromo ketones by α,α-dibromo ketones in the

Table 2. Plant-growth-regulatory activities of the title compounds (%) (10 μg/L)

Compound	Ratio
5a	18.8
5b	8.3
5c	1.3
5d	16.5
5e	10.4
5f	16.5
5g	7.3
5h	4.2
5i	7.8
5j	47.2
5k	22.6
5l	50
5m	7.9
5n	22.6
5o	13.4

Hantzsch reaction was reported, and this method maybe useful for the synthesis of thiazol-2-amine derivatives, which contain the bulky group in the 5 position of thiazol-2-amine derivatives. The results of the bioassay showed that some title compounds exhibited some degree of antifungal and plant-growth-regulatory activities.

EXPERIMENTAL

Instruments

All reactions were monitored by thin-layer chromatography (TLC). The ^{1}H NMR spectra were measured on a Bruker AC 200, using tetramethylsilane (TMS) as internal standard and dimethylsulfoxide (DMSO-d_6) and $CDCl_3$ as solvent. Chemical shift values (δ) are given in parts per million (ppm). Elemental analyses were determined with a Yanaco CHN Corder MT-3 elemental analyzer. Melting points were determined with X-4 digital melting-point apparatus, and the thermometer was uncorrected.

Synthesis of Intermediates 1, 2, 3, and 4

The intermediates **1** and **2** were synthesized according to the literature method.[26] The intermediates **4** were prepared according to Ref.[27]

Synthesis of 2-Bromo-1-(2,4-difluorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone (3-1)

A solution of 8.8 g (0.055 mol) bromine in acetic acid (20 mL) to a stirred solution of the intermediate **2** (11.15 g, 0.05 mol) in acetic acid (100 mL), was added dropwise in 2 h at room temperature. The mixtures were stirred in another 2 h at room temperature, and then 500 mL ice water was added to the mixtures. After 1 h, the solution was filtered, and the solid obtained was recrystallized from ethanol/water to give a white solid with yield of 69%, mp, 72–74 °C. ^{1}H NMR ($CDCl_3$/TMS, 200 MHz): δ 9.07 (s, 1H, TrH), 9.16 (s, 1H, TrH), 8.08–8.16 (m, 1H, PhH), 7.67 (d, J = 2.1 Hz, 1H, CH), 7.07–7.13 (m, 1H, PhH), 6.96–7.03 (m, 1H, PhH). Anal. calcd. for $C_{10}H_6BrF_2N_3O$: C, 39.76; H, 2.00; N, 13.99. Found: C, 39.58; H, 2.25; N, 14.17.

Synthesis of 2, 2-Dibromo-1-(2,4-difluorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone (3-2)

This product can be obtained by the previous method. The dosages of the substances were the same as before, except the molar quantity of the bromine was 0.11 mol. Yield: 51.2%, mp 90–92 °C. ^{1}H NMR ($CDCl_3$/TMS, 200 MHz): δ 8.00–8.07 (m, 1H, PhH), 7.93 (s, 1H, TrH), 7.56 (s, 1H, TrH), 7.02–7.08 (m, 1H, PhH), 6.83–6.90 (m, 1H, PhH). Anal. calcd. for $C_{10}H_5Br_2F_2N_3O$: C, 31.53; H, 1.32; N, 11.03. Found: C, 31.45; H, 2.41; N, 11.19.

General Procedure for the Preparation of Title Compounds 5e–5o

Intermediate (3-1) (1.51 g, 0.005 mol), 0.06 mol of compound **4,** and 20 mL of 1,4-dioxane were added into a 100-mL, four-necked, round-bottomed flask. The mixture was refluxed for 5–8 h (monitored by TLC). After the solution was cooled to room temperature, it was poured into a beaker containing 50 mL water at 50–60 °C. The solution was filtered, and the solid was recrystallized from ethanol to give white solid **5e**–**5o** in various yields.

Selected Data

4-(2, 4-Difluorophenyl)-N-(4-fluorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5e). White solid; yield: 39.6%; mp 178–180 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.17 (s, 1H, NH), 8.52 (s, 1H, TrH), 7.99 (s, 1H, TrH), 7.70 (d, d, $J = 8.7$ Hz, 1H, PhH), 7.20–7.26 (m, 2H, PhH), 7.01 (d, $J = 8.1$ Hz, 4H, PhH). Anal. calcd. for $C_{17}H_{10}F_3N_5S$: C, 54.69; H, 2.70; N, 18.76. Found: C, 54.91; H, 2.56; N, 18.98.

4-(2, 4-Difluorophenyl)-N-(2-chlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5f). White solid; yield: 35.4%; mp 172–174 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.11 (s, 1H, NH), 8.70 (s, 1H, TrH), 8.26–8.29 (m, 1H, PhH), 8.20 (s, 1H, TrH), 7.58–7.63 (m, 1H, PhH), 7.51–7.56 (m, 1H, PhH), 7.33–7.39 (m, 1H, PhH), 7.25–7.29 (m, 1H, PhH), 7.15–7.20 (m, 1H, PhH), 7.10–7.12 (m, 1H, PhH). Anal. calcd. for $C_{17}H_{10}ClF_2N_5S$: C, 52.38; H, 2.59; N, 17.97. Found: C, 52.14; H, 2.56; N, 18.16.

4-(2,4-Difluorophenyl)-N-(3-chlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5g). White solid; yield: 37.9%; mp 236–239 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.80 (s, 1H, NH), 8.71 (s, 1H, TrH), 8.22 (s, 1H, TrH), 7.86 (t, $J = 1.8$ Hz, 1H, PhH), 7.61 (d, d, $J = 8.4$ Hz, 1H, PhH), 7.53 (d, d, $J = 1.2$ Hz, 1H, PhH), 7.39 (d, $J = 8.1$ Hz, 1H, PhH), 7.17–7.35 (m, 2H, PhH), 7.07 (d, d, $J = 1.2$ Hz, 1H, PhH). Anal. calcd. for $C_{17}H_{10}ClF_2N_5S$: C, 52.38; H, 2.59; N, 17.97. Found: C, 52.25; H, 2.45; N, 18.18.

4-(2,4-Difluorophenyl)-N-(4-chlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5h). White solid; yield: 36.1%; mp 239–241 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.21 (s, 1H, NH), 8.68 (s, 1H, TrH), 8.18 (s, 1H, TrH), 7.78 (d, d, $J = 8.7$ Hz, 1H, PhH), 7.32–7.38 (m, 2H, PhH), 7.21 (d, $J = 8.1$ Hz, 2H, PhH), 7.15 (d, $J = 7.8$, Hz, 2H, PhH). Anal. calcd. for $C_{17}H_{10}ClF_2N_5S$: C, 52.38; H, 2.59; N, 17.97; Found: C, 52.16; H, 2.33; N, 18.09.

4-(2,4-Difluorophenyl)-N-(3-bromophenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5i). White solid; yield: 31.5%; mp 236–238 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.78 (s, 1H, NH), 8.71 (s, 1H, TrH), 8.21 (s, 1H, TrH), 7.98 (s, 1H, PhH), 7.56–7.64 (m, 2H, PhH), 7.29–7.34(m, 2H, PhH), 7.18–7.26 (m, 2H, PhH). Anal. calcd. for $C_{17}H_{10}BrF_2N_5S$: C, 47.02; H, 2.32; N, 16.13. Found: C, 46.86; H, 2.33; N, 16.31.

4-(2,4-Difluorophenyl)-N-(4-bromophenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5j). White solid; yield: 33.6%; mp 234–236 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.73 (s, 1H, NH), 8.69 (s, 1H, TrH), 8.20 (s, 1H, TrH), 7.59–7.67 (m,

3H, PhH), 7.52 (d, $J = 9$ Hz, 1H, PhH), 7.16–7.31(m, 2H, PhH). Anal. calcd. for $C_{17}H_{10}BrF_2N_5S$: C, 47.02; H, 2.32; N, 16.13. Found: C, 46.79; H, 2.11; N, 16.40.

4-(2,4-Difluorophenyl)-N-(2-(trifluoromethyl)phenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5k). White solid; yield: 41.6%; mp 219–221 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.94 (s, 1H, NH), 8.72 (s, 1H, TrH), 8.22 (s, 1H, TrH), 8.17 (s, 1H, PhH), 7.86 (d, $J = 8.7$ Hz, 1H, PhH), 7.55–7.64 (m, 2H, PhH), 7.35 (d, $J = 8.1$ Hz, 1H, PhH), 7.17–7.30 (m, 2H, PhH). Anal. calcd. for $C_{18}H_{10}BrF_5N_5S$: C, 51.07; H, 2.38; N, 16.54. Found: C, 51.21; H, 2.26; N, 16.69.

4-(2,4-Difluorophenyl)-N-(4-(trifluoromethyl)phenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5l). White solid; yield: 42.7%; mp 234–235 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.98 (s, 1H, NH), 8.71 (s, 1H, TrH), 8.21 (s, 1H, TrH), 7.85 (d, $J = 8.7$ Hz, 2H, PhH), 7.70 (d, $J = 8.7$ Hz, 2H, PhH), 7.61–7.66 (m, 1H, PhH), 7.16–7.31 (m, 2H, PhH). Anal. calcd. for $C_{18}H_{10}BrF_5N_5S$: C, 51.07; H, 2.38; N, 16.54. Found: C, 49.89; H, 2.11; N, 16.40.

4-(2,4-Difluorophenyl)-N-(2-chloro-4-methylphenyl)-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5m). White solid; yield: 29.6%; mp 262–264 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.68 (s, 1H, NH), 8.70 (s, 1H, TrH), 8.21 (s, 1H, TrH), 7.85 (d, $J = 1.8$ Hz, 1H, PhH), 7.58 (d, d, $J = 8.7$ Hz, 1H, PhH), 7.40–7.44 (m, 1H, PhH), 7.33 (s, 1H, PhH), 7.17–7.30 (m, 1H, PhH), 2.28 (s, 1H, CH_3). Anal. calcd. for $C_{18}H_{12}ClF_2N_5S$: C, 53.53; H, 3.00; N, 17.34. Found: C, 53.79; H, 2.75; N 17.49.

4-(2,4-Difluorophenyl)-N-(2,4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl) thiazol-2-amine (5n). White solid; yield: 37.1%; mp 176–178 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 8.68 (s, 1H, TrH), 8.35 (d, $J = 9$ Hz, 1H, PhH), 8.19 (s, 1H, TrH), 7.65 (d, $J = 2.4$ Hz, 1H, PhH), 7.59 (d, d, $J = 8.7$ Hz, 1H, PhH), 7.41 (d, d, $J = 2.4$ Hz, 1H, PhH), 7.13–7.29 (m, 2H, PhH). Anal. calcd. for $C_{17}H_9Cl_2F_2N_5S$: C, 48.13; H, 2.14; N, 16.51; Found: C, 47.99; H, 2.03; N, 16.79.

4-(2,4-Difluorophenyl)-N-(2, 4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl) thiazol-2-amine (5o). White solid; yield: 35.6%; mp 224–228 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.26 (s, 1H, NH), 8.71 (s, 1H, TrH), 8.57 (s, 1H, TrH), 8.21 (s, 1H, PhH), 7.53 (d, $J = 6.3$ Hz, 2H, PhH), 7.12–7.31 (m, 3H, PhH). Anal. calcd. for $C_{17}H_9Cl_2F_2N_5S$: C, 48.13; H, 2.14; N, 16.51. Found: C, 48.29; H, 2.22; N, 16.63.

General Procedure for the Preparation of Title Compounds 5a–5d

Intermediate (3-2) (1.9 g, 0.005 mol), 0.06 mol of compound **4**, and 20 mL of ethanol were added into a 100-mL, four-necked, round-bottomed flask. The mixtures were refluxed for 5–8 h (monitored by TLC). After the solution was cooled to room temperature, it was poured into a beaker containing 50 mL water at 50–60 °C. The solution was filtered, and the solid was recrystallized from ethanol to give white solids **5a**–**5d** in various yields.

Selected Data

4-(2,4-Difluorophenyl)-N-phenyl-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5a). White solid; yield: 30.6%; mp 218–220 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.58 (s, 1H, NH), 8.69 (s, 1H, TrH), 8.20 (s, 1H, TrH), 8.21 (s, 1H, PhH), 7.59–7.66 (m, 3H, PhH), 7.15–7.38 (m, 4H, PhH), 7.00–7.05 (m, 1H, PhH). Anal. calcd. for $C_{17}H_{11}F_2N_5S$: C, 57.46; H, 3.12; N, 19.71. Found: C, 57.21; H, 3.01; N 19.98.

4-(2,4-Difluorophenyl)-N-o-tolyl-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5b). White solid; yield: 25.5%; mp 170–171 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 9.78 (s, 1H, NH), 8.66 (s, 1H, TrH), 8.17 (s, 1H, TrH), 7.83 (d, $J = 7.5$ Hz, 1H, PhH), 7.57 (d, d, $J = 8.7$ Hz, 1H, PhH), 7.05–7.28 (m, 5H, PhH), 2.21 (s, 1H, CH_3). Anal. calcd. for $C_{18}H_{13}F_2N_5S$: C, 58.53; H, 3.55; N, 18.96. Found: C, 58.67; H, 3.41; N 19.21.

4-(2,4-Difluorophenyl)-N-m-tolyl-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5c). White solid; yield: 27.4%; mp 203–205 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.80 (s, 1H, NH), 8.94 (s, 1H, TrH), 8.20 (s, 1H, TrH), 7.91–8.01 (m, 1H, PhH), 7.58 (d, $J = 9$ Hz, 1H, PhH), 7.45 (s, 1H, PhH), 7.26–7.36 (m, 2H, PhH), 6.88 (d, $J = 7.5$ Hz, 2H, PhH), 2.34 (s, 1H, CH_3). Anal. calcd. for $C_{18}H_{13}F_2N_5S$: C, 58.53; H, 3.55; N, 18.96. Found: C, 58.29; H, 3.69; N, 19.22.

4-(2,4-Difluorophenyl)-N-m-tolyl-5-(1*H*-1,2,4-triazol-1-yl)thiazol-2-amine (5d). White solid; yield: 27.4%; mp 203–205 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 10.45 (s, 1H, NH), 8.68 (s, 1H, TrH), 8.19 (s, 1H, TrH), 7.62 (d, d, $J = 8.4$ Hz, 1H, PhH), 7.52 (d, $J = 8.4$ Hz, 2H, PhH), 7.21–7.30 (m, 2H, PhH), 7.16 (d, $J = 8.1$ Hz, 2H, PhH), 2.26 (s, 1H, CH_3). Anal. calcd. for $C_{18}H_{13}F_2N_5S$: C, 58.53; H, 3.55; N, 18.96. Found: C, 58.36; H, 3.62; N, 19.10.

Biological Activities

The title compounds **5** were screened for their biological activities in vitro against the *G. zeae*, *A. solani*, *P. asparagi*, *P. piricola*, *C. rachidicola*, *C. cucumerinum* at the concentration of 50 μg/L, and the relative inhibitory ratios (%) against these fungi were listed in Table **1**. The plant growth regulatory activities of the title compounds were tested by wheat coleoptile and cucumber cotyledon test at the concentration of 10 μg/L. The biological activity of the title compounds were assayed at the Biological Assay Centre, Nankai University according to procedures described previously.[28]

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