Synthesis of Novel Disubstituted Pyrazolo[1,5-*a*]pyrimidines, Imidazo[1,2-*a*]pyrimidines, and Pyrimido[1,2-*a*]benzimidazoles Containing Thioether and Aryl Moieties

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A series of novel 6-[(1,3,4-thiadiazol-2-yl)sulfanyl]-7-phenylpyrazolo[1,5-*a*]pyrimidines, 5-phenyl-6-[(1,3,4-thiadiazol-2-yl)sulfanyl]imidazo[1,2-*a*]pyrimidines, and 2-phenyl-3-[(1,3,4-thiadiazol-2-yl)sulfanyl]pyrimido[1,2-*a*]benzimidazoles have been synthesized in four steps starting with 2-hydroxyacetophenone. The intermediate 3-[(1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-ones reacted with pyrazol-3-amines, 5-methylpyrazol-3-amine, and 1*H*-imidazol-2-amine, 1*H*-benzimidazol-2-amine *via* a cyclocondensation to give the title compounds in the presence of MeONa as base, respectively. The approach affords the target compounds in acceptable-to-good yields. The new compounds were characterized by their IR, NMR, and HR mass spectra.

Introduction. – Fused heterocyclic compounds commonly exhibit various biological activities, and they mainly include [5,6], [6,6], and [7,6] ring systems [1]. In particular, the fused [5,6] structural scaffold occurs in many pharmaceutical agents with diverse physiological and pharmacological activities. For this reason, organic chemists paid high attention to pyrimidine derivatives due to their chemotherapeutic relevance [2][3]. There are a great number of compounds involving pyrimidines, such as pyrazolo[1,5-*a*]pyrimidines (**a**), imidazo[1,2-*a*]pyramidines (**b**), and pyrimido[1,2-*a*]benzimidazoles (**c**; *Fig.*).

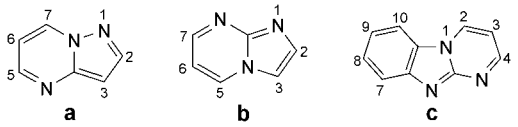


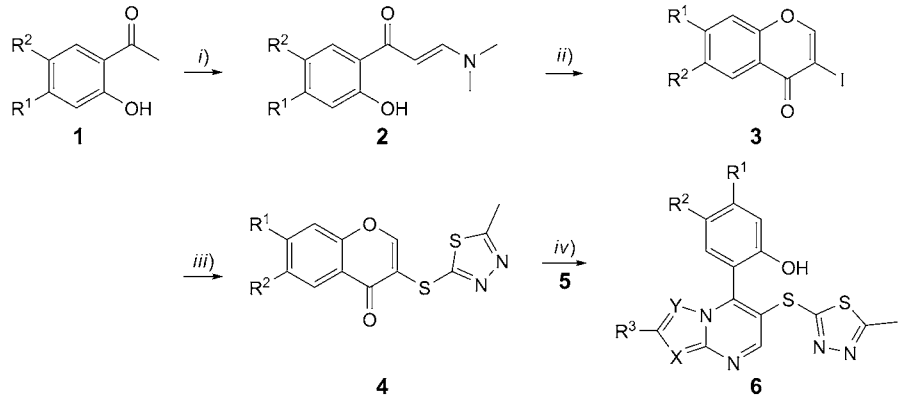
Figure. *Structures of pyrazolo[1,5-*a*]pyrimidines, imidazo[1,2-*a*]pyrimidines, and pyrimido[1,2-*a*]benzimidazoles,* **a**–**c**, *respectively*

Pyrazolo[1,5-*a*]pyrimidines have shown biological activities, *e.g.*, as inhibitors of protein kinases [4] and in the treatment of *Alzheimer*'s disease [5]. Meanwhile, the importance of the imidazo[1,2-*a*]pyrimidines has been well established in pharmaceutical chemistry due to their activities as HIV inhibitors [6]. Similarly, some pyrimido[1,2-*a*]benzimidazoles are known as compounds with antiparasitic [7] and substance P receptor-binding activity [8], as antibacterial drugs [9], anti-arrhythmics [10], and central nervous system-depressing agents [11], as well as substances with marked

herbicidal activity [12]. The synthesis of pyrazolo[1,5-*a*]pyrimidines involved the reaction between aminopyrazoles and 1,3-biselectrophilic compounds [13][14]. The formation of imidazo[1,2-*a*]pyrimidines relied on the condensation of substituted pyridin-2-amine or pyrimidin-2-amine with the appropriate α-halogenocarbonyl compounds [15]. Construction of the pyrimido[1,2-*a*]benzimidazole scaffold involved the condensation of 1*H*-benzimidazol-2-amine with acetylene esters [16], enamino ester [17], 1,3-diketone [10], and α,β-unsaturated ketones [18], respectively.

Recently, we reported the synthesis of new 6,7-diarylpyrazolo[1,5-*a*]pyrimidines, 2,3-diarylpyrimido[1,2-*a*]benzimidazoles, and 1,2,4-triazole[4,3-*a*]pyrimidines based on reactions with isoflavones [19]. Continuing our studies on the intriguing fused [5,6] ring system, here, we describe a simple and concise method to synthesize a range of 6,7-disubstitued pyrazolo[1,5-*a*]pyrimidines, 5,6-disubstitued imidazo[1,2-*a*]pyrimidines, and 2,3-disubstituted pyrimido[1,2-*a*]benzimidazole derivatives, which contain thioether and aryl moieties *via* the intermediate 3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-ones **4** and its reaction with azol-amines **5** (*Scheme 1*).

Scheme 1. *Synthesis of Pyrimidine Derivatives*



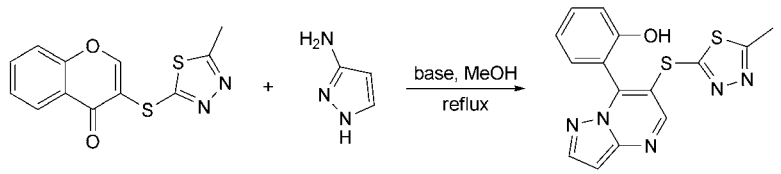
i) *N,N*-Dimethylformamide dimethyl acetal, oil bath, 70–75°, 30 min. *ii*) I_2 in $CHCl_3$, room temperature, 30 min. *iii*) 5-Methyl-1,3,4-thiadiazole-2-thiol, ^{t}BuOK, DMF, 85°, MW 240 W. *iv*) Azol-amines, MeONa, MeOH, 20–30 min.

Results and Discussion. – To the best of our knowledge, the first synthetic route of 3-iodochromones **3** was reported by *Gammill* [20a], and substituted compounds **3** were also synthesized [20b][20c]. The condensation of 2-hydroxyacetophenones **1** with *N,N*-dimethylformamide dimethyl acetal (3.5 equiv.) gave enamines **2** in desired yield. Cyclization of **2** without further purification using I_2 (3 equiv.) in $CHCl_3$ afforded 3-iodochromones in good yield (*Scheme 1*). The reaction of **3** with 5-methyl-1,3,4-thiadiazole-2-thiol in the presence of ^{t}BuOK (1.1 equiv.) at 85° afforded compounds **4** in moderate-to-good yields [21]. A plausible mechanism for the reaction of **3** with azolethiols was proposed by *Sugita et al.* [22]. Under basic reaction conditions (3 equiv. MeONa, MeOH, reflux, 30 min), **4** reacted with **5** (1*H*-pyrazol-3-amine (**5a**), 5-methyl-

1*H*-pyrazol-3-amine (**5b**), 1*H*-imidazol-2-amine (**5c**)) to give cyclocondensation products **6** in fair yields.

The synthesis of compound **6a** was chosen as model to optimize the reaction (*Table 1*). A mixture of **4a** (1 mmol) and **5a** (3 mmol) was heated to reflux in MeOH. In the course of optimizing the reaction, it was noted that 3 equiv. of MeONa gave **6a** in the highest yield (*Table 1*, *Entry 3*; 75%). NaOH, K_2CO_3, and Et_3N were also investigated, and their yields were inferior to those with MeONa as base (*Table 1*, *Entries 6–8*).

Table 1. *Base Effects on the Cyclocondensations of* **4a** *and* **5a**[a])



4a **5a** **6a**

Entry	Base	Molar ratios (**4a**/**5a**/base)	Yield[b]) [%]
1	MeONa	1 : 3 : 1	46
2	MeONa	1 : 3 : 2	52
3	MeONa	1 : 3 : 3	75
4	MeONa	1 : 3 : 4	60
5	MeONa	1 : 3 : 5	51
6	NaOH	1 : 3 : 3	28
7	K_2CO_3	1 : 3 : 3	19
8	Et_3N	1 : 3 : 3	13

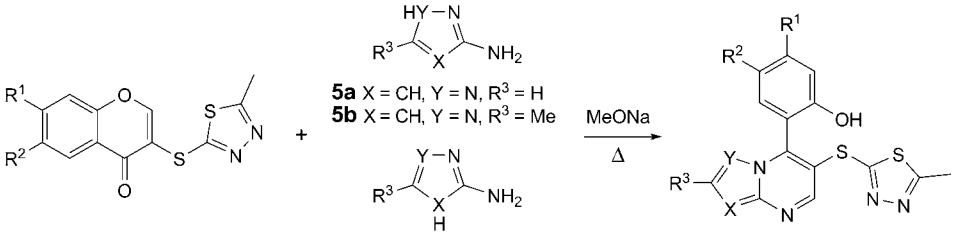
[a]) All reactions were carried out in boiling MeOH (8 ml) for 20–30 min. [b]) Yields of isolated products after chromatography.

To evaluate the scope of the cyclocondensation, F-, Br-, and MeO-substituted **4** were examined, and the expected compounds **6a–6i** were obtained (*Table 2*). Whereas the yields of **6c–6g** were *ca.* 80%, the results of the cyclocondensation to give imidazo[1,2-*a*]pyrimidines **6h** and **6i** under the optimized conditions were unsatisfactory (*Table 2*, *Entries 8* and *9*), but in DMSO as solvent, **6h** and **6i** were formed in good yields (*Table 2*, *Entries 8* and *9*).

Focusing on the synthesis of disubstituted pyrimido[1,2-*a*]benzimidazole **6j–6l**, we reacted 3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-ones **4** with 1*H*-benzimidazol-2-amine (**5d**) in boiling MeOH. The products were obtained in good yields (*Table 3*).

A proposed mechanism for the formation of compounds **6** by cyclocondensation of **4a** with azol-amines **5a–5d** in the presence of MeONa is depicted in *Scheme 2* in analogy to reactions with isoflavone [19b][23]. Compounds **4** undergo ring opening in the presence of a base to form α,β-unsaturated ketone intermediates **7**, followed by the attack of the NH_2 group of **5a** on the β-C-atom of **7**. Subsequently, a condensation between the ring N-atom and the C=O group affords the target compounds **6**. Additionally, the concentration of base is very important for the cyclocondensations.

Table 2. *Synthesis of Pyrazolo[1,5-*a*]pyrimidines and Imidazo[1,2-*a*]pyrimidines*

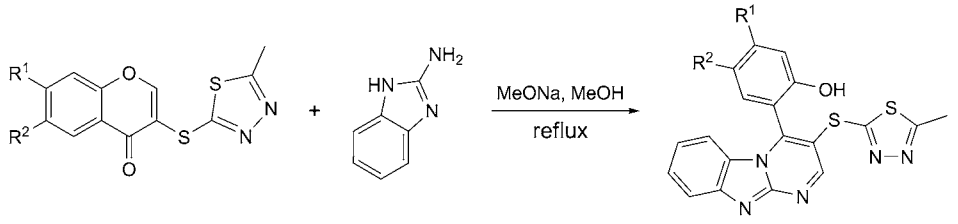


4 **6**

Entry	R^1	R^2	R^3	X	Y	Substrate **5**	Product	Yield[a]) [%]
1	H	H	H	CH	N	**5a**	**6a**	75[b])
2	H	F	H	CH	N	**5a**	**6b**	79[b])
3	MeO	H	H	CH	N	**5a**	**6c**	83[b])
4	H	H	Me	CH	N	**5b**	**6d**	85[b])
5	H	F	Me	CH	N	**5b**	**6e**	80[b])
6	H	Br	Me	CH	N	**5b**	**6f**	82[b])
7	MeO	H	Me	CH	N	**5b**	**6g**	88[b])
8	H	H	H	N	CH	**5c**	**6h**	36[b]), 78[c])
9	H	F	H	N	CH	**5c**	**6i**	47[b]), 84[c])

[a]) Yields of isolated products after chromatography. [b]) Reaction in boiling MeOH as solvent. [c]) Reaction in DMSO as solvent at 100°.

Table 3. *Synthesis of Pyrimido[1,2-*a*]benzimidazoles from* **4** *and 1*H*-Benzimidazol-2-amine* (**5d**)



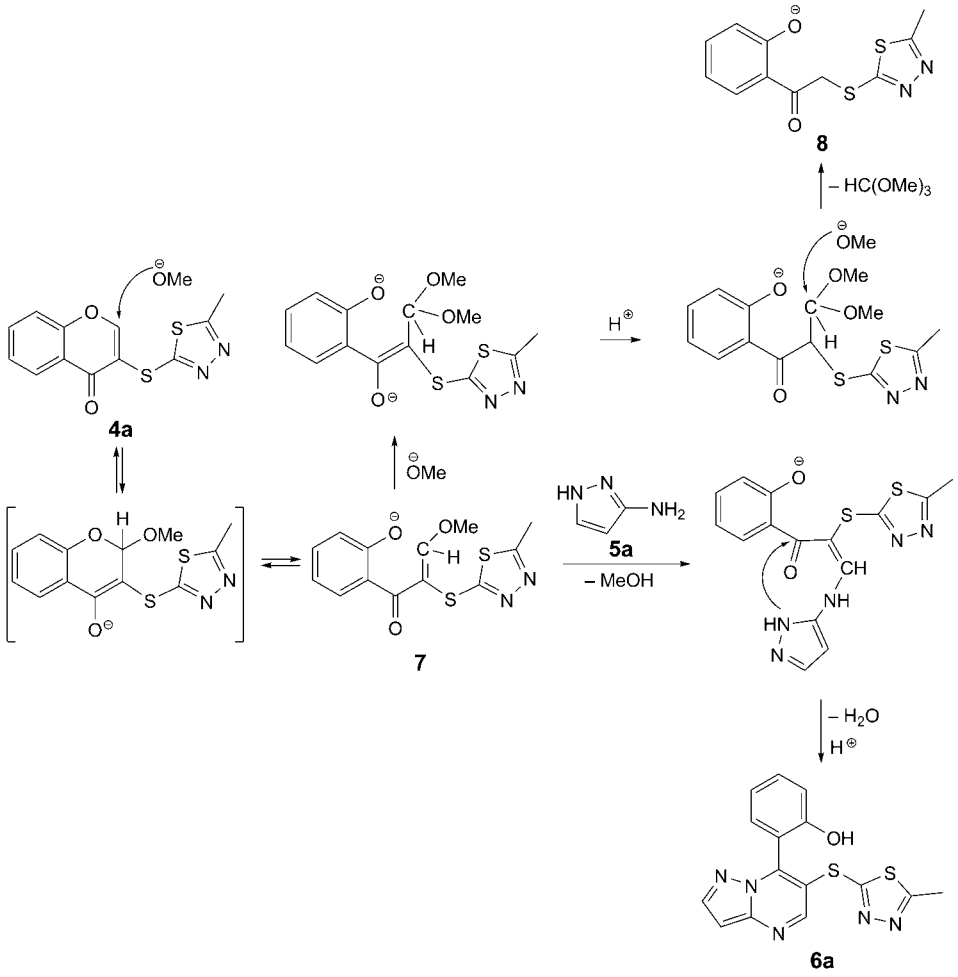
4 **5d** **6j – 6l**

Entry	R^1	R^2	Product	Yield[a]) [%]
1	H	H	**6j**	83
2	H	F	**6k**	75
3	MeO	H	**6l**	82

[a]) Yields of isolated products after chromatography.

Intermediate **7** would be converted to the ketone **8** at high concentration of base by elimination of $HC(OMe)_3$. However, it would be too difficult for **4** to produce the intermediate **7** in low base concentration.

Scheme 2. *Proposed Mechanism of Cyclocondensation* **4a** *with* **5a**



Conclusions. – In summary, we have developed a simple and efficient method for the synthesis of 6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-7-phenylpyrazolo[1,5-*a*]pyrimidines, 5-phenyl-6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]imidazol[1,2-*a*]pyrimidines, and 2-phenyl-3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrimido[1,2-*a*]benzimidazoles in the presence of base by reaction of 3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-ones **4** with azol-amines **5**. The target compounds present an imported core with respect to biological activity. In further studies, we will investigate the biological activities.

Experimental Part

General. TLC: silica gel *60 GF*$_{254}$ plates (SiO_2); visualization under UV light (254 nm). M.p.: *X-5 Macro* melting-point instrument; uncorrected. IR Spectra: *Nicolet 170SX* FT-IR spectrophotometer; in

KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker Avance 300* at 300 and 75 MHz, resp.; in (D_6)DMSO, unless otherwise indicated; δ in ppm rel. to Me_4Si as internal standard, J in Hz. LC/MS: *Mson Brukermicro TOF-Q II ESI-Q-ToF*; in *m/z*. Elemental Analyses: *elementar Analysensysteme GmbH Vario EL III*.

General Procedure for the Preparation of 3-Iodochromone (**3**) [20c]. A mixture of a substituted 2-hydroxyacetophenone **1** (5 mmol) and *N,N*-dimethylformamide dimethyl acetal (17.5 mmol, 3.5 equiv.) was heated to 70–75° in DMF (25 ml) for 30 min in an oil bath. The mixture was washed with sat. aq. NaCl (100 ml), a yellow precipitation of 3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-enone (**2**; 99%) was obtained. Then, to a soln. of **2** (10 mmol) in $CHCl_3$ (15 ml) was added I_2 (30 mmol, 3 equiv.), and the mixture was stirred at r.t. for 30 min. The reaction was quenched with 5% aq. $NaHSO_3$ (30 ml), and the aq. layer was extracted with $CHCl_3$ (3×10 ml). The org. phase was washed neutrally with 5% aq. $NaHCO_3$, dried (Na_2SO_4), and concentrated *in vacuo*, and recrystallized from abs. EtOH to give **3** as colorless crystals.

*General Procedure for the Preparation of Substituted 3-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-ones* **4** [21]. Compound **3** (1 mmol) was added to a soln. of 5-methyl-1,3,4-thiadiazole-2-thiol (132 mg, 1 mmol) and *t*BuOK (134 mg, 1.2 mmol) in 8 ml of DMF. The mixture was irradiated by 240 W microwave (MW) at 85° for 20–30 min. The reaction was monitored by TLC. The resulting mixture was cooled and diluted with 40 ml of ice H_2O. The obtained solid product was filtered and purified by CC (SiO_2; petroleum ether/AcOEt 5: 1) to afford the product **4**.

*3-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-one* (**4a**) [21]. Yield: 215.5 mg (78%). Yellow powder. M.p. 75–76°. ^1H-NMR (300 MHz, (D_6)DMSO): 9.10 (*s*, 1 H); 8.11 (*d*, $J = 7.5$, 1 H); 7.90 (*d*, $J = 7.5$, 1 H); 7.77 (*d*, 1 H); 7.61 (*m*, 1 H); 2.63 (*s*, 3 H). Anal. calc. for $C_{12}H_8N_2O_2S_2$ (276.33): C 52.16, H 2.92, N 10.14; found: C 52.00, H 2.99, N 10.06.

*6-Fluoro-3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-one* (**4b**). Yield: 247.3 mg (84%). Yellow powder. M.p. 179–180°. ^1H-NMR (300 MHz, $CDCl_3$): 8.51 (*s*, 1 H); 7.80 (*d*, $J = 7.5$, 1 H); 7.42 (*m*, 2 H); 2.63 (*s*, 3 H). Anal.calc. for $C_{12}H_7FN_2O_2S_2$ (294.32): C 48.97, H 2.40, N 9.52; found: C 48.99, H 2.38, N 9.51.

*6-Bromo-3-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-one* (**4c**). Yield: 284.2 mg (80%). Yellow powder. M.p. 145–146°. ^1H-NMR (300 MHz, $CDCl_3$): 8.44 (*s*, 1 H); 8.29 (*s*, 17.75 (*d*, $J =$ 7.4, 17.3 (*d*, $J = 8.9$, 12.68 (*s*, 3 H). Anal. calc. for $C_{12}H_7BrN_2O_2S_2$ (355.23): C 40.57, H 1.99, N 7.89; found: C 40.60, H 1.98, N 7.88.

*7-Methoxy-3-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-4*H*-1-benzopyran-4-one* (**4d**). Yield: 229.8 mg (75%). Yellow powder. M.p. 190–191°. ^1H-NMR (300 MHz, $CDCl_3$): 8.44 (*s*, 1 H); 8.15 (*d*, $J = 8.9$, 1 H); 7.03 (*d*, $J = 8.8$, 1 H); 6.88 (*s*, 1 H); 3.92 (*s*, 3 H); 2.69 (*s*, 3 H). Anal. calc. for $C_{13}H_{10}N_2O_3S_2$ (306.36): C 50.97, H 3.29, N 9.14; found: C 50.94, H 3.30, N 9.16.

General Procedure for the Preparation of the Compounds **6a–6l** (*Table 2*, *Entry 1–9*; and *Table 3*, *Entry 1–3*). A mixture of **4** (1mmol), **5** (3.0 mmol), and MeONa (3 mmol) in boiling MeOH (DMSO, at 100°, **5c**) was heated for 20–30 min. The reaction was monitored by TLC, until the disappearances of the starting materials. After addition of H_2O (25 ml), the soln. was washed neutrally with aq. 5% HCl. A yellow precipitate was formed and filtered. The crude product was obtained and purified by CC (SiO_2; $CHCl_3$/MeOH 30 : 1) to give the corresponding pure product **6**.

*2-{6-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}phenol* (**6a**). Yield: 256.1 mg (75%). Yellow solid. M.p. 207–208°. IR (KBr): 3289, 3186, 3131, 1585, 1517, 1448, 1371, 755. ^1H-NMR (300 MHz, (D_6)DMSO): 10.08 (*s*, 1 H); 8.78 (*s*, 1 H); 8.26 (*s*, 1 H); 7.34 (*m*, 2 H); 7.04 (*m*, 2 H); 6.91 (*s*, 1 H); 2.62 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.7; 98.2; 112.1; 116.4; 117.1; 119.2; 130.7; 132.5; 146.7; 148.6; 149.5; 153.9; 155.6; 166.6; 166.9. ESI-HR-MS: 364.0304 ($[M+K]^+$, $C_{15}H_{11}KN_5S_2^+$; calc. 364.0303).

*4-Fluoro-2-{6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}phenol* (**6b**). Yield: 283.9 mg (79%). Yellow solid. M.p. 219–220°. IR (KBr): 3243, 3186, 3068, 1588, 1427, 1380, 1182, 819, 780. ^1H-NMR (300 MHz, (D_6)DMSO): 10.16 (*s*, 1 H); 8.80 (*s*, 1 H); 8.29 (*s*, 1 H); 7.28 (*d*, $J =$ 8.1, 2 H); 7.01 (*s*, 1 H); 6.94 (*s*, 1 H); 2.62 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.2; 97.8; 111.8; 116.3; 116.7; 117.0; 117.1; 118.8; 146.3; 148.1; 151.6; 153.3; 156.2; 165.5; 166.7. ESI-HR-MS: 382.0200 ($[M+Na]^+$, $C_{15}H_{10}FN_5NaOS_2^+$; calc. 382.0208).

*5-Methoxy-2-{6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}phenol* (**6c**). Yield: 308.3 mg (83%). Yellow solid. M.p. 119–120°. IR (KBr): 3378, 3079, 1615, 1589, 1494, 1197, 839, 781. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.24 (*s*, 1 H); 8.75 (*s*, 1 H); 8.26 (*s*, 1 H); 7.30 (*d*, J = 8.8, 2 H); 6.90 (*s*, 1 H); 6.56 (*s*, 1 H); 3.79 (*s*, 3 H); 2.50 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.7; 55.7; 98.1; 101.6; 105.6; 109.7; 112.3; 131.8; 146.5;148.7; 149.4; 153.8; 156.9; 157.2; 162.8; 166.8. ESI-HR-MS: 394.0411 ([M + Na]$^+$, $C_{16}H_{13}N_5NaO_2S_2^+$; calc. 394.0408).

*2-{2-Methyl-6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}phenol* (**6d**). Yield: 302.1 mg (85%).Yellow solid. M.p. 232–233°. IR (KBr): 3400, 3033, 1594, 1492, 1380, 1148, 760. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.10 (*s*, 1 H); 8.71 (*s*, 1 H); 7.36 (*m*, 2 H); 7.00 (*m*, 2 H); 6.72 (*s*, 1 H); 2.62 (*s*, 3 H); 2.38 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 14.9; 15.7; 97.6; 111.1; 116.5; 117.4; 119.3; 130.5; 132.4; 149.1; 149.3; 153.7; 155.5; 156.5; 166.8; 170.0. ESI-HR-MS: 378.0460 ([M + Na]$^+$, $C_{16}H_{13}N_5NaOS_2^+$; calc.378.0459).

*4-Fluoro-2-{2-methyl-6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}phenol* (**6e**). Yield: 298.7 mg (80%). Yellow solid. M.p. 107–108°. IR (KBr): 3371, 3066, 1592, 1500, 1268, 1183, 819, 784. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.13 (*s*, 1 H); 8.73 (*s*, 1 H); 7.25 (*d*, J = 8.2, 2 H); 7.00 (*s*, 1 H); 6.74 (*s*, 1 H); 2.62 (*s*, 3 H); 2.35 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 14.4; 15.2; 97.2; 110.7; 115.8; 116.4; 117.3; 118.3; 118.7; 147.0; 148.8; 151.5; 153.1; 155.5; 166.0; 166.5. ESI-HR-MS: 396.0369 ([M + Na]$^+$; $C_{16}H_{12}FN_5NaOS_2^+$; calc. 396.0365).

*4-Bromo-2-{2-methyl-6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}-phenol* (**6f**). Yield: 356.2 mg (82%). Yellow solid. M.p. 219–220°. IR (KBr): 3404, 3125, 1591, 1485, 1285, 813, 784. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.43 (*s*, 1 H); 8.72 (*s*, 1 H); 7.53 (*t*, 2 H); 6.98 (*d*, J = 8.6, 1 H); 6.73 (*s*, 1 H); 2.62 (*s*, 3 H); 2.39 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 14.9; 15.7; 97.7; 110.0; 111.3; 118.7; 119.5; 132.7; 134.9; 147.3; 149.2; 153.5; 155.0; 156.7; 166.3; 167.0. ESI-HR-MS: 455.9574 ([M + Na]$^+$, $C_{16}H_{12}BrN_5NaOS_2^+$; calc.455.9564).

*5-Methoxy-2-{2-methyl-6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazolo[1,5-*a*]pyrimidin-7-yl}-phenol* (**6g**). Yield: 339.2 mg (88%). Yellow solid. M.p. 135–136°. IR (KBr): 3401, 1615, 1591, 1494, 1204, 1033, 837, 788. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.19 (*s*, 1 H); 8.68 (*s*, 1 H); 7.25 (*d*, J = 8.9, 2 H); 6.70 (*s*, 1 H); 6.62 (*s*, 1 H); 3.76 (*s*, 3 H); 2.60 (*s*, 3 H); 2.38 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 14.9; 15.7; 55.5; 97.3; 101.7; 105.0; 109.9; 111.4; 131.5; 148.9; 149.4; 153.4; 156.8; 157.0; 162.5; 166.7; 167.4. ESI-HR-MS: 408.0568 ([M + Na]$^+$, $C_{17}H_{15}N_5NaO_2S_2^+$; calc. 408.0565).

*2-{6-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]imidazo[1,2-*a*]pyrimidin-5-yl}phenol* (**6h**). Yield: 266.3 mg (78%). Yellow solid. M.p. 194–195°. IR (KBr): 3440, 1576, 1488, 1296, 1142, 1053, 755. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.41 (*s*, 1 H); 8.82 (*s*, 1 H); 7.81 (*s*, 1 H); 7.50–7.37 (*m*, 3 H); 7.10–6.98 (*m*, 3 H); 2.61 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.7; 112.4; 112.6; 116.9; 117.2; 119.9; 130.4; 133.3; 136.2; 147.9; 148.7; 154.4; 155.5; 166.5; 167.0. ESI-HR-MS: 364.0304 ([M + Na]$^+$, $C_{15}H_{11}N_5NaOS_2^+$; calc. 364.0303).

*4-Fluoro-2-{6-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]imidazo[1,2-*a*]pyrimidin-5-yl}phenol* (**6i**). Yield: 301.9 mg (84%). Yellow solid. M.p. 149–150°. IR (KBr): 3430, 1582, 1496, 1426, 1250, 1194, 817, 733. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.33 (*s*, 1 H); 8.81 (*s*, 1 H); 7.81 (*s*, 1 H); 7.44 (*s*, 1 H); 7.36 (*m*, 2 H); 7.06 (*m*, 1 H); 2.50 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.2; 112.1; 116.1; 116.5; 117.7; 119.3; 119.6; 135.8; 146.6; 147.4; 151.4; 153.5; 156.5; 165.4; 166.7. ESI-HR-MS: 382.0218 ([M + Na]$^+$, $C_{15}H_{10}FN_5NaOS_2^+$; calc. 382.0208).

*2-{3-[(5-Methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrimido[1,2-*a*]benzimidazol-4-yl}phenol* (**6j**). Yield: 324.9 mg (83%). Yellow solid. M.p. 263–264°. IR (KBr): 3408, 1604, 1572, 1481, 1447, 1368, 1196, 756. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.48 (*s*,1 H); 9.30 (*s*,1 H); 8.12 (*d*, J = 6.8, 1 H); 7.76 (*t*, 2 H), 7.62 (*d*, J = 6.6, 1 H); 7.34 (*t*, 3 H); 6.65 (*d*, J = 8.0, 1 H); 2.83 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.7; 110.8; 114.7; 116.9; 117.7; 120.3; 120.4; 122.9; 127.0; 128.1; 129.9; 133.6; 144.9; 150.5; 152.4; 155.4; 160.3; 166.5; 167.0. ESI-HR-MS: 414.0474 ([M + Na]$^+$, $C_{19}H_{13}N_5NaOS_2^+$; calc. 414.0459).

*4-Fluoro-2-{3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrimido[1,2-*a*]benzimidazol-4-yl}phenol* (**6k**). Yield: 307.1 mg (75%). Yellow solid. M.p. 278–279°. IR (KBr): 3425, 1574, 1486, 1443, 1269, 1199, 767. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.28 (*s*, 1 H); 9.11 (*s*, 1 H); 7.94 (*d*, J = 8.2, 1 H); 7.55 (*m*, 3 H); 7.43 (*m*, 2 H); 6.54 (*d*, J = 8.5, 1 H); 2.50 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.3; 110.5; 114.0;

115.9; 116.2; 117.7; 119.6; 119.9; 122.6; 126.5; 127.5; 144.4; 150.5; 151.4; 153.7; 156.8; 159.6; 165.4; 166.8. ESI-HR-MS: 432.0377 ($[M+Na]^+$, $C_{19}H_{12}FN_5NaOS_2^+$; calc. 432.0365).

5-Methoxy-2-{3-[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrimido[1,2-a]benzimidazol-4-yl}phenol (**6l**). Yield: 345.6 mg (82%). Yellow solid. M.p. 278–279°. IR (KBr): 3438, 2359, 1613, 1485, 1442, 1296, 1200, 742. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.31 (*s*, 1 H); 9.05 (*s*,1 H); 7.90 (*s*,1 H); 7.51 (*d*, *J* = 6.4, 1 H); 7.34 (*d*, *J* = 7.34, 1 H); 7.20 (*d*, *J* = 6.2, 1 H); 6.66 (*s*, 3 H); 3.84 (*s*, 3 H); 2.50 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 15.7; 55.8; 102.2; 106.5; 110.4; 111.4; 120.2; 122.8;126.9; 128.3; 130.9; 144.9; 150.6; 152.4; 156.9; 160.1; 163.4; 166.7; 166.8; 166.9. ESI-HR-MS: 444.0576 ($[M+Na]^+$, $C_{20}H_{15}N_5NaO_2S_2^+$, calc. 444.0565).

We thank the *National Natural Science Foundation of China* (No. 20772076) and *the Fundamental Funds Research for the Central Universities* (No. Gk200901010) for financial support of this research.

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Received December 9, 2011