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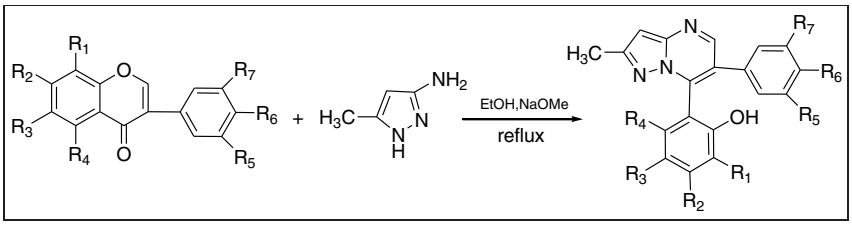

A new facile and straightforward method for synthesis of 2-methyl-6,7-diphenyl- pyrazolo[1,5-*a*] pyrimidines has been described. The cyclocondensation of isoflavones with 3-amino-5-methylpyrazole in the presence of sodium methoxide gave fused 2-methyl-6,7-diphenylpyrazolo[1,5-*a*]pyrimidines in moderate to good yields. A series of 20 new compounds were obtained and characterized by FT-IR, NMR, and elemental analysis.

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INTRODUCTION

In general, the fused heterocyclic compound, pyrazolo [1,5-*a*]pyrimidines are known to possess pharmacological activity and anxiolytic properties, such as translocator protein ligands [1,2] (Scheme 1), HIV (human immunodeficiency virus)reverse transcriptase inhibitors [3], estrogen receptor ligands [4], KDR (kinase insert domain-containing receptor) kinase inhibitors [5], COX-2-selective inhibitors [6], and CRF-1 receptor antagonists. [7] They are also used as intermediates in the dyestuff industry. [8,9] These interesting activities have stimulated chemists to develop the chemistry of this class of compounds.

Numerous methods for the synthesis of pyrazolo[1,5-*a*] pyrimidines have been reported in the last 20 years, which involved the reaction between aminopyrazoles and 1,3-biselectrophilic compounds, including α,β-unsaturated ketones [10], dithioacetals [11], and enaminone compounds. [12] It was reported that the chromone fragment of the isoflavone can generate a 1,3-diketone equivalent in the present of alkali, which readily reacts with amidine [13], hydrazine [14], biguanidine [15], and 2-aminobenzimidazole [16] to form the corresponding pyrimidines and diarylpyrazoles. Recently, we have reported the synthesis of diarylpyrazolo[3,4-*b*]pyridines [17] and diphenylpyrazolo[1,5-*a*] pyrimidines [18] by using one-step reaction of 3-amino-5-hydroxypyrazole (X=OH) and 3-aminopyrazole (X=H) with isoflavones (Scheme 2). The different fused nitrogen was obtained, because hydroxyl located at pyrazole ring is donating electron to the ring. [18] For the methyl of 3-amino-5-methylpyrazole, (X=Me) is also an electron donating group, but its electron donating effect is weaker than hydroxyl located at pyrazole ring. In this paper, in order to explore forming-fused pyrazolo[3,4-*b*]-pyridines or pyrazolo[1,5-*a*]pyrimidines, the cyclocondensation of 3-amino-5-methylpyrazole with isoflaovens was carried out.

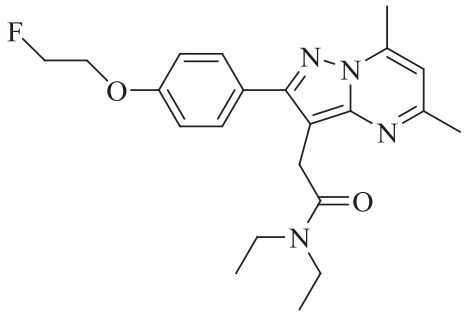
RESULT AND DISCUSSION

Reaction of 7-isopropoxyisoflavone **1a** (1.0 equiv) and] 3-amino-5-methylpyrazole **2** (1.2 equiv) were carried out in refluxing ethanol in the presence of sodium methoxide as base to promote the ring-opening of isoflavone. The progress of the reaction was monitored by thin layer chromatography (TLC) until the starting **1a** disappeared. The product that was purified by column chromatography on silica gel, and characterized by IR, ^{1}H NMR, and ^{13}C NMR, finally confirmed condensation of **1a** and **2** mainly product 2-methyl-6-phenyl-7-(2-hydroxyl-4-isopropoxyphenyl)-pyrazo[1,5-*a*]pyrimidine (**3a**).

Then we turned our attention to optimize the conditions to improve yields (Table 1). Under different equivalency of NaOH and NaOMe, it was found that 3.0 equivalency of NaOMe gave the best result (Table 1, entry 4). EtOH was an ideal solvent. The best condition to obtain the maximum yield (83%) was using NaOMe (0.5 mol·L^{-1}, 3.0 eq) as base in ethanol with 1:1.5 as the ratio of **1a/2**.

Having the optimized conditions, the scope of the reaction was examined and summarized in Table 2. All products were characterized by IR, ^{1}H NMR, ^{13}C NMR spectra, and elemental analysis.

Scheme 1. Pyrazolo[1,5-*a*]pyrimidine as a TSPO (translocator protein) ligand.



As shown in Table 2, isoflavones containing fluorine group take reaction easily and give **3** in high yields. The yields become the lowest when isoflavones with hydroxyl group. Isoflavones **1o, 1p**, and **1q** (Table 2, entries15–17), which contain fluorine group, gave **3** about 85%. Isoflavone with hydroxyl group **1g, 1h**, and **1i** (Table 2, entries7–9) afforded **3** about 50%. The yields of **3** directly depended on the substituents present on the engaged isoflavones. It seems possible that strong electronegativity of fluorine might be beneficial to take reaction. Although the hydroxyl groups under the basic conditions would become oxyanions, which possess stronger electron donating ability than alkoxy and benzyoxyl groups, preventing condensation with **2**.

According to the report [19], isoflavone may undergo ring opening reaction in the presence of alkali to form an α,β-unsaturated ketone intermediate **5** (Scheme 3) which at high concentration of base may eliminate $HC(OMe)_3$ to generate byproduct **6**. 3-amino-5-hydroxypyrazole react with isoflavones formed pyrazolo[3,4-*b*]pyridine because of the hydroxyl group that would become an oxyanion in basic condition, enhancing the nucleophilicity of **C4** of 3-amino-5-hydroxypyrazole that attacks the β-carbon of **5** more easily [18]. On the contrast, the electron donating ability of methyl is weaker than hydroxyl, the **C4** of 3-amino-5-methylpyrazole has poor nucleophilicity, and the proposed mechanism is similar to the reaction of 3-aminopyrazole with isoflavones [19], as shown in Scheme 3; the primary amine group of the **2** first attacks the β-carbon of **5**, followed by ring closure, then pyrazolo[1,5-*a*]pyrimidine is formed.

Table 1

Optimization of cyclocondensation of 7-isopropoxyisoflavone **1a** with 3-amino-5-methylpyrazole **2**.[a]

Entry	Solvent [b]	Base	Molar ratios **1a/2**/base	**3a** yield (%)[c]
1	MeOH	NaOH(s)	1/1.2/2	30
2	MeOH	NaOH(3 mol·L^{-1})	1/1.2/2	45
3	MeOH	NaOMe(0.5 mol·L^{-1})	1/1.2/2	57
4	MeOH	NaOMe(0.5 mol·L^{-1})	1/1.2/3	64
5	MeOH	NaOMe(0.5 mol·L^{-1})	1/1.2/4	58
6	EtOH	NaOMe(0.5 mol·L^{-1})	1/1.2/3	74
7	THF	NaOMe(0.5 mol·L^{-1})	1/1.2/3	55
8	DMF [d]	NaOMe(0.5 mol·L^{-1})	1/1.2/3	58
9	EtOH	NaOMe(0.5 mol·L^{-1})	1/1.3/3	79
10	EtOH	NaOMe(0.5 mol·L^{-1})	1/1.5/3	83
11	EtOH	NaOMe(0.5 mol·L^{-1})	1/1.7/3	82

[a]All reactions were carried out with 7-isopropoxyisoflavone **1a** (2 mmol), 3-amino-5-methylpyrazole **2**, and different kinds of bases in indicated solvents (20 mL) for 24 h.
[b]Reactions with MeOH, EtOH, and THF as solvent were carried out at reflux.
[c]Isolated yield on the basis of isoflavone **1a**.
[d]The reaction with DMF as solvent was carried at 100°C.

Scheme 2. Cyclocondensations of 3-amino-5-hydroxypyrazole and 3-aminopyrazole with isoflavones. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

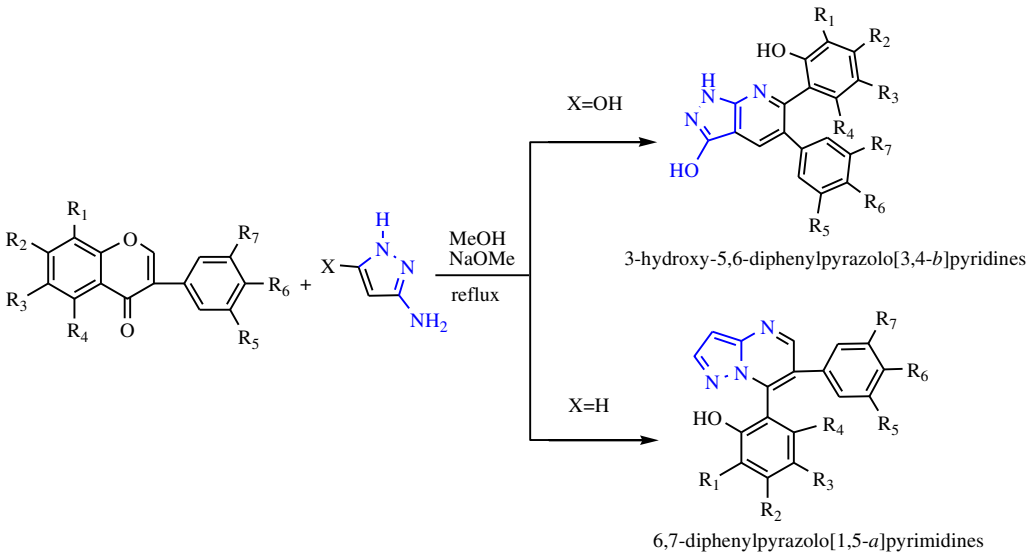
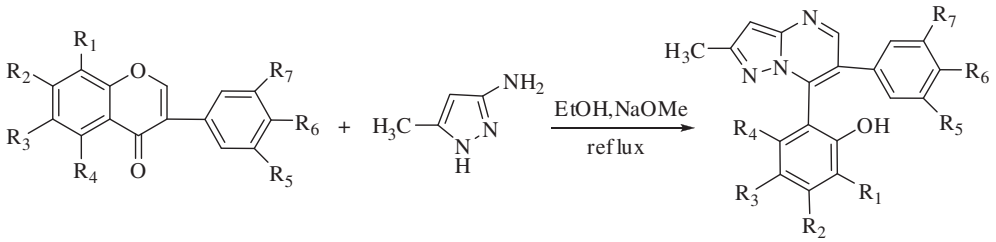


Table 2

Synthesis of 6,7-diphenylpyrazolo[1,5-*a*]pyrimidines **3**.[a]



Entry	Substance	R_1	R_2	R_3	R_4	R_5	R_6	R_7	Product	Yield (%)[b]	Time (h)
1	1a	H	i-OPr	H	H	H	H	H	**3a**	83	20
2	1b	H	OMe	H	H	H	OMe	H	**3b**	80	24
3	1c	H	OMe	H	OMe	H	OMe	H	**3c**	77	24
4	1d	H	OMe	H	Me	H	H	H	**3d**	75	24
5	1e	H	OBn	H	H	H	OMe	H	**3e**	77	27
6	1f	H	OMe	H	H	H	H	H	**3f**	71	24
7	1g	H	OH	H	H	H	OMe	H	**3g**	56	72
8	1h	H	OMe	H	H	H	OH	H	**3h**	60	48
9	1i	H	OMe	H	OH	H	OMe	H	**3i**	58	56
10	1j	Br	i-OPr	H	H	H	H	H	**3j**	78	18
11	1k	H	OMe	H	H	i-Pr	OMe	i-Pr	**3k**	76	27
12	1l	H	H	H	H	H	H	H	**3l**	75	30
13	1m	H	H	H	H	H	Me	H	**3m**	82	24
14	1n	H	H	H	H	H	OMe	H	**3n**	81	24
15	1o	H	H	F	H	H	H	H	**3o**	87	18
16	1p	H	H	F	H	H	Me	H	**3p**	88	18
17	1q	H	H	F	H	H	OMe	H	**3q**	86	16
18	1r	H	H	Br	H	H	H	H	**3r**	83	18
19	1s	H	H	Br	H	H	Me	H	**3s**	85	24
20	1t	H	H	H	H	H	F	H	**3t**	82	20

[a]Isoflavones **1** (2 mmol), **2** (3.0 mmol), and NaOMe (4 mmol were used for fluorine group and 8 mmol were used for 1 hydroxyl group in **1**, respectively) in ethanol.
[b]Isolated yield.

CONCLUSION

Make the comparison of isoflavones react with 3-amino-5-hydroxypyrazole, 3-aminopyrazole and 3-amino-5-methylpyrazole under the basic condition afforded chemoselectivity fused pyrazolo[3,4-*b*]pyridines and pyrazolo [1,5-*a*]pyrimidines. It is indicative that the electron donating ability of substituents probably is one of the key factors that will lead to form different structures. Extended to all the alkyl-3-aminopyrazole, which react with isoflavones under the aforementioned conditions will be mainly formed the structure of pyrazolo[1,5-*a*]pyrimidines.

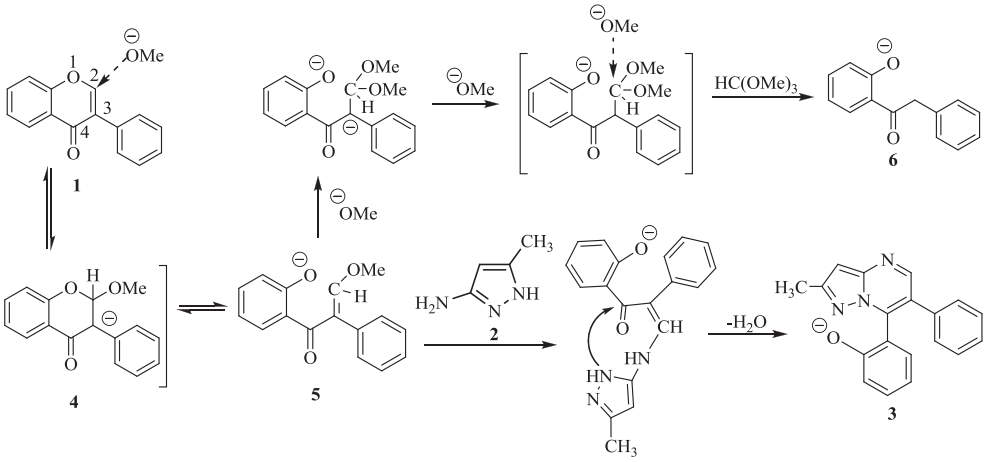
EXPERIMENTAL

General procedure for the reaction of isoflavones with 3-amino-5-methylpyrazole to synthesize pyrazolo[1,5-*a*] pyrimidine. The corresponding isoflavones **1** (2 mmol), 3-amino-5-methyl-pyrazole **2** (3 mmol), and sodium methoxide (6 mmol) were refluxed in ethanol (20 mL) for 16–72 h. All reactions were monitored by usingTLC, which showed the disappearance of **1** that was indicative of the reaction being complete. The reaction mixture was adjusted to neutrality with the solution of 5% HCl and then poured into water (30 mL). A yellow precipitate appeared and was filtered. Finally, the precipitate was recrystallized from absolute ethanol or purified by column chromatography on silica gel using petroleum ether-ethyl acetate (4:1) to give the corresponding pure product **3a–3t**.

Characterizations of products

2-Methyl-6-phenyl-7-(2-hydroxyl-4-isopropoxyphenyl)pyrazolo [1,5-a]pyrimidine (3a). Mp 223.7–224.1°C. IR (KBr), ν (cm^{-1}): 3842, 2980, 2926, 1604, 1497, 1271, 1179, 1108, 990, 463. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 1.29 (d, 6H, J = 5.8 Hz), 2.40 (s, 3H), 4.56 (m, 1H), 6.42 (d, 1H, J = 8.7 Hz), 6.46 (s, 1H), 6.55 (s, 1H), 6.98 (d, 1H, J = 8.7 Hz), 7.30 (s, 5H), 8.55 (s, 1H), 9.78 (s, 1H). ^{1}H NMR [300 MHz, DMSO-d_6 + D_2O/TMS, δ (ppm)]: 1.29 (d, 6H, J = 5.8 Hz), 2.40 (s, 3H), 4.56 (m, 1H), 6.42 (d, 1H, J = 8.7 Hz), 6.46 (s, 1H), 6.55 (s, 1H), 6.98 (d, 1H, J = 8.7 Hz), 7.30 (s, 5H), 8.55 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 22.2, 69.8, 95.9, 103.0, 106.6, 110.8, 121.9, 127.7, 128.9, 129.7, 132.0, 135.9, 142.6, 148.9, 150.6, 154.4, 157.1, 160.1. *Anal*. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69; Found C, 73.48; H, 5.96; N, 11.75.

Scheme 3. Proposed mechanism for the formation of **3**.



2-Methyl-6-(4-methoxyphenyl)-7-(2-hydroxyl-4-methoxyphenyl) pyrazolo[1,5-a]pyrimidine (3b). Mp 227.1–228.5°C. IR (KBr), ν (cm^{-1}): 3845, 2948, 1609, 1504, 1416, 1295, 1248, 1093, 1020, 828, 742, 568. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.36 (s, 3H), 3.73 (s, 6H), 6.40 (d, 1H, *J* = 8.4 Hz), 6.44 (s, 1H), 6.57 (s, 1H), 6.86 (d, 2H, *J* = 7.9 Hz), 6.98 (d, 1H, *J* = 8.4 Hz), 7.20 (d, 2H, *J* = 7.9 Hz), 8.50 (s, 1H), 9.79 (s, 1H). ^{1}H NMR [300 MHz, DMSO-d_6 + D_2O/TMS, δ (ppm)]: 2.35 (s, 3H), 3.72 (s, 6H), 6.39 (d, 2H, *J* = 8.4 Hz), 6.45 (s, 1H), 6.45 (s, 1H), 6.57 (s, 1H), 6.85 (d, 2H, *J* = 7.9 Hz), 6.97 (d, 1H, *J* = 8.4 Hz), 7.19 (d, 2H, *J* = 7.9 Hz), 8.50 (s, 1H). ^{13}C NMR [75 MHz, DMSO- d_6/TMS, δ (ppm)]: 14.9, 55.5, 95.8, 101.6, 105.4, 111.4, 114.2, 121.7, 128.0, 130.5, 132.0, 142.2, 148.8, 150.7, 154.1, 157.0, 159.0, 161.8. *Anal*. Calcd for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63; Found C, 69.85; H, 5.24; N, 11.67.

2-Methyl-6-(4-methoxyphenyl)-7-(2-hydroxyl-4,6-dimethoxyphenyl) pyrazolo[1,5-a]pyrimidine (3c). Mp 227.7–118.9°C. IR (KBr), ν (cm^{-1}): 3482, 3136, 2803, 1597, 1506, 1462, 1354, 1289, 1108, 1034, 816, 571. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.35 (s, 3H), 3.51 (s, 3H), 3.73 (s, 6H), 6.06 (s, 1H), 6.10 (s, 1H), 6.53 (s, 1H), 6.86 (d, 2H, *J* = 7.9 Hz), 7.20 (d, 2H, *J* = 7.9 Hz), 8.46 (s, 1H), 9.69 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.4, 55.0, 55.5, 89.9, 93.6, 95.0, 101.6, 113.5, 123.0, 126.2, 129.8, 143.6, 148.1, 149.8, 154.0, 156.7, 158.6, 158.9, 162.0. *Anal.* Calcd for $C_{22}H_{21}N_3O_4$: C, 67.51; H, 5.41; N, 10.74; Found C, 67.46; H, 5.49; N, 10.68.

2-Methyl-6-phenyl-7-(2-hydroxyl-4-methoxy-6-methylphenyl) pyrazolo[1,5-a]pyrimidine (3d). Mp 222.3–223.0°C. IR (KBr), ν (cm^{-1}): 3478, 3013, 2802, 1517, 1269, 1145, 1058, 995, 832, 789, 694, 535. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 1.71 (s, 3H), 2.36 (s, 3H), 3.70 (s, 3H), 6.28 (s, 2H), 6.59 (s, 1H), 7.30 (s, 5H), 8.53 (s, 1H), 9.70 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 19.6, 55.3, 95.8, 99.1, 106.6, 111.4, 122.4, 127.9, 128.7, 129.9, 135.8, 138.5, 141.9, 148.9, 150.4, 154.4, 157.0, 161.3. *Anal*. Calcd for $C_{21}H_{19}N_3O_2$: C, 73.03; H, 5.54; N, 12.17; Found C, 73.10; H, 5.46; N, 12.24.

2-Methyl-6-(4-methoxyphenyl)-7-(2-hydroxyl-4-benzyloxyphenyl) pyrazolo[1,5-a]pyrimidine (3e). Mp 228.2–229.6°C. IR (KBr), ν (cm^{-1}): 3487, 3096, 3025, 2963, 1609, 1503, 1447, 1293, 1243, 1181, 1032, 828,739. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.38 (s, 3H), 3.76 (s, 3H), 5.09 (s, 2H), 6.47–6.59 (m,3H), 6.87 (d, 2H, *J* = 8.1 Hz), 6.99 (m, 1H), 7.21 (d, 2H, *J* = 8.1 Hz), 7.37–7.47 (m, 5H), 8.52 (s, 1H), 9.85 (s, 1H). ^{13}C NMR [75MHz, DMSO-d_6/TMS, δ (ppm)]:14.4, 55.0, 69.2, 95.2, 102.1, 105.6, 111.2, 113.7 121.2, 127.5, 127.9, 128.4, 130.4, 131.5, 136.9, 141.7, 148.3, 150.2, 153.5, 156.7, 158.4, 160.4. *Anal*. Calcd for $C_{27}H_{23}N_3O_3$: C, 74.12; H, 5.30; N, 9.60; FoundC, 74.20; H, 5.25; N, 9.56.

2-Methyl-6-phenyl-7-(2-hydroxyl-4-methoxyphenyl)pyrazolo [1,5-a]pyrimidine (3f). Mp 223.4–224.9°C. IR (KBr), ν (cm^{-1}): 3431, 3029, 2962, 1606, 1497, 1440, 1338, 1294, 1205, 1160, 695. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.36 (s, 3H), 3.72 (s, 3H), 6.38 (d, 2H, *J* = 8.1 Hz), 6.43 (s, 1H), 6.58 (s, 1H), 6.97 (d, 2H, *J* = 8.1 Hz), 7.28 (s, 5H), 8.52 (s, 1H), 9.81 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.4, 55.3, 95.3, 101.2, 104.8, 110.8, 121.4, 127.2, 128.2, 129.2, 131.5, 135.4, 142.1, 148.5, 150.1, 153.7, 156.7, 161.3. *Anal*. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68; Found C, 72.55; H, 5.12; N, 12.72.

2-Methyl-6-(4-methoxyphenyl)-7-(2,4-dihydroxylphenyl)pyrazolo [1,5-a]pyrimidine (3g). Mp 273.8–274.6°C. IR (KBr), ν (cm^{-1}): 3283, 3134, 3001, 1600, 1514, 1439, 1382, 1318, 1265, 1169, 829, 742, 642, 593. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.36 (3H), 3.72 (3H), 6.22 (d, 1H, *J* = 8.1 Hz), 6.35 (s, 1H), 6.55 (s, 1H), 6.85 (d, 2H, *J* = 7.8 Hz), 6.87 (d, 1H, *J* = 8.1 Hz), 7.19 (d, 2H, *J* = 7.8 Hz), 8.48 (s, 1H), 9.57 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 55.5, 95.6, 103.0, 107.1, 109.8, 114.1, 121.6, 128.2, 130.9, 131.9, 142.7, 148.9, 150.7, 153.9, 157.0, 158.9, 160.0. *Anal*. Calcd for $C_{20}H_{17}N_3O_3$: C, 69.15; H, 4.93; N, 12.10; Found C, 69.22; H, 4.86; N, 12.13.

2-Methyl-6-(4-hydroxylphenyl)-7-(2-hydroxyl-4-methoxyphenyl) pyrazolo[1,5-a]pyrimidine (3h). Mp 263.0–264.5°C. IR (KBr), ν (cm^{-1}): 3263, 3110, 3003, 1598, 1504, 1439, 1382, 1318, 1265,1169, 829, 742, 642, 593. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.34 (s, 3H), 3.73 (s, 3H), 6.38 (d, 1H, *J* = 8.1 Hz), 6.43 (s, 1H), 6.58 (s, 1H), 6.66 (d, 2H, *J* = 8.4 Hz), 6.95 (d, 1H, *J* = 8.1 Hz), 7.06 (d, 2H, *J* = 8.4 Hz), 8.47 (s, 1H), 9.62 (s, 1H), 9.85 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 55.5, 95.6, 101.6, 105.2, 111.6, 115.5, 122.0, 126.3, 130.9, 131.9, 142.1, 148.7, 150.8, 153.8, 157.1, 157.2, 161.7. *Anal*. Calcd for $C_{20}H_{17}N_3O_3$: C, 69.15; H, 4.93; N, 12.10; Found C, 69.09; H, 4.97; N, 12.14.

2-Methyl-6-(4-methoxyphenyl)-7-(2,6-dihydroxyl-4-methoxyphenyl) pyrazolo[1,5-a]pyrimidine (3i). Mp 267.6–277.4°C. IR (KBr), ν (cm^{-1}): 3256, 3001, 1602, 1502, 1439, 1233, 827, 741, 642, 589. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.35 (s, 3H), 3.62

(s, 3H), 3.72 (s, 3H), 5.84 (s, 2H), 6.43 (s, 1H), 6.83 (d, 2H, J = 5.5 Hz), 7.23 (d, 2H, J = 5.5 Hz), 8.80 (s, 1H), 9.22 (s, 2H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.7, 55.1, 55.5, 92.8, 94.9, 113.8, 124.4, 128.8, 130.3, 132.9, 148.1, 154.5, 155.6, 156.8, 159.0, 160.8. *Anal*. Calcd for $C_{21}H_{19}N_3O_4$: C, 66.83; H, 5.07; N, 11.13; Found C, 66.90; H, 5.04; N, 11.08.

2-Methyl-6-phenyl-7-(2-hydroxyl-3-bromo-4-isopropoxyphenyl) pyrazolo[1,5-a]pyrimidine (3j). Mp 223.3–223.9°C. IR (KBr), ν (cm^{-1}): 3483, 2977, 1600, 1487, 1403, 1331, 1260, 1201, 1103, 1031, 889, 751, 697. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 1.32 (d, 6H, J = 5.8 Hz), 2.38 (s, 3H), 4.56 (m, 1H), 6.58 (s, 1H), 6.60 (s, 1H), 7.31 (s, 6H), 8.52 (s, 1H), 10.04 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 22.3, 71.7, 96.0, 101.0, 102.9, 112.3 122.2, 127.9, 128.7, 129.8, 134.5, 135.6, 140.9, 148.9, 150.6,154.4, 155.9, 156.7. *Anal*. Calcd for $C_{22}H_{20}BrN_3O_2$: C, 60.28; H, 4.60; Br, 18.23; N, 9.59; Found C, 60.34; H, 4.58; Br, 18.31; N, 9.51.

2-Methyl-6-(3,5-diisopropyl-4-methoxyphenyl)-7-(2-hydroxyl-4-methoxyphenyl)pyrazolo[1,5-a]pyrimidine (3k). Mp 229.4–231.0°C. IR (KBr), ν (cm^{-1}): 3478,3083, 2960, 1607, 1499, 1298, 1202, 1114, 1009, 789. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 1.02–1.09 (m,12H), 2.36 (s, 3H), 3.16 (m, 2H), 3.63 (s, 3H), 3.71 (s, 3H), 6.42 (d, 1H, J = 8.4 Hz), 6.49 (s, 1H), 6.57 (s, 1H), 6.92 (d, 1H, J = 8.4 Hz), 7.04 (s, 2H), 8.59 (s, 1H), 9.83 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.4, 23.6, 25.8, 55.1, 61.8, 95.2, 101.3, 104.9, 111.2, 121.3, 125.1, 130.9, 131.1, 140.7, 141.8, 148.3, 150.1, 153.2, 153.6, 156.8, 161.4. *Anal*. Calcd for $C_{27}H_{31}N_3O_3$: C, 72.78; H, 7.01; N, 9.43; Found C, 72.85; H, 7.03; N, 9.36.

2-Methyl-6-phenyl-7-(2-hydroxylphenyl)pyrazolo[1,5-a]pyrimidine (3l). Mp 260.2–261.4°C. IR (KBr), ν (cm^{-1}): 3475, 3039, 2967, 1603, 1527, 1451, 1352, 1284, 1231, 844, 752, 697. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.36 (s, 3H), 6.60 (s, 1H), 6.77 (m, 2H), 6.93 (d, 1H, J = 7.6 Hz), 7.04 (d, 1H, J = 7.6 Hz), 7.27 (s, 5H), 8.55 (s, 1H), 9.88 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 95.9, 116.2, 118.6, 119.2, 121.8, 127.8, 128.6, 129.8, 131.1, 131.3, 135.6, 142.6, 148.9, 150.6, 154.4, 156.1. *Anal*. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94; Found C, 75.77; H, 5.05; N, 13.87.

2-Methyl-6-(4-methylphenyl)-7-(2-hydroxylphenyl)pyrazolo[1,5-a] pyrimidine (3m). Mp 256.6–256.9°C. IR (KBr), ν (cm^{-1}): 3461, 3047, 2736, 1602, 1508, 1453, 1350, 1279, 1224, 932, 816, 753, 679. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.24 (s, 3H), 2.35 (s, 3H), 6.59 (s, 1H), 6.77 (m, 2H), 6.93 (d, 1H, J = 7.8 Hz), 7.07 (d, 2H, J = 8.4 Hz), 7.16 (d, 2H, J = 8.4 Hz), 7.25 (d, 1H, J = 7.8 Hz), 8.52 (s, 1H), 9.90 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.4, 20.6, 95.3, 115.7, 118.2, 118.7, 121.1, 128.8, 129.1, 130.6, 130.8, 132.1, 136.6, 141.9, 148.6, 150.2, 153.8, 155.6. *Anal*. Calcd for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.32; Found C, 76.25; H, 5.40; N, 13.28.

2-Methyl-6-(4-methoxyphenyl)-7-(2-hydroxylphenyl)pyrazolo [1,5-a]pyrimidine (3n). Mp 239.3–240.2°C. IR (KBr), ν (cm^{-1}): 3469, 3189, 1821, 1601, 1506, 1453, 1356, 1241, 1172, 1089, 835, 757. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.35 (s, 3H), 3.71 (s, 3H), 6.58 (s, 1H), 6.83 (d, 2H, J = 8.4 Hz), 6.90 (m, 2H), 7.05 (d, 1H, J = 6.3 Hz), 7.19 (d, 2H, J = 8.4 Hz), 7.26 (d, 1H, J = 6.3 Hz), 8.52 (s, 1H), 9.77 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 55.5, 95.8, 114.2, 116.2, 118.8, 119.3, 121.4, 127.7, 130.9, 131.1, 131.3, 142.2, 148.8, 150.8, 154.2, 155.9, 159.0. *Anal*. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68; Found C, 72.54; H, 5.13; N, 12.72.

2-Methyl-6-phenyl-7-(2-hydroxyl-5-fluorophenyl)pyrazolo[1,5-a]pyrimidine (3o). Mp 25 8.6–259.2°C. IR (KBr), ν (cm^{-1}): 3439, 2983, 2721, 1604, 1511, 1438, 1271, 1235, 1183, 759, 462. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.37 (s, 3H), 6.62 (s, 1H), 6.87 (s, 1H), 6.06 (m, 2H), 7.30 (s, 5H), 8.56 (s, 1H), 9.80 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 96.0, 117.1, 117.3, 117.6, 117.8, 118.1, 119.3, 121.8, 128.0, 128.7, 129.8, 135.3, 141.0, 148.9, 150.6, 152.4, 153.7, 154.6, 156.8. *Anal*. Calcd for $C_{19}H_{14}FN_3O$: C, 71.46; H, 4.42; F, 5.95; N, 13.16; Found C, 71.52; H, 4.39; F, 5.99; N, 13.12.

2-Methyl-6-(4-methylphenyl)-7-(2-hydroxyl-5-fluorophenyl)pyrazolo [1,5-a]pyrimidine (3p). Mp 237.1–237.6°C. IR (KBr), ν (cm^{-1}): 3420, 3182, 1606, 1507, 1429, 1253, 1183, 824, 786. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.26 (s, 3H), 2.36 (s, 3H), 6.61 (s, 1H), 6.87 (m, 2H), 7.02 (s, 1H), 7.11 (d, 2H, J = 7.5 Hz), 7.18 (d, 2H, J = 7.5 Hz), 8.53 (s, 1H), 9.78 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]:14.9, 21.1, 96.0, 117.1, 117.3, 117.7, 118.0, 119.3, 121.8, 129.3, 129.6, 132.3, 137.3, 140.8, 148.8, 150.7, 152.2, 153.8, 154.4, 156.9. *Anal*. Calcd for $C_{20}H_{16}FN_3O$: C, 72.06; H, 4.84; F, 5.70; N, 12.61; Found C, 72.12; H, 4.80; F, 5.74; N, 12.57.

2-Methyl-6-(4-methoxyphenyl)-7-(2-hydroxyl-5-fluorophenyl) pyrazolo[1,5-a]pyrimidine (3q). Mp 222.7–223.3°C. IR (KBr), ν (cm^{-1}): 3406, 3058, 1599, 1488, 1330, 1268, 1223, 1185, 1135, 781. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.36(s, 3H), 3.72 (s, 3H), 6.60 (s, 1H), 6.87 (d, 2H, J = 8.4 Hz), 7.05 (m, 2H), 7.09 (s, 1H), 7.22 (d, 2H, J = 8.4 Hz), 8.53 (s, 1H), 9.76 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 13.9, 54.6, 95.0, 113.3, 116.2, 116.3, 116.4, 116.7, 117.1, 118.6, 120.6, 126.4, 130.0, 139.7, 147.8, 149.9, 151.4, 152.8, 153.4, 155.9, 158.2. *Anal*. Calcd for $C_{20}H_{16}FN_3O_2$: C, 68.76; H, 4.62; F, 5.44; N, 12.03; Found C, 68.82; H, 4.60; F, 5.50; N, 12.07.

2-Methyl-6-phenyl-7-(2-hydroxyl-5-bromophenyl)pyrazolo[1,5-a]pyrimidine (3r). Mp 259.4–260.9°C. IR (KBr), ν (cm^{-1}): 3470, 3031, 2943, 2706, 2602, 1602, 1525, 1488, 1413, 1280, 1227, 741, 692. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.37 (s, 3H), 6.62 (s, 1H), 6.86 (d, 1H, J = 8.7 Hz), 7.30 (s, 6H), 7.42 (d, 1H, J = 8.7 Hz), 8.55 (s, 1H), 10.07 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 96.1, 110.0, 118.3, 120.8, 122.0, 128.0, 128.7, 129.7, 133.2, 134.0, 135.3, 140.7, 148.8, 150.6, 154.6, 155.5. *Anal*. Calcd for $C_{20}H_{16}FN_3O$: C, 72.06; H, 4.84; F, 5.70; N, 12.61; Found C, 72.13; H, 4.80; F, 5.76; N, 12.68.

2-Methyl-6-(4-methylphenyl)-7-(2-hydroxyl-5-bromophenyl)pyrazolo [1,5-a]pyrimidine (3s). Mp 242.5–244.0°C. IR (KBr), ν (cm^{-1}): 3478, 3046, 1603, 1514, 1404, 1278, 1225, 815, 741, 587. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.27 (s, 3H), 2.36 (s, 3H), 6.61 (s, 1H) 6.85 (d, 1H, J = 8.7 Hz), 7.12 (d, 2H, J = 7.5 Hz), 7.18 (d, 2H, J = 7.5 Hz), 7.32 (s, 1H), 7.41 (d, 1H, J = 8.7 Hz), 8.52 (s, 1H), 10.12 (s, 1H). ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 21.1, 96.0, 110.0, 118.4, 121.0, 121.8, 129.4, 129.6, 132.3, 133.2, 134.0, 137.4, 140.5, 148.8, 150.7, 154.4, 155.5. *Anal*. Calcd for $C_{20}H_{16}BrN_3O$: C, 60.93; H, 4.09; Br, 20.27; N, 10.66; Found C, 60.98; H, 4.13; Br, 20.34; N, 10.59.

2-Methyl-6-(4-fluorophenyl)-7-(2-hydroxylphenyl)pyrazolo[1,5-a] pyrimidine (3t). Mp 237.1–238.5°C. IR (KBr), ν (cm^{-1}): 3481, 3050, 2737, 1604, 1509, 1457, 1279, 1229, 837, 752, 590, 530. ^{1}H NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 2.36 (s, 3H), 6.61

(s,1H), 6.81 (d, 1H, $J = 7.5$ Hz), 6,89 (d, 1H, $J = 7.5$ Hz), 7.11 (m, 3H), 7.29 (m, 3H), 8.54 (s, 1H), 9.80 (s, 1H) . ^{13}C NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 14.9, 95.9, 115.4, 116.1, 116.2, 118.4, 119.4, 120.8, 131.1, 131.5, 131.8, 131.9, 132.0, 142.5, 148.9, 150.5, 154.5, 155.7, 160.4, 163.6. *Anal*. Calcd for $C_{19}H_{14}FN_3O$: C, 71.46; H, 4.42; F, 5.95; N, 13.16; Found C, 71.54; H, 4.40; F, 6.03; N, 13.20.

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