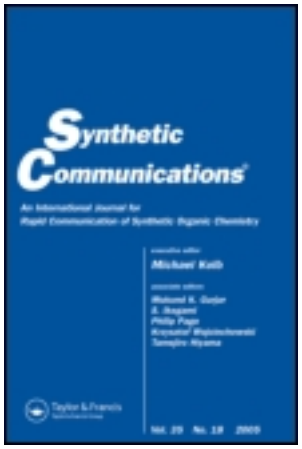

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Microwave Irradiation for Accelerating Synthesis of 5,6-Diphenylimidazo[1,2-a]pyrimidines Based on Isoflavones

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MICROWAVE IRRADIATION FOR ACCELERATING SYNTHESIS OF 5,6-DIPHENYLIMIDAZO[1,2-*a*]PYRIMIDINES BASED ON ISOFLAVONES

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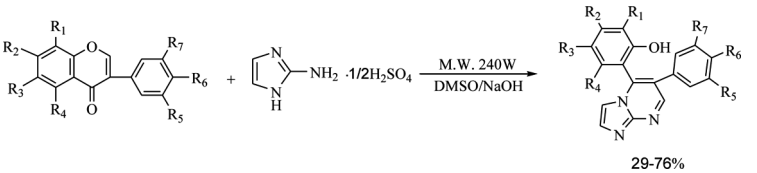
GRAPHICAL ABSTRACT



Abstract *Microwave irradiation was used to accelerate the cyclocondensation of isoflavones with 2-aminoimidazole to synthesize 5,6-diphenylimidazo[1,2-a]pyrimidines. A series of 17 new compounds were characterized by Fourier transform infrared, NMR, and elemental analysis. 5-(2-Hydroxyl-4-isopropoxyphenyl)-6-phenylimidazo-[1,2-a]pyrimidine was determined by x-ray diffraction. A variety of substrates can participate in the process with good yields and purities, making this methodology suitable for library synthesis in drug discovery.*

Keywords Cyclocondensation; imidazo[1,2-*a*]pyrimidine; isoflavone; microwave irradiation

INTRODUCTION

The importance of the imidazo[1,2-*a*]pyrimidine nucleus has been well established in pharmaceutical chemistry on account of its pharmacological activities as antiviral,[1] anti-inflammatory,[2] antibacterial,[3] and antiarrhythmic drugs.[4] Chemical modifications of the imidazopyrimidine ring, such as the introduction of different substituents, have allowed expansion of the research on the structure–activity relationship to afford new insight into the molecular interaction at the

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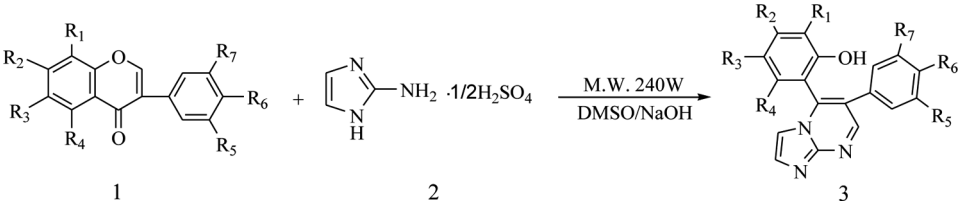
receptor level, revealing new information such as that imidazo[1,2-*a*]pyrimidines are $GABA_A$ receptor benzodiazepine binding site ligands that can exhibit functional selectivity for the α_3 subtype over the α_1 subtype.[5] Because of the range of biological activity they exhibited, these compounds have distinguished themselves as heterocycles of profound chemical and biological significance. Thus, the synthesis of these molecules attracted our interest. The existing methods for building up the imidazo[1,2-*a*] pyrimidine parent nucleus involve condensation of 2-aminobenzimidazole with acetylene esters,[6] enamino esters,[7] 1,3-diketone,[4] and α,β-unsaturated ketones.[8] It was reported that the chromone fragment present in isoflavones can generate a 1,3-diketone equivalent that readily react with amidines[9] and guanidine[10] to form the corresponding 2-substituted pyrimidines. In the previous work from our laboratory, we reported the synthesis of a number of 3,4-diarylpyrazoles and 4,5-diphenyl-2-pyrimidinylguanidines by using a one-pot reaction of hydrazine[11] or bisguanidine[12] with isoflavones by conventional methods. We were interested in the use of microwave irradiation in organic synthesis, because its use can provide improvements in environmental and economical aspects.[13–15] Moreover, speculation about the influence of microwaves on reaction rates have been

Table 1. Synthesis of 5,6-diphenylimidazo[1,2-*a*]pyrimidine by cyclocondensation of various isoflavones with 2-aminoimidazole slulfate in DMSO



1 2 3

Entry	Substrate	R_1	R_2	R_3	R_4	R_5	R_6	R_7	Time (min)	Yield (%)[a]
1	**1a**	H	O^{i}Pr	H	H	H	H	H	30	70
2	**1b**	H	OMe	H	H	H	H	H	35	63
3	**1c**	H	OMe	H	H	H	OMe	H	30	72
4	**1d**	H	OMe	H	OMe	H	OMe	H	35	67
5	**1e**	H	OMe	OMe	OMe	H	OMe	H	35	76
6	**1f**	H	OEt	H	H	H	OMe	H	30	69
7	**1g**	H	OMe	H	Me	H	H	H	30	65
8	**1h**	Br	O^{i}Pr	H	H	H	H	H	35	75
9	**1i**	H	OBn	H	H	H	OMe	H	35	66
10	**1j**	H	OMe	H	H	H	OH	H	40	56
11	**1k**	H	OMe	H	H	^{i}Pr	OH	^{i}Pr	40	58
12	**1l**	H	OH	H	H	H	OMe	H	45	52
13	**1m**	H	OH	H	H	H	H	H	50	49
14	**1n**	H	OH	H	H	H	OH	H	55	40
15	**1o**	H	OH	H	H	H	OH	NO_2	55	42
16	**1p**	H	OH	H	H	^{i}Pr	OH	^{i}Pr	55	45
17	**1q**	H	OH	H	OH	H	OH	H	70	29

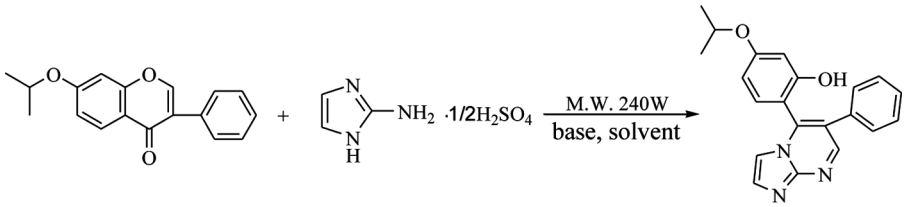
[a]Isolated yield after silica chromatography.

reported whereby the reaction could proceed faster than that under conventional conditions at the same temperature.[16–18] To the best of our knowledge, using isoflavone as a starting material to synthesize the fused heterocycle has not been reported so far. Herein, we report a new strategy for the preparation of the unknown class of 5,6-diphenylimidazo[1,2-*a*]pyrimidine by the cyclocondensation of isoflavones (**1**) with 2-aminoimi-dazole (**2**) (Table 1) under microwave irradiation.

RESULTS AND DISCUSSION

We turned our attention to optimize the condition of the cyclocondensations of isoflavones (**1**) with 2-aminoimidazole (**2**) and designed a process by the cyclocondensation of ipriflavone (**1a**) with 2-aminoimidazole sulfate (**2**) as a model substrate (Table 2). As shown in Table 2, we used NaOH as base, and solvents MeOH, EtOH, *n*-BuOH, glycol, and dimethylsulfoxide (DMSO) were attempted. DMSO gave expected result (Table 2, entry 5). A comparative reactivity study of bases in the reaction showed that NaOH proved to be the most effective for this cyclocondensation (Table 2, entry 5). Further study with varying NaOH equivalents revealed that

Table 2. Optimization of cyclocondensation of ipriflavone **1a** with 2-aminoimidazole sulfate **2**[a]



1a 2 3a

Entry	Solvent	Base	Molar ratios **1a**/**2**/base	Yield (%)[b] **3a**
1	MeOH	NaOH	1:1:2	NR[c]
2	EtOH	NaOH	1:1:2	NR[c]
3	*n*-BuOH	NaOH	1:1:2	18
4	glycol	NaOH	1:1:2	25
5	DMSO	NaOH	1:1:2	32
6	DMSO	K_2CO_3	1:1:2	19
7	DMSO	NaOMe	1:1:2	22
8	DMSO	NaOH	1:1:3	39
9	DMSO	NaOH	1:1:4	46
10	DMSO	NaOH	1:1:5	42
11	DMSO	NaOH	1:2:4	58
12	DMSO	NaOH	1:3:4	70
13	DMSO	NaOH	1:4:4	67

[a]All reactions were carried out in the appropriate solvent (8 mL) using ipriflavone (**1a**, 1 mmol), 2-aminoimidazole sulfate (**2**), and base until complete disappearance of **1a** (microwave irradiation for 0.5 h, MeOH, EtOH at boiling point and *n*-BuOH, glycol, and DMSO at 100 °C, output 240 W, TLC check).
[b]Isolated yield after silica chromatography.
[c]No reaction.

4.0 equiv of base is necessary to obtain a good yield of the condensation product (Table 2, entry 9). Finally, the ratio of **1a** and **2** was also evaluated. Using the ratio of **1a**/**2** (1:3), we obtained a high yield of **3a** for the cyclocondensation reaction (Table 2, entry 12).

With the optimized reaction conditions and proven results in hand, the condensation of a variety of structurally divergent isoflavones (**1**) and 2-aminoimidazole (**2**) were studied to illustrate this concise and general method for the synthesis of 5,6-diphenylimidazo[1,2-*a*]pyrimidine. All substrates smoothly reacted to give the corresponding 5,6-diphenylimidazo[1,2-*a*]pyrimidine in 30–70 min in moderate to good yields, and the results were summarized in Table 1. All products were characterized by infrared (IR), ^{1}H NMR, ^{13}C NMR, and elemental analysis. Single-crystal x-ray diffraction analysis of **3a** (Fig. 1) was used to corroborate the postulated structures unequivocally, which added evidence for the structure.

In general, isoflavone **1** substituted with alkoxy and benzyoxyl groups gave goods yields. In contrast, the presence of the hydroxyl groups gave lower yields. As shown in Table 1, isoflavones **1a–i** (Table 1, entries 1–9), which do not contain hydroxyl groups, gave yields **3** of about 70%. Isoflavone with one hydroxyl group, **1j–m** (Table 3, entries 10–13), gave yields of **3** of only about 55%, whereas those with two free hydroxyls, **1n–p** (Table 3, entries 14–16), gave yields of roughly 40%. Genistein (4′,5,7-trihydroxyisoflavone), **1q** (Table 3, entry 17), was even more difficult to condensate, and the yield of **3q** was only 29%. The yields of **3** are directly dependent on the number of free hydroxyl group present on the engaged isoflavone. Because the hydroxyls of isoflavone **1** under the base condition would be oxygenions, which possess stronger electron-donating abilities than alkoxy and benzyoxyl groups of the isoflavone, they prevent condensation of the reaction.

To explain the mechanism for the formation of 5,6-diphenylimidazo[1,2-*a*]pyrimidine (**3**) by the cyclocondensation of isoflavones (**1**) with 2-aminoimidazole (**2**) in the presence of NaOH, a postulated reaction course is illustrated in Scheme 1. It was reported that isoflavone may undergo a ring-opening reaction when refluxing in the presence of alkali to form a β-diketone intermediate **4**.[19] Subsequent attack of the primary amine group from the 2-aminoimidazole (**2**) on the aldehyde carbon in **4**, followed by a ring-closure reaction between the secondary amine and the carbonyl

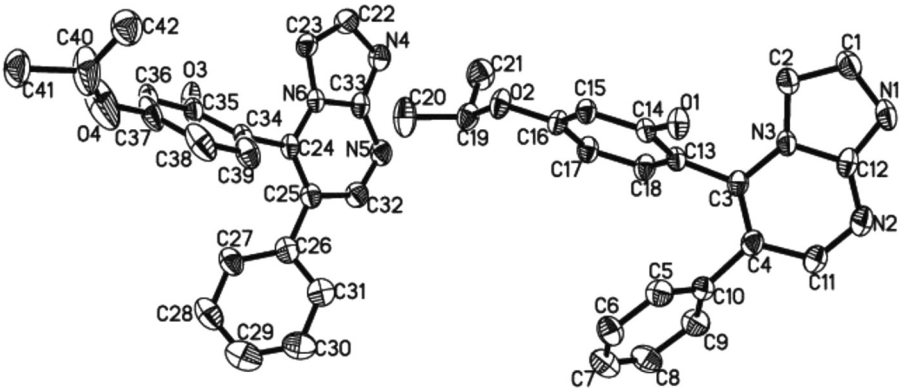
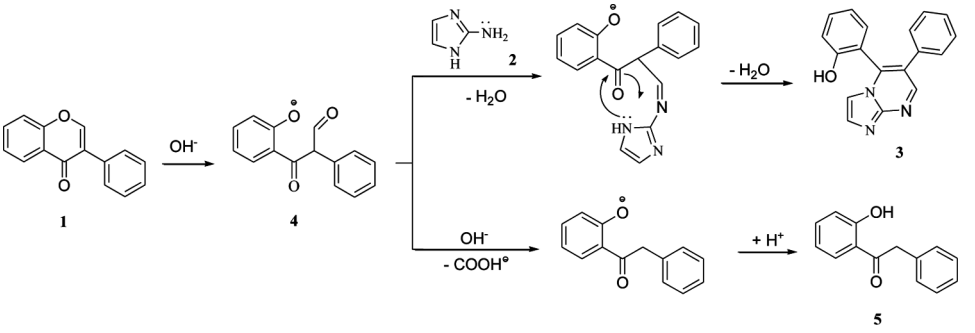


Figure 1. Unit of asymmetry of **3a**. Hydrogen atoms were omitted for clarity.



Scheme 1. Proposed mechanism for the formation of **3**.

carbon, produced **3**. Meanwhile, the intermediate **4** at high concentration of base may eliminate HCOOH to generate by-product **5**.[19]

CONCLUSION

In summary, we have developed a simple, efficient, one-step method for the synthesis of functionalized 5,6-diphenylimidazo[1,2-*a*]pyrimidine by the cyclocondensations of isoflavones with 2-aminoimidazole under microwave irradiation conditions. These compounds present a privileged core from a biological point of view. Also, we report here for the first time that reaction of an aminoimidazole with isoflavones in the presence of a base affords the fused 5,6-diphenylimidazo[1,2-*a*]pyrimidine. Efforts to expand the scope of the method in combination with its application to the synthesis of pharmaceutical molecules are ongoing in our laboratory.

EXPERIMENTAL

All other commercially obtained reagents were used as received without further purification, including 2-aminoimidazole slulfate, ipriflavone, daiazein, genistein, formonone, and 5-methyl-7-methoxylisoflavone. Substrates **1b**, **1h**, and **1m** were derived from ipriflavone. Substrates **1c, 1j, 1k, 1o**, and **1p** were derived from daiazein. Substrate **1d** was derived from genistein. Substrate **1f** and **1i** were derived from formonone. Substrate **1e** derived from irisolidone (4′,6-dialkoxy-5,7-dihydroxyisoflavone) was separated from the flower of *pueraria lobata* by our group. The microwave-assisted reactions were performed using a MCR-3 microwave oven quipped with a Teflon Resin plus temperature probe as sensor. Melting points were measured on X-5 micromelting-point apparatus and were uncorrected. IR spectra were recorded on a Fourier transform (FT)–IR spectrometer using KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-300 Avance spectrometer at 300.00 MHz in dimethylsulfoxide (DMSO-d_6) with tetramethylsilane (TMS) as internal standard. The elemental analyses were performed with an Elementar Analysensyteme GmbH Vario EL III instrument. X-ray crystallography dates were given by a Bruker Smart-1000 CCD diffactometer.

General Procedure for the Condensation Reaction

The corresponding isoflavones **1** (1 mmol), 2-aminoimidazole sulfate (**2**, 3 mmol), sodium hydroxide (4, 5, 6, and 7 mmol were used for 0, 1, 2, and 3 free hydroxyls, of **1**, respectively), and water (1.0 mL) were mixed in DMSO (8 mL) under microwave irradiation (output 240 W, 100 °C) for 30–70 min. All reactions were monitored by thin-layer chromatography (TLC), which showed the disappearance of **1** that was indicative of the reaction being complete. The mixture was added to water (30 mL) and adjusted to neutrality with a solution of 5% HCl. A precipitate appeared and was filtered. The precipitate was dissolved in a solution of 10% HCl (20 mL) and filtered. The mother liquid was neutralized with sodium hydroxide until the crude product was completely precipitated. The crude product was filtered and purified by column chromatography on silica gel using chloroform–methanol to give the corresponding pure product.

Data for Compounds 3a–3q

5-(2-Hydroxyl-4-isopropoxyphenyl)-6-phenylimidazo[1,2-*a*]pyrimidine (3a). White solid, mp 207.6–208.5 °C. IR (KBr), ν (cm^{-1}): 3435, 2979, 2931, 2579, 1612, 1487, 1178, 1119, 1110, 993, 702. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.26 (d, $J = 5.9$ Hz, 6H), 4.51–4.59 (m, 1H), 6.37 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.7$ Hz, 1H), 6.52 (d, 1H), 6.91 (d, $J = 8.5$ Hz, 1H), 7.28–7.35 (m, 6H), 7.71 (s, 1H), 8.62 (s, 1H), 10.15 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 21.6, 69.6, 102.7, 107.0, 110.0, 111.0, 122.4, 127.6, 128.3, 129.3, 131.4, 134.3, 134.9, 141.6, 147.5, 151.3, 156.5, 160.2. Anal. calcd. for $C_{21}H_{19}N_3O_2$: C, 73.03; H, 5.54; N, 12.17. Found: C, 72.86; H, 5.79; N, 12.28.

5-(2-Hydroxyl-4-methoxyphenyl)-6-phenylimidazo[1,2-*a*]pyrimidine (3b). White solid, mp 243.6–244.8 °C. IR (KBr), ν (cm^{-1}): 3493, 2961, 2931, 1613, 1492, 1437, 1206, 1033, 706. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.69 (s, 3H), 6.36 (d, $J = 8.4$ Hz, 1H), 6.52 (s, 1H), 6.87 (d, $J = 8.6$ Hz, 1H), 7.16–7.27 (m, 6H), 7.67 (s, 1H), 8.58 (s, 1H), 10.22 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 55.6, 101.9, 106.1, 111.0, 111.3, 122.7, 127.9, 128.8, 129.8, 132.0, 135.0, 135.6, 141.9, 148.2, 151.6, 157.3, 162.4. Anal. calcd. for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.72; H, 4.93; N, 13.45.

5-(2-Hydroxyl-4-methoxyphenyl)-6-(4-methoxyphenyl)imidazo[1,2-*a*]-pyrimidine (3c). White solid, mp 176.6–177.5 °C. IR (KBr), ν (cm^{-1}): 3436, 2936, 2834, 2567, 1612, 1495, 1432, 1295, 1238, 1174, 1129, 1033, 976, 810, 745; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.74 (s, 6H), 6.42 (d, $J = 8.2$ Hz, 1H), 6.55 (s, 1H), 6.88 (d, $J = 7.6$ Hz, 2H), 6.95 (d, $J = 8.2$ Hz, 1H), 7.19 (d, $J = 8.0$ Hz, 3H), 7.69 (s, 1H), 8.59 (s, 1H), 10.09 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 55.1, 101.6, 105.7, 110.6, 110.7, 113.8, 121.9, 127.3, 130.5, 131.4, 134.4, 141.0, 147.7, 151.2, 156.7, 158.6, 161.8. Anal. calcd. for $C_{20}H_{17}N_3O_3$: C, 69.15; H, 4.93; N, 12.10. Found: C, 69.37; H, 4.79; N, 11.88.

5-(2-Hydroxyl-4,6-dimethoxyphenyl)-6-(4-methoxyphenyl)imidazo[1,2-*a*]pyrimidine (3d). White solid, mp 149.7–150.9 °C. IR (KBr), ν (cm^{-1}): 3003, 2936, 2839, 2567, 1612, 1494, 1248, 1107, 1030, 828, 560; ^{1}H NMR (300 MHz,

DMSO-d_6), δ (ppm): 3.51 (s, 3H), 3.71 (s, 3H), 3.73 (s, 3H), 6.15 (s, 2H), 6.87 (d, $J = 8.0$ Hz, 2H), 7.20 (d, 3H), 7.66 (s, 1H), 8.56 (s, 1H), 10.07 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 55.5, 55.6, 55.9, 90.8, 94.3 100.4, 110.9, 114.1, 114.2, 123.7, 128.2, 130.2, 134.8, 138.8, 148.3, 151.4, 157.4, 159.2, 163.2. Anal. calcd. for $C_{21}H_{19}N_3O_4$: C, 66.83; H, 5.07; N, 11.13. Found: C, 66.97; H, 5.21; N, 10.93.

5-(2-Hydroxyl-4,5,6-trimethoxyphenyl)-6-(4-methoxyphenyl)imidazo[1,2-*a*]pyrimidine (3e). Yellow solid, mp 153.2–154.6 °C. IR (KBr), ν (cm^{-1}): 3235, 2938, 1608, 1499, 1463, 1413, 1247, 1105, 1034, 831, 561; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.33 (s, 3H), 3.54 (s, 3H), 3.67 (s, 3H), 3.73 (s, 3H), 6.33 (s, 1H), 6.84 (d, $J = 8.0$ Hz, 2H), 7.19–7.21 (t, 3H), 7.63 (s, 1H), 8.56 (s, 1H), 9.86 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 55.6, 56.1, 60.9, 61.0, 96.1, 104.2, 111.0, 114.0, 114.3, 123.3, 127.9, 130.4, 134.9, 138.3, 148.3, 151.4, 151.5, 152.2, 156.1, 159.3. Anal. calcd. for $C_{22}H_{21}N_3O_5$: C, 64.86; H, 5.20; N, 10.31. Found: C, 64.98; H, 5.45; N, 10.12.

5-(2-Hydroxyl-4-ethoxyphenyl)-6-(4-methoxyphenyl)imidazo[1,2-*a*]pyrimidine (3f). Yellow solid, mp 199.4–201.5 °C. IR (KBr), ν (cm^{-1}): 3410, 2930, 1607, 1489, 1252, 1187, 1036, 831, 466; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.32 (s, 3H), 3.73 (s, 3H), 3.99 (d, $J = 5.9$ Hz, 2H), 6.40 (d, $J = 6.8$ Hz, 1H), 6.55 (s, 1H), 6.88–6.94 (t, 3H), 7.20 (d, $J = 8.2$ Hz, 3H), 7.70 (s, 1H), 8.60 (s, 1H), 10.18 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 15.1, 55.5, 63.6, 102.4, 106.5, 111.0, 111.2, 114.3, 122.4, 127.7, 131.0, 131.9, 134.8, 141.5, 148.2, 151.8, 157.2, 159.1, 161.6. Anal. calcd. for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63. Found: C, 69.60; H, 5.12; N, 11.87.

5-(2-Hydroxyl-4-methoxy-6-methylphenyl)-6-phenylimidazo[1,2-*a*]pyrimidine (3g). White solid, mp 231.8–232.9 °C. IR (KBr), ν (cm^{-1}): 3407, 2964, 1614, 1585, 1491, 1445, 1332, 1271, 1143, 1038, 836, 704. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.67 (s, 3H), 3.73 (s, 3H), 6.33 (s, 1H), 6.42 (s, 1H), 7.16 (s, 1H), 7.33 (s, 5H), 7.72 (s, 1H), 8.66 (s, 1H), 10.09 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 18.8, 54.9, 99.0, 106.8, 110.2, 110.4, 122.8, 127.7, 128.3, 128.7, 134.8, 135.1, 137.9, 140.5, 147.8, 151.0, 156.8, 161.4. Anal. calcd. for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.27; H, 5.02; N, 12.85.

5-(2-Hydroxyl-3-bromo-4-isopropoxyphenyl)-6-phenylimidazo[1,2-*a*]pyrimidine (3h). White solid, mp 262.1–262.9 °C. IR (KBr), ν (cm^{-1}): 3504, 3433, 2982, 2608, 1593, 1485, 1263, 1203, 1141, 1109, 1029, 703. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.30 (d, $J = 5.6$ Hz, 6H), 4.58 (m, 1H), 6.68 (s, 1H), 7.24–7.31 (m, 7H), 7.70 (s, 1H), 8.59 (s, 1H), 10.45 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 22.1, 22.2, 71.9, 101.6, 103.1, 111.4, 112.1, 122.9, 128.1, 128.8, 129.8, 134.3, 135.1, 135.4, 140.4, 148.2, 151.5, 156.4, 156.9. Anal. calcd. for $C_{21}H_{18}BrN_3O_2$: C, 59.45; H, 4.28; N, 9.90. Found: C, 59.26; H, 4.41; N, 9.78.

5-(2-Hydroxyl-4-benzyloxyphenyl)-6-(4-methoxyphenyl)imidazo[1,2-*a*]-pyrimidine (3i). Yellow solid, mp 157.8–158.9 °C. IR (KBr), ν (cm^{-1}): 3417, 3033, 2924, 1610, 1491, 1433, 1249, 1179, 1027, 834, 734; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.74 (s, 3H), 5.07 (s, 2H), 6.52 (d, $J = 8.4$ Hz, 1H), 6.65 (s, 1H), 6.89 (d, $J = 8.4$ Hz, 2H), 6.97 (d, $J = 8.4$ Hz, 1H), 7.21 (d, $J = 8.7$ Hz, 3H), 7.35–7.47 (m,

5H), 7.70 (s, 1H), 8.60 (s, 1H), 10.26 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 55.5, 69.8, 102.9, 106.8, 111.2, 111.5, 114.3, 122.4, 127.7, 128.1, 128.4, 128.9, 131.0, 132.0, 134.9, 137.1, 141.4, 148.2, 151.8, 157.2, 159.1, 161.4. Anal. calcd. for $C_{26}H_{21}N_3O_3$: C, 73.74; H, 5.00; N, 9.92. Found: C, 73.50; H, 4.89; N, 10.12.

5-(2-Hydroxyl-4-methoxyphenyl)-6-(4-hydroxylphenyl)imidazo[1,2-*a*]pyrimidine (3j). White solid, mp 272.3–273.8 °C. IR (KBr), ν (cm^{-1}): 3548, 2929, 2600, 1607, 1498, 1442, 1378, 1276, 1219, 1160, 1113, 1027, 956, 832, 716; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.74 (s, 3H), 6.42 (t, 1H), 6.55 (s, 1H), 6.69 (d, $J = 7.8$ Hz, 2H), 6.92 (t, 1H), 7.06 (d, $J = 8.0$ Hz, 2H), 7.21 (d, $J = 0.9$ Hz, 1H), 7.67 (d, $J = 1.0$ Hz, 1H), 8.57 (s, 1H), 9.54 (s, 1H), 10.17 (s, 1H). ^{13}C HMR (75 MHz, DMSO-d_6), δ (ppm): 55.1, 101.6, 105.6, 110.7, 110.9, 115.3, 122.4, 125.5, 130.5, 131.4, 134.0, 141.0, 147.7, 151.5, 156.8, 156.9, 161.8. Anal. calcd. for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.29; H, 4.75; N, 12.46.

5-(2-Hydroxyl-4-methoxyphenyl)-6-(3,5-diisopropyl-4-hydroxyphenyl) imidazo[1,2-*a*]pyrimidine (3k). White solid, mp 247.2–248.6 °C. IR (KBr), ν (cm^{-1}): 3437, 2961, 1619, 1496, 1467, 1318, 1205, 1107, 1033, 880, 723; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 0.99–1.07 (m, 12H), 3.18–3.27 (m, 2H), 3.72 (s, 3H), 6.42 (d, $J = 8.3$ Hz, 1H), 6.61 (s, 1H), 6.88 (d, $J = 8.5$ Hz, 1H), 6.92 (s, 2H), 7.23 (s, 1H), 7.67 (s, 1H), 8.19 (s, 1H), 8.69 (s, 1H), 10.24 (s, 1H). ^{13}C HMR (75 MHz, DMSO-d_6), δ (ppm): 23.2, 23.3, 26.4, 55.6, 102.1, 106.1, 111.1, 111.8, 123.1, 124.7, 126.4, 131.6, 134.7, 135.5, 141.2, 148.1, 150.6, 151.7, 157.5, 162.3. Anal. calcd. for $C_{25}H_{27}N_3O_3$: C, 71.92; H, 6.52; N, 10.06. Found: C, 71.78; H, 6.35; N, 10.27.

5-(2,4-Dihydroxylphenyl)-6-(4-methoxyphenyl)imidazo[1,2-*a*]pyrimidine (3l). White solid, mp 211.2–212.0 °C. IR (KBr), ν (cm^{-1}): 3420, 2915, 1607, 1501, 1395, 1248, 1177, 1097, 1026, 980, 829, 713; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 3.74 (s, 3H), 6.23 (d, $J = 8.2$ Hz, 1H), 6.46 (s, 1H), 6.80 (d, $J = 8.3$ Hz, 1H), 6.89 (d, $J = 8.4$ Hz, 2H), 7.19 (d, $J = 8.3$ Hz, 2H), 7.24 (s, 1H), 7.69 (s, 1H), 8.59 (s, 1H), 9.79 (s, 1H), 9.98 (s, 1H). ^{13}C HMR (75 MHz, DMSO-d_6), δ (ppm): 55.1, 102.9, 107.4, 109.1, 110.8, 114.0, 121.8, 127.4, 130.7, 131.2, 134.3, 141.5, 147.7, 151.2, 156.7, 158.6, 160.2. Anal. calcd. for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.58; H, 4.37; N, 12.49.

5-(2,4-Dihydroxylphenyl)-6-phenylimidazo[1,2-*a*]pyrimidine (3m). Yellow solid, mp 189.1–190.3 °C. IR (KBr), ν (cm^{-1}): 3666, 3389, 1611, 1487, 1111, 701, 463. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 6.24 (d, 1H), 6.45 (d, 1H), 6.74–6.83 (m, 1H), 7.03–7.30 (s, 6H), 7.73 (t, 1H), 8.57-8.67 (m, 1H), 9.81 (d, 1H), 10.02 (d, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 103.3, 107.9, 109.4, 111.3, 122.6, 127.8, 128.7, 129.8, 131.8, 134.9, 135.8, 142.4, 148.2, 151.5, 157.2, 160.8. Anal. calcd. for $C_{18}H_{13}N_3O_2$: C, 71.28; H, 4.32; N, 13.85. Found: C, 71.09; H, 4.56; N, 14.02.

5-(2,4-Dihydroxylphenyl)-6-(4-hydroxylphenyl)imidazo[1,2-*a*]pyrimidine (3n). Yellow solid, mp 212.6–213.9 °C. IR (KBr), ν (cm^{-1}): 3558, 3236, 3150, 2929, 1611, 1493, 1243, 837, 555; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 6.22 (d, $J = 6.9$ Hz, 1H), 6.46 (s, 1H), 6.69 (d, $J = 7.7$ Hz, 2H), 6.76 (d, $J = 8.0$ Hz, 1H),

7.05 (d, $J = 7.5$ Hz, 2H), 7.22 (s, 1H), 7.67 (s, 1H), 8.56 (s, 1H), 9.56 (s, 1H), 9.81 (s, 1H), 9.99 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 103.3, 107.8, 109.7, 111.2, 115.7, 122.6, 126.2, 131.0, 131.8, 134.6, 141.8, 148.1, 151.8, 157.2, 157.3, 160.7. Anal. calcd. for $C_{18}H_{13}N_3O_3$: C, 67.71; H, 4.10; N, 13.16. Found: C, 67.52; H, 4.35; N, 13.29.

5-(2,4-Dihydroxylphenyl)-6-(3-nitro-4-hydroxylphenyl)imidazo[1,2-*a*]-pyrimidine (3o). Yellow solid, mp 230.2–231.5 °C. IR (KBr), ν (cm^{-1}): 3499, 3454, 1613, 1489, 1328, 1267, 1210, 1176, 719; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 6.22 (s, 1H), 6.25 (s, 1H), 6.47 (s, 1H), 6.54 (d, $J = 8.0$ Hz, 1H), 6.59 (s, 1H), 6.78 (d, $J = 8.3$ Hz, 1H), 7.20 (s, 1H), 7.66 (s, 1H), 8.50 (s, 1H), 9.19 (s, 1H), 9.79 (s, 1H), 9.96 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 103.3, 107.7, 109.9, 111.2, 114.6, 115.9, 118.4, 123.4, 126.8, 131.8, 134.4, 136.9, 141.7, 144.0, 148.1, 152.0, 157.1, 160.5. Anal. calcd. for $C_{18}H_{12}N_4O_5$: C, 59.34; H, 3.32; N, 15.38. Found: C, 59.19; H, 3.46; N, 15.51.

5-(2,4-Dihydroxylphenyl)-6-(3,5-diisopropyl-4-hydroxyphenyl)imidazo[1,2-*a*]pyrimidine (3p). Yellow solid, mp 194.7–195.5 °C. IR (KBr), ν (cm^{-1}): 3602, 3544, 2964, 1613, 1466, 1442, 1109, 471; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.00–1.08 (m, 12H), 3.24 (d, 2H), 6.23 (d, $J = 7.8$ Hz, 1H), 6.50 (s, 1H), 6.73 (d, $J = 8.0$ Hz, 1H), 6.95 (t, 2H), 7.24 (d, $J = 7.7$ Hz, 1H), 7.68 (d, $J = 7.9$ Hz, 1H), 8.16 (s, 1H), 8.70 (t, 1H), 9.73 (s, 1H), 10.00 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 23.3, 26.4, 103.1, 107.8, 110.0, 111.1, 123.0, 124.7, 126.5, 131.4, 134.6, 135.4, 141.6, 148.1, 150.6, 151.7, 157.3, 160.7. Anal. calcd. for $C_{24}H_{25}N_3O_3$: C, 71.44; H, 6.25; N, 10.41. Found: C, 71.28; H, 6.41; N, 10.59.

5-(2,4,6-Trihydroxylphenyl)-6-(4-hydroxylphenyl)imidazo[1,2-*a*]pyrimidine (3q). White solid, mp 292.2–293.5 °C. IR (KBr), ν (cm^{-1}): 3494, 3445, 3221, 1643, 1512, 1438, 1267, 1184, 836; ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 5.87 (s, 1H), 6.15 (s, 1H), 6.81 (s, 2H), 7.21–7.30 (m, 2H), 7.48 (d, 2H), 8.04 (d, 1H), 9.51 (s, 1H), 10.47 (s, 1H), 12.96 (s, 1H), 14.76 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm): 91.9, 98.8, 107.3, 115.4, 119.9, 124.5, 130.4, 140.0, 141.3, 143.3, 157.2, 163.3, 164.0, 180.1. Anal. calcd. for $C_{18}H_{13}N_3O_4$: C, 64.47; H, 3.91; N, 12.53. Found: C, 64.62; H, 3.69; N, 12.70.

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