Microwave-assisted Efficient Synthesis of benzo[4,5]imidazo[1,2-*a*]-pyrimidine Derivatives in Water under Catalyst-free Conditions

Shujiang Tu, * Qingqing Shao, Dianxiang Zhou, Longji Cao, Feng Shi, Chunmei Li

Department of Chemistry, Xuzhou Normal University, Key Laboratory of Biotechnology on Medical Plant, Xuzhou, Jiangsu 221116, PR China

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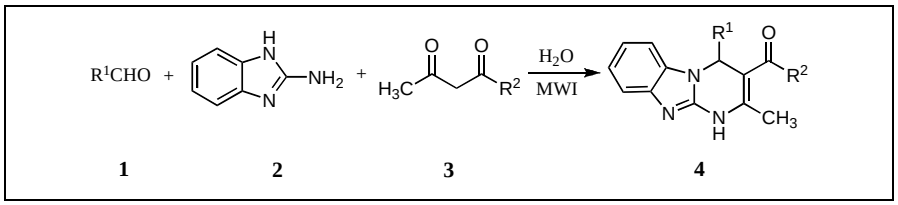

Benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives were synthesized *via* the three-component reaction of aldehyde, β-dicarbonyl compound and 2-aminobenzimidazole in water under microwave irradiation and without catalyst conditions. The new protocol has the advantages of higher yield, lower cost, reduced environment impact, wider scope and convenient procedure.

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INTRODUCTION

The rapid assembly of molecular diversity is an important goal of synthetic organic chemistry and one of the key paradigms of modern drug discovery [1,2]. One approach to address this challenge involves the development of multicomponent reactions (MCRs), in which three or more reactants are combined together in a single reaction flask to generate a product incorporating most of the atoms contained in the starting materials [3,4]. Diversity can be achieved by simply varying each component or just changing the reaction conditions [5,6]. In addition to the intrinsic atom economy and selectivity underlying such reactions, simpler procedures and equipment, time, and energy savings, as well as environmental friendliness have all led to a sizable effort to design and implement MCRs in both academia and industry [7].

As early as in the 1980's Breslow demonstrated hydrophobic effects could strongly enhance the rate of some organic reactions and rediscovered the use of water as solvent in organic chemistry [8,9]. Since then, the use of water as a solvent has attracted considerable research interest [10-12]. Water, compared with organic solvents, is abundant, nontoxic and environment-friendly. Therefore, it has become an attractive medium for many organic reactions [13-15], not only for the advantages concerning the avoidance of expensive drying agents, catalysts and solvents, but also for some unique reactivity and selectivity [16-19].

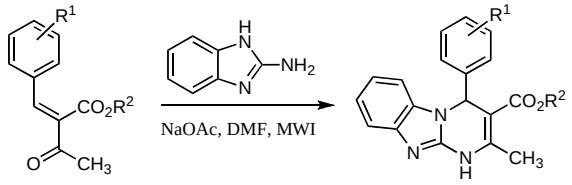
The microwave (MW) assisted organic synthesis has been a topic of continued studies as it could lead to higher yields of pure products, easier operation and shorter reaction time as compared to the traditional heating methods [20-23]. Use of MW irradiation for the formation of carbon-heteroatoms, especially carbon-nitrogen bonds, has been reported [24-27].

The classic version of the Biginelli three-component condensation reaction [28], which combines an aldehyde, urea or thiourea and an open-chain β-dicarbonyl compound under acidic conditions in ethanol to give a monocyclic 3,4-dihydropyrimidin-2(1*H*)-one (DHPs), has extended into widespread use of generating large collections of molecules in combinatorial synthesis [29,30].

Recently much attention has been devoted towards dihydropyrimidine derivatives due to their significant therapeutic and medicinal properties [31-33]. Several marine alkaloids having the dihydropyrimidine core unit were found to show interesting biological activities such as antiviral, antibacteriala and anti-inflammatory activities [34,35]. Many functionalized derivatives are used as calcium channel blockers, antihypertensive agents and α-la antagonists [36,37]. Therefore, the preparation of this heterocyclic core unit has gained much importance.

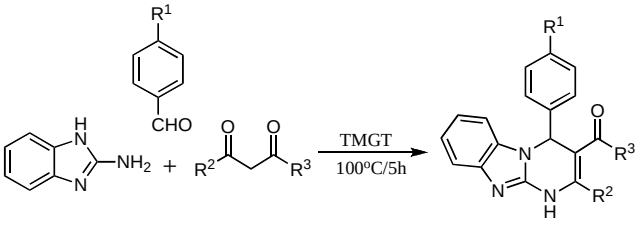
Julio Alvarez-Builla and co-workers reported the synthesis of benzo[4,5]imidazo[1,2-*a*]-pyrimidine derivatives with an requisite arylmethyleneacetoacetate, which could be synthesized *via* standard Knoevenagel reaction of aldehyde and β-ketoester. NaOAc was used as catalyst and DMF as organic solvent in the protocol [38] (Scheme 1).

Scheme 1



Ahmad Shaabani and co-workers also reported the three-component condensation reaction of an aldehyde, β-ketoester and 2-aminobenzimidazole in 1,1,3,3-N,N,N',N'-tetramethylguanidinium trifluoroacetate (TMGT) as an ionic liquid affording 4*H*-pyrimido[2,1-*b*]benzazolea derivatives, with the shortage of long reaction time and the limitation that the benzaldehydes must be substituted in the *para*-position (Scheme 2) [39].

Scheme 2



Interested in biological activity of a significant number of compounds containing condensed pyrimidine ring system, MCRs and Biginelli-like reactions, we wish to report a facile, rapid and green protocol for the three component condensation reactions of an aldehyde, a β-dicarbonyl compound and 2-aminobenzimidazole.

RESULTS AND DISCUSSION

Choosing an appropriate solvent is of crucial importance for successful MW promoted synthesis in view of a rapid rise of temperature in the reaction mixture. In order to search for the optimum solvent, the MW assisted reaction of 4-chlorobenzaldehyde (**1b**), ethyl 3-oxobutanoate and 2-aminobenzimidazole was examined using water, ethyleneglycol, ethanol, glacial acetic acid and DMF as solvent, respectively, at 90 °C. All the reactions were carried out at the power of 200 W. The results are summarized in Table 1.

Table 1

Solvent Optimization for the Synthesis of **4b** under MWI at 90 °C

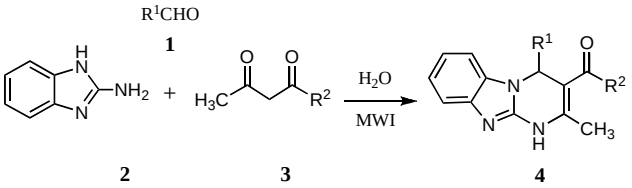
Entry	Solvent	Power (W)	Time (min)	Yield (%)
1	Water	200	6	92
2	ethyleneglycol	200	8	90
3	EtOH	200	10	76
4	HOAc	200	20	50
5	DMF	200	14	45

It is shown in Table 1 the reaction with water as solvent resulted in the most excellent yield and shortest reaction time. Water was used as the solvent for all further microwave-assisted reactions as it is also environmentally friendly and the use of expensive organic reagents can be avoided.

Microwave irradiation power was also optimized for the synthesis of **4b**. The most suitable irradiation power was 200 W.

Based on these optimized reaction conditions, a series of benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives were synthesized by equimolecular amounts of aldehyde, β-dicarbonyl compound and 2-aminobenzimidazole in water under microwave irradiation. After irradiation for 3-6 min, the benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives were obtained in excellent yields (84-95%) (Scheme 3). The results were summerized in Table 2.

Scheme 3



As shown in Table 2, this protocol could be applied not only to the aromatic aldehydes with either electron-withdrawing groups or electron-donating groups, but also to aliphatic aldehydes, which highlighted the wide scope of this three-component condensation. Furthermore, the procedure is easy to operate and the workup procedure is just simple filtration.

Moreover, we performed the synthesis of **4b** under both MWI and classical heating conditions. The reaction was efficiently promoted by MWI and the reaction time was strikingly shortened to 6 min from 5 h required under traditional heating condition and the yield was increased to 92% from 51%. Therefore, microwave irradiation exhibited several advantages over the conventional heating by significantly reducing the reaction time and dramatically improving the reaction yield owing to a specific nonthermal microwave effect [40].

Although the detailed mechanism of the above reaction remains to be fully clarified, the formation of benzo[4,5]-imidazo[1,2-*a*]pyrimidine derivatives **4** could be explained by the reaction sequence presented in Scheme 4. During the course of reaction, the colour of bright yellow appeared first, while the reaction system was rather pale when the reaction ended. The bright yellow substance was Schiff base **5**, condensed of aldehyde and 2-aminobenzimidazole, which was characterized by IR and ^{1}H NMR spectral data.

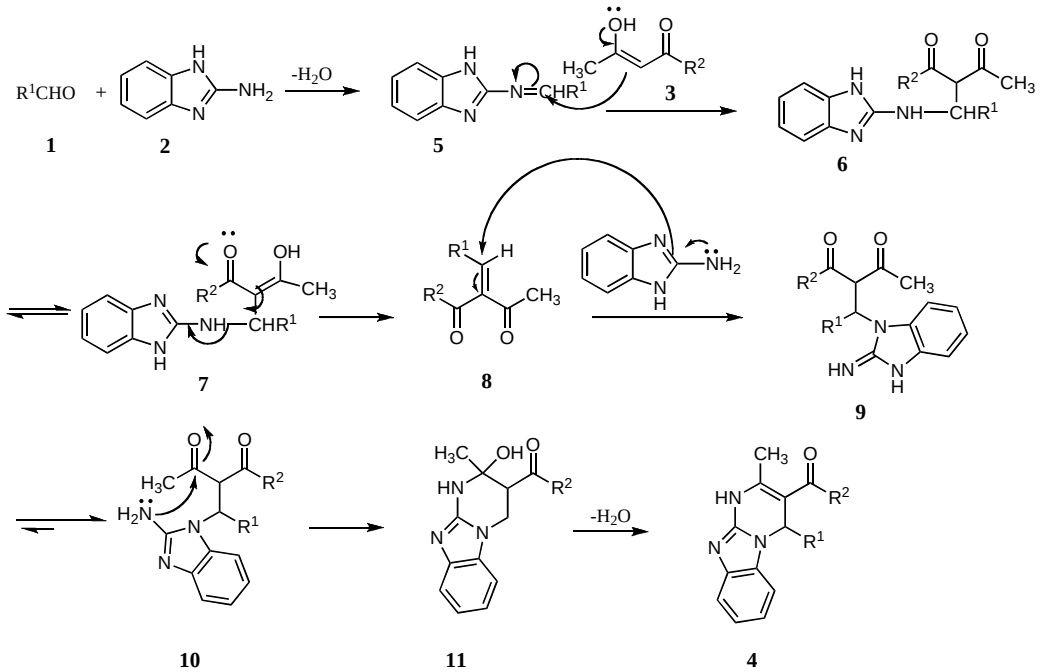
We therefore proposed that the reaction proceeded *via* a sequence of condensation, addition, elimination, addition, cyclization and dehydration. First, the condensation of aldehyde and 2-aminobenzimidazole gave Schiff base **5**. The addition of Schiff base to 1,3- dicarbonyl compound, then after elimination furnished the intermediate product **8**. Then the addition of 2-aminobenzimidazole to **8** gave the intermediate product **10**, which upon intermolecular cyclization and dehydration gave rise to **4**.

Table 2

Physical Data of Compounds **4**

Compound No.	R^1	**3**	R^2	Time(min)	Yield(%)	Mp(℃)
4a	4-FC_6H_4	**3a**	C_2H_5O	5	91	>300
4b	4-ClC_6H_4	**3a**	C_2H_5O	6	92	>300
4c	4-BrC_6H_4	**3a**	C_2H_5O	6	90	>300
4d	4-$MeOC_6H_4$	**3a**	C_2H_5O	5	88	272-273
4e	4-$NO_2C_6H_4$	**3a**	C_2H_5O	4	91	>300
4f	3-$NO_2C_6H_4$	**3a**	C_2H_5O	4	90	294-297
4g	C_6H_5	**3a**	C_2H_5O	5	90	294-297
4h	2,4-$Cl_2C_6H_3$	**3a**	C_2H_5O	3	94	>300
4i	2-ClC_6H_4	**3a**	C_2H_5O	5	90	>300
4j	4-FC_6H_4	**3b**	CH_3	4	87	>300
4k	4-ClC_6H_4	**3b**	CH_3	5	89	>300
4l	4-BrC_6H_4	**3b**	CH_3	5	88	>300
4m	4-$MeOC_6H_4$	**3b**	CH_3	6	85	279-282
4n	4-$NO_2C_6H_4$	**3b**	CH_3	4	90	>300
4o	3-$NO_2C_6H_4$	**3b**	CH_3	5	91	290-292
4p	C_6H_5	**3b**	CH_3	6	86	>300
4q	2,4-$Cl_2C_6H_3$	**3b**	CH_3	4	95	>300
4r	2-ClC_6H_4	**3b**	CH_3	5	89	>300
4s	n-C_4H_9	**3b**	CH_3	5	84	236.3-237

Scheme 4



To test the proposed mechanism, we carried out the synthesis of **4b** in two steps, first of which was to get the pure Schiffe base **5b**, and then reacted with **3a** under similar conditions. The target compound of **4b** was obtained with yield similar to the one-pot reaction. The fact supported the proposed mechanism (Scheme 4).

In this study, all the products were characterized by melting point, IR and ^{1}H NMR spectral data, as well as elemental analyses. Furthermore, the structure of **4d** was established by X-ray crystallographic analysis (Figure 1).

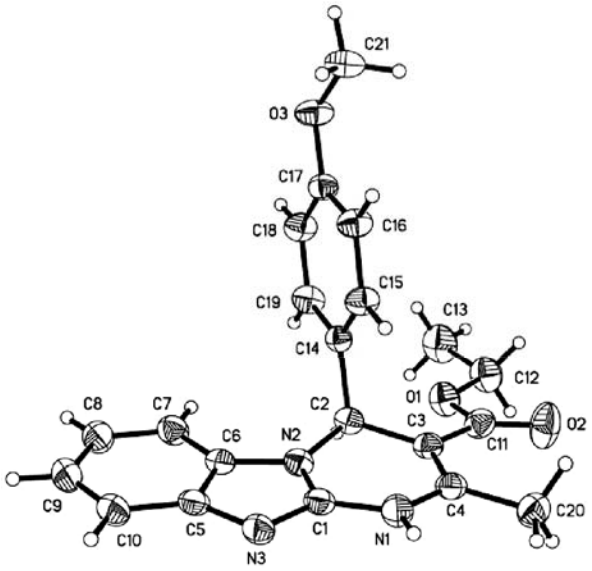


Figure 1

In conclusion, we have developed a three-component reaction of an aldehyde, β-dicarbonyl compound and 2-aminobenzimidazole in water under microwave irradiation conditions for the synthesis of benzo[4,5]imidazo[1,2-*a*]-pyrimidine derivatives. Particularly valuable features of this method include excellent yields of the products, shorter reaction time, reduced environmental impact, and straightforward procedure.

EXPERIMENTAL

Microwave irradiation was carried out in a monomodal Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27 spectrometer in KBr. ^{1}H NMR spectra were measured on a DPX 400 spectrometer operating at 400 MHz, using DMSO-d_6 as solvent and TMS as internal standard. Elemental analyses were determined by using a Perkin-Elmer 240c elemental analysis instrument.

General Procedure for the synthesis of benzo[4,5]imidazo-[1,2-*a*]pyrimidine derivatives (4a-4s). In a 10 mL Emrys™ reaction vial, aldehyde (1 mmol), β-dicarbonyl compound (1 mmol), 2-aminobenzimidazole (1 mmol) and water (2 mL) were mixed and then capped. After irradiation for 3-6 min, the reaction mixture was cooled to room temperature. Then the mixture was filtered to give the crude product, which was further purified by crystallized from 95% EtOH.

4-(4-Fluoro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxylic acid ethyl ester (4a). This compound was obtained according to above general procedure; ir (potassium bromide): cm^{-1} 3235, 3039, 2929, 1697, 1617, 1458, 1303, 1096, 792, 637; ^{1}H nmr (DMSO-d_6): δ 10.84 (s, 1H, NH), 7.43-7.40 (m, 2H, ArH), 7.35 (d, 1H, J = 8.0 Hz, ArH), 7.28 (d, 1H, J = 7.6 Hz,ArH), 7.12-7.03 (m, 3H, ArH), 6.96 (t, 1H, J = 7.6 Hz, ArH), 6.46(s, 1H, CH), 4.02 (q, 2H, J = 7.2 Hz, CH_2), 2.46 (s, 3H, CH_3), 1.15 (t, 3H, J = 7.2 Hz, CH_3). *Anal* calcd. for $C_{20}H_{18}FN_3O_2$: C, 68.36; H, 5.16; N, 11.96. Found: C, 68.46; H, 5.11; N, 11.89.

4-(4-Chloro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxylic acid ethyl ester (4b). This compound was obtained according to above general procedure; ir (potassium bromide): 3234, 3101, 3025, 2981, 2863, 1696, 1617, 1572, 1516, 1385, 1284, 1168, 893, 753cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.87 (s, 1H, NH), 7.40-7.26 (m, 6H, ArH), 7.05 (t, 1H, J = 7.6 Hz, ArH), 6.96 (t, 1H, J = 7.2 Hz, ArH), 6.46 (s, 1H, CH), 4.02 (q, 2H, J = 8.0 Hz, CH_2), 2.46 (s, 3H, CH_3), 1.15 (t, 3H, J = 7.2 Hz, CH_3). *Anal*. Calcd. for $C_{20}H_{18}ClN_3O_2$: C, 65.31; H, 4.93; N, 11.42. Found: C, 65.41; H, 4.89; N, 11.44.

4-(4-Bromo-phenyl)-2-methyl-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxylic acid ethyl ester (4c). This compound was obtained according to above general procedure; ir (potassium bromide): 3233, 3101, 3023, 2978, 2849, 1698, 1618, 1571, 1487, 1385, 1234, 1010, 893, 801, 730 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.87 (s, 1H, NH), 7.47 (d, 2H, J = 8.4 Hz, ArH), 7.36-7.32 (m, 3H, ArH), 7.26 (d, 1H, J = 8.0 Hz, ArH), 7.06 (t, 1H, J = 7.6 Hz, ArH), 6.96 (t, 1H, J = 8.0 Hz, ArH), 6.45 (s, 1H, CH), 4.02 (q, 2H, J = 8.0 Hz, CH_2), 2.46 (s, 3H, CH_3), 1.16 (t, 3H, J = 7.2 Hz, CH_3). *Anal*. Calcd. for $C_{20}H_{18}BrN_3O_2$: C, 58.26; H, 4.40; N, 10.19. Found: C, 58.16; H, 4.52; N, 10.20.

4-(4-Methoxy-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidine-3-carboxylic acid ethyl ester (4d). This compound was obtained according to above general procedure; ir (potassium bromide): 3231, 3011, 2907, 2839, 1703, 1511, 1297, 1179, 1022, 911, 876, 734, 632 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.77 (s, 1H, NH), 7.34 (d, 1H, J = 8.0 Hz, ArH), 7.29-7.25 (m, 3H, ArH), 7.04 (t, 1H, J = 7.2 Hz, ArH), 6.95 (t, 1H, J = 7.6 Hz, ArH), 6.81 (d, 2H, J = 4.8 Hz, ArH), 4.02 (q, 2H, J = 8.0 Hz, CH_2), 3.67 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3), 1.16 (t, 3H, J = 7.2 Hz, CH_3). *Anal*. Calcd. for $C_{21}H_{21}N_3O_3$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.52; H, 5.78; N, 11.61.

4-(4-Nitro-phenyl)-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]-pyrimidine-3-carboxylic acid ethyl ester (4e). This compound was obtained according to above general procedure; ir (potassium bromide): 3234, 3105, 2978, 2861, 1697, 1619, 1572, 1518, 1458, 1235, 870, 755, 715, 608 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.99 (s, 1H, NH), 8.15 (d, 2H, J = 8.4 Hz, ArH), 7.66 (d, 2H, J = 8.8 Hz, ArH), 7.37 (d, 1H, J = 7.6 Hz, ArH), 7.28 (d, 1H, J = 7.6 Hz, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.96 (t, 1H, J = 7.2 Hz, ArH), 6.62 (s, 1H, CH), 4.03 (q, 2H, J = 7.6 Hz CH_2), 2.48 (s, 3H, CH_3), 1.16 (t, 3H, J = 7.2 Hz, CH_3). *Anal*. Calcd. for $C_{20}H_{18}N_4O_4$: C, 63.48; H, 4.79; N, 14.81. Found: C, 63.35; H, 4.81; N, 14.79.

4-(3-Nitro-phenyl)-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]-pyrimidine-3-carboxylic acid ethyl ester (4f). This compound was obtained according to above general procedure; ir (potassium bromide): 3232, 3092, 3023, 2980, 2903, 2844, 1707, 1618, 1573, 1457, 1350, 1170, 891, 820, 743 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.99 (s, 1H, NH), 8.08–8.06 (m, 1H, ArH), 7.76 (d, 2H, J = 8.0 Hz, ArH), 7.58 (t, 1H, J = 8.0 Hz, ArH), 7.37 (d, 1H, J = 8.0 Hz, ArH), 7.32 (d, 1H, J = 8.0 Hz, ArH), 7.07 (t, 1H, J = 7.6 Hz, ArH), 6.96 (t, 1H, J = 7.2 Hz, ArH), 6.67 (s, 1H, CH), 4.02 (q, 2H, J = 7.2 Hz, CH_2), 2.48 (s, 3H, CH_3), 1.17 (t, 3H, J = 6.8 Hz, CH_3). *Anal*. Calcd. for $C_{20}H_{18}N_4O_4$: C, 63.48; H, 4.79; N, 14.81. Found: C, 63.35; H, 4.81; N, 14.79.

2-methyl-4-phenyl-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]-pyrimidine-3-carboxylic acid ethyl ester (4g). This compound was obtained according to above general procedure; ir (potassium bromide): 3234, 3103, 3026, 2928, 2865, 1698, 1615, 1572, 1365, 1255, 1092, 893, 794, 730 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.82 (s, 1H, NH), 7.35 (t, 3H, J = 6.8 Hz, ArH),

7.27 (t, 3H, J = 8.0 Hz, ArH), 7.20-7.16 (m, 1H, ArH), 7.04(t, 1H, J = 8.0 Hz, ArH), 6.95 (t, 1H, J = 7.6 Hz, ArH), 6.43 (s, 1H, CH), 4.02 (q, 2H, J = 7.2 Hz, CH_2), 2.46 (s, 3H, CH_3), 1.14 (t, 3H, J = 7.2 Hz, CH_3). *Anal.* Calcd. for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60. Found: C, 72.18; H, 5.82; N, 12.54.

4-(2,4-Dichloro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidine-3-carboxylic acid ethyl ester (4h). This compound was obtained according to above general procedure; ir (potassium bromide): 3233, 3101, 2973, 2929, 2863, 1698, 1618, 1515, 1458, 1385, 1046, 909, 866, 694 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.98 (s, 1H, NH), 7.58-7.49 (m, 2H, ArH), 7.40-7.36 (m, 2H, ArH), 7.16 (d, 1H, J = 8.0 Hz, ArH), 7.07 (t, 1H, J = 7.2 Hz, ArH), 6.98 (t, 1H, J = 7.2 Hz, ArH), 6.75 (s, 1H, CH), 4.01 (q, 2H, J = 8.0 Hz, CH_2), 2.47 (s, 3H, CH_3), 1.11(t, 3H, J = 7.2 Hz, CH_3).*Anal.* Calcd. for $C_{20}H_{17}Cl_2N_3O_2$: C, 59.71; H, 4.26; N, 10.45. Found: C, 59.82; H, 4.32; N, 10.42.

4-(2-Chloro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]imi-dazo[1,2-*a*]pyrimidine-3-carboxylic acid ethyl ester (4i). This compound was obtained according to above general procedure; ir (potassium bromide): 3238, 3157, 3106, 2978, 2927, 2849, 1700, 1662, 1576, 1520, 1473, 1366, 1019, 892, 833, 796, 718 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.93 (s, 1H, NH), 7.46 (d, 1H, J = 8.0 Hz, ArH), 7.40-7.35 (m, 2H, ArH), 7.30-7.19 (m, 3H, ArH), 7.05 (t, 1H, J = 7.2 Hz, ArH), 6.96 (t, 1H, J = 7.6 Hz, ArH), 6.76 (s, 1H, CH), 3.97 (q, 2H, J = 8.0 Hz CH_2), 2.47 (s, 3H, CH_3), 1.09 (t, 3H, J = 7.2 Hz, CH_3). *Anal.* Calcd. for $C_{20}H_{18}ClN_3O_2$: C, 65.31; H,4.93; N, 11.42. Found: C, 65.48; H, 4.88; N, 11.36.

1-[4-(4-Fluoro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidin-3-yl]-ethanone (4j). This compound was obtained according to above general procedure; ir (potassium bromide): 3227, 3100, 3022, 2914, 2840, 1653, 1627, 1565, 1459, 1330, 1229, 1006, 954, 854, 747 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.85 (s, 1H, NH), 7.48-7.42 (m, 3H, ArH), 7.35 (d, 1H, J = 8.0 Hz, ArH), 7.12-6.98 (m, 4H, ArH), 6.62 (s, 1H, CH), 2.49 (s, 3H, CH_3), 2.24 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{16}FN_3O$: C, 71.01; H, 5.02; N, 13.08. Found: C, 71.00; H, 5.04; N, 13.05.

1-[4-(4-Chloro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidin-3-yl]-ethanone (4k). This compound was obtained according to above general procedure; ir (potassium bromide): 3227, 3100, 3022, 2838, 1654, 1610, 1566, 1522, 1436, 1380, 1228, 830, 747, 694 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.88 (s, 1H, NH), 7.44-7.33 (m, 6H, ArH), 7.08-6.98 (m, 2H, ArH), 6.61 (s, 1H, CH), 2.49 (s, 3H, CH_3), 2.25 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{16}ClN_3O$: C, 67.56; H, 4.77; N, 12.44. Found: C, 67.67; H, 4.67; N, 12.48.

1-[4-(4-Bromo-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidin-3-yl]-ethanone (4l). This compound was obtained according to above general procedure; ir (potassium bromide): 3297, 3227, 3099, 2918, 2839, 1650, 1607, 1560, 1456, 1308, 887, 742, 655 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.86 (s, 1H, NH), 7.47 (d, 2H, J = 8.0 Hz, ArH), 7.41-7.34 (m, 4H, ArH), 7.08-7.04 (m, 1H, ArH), 7.01-6.97 (m, 1H, ArH), 6.59 (s, 1H, CH), 2.49 (s, 3H, CH_3), 2.25 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{16}BrN_3O$: C, 59.70; H, 4.22; N, 10.99. Found: C, 59.81; H, 4.38; N, 11.10.

1-[4-(4-Hydroxy-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidin-3-yl]-ethanoe; compound with ethane (4m). This compound was obtained according to above general procedure; ir (potassium bromide): 3227, 3099, 3002, 2832, 1654, 1628, 1590, 1514, 1459, 1335, 1228, 958, 807, 744, 659 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.75 (s, 1H, NH), 7.43 (d, 1H, J = 8.0 Hz, ArH), 7.05-6.97 (m, 2H, ArH), 6.83 (d, 2H, J = 8.0 Hz, ArH), 6.57 (s, 1H, CH), 3.67 (s, 3H, OCH_3), 2.47 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). *Anal.* Calcd. for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60. Found: C, 72.13; H, 5.66; N,12.50.

1-[4-(4-Nitro-phenyl)-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]-pyrimidin-3-yl]-ethanone (4n). This compound was obtained according to above general procedure; ir (potassium bromide): 3229, 3022, 2840, 1655, 1592, 1455, 1347, 1230, 824, 742 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.00(s, 1H, NH), 8.13 (d, 2H, J = 8.0 Hz, ArH), 7.67 (d, 2H, J = 8.0 Hz, ArH), 7.41-7.36 (m, 2H, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.99 (t, 1H, J = 7.6 Hz, ArH), 6.73 (s, 1H, CH), 2.52 (s, 3H, CH_3), 2.29 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{16}N_4O_3$: C, 65.51; H, 4.63; N, 16.08. Found: C, 65.60; H, 4.58; N, 16.02.

1-[4-(3-Nitro-phenyl)-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]-pyrimidin-3-yl]-ethanone (4o). This compound was obtained according to above general procedure; ir (potassium bromide): 3215, 3087, 2881, 1649, 1560, 1458, 1267, 1059, 959, 888, 737, 690 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.01 (s, 1H, NH), 8.28 (s, 1H, ArH), 8.05 (d, 1H, J = 8.0 Hz, ArH), 7.81 (d, 1H, J = 8.0 Hz, ArH), 7.58 (t, 1H, J = 7.6 Hz, ArH), 7.45 (d, 1H, J = 8.0 Hz, ArH), 7.37 (d, 1H, J = 8.0 Hz, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.99 (t, 1H, J = 7.6 Hz, ArH), 6.77 (s, 1H, CH), 2.53 (s, 3H, CH_3), 2.30 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{16}N_4O_3$: C,65.51; H, 4.63; N,16.08. Found: C, 65.60; H, 4.58; N, 16.02.

1-(2-Methyl-phenyl-4-methyl-1,4-dihydro-benzo[4,5]imi-dazo[1,2-*a*]pyrimidin-3-yl)-ethanone (4p). This compound was obtained according to above general procedure; ir (potassium bromide): cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.83 (s, 1H, NH), 7.42 (d,3H, J = 8.0 Hz, ArH), 7.35-7.26 (m, 3H, ArH), 7.20-7.16 (m, 1H, ArH), 7.06-6.95 (m, 2H, ArH), 6.60 (s, 1H, CH), 2.49 (s, 3H, CH_3), 2.23(s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{17}N_3O$: C, 75.23; H, 5.65; N, 13.85. Found: C, 75.26; H, 5.76; N, 13.91.

1-[4-(2,4-Dichloro-phenyl)-1,4-dihydro-benzo[4,5]imidazo-[1,2-*a*]pyrimidin-3-yl]-ethanone (4q). This compound was obtained according to above general procedure; ir (potassium bromide) 3230, 3104, 3022, 2840, 1659, 1612, 1523, 1457, 1270, 866, 806, 739: cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.98 (s, 1H, NH), 7.54-7.49 (m, 2H, ArH), 7.37 (d, 2H, J = 8.0 Hz, ArH), 7.24 (d, 1H, J = 8.0 Hz, ArH), 7.07 (t, 1H, J = 7.6 Hz, ArH), 6.99 (t, 1H, J = 7.6 Hz, ArH), 6.79 (s, 1H, CH), 2.50 (s, 3H, CH_3), 2.27 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{15}ClN_3O$: C, 61.30; H, 4.06; N, 11.29. Found: C, 61.48; H, 4.08; N, 11.32.

1-[4-(2-Chloro-phenyl)-2-methyl-1,4-dihydro-benzo[4,5]-imidazo[1,2-*a*]pyrimidin-3-yl]-ethanone (4r). This compound was obtained according to above general procedure; ir (potassium bromide): 3225, 3097, 3019, 2835, 1654, 1611, 1564, 1472, 1436, 1327, 1266, 984, 889, 742, 699 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.92 (s, 1H, NH), 7.48 (d, 1H, J = 6.8 Hz, ArH), 7.31-7.20 (m, 3H, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.98 (t, 3H, J = 8.0 Hz, ArH), 6.82 (s, 1H, CH), 2.49 (s, 3H, CH_3), 2.25 (s, 3H, CH_3). *Anal.* Calcd. for $C_{19}H_{16}ClN_3O$: C, 67.56; H, 4.77; N, 12.44. Found: C, 67.64; H, 4.85; N, 12.39.

1-(4-Butyl-1,4-dihydro-benzo[4,5]imidazo[1,2-*a*]pyrimidin-3-yl]-ethanone (4s). This compound was obtained according to above general procedure; ir (potassium bromide): 3225, 3097, 3019, 2834, 1654, 1610, 1564, 1472, 1436, 1327, 1266, 984, 889, 742, 699 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.50 (s, 1H, NH), 7.50-7.48 (m, 1H, ArH), 7.40-7.38 (m, 1H, ArH), 7.13-7.06 (m, 2H, ArH), 5.70 (s, 1H, CH), 2.40 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 1.91-1.57 (m, 2H, CH_2), 1.11-0.73 (m, 4H, $2CH_2$), 0.70 (t,

3H, J = 8.0 Hz, CH_3).*Anal*. Calcd. for $C_{17}H_{21}N_3O$: C, 72.06; H, 7.47; N, 14.83. Found: C, 72.14; H, 7.45; N, 14.78.

(*E*)-*N*-(4-chlorobenzylidene)-1*H*-benzo(*d*)imidazol-2-amine (5b). In a 10-mL Emrys™ reaction vial, 4-chlorobenzaldehyde (1 mmol), 2-aminobenzimidazole (1 mmol) and water (2 mL) were mixed and then capped. After irradiation for 1 min, the reaction mixture was cooled to room temperature. Then the mixture was filtered to give the crude product, which was further purified by recrystallization from 95% EtOH. Ir (potassium bromide): 3245, 3078, 2973, 2764, 1684, 1585, 1389, 1090, 852, cm^{-1}; ^1H nmr (DMSO-d_6): δ 12.74 (s, 1H, NH), 9.47 (s, 1H, CH), 8.11-8.10 (d, 2H, J = 8.0 Hz, ArH), 7.67 (d, 2H, J = 8.0 Hz, ArH), 7.61-7.59 (m, 1H, ArH), 7.46-7.45(m, 1H, ArH), 7.21-7.19(m, 2H, ArH). *Anal*. Calcd. for $C_{14}H_{10}N_3Cl$: C, 65.76; H, 3.94; N, 16.43. Found: C, 65.71; H, 3.96; N, 16.39.

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