A Rapid and Efficient Method for Synthesis of Pyrimido[1,2-*a*]-benzimidazole Derivatives under Microwave Irradiation

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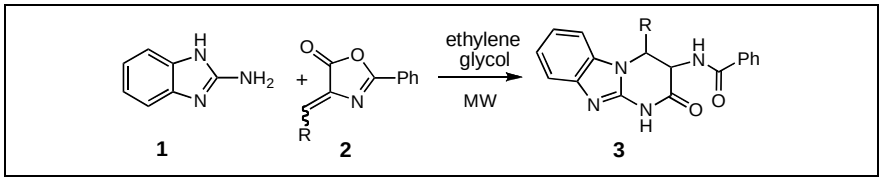

A rapid and efficient method for synthesis pyrimido[1,2-*a*]benzimidazole derivatives from readily available starting materials is accomplished under microwave irradiation. This method has the advantages of short reaction time, operational simplicity, increased safety for small-scale high-speed synthesis, and minimal environment impact.

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INTRODUCTION

For small organic molecules, simple nitrogen-containing heterocycles receive a large amount of attention in the literature, as a consequence of their exciting biological properties and their role as pharmacophores of considerable historical importance. Of these heterocycles, the synthesis, reactions and biological activities of pyridine containing molecules stands as an ever expanding area of research in heteroaromatic chemistry and this structural motif appears in a large number of pharmaceutical agents and natural products [1].

Many biologically active compounds contain bicyclic heterocycles with a bridgehead nitrogen atom.

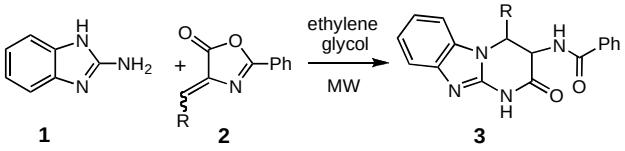
Imidazo[1,2-*a*]pyrimidine structural moieties are important as benzodiazepine receptor agonists [2], antiviral agents [3], antibacterials [4], antifungal agents [5], and calcium channel blockers [6]. Significant effort has been devoted to new synthetic methods and chemical reactivities regarding these ring systems [7,8]. We are interested in preparing imidazo[1,2-*a*]pyrimidine skeleton as intermediates for synthesizing pharmaceutically active compounds.

In the context of our interest in the design and development of useful tactics and strategies for the synthesis of nitrogen heterocycles [9,10,11], in this communication, we reported a new, rapid and efficient method for the synthesis of pyrimido[1,2-*a*]benzimidazole derivatives including imidazo[1,2-*a*]pyrimidine core from readily available starting materials under microwave irradiation (MW).

Although the synthesis of these compounds was reported in the literature with the shortage of long reaction time and the limitation that benzaldehydes must be substituted with electron-rich groups [12], to obtain the potential pharmacological molecules, a shorter, more efficient and more extensive method with minimal environment impact was desired.

The starting material **2** were easily prepared according to our reported procedure [13]. Treatment of **2** with an equimolar amount of 1*H*-benzo[*d*]imidazol-2-amine **1** under MW in ethylene glycol, to our great satisfaction proceeded smoothly to afford a series of pyrimido[1,2-*a*]-benzimidazole derivatives (Scheme 1).

Scheme 1



RESULTS AND DISCUSSION

To explore the scope and versatility of this method, various reaction conditions were investigated, including solvent and temperature. In order to find the optimum reaction condition, different solvents, such as ethanol (EtOH), water, glacial acetic acid (AcOH), and ethylene glycol, were tested in the synthesis of **3a** at 100 °C, respectively. All the reactions were carried out under microwave irradiation (initial power 100 W and maximum power 200 W) (Table 1).

As shown in Table 1, the reaction in ethylene glycol gave the best results (Table 1, entry 3).

Moreover, to further optimize the reaction temperature, reaction of 4-(4-chlorobenzylidene)-2-phenyloxazol-

5(4*H*)-one (**2a**) and **1** was carried out in ethylene glycol at the temperature ranging from 80 °C to 140 °C with an increment of 10 °C. As shown in Table 2, when the temperature was increased from 80 °C to 110 °C, the yield of product **3a** improved from 49% to 81%. However, no significant increase in the yield of product **3a** was observed as the reaction temperature was raised from 120 °C to 140 °C. Therefore, the temperature of 110 °C was chosen for all further microwave-assisted reactions.

Table 1

Solvent Optimization for the Synthesis of **3a** under MW

Entry	Solvent	Time (min)	Yield (%)
1	EtOH	9	52
2	HOAc	8	63
3	Ethylene glycol	7	78
4	water	12	16

Table 2

Temperature optimization for the synthesis of **3a** under MW

Entry	T (°C)	Time (min)	Yield (%)
1	80	10	49
2	90	9	54
3	100	7	78
4	110	5	81
5	120	5	81
6	130	4	80
7	140	5	79

Under these optimized reaction conditions, a series of polysubstituted pyrimido[1,2-*a*]benzimidazole **3** were synthesized with this simple reaction procedure. The results are collected in Table 3.

In addition, compound **3** should have two possible diastereoisomers: *trans*-isomer and *cis*-isomer. Identified by the coupling constant (J) of the vicinal protons adjacent to R and NH in their ^{1}H nmr spectra [14], only the *trans*-isomer was obtained. The reason may be attributed to their steric hindrance.

For comparison, we performed the synthesis of **3a** under both microwave irradiation and classical heating conditions at 110 °C The reactions were efficiently promoted by microwave irradiation; under classical conditions the reaction time was eight hours and the yield of **3a** was 56%, however, using microwave irradiation the reaction time was five minutes and the yield of **3a** increased to 81%. Therefore, microwave irradiation exhibited several advantages over conventional heating by significantly reducing the reaction time and dramatically improving the yield of the reaction. The electronic effect of the aryl group was investigated. Under our reaction conditions, both electron-withdrawing (such as nitro) and electron-donating (such as alkoxy) groups readily provided pyrimido[1,2-*a*]benzimidazole **3** in good yields. At the same time, we have also observed delicate electronic effects: that is, aldehydes with electron-withdrawing groups (Table 3, entries1-6) reacted rapidly, while electron-donating groups (Table 3, entries 8-13) decreased the reactivity, requiring longer reaction times. Moreover, the heterocyclic aldehydes such as thiophene-2-carbaldehyde (Table 3, entry 13) still displayed high reactivity under this standard condition.

Although the detailed mechanism of the reaction has not been established in experimental manner, the formation of **3** could be explained by a reaction sequence presented in Scheme 2. We propose that the reaction proceeds *via* a sequence of Michael addition, cyclization and ring opening [10].

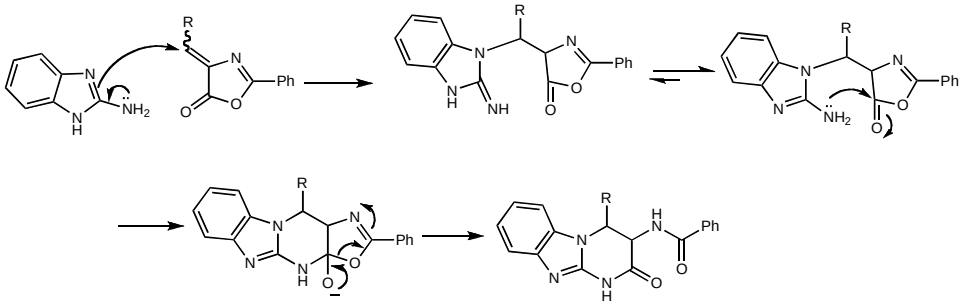
In summary, we have successfully constructed the pyrimido[1,2-*a*]benzimidazole skeleton from readily obtainable and cheap materials. Particularly valuable

Table 3

Synthesis of **4** and **5** under Microwave Irradiation

Entry	**3**	R	Time (min)	Yield (%)	Mp (°C)
1	**3a**	4-ClC_6H_4	5	81	>300
2	**3b**	4-FC_6H_4	5	80	258-259
3	**3c**	4-$NO_2C_6H_4$	4	81	>300
4	**3d**	4-BrC_6H_4	5	78	>300
5	**3e**	2-OHC_6H_4	6	77	>300
6	**3f**	2-ClC_6H_4	6	80	>300
7	**3g**	C_6H_5	7	76[58]	>300 [223-225]
8	**3h**	4-$MeOC_6H_4$	8	78	259-260
9	**3i**	2,3-$(MeO)_2C_6H_3$	7	76	294-295
10	**3j**	3,4,5-$(MeO)_3C_6H_2$	9	77	255-256
11	**3k**	3,4-$(OCH_2O)C_6H_3$	9	74	299-300
12	**3l**	4-$CH_3C_6H_4$	8	75	>300
13	**3m**	thiophen-2-yl	7	71	>300

Scheme 2



features of this method include the broader substrate scope and operational simplicity as well as increased safety for small-scale high-speed synthesis. In addition, this series of polysubstituted pyrimido[1,2-*a*]benzimidazole derivatives may result in a new biologically active compound librarie for biomedical screening, which is in progress in our laboratories.

EXPERIMENTAL

All reactions were performed 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 FT-IR-tensor 27 spectrometer. ^{1}H NMR (^{13}C NMR) spectra were measured on a DPX 400 MHz (100 MHz) spectrometer using TMS as an internal standard and DMSO-d_6 as solvent. Elemental analysis was determined by using a Perkin-Elmer 240c elemental analysis instrument. ESI-MS was determined by using the LCQ Advantage HPLC/MS instrument (Thermo Finnigan).

General procedure for the one-pot synthesis of compounds 4 under microwave irradiation conditions. In a 10-mL reaction vial, 4-arylidene-3-methylisoxazol-5(4*H*)-ones **2** (1 mmol), 1*H*-benzo[*d*]imidazol-2-amine **1** (1 mmol), ethylene glycol (2 mL) were mixed and then capped. The mixture was irradiated at 200 W (initial power 100 W, maximum power 200 W) at 110 °C for a given time. The reaction mixture was cooled to room temperature and poured into water (30 mL), the insoluble portion was collected by filtration to give the crude product, which was further purified by recrystallization from 95% aqueous EtOH to give pure polysubstituted pyrimido[1,2-*a*]benzimidazole **3** (Table 3).

***N*-[4-(4-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimido-[1,2-*a*]benzimidazol-3-yl]benzamide (3a).** This compound was obtained according to above general procedure; ir (potassium bromide): 3399, 3255, 3061, 2932, 1708, 1637, 1571, 1509, 1489, 1455, 1382, 1270, 1238, 1093, 736, 697 cm^{-1}; ^{1}H nmr: 12.17 (s, 1H, NH), 8.50 (d, 1H, J = 7.6 Hz, NH), 7.84 (d, 2H, J = 7.6 Hz), 7.59-7.34 (m, 7H, ArH), 7.16-7.05 (m, 2H, ArH), 7.01 (d, 2H, J = 8.4 Hz, ArH), 6.16 (d, 1H, J = 8.8 Hz, CH), 5.84-5.80 (m, 1H, CH); ^{13}C nmr: 167.0, 161.4, 150.2, 141.3, 134.1, 133.4, 133.3, 131.9, 128.9, 128.8, 127.6, 122.1, 121.4, 117.3, 115.4, 109.4, 54.4, 52.0; ms: m/z 417.4 (M+H)$^+$, 379.2, 301.4, 279.5. *Anal*. calcd for $C_{23}H_{17}ClN_4O_2$: C, 66.27; H, 4.11; N, 13.44. Found: C, 66.24; H, 4.18; N, 13.40.

***N*-[4-(4-Fluorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimido-[1,2-*a*]benzimidazol-3-yl]benzamide (3b).** This compound was obtained according to above general procedure; ir (potassium bromide): 3401, 3257, 3004, 1702, 1692, 1642, 1540, 1409, 1277, 1213, 1051, 746, 711 cm^{-1}; ^{1}H nmr: 12.06 (s, 1H, NH), 8.77 (d, 1H, J = 8.0 Hz, NH), 7.88 (d, 2H, J = 7.2 Hz, ArH), 7.57-7.47 (m, 7H, ArH), 7.13-7.10 (m, 2H, ArH), 6.89-6.87 (m, 2H, ArH), 6.30 (d, 1H, J = 8.0 Hz, CH), 5.85-5.81 (m, 1H, CH); ^{13}C nmr: 170.9, 163.1, 157.8, 152.2, 140.3, 135.9, 133.8, 133.4, 130.8, 129.9, 128.3, 127.9, 126.8, 122.5, 122.0, 121.7, 114.5, 108.9, 54.6, 52.7; ms: m/z 401.5 (M+H)$^+$, 361.9, 340.0, 280.6, 268.5. *Anal*. calcd for $C_{23}H_{17}FN_4O_2$: C, 68.99; H, 4.28; N, 13.99. Found: C, 69.03; H, 4.21; N, 14.06.

***N*-[4-(4-Nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimido-[1,2-*a*]benzimidazol-3-yl]benzamide (3c).** This compound was obtained according to above general procedure; ir (potassium bromide): 3410, 3208, 3065, 2866, 1714, 1661, 1632, 1572, 1485, 1458, 1350, 1240, 1037, 743, 709 cm^{-1}; ^{1}H nmr: 12.18 (s, 1H, NH), 8.51 (d, 1H, J = 7.6 Hz, NH), 8.18 (d, 2H, J = 8.4 Hz, ArH), 7.81 (d, 2H, J = 7.6 Hz, ArH), 7.58-7.45 (m, 5H, ArH), 7.34-7.26 (m, 3H, ArH), 7.17-7.05 (m, 1H, ArH), 6.31 (d, 1H, J = 7.6 Hz, CH), 5.91-5.87 (m, 1H, CH); ^{13}C nmr: 167.0, 165.9, 154.2, 147.7, 142.6, 133.4, 131.7, 128.7, 128.3, 127.7, 123.9, 122.2, 121.4, 117.3, 109.4, 54.5, 51.7; ms: m/z 428.4 (M+H)$^+$, 384.1, 301.6, 279.5. *Anal*. calcd for $C_{23}H_{17}N_5O_4$: C, 64.63; H, 4.01; N, 16.39. Found: C, 64.66; H, 4.15; N, 16.31.

***N*-[4-(4-Bromophenyl)-2-oxo-1,2,3,4-tetrahydropyrimido-[1,2-*a*]benzimidazol-3-yl]benzamide (3d).** This compound was obtained according to above general procedure; ir (potassium bromide): 3395, 3254, 3059, 2932, 1708, 1639, 1577, 1543, 1488, 1409, 1380, 1269, 1239, 1073, 819, 736 cm^{-1}; ^{1}H nmr: 12.12 (s, 1H, NH), 8.51 (d, 1H, J = 7.2 Hz, NH), 7.85 (d, 2H, J = 8.4 Hz, ArH), 7.57-7.34 (m, 7H, ArH), 7.16-7.05 (m, 2H, ArH), 6.95 (d, 2H, J = 8.0 Hz, ArH), 6.15 (d, 1H, J = 7.6 Hz, CH), 5.84-5.82 (m, 1H, CH); ^{13}C nmr: 166.9, 161.9, 151.2, 140.1, 135.9, 134.5, 133.4, 131.7, 129.2, 128.4, 128.3, 127.7, 127.3, 122.1, 122.0, 121.4, 112.7, 109.4, 54.4, 53.0; ms: m/z 461.4 (M+H)$^+$, 384.7, 329.0, 299.2, 273.3. *Anal*. calcd for $C_{23}H_{17}BrN_4O_2$: C, 59.88; H, 3.71; N, 12.15. Found: C, 59.86; H, 3.79; N, 12.09.

***N*-[4-(2-Hydroxyphenyl)-2-oxo-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-3-yl]benzamide (3e).** This compound was obtained according to above general procedure; ir (potassium bromide): 3388, 3365, 3217, 2980, 1711, 1659, 1604, 1535, 1362, 1257, 1176, 1157, 1064, 911, 756, 702 cm^{-1}; ^{1}H nmr: 11.99 (s, 1H, NH), 9.68 (s, 1H, OH), 8.64 (d, 1H, J =

7.6 Hz, NH), 7.98 (d, 2H, J = 8.8 Hz, ArH), 7.79 (d, 2H, J = 7.6 Hz, ArH), 7.67-7.55 (m, 7H, ArH), 7.47-7.38 (m, 2H, ArH), 6.14 (d, 1H, J = 8.8 Hz, CH), 5.85-5.81 (m, 1H, CH); ^{13}C nmr: 167.9, 163.6, 157.8, 150.2, 136.7, 134.2, 133.5, 133.1, 132.3, 130.2, 128.7, 128.1, 126.9, 125.6, 124.1, 121.3 119.3, 116.0, 58.6, 49.2. *Anal*. calcd for $C_{23}H_{18}N_4O_3$: C, 69.34; H, 4.55; N, 14.06. Found: C, 69.37; H, 4.48; N, 14.11.

***N*-[4-(2-Chlorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimido-[1,2-*a*]benzimidazol-3-yl]benzamide (3f).** This compound was obtained according to above general procedure; ir (potassium bromide): 3379, 3249, 3061, 2942, 1711, 1675, 1579, 1553, 1378, 1319, 1301, 1119, 1105, 735 cm^{-1}; ^{1}H nmr: 12.00 (s, 1H, NH), 8.51 (d, 1H, J = 7.6 Hz, NH), 7.83 (d, 2H, J = 8.4 Hz, ArH), 7.57-7.34 (m, 3H, ArH), 7.32-6.96 (m, 8H, ArH), 6.16 (d, 1H, J = 7.6 Hz, CH), 5.82-5.80 (m, 1H, CH); ^{13}C nmr: 167.7, 161.6, 152.2, 140.3, 135.9, 134.2, 134.0, 133.8, 130.6, 129.9, 128.3, 127.9, 125.6, 122.9, 122.0, 121.7, 114.2, 109.1, 54.8, 51.9; ms: m/z 417.5 $(M+H)^+$, 389.4, 351.9, 284.3. *Anal*. calcd for $C_{23}H_{17}ClN_4O_2$: C, 66.27; H, 4.11; N, 13.44; Found: C, 66.25; H, 4.18; N, 13.47.

***N*-(2-Oxo-4-phenyl-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-3-yl)benzamide (3g).** This compound was obtained according to above general procedure; ir (potassium bromide): 3348 3275, 3061, 2932, 1707, 1637, 1576, 1537, 1454, 1385, 1273, 1239, 735, 694 cm^{-1}; ^{1}H nmr: 12.17 (s, 1H, NH), 8.35 (d, 1H, J = 7.6 Hz, NH), 7.80 (d, 2H, J = 7.6 Hz, ArH), 7.58-7.54 (m, 1H, ArH), 7.48-7.44 (m, 3H, ArH), 7.35-7.29 (m, 4H, ArH), 7.15-7.01 (m, 4H, ArH), 6.15 (d, 1H, J = 7.6 Hz, CH), 5.80-5.77 (m, 1H, CH); ^{13}C nmr: 166.9, 162.0, 152.2, 151.7, 135.1, 133.5, 132.1, 131.6, 128.7, 127.6, 127.0, 126.2, 122.0, 121.3, 109.4, 54.9, 52.3; ms: m/z 383.6 $(M+H)^+$, 337.0, 308.7, 279.4. *Anal*. calcd for $C_{23}H_{18}N_4O_2$: C, 72.24; H, 4.74; N, 14.65. Found: C, 72.20; H, 4.68; N, 14.71.

***N*-[4-(4-Methoxylphenyl)-2-oxo-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-3-yl]benzamide (3h).** This compound was obtained according to above general procedure; ir (potassium bromide): 3389, 3257, 3058, 2956, 1717, 1650, 1589, 1550, 1374, 1312, 1247, 1109, 735 cm^{-1}; ^{1}H nmr: 12.11 (s, 1H, NH), 8.37 (d, 1H, J = 7.6 Hz, NH), 7.82 (d, 2H, J = 8.0 Hz, ArH), 7.59-7.55 (m, 1H, ArH), 7.47-7.34 (m, 2H, ArH), 7.16-7.00 (m, 6H, ArH), 6.83 (d, 2H, J = 8.4 Hz, ArH), 6.14 (d, 1H, J = 7.6 Hz, CH), 5.84-5.81 (m, 1H, CH), 3.72 (s, 3H, OCH_3); ^{13}C nmr: 167.4, 166.4, 152.6, 147.0, 138.4, 134.6, 133.5, 132.2, 131.9, 129.8, 128.5, 127.7, 125.6, 125.2, 117.3, 112.9, 108.4, 60.2, 55.1, 52.6; ms: m/z 413.3 $(M+H)^+$, 364.4, 292.5, 280.4. *Anal*. calcd for $C_{24}H_{20}N_4O_3$: C, 69.89 ; H, 4.89; N, 13.58. Found: C, 69.88; H, 4.95; N, 13.55.

***N*-[4-(2,3-Dimethoxylphenyl)-2-oxo-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-3-yl]benzamide (3i).** This compound was obtained according to above general procedure; ir (potassium bromide): 3417, 3353, 3000, 2937, 1712, 1661, 1581, 1513, 1457, 1413, 1378, 1270, 747, 714 cm^{-1}; ^{1}H nmr: 12.04 (s, 1H, NH), 8.35 (d, 1H, J = 7.6 Hz, NH), 7.71 (d, 2H, J = 7.2 Hz, ArH), 7.54-7.40 (m, 5H, ArH), 7.17-6.98 (m, 5H, ArH), 6.28 (d, 1H, J = 8.4 Hz, CH), 5.80-5.76 (m, 1H, CH), 3.74 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3); ^{13}C nmr: 167.1, 166.4, 152.2, 147.0, 133.7, 132.7, 132.1, 131.5, 128.3, 128.1, 127.5, 127.3, 124.1, 121.7, 117.2, 113.7, 112.7, 108.9, 60.2, 55.1, 52.6; ms: m/z 443.5 $(M+H)^+$, 359.8, 310.5, 284.4. *Anal*. calcd for $C_{25}H_{22}N_4O_4$: C, 67.86; H, 5.01; N, 12.66. Found: C, 67.89; H, 5.07; N, 12.59.

***N*-[4-(3,4,5-Trimethoxylphenyl)-2-oxo-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-3-yl]benzamide (3j).** This compound was obtained according to above general procedure; ir (potassium bromide): 3393, 3225 3038, 2937, 2750, 1714, 1655, 1632, 1593, 1569, 1528, 1456, 1228, 758, 716 cm^{-1}; ^{1}H nmr: 12.12 (s, 1H, NH), 8.45 (d, 1H, J = 6.0 Hz, NH), 7.83 (d, 2H, J = 7.2 Hz, ArH), 7.58-7.40 (m, 6H, ArH), 7.15-7.09 (m, 3H, ArH), 6.04 (d, 1H, J = 7.2 Hz, CH), 5.79-5.62 (m, 1H, CH), 3.59 (s, 3H, OCH_3), 3.54 (s, 6H, OCH_3); ^{13}C nmr: 167.0, 166.4, 152.9, 137.6, 133.5, 132.2, 131.7, 131.0, 130.7, 128.2, 127.7, 126.6, 126.0, 125.2, 122.0, 117.7, 112.7, 104.4, 59.8, 55.5, 54.9, 52.3; ms: m/z 473.3 $(M+H)^+$, 383.5, 339.5, 314.3, 279.4. *Anal*. calcd for $C_{26}H_{24}N_4O_5$: C, 66.09; H, 5.12; N, 11.86. Found: C, 66.07; H, 5.17; N, 11.84.

***N*-[4-(1,3-Benzodioxol-5-yl)-2-oxo-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-3-yl]benzamide (3k).** This compound was obtained according to above general procedure; ir (potassium bromide): 3387, 3228, 3058, 2882, 1707, 1669, 1630, 1598, 1505, 1444, 1374, 1247, 932, 748, 714 cm^{-1}; ^{1}H nmr: 12.11 (s, 1H, NH), 8.38 (d, 1H, J = 6.4 Hz, NH), 7.83 (d, 2H, J = 8.8 Hz, ArH), 7.58-7.37 (m, 5H, ArH), 7.16-7.06 (m, 2H, ArH), 6.83 (d, 1H, J = 8.0 Hz, ArH), 6.58-6.53 (m, 2H, ArH), 6.05 (d, 1H, J = 7.2 Hz, CH), 5.96 (d, 2H, J = 8.8 Hz, OCH_2O), 5.77-5.73 (m, 1H, CH); ^{13}C nmr: 167.0, 165.1, 153.9, 148.7, 142.7, 138.0, 133.9, 133.6, 133.2, 128.6, 128.1, 127.9, 126.3, 126.0, 121.0, 116.9, 112.4, 104.3, 98.9, 55.1, 52.6. *Anal*. calcd for $C_{24}H_{18}N_4O_4$: C, 67.60; H, 4.25; N, 13.14. Found: C, 67.64; H, 4.29; N, 13.08.

***N*-[4-(4-Methylphenyl)-2-oxo-1,2,3,4-tetrahydropyrimido-1,2-*a*]benzimidazol-3-yl]benzamide (3l).** This compound was obtained according to above general procedure; ir (potassium bromide): 3387, 3243, 3050, 2950, 1720, 1649, 1566, 1526, 1376, 1315, 1295, 1205, 1184, 736, 708 cm^{-1}; ^{1}H nmr: 12.17 (s, 1H, NH), 8.35 (d, 1H, J = 7.6 Hz, NH), 7.71 (d, 2H, J = 8.0 Hz, ArH), 7.41-7.34 (m, 7H, ArH), 7.12-6.98 (m, 4H, ArH), 6.11 (d, 1H, J = 7.6 Hz, CH), 5.71-5.66 (m, 1H, CH), 2.23 (s, 3H, CH_3); ^{13}C nmr: 168.0, 165.7, 157.9, 139.5, 139.4, 134.3, 133.6, 133.4, 132.8, 131.9, 129.9, 128.5, 127.6, 125.7, 122.2, 122.1, 119.0, 117.4, 115.7, 112.7, 55.1, 53.0, 21.0. *Anal*. calcd for $C_{24}H_{20}N_4O_2$: C, 72.71; H, 5.08; N, 14.13. Found: C, 72.75; H, 5.04; N, 14.15.

***N*-(2-Oxo-4-thien-2-yl-1,2,3,4-tetrahydropyrimido[1,2-*a*]-benzimidazol-3-yl)benzamide (3m).** This compound was obtained according to above general procedure; ir (potassium bromide): 3390, 3276, 3101, 2968, 1724, 1669, 1603, 1570, 1417, 1380, 1028, 773, 718 cm^{-1}; ^{1}H nmr: 12.17 (s, 1H, NH), 8.49 (d, 1H, J = 7.6 Hz, NH), 7.80 (d, 2H, J = 8.0 Hz, ArH), 7.58-7.31 (m, 4H, ArH), 7.14-6.89 (m, 6H, ArH), 6.14 (d, 1H, J = 7.6 Hz, CH), 5.84-5.80 (m, 1H, CH); ^{13}C nmr: 169.2, 162.7, 151.7, 137.7, 134.0, 132.8, 131.9, 129.7, 128.6, 128.1, 127.1, 125.9, 122.2, 122.1, 118.7, 117.9, 112.7, 54.8, 52.5. *Anal*. calcd for $C_{21}H_{16}N_4O_2S$: C, 64.93; H, 4.15; N, 14.42; S, 8.25. Found: C, 64.89; H, 4.21; N, 14.40; S, 8.21.

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REFERENCES AND NOTES

[1] Roth, H. J.; Kleemann, A. In *Pharmaceutical Chemistry. Volume 1: Drug Synthesis*; John Wiley & Sons: New York, 1988.

[2] Tully, W. R.; Gardner, C. R.; Gillespie, R. J.; Westwood, R. *J. Med. Chem*. **1991**, *34*, 2060.

[3] Gueiffier, A.; Lhassani, M.; Elhakmaoui, A.; Snoeck, R.; Andrei, G.; Chavignon, O.; Teulade, J.-C.; Kerbal, A.; Essassi, E. M.; Debouzy, J.-C.; Witvrouw, M.; Blache, Y.; Balzarini, J.; De Clercq, E.; Chapat, J.-P. *J. Med. Chem.* **1996,** *39*, 2856.

[4] Rival, Y.; Grassy, G.; Michel, G. *Chem. Pharm. Bull.* **1992**, *40*, 1170.

[5] Rival, Y.; Grassy, G.; Taudou, A.; Ecalle, R. *Eur. J. Med. Chem.* **1991**, *26*, 13.

[6] Sanfilippo, P. J.; Urbanski, M.; Press, J. B.; Dubinsky, B.; Moore, J. B. *J. Med. Chem.* **1988**, *31*, 2221.

[7] Katritzky, A. R.; Rees, C. W. In *Comprehensive Heterocyclic Chemistry*; Potts, K. T., Ed.; Pergamon Press: Oxford, 1984; Vol. 5, part 4A.

[8] Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V. In *Comprehensive Heterocyclic Chemistry* II; Jones, G., Ed.; Pergamon Press: Oxford, 1996; Vol. 8.

[9] Tu, S. J.; Zhang, Y.; Jiang, H.; Jiang, B.; Zhang, J. Y.; Jia, R. H.; Shi, F. *Eur. J. Org. Chem.* **2007**, 1552.

[10] Tu, S. J.; Zhang, J. Y.; Jia, R. H.; Jiang, B.; Zhang, Y.; Jiang, H. *Org. Biomol. Chem.*, **2007**, *5*, 1450.

[11] Tu, S. J.; Li, T. J.; Shi, F.; Wang, Q.; Zhang, J. P.; Xu, J. N.; Zhu, X. T.; Zhang, X. J.; Zhu, S. L.; Shi, D. Q. *Synthesis* **2005**, 3045.

[12] Chebanov, V. A.; Desenko, S. M.; Kuzmenko, S. A.; Borovskoy, V. A.; Musatov, V. I.; Sadchikova, Yu. V. *Russian Chemical Bulletin, International Edition*, **2004**, *53*, 2845.

[13] Tu, S. J.; Jiang, H.; Zhuang, Q. Y.; Miao, C. B.; Shi, D. Q.; Wang, X. S.; Gao, Y. *Chin. J. Org. Chem.* **2003**, *23*, 491.

[14] Wu, H.; Shen, Y.; Fan, L. Y; Wan, Y.; Zhang, P.; Chen, C. F.; Wang, W. X. *Tetrahedron*, **2007**, *63*, 2404.