Synthesis and Antimicrobial Activity of Some Novel 4-(1*H*-Benz[*d*]imidazol-2yl)-1,3-thiazol-2-amines

Vanga Malla Reddy* and Kunduru Ravinder Reddy

Dr. Ch. Ravishanker Memorial Medicinal Chemistry Research Laboratory, University College of Pharmaceutical Sciences, Kakatiya University; Warangal–506009, India.

Received December 21, 2009; accepted April 9, 2010; published online April 19, 2010

A new series of novel 4-(1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amines 5a—d and 4-(1*H*-benz[*d*]imidazol-2yl)-3-alkyl-2,3-dihydro-1,3-thiazol-2-amine 8a—d has been synthesized by the cyclocondensation of 2-acetyl benzimidiazoles 4a—d and 2-bromo-1-(1-alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone 7a—d with thiourea respectively, and evaluated for their antibacterial and antifungal activity against clinical isolates of Gram-positive and Gram-negative bacteria. Some of these hybrids in these series exhibited antibacterial activity comparable to standard Streptomycin and Benzyl penicillin and antifungal activity against Fluconazole. All the newly synthesized compounds were characterized by their spectral data and further used to estimate their ability towards antimicrobial activity.

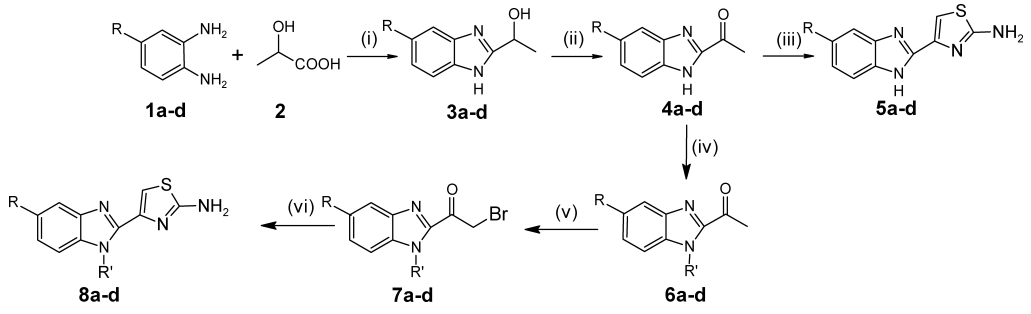
Key words thiazol-2-amine; benzimidazole; antimicrobial activity

Benzimidazoles show significant activity against several viruses such as human cytomegalovirus (HCMV),[1] human immunodeficiency virus (HIV),[2] herpes (HSV-1),[3] RNA[4] and influenza.[5] In view of the tremendous activities of benzimidazoles, their preparation has gained considerable attention. While many strategies are available for benzimidazole synthesis.[6—9] Almost all benzimidazoles with their two ring systems bear different functional substituents and this leads to essential modification of the physico-chemical, metabolic and pharmacokinetic properties of drugs.

Thiazoles are an important group of heterocyclic compounds contains sulfur and nitrogen in a five member ring. A lot of research work on thiazoles has been done in the past. The nucleus is also known as wonder nucleus because it gives out different derivatives with all different types of biological activities. Various methods are available in the literature for synthesis of thiazoles by using various agents.[10—15] Heterocycles based on thiazole ring systems are biologically active. Hence, thiazole ring systems containing molecules are known in pharmaceuticals such as Meloxicam,[16] Nitazoxamide,[17] Thiabendazole,[18] Cefdinir,[19] Nizatidine,[20] Alagebrium,[21] Sulfathiazole,[22] Amthamine,[23] Pramipexole.[24]

Inspired with the biological profile of benzimidazoles and thiazoles and their increasing importance in pharmaceutical and biological fields, and in connection with our research on the design and synthesis of biologically active and pharmacologically important new heterocycles,[25—30] it was thought worthwhile to synthesize the title compounds with a view to obtain certain new chemical entities with two active pharmacophores in a single molecular frame work in order to prepare molecules having with potentially enhanced biological activities and to have them evaluated for their antimicrobial activity. On the other hand, to the best of my knowledge previously there is no report, on the synthesis of 4-(1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine **5** and 4-(1*H*-benz[*d*]imidazol-2yl)-3-alkyl-2,3-dihydro-1,3-thiazol-2-amine **8** skeleton system represented as in Chart 1.

Chart 1 outlines the synthetic strategy developed to obtain the 4-(1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine **5** from 2-acetyl benzimidiazole **4** with thiourea. For the synthesis of target compounds, 2-(α-hydroxy) ethyl benzimidazole **3** was prepared by the reaction of substituted *o*-phenylenediamine **1** with α-hydroxy propionic acid **2** in presence of hydrochloric acid under reflux, followed by oxidation of compound **3** in presence of potassium dichromate and sulfuric acid at room temperature yields 2-acetyl benzimidazoles, **4** which on cyclo condensation reaction with thiourea under reflux in presence of iodine and isopropanol gave 4-(1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine **5**. Similarly, the synthesis of 4-(1*H*-benz[*d*]imidazol-2yl)-3-alkyl-2,3-dihy-



(i) HCl, reflux, 24 h; (ii) $K_2Cr_20_7$, H_2SO_4, 2.5 h; (iii) thiourea, I_2, isopranol, reflux, 3 h; (iv) TEBAC, DMS/$PhCH_2Cl$, K_2CO_3, CH_3CN, 30 min; (v) Br_2, AcOH, reflux, 3 h; (vi) Thiourea, DMF, rt, 3 h.

1R=a) H; b) 4-CH_3; c) 4-Cl; d) 4-NO_2; 3/4/5 R=a) H; b) 5-CH_3; c) 5-Cl; d) 5-NO_2; 6/7/8/ R=a) 5-CH_3; b) 5-CH_3; c) 5-Cl; d) 5-Cl; 6/7/8/ R′=a) CH_3; b) $CH_2C_6H_5$; c) CH_3; d) $CH_2C_6H_5$.

Chart 1

* To whom correspondence should be addressed. e-mail: vanga_mreddy@rediffmail.com

Table 1. Antibacterial and Antifungal Activity of 4-(1*H*-Benz[*d*]imidazol-2yl)-1,3-thiazol-2-amines **5a**—**d** and 4-(1*H*-Benz[*d*]imidazol-2yl)-3-alkyl-2,3-dihydro-1,3-thiazol-2-amine **8a**—**d**

Compound	Antibacterial activity[a,b]				Antifungal activity[a,b]	
	B. subtilus	*S. aureus*	*E. coli*	*K. pneumoniae*	*F. oxysporum*	*A. niger*
5a	06/05	07/06	04/04	06/05	03/02	02/02
5b	12/11	13/12	10/08	11/09	04/03	04/03
5c	14/13	13/11	12/11	14/12	05/04	04/03
5d	15/14	13/12	14/12	13/12	05/04	04/03
8a	09/08	08/07	09/07	07/06	03/02	03/02
8b	13/12	15/14	14/13	13/12	05/04	03/02
8c	15/14	14/13	13/12	10/08	05/04	05/04
8d	14/12	11/10	12/11	14/12	04/03	04/03
Streptomycin[c]	—	—	16	16	—	—
Benzyl penicillin[c]	16	16	—	—	—	—
Fluconazole[c]	—	—	—	—	06	06

a) Zone of inhibition in mm at 500 μg/ml concentration. *b*) Zone of inhibition in mm at 250 μg/ml concentration. *c*) Zone of inhibition in mm at 40 μg/ml concentration.

dro-1,3-thiazol-2-amine **8** was obtained by the cyclocondensation of 2-bromo-1-(1-alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone **7** with thiourea in *N*,*N*-dimethylformamide (DMF) solvent under reflux. The compound **7** was achieved through α-bromination of acetyl group of 1-(1-alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone **6** with the mixture of molecular bromine and acetic acid. The intermediate **6** was resulted through *N*-methylation/benzylation of 2-acetyl benzimidiazoles **4** with dimethyl sulphate/benzyl chloride in presence of triethyl benzyl ammonium chloride (TEBAC) at room temperature. The chemical structures of all the newly synthesized compounds were confirmed by their IR, ^{1}H-NMR and mass spectral analysis and further used to estimate their ability towards antimicrobial activity.

Antibacterial Activity In an approach, we have synthesized a new class of compounds and evaluated them for their *in vitro* antimicrobial activities against clinical isolates two Gram-positive bacteria namely *Bacillus subtilus* and *Staphylococcus aureus* and two Gram-negative bacteria viz., *Escherichia coli* and *Klebsiella pneumoniae* by Cup-plate method[31] using Streptomycin and Benzyl penicillin as control drugs. The Minimum Inhibitory Concentration (MIC) was determined according to the protocols of National Committee for Clinical Laboratory Standards (NCCLS). In general the compounds showed improved antibacterial activity to their antifungal activity. It is observed from the results as illustrated in Table 1 that almost all the compounds exhibited good to moderate antibacterial activity towards all the organisms employed. Compounds **5d** and **8c** exhibited almost equipotent inhibitory activity as compared to the control against *B. subtilus*, whereas compounds **8b** and **8d** have shown high activity and none of the compounds showed better activity than the control against the same organism. Compounds **5c**, **5d**, **8b** and **8d** are the most effective against *S. aureus*. Similarly only compound **8b** against *E. coli* and **5c** against *K. pneumoniae* showed effective activity.

Antifungal Activity The synthesized compounds have also been evaluated for their antifungal activity against two representative fungi *viz.*, *Fusarium oxysporum* and *Aspergillus niger* by Cup-plate method[31] using Fluconazole as standard drug at 40 μg/ml concentration. Compounds **5c**, **5d**, **8b** and **8c** are most active which possessed higher activity against *F. oxysporum* in comparison to standard drug. For activity against *A. niger* compounds **5b**, **5d**, **8c** and **8d** yielded better activity in comparison to other compounds synthesized. However almost all synthesized benzoimidazolyl-1,3-thiazol-2-amines have shown moderate to significant antifungal activity against the two organisms employed. From the above discussion it is evident that compounds **5d** and **8c** have emerged as the most effective antibacterial agents whereas compounds **8c** and **8d** were the most active ones towards antifungal activity.

Experimental

General All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by column chromatography on silica gel of 60—120 mesh. IR spectra were obtained on a Perkin Elmer BX serried FTIR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a Varian 300 MHz spectrometer for ^{1}H-NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

Typical Procedure 2-(α-Hydroxy)ethyl Benzimidazoles (3) *o*-Phenelen-ediamine (0.01 mol) was treated with lactic acid (0.01 mol) in presence of 4 N-hydrochloric acid (5 ml) and refluxed on water both for 24 h. After completion of the reaction (monitored by TLC) the reaction mixture was cooled and neutralized with NH_3 solution. The solid was separated through filter and recrystallized from absolute ethanol.

2-Acetyl Benzimidazoles (4) To a solution of 2-(α-hydroxy)ethyl benzimidazoles **3** (0.01 mol) in dil.H_2SO_4 (5%, 40 ml) was drop wise added the solution of $K_2Cr_2O_7$ (0.15 mol) and aqueous H_2SO_4 (25%, 80 ml) with constant stirring at room temperature over a period of 20 min. Further the reaction mixture was stirred at room temperature for 2 h. After completion of the reaction, (monitored by TLC), the reaction mixture neutralized with NH_3 solution (1 : 1) and formed orange solid was filtered, washed with water and dried, recrystallized from ethyl acetate.

4-(1*H*-Benz[*d*]imidazol-2yl)-1,3-thiazol-2-amines (5) A solution of 2-acetyl benzimidazoles (**4**) (0.01 mol) in isopropanol (20 ml) was added to the mixture of thiourea (0.01 mol) and iodine (0.12 mol) in isopropanol (20 ml). Then the reaction mixture was heated under reflux for 3 h. After completion of the reaction, (monitored by TLC) the solvent was removed *in vacuo*. The solid separated was washed with aq. sodium bicarbonate solution, dried and recrystallized from ethanol to give product **5** in pure state.

1-(1-Alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanones (6) To a suspension of potassium carbonate (0.01 mol) in acetonitrile (20 ml) was added triethyl benzyl ammonium chloride and the reaction was stirred for 10 min. To this mixture, added 2-acetyl benzimidiazole **4** was added and continued stirring for 30 min followed by the addition of dimethyl sulphate/benzyl chloride (0.01 mol) in acetonitrile. After completion of the reaction, the solvent was removed *in vacuo*. The solid separated was dissolved in chloroform (15 ml). The chloroform layer was washed with water (2×250 ml), dried and recrystallized from ethyl acetate to give product **6** in pure form.

2-Bromo-1-(1-alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (7) To a solution of 1-(1-alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanones **6** (0.01 mol) in acetic acid (15 ml) at reflux, drop wise added a solution of bromine (0.01 mol) in acetic acid. Then the reaction mixture was maintained under similar conditions for 3 h with constant stirring. After completion of the reaction, the mixture was cooled into room temperature, poured into ice cold water and washed with aq. Sodium bicarbonate solution, dried and recrystallized from ethanol.

4-(1*H*-Benz[*d*]imidazol-2yl)-3-alkyl-2,3-dihydro-1,3-thiazol-2-amines (8) To a solution of 2-bromo-1-(1-alkyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone **7** (0.01 mol) in dimethylformamide (DMF) (20 ml) was added the solution of thiourea (0.01 mol) in DMF (15 ml). The reaction mixture was then stirred at room temperature for 2 h. When the reaction was completed (monitored by TLC), the reaction mixture was poured into ice cold water to separate the product in solid form, dried and recrystallized from ethanol.

1-(1*H*-Benzo[*d*]imidazol-2-yl)-1-ethanol (**3a**): Yellow solid, yield 90%, mp 180—182 °C. IR (KBr) cm^{-1}: 2971, 1623, 1458, 1215, 1103. ^{1}H-NMR ($CDCl_3$) δ: 10.30 (1H, br s), 7.52 (2H, d, J=7.8 Hz), 7.32 (2H, d, J=1.9 Hz), 4.8 (1H, s), 3.05 (1H, q, J=7.4 Hz), 1.62 (3H, d, J=7.2 Hz). MS m/z: 163 (M^++1).

1-(5-Methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (**3b**): Dark yellow solid, yield 90%, mp 160—162 °C. IR (KBr) cm^{-1}: 3038, 2701, 1629, 1449, 1316, 1101. ^{1}H-NMR ($CDCl_3$) δ: 11.61 (1H, br s), 7.32 (2H, d, J=8.0 Hz), 7.24 (1H, d, J=1.9 Hz), 4.85 (1H, s), 3.05 (1H, q, J=7.8 Hz), 2.30 (3H, s), 1.52 (3H, d, J=7.4 Hz). MS m/z: 177 (M^++1).

1-(5-Chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (**3c**): Brown solid, yield 65%, mp 171—173 °C. IR (KBr) cm^{-1}: 2981, 1623, 1444, 1210, 1082. ^{1}H-NMR ($CDCl_3$) δ: 12.50 (1H, s), 7.55 (2H, d, J=7.2 Hz), 7.20 (1H, d, J=2.1 Hz), 4.91 (1H, s), 3.10 (1H, q, J=7.8 Hz), 1.56 (3H, d, J=7.2 Hz). MS m/z: 197 (M^++1).

1-(5-Nitro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (**3d**): Brown solid, yield 75%, mp 148—150 °C. IR (KBr) cm^{-1}: 3342, 3215, 3024, 2865, 2240, 1420, 1248. ^{1}H-NMR ($CDCl_3$) δ: 10.63 (1H, br s) 7.91 (1H, d, J=1.9 Hz), 7.76 (2H, d, J=7.4 Hz), 5.16 (1H, s), 3.06 (1H, q, J=7.5 Hz), 1.64 (3H, d, J=7.5 Hz). MS m/z: 208 (M^++1).

1-(1*H*-Benzo[*d*]imidazol-2-yl)-1-ethanone (4a): Yellow solid, yield 78%, mp 189—191 °C. IR (KBr) cm^{-1}: 3289, 3059, 3015, 1674, 1580, 1445, 1235, 1147. ^{1}H-NMR ($CDCl_3$) δ: 13.02 (1H, s), 7.85 (1H, d, J=7.8 Hz), 7.52 (1H, d, J=7.6 Hz), 7.32 (2H, t, J=7.4 Hz), 2.74 (3H, s). MS m/z: 161 (M^++1).

1-(5-Methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**4b**): Yellow solid, yield 80%, mp 170—172 °C. IR (KBr) cm^{-1}: 3365, 2919, 2852, 1693. ^{1}H-NMR ($CDCl_3$) δ: 11.23 (1H, s), 7.65 (1H, d, J=8.0 Hz), 7.48 (1H, d, J=7.8 Hz), 7.24 (1H, s), 3.42 (3H, s), 2.45 (3H, s). MS m/z: 174 (M^++1).

1-(5-Chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**4c**): Yellow solid, yield 65%, mp 185—187 °C. IR (KBr) cm^{-1}: 3294, 3066, 3021, 1677, 1574, 1335, 1219, 1060. ^{1}H-NMR ($CDCl_3$) δ: 13.02 (1H, s), 7.52 (2H, d, J=7.4 Hz), 7.32 (1H, s), 2.74 (3H, s). MS m/z: 195 (M^++1).

1-(5-Nitro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**4d**): Pale yellow solid, yield 70%, mp 155—157 °C. IR (KBr) cm^{-1}: 3360, 3040, 2865, 2160, 1720, 1356, 1240. ^{1}H-NMR ($CDCl_3$) δ: 8.91 (1H, s), 8.77 (1H, s), 8.13 (1H, d, J=7.2 Hz), 8.09 (1H, d, J=7.4 Hz), 2.79 (3H, s). MS m/z: 206 (M^++1).

4-(1*H*-Benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**5a**): Colorless solid, yield 62%, mp 109—111 °C. IR (KBr) cm^{-1}: 3285, 3240, 3045, 2990, 1605, 1596, 780. ^{1}H-NMR ($CDCl_3$) δ: 7.41 (2H, dd, J=7.4 Hz), 7.73 (2H, d, J=7.8 Hz), 7.51 (1H, s), 6.31 (3H, s). MS m/z: 217 (M^++1).

4-(5-Methyl-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**5b**): Yellow solid, yield 68%, mp 146—148 °C. IR (KBr) cm^{-1}: 3356, 3145, 2872, 2174, 1735, 1362, 1254. ^{1}H-NMR ($CDCl_3$) δ: 7.39 (1H, d, J=7.6 Hz), 7.39 (1H, s), 7.11 (1H, d, J=8.0 Hz), 7.51 (1H, s), 6.31 (3H, s), 2.43 (3H, s). MS m/z: 231 (M^++1).

4-(5-Chloro-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**5c**): Brown solid, yield 66%, mp 136—138 °C. IR (KBr) cm^{-1}: 3266, 3254, 3038, 2982, 1614, 1565, 875. ^{1}H-NMR ($CDCl_3$) δ: 7.76 (1H, d, J=7.1 Hz), 7.69 (1H, d, J=7.2 Hz), 7.64 (1H, s), 7.42 (1H, s), 7.15 (1H, s), 6.31 (2H, s). MS m/z: 251 (M^++1).

4-(5-Nitro-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**5d**): Orange solid, yield 71%, mp 142—144 °C. IR (KBr) cm^{-1}: 3274, 3258, 3043, 2982, 1647, 1552, 1023, 845. ^{1}H-NMR ($CDCl_3$) δ: 8.62 (1H, s), 8.01 (1H, d, J=8.2 Hz), 7.87 (1H, d, J=7.6 Hz), 7.51 (1H, s), 6.31 (3H, s). MS m/z: 262 (M^++1).

1-(1,5-Dimethyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**6a**): Yellow solid, yield 80%, mp 70—72 °C. IR (KBr) cm^{-1}: 3030, 2965, 2910, 1702, 1640, 1605. ^{1}H-NMR ($CDCl_3$) δ: 7.36 (1H, s), 7.29 (1H, d, J=7.4 Hz), 7.25 (1H, d, J=7.6 Hz), 3.84 (3H, s), 2.56 (3H, s), 2.43 (3H, s). MS m/z: 189 (M^++1).

1-(1-Benzyl-5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**6b**): Orange solid, yield 78%, mp 92—94 °C. IR (KBr) cm^{-1}: 3045, 2974, 2922, 1707, 1636, 1625. ^{1}H-NMR ($CDCl_3$) δ: 7.39 (1H, s), 7.37 (2H, d, J=7.2 Hz), 7.31 (1H, d, J=7.8 Hz), 7.29 (2H, dd, J=7.4 Hz), 7.27 (1H, d, J=7.2 Hz), 7.12 (1H, dd, J=8.0 Hz), 5.62 (2H, s), 2.56 (3H, s), 2.43 (3H, s). MS m/z: 265 (M^++1).

1-(5-Chloro-1-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**6c**): Orange solid, yield 84%, mp 124—126 °C. IR (KBr) cm^{-1}: 3064, 2975, 2921, 1714, 1635, 1616, 762. ^{1}H-NMR ($CDCl_3$) δ: 7.52 (1H, s), 7.23 (1H, d, J=6.8 Hz), 7.22 (1H, d, J=7.2 Hz), 3.84 (3H, s), 2.56 (3H, s). MS m/z: 209 (M^++1).

1-(1-Benzyl-5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**6d**): Brown solid, yield 81%, mp 70—72 °C. IR (KBr) cm^{-1}: 3054, 2982, 2919, 1712, 1642, 1632, 754. ^{1}H-NMR ($CDCl_3$) δ: 7.54 (1H, s), 7.40 (2H, d, J=7.6 Hz), 7.29 (2H, dd, J=7.4 Hz), 7.12 (1H, dd, J=8.0 Hz), 7.25 (2H, d, J=7.8 Hz), 5.62 (2H, s), 2.56 (3H, s). MS m/z: 285 (M^++1).

2-Bromo-1-(1,5-dimethyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**7a**): Yellow solid, yield 77%, mp 106—106 °C. IR (KBr) cm^{-1}: 3045, 2975, 2921, 1708, 1632, 1641, 545. ^{1}H-NMR ($CDCl_3$) δ: 7.65 (1H, s), 7.56 (1H, d, J=8.0 Hz), 7.38 (1H, d, J=8.2 Hz), 4.27 (2H, s), 3.76 (3H, s), 2.43 (3H, s). MS m/z: 268 (M^++1).

1-(1-Benzyl-5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-2-bromo-1-ethanone (**7b**): Pale brown solid, yield 84%, mp 65—67 °C. IR (KBr) cm^{-1}: 3055, 2964, 2923, 1707, 1623, 1635, 561. ^{1}H-NMR ($CDCl_3$) δ: 7.67 (1H, s), 7.62 (2H, d, J=8.0 Hz), 7.58 (1H, d, J=7.8 Hz), 7.40 (1H, d, J=7.8 Hz), 7.24 (2H, dd, J=7.6 Hz), 7.12 (1H, dd, J=7.4 Hz), 5.58 (2H, s), 4.27 (2H, s), 2.43 (3H, s). MS m/z: 344 (M^++1).

2-Bromo-1-(5-chloro-1-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (**7c**): Brown-yellow solid, yield 65%, mp 78—80 °C. IR (KBr) cm^{-1}: 3062, 2973, 2926, 1710, 1624, 1638, 714, 568. ^{1}H-NMR ($CDCl_3$) δ: 7.80 (1H, s), 7.46 (1H, d, J=7.6 Hz), 7.32 (1H, d, J=7.4 Hz), 4.27 (2H, s), 3.76 (3H, s). MS m/z: 288 (M^++1).

1-(1-Benzyl-5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-2-bromo-1-ethanone (**7d**): Pale yellow solid, yield 65%, mp 78—80 °C. IR (KBr) cm^{-1}: 3068, 2973, 2928, 1708, 1632, 1614, 710, 556. ^{1}H-NMR ($CDCl_3$) δ: 7.83 (1H, s), 7.62 (2H, d, J=7.8 Hz), 7.49 (1H, d, J=7.6 Hz), 7.43 (1H, d, J=8.0 Hz), 7.24 (2H, dd, J=7.8 Hz), 7.12 (1H, dd, J=7.6 Hz), 5.58 (2H, s), 4.27 (2H, s). MS m/z: 364 (M^++1).

4-(1,5-Dimethyl-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**8a**): Yellow solid, yield 74%, mp 130—132 °C. IR (KBr) cm^{-1}: 3184, 3027, 1603, 1555, 1523, 1496. ^{1}H-NMR ($CDCl_3$) δ: 7.36 (1H, s), 7.20 (1H, d, J=7.4 Hz), 7.16 (1H, s), 7.08 (1H, d, J=7.8 Hz), 5.02 (2H, s), 3.70 (3H, s), 2.43 (3H, s). MS m/z: 245 (M^++1).

4-(1-Benzyl-5-methyl-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**8b**): Colorless solid, yield 774%, mp 132—134 °C. IR (KBr) cm^{-1}: 3178, 3032, 1612, 1565, 1527, 1487. ^{1}H-NMR ($CDCl_3$) δ: 7.38 (1H, s), 7.33 (2H, d, J=7.6 Hz), 7.22 (2H, d, J=7.4 Hz), 7.17 (2H, dd, J=7.8 Hz), 7.12 (1H, dd, J=8.0 Hz), 7.10 (1H, s), 5.26 (2H, s), 5.02 (2H, s), 2.43 (3H, s). MS m/z: 321 (M^++1).

4-(5-Chloro-1-methyl-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**8c**): Yellow solid, yield 70%, mp 120—122 °C. IR (KBr) cm^{-1}: 3166, 3032, 1610, 1565, 1532, 1486, 745. ^{1}H-NMR ($CDCl_3$) δ: 7.50 (1H, s), 7.31 (1H, d, J=7.8 Hz), 7.18 (1H, d, J=7.6 Hz), 7.16 (1H, s), 5.02 (2H, s), 3.70 (3H, s). MS m/z: 245 (M^++1).

4-(1-Benzyl-5-chloro-1*H*-benz[*d*]imidazol-2yl)-1,3-thiazol-2-amine (**8d**): Yellow solid, yield 65%, mp 116—118 °C. IR (KBr) cm^{-1}: 3174, 3038, 1618, 1574, 1544, 1474, 754. ^{1}H-NMR ($CDCl_3$) δ: 7.52 (1H, s), 7.33 (3H, d, J=7.6 Hz), 7.21 (1H, d, J=7.8 Hz), 7.19 (2H, dd, J=7.4 Hz), 7.12 (1H, dd, J=8.0 Hz), 7.10 (1H, s), 5.26 (2H, s), 5.02 (2H, s). MS m/z: 341 (M^++1).

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