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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis and evaluation of novel benzimidazole derivatives as antimicrobial agents

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Abstract Benzimidazole analogs bearing electron-withdrawing as well as electron-donating substituent were synthesized to achieve bioactive molecules with significant antimicrobial property. The desired compounds were prepared by multi-step synthesis process. The formation of intermediates and their corresponding derivatives ($\mathbf{III_{1–13}}$) was confirmed by spectral characterization such as ^{1}H NMR, ^{13}C NMR, mass spectra, IR, and elemental analysis. The compounds were screened for their antimicrobial properties against a broad panel of Gram-positive and Gram-negative bacteria as well as fungi. From the SAR study data, it was observed that the derivatives with electron-withdrawing functional groups were more bioactive than that with electron-donating functional groups.

Keywords Benzimidazole · Antifungal · Antibacterial · MIC · SAR study

Introduction

The versatility of benzimidazole and its property of exhibiting high potency against several microbial strains (Tuncbilek *et al.*, 2009) and cancer cell lines (O'Sullivan and Wallis, 1963) has drawn attention of many researchers to concentrate their work around it. Different derivatives of benzimidazole are found to possess antibacterial, antifungal, and molluscicidal activities (Nofal *et al.*, 2002). Benzimidazoles are the class of heterocyclic scaffolds exhibiting antiparasitic (Castilloa *et al.*, 2002), analgesic (Dixit *et al.*, 2013), anticancer (Reffat, 2011), antiprotozoal (Navarette-Vázquez *et al.*, 2001; Kazimierczuk *et al.*, 2002), and chemotherapeutic properties (Youssef *et al.*, 2013). Some of the benzimidazole derivatives are utilized as inhibitors of MDA-MB-231 human breast cell proliferation (Rangappa *et al.*, 2008). Several benzimidazole derivatives are observed to exhibit anti-inflammatory (Tsukamoto *et al.*, 1980), antihypertensive (Jat *et al.*, 2006), antidiabetic, as well as anti-asthametic properties (Ramanatham *et al.*, 2008).

Presence of benzimidazole nucleus in several categories of therapeutic molecules such as antimicrobial (Patel *et al.*, 2013), proton pump inhibitor (Iwahi *et al.*, 1991), antihypertensive (Shah *et al.*, 2008), anticoagulant, anti-inflammatory, antioxidants (Narasimhan *et al.*, 2012) has made it an important part in development of novel therapeutic agents. Benzimidazole nucleus serves as an important core in several antiulcer (Patil *et al.*, 2008) and antihelmintic drugs (Dubey *et al.*, 1985). Majority of the drugs available in the market viz. omeprazole, lansoprazole, pantoprazole as proton pump have benzimidazole as its center nuclei (Iwahi *et al.*, 1991). Other drugs available in market such as albendazole comprising of benzimidazole nucleus is used for the treatment of various parasitic worm infestations. Also mebendazole and bendamustine used as antihelmintic and in treatment of chronic lymphocytic leukemia (Kath *et al.*, 2001) are found to contain benzimidazole as their core (Fig. 1).

Substituted 2-mercapto benzimidazole (Saxena *et al.*, 1982; Scherhag *et al.*, 1974) is used as a precursor for the synthesis of desired compounds $\mathbf{III_{1–13}}$. It is also found that benzimidazole derivatives are capable of possessing antioxidant properties (Ayhan-Kilcigil *et al.*, 2004). Keeping in light all the above findings and in accordance with our

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previous research (Parikh and Joshi, 2013); we have reported the synthesis 2-(5-methoxy-1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-arylacetamides derivatives **III$_{1–13}$**. The precursor 5-methoxy-1*H*-benzo[*d*]imidazole-2-thiol used was synthesized by using the reported procedure (Wang and Liu, 2007).

Result and discussion

Chemistry

The formation of the titled compounds **III$_{1–13}$** was achieved in three steps. Initially synthesis of 5-methoxy-1*H*-benzo[*d*]imidazole-2-thiol **I** was undertaken by reacting 4-methoxybenzene-1,2-diamine in presence of carbondisulphide and KOH using ethanol as solvent (Wang and Liu, 2007). Simultaneously different derivatives of 2-chloro-*N*-(aryl)acetamide **II$_{1–13}$** were prepared by reacting substituted anilines with chloroacetylchloride, where triethylamine was used as a catalyst. The obtained intermediates 5-methoxy-1*H*-benzo[*d*]imidazole-2-thiol **I** and 2-chloro-*N*-(aryl)acetamide **II$_{1–13}$** were reacted in presence of K_2CO_3 using acetone as a suitable solvent, which resulted in the formation of titled compounds **III$_{1–13}$** in good yield as indicated in Scheme 1. The minimum inhibitory concentration (MIC) value for each final product against the wide panel of microorganisms was studied and is demonstrated in Table 1.

Table 1 Results of antibacterial and antifungal screening for compounds **III$_{1-13}$**

-R (derivatives)	MIC in μg/ml					
	Gram-positive bacteria		Gram-negative bacteria		Fungi	
	S. aureus	*E. faecalis*	*E. coli*	*P. aeruginosa*	*C. albicans*	*A. niger*
-3-NO_2	250	250	125	62.5	250	250
-4-NO_2	125	250	125	62.5	125	250
-3-Cl	125	125	125	62.5	125	250
-3-F-4-Cl	125	125	62.5	62.5	125	250
-H	125	125	62.5	125	125	125
-4-F	125	250	62.5	125	125	125
-2-OCH_3	31.25	125	62.5	125	250	125
-3-CH_3	250	250	125	250	250	250
-3-OCH_3	62.5	125	125	62.5	250	250
-2-NO_2	62.5	125	62.5	125	250	250
-2-CH_3	125	125	62.5	125	125	125
-4-CH_3	250	250	62.5	125	250	250
-3-CF_3	250	250	62.5	125	250	125
Fluconazole	–	–	–	–	**125**	**62.5**
Ciprofloxacin	**62.5**	**125**	**125**	**125**	–	–

MIC minimum inhibitory concentration, *Std*. Standard drug fluconazole for antifungal and ciprofloxacin for antibacterial tests

Characterization

IR data

IR data obtained for the final compounds **III$_{1–13}$** help us to a great extent to confirm their formation. If we observe the data for 2-(5-methoxy-1*H*-benzo[*d*]imidazol-2-ylthio)-*N*-(3-(trifluoromethyl)phenyl)acetamide **III$_{13}$**; an absorption peak obtained at 3,393 cm^{-1} has helped in confirming the presence of –NH in vicinity to the carbonyl group. The presence of aromatic C–H linkage is confirmed by the peak obtained at 3,095 cm^{-1}. A sharp peak at 2,921 cm^{-1} helped to assign the presence of –C–H bond in –OCH_3 group. A stretching band at 2,853 cm^{-1} concluded the presence of methylene group in the final motif. The presence of carbonyl (–C=O) in the structure is proved due to the presence of a sharp peak at 1,698 cm^{-1}. The presence of –C=N in the benzimidazole nucleus was also confirmed by the presence of a sharp absorption band at 1,580 cm^{-1}.

^{1}H NMR

Compound **III$_{13}$** when observed under ^{1}H NMR, the different peaks obtained at desirable δ values (in ppm) confirmed its formation. A singlet at $\delta = 3.75$ helped to prove the presence of three protons of the methoxy group. The presence of the protons of the methylene group was indicated by $\delta = 4.11$ showing a sharp singlet peak. The aromatic protons present in the phenyl ring were confirmed by the multiplet peak obtained in the range of $\delta = 6.74–8.03$. In the structure there are two –NH (secondary amine) present; the two protons of each secondary amine can be easily differentiated from the shift observed in the peaks of the corresponding amines. The proton of –NH in the vicinity of –C=O group was confirmed by the value $\delta = 11.21$ whereas the proton of secondary amine in the ring confirmed its presence by showing a singlet at downfield shift of $\delta = 12.33$.

^{13}C NMR data

The δ values obtained between 39.4 and 167.3 helped to confirm the formation of the final products **III$_{1–13}$**. The formation of the linkage between the two derivatives resulting in the formation of final compounds in the form of Methylene group (–CH_2) was proved by the peak obtained at $\delta = 39.4$. With respect to the other carbon of phenyl group, the one possessing the –OCH_3 substitution showed more downfield shift exhibiting the δ value to 157.2. The carbonyl carbon (C-7) also exhibited a downfield shift $\delta = 166.1$ due

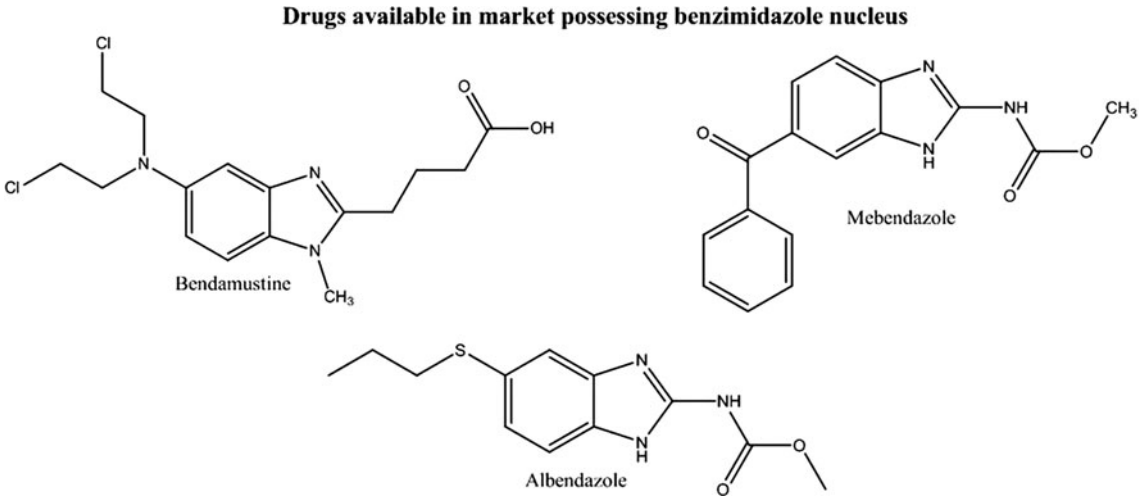


Fig. 1 Drugs with benzimidazole nucleus

to the presence of electronegative environment. A drastic shift in the δ value was observed when the protons of the phenyl ring were replaced by the different substituents. When $-NO_2$ was introduced as a substituent at para position in the phenyl ring, the shift was observed to $\delta = 136.8$ (**III$_2$**). Similarly when $-OCH_3$ was used in compound **III$_7$** and **III$_9$**; the shifts were observed for that particular carbon at δ value 149.6 and 159.1, respectively. When electronegative functional groups like fluorine and chlorine were introduced at meta position in the phenyl ring, the δ values were observed at 135.0 (**III$_3$**) and 163.0 (**III$_4$**), respectively. The carbon enumeration is given in Fig. 2.

Antimicrobial activity

A broad panel of bacterial and fungal strains was used for testing the antimicrobial properties of the synthesized molecules **III$_{1–13}$**. The results obtained were depicted in the form of MIC values for the synthesized derivatives **III$_{1–13}$**. The samples were tested by standard protocols like Micro dilution/Broth titer method. The screening for antimicrobial activity was carried out by diluting the solution and preparing the sets consecutively from 1000, 500, 250, 125, 62.5, 31.25, 15.62 up to 7.8 μg/ml. Ciprofloxacin was used as a standard drug for antibacterial activity and fluconazole was used as a standard for antifungal activity tests. The MIC values for standards fluconazole against *Candida albicans* and *Aspergillus niger* were recorded as 125 and 62.5 μg/ml, respectively. On the other hand, the MIC values obtained for the standard ciprofloxacin against Gram-positive bacteria *Staphylococcus aureus* and *Enterococcus faecalis* were 62.5 and 125 μg/ml, respectively; similarly the MIC value was recorded 125 μg/ml when tested against both the Gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa* for the same standard drug ciprofloxacin. The antibacterial and antifungal details for each compound (**III$_{1–13}$**) are discussed below.

Antibacterial activity and antifungal activity

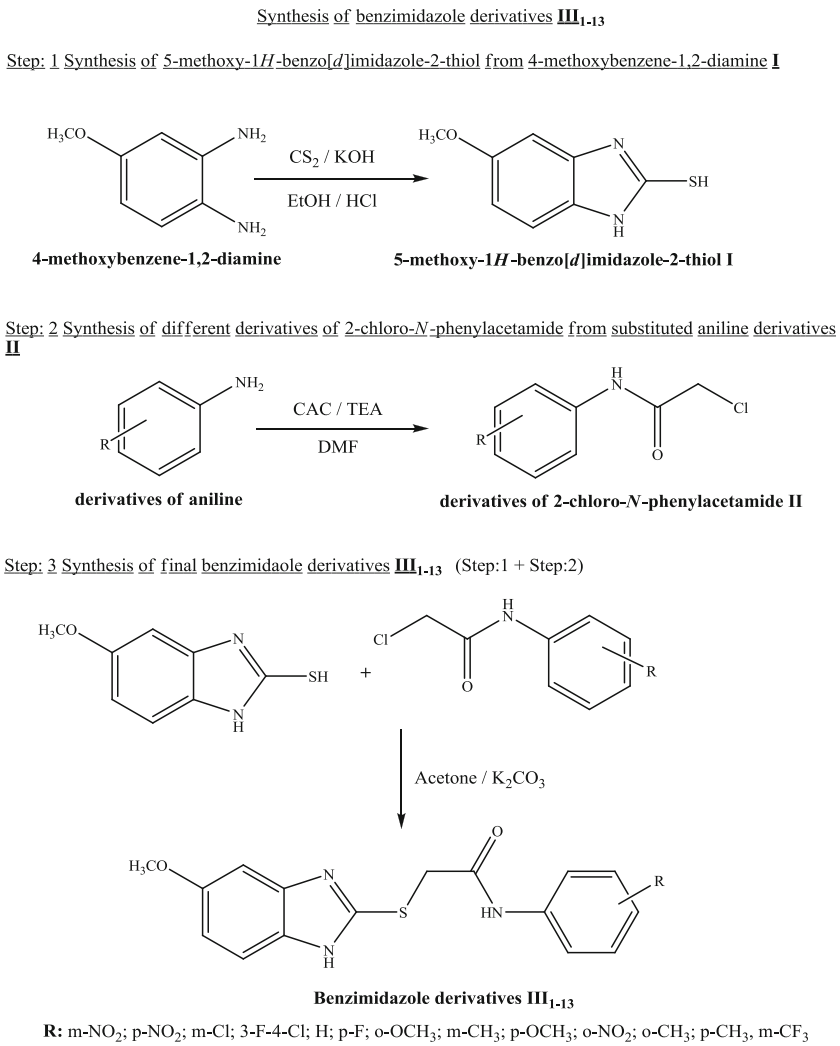
Gram-positive bacteria *S. aureus* (ATCC No. 25923) and *E. faecalis* (ATCC No. 27853) were introduced for testing the antibacterial potential of the synthesized molecules **III$_{1–13}$**. When tested against *S. aureus*, it was found that from the complete series synthesized; compounds **III$_9$** (*p*-OCH_3) and **III$_{10}$** (*o*-NO_2) exhibited activity equivalent to that of the standard ciprofloxacin (62.5 μg/ml). Other derivatives from the series exhibited higher MIC value than the standard resulting in poor results against Gram-positive bacteria *S. aureus*. Similarly the synthesized compounds were tested against another Gram-positive bacterial strain *E. faecalis*, where it was observed that the derivatives **III$_3$** (*m*-Cl), **III$_4$** (3-F-4-Cl), **III$_5$** (H), **III$_9$** (*p*-OCH_3), **III$_{10}$** (*o*-NO_2), and **III$_{11}$** (*o*-CH_3) exhibited equivalent (125 μg/ml) activity as compared to the standard. Overall half of the derivatives showed equivalent activity against Gram-positive bacteria *S. aureus* and *E. faecalis*. The final derivatives **III$_{1–13}$** were also tested against two Gram-negative bacteria *E. coli* (ATCC No. 25922) and *P. aeruginosa* (27853) and compared with the same standard ciprofloxacin. The results of most of the compounds as antibacterial were excellent against both the Gram-negative bacterial strains. The compounds **III$_4$** (3-F-4-Cl), **III$_5$** (H), **III$_6$** (*p*-F), **III$_{10}$** (*o*-NO_2), **III$_{11}$** (*o*-CH_3), **III$_{12}$** (*p*-CH_3), and **III$_{13}$** (*m*-CF_3) showed MIC value (62.5 μg/ml) even better than that of the standard drug ciprofloxacin proving excellent potency as antibacterial. The remaining derivatives from the same series which included **III$_1$** (*m*-NO_2), **III$_2$** (*p*-NO_2), **III$_3$** (*m*-Cl), **III$_8$** (*m*-CH_3), **III$_9$** (*p*-OCH_3) exhibited activity equivalent to the standard (125 μg/ml). These derivatives

when tested against *P. aeruginosa* also resulted in very good antibacterial activity, where compounds **III$_1$** (*m*-NO_2), **III$_2$** (*p*-NO_2), **III$_3$** (*m*-Cl), **III$_4$** (3-F-4-Cl), and **III$_9$** (*p*-OCH_3) were showing excellent activity (62.5 μg/ml). There were other compounds exhibiting equivalent activity (125 μg/ml) as compared to the standard drug, viz. **III$_5$** (H), **III$_6$** (*p*-F), **III$_{10}$** (*o*-NO_2), **III$_{11}$** (*o*-CH_3), **III$_{12}$** (*p*-CH_3), and **III$_{13}$** (*m*-CF_3). Thus from the series of synthesized derivatives **III$_{1–13}$** more than half of the compounds showed equivalent activity against Gram-positive bacteria and all the compounds were excellent or equivalent when tested against Gram-negative bacteria when compared to ciprofloxacin.

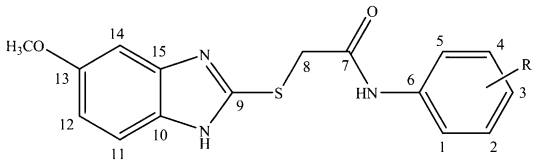
The antifungal tests were carried against two fungal strains *C. albicans* and *A. niger*, where fluconazole was used as a standard drug for comparison and evaluation of the antifungal activity of the synthesized molecules **III$_{1–13}$**. The derivatives **III$_2$** (*p*-NO_2), **III$_3$** (*m*-Cl), **III$_4$** (3-F-4-Cl), **III$_5$** (H), **III$_6$** (*p*-F), and **III$_{11}$** (*o*-CH_3) showed equivalent activity (125 μg/ml) to that of the standard drug when tested against fungal strain *C. albicans*. The rest of the compounds exhibited poor activity as compared to the standard drug result. *A. niger* when introduced for anti-fungal activity test, none of the compounds exhibit even equivalent activity to that of the standard drug. All the compounds were seen to exhibit poor activity. Very few compounds among the synthesized derivatives **III$_{1–13}$** were capable of exhibiting antifungal property.

SAR study

It was observed that the use of electron-withdrawing and electron-donating groups to confer different electronic environments on the molecules showed a great impact on their biological properties. It is very clear from the data showed in Table 1 that the derivatives possessing electron-withdrawing substituent like –NO_2, –F, and –Cl exhibit much better activity than the other derivatives, sometimes



Scheme 1 Scheme for synthesis of benzimidazole derivatives



Final derivatives $\mathbf{III_{1\text{-}13}}$

Fig. 2 Carbon enumeration of synthesized compounds $\mathbf{III_{1–13}}$

even better than the standard drugs ciprofloxacin and fluconazole. Compounds $\mathbf{III_3}$ (*m*-Cl), $\mathbf{III_4}$ (3-F-4-Cl), and $\mathbf{III_{10}}$ (*o*-NO_2) possessing electron-withdrawing functional groups exhibited excellent activity against Gram-positive bacterial strains *S. aureus* and *E. faecalis*. One more electron-withdrawing functional group fluorine was added to the list, as the compound $\mathbf{III_6}$ (*p*-F) and $\mathbf{III_{13}}$ (*m*-CF_3) also exhibited excellent activity along with the other derivatives possessing electro-withdrawing groups when tested against the Gram-negative bacteria *E. coli* and *P. aeruginosa*. It was found that only the derivatives with electron-withdrawing groups were present among the few exhibiting equivalent antifungal activity as that of the standard drug fluconazole. SAR study helped to lead to a conclusion that modifications if undertaken by introducing electron-withdrawing functional group can help to enhance the antimicrobial properties of the synthesized compounds.

Experimental

Methods, materials, and physical measurements

All the chemicals required for the synthesis were purchased from Merck ltd., HIMEDIA, LOBA Chemie, and sdfine chemicals. Melting points of the final compounds as well as derivatives were determined by open end capillary method and were uncorrected. The monitoring of the completion of reaction was determined by using TLC plates purchased from Merck (TLC Silica gel 60 F_{254}). Bruker spectrophotometer-400 MHz and -100 MHz were used to determine the ^{1}H NMR and ^{13}C NMR, respectively, for the designed compounds $\mathbf{III_{1–13}}$ using DMSO-d_6 as solvent and TMS as reference. The IR spectral data were recorded using Bruker FT-IR alpha-t (ATR). The mass spectral analysis was conducted on Shimadzu mass spectrophotometer. The elemental analysis was carried out on Perkin-Elmer 2400 CHN Analyzer.

Synthesis and physical data

Synthesis of 5-methoxy-1H-benzo[d]imidazole-2-thiol ***I***

The titled compound **I** was obtained by the literature procedure (Castilloa *et al.*, 2002).

Solid light brown; Yield: 72 %; m.p.: 258 °C; IR (ATR, cm^{-1}): 1580 (–C=N str. benzimidazole nucleus), 2923 (–CH str. methoxy group), 3090 (–CH str. aromatic ring), 3390 (–NH str. sec. amine); 1H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.75 (1H, s, –OC*H*$_3$), 6.74–7.79 (3H, m, Ar–*H*), 12.33 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 147.8 (C_9), 157.2 (C_{13}); MS (*m*/*z*): 181; For $C_8H_8N_2OS$ C, 53.3; H, 4.47; N, 15.54; S, 17.79 % Found: C, 53.35; H, 4.50; N, 15.58; s, 17.83 %.

General procedure for the synthesis of 2-chloro-N-(aryl)acetamide derivatives $\boldsymbol{II_{1–13}}$

Various substituted amines (0.01 mol) were added to a solution of DMF (35 ml) containing TEA (3–4 drops). The mixture was stirred for 10 min at room temperature. Chloroacetylchloride (0.015 mol, 113 g/mol, 1.19 ml) was added to the above mixture, maintaining the temperature between 0 and 5 °C. The obtained solution was then stirred at room temperature for 4–6 h. The completion of reaction was monitored with TLC using toluene:acetone (8:2) as mobile phase. The solution was then added onto crushed ice and the separated precipitates were filtered and dried. The product was crystallized from methanol.

2-Chloro-N-(3-nitrophenyl)acetamide $\boldsymbol{II_1}$ Solid buff; yield: 71 %; m.p.: 130 °C; IR (ATR, cm^{-1}): 1692 (–C=O str.), 2854 (–CH_2 str. methylene), 3092 (–CH str. aromatic ring), 3396 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.16 (2H, s, –C*H*$_2$), 6.69–8.19 (4H, m, Ar–*H*), 11.29 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 114.5 (C_1), 119.8 (C_3), 127.8 (C_5), 129.9 (C_4), 141.7 (C_6), 148.2 (C_2), 166.1 (C_7); MS (*m*/*z*): 215; For $C_8H_7ClN_2O_3$: C, 44.77; H, 3.29; N, 13.05 %. Found: C, 44.81; H, 3.34; N, 13.09 %.

2-Chloro-N-(4-nitrophenyl)acetamide $\boldsymbol{II_2}$ Solid light yellow; yield: 84 %; m.p.: 195 °C; IR (ATR, cm^{-1}): 1699 (–C=O str.), 2859 (–CH_2 str. methylene), 3087 (–CH str. aromatic ring), 3385 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.12 (2H, s, –C*H*$_2$), 6.74–8.09 (7H, m, Ar–*H*), 11.32 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 143.8 (C_3), 121.7 (C_5), 124.2 (C_4), 141.7 (C_6), 124.2 (C_2), 166.1 (C_7); MS (*m*/*z*): 215; For $C_8H_7ClN_2O_3$ C, 44.77; H, 3.29; N, 13.05 %. Found: C, 44.80; H, 3.35; N, 13.10 %.

2-Chloro-N-(3-chlorophenyl)acetamide $\boldsymbol{II_3}$ Solid light yellow; yield: 84 %; m.p.: 110 °C; IR (ATR, cm^{-1}): 1692 (–C=O str.), 2843 (–CH_2 str. methylene), 3099 (–CH str. aromatic ring), 3383 (–NH str. sec. amine); ^{1}H NMR

(400 MHz, DMSO-d_6, δ, ppm): 4.15 (2H, s, –CH_2), 6.79–8.12 (4H, m, Ar–*H*), 11.30 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 128.2 (C_3), 120.1 (C_5), 130.3 (C_4), 141.7 (C_6), 135.0 (C_2), 166.1 (C_7); MS (*m*/*z*): 205; For $C_8H_7Cl_2NO$ C, 47.09; H, 3.46; N, 6.86 %. Found: C, 47.13; H, 3.50; N, 6.90 %.

2-Chloro-N-(4-chloro-3-fluorophenyl)acetamide ***II*****$_4$** Solid white; yield: 74 %; m.p.: 122 °C; IR (ATR, cm^{-1}): 1688 (–C=O str.), 2852 (–CH_2 str. methylene), 3090 (–CH str. aromatic ring), 3395 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.31 (2H, s, –CH_2), 6.74–8.05 (3H, m, Ar–*H*), 11.21 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 112.0 (C_1), 116.8 (C_3), 120.1 (C_5), 128.2 (C_4), 137.7 (C_6), 163.0 (C_2), 166.1 (C_7); MS (*m*/*z*): 205; For $C_8H_6Cl_2NOF$ C, 43.27; H, 2.72; N, 6.31 %. Found: C, 43.31; H, 2.76; N, 6.35 %.

2-Chloro-N-phenylacetamide ***II*****$_5$** Solid white; yield: 66 %; m.p.: 150 °C; IR (ATR, cm^{-1}): 1690 (–C=O str.), 2858 (–CH_2 str. methylene), 3088 (–CH str. aromatic ring), 3387 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.19 (2H, s, –CH_2), 6.66–8.12 (5H, m, Ar–*H*), 11.14 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 128.2 (C_3), 121.7 (C_5), 128.2 (C_4), 141.7 (C_6), 129.0 (C_2), 166.1 (C_7); MS (*m*/*z*): 170; For C_8H_8ClNO C, 56.65; H, 4.75; N, 8.26 %. Found: C, 56.69; H, 4.79; N, 8.30 %.

2-Chloro-N-(4-fluorophenyl)acetamide ***II*****$_6$** Solid off-white; yield: 76 %; m.p.: 145 °C; IR (ATR, cm^{-1}): 1688 (–C=O str.), 2856 (–CH_2 str. methylene), 3099 (–CH str. aromatic ring), 3391 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.22 (2H, s, –CH_2), 6.56–8.02 (4H, m, Ar–*H*), 11.23 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 163.2 (C_3), 121.7 (C_5), 115.2 (C_4), 141.7 (C_6), 115.2 (C_2), 166.1 (C_7); MS (*m*/*z*): 188; For C_8H_8ClFNO C, 51.22; H, 3.76; N, 7.47 %. Found: C, 51.25; H, 3.80; N, 7.50 %.

2-Chloro-N-(2-methoxyphenyl)acetamide ***II*****$_7$** Solid brown; yield: 61 %; m.p.: 159 °C; IR (ATR, cm^{-1}): 1690 (–C=O str.), 2859 (–CH_2 str. methylene), 3087 (–CH str. aromatic ring), 3402 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.17 (2H, s, –CH_2), 6.71–8.06 (4H, m, Ar–*H*), 11.14 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 149.6 (C_1), 128.5 (C_3), 120.5 (C_5), 124.5 (C_4), 126.9 (C_6), 113.0 (C_2), 166.1 (C_7); MS (*m*/*z*): 201; For $C_9H_{10}ClNO_2$ C, 54.15; H, 5.05; N, 7.02 %. Found: C, 54.19; H, 5.09; N, 7.05 %.

2-chloro-N-m-tolylacetamide ***II*****$_8$** Solid white; yield: 63 %; m.p.: 95 °C; IR (ATR, cm^{-1}): 1691 (–C=O str.), 2852 (–CH_2 str. methylene), 3092 (–CH str. aromatic ring), 3396 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.22 (2H, s, –CH_2), 6.66–8.02 (4H, m, Ar–*H*), 11.21 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 124.5 (C_3), 119.2 (C_5), 128.5 (C_4), 141.7 (C_6), 136.6 (C_2), 166.1 (C_7); MS (*m*/*z*): 184; For $C_9H_{10}ClNO$ C, 58.86; H, 5.49; N, 7.63 %. Found: C, 58.90; H, 5.54; N, 7.68 %.

2-Chloro-N-(4-methoxyphenyl)acetamide ***II*****$_9$** Solid gray; yield: 67 %; m.p.: 138 °C; IR (ATR, cm^{-1}): 1698 (–C=O str.), 2846 (–CH_2 str. methylene), 3086 (–CH str. aromatic ring), 3391 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.16 (2H, s, –CH_2), 6.74–8.10 (4H, m, Ar–*H*), 11.28 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 159.1 (C_3), 121.7 (C_5), 115.2 (C_4), 141.7 (C_6), 115.2 (C_2), 166.1 (C_7); MS (*m*/*z*): 201; For $C_9H_{10}ClNO_2$ C, 54.15; H, 5.05; N, 7.02 %. Found: C, 54.19; H, 5.09; N, 7.05 %.

2-Chloro-N-(2-nitrophenyl)acetamide ***II*****$_{10}$** Chrome yellow; yield: 84 %; m.p.: 100 °C; IR (ATR, cm^{-1}): 1693 (–C=O str.), 2848 (–CH_2 str. methylene), 3098 (–CH str. aromatic ring), 3388 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.18 (2H, s, –CH_2), 6.70–8.19 (4H, m, Ar–*H*), 11.15 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 131.9 (C_1), 118.0 (C_3), 115.0 (C_5), 135.8 (C_4), 145.2 (C_6), 126.0 (C_2), 166.1 (C_7); MS (*m*/*z*): 215; For $C_8H_7ClN_2O_3$ C, 44.77; H, 3.29; N, 13.05 %. Found: C, 44.80; H, 3.34; N, 13.10 %.

2-Chloro-N-o-tolylacetamide ***II*****$_{11}$** Solid white; yield: 44 %; m.p.: 125 °C; IR (ATR, cm^{-1}): 1687 (–C=O str.), 2856 (–CH_2 str. methylene), 3091 (–CH str. aromatic ring), 3397 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.14 (2H, s, –CH_2), 6.80–8.21 (4H, m, Ar–*H*), 11.27 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 132.0 (C_1), 129.5 (C_3), 125.2 (C_5), 126.0 (C_4), 137.7 (C_6), 130.8 (C_2), 166.1 (C_7); MS (*m*/*z*): 184; For $C_9H_{10}ClNO$ C, 58.86; H, 5.49; N, 7.63 %. Found: C, 58.90; H, 5.55; N, 7.68 %.

2-chloro-N-p-tolylacetamide ***II*****$_{12}$** Solid white; yield: 66 %; m.p.: 170 °C; IR (ATR, cm^{-1}): 1692 (–C=O str.), 2848 (–CH_2 str. methylene), 3088 (–CH str. aromatic ring), 3387 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.20 (2H, s, –CH_2), 6.96–8.12 (4H, m, Ar–*H*), 11.17 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 121.7 (C_1), 136.8 (C_3), 123.5 (C_5), 129.4 (C_4), 141.7 (C_6), 129.4 (C_2), 166.1 (C_7); MS (*m*/*z*): 184; For $C_9H_{10}ClNO$ C, 58.86; H, 5.49; N, 7.63 %. Found: C, 58.91; H, 5.54; N, 7.68 %.

2-Chloro-N-(3-(trifluoromethyl)phenyl)acetamide ***II*****$_{13}$** Solid light brown; yield: 68 %; m.p.: 102 °C; IR (ATR, cm^{-1}): 1698 (–C=O str.), 2853 ($–CH_2$ str. methylene), 3095 (–CH str. aromatic ring), 3393 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.11 (2H, s, $–CH_2$), 6.74–8.03 (4H, m, Ar–*H*), 11.21 (1H, s, –N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 43.4 (C_8), 123.4 (C_1), 120.9 (C_3), 123.5 (C_5), 129.4 (C_4), 141.7 (C_6), 131.6 (C_2), 166.1 (C_7); MS (*m*/*z*): 238; For $C_9H_7ClF_3NO$: C, 45.49; H, 2.97; N, 5.89 %. Found: C, 45.53; H, 3.01; N, 5.93 %.

General method for the synthesis of final derivatives ***III*****$_{1–13}$**

5-Methoxy-1*H*-benzo[*d*]imidazole-2-thiol **I** (0.01 mol, 180 g/mol, 1.8 g) was made soluble in acetone. To this well-stirred solution different acetamide derivatives **II$_{1–13}$** (0.01 mol) were added. K_2CO_3 (0.02 mol, 138 g/mol, 2.76 g) was added to the above mixture and was allowed to stir for 4 h at room temperature. The completion of reaction was monitored using TLC plate with mobile phase ethyl acetate:*n*-hexane (6:4). The final products thus obtained were poured into ice cold water and stirred for 30 min. The precipitates were filtered and washed occasionally. The final products **III$_{1–13}$** obtained were crystallized from alcohol.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-(3-nitrophenyl)acetamide ***III*****$_1$** Solid dark yellow; yield: 50 %; m.p.: 118 °C; IR (ATR, cm^{-1}): 1587 (–C=N str. benzimidazole nucleus), 1692 (–C=O str.), 2854 ($–CH_2$ str. methylene), 2926 (–CH str. methoxy group), 3092 (–CH str. aromatic ring), 3396 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.72 (3H, s, $–OCH_3$), 4.16 (2H, s, $–CH_2$), 6.69–8.19 (7H, m, Ar–*H*), 11.29 (1H, s, –N*H*), 12.31 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 114.5 (C_1), 117.1 (C_{11}), 119.8 (C_3), 127.8 (C_5), 129.9 (C_4), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 148.2 (C_2), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 359 (M^+). For $C_{16}H_{14}N_4O_4S$: C, 53.62; H, 3.94; N, 15.63; S, 8.95 %. Found: C, 53.67; H, 3.98; N, 15.67; S, 8.98 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-(4-nitrophenyl)acetamide ***III*****$_2$** Solid yellow; yield: 59 %; m.p.: 125 °C; IR (ATR, cm^{-1}): 1584 (–C=N str. benzimidazole nucleus), 1699 (–C=O str.), 2859 ($–CH_2$ str. methylene), 2915 (–CH str. methoxy group), 3087 (–CH str. aromatic ring), 3385 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.75 (3H, s, $–OCH_3$), 4.12 (2H, s, $–CH_2$), 6.74–8.09 (7H, m, Ar–*H*), 11.32 (1H, s, –N*H*), 12.36 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 121.7 (C_5), 121.7 (C_1), 124.2 (C_2), 124.2 (C_4), 139.0 (C_{15}), 141.7 (C_6), 143.8 (C_3), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 359 (M^+). For $C_{16}H_{14}N_4O_4S$: C, 53.62; H, 3.94; N, 15.63; S, 8.95 %. Found: C, 53.66; H, 3.99; N, 15.66; S, 8.99 %.

N-(3-Chlorophenyl)-2-(5-methoxy-1H-benzo[d]imidazol-2-ylthio)acetamide ***III*****$_3$** Solid off-white; yield: 63 %; m.p.: 121 °C; IR (ATR, cm^{-1}): 1587 (–C=N str. benzimidazole nucleus), 1692 (–C=O str.), 2843 ($–CH_2$ str. methylene), 2935 (–CH str. methoxy group), 3099 (–CH str. aromatic ring), 3383 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.71 (3H, s, $–OCH_3$), 4.15 (2H, s, $–CH_2$), 6.79–8.12 (7H, m, Ar–*H*), 11.30 (1H, s, –N*H*), 12.29 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 120.1 (C_5), 121.7 (C_1), 128.2 (C_3), 130.3 (C_4), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 163.0 (C_2), 167.3 (C_7); MS (*m*/*z*): 348 (M^+). For $C_{16}H_{14}N_3O_2SCl$: C, 55.25; H, 4.06; N, 12.08; S, 9.22 %. Found: C, 55.29; H, 4.10; N, 12.11; S, 9.25 %.

N-(4-Chloro-3-fluorophenyl)-2-(5-methoxy-1H-benzo[d]imidazol-2-ylthio)acetamide ***III*****$_4$** Solid white; 59 %; m.p.: 202 °C; IR (ATR, cm^{-1}): 1592 (–C=N str. benzimidazole nucleus), 1688 (–C=O str.), 2852 ($–CH_2$ str. methylene), 2930 (–CH str. methoxy group), 3090 (–CH str. aromatic ring), 3395 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.72 (3H, s, $–OCH_3$), 4.31 (2H, s, $–CH_2$), 6.74–8.05 (6H, m, Ar–*H*), 11.21 (1H, s, –N*H*), 12.35 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.0 (C_1), 112.2 (C_{12}), 116.8 (C_3), 117.1 (C_{11}), 121.8 (C_5), 130.6 (C_4), 139.0 (C_{15}), 137.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 163.0 (C_2), 167.3 (C_7); MS (*m*/*z*): 366 (M^+). For $C_{16}H_{13}N_3O_2SClF$: C, 52.53; H, 3.58; N, 11.49; S, 8.77 %. Found: C, 53.56; H, 3.62; N, 11.53; S, 8.80 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-phenylacetamide ***III*****$_5$** Solid white; yield: 55 %; m.p.: 118 °C; IR (ATR, cm^{-1}): 1586 (–C=N str. benzimidazole nucleus), 1690 (–C=O str.), 2858 ($–CH_2$ str. methylene), 2928 (–CH str. methoxy group), 3088 (–CH str. aromatic ring), 3387 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.71 (3H, s, $–OCH_3$), 4.19 (2H, s, $–CH_2$), 6.66–8.12 (8H, m, Ar–*H*), 11.14 (1H, s, –N*H*), 12.32 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 121.7 (C_5), 121.7 (C_1), 128.2 (C_3), 129.0 (C_4), 129.0 (C_2), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 314 (M^+). For $C_{16}H_{15}N_3O_2S$: C, 61.32; H, 4.82; N, 13.41; S, 10.23 %. Found: C, 61.35; H, 4.85; N, 13.45; S, 10.26 %.

N-(4-Fluorophenyl)-2-(5-methoxy-1H-benzo[d]imidazol-2-ylthio)acetamide ***III*****$_6$** Solid off-white; yield: 58 %; m.p.: 158 °C; IR (ATR, cm^{-1}): 1592 (–C=N str. benzimidazole

nucleus), 1688 (–C=O str.), 2856 (–CH_2 str. methylene), 2926 (–CH str. methoxy group), 3099 (–CH str. aromatic ring), 3391 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.69 (3H, s, –O*CH*$_3$), 4.22 (2H, s, –*CH*$_2$), 6.56–8.03 (7H, m, Ar–*H*), 11.23 (1H, s, –N*H*), 12.37 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 115.2 (C_4), 115.2 (C_2), 117.1 (C_{11}), 121.7 (C_5), 121.7 (C_1), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 163.2(C_3), 167.3 (C_7); MS (*m*/*z*): 332 (M^+). For $C_{16}H_{14}N_3O_2FS$: C, 57.99; H, 4.26; N, 12.68; S, 9.68 %. Found: C, 58.02; H, 4.30; N, 12.72; S, 9.71 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-(2-methoxyphenyl)acetamide ***III*****$_7$** Solid cream; yield: 44 %; m.p.: 156 °C; IR (ATR, cm^{-1}): 1586 (–C=N str. benzimidazole nucleus), 1690 (–C=O str.), 2859 (–CH_2 str. methylene), 2920 (–CH str. methoxy group), 3087 (–CH str. aromatic ring), 3402 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.72 (3H, s, –O*CH*$_3$), 4.17 (2H, s, –*CH*$_2$), 6.71–8.06 (7H, m, Ar–*H*), 11.14 (1H, s, –N*H*), 12.37 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 120.5 (C_5), 149.6 (C_1), 128.5(C_3), 124.5 (C_4), 113.0 (C_2), 139.0 (C_{15}), 126.9 (C_6), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 344 (M^+). For $C_{17}H_{17}N_3O_3S$: C, 59.46; H, 4.99; N, 12.24; S, 9.34 %. Found: C, 59.51; H, 5.04; N, 12.28; S, 9.39 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-m-tolylacetamide ***III*****$_8$** Solid white; yield: 54 %; m.p.: 105 °C; IR (ATR, cm^{-1}): 1576 (–C=N str. benzimidazole nucleus), 1691 (–C=O str.), 2852 (–CH_2 str. methylene), 2944 (–CH str. methoxy group), 3092 (–CH str. aromatic ring), 3396 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.69 (3H, s, –O*CH*$_3$), 4.22 (2H, s, –*CH*$_2$), 6.66–8.02 (7H, m, Ar–*H*), 11.21 (1H, s, –N*H*), 12.32 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 119.2 (C_5), 121.7 (C_1), 124.5(C_3), 128.8 (C_4), 136.6 (C_2), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 328 (M^+). For $C_{17}H_{17}N_3O_2S$: C, 62.36; H, 5.23; N, 12.83; S, 9.79 %. Found: C, 62.41; H, 5.28; N, 12.87; S, 9.84 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-(4-methoxyphenyl)acetamide ***III*****$_9$** Solid off-white; yield: 62 %; m.p.: 195 °C; IR (ATR, cm^{-1}): 1587 (–C=N str. benzimidazole nucleus), 1698 (–C=O str.), 2846 (–CH_2 str. methylene), 2936 (–CH str. methoxy group), 3086 (–CH str. aromatic ring), 3391 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.80 (3H, s, –O*CH*$_3$), 4.16 (2H, s, –*CH*$_2$), 6.74–8.10 (7H, m, Ar–*H*), 11.28 (1H, s, –N*H*), 12.29 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 115.2 (C_2), 115.2 (C_4), 117.1 (C_{11}), 121.7 (C_5), 121.7 (C_1), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 159.1 (C_3), 167.3 (C_7); MS (*m*/*z*): 344 (M^+). For $C_{17}H_{17}N_3O_3S$: C, 59.46; H, 4.99; N, 12.24; S, 9.34 %. Found: C, 59.50; H, 5.04; N, 12.27; S, 9.38 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-(2-nitrophenyl)acetamide ***III*****$_{10}$** Solid yellow; yield: 60 %; m.p.: 105 °C; IR (ATR, cm^{-1}): 1582 (–C=N str. benzimidazole nucleus), 1693 (–C=O str.), 2848 (–CH_2 str. methylene), 2925 (–CH str. methoxy group), 3098 (–CH str. aromatic ring), 3388 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.75 (3H, s, –O*CH*$_3$), 4.18 (2H, s, –*CH*$_2$), 6.70–8.19 (7H, m, Ar–*H*), 11.15 (1H, s, –N*H*), 12.27 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 115.0 (C_5), 118.0 (C_3), 126.0 (C_2), 131.9 (C_1), 135.8 (C_4), 139.0 (C_{15}), 145.2 (C_6), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 359 (M^+). For $C_{16}H_{16}N_4O_4S$: C, 53.62; H, 3.94; N, 15.63; S, 8.95 %. Found: C, 53.66; H, 3.95; N, 15.66; S, 8.99 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-o-tolylacetamide ***III*****$_{11}$** Solid light brown; yield: 53 %; m.p.: 156 °C; IR (ATR, cm^{-1}): 1576 (–C=N str. benzimidazole nucleus), 1687 (–C=O str.), 2856 (–CH_2 str. methylene), 2918 (–CH str. methoxy group), 3091 (–CH str. aromatic ring), 3397 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.53 (3H, s, –C*H*$_3$); 3.76 (3H, s, –O*CH*$_3$), 4.14 (2H, s, –*CH*$_2$), 6.80–8.21 (7H, m, Ar–*H*), 11.27 (1H, s, –N*H*), 12.33 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 125.2 (C_5), 126.0 (C_4), 129.5(C_3), 130.8 (C_2), 132.0 (C_1), 137.7 (C_6), 139.0 (C_{15}), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 328 (M^+). For $C_{17}H_{17}N_3O_2S$: C, 62.36; H, 5.23; N, 12.83; S, 7.79 %. Found: C, 62.41; H, 5.26; N, 12.87; S, 7.74 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-p-tolylacetamide ***III*****$_{12}$** Solid light brown; yield: 76 %; m.p.: 175 °C; IR (ATR, cm^{-1}): 1584 (–C=N str. benzimidazole nucleus), 1692 (–C=O str.), 2848 (–CH_2 str. methylene), 2926 (–CH str. methoxy group), 3088 (–CH str. aromatic ring), 3387 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.49 (3H, s, –C*H*$_3$); 3.79 (3H, s, –O*CH*$_3$), 4.20 (2H, s, –*CH*$_2$), 6.96–8.12 (7H, m, Ar–*H*), 11.17 (1H, s, –N*H*), 12.30 (1H, s, benzimidazole-N*H*); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 121.7 (C_1), 123.5 (C_5), 129.4 (C_2), 129.4 (C_4), 136.8(C_3), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (*m*/*z*): 328 (M^+).

For $C_{17}H_{17}N_3O_2S$: C, 62.36; H, 5.23; N, 12.83; S, 7.79 %. Found: C, 62.41; H, 5.28; N, 12.87; S, 7.73 %.

2-(5-Methoxy-1H-benzo[d]imidazol-2-ylthio)-N-(3-(trifluoromethyl)phenyl)acetamide ***III*****$_{13}$** Solid light cream; yield: 66 %; m.p.: 109 °C; IR (ATR, cm^{-1}): 1161 (–C–F str. $–CF_3$), 1580 (–C=N str. benzimidazole nucleus), 1698 (–C=O str.), 2853 ($–CH_2$ str. methylene), 2921 (–CH str. methoxy group), 3095 (–CH str. aromatic ring), 3393 (–NH str. sec. amine); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.75 (3H, s, $–OCH_3$), 4.11 (2H, s, $–CH_2$), 6.74–8.03 (7H, m, Ar–H), 11.21 (1H, s, –NH), 12.33 (1H, s, benzimidazole-NH); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 39.4 (C_8), 103.2 (C_{14}), 112.2 (C_{12}), 117.1 (C_{11}), 120.9 (C_3), 123.4 (C_1), 123.5 (C_5), 129.4 (C_4), 131.6 (C_2), 139.0 (C_{15}), 141.7 (C_6), 147.8 (C_9), 157.2 (C_{13}), 167.3 (C_7); MS (m/z): 382 (M^+). For $C_{17}H_{14}F_3N_3O_2S$: C, 53.54; H, 3.70; N, 11.02; S, 8.41 %. Found: C, 53.58; H, 3.74; N, 11.05; S, 8.45 %.

Conclusion

The bioactive molecules synthesized by the authors were found to possess excellent antibacterial property. The SAR study undertaken for the synthesized derivatives (**III$_{1–13}$**) clearly lead to a conclusion that the use of electron-withdrawing functional groups as substituent helped to enhance the antimicrobial property. The molecules synthesized here can be further optimized by introducing more electron-withdrawing sites, which may help to develop few newer potent leads. On the basis of above results, attempts are made to optimize the lead structure to obtain more potent antimicrobial molecules. The modifications undertaken for future study will help to develop much better antimicrobial heterocyclic scaffolds.

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