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Synthesis and Antimicrobial Activity of Some New Benzimidazole Derivatives

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Abstract: Reaction of 3-(2-methylbenzimidazol-1-yl)propanoic acid hydrazide (**1**) with CS_2/KOH gave oxadiazole **2** which underwent Mannich reaction to give **3**. Compound **2** was treated with hydrazine hydrate to give triazole **4** which was treated with both aldehydes and acetic anhydride to give **5** and **6**, respectively. Carbohydrazide **1** was reacted with ethyl acetoacetate, acetylacetone and aldehydes to give **7**, **8** and **9**, respectively. Cyclocondensation of **9** with thioglycolic and thiolactic acids gave **10** and **11**, respectively. Some of these compounds showed potential antimicrobial activities.

Keywords: Methylbenzimidazole, oxadiazole, thioglycolic, thiolactic, triazole, pyrazole, antimicrobial.

Introduction

A wide variety of benzimidazole derivatives have been described for their chemotherapeutic importance [1-6]. Oxadiazole compounds have shown biological activity against parasites [7] and bacteria [8]. Also, the presence of basic Mannich side chains in a drug may overcome the water insolubility problem through the formation of hydrochlorides [9]. Also, some heterocyclic moieties such as triazole nucleus are known to possess antibacterial [10] and fungicidal [11] properties. Furthermore, Schiff's bases possess anticancer [12,13] activity in animal screening, and pyrazoles, pyrazolones and alkylpyrazoles have shown wide ranging pharmacological applications [14]. We

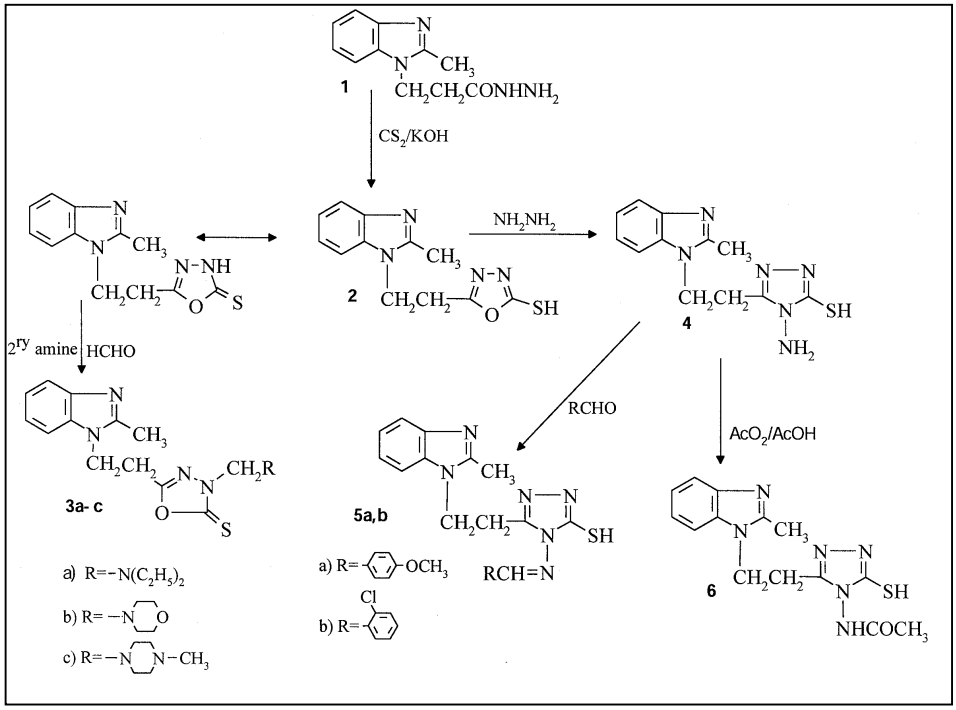
report here the synthesis of some derivatives of the title structure type containing the above mentioned moieties for evaluation of their antimicrobial activity.

Results and Discussion

In the present work, 3-(2-methylbenzimidazol-1-yl)propanoic acid hydrazide (**1**), which was previously prepared by one of us [15], was used as the key intermediate for further synthesis. Thus, when compound **1** was treated with carbon disulphide and potassium hydroxide according to a reported method of Young and Wood [8,16], 5-[2-(2-methylbenzimidazol-1-yl)ethyl]-[1,3,4]-oxadiazole-2(3H)-thione (**2**) was obtained, (Scheme 1, Tables 2 and 3). One of the earliest discoveries concerning the utility of Mannich bases as intermediates in drug synthesis was made by Burckhalter and co-workers [17]. Similarly, compound **2** was allowed to undergo the Mannich reaction with different secondary amines namely, diethylamine, morpholine or *N*-methylpiprazine and paraformaldehyde in absolute ethanol to give compounds **3a-c** respectively. (Scheme 1, Tables 2 and 3).

A benzimidazole incorporated into a triazole moiety was synthesized by the reaction of **2** with hydrazine hydrate (99%) in absolute ethanol which afforded 1-[(1-amino-2-mercapto-1,3,4-triazol-5-yl)ethyl]-2-methylbenzimidazole (**4**). (Scheme 1, Tables 2 and 3).

A number of arylidine hydrazones incorporated into the parent benzimidazole were also synthesized. Thus condensation of compound **4** with aromatic aldehydes, namely, *p*-methoxy benzaldehyde and *o*-chlorobenzaldehyde in absolute ethanol afforded the corresponding Schiff's bases **5a,b** respectively. (Scheme 1, Tables 2 and 3).

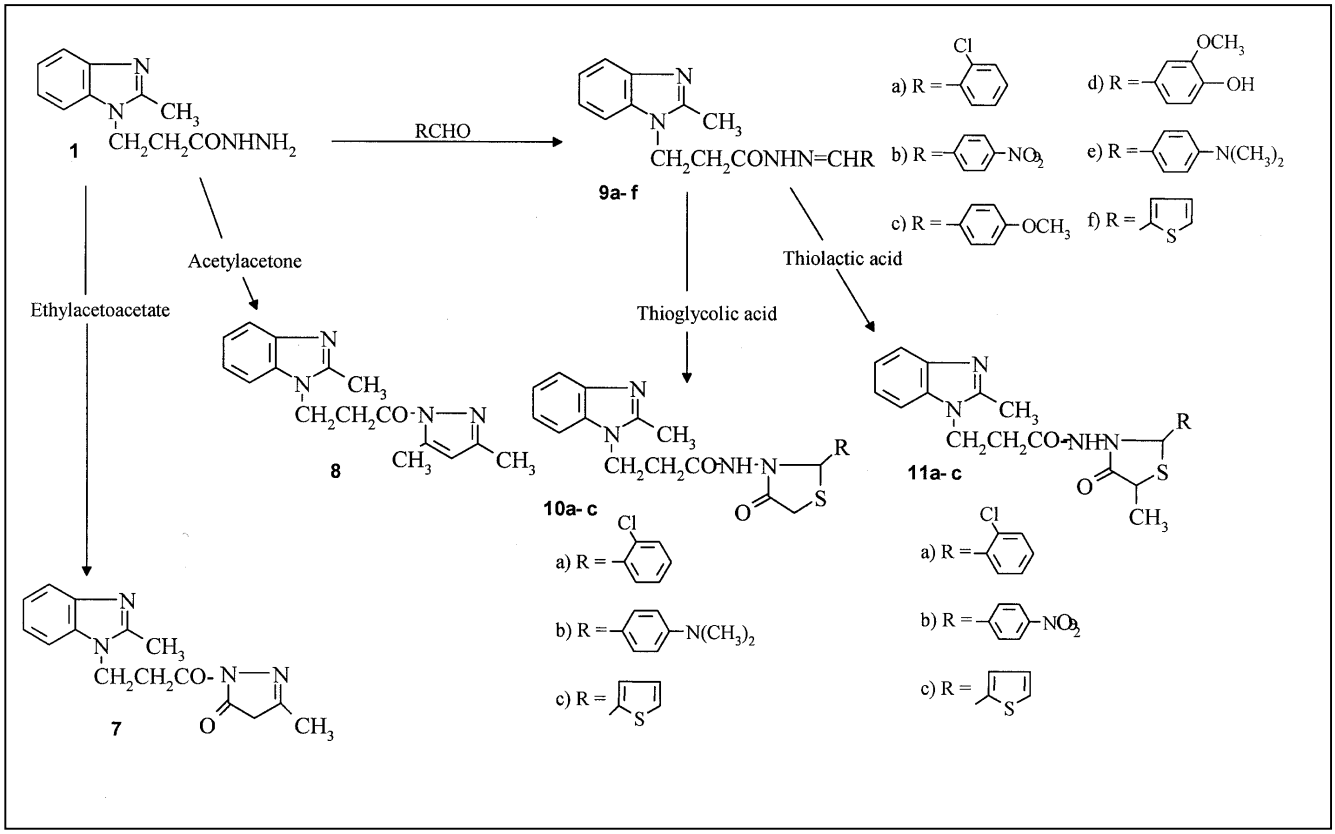


Scheme 1.

On the other hand, reaction of **4** with acetic anhydride in the presence of glacial acetic acid leads to the formation of monoacetyl derivative **6**. (Scheme 1, Tables 2 and 3).

Carbohydrazide **1** was also allowed to react with ethyl acetoacetate and acetylacetone to give the corresponding methylpyrazolone derivative **7** and dimethylpyrazole derivative **8** respectively. (Scheme 2, Tables 1 and 3). Condensation of compound **1** with aromatic and heterocyclic aldehydes in absolute ethanol afforded the corresponding Schiff's bases **9a-f**. (Scheme 2, Tables 2 and 3).

Also, the cyclocondensation of some substituted Schiff's bases with thioglycolic acid and thiolactic acid afforded the corresponding thiazolidinone **10a-c** and methylthiazolidines **11a-c** respectively. (Scheme 2, Tables 2 and 3). This result is in accordance with previous reported results [18, 19].



Scheme 2.

Biological Screening. Antimicrobial activity test

The test was performed according to the disk diffusion method [20] adopted with some modifications for the prepared compounds using Gentamycine and Ampicelline as references. The prepared compounds were tested against one strain of Gram +ve bacteria (*Bacillus cereus*), Gram –ve bacteria (*Escherichia coli*), Yeast (*Saccharomyces cerevisae*) and Fungi (*Aspergillus niger*). Whatman No. 1 filter paper disk of 5mm diameter were sterilized by autoclaving for 15 min at 121°C . The

sterile disks were impregnated with different compounds (600 μg / disk). Agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. The impregnated disks were placed on the medium suitably spaced apart and the plates were incubated at 5 °C for 1 h. to permit good diffusion and then transferred to an incubator at 37 °C for 24 h. for bacteria, and at 28 °C for 72 h. for yeast and fungi. The inhibition zones caused by the various compounds on the microorganisms were examined. The results of the preliminary screening test are listed in Table 1. The antibacterial and antifungal activity of compounds **1**, **2**, **3a**, **4**, **5b**, **8**, **9a**, **10a,c** and **11a,c** were tested. From the data obtained in Table 1, it is clear that compound **2** was found to be highly active against *Bacillus cereus* but, slightly active against *Escherichia coli*. Compounds **4** and **9a** were found to be moderately active against *Bacillus cereus* while compounds **3a** and **10c** were found to be slightly active against *Bacillus cereus*. But all the tested compounds were found to be inactive against *Saccharomyces cerevisae* and *Aspergillus niger*. Also, compounds **1**, **5b**, **8**, **10a** and **11a** were found to be inactive against all microorganisms used.

Table 1. Results of antimicrobial activity of the tested compounds.

Compound No.	***B. cereus* .**	***E. coli* .**	***S. cerevisae* .**	***A. niger* .**
Gentamycine	+++	+++	-	-
Ampicelline	+++	+++	-	-
1	-	-	-	-
2	+++	+	-	-
3a	+	-	-	-
4	++	-	-	-
5b	-	-	-	-
8	-	-	-	-
9a	++	-	-	-
10a	-	-	-	-
10c	+	-	-	-
11a	-	-	-	-
11c	-	+	-	-

Key to symbols:

Highly active = +++ (inhibition zone > 12 mm)
Moderately active = ++ (inhibition zone 9 - 12 mm)
Slightly active = + (inhibition zone 6 - 9 mm)
Inactive = - (inhibition zone < 6 mm)

Experimental

Materials and Methods

All melting points are uncorrected and were taken in open capillaries on a Gallenkamp apparatus. Infrared spectra were determined in KBr on a Perkin Elmer Model-137 Infracord. The ^{1}H-NMR spectra were measured in DMSO-d6 or $CDCl_3$ solutions using a JEOL EX-270MHz spectrometer. The mass spectra were recorded on a GCMS-QP 1000 EX Shimadzu Gas Chromatography-MS apparatus. Spectroscopic and physical data is listed in Tables 2 and 3.

Synthesis of compounds

5-[2-(2-Methylbenzimidazol-1-yl) ethyl][1,3,4]oxadiazole-2(3H)-thione (2)

To a mixture of carbohydrazide **1** (2.18 g, 0.01 mole) in ethanol (200 mL) was added a solution of KOH (0.84 gm , 0.015 mole) in ethanol (20 mL), followed by CS_2 (20mL). The reaction mixture was heated under reflux for 8 hr. Then it was concentrated, acidified with dilute hydrochloric acid and the resulting solid was collected, washed with water and recrystallized to give compound **2.**

5-[2-(2-Methylbenzimidazol-1-yl) ethyl]-3-diethylaminomethyl (or 3-*N*-morpholinylmethyl, or 3-*N*-piprazinylmethyl)[1,3,4]oxadiazole-2(3H)-thione (3a-c).

General method

A mixture of paraformaldehyde (0.9 g, 0.001mole) and the appropriate secondary amine, namely, diethylamine, morpholine or *N*-methylpiprazine (0.015 mole) was refluxed for 30 minutes in absolute ethanol (10 mL) until complete solubilization of the paraformaldehyde was observed. Compound **2** (1.04g, 0.004mole) was heated in absolute ethanol (10 mL), then added to the reaction mixture which was refluxed for 2 h. The reaction mixture was concentrated and the separated product was filtered off and recrystallized form chloroform/petroleum ether to give compounds **3a-c,** respectively.

5-[2-(2-Methylbenzimidazol-1-yl) ethyl]-4-amino[1,2,4]triazole-3-thiol (4)

A mixture of compound **2** (2.6 g, 0.01 mole) and 99% hydrazine hydrate (2 mL, 0.03 mole) in absolute ethanol (20 mL) was refluxed for 6 h. The solvent and the excess hydrazine hydrate were removed under reduced pressure, the residue washed with ether, then recrystallized to give the product **4**.

5-[2-(2-Methylbenzimidazol-1-yl)ethyl]-4-arylidenimino-[1,2,4]triazole-3-thiol (5a,b)

General method

To a solution of compound **4** (2.74 g, 0.01 mole) in absolute ethanol (30 mL), the appropriate aromatic aldehyde, namely, *p*–methoxybenzaldehyde or *o*-chlorobenzaldehyde (0.012 mole) was added. The reaction mixture was refluxed for 4 h. The formed solid after cooling was filtered off and recrystallized to give the title compounds **5a,b,** respectively.

5-[2-(2-Methylbenzimidazol-1-yl)ethyl]-4-actamido-[1,2,4]triazole-3-thiol (6)

Acetic anhydride (0.19 mL, 0.002 mole) was added to a boiling solution of 5-[2-(2-methyl-benzimidazol-1-yl) ethyl]-4amino[1,2,4]triazole-3-thiol (**4**) (0.28 g, 0.001 mole) in glacial acetic acid (3 mL). After refluxing for 2 h., the reaction mixture was cooled and poured into ice/cold water. The formed precipitate was filtered off and recrystallized from ethanol to give the title compound **6** .

1-[3-(2-Methylbenzimidazol-1-yl)propanoyl]-4,5-dihydro-3-methylpyrazol-5-one (7)

A mixture of carbohydrazide **1** (0.6 g, 0.0028 mole) and ethyl acetoacetate (0.364 g, 0.0028 mole) in absolute ethanol (20 mL) was heated at reflux temperature for 3 h. The reaction mixture was cooled and the formed precipitate was filtered off and recrystallized to give the title compound **7**.

1-[3-(2-Methylbenzimidazol-1-yl)propanoyl]-3,5-dimethylpyrazole (8)

A mixture of compound **I** (0.6 g, 0.0028 mole) and acetylacetone (0.28 g, 0.0028 mole) in absolute ethanol (20 mL) was treated according to the procedure described above to give compound **8**.

3-(2-Methylbenzimidazol-1-yl)propanoic acid hydrazide Schiff's bases (9a-f)

General method

A mixture of compound **1** (2.2 g, 0.01 mole) and the appropriate aromatic or heterocyclic aldehyde, namely, *o*-chlorobenzaldehyde, *p*-nitrobenzaldehyde, *p*-methoxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde, *p*-*N*,*N*-dimethylaminobenzaldehyde or 2-thiophenecarboxaldehyde (0.012 mole) was refluxed in absolute ethanol (20 mL) for 5 h. The reaction mixture was concentrated, cooled and the formed precipitate was filtered off, dried and then recrystallized to give the title compounds **9a-f** respectively.

3-(2-Methylbenzimidazol-1-yl)-N-(2-aryl-4-oxo[1,3]thiazolidin-3-yl)propionamide (10a-c)

General method

A mixture of compound **9a,e,f** (0.005 mole) and thioglycolic acid (0.55 g, 0.006 mole) was refluxed in dry benzene (50 mL) for 6 hr. The solvent was evaporated and the reaction mixture was neutralized with cold dilute sodium bicarbonate solution, the formed product was filtered off and recrystallized to give the title compounds **10a-c** respectively.

3-(2-Methylbenzimidazol-1-yl)-N-(2-aryl-5-methyl-4-oxo[1,3]thiazolidin-3-yl)propionamide (11a-c)

General method

A mixture of compound **9a,b,f** (0.005 mole) and thiolactic acid (0.65 g, 0.006 mole) was heated to fusion at 110-120 °C in an oil bath for 8 hr. The reaction mixture was neutralized with sodium bicarbonate solution, the formed product was filtered off and recrystallized to give the title compounds **11a-c** respectively.

Table 2. Spectral data for the newly synthesized compounds.

Compd. No	Spectral data
2	IR (KBr, cm^{-1}): 3300 (NH), 2923 (CH), 2600 (SH), 1624 (C=N) and 1136.0 (C=S), [(SH) and (C=S) absorptions indicate thiol-thione tautomers]. ^{1}H-NMR (DMSO-d_6, δ ppm): 2.55 (3H, s, CH_3 at C-2 of benzimidazole), 3.25 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 4.6 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$) and 7.25-7.6 (5H, m, aromatic protons, and SH). MS, m/z (%): 260 (M^+, 57.72), 145 (100).
3a	IR (KBr, cm^{-1}): 2991 (CH), 1180 (C-O), 1654 (C=N) and 1150 (C=S). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.2 (6H, t, *J* = 7 Hz, 2 $CH_2\underline{CH_3}$), 2.55 (3H, s, CH_3 at C-2 of benzimidazole), 2.75 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.6 (4H, q, *J* = 6 Hz, 2 $\underline{CH_2}$ CH_3), 4.45 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 4.9 (2H, s, NCH_2N) and 7.15-7.6 (4H, m, aromatic protons).
3b	IR: (KBr, cm^{-1}), 2985 (CH), 1177 (C-O), 1660 (C=N) and 1147 (C=S). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.55 (4H, t, *J* = 7 Hz, $N(CH_2)_2$ of morpholine ring), 2.6 (3H, s, CH_3 at C-2 of benzimidazole), 3.2 (2H, t, $NCH_2\underline{CH_2}$), 3.65 (4H, t, *J* = 7 Hz, $O(CH_2)_2$ of morpholine ring), 4.5 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$) 4.85 (2H, s, NCH_2N) and 7.15-7.7 (4H, m, aromatic protons).
3c	IR (KBr, cm^{-1}): 2988 (CH), 1176 (C-O), 1658 (C=N) and 1148 (C=S). MS: ($M^{+\cdot}$,$C_{18}H_{24}N_6OS$), m/z 372.5 (0.09, unstable) and the base peak at m/z 145 (100).
4	IR (KBr, cm^{-1}): 3420, 3300, 3145 (NH_2 sym., asym-stretch and NH), 2600 (SH), 1155 (C=S) (thiol-thione tautomers) and 1620 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 3.2 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 4.55 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 5.6 (2H, s, NH_2) and 7.25-7.6 (5H, m, aromatic protons and SH). MS, m/z (%):274 (M^+, 76.46), 145 (100).
5a	IR (KBr, cm^{-1}): 3047 (NH), 2993 (CH), 2580 (SH), 1267 (C=S) and 1153 (C-O). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 3.2 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.85 (3H, s, OCH_3), 4.55 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$) and 7.1-7.8 (8H, m, aromatic protons), 9.4 (1H, s, $\underline{CH}$=N) and 13.8 (1H, s, NH). MS, m/z (%): 392 (M^+, 14.05), 132 (100).
5b	IR (KBr, cm^{-1}): 3162 (NH), 2986 (CH), 2593 (SH), 1282 (C=S) and 746 (C-Cl). MS, m/z (%): 398 (M^+, ^{37}Cl, 0.29), 396 (M^+, ^{35}Cl, 0.60), 132 (100).
6	IR (KBr, cm^{-1}): 3157 (NH), 2964 (CH), 2486 (SH) and 1697 (C=O). MS, m/z (%): 316 (M^+, 16.1), 145 (100).

Compd. No	Spectral data
7	IR (KBr, cm^{-1}): 3210 (NH), 3005, 2995 (CH), 1732 (C=O, of pyrazolone), 1682 (C=O) and 1663 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.2 (3H, s, CH_3 at C-3 of pyrazolone), 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 2.75 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.1 (2H, s, CH_2 of pyrazolone), 4.5 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), and 7.15-7.6 (4H, m, aromatic protons). MS, m/z (%): 284 (M^+, 0.33), 145 (100).
8	IR (KBr, cm^{-1}): 2990 (CH) and 1668 (C=O). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.55, 1.75 (6H, 2s, $2CH_3$ of pyrazoline), 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 2.95 (2H, t, *J* = 7 Hz,$NCH_2\underline{CH_2}$), 4.45 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$) and 7.0-7.6 (5H, m, 4 aromatic protons and 1H of pyrazoline).
9a	IR (KBr, cm^{-1}): 3100 (NH), 2990 (CH), 1671 (C=O). MS, m/z (%): 342 (M^+, ^{37}Cl, 20.7), 340 (M^+, ^{35}Cl, 58.3), 145 (100).
9b	IR (KBr, cm^{-1}): 3045 (NH), 2964 (CH), 1671 (C=O), 1514, 1327 (NO_2).
9c	IR (KBr, cm^{-1}): 3190 (NH), 3000 (CH), 1670 (C=O). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.45 (3H, s, CH_3 at C-2 of benzimidazole), 3.0 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.6 (3H, s, OCH_3), 4.35 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 6.65-7.7 (9H, m, 8 aromatic protons and 1H of N=$\underline{CH}$) and 10.3 (1H, s, NH). MS, m/z (%): 336 (M^+, 100).
9d	IR (KBr, cm^{-1}): 3400 (OH), 3200 (NH), 2968(CH), 1664 (C=O). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 3.0 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.7 (3H, s, OCH_3), 4.35 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 6.65-7.9 (8H, m, 7 aromatic protons and 1H of N=$\underline{CH}$), 9.5 (1H, s, OH) and 11.1 (1H, s, NH). MS, m/z (%): 352 (M^+, 57), 145 (100).
9e	IR (KBr, cm^{-1}): 3251 (NH), 2984 (CH), 1672 (C=O). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 2.95 (6H, s, $N(CH_3)_2$), 3.2 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 4.45 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 6.7-7.9 (9H, m, 8 aromatic protons and 1H of N=$\underline{CH}$) and 11.1 (1H, s, NH).
9f	IR (KBr, cm^{-1}): 3209 (NH), 2997 (CH), 1668 (C=O).
10a	IR (KBr, cm^{-1}): 3417 (NH), 2930 (CH), 1716 (C=O of thiazolidinone), 1673 (C=O amide) and 746 (C-Cl). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.5 (3H, s, CH_3 at C-2 of benzimidazole), 2.65 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.75 (1H, d, *J* = *6* Hz, A part of an AB system, equatorial proton of thiazolidinone at C-5), 3.9 (1H, d, *J* = *6* Hz, B part of an AB system, axial proton of thiazolidinone at C-5), 4.35 (2H, t, $N\underline{CH_2}CH_2$), 6.00 (1H, s,CH of thiazolidinone at C-2), 7.1-7.5 (8H, m, aromatic protons) and 10.4 (1H, s, NH). MS, m/z (%): 416 (M^+, ^{37}Cl, 3.62), 414 (M^+, ^{35}Cl, 10.70), 132 (100).
10b	IR (KBr, cm): 3415 (NH), 2951 (CH), 1719 (C=O of thiazolidinone), 1676 (C=O amide).
10c	IR (KBr, cm^{-1}): 3418 (NH), 2930 (CH), 1720 (C=O of thiazolidinone), 1677 (C=O amide). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.45 (3H, s, CH_3 at C-2 of benzimidazole), 2.65 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.7 (1H, d, *J* = *6* Hz, A part of an AB system, equatorial proton of thiazolidinone at C-5), 4.0 (1H, d, *J* = *6* Hz, B part of an AB system, axial proton of thiazolidinone at C-5), 4.45 (2H, t, $N\underline{CH_2}CH_2$), 5.95 (1H, s,CH of thiazolidinone at C-2), 6.7-7.5 (7H, m, aromatic protons) and 10.5 (1H, s, NH). MS, m/z (%): 386 (M^+, 0.7), 132 (100).
11a	IR (KBr, cm-1): 3400 (NH), 3000 (CH), 1715 (C=O of thiazolidinone), 1670 (C=O amide). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.45 (3H, d, *J* = 6 Hz, CH_3 at C-5 of thiazolidinone), 2.45 (3H, s, CH_3 at C-2 of benzimidazole), 2.65 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.65 (1H, q, CH of thiazolidinone at C-5), 4.35 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 6.1 (1H, s, CH of thiazolidinone at C-2), 7.1-7.55 (8H, m, aromatic protons) and 10.4 (1H, s, NH). MS, m/z (%): 430 (M^+, ^{37}Cl, 8.89), 428 (M^+, ^{35}Cl, 25.78), 160 (100).
11b	IR (KBr, cm^{-1}): 3440 (NH), 2930 (CH), 1720 (C=O of thiazolidinone), 1677 (C=O amide) and 1520, 1325 (NO_2).
11c	IR (KBr, cm^{-1}): 3341 (NH), 3008 (CH), 1711 (C=O of thiazolidinone), 1675 (C=O amide). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.43 (3H, d, *J* = 6 Hz, CH_3 at C-5 of thiazolidinone), 2.42 (3H, s, CH_3 at C-2 of benzimidazole), 2.65 (2H, t, *J* = 7 Hz, $NCH_2\underline{CH_2}$), 3.65 (1H, q, CH of thiazolidinone at C-5), 4.4 (2H, t, *J* = 7 Hz, $N\underline{CH_2}CH_2$), 6.2 (1H, s, CH of thiazolidinone at C-2), 6.9-7.5 (7H, m, aromatic protons) and 10.4 (1H, s, NH). MS, m/z (%): 400 (M^+, 0.6), 132 (100).

Table 3. Yields, physical and analytical data of the prepared compounds.

Comp No.	M.P. °C (Recryst. Solvents)	Yield %	Formulae (M.Wt.)	Analysis % ,Calculated / Found			
				C	H	N	S
2	208-210 (AcOH/H_2O)	86	$C_{12}H_{12}N_4OS$ (260.28)	55.37 55.29	4.65 4.63	21.52 21.45	12.32 12.28
3a	89-91 ($CHCl_3$/Pet.ether)	65	$C_{17}H_{23}N_5OS$ (345.51)	59.10 59.18	6.71 6.77	20.27 20.32	-
3b	183-185 ($CHCl_3$/Pet.ether)	60	$C_{17}H_{21}N_5O_2S$ (359.49)	56.80 56.85	5.89 5.93	19.48 19.51	-
3c	149-150 ($CHCl_3$/Pet.ether)	63	$C_{18}H_{24}N_6OS$ (372.54)	58.04 58.15	6.49 6.51	22.56 22.62	-
4	304-306 (AcOH/H_2O)	85	$C_{12}H_{14}N_6S$ (274.35)	52.53 52.45	5.14 5.12	30.63 30.54	11.68 11.65
5a	261-263 (AcOH/H_2O)	80	$C_{20}H_{20}N_6OS$ (392.48)	61.20 61.27	5.15 5.17	21.42 21.43	-
5b	249-251 (AcOH/H_2O)	85	$C_{19}H_{17}ClN_6S$ (396.93)	57.49 57.53	4.32 4.37	21.18 21.21	-
6	282-284 (Ethanol)	68	$C_{14}H_{16}N_6OS$ (316.43)	53.14 53.09	5.11 5.20	26.56 26.54	-
7	123-124 (Ethanol)	65	$C_{15}H_{16}N_4O_2$ (284.35)	63.36 63.32	5.68 5.67	19.71 19.69	-
8	139-141 (Ethanol)	75	$C_{16}H_{18}N_4O$ (282.38)	68.06 68.09	6.43 6.47	19.85 19.90	-
9a	187-189 (Ethanol/H_2O)	87.5	$C_{18}H_{17}ClN_4O$ (340.84)	63.43 63.41	5.04 5.01	16.44 16.40	-
9b	199-201 (Ethanol/H_2O)	82.6	$C_{18}H_{17}N_5O_3$ (351.36)	61.53 61.59	4.88 4.82	19.93 19.99	-
9c	167-169 (Ethanol/H_2O)	88	$C_{19}H_{20}N_4O_2$ (336.43)	67.84 67.87	6.00 6.12	16.66 16.69	-
9d	229-231 (Ethanol/H_2O)	90	$C_{19}H_{20}N_4O_3$ (352.43)	64.74 64.71	5.73 5.69	15.90 15.96	-
9e	179-181 (Ethanol/H_2O)	91	$C_{20}H_{23}N_5O$ (349.48)	68.73 68.68	6.65 6.60	20.04 20.12	-
9f	89-91 (Ethanol/H_2O)	85	$C_{16}H_{16}N_4OS$ (312.42)	61.51 61.56	5.17 5.20	17.93 17.99	-
10a	249-251 (Ethanol/H_2O)	71	$C_{20}H_{19}ClN_4O_2S$ (414.94)	57.89 57.84	4.62 4.65	13.51 13.48	7.73 7.69
10b	264-266 (Ethanol/H_2O)	64	$C_{22}H_{25}N_5O_2S$ (423.58)	62.39 62.45	5.96 5.98	16.54 16.58	7.55 7.60
10c	120-122 (Ethanol/H_2O)	40	$C_{18}H_{18}N_4O_2S_2$ (386.52)	55.94 55.98	4.70 4.69	14.49 14.46	16.59 16.55
11a	193-195 ($CHCl_3$/Pet.ether)	74	$C_{21}H_{21}ClN_4O_2S$ (428.97)	58.80 58.87	4.94 4.96	13.06 13.11	7.47 7.50
11b	159-161 (Ethanol/H_2O)	53	$C_{21}H_{21}N_5O_4S$ (439.53)	57.38 57.35	4.83 4.82	15.94 15.91	7.29 7.25
11c	131-133 ($CHCl_3$/Pet.ether)	44	$C_{19}H_{20}N_4O_2S_2$ (400.5)	56.97 57.12	5.04 5.11	13.99 14.13	16.00 16.10

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