Synthesis and Biological Activities of Some Benzimidazolone Derivatives

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The reaction of 5-nitrobenzimidazolone with phenoxyethyl bromide in presence of potassium carbonate in dimethyl formamide obtained 6-nitro-1,3-bis(2-phenoxyethyl)-1,3-dihydro-2*H*-benzimidazol-2-one. It was reduced using stannous chloride to get 6-amino -1,3-bis(2-phenoxyethyl)-1, 3-dihydro-2*H*-benzimidazol -2-one, which was further treated with aromatic sulphonyl chloride to obtain benzimidazolone derivatives, 6a-k. These compounds were tested for antibacterial, antituberculosis and antifungal activity. Most of them have shown very good activity against some gram positive and gram negative microorganisms and fungal strains. Some of them have shown moderate activity against *Mycobacterium tuberculosis*.

Key words: Benzimidazolone, antifungal, antibacterial and antituberculosis activity

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The incidence of bacterial and fungal infections has increased dramatically in the past 20 years partly because of the increase in the number of people whose immune systems are compromised by with AIDS, aging, organ transplantation or cancer therapy. Accordingly, the increase in rates of morbidity and mortality because of bacterial and fungal infections has been now recognized as a major problem. In response to the increased incidence of bacterial and fungal infections, researchers are working on the development of newer less toxic antiinfective agents for clinical use.

Sulfonamide drugs were the first antimicrobial drugs, and paved the way for the antibiotic revolution in medicine. There are several sulfonamide-based groups of antiinfective drugs e.g. sulfamethoxazole, which are known as the reversible inhibitors of folic acid synthesis[1]. Sulfa drugs are still widely used for conditions such as acne and urinary tract infections, and are receiving renewed interest for the treatment of infections caused by bacteria resistant to other antibiotics.

In the last few years, benzimidazole and benzimidazolone have been studied extensively for their antitumor[2], antiviral[3] and antibiotic activities such as the antiprotozoal and antibacterial[4]. Recently, Monforte *et al.* identified some 1,3-dihydrobenzimidazol-2-one derivative and their sulfones as a potent and novel class of non-nucleoside reverse transcriptase inhibitor[5]. Aryloxyalkyl benzimidazole derivatives have been explored for antimicrobial activity by Khalafi-Nezhad *et al.* and have suggested that negative electrostatic potentials around oxygen of the phenoxy and nitrogen of the imidazole moieties have direct effect on the antibacterial activity towards *Staphylococcus aureus*[6].

Very few attempts have been made so far to explore antimicrobial activity of sulfonamide linked benzimidazolone. In order to explore the potential role of sulfonamide linked benzimidazolone in antiinfective treatment, we have synthesized some aryloxyalkyl benzimidazolone linked to various heterocyclic ring systems through sulfonamide linkage and tested them for antimicrobial activity.

All the recorded melting points were determined in open capillary and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on 400 MHz spectrophotometer in DMSO-d_6 as a solvent and TMS as an internal standard. Peak positions are shown in ppm values. Mass spectra were obtained by Waters mass spectrometer. Thin layer chromatography (TLC) was performed on precoated aluminum sheets of Silica Gel 60 F254 (Merck, Art. 5554), visualization of products being accomplished by UV absorption.

General procedure used for the synthesis of 6-nitro-1,3-bis(2-phenoxyethyl)-1,3-dihydro-2*H*-benzimidazol-2-one (3) was as follows. Compound 1 (0.01 mol) and 2 (0.01 mol) were dissolved in DMF along with K_2CO_3. The reaction mixture was stirred at 45° for 14 h. The reaction mixture was cooled to room temperature and poured into water and extracted by ethyl acetate. The organic layer separated, dried over sodium sulphate and concentrated under vacuum. The crude product was recystallised from ethanol.

Compound (3) was obtained in a yield of 86%; yellow solid, mp: 90-92°. Analysis calculated for $C_{23}H_{21}N_3O_5$: C, 65.86; H, 5.05; N, 10.02. Found: C, 65.70; H, 5.01; N, 9.90. IR (KBr): 3432 s, 3111 s, 1678 s, 1560 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 8.27 d, 1H, J=2.4 (Ar-H); 8.10 dd, 1H, J=8.8, 2.0 (Ar-H); 7.53 d, 1H, J=8.8 (Ar-H), 7.21 m, 4H (Ar-H); 6.8 m, 6H (Ar-H); 4.35 m, 4H, (OCH_2), 4.27 m, 4H (NCH_2). MS m/z: 420 (M+1) with all isotopic and other peaks.

General procedure used for the synthesis of 6-amino-1,3-bis(2-phenoxyethyl)-1,3-dihydro-2*H*-benzimidazol-2-one (4) was as follows, to a solution of nitro derivative 3 (0.1 mol) in methanol (50 ml) was added 5 equivalent $SnCl_2$:$2H_2O$ and the reaction mixture was heated at 60° for 4 h. The reaction mixture was cooled to room temperature and poured into liquid NH_3 and filtered through hyflow. The filtrate was extracted by ethyl acetate. The organic layer was separated, dried over sodium sulphate and concentrated under vacuum. The product was recrystallized from ethanol.

Compound (4) was obtained in a yield of 80%; white solid, mp: 64-66°. Analysis calculated for $C_{23}H_{23}N_3O_3$: C, 70.93; H, 5.95; N, 10.79. Found: C, 70.74; H, 5.90; N, 10.70. IR (KBr): 3600 s, 3432 s, 3111 s, 1678 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 7.28 m, 4H (Ar-H); 6.96 m, 7H (Ar-H); 6.62 s, 1H (Ar-H), 6.39 d, 1H, J=8.0 (Ar-H); 4.91 s, 2H (NH_2), 4.23 s,

4H (OCH_2), 4.16 s, 4H (NCH_2). MS m/z: 390 (M+1) with all isotopic and other peaks.

General procedure used for the synthesis of 5i-j was as follows; compound 7 (0.01 mol) was added in portions to the solution of chlorosulfonic acid (10 ml) at 0° and stirred for 1 h. The reaction mixture was poured into cold water and solid separated by filtration.

Compound 5i was obtained with an yield of 60%; white solid, mp: 182-184°. Analysis calculated for $C_{10}H_6Cl_2O_4S_2$: C, 36.94; H, 1.86. Found: C, 36.85; H, 1.85. IR (KBr): 1735 s, 1598 s, 800 s. ^{1}H-NMR (400 MHz, DMSO): 8.16 s, 1H (Ar-H); 8.10 d, 1H, J=8.4 (Ar-H); 7.84 d, 1H, J=8.4 (Ar-H); 3.92 s, 3H (OCH_3). ^{13}C-NMR (400 MHz, DMSO): 160.6, 146.3, 137.8, 135.4, 126.5, 126.2, 125.97, 123.2, 119.7, 52.8. MS m/z: 323 (M-1) with all isotopic and other peaks.

Compound 5j was obtained with an yield of 66%; white solid, mp:152-154°. Analysis calculated for $C_{11}H_9ClO_5S$: C, 45.76; H, 3.14. Found: C, 45.60; H, 3.13. IR (KBr): 2937 s, 2840 s, 1735 s, 1598 s. ^{1}H-NMR (400 MHz, DMSO): 8.39 d, 1H, J=1.6 (Ar-H); 8.14 dd, 1H, J=8.8, 2 (Ar-H); 7.75 d, 1H, J=8.8 (Ar-H); 4.00 s, 3H (OCH_3); 2.64 s, 3H (Ar-CH_3). ^{13}C-NMR (400 MHz, DMSO): 159.9, 156.8, 143.6, 139.7, 129.6, 126.1, 125.8, 122.0, 113.7, 52.5, 9.3. MS m/z: 289 (M+1) with all isotopic and other peaks.

General procedure used for the synthesis of 6a-g and 6k was as follows, compound 4 (0.01 mol) and aryl sulphonyl chloride (in case of 6k, 6-chloronicotinyl chloride, 0.01 mol) were dissolved in THF along with dimethylaminopyridine (DMAP) and pyridine (0.03 mol). The reaction mixture was stirred at room temperature for 6 h. The reaction mixture poured into dilute HCl and extracted by ethyl acetate. The organic layer was washed by water, separated, dried over sodium sulphate and concentrated under vacuum. The crude product was purified by using silica gel column chromatography with hexane and ethyl acetate as solvent.

Compound 6a was obtained with an yield of 76%, yellow solid, mp: 148-150°. Analysis calculated for $C_{28}H_{25}ClN_4O_5S$: C, 59.52; H, 4.46; N, 9.92. Found: C, 59.46; H, 4.44; N, 9.88. IR (KBr): 3432 s, 3111 s, 1678 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 10.36 s, 1H (NH); 8.64 d, 1H, J=2.4 (Ar-H); 8.06 dd, 1H, J=8.4, 2.4 (Ar-H); 7.67 d, 1H, J=8.4 (Ar-H), 7.18 m, 6H (Ar-H); 6.8 m, 6H (Ar-H); 6.7 dd, 1H, J=8.4, 2 (Ar-H); 4.16 s, 8H, (CH_2). MS m/z: 565 (M+1) with all isotopic and other peaks.

Compound 6b was obtained with an yield of 66%, brown microcrystalline, mp: 82-84°. Analysis calculated for $C_{33}H_{32}N_4O_6S$: C, 64.69; H, 5.26; N, 9.14. Found: C, 64.58; H, 5.25; N, 9.10. IR (KBr): 3430 s, 3119 s, 1645 s, 1677 s, 1499 s. ^{1}H-NMR (400 MHz, DMSO): 9.97 s, 1H (NH); 7.51 m, 2H (Ar-H); 7.20 m, 5H (Ar-H); 7.10 m, 2H, (Ar-H); 6.80 m, 6H (Ar-H); 6.72 m, 1H (Ar-H); 4.24 s, 4H (OCH_2); 4.09 s, 4H (NCH_2); 4.04 t, 2H (NCH_2); 3.03 t, 2H (CH_2); 2.13 s, 3H ($COCH_3$). MS m/z: 613 (M+1) with all isotopic and other peaks.

Compound 6c was obtained with an yield of 68%, yellow crystalline, mp: 85-87°. Analysis calculated for $C_{32}H_{32}N_4O_7S_2$: C, 59.24; H, 4.97; N, 8.64. Found: C, 59.16; H, 4.95; N, 8.60. IR (KBr): 3435 s, 3109 s, 1678 s, 1500 s. ^{1}H-NMR (400 MHz, DMSO): 10.19 s, 1H, (NH); 7.52 m, 2H (Ar-H); 7.22 m, 5H (Ar-H); 7.10 m, 2H, (Ar-H); 6.81 m, 6H (Ar-H); 6.74 m, 1H (Ar-H); 4.15 s, 8H (CH_2); 3.82 t, 2H (NCH_2); 3.12 s, 3H (SO_2CH_3); 3.07 t, 2H (indoline CH_2). MS m/z: 648 (M^+) with all isotopic and other peaks.

Compound 6d was obtained with an yield of 88%, yellow crystalline, mp: 83-85°. Analysis calculated for $C_{32}H_{27}N_3O_7S$: C, 64.31; H, 4.55; N, 7.03. Found: C, 64.25; H, 4.57; N, 7.06. IR (KBr): 3433 s, 3112 s, 1693 s, 1675 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 10.22 s, 1H (NH); 8.20 m, 2H (Ar-H); 7.86 d, 1H, J=10.8 (Ar-H); 7.50 d, 1H, J=10.8 (Ar-H); 7.20 m, 6H (Ar-H); 6.80 m, 7H (Ar-H); 6.55 m, 1H, (Ar-H); 4.14 s, 8H (CH_2); MS m/z: 596 (M-1) with all isotopic and other peaks.

Compound 6e was obtained with an yield of 75%, yellow crystalline, mp: 92-94°. Analysis calculated for $C_{35}H_{34}N_4O_5S$: C, 67.51; H, 5.50; N, 9.00. Found: C, 67.44; H, 5.51; N, 8.97. IR (KBr): 3435 s, 3111 s, 1677 s, 1501 s, 1350 s. ^{1}H-NMR (400 MHz, DMSO): 10.46 s, 1H, (NH); 8.40 q, 2H (Ar-H); 8.13 d, 1H, J=6.4 (Ar-H); 7.62 t, 1H (Ar-H); 7.48 t, 1H (Ar-H); 7.18 m, 5H (Ar-H); 7.04 m, 2H (Ar-H); 6.88 m, 2H (Ar-H); 6.75 m, 4H (Ar-H); 6.67 dd, 1H, J=8.4, 1.6 (Ar-H); 4.09 s, 8H (CH_2); 2.76 s, 6H (NCH_3). MS m/z: 623 (M+1) with all isotopic and other peaks.

Compound 6f was obtained with an yield of 78%, yellow crystalline, mp: 85-87°. Analysis calculated for $C_{33}H_{34}N_4O_7S_2$: C, 59.80; H, 5.17; N, 8.45. Found: C, 59.72; H, 5.15; N, 8.48. IR (KBr): 3435 s 3109 s 1678 s, 1500 s. ^{1}H-NMR (400 MHz, DMSO): 10.05 s, 1H, (NH); 7.64 d, 1H, J=2 (Ar-H); 7.51 m, 2H (Ar-H); 7.20 m, 6H (Ar-H); 6.81 m, 7H (Ar-H); 4.16 s, 8H (CH_2); 3.64 t, 2H (tetrahydroquinoline NCH_2); 3.09 s, 3H (SO_2CH_3) 2.70 t, 2H (tetrahydroquinoline CH_2); 1.80 m, 2H (tetrahydroquinoline CH_2). MS m/z: 663(M+1) with all isotopic and other peaks.

Compound 6g was obtained with an yield of 44%, yellow crystalline, mp: 89-91°. Analysis calculated for $C_{41}H_{40}N_6O_8S_2$: C, 60.88; H, 4.98; N, 10.39. Found: C, 60.74; H, 4.96; N, 10.42. IR (KBr): 3455 s, 3050 s, 2927 s, 2830 s, 1677 s. ^{1}H-NMR (400 MHz, DMSO): 10.04 s, 1H (NH); 8.25 s, 1H (N=CH); 7.85 d, 1H, J=8 (Ar-H); 7.68 m, 3H (Ar-H); 7.21 m, 7H (Ar-H); 6.85 m, 9H (Ar-H); 4.16 s, 8H (CH_2); 4.10 t, 2H (indoline NCH_2); 3.15 s, 3H (NCH_3); 2.98 t, 2H (indoline CH_2); 2.92 t, 3H (NCH_3); MS m/z: 807 (M-1) with all isotopic and other peaks.

Compound 6k was obtained with an yield of 88%, yellow solid, mp: 110-112°. Analysis calculated for $C_{29}H_{25}ClN_4O_4$: C, 65.85; H, 4.76; N, 10.59. Found: C, 65.70; H, 4.74; N, 10.55. IR (KBr): 3432 s, 3111 s, 1668 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 10.26 s, 1H (NH); 8.60 d, 1H, J=2.4 (Ar-H); 8.00 dd, 1H, J=8.4, 2.4 (Ar-H); 7.66 d, 1H, J=8.4 (Ar-H), 7.21 m, 6H (Ar-H); 6.79 m, 6H (Ar-H); 6.7 dd, 1H, J=8.0, 2 (Ar-H); 4.12 s, 8H, (CH_2). MS m/z: 527 (M-1) with all isotopic and other peaks.

General procedure used for the synthesis of 6h-j was as follows, compound 4 (0.01 mol) and aryl sulphonyl chloride (0.01 mol) were dissolved in THF along with DMAP and pyridine (0.03 mol). The reaction mixture was stirred at room temperature for 4 h. The reaction mixture poured into dilute HCl and extracted by ethyl acetate. The organic layer was washed by water, separated, dried over sodium sulphate and concentrated under vacuum. The product was dissolved in 50 ml MeOH and (1 mol) NaOH in water added to the reaction mixture and stirred at room temperature for 3 h. Reaction mixture poured in excess of water and acidified by dilute HCl to pH 2. Precipitate formed was filtered and washed by water, ether and Hexane.

Compound 6h was obtained with an yield of 86%, brown microcrystalline, mp: 68-70°. Analysis calculated for $C_{32}H_{31}N_3O_7S$: C, 63.88; H, 5.19; N, 6.98. Found: C, 63.79; H, 5.21; N, 6.96. IR (KBr): 3600 s, 3435 s, 3113 s, 1724 s, 1678 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 12.05 s, 1H (COOH); 10.05 s, 1H (NH); 7.62 d, 2H, J=8 (Ar-H); 7.32 d, 2H, J=8 (Ar-H); 7.22 m, 4H (Ar-H); 7.12 m, 2H (Ar-H); 6.90 m, 6H (Ar-H); 6.72 dd, 1H, J=8, 1.6 (Ar-H); 4.17 t, 2H (CH_2); 4.15 s, 8H (CH_2); 3.42 t, 2H (CH_2). MS m/z: 602 (M+1) with all isotopic and other peaks.

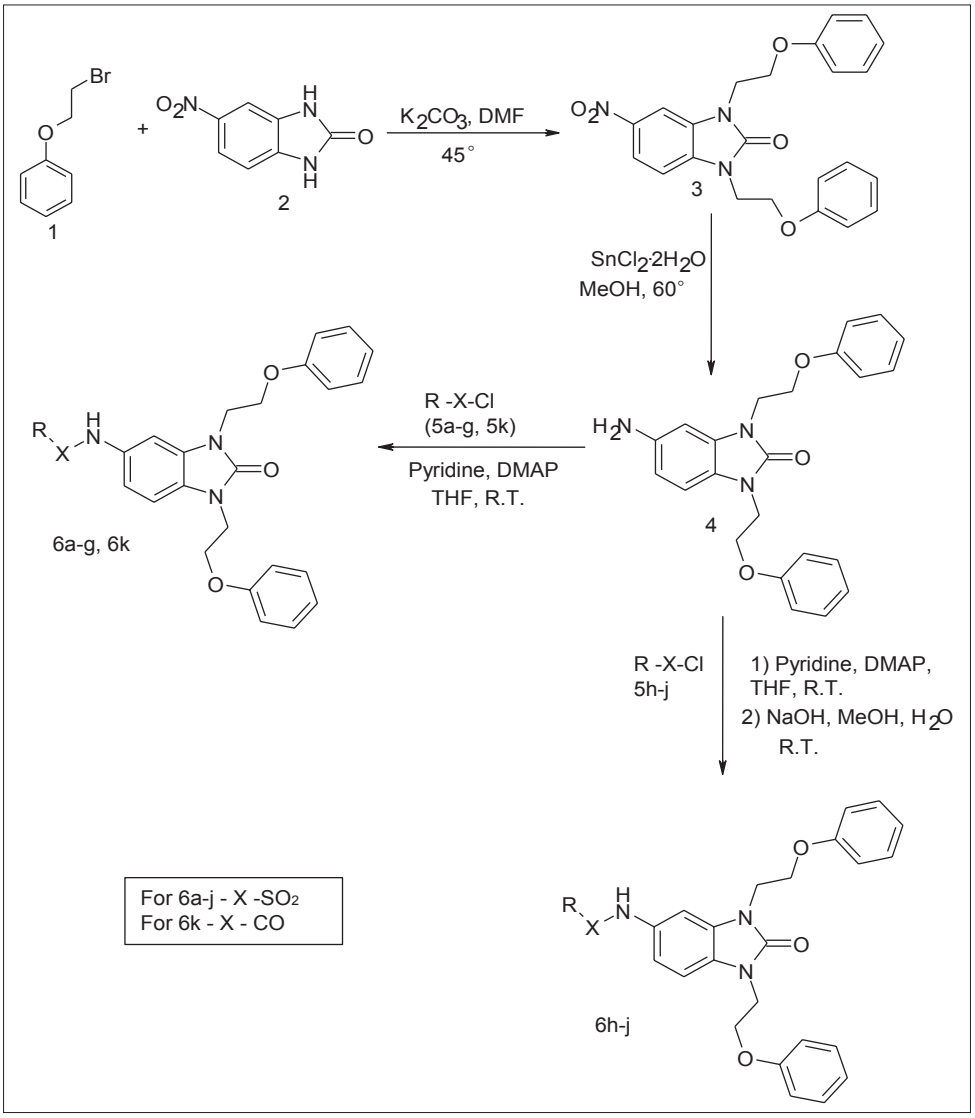
Compound 6i was obtained with an yield of 70%, yellow crystalline, mp: 101-103°. Analysis calculated for $C_{32}H_{26}ClN_3O_7S_2$: C, 57.87; H, 3.95; N, 6.33. Found: C, 57.70; H, 3.97; N, 6.36. IR (KBr): 3600 s, 3430 s, 3110 s, 1725 s, 1678 s, 1498 s. ^{1}H-NMR (400 MHz, DMSO): 12.05 s, 1H (COOH); 10.67 s, 1H (NH); 8.24 m, 2H (Ar-H); 7.87 m, 1H (Ar-H); 7.20 m, 6H (Ar-H); 6.80 m, 7H (Ar-H); 4.15 s, 8H (CH_2). MS m/z: 662 (M-1) with all isotopic and other peaks.

Compound 6j was obtained with an yield of 65%, yellow crystalline, mp: 103-105°. Analysis calculated for $C_{33}H_{29}N_3O_8S$: C, 63.15; H, 4.66; N, 6.69. Found: C, 63.00; H, 4.64; N, 6.66. IR (KBr): 3602 s, 3434 s, 3112 s, 1722 s, 1677 s, 1499 s. ^{1}H-NMR (400 MHz, DMSO): 12.05 s, 1H (COOH); 10.14 s, 1H (NH); 8.16 s, 1H (Ar-H); 7.80 m, 2H (Ar-H); 7.17 m, 5H (Ar-H); 7.10 m, 1H (Ar-H); 6.87 m, 2H (Ar-H); 6.76 m, 5H (Ar-H); 4.12 s, 8H (CH_2); 2.42 s, 3H (Ar-CH_3); MS m/z: 628 (M+1) with all isotopic and other peaks.

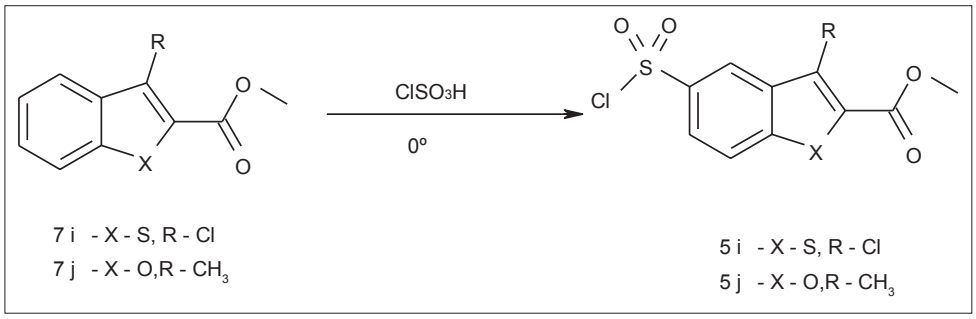
The *in vitro* antimicrobial activity of test compounds was assessed against 24 h culture of several selected bacteria and fungi. The Gram +ve and Gram -ve bacteria used were, *Escherichia coli, Pseudomonas aeruginosa*, *Streptococcus pyogenes* and *Staphylococcus aureus* and the fungi used were *Candida albicans, Aspergillus niger and Aspergillus clavatus*. Antimicrobial activity of all the compounds was tested using Muller Hinton broth (Hi Media M 391) as nutrient medium for bacteria. Growth inhibition activities for test compounds were tested using disc diffusion method. The media were prepared using distilled deionized water and dispensed in 25 ml amounts into 100 mm petri dishes. One milliliter of inoculum suspension was used to inoculate by flooding the surface of Mueller-Hinton Agar petri dish. Excess

liquid was air dried under a sterile hood. Different dilutions of test compounds and standard were loaded on 6 mm sterile disc. Dimethyl sulphoxide (DMSO) was used as negative control. The loaded disc was placed on the surface of medium and the compound was allowed to diffuse for 5 min and the plates were kept for incubation at 37° for 24 h. At the end of incubation, inhibition zones formed around the disc were measured with transparent ruler in mm.

Determination of antifungal activity of test compounds was accomplished by agar disc diffusion method



Scheme 1: Synthetic route for the preparation of benzimidazolone derivatives 6(a-k).



Scheme 2: Synthetic route for the preparation of 5i and 5j.

on Sabouraud dextrose broth. Different dilutions of test compounds and standard were loaded on 6 mm sterile disc. The loaded disc was placed on the surface of medium and the compound was allowed to diffuse for 5 min and the plates were kept for incubation at 37° for 72 h. DMSO was used as the negative control. At the end of incubation, inhibition zones formed around the disc were measured with transparent ruler in mm.

All the compounds were screened for their *in vitro* antimycobacterial activity against *M. tuberculosis* by broth macro dilution method. The activity of compounds was confirmed by MIC determination against *M. tuberculosis*. A stock solution of each compound (1 mg/ml) was diluted in sterile distilled water to test the range. Each tube contained 4 ml sterile Middle brook 7H9 broth containing albumin-dextrose-catalase, Tween 80, glycerol and 4 ml of the compound solution was added to make serial double dilutions. Tubes were incubated at 37° for 7 days and then read visually. MIC was determined as the lowest concentration of antibiotic that prevented turbidity. Streptomycin, isoniazid, rifampicin and ethambutol were used as reference standards.

TABLE 1: STRUCTURAL DATA OF THE SYNTHESIZED COMPOUNDS 6a-k

Compound code	R-X
6a	6-Chloropyridine-3-sulfonyl
6b	1-Acetyl-5-indolinesulfonyl
6c	1-(Methylsulfonyl) indoline-5-sulfonyl
6d	Coumarin-6-sulfonyl
6e	5-Dimethylamino-naphthalene-1-sulfonyl
6f	1-Methanesulfonyl-1,2,3,4-tetrahydroquinoline-6-sulfonyl
6g	1-[4-({[(1E)-(Dimethyl amino) methylene] amino} sulphonyl) benzoyl] indoline-5-sulphonyl
6h	3-[4-(sulfonyl) Phenyl] Propanoic Acid
6i	5-(sulfonyl)- 3-chlorobenzo[b] thiophene-2-carboxylic acid
6j	5-(sulfonyl)-3-methyl-1-benzofuran-2-carboxylic acid
6k	6-Chloropyridine-3-carbonyl

In the present work, 5-nitrobenzimidazolone (2) was treated with phenoxyethyl bromide (1) at 45° in DMF using potassium carbonate as a base to obtain nitro derivative (3), which was further reduced to amino derivative (4) using stannous chloride dihydrate. Amino derivative (4) was reacted with aromatic sulphonyl chloride (5a–g) in presence of pyridine and DMAP using THF as a solvent to get benzimidazolone derivatives 6a-g. Compounds 6h-j were synthesized by treating aromatic sulphonyl chlorides 5h-j, with amino compound (4) in presence of pyridine and DMAP in THF and further hydrolyzed using sodium hydroxide in methanol and water as shown in Scheme 1.

Compound (5i) was synthesized by the reaction of methyl-3-chlorobenzo[b]thiophene-2-carboxylate (7i) with chlorosulfonic acid. Similarly, compound (5j) was synthesized by treating methyl-3-methylbenzofuran-2-carboxylate (7j) with chlorosulfonic acid as shown in Scheme 2. The structure of (5i) and (5j) were confirmed by ^{13}C-NMR

TABLE 2: ANTIFUNGAL AND ANTIBACTERIAL ACTIVITY OF THE BENZIMIDAZOLONES

Comp. No.	Concentration in µg/ml																			
	A. niger				*A. clavatus*				*E. coli*				*P. aeruginosa*				*S. aureus*			
	25	50	100	250	25	50	100	250	25	50	100	250	25	50	100	250	25	50	100	250
Ampicillin									15	16	19	20	15	15	18	20	14	16	18	19
Ciprofloxacin									23	28	28	28	23	24	26	27	19	21	21	22
Norfloxacin									25	26	27	29	19	21	23	23	19	20	21	21
Griseofulvin	23	25	25	28	21	22	22	24												
Nystatin	19	24	29	29	21	24	25	26												
6a	13	16	18	20	13	17	18	21	17	18	18	19	12	13	15	17	11	15	18	20
6b	-	-	-	-	-	-	-	-	-	-	-	9	-	-	-	10	-	-	-	9
6c	-	-	-	9	-	-	9	10	-	-	-	10	-	-	-	9	-	-	-	10
6d	14	16	19	21	15	16	19	20	11	12	14	16	14	17	18	20	13	17	19	23
6e	15	18	21	22	14	17	22	22	12	12	14	15	10	11	14	16	12	14	15	17
6f	14	17	20	23	15	18	21	23	11	13	15	16	11	15	18	21	10	14	16	19
6g	15	18	21	22	14	18	19	20	15	15	18	26	12	15	20	23	13	17	18	22
6h	14	17	22	22	13	16	20	22	15	16	18	22	15	16	17	20	10	14	17	19
6i	12	15	19	19	13	15	19	21	12	13	16	17	11	11	14	16	12	15	17	19
6j	15	18	20	20	15	19	20	21	15	17	19	24	12	15	18	20	12	14	17	20
6k	-	-	10	11	-	-	9	13	-	-	-	13	-	-	-	11	-	-	-	12

Zone of inhibition (mm) excluding well size 6 mm

TABLE 3: ANTITUBERCULAR ACTIVITY OF THE BENZIMIDAZOLONES

Compound	MIC in µg/ml
Streptomycin	4
Isoniazid	0.2
Rifampicin	40
Ethambutol	2
6a	250
6b	-
6c	-
6d	500
6e	200
6f	500
6g	250
6h	100
6i	250
6j	500
6k	>1000

MIC: Minimum inhibitory concentration

and ^{1}H-NMR spectroscopy. Compound (5g) was synthesized by chlorosulfonation of 1-[4-[(1E)-(dimethylamino)methylene]aminosulphonyl)benzoyl] indoline[7].

The structural data of the compounds 6a-k is given in Table 1. All the compounds, 6a-k were characterized by FTIR, ^{1}H-NMR and mass spectroscopy. All of them were tested for their antibacterial, antifungal, and antituberculosis activities.

Except indoline derivatives 6b and 6c, all other compounds have shown very good antibacterial and antifungal activities as shown in Table 2. In order to evaluate the role of sulfonamide group in antimicrobial activity of these benzimidazolone derivatives, carboxamide analogue (6k) of one of the potent compound 6-chloropyridyl derivative (6a) was synthesized and tested for antibacterial and antifungal activity. Insignificant activity of 6-chloropyridyl derivative (6k) against bacterial and fungal strains, suggest that sulfonamide group plays vital role in antimicrobial activity of the tested compounds along with phenoxy group and nitrogen of benzimidazolone. Phenylpropionic acid derivative (6h, MIC 100 µg/ml) has shown promising antituberculosis activity. Chloropyridyl, dansyl, sulfamoylbenzoyl indoline and benzothiophene derivatives (6a, 6e, 6g and 6i) did exhibit low to moderate antituberculosis activity as shown in Table 3.

In conclusion, a series of novel sulfonamide linked benzimidazolone derivatives were synthesized and subjected to various biological activities viz. antifungal, antituberculosis and antibacterial activity. Most of the compounds have shown very good antiinfective activity, which suggest that sulfonamide linked benzimidazolone derivatives are of very high therapeutic value and need to be explored for further studies.

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