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Synthesis of New Thiazolidinyl benzimidazole and Azetidiniyl benzimidazole derivatives

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Abstract: A Series of 2-[(2′-Substitutedbenzylidenylimino-1′,3′-thiazol-4′-yl)hydrazido]benzimidazoles (**5a-5f**) 2-{[2′-(3″-Chloro-2″-oxo-4″-substitutedaryl-1″-azetidinyl)-1′,3′-thiazol-4′-yl] hydrazido} benzimidazoles (**6a-6f**) 2-{[2′-(2″-Substitutedaryl-4″-thiazoli dinon-3″-yl)-1′,3′-thiazol-4′-yl]hydrazido} benzimidazoles (**7a-7f**) were prepared in present study. The structure of all these newly synthesized compounds was confirmed on the basis of spectral (IR, ^{1}HNMR and mass) and analytical data.

Key words: Thiazolidinyl benzimidazole ,Azetidiniyl benzimidazole.

Introduction

The benzimidazole derivatives are well known in medicinal chemistry due to their diverse biological activities like insecticidal[1], antimicrobial, pesticidal[2-3] etc. Furthermore, it has also been found that the thiazole[4-5] bearing compounds show varied biological properties. Therefore there are a large number of synthetic compounds with thiazole nucleus having application is insecticidal, pesticidal, antimicrobial, anti-inflammatory etc. Moreover, certain azetidinone[6] and thiazolidinone[7-8]congeners have also found to be associated with insecticidal, antimicrobial and pesticidal profiles. Wide range of above said activities in different heterocyclic nuclei having azetidinone and thizolidinone rings prompted us to synthesize azetidinylthiazolylbenzimidazoles and thiazolidinylthiazilylbenzimidazoles and screened them for insecticidal, antifungal and antibacterial activities.

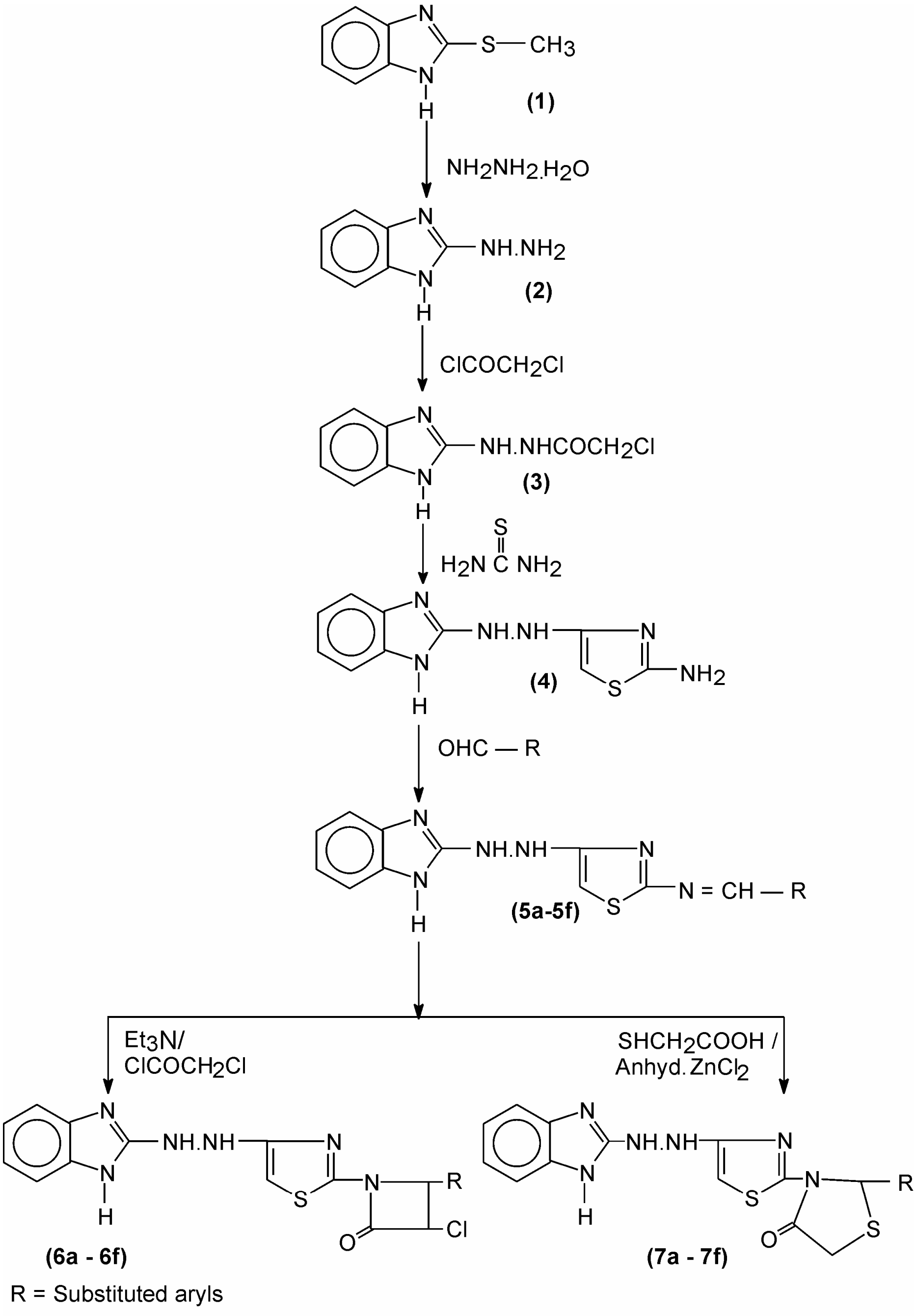
Chemistry

The starting material i.e 2-methylthiobenzimidazole **(1)** was prepared by reported method. This compound on treated with hydrazine hydrate afforded 2-hydrazido-benzimidazole **(2).** Compound 2 on reaction with chloroacetyl chloride gave 2-chloroacetyl hydrazidobenzimidazole **(3).** Further, compound 3 was converted into thiazole congener i.e 2-[(2’-amino-1’,3’-thiazol-4’-yl) hydrazido] benzimidazole **(4).** Further, compound 4 was reacted with different aromatic aldehydes to give 2-[(2’- substitutedbenzylidenylimino-1’,3’-thiazol-4’-yl) hydrazido] benzimidazoles **(5a-5f).** 2-{[2’-(3”-chloro-2”-oxo-4”-substitutedaryl-1”-azetidinyl)-1’,3’-thiazol--4’-yl) hydrazido]benzimidazoles **(6a-6f)** were prepared from compounds 5a-5f ontreatement with triethylamine/ chloroacetyl chloride. Substitutedbenzylidene congeners (5a-5f) were cyclized on reacting with thioglycolic acid and anfydrous $ZnCl_2$ to yield 2-{[2’-(2”-substitutedaryl-4”-thiazolidinon-3”-yl)-1’,3’-thiazol--4’-yl)hydrazido] benzimida- zoles **(7a-7f).**

Results

Insecticidal Activity

Compounds **5a-5f**, **6a-6f** and **7a-7f** and the reference drug, parathion, were screened at a concentration of 5 g/L against *periplaneta americana*. All the compounds were found to be more active than the parathion (Table I). Only compound **6a** possessed greater degree of insecticidal activity in comparison to standard and rest of the compounds. By considering the potentiality of this compound, it was further tested along with parathion at two graded concentrations i.e. 10 g/L and 20 g/L (Table I).



Scheme I

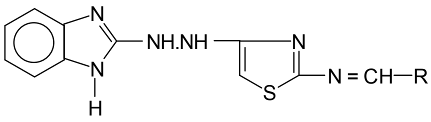
Antifungal Activity

All the compounds **5a-5f**, **6a-6f**, **7a-7f** and standard drug, fluconazole, were evaluated for *in vitro* antifungal profile against different strains of fungi at a concentration of 250 µg/mL. Results given in table II indicated that except compounds **5d**, **5f**, **7c**, **7e** and **7f**, rest compounds possessed antifungal property. Among these tested compounds, only compounds **6a** revealed better antifungal activity against *A. fumigatus, C. albicans 2091, C. albicans ATCC 10231* and *C. glabrata H05* than the standard drug (Table II).

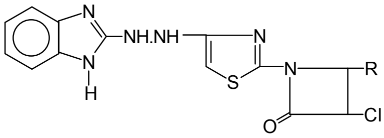
Antibacterial Activity

It is clear from the results (Table II) that only compounds **6a-6f** and **7d** exhibited antibacterial activity against *S. aureus 209P* and *E. coli ESS 2231*. However, none of these compounds showed antibacterial activity more than the standard, chloramphenicol.

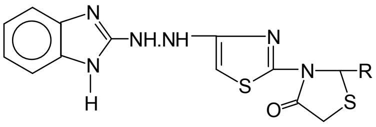
Table I: Insecticidal activity of compounds 5a-5f, 6a-6f and 7a-7f against cockroaches (*periplaneta americana*).



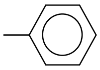
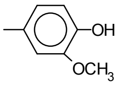
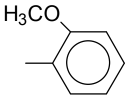
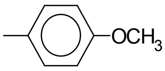
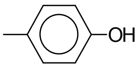
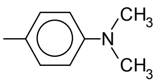
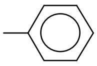
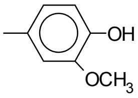
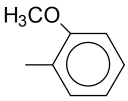
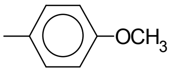
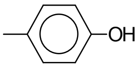
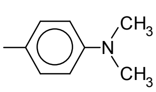
(5a-5f)

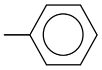
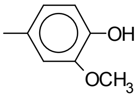
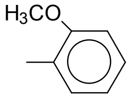
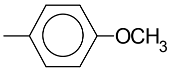
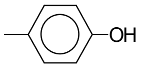
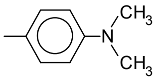


(6a-6f)



(7a-7f)

Compounds	R	Concentration	Mean killing time (minutes) ± S.E.M.
$^{@}$Control		0.02 mL	720 ± 10.29
Parathion		5 g/L 10 g/L 20 g/L	280 ± 11.74 $^{\Delta\Delta\Delta}$ 247 ± 9.29 $^{\Delta\Delta\Delta}$ 231 ± 13.75$^{\Delta\Delta\Delta}$
5a		5 g/L	188.2 ± 9.35***
5b		5 g/L	213.8 ± 13.34**
5c		5 g/L	200 ± 8.34***
5d		5 g/L	203.6 ± 10.04**
5e		5 g/L	222.3 ± 7.27**
5f		5 g/L	231.5 ± 5.27*
6a		5 g/L 10 g/L 20 g/L	140 ± 6.51*** 126 ± 8.78*** 100 ± 10.69***
6b		5 g/L	192 ± 4.29***
6c		5 g/L	166 ± 6.12***
6d		5 g/L	185 ± 4.63***
6e		5 g/L	198 ± 5.13***
6f		5 g/L	211.4 ± 5.27***

7a		5 g/L	218.6 ± 8.65 **
7b		5 g/L	257.6 ± 4.55*
7c		5 g/L	262 ± 6.43
7d		5 g/L	253.6 ± 4.98*
7e		5 g/L	270 ± 7.10
7f		5 g/L	283.6 ± 6.16

n = 5 in each group; □P < 0.05, □□P < 0.01, □□□P < 0.001 in comparison to control;
*P < 0.05, **P < 0.01, ***P < 0.001 in comparison to standard; $^{@}$acetone.

Table II: Antifungal and antibacterial activities of compounds 5a-5f, 6a-6f and 7a-7f by agar diffusion and filter paper disc methods, respectively.

Compounds	Antifungal activity$^{\#}$ **[Diameter of the inhibition zone (mm)]**					Antibacterial activity$^{\#}$ [Diameter of the inhibition zone (mm)]	
	Aspergillus fumigatus	*Candida albicans ATCC 2091*	*Candida albicans ATCC 10231*	*Candida krusei G03*	*Candida glabrata H05*	*Staphylococcus aureus 209p*	*Eschericia coli ESS 2231*
$^{@}$Control	0	0	0	0	0	0	0
Fluconazole	0	29	25	19	15	—	—
Chloramphenicol	—	—	—	—	—	20	20
5a	12	14	16	0	11	0	0
5b	0	08	13	0	10	0	0
5c	0	11	10	0	08	0	0
5d	0	0	0	0	0	0	0
5e	10	14	10	0	10	0	0
5f	0	0	0	0	0	0	0
6a	18	32	30	0	21	14	13
6b	15	18	12	0	11	12	14
6c	12	13	11	0	13	10	12
6d	10	12	10	0	13	09	10
6e	10	11	13	0	10	11	13
6f	14	12	10	0	12	08	12
7a	11	13	14	0	10	0	0
7b	11	08	10	0	09	0	0
7c	0	0	0	0	0	0	0
7d	08	10	11	0	0	10	08
7e	0	0	0	0	0	0	0
7f	0	0	0	0	0	0	0

$^{\#}$Concentration was 250µg/mL., $^{@}$ 10 % DMSO in methanol.
— : No activity done. , — : No inhibition zone.

Discussion

Eighteen compounds **5a-5f**, **6a-6f** and **7a-7f** were evaluated for their biological profiles i.e. insecticidal, antifungal and antibacterial and the results are reported (Table I and II respectively). The characteristic feature of compounds **5a-5f** is the presence of substituted arylidenylimino moiety. It was found that substitution at 2-position of the thiazole ring gave analogs with prominent insecticidal activity than the standard parathion. Out of these six compounds, compound **5a**, substituted with phenyl group at 2-position of thiazole ring, was found to be most active than the rest of the compounds (**5b-5f**). Among the compounds **5b-5f**, compounds **5c** and **5d** brought about an increase in the insecticidal activity than the compounds **5c**, **5e** and **5f**. It may be just because of the presence of methoxy group at *o*-position and *p*-position in phenyl ring of compounds **5c** and **5d**, respectively. On the other hand, it is observed that compounds **5a**, **5b**, **5c** and **5e** displayed antifungal activity against few strains of fungi. However, compound **5a** possessed good antifungal activity than rest of the compounds **5b**, **5c** and **5e**. Compounds **5a-5f** were devoid of antibacterial activity.

Furthermore, introduction of azetidinone ring in compounds **6a-6f** enhances the insecticidal and antifungal activities. It has also been observed that compounds with azetidinone moiety were found to be associated with antibacterial property. It is interesting to note from the results that compound **6a** exhibited more potent insecticidal activity in comparison to standard (*Figure-6*). This compound also displayed better antifungal activity than fluconazole and considerable antibacterial activity. It is significant to mention that compounds **6c** and **6d** having methoxy group at *o*- and *p*-position, respectively, seems to be more efficacious than rest of the compounds **6b**, **6e** and **6f**.

Cyclization of arylidene derivatives (**5a-5f**) into their corresponding thiazolidinones (**7a-7f**) has reduced the insecticidal activity. However, it is indicated from the results that compounds **7a-7e** are associated with better insecticidal property than the standard and compound **7f**, which was found to be equipotent to standard. In addition to this, the screening data of antifungal and antibacterial activities indicated that **7a**, **7b** and **7d** exhibited antifungal activity against one or more fungus tested. None of the derivatives **7a–7f** showed inhibition against both bacteria, except compound **7d**, which revealed marginal activity. From the above results and discussion, following conclusions can be drawn –

- Substituted arylidene congeners (**5a-5f**) exhibited moderate insecticidal activity.
- Conversion of compounds **5a-5f** into azetidinone derivatives (**6a-6f**) enhanced the insecticidal property.
- The presence of β-lactam ring (azetidinone moiety) in compounds (**6a-6f**) introduces, antifungal and antibacterial activities.
- Appearance of methoxy group, at *o*- or *p*-position of phenyl ring, may play a significant role in the modulation of insecticidal activity.
- The highest insecticidal and antifungal activity was evoked by substitution with phenyl group.

Biological Study

Various compounds have been synthesized and evaluated for insecticidal activity against male or female cockroaches (*Periplaneta americana*). These compounds were also assayed *in vitro* for their antifungal and antibacterial activities.

Insecticidal Activity

The insecticidal activity was determined by the method of Joshi and Tholia (1973). The cockroaches of either sex were divided in groups having five cockroaches each. An acetone solution (0.02 mL of 5 g/L) of standard insecticide, parathion, and different test compounds were injected on the ventral side of the insect, between the fourth and fifth abdominal segments with the help of a micrometer syringe. Insects receiving 0.02 mL of acetone by the same route served as control.

The treated cockroaches were kept under observation to record the time taken until 100 % mortality. During this period, no food was given. In an other set of experiment, most active compound of each *Series* at two graded doses i.e. 0.2 ml of 10 g/l and 20 g/l were also injected to groups of insects with identical doses of parathion. The statistical significance of the difference between the data of standard and test compounds was calculated by employing student's 't' test (A 1).

Antifungal Activity

The standard agar disc diffusion method (Pai and Platt, 1995) was performed to evaluate the antifungal property of test compounds and standard fluconazole.

Aspergillus fumigatus, Candida albicans ATCC 2091, Candida albicans ATCC 10231, Candida Krusei GO3 and *Candida glabrata HO5* were used in this study. All cultures were routinely maintained on SDA (A 2) and incubated at 30 ºC. In order to prepare homogeneous suspensions of these fungi for disc assays, they were grown overnight in sabouraud broth, centrifuged to collect the pellet and re-suspended in sterile phosphate buffered saline. The fungal pellet was homogenized in a sterile hand–held homogenizer. This suspension was then plated onto SDA using a bacterial spreader to obtain an even growth field.

Sterile 6 mm what man filter paper discs (A 3) were impregnated with 250 μg/mL concentration of various test compounds and standard drug, fluconazole. These discs were then placed in the centre of each quadrant of an SDA plate. Each plate had one control disc impregnated with 10% DMSO in methanol. The plates were incubated at 30 ºC. After 48 hours, the plates were removed and the radius of the zone of inhibition (in mm) was measured.

Antibacterial Activity

The antibacterial activity of test compounds and standard chloramphenicol was done by filter paper disc method (Gould and Bowie, 1952) against *Staphyloccous aureus 209 p* and *Eschericia coli ESS 2231*, at a concentration of 250 μg/mL. Media with 10% DMSO in methanol was set up as control. The presence of methanol caused no visible change in the bacterial growth.

The Whatman filter paper discs of standard size (7 mm) were prepared. These discs were put into 1 oz screw capped wide-mouthed containers. These bottles are then sterilised in hot-air oven at 150 ºC. Solution is then added to each bottle. Before use, the bottles should be shaken to distribute the discs around the walls of the container and this allows them to be picked up more easily with the forceps.

The discs are transferred to the inoculated plates with a pair of fine pointed tweezers. The tweezers may be kept with their tips immersed in 70 % alcohol, which is flamed off before use to prevent contamination.

The test organisms were grown on nutrient agar (A 4) and, before use, were subcultured in nutrient broth at 37 ºC for 18-20 hours. Each disc was applied carefully to the surface of the agar without lateral movement once the surface had been touched; where necessary they were flattened down with the points of the forceps. The plates were then incubated for 24 hours at 37 ºC, and the resulting zones of inhibition (in mm) were measured.

Experimental

General

All reagents and solvents were of analytical grade and used directly. The chemicals and solvents used for the experimental work here commercially procured from E. Merck, HIMEDIA, CDH, s. d. and Qualigens, India. All reagents and solvents were generally used as received from the commercial supplier. Reactions were routinely performed in oven-dried borosil glassware. The melting points of compounds were determined in open capillaries with the help of thermonic melting point apparatus and were uncorrected. Homogeneity of all the newly synthesized compounds was routinely checked by thin layer chromatography (TLC) on silica gel G coated plate of 0.5 mm thickness. The eluent was a mixture of different polar and nonpolar solvents in different proportions, and spots were visualized under iodine chamber. Elemental analysis (C, H, N) of all the compounds were performed on CHN analyzer, Carlo Erba 1108 analyzer at the Central Drug Research Institute (Lucknow, India). The IR spectra were recorded on Perkin Elmer 881 FTIR spectrophotometer (nmax in cm_1). The 1H NMR spectra were recorded in $CDCl_3$ and DMSO-d6 on Brucker DRX-300 FTNMR instrument.

Synthesis of 2-methylthiobenzimidazole (1).

This compound has been prepared by the procedure of Futaki (1954) and Anzai and Suzuki (1967), observed m. p. 202 ^{0}C (reported m. p. 203 ^{0}C)

Synthesis of 2-hydrazidobenzimidazole (2).

Compound **1** (0.02 mole) and hydrazine hydrate (99 %, 0.04 mole) in absolute ethanol (65 mL) were refluxed for 12 hours. The mixture was concentrated, cooled, poured in crushed ice in small proportions. The solid thus separated out was filtered, dried and recrystallized from methanol.

Yield 68%, m.p.135 ºC, Compound **2** (Found: C, 56.92; H, 5.22; N, 37.55; Calc. for $C_7H_8N_4$.: C, 56.76; H, 5.41; N, 37.84 %). IR (KBr) ν in cm^{-1}: 3388.243 (N-H), 3054.138 (C-H aromatic), 1603.501 (C=N), 1575.364 ($\mathrm{C}\overset{\cdots\cdots}{-\!-}\mathrm{C}$ of aromatic ring), 1210.093 (C-N).^{1}H-NMR ($CDCl_3$) δ in ppm: 8.05 (s, 1H, N*H* of benzimidazole ring, exchangeable with D_2O), 7.84 (brs, 3H, N*H*N*H*$_2$, exchangeable with D_2O), 7.75-7.45 (m, 4H, Ar-*H*). MS:[M]$^+$ at *m/z* 148.

Synthesis of 2-chloroacetylhydrazidobenzimidazole (3).

To the solution of 2-hydrazidobenzimidazole (**2**, 0.01 mole) in dry benzene (50 mL), chloroacetyl chloride (0.02 mole) was added gradually with stirring under cool condition. The reaction mixture was further stirred for another 2 hours at room temperature and then refluxed for 4 hours. Benzene was removed by distillation, to yield the product, which was finally recrystallized from methanol.

Yield 61%, m.p.110 ºC, Compound **3** (Found: C, 48.341; H, 4.26; N, 24.62; Calc. for $C_9H_9N_4OCl$: C, 48.11; H, 4.01; N, 24.94 %). IR (KBr) ν in cm^{-1}: 3373.329 (N-H), 3056.436 (C-H aromatic), 2955.572 (C-H aliphatic), 1681.555 (C=O), 1617.214 (C=N), 1588.355 (C⎓C of aromatic ring), 1219.087 (C-N), 760.817 (C-Cl). ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.22 (brs, 1H, N*H*CO, exchangeable with D_2O), 8.02 (s, 1H, N*H* of benzimidazole ring, exchangeable with D_2O), 7.81 (s, 1H, N*H,* exchangeable with D_2O), 7.75-7.40 (m, 4H, Ar-*H*), 4.35 (s, 2H, C*H*$_2$). MS: $[M]^+$ at *m/z* 224.

Synthesis of 2-[(2′-amino-1′,3′-thiazol-4′-yl)hydrazido]benzimidazole (4).

A mixture of compound **3** (0.02 mole), thiourea (0.02 mole) and acetone (80 mL) was refluxed for 12 hours. The purity of the reaction was proved by TLC. It was then concentrated and cooled, whereupon the solid separated out was filtered and then recrystallized from methanol. The solid thus obtained was washed with 2% saturated sodium carbonate solution and water to liberate the base completely, dried and recrystallized from ethanol/water.

Yield 60%, m.p.176 ºC, Compound **4** (Found: C, 48.351; H, 4.32; N, 33.90; Calc. for $C_{10}H_{10}N_6S$. C, 48.78; H, 4.07; N, 44.15 %). IR (KBr) ν in cm^{-1}: 3390.249 (N-H), 3064.421 (C-H aromatic), 1616.138 (C=N), 1580.342 (C⎓C of aromatic ring), 1221.051 (C-N), 690.382 (C-S-C). ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.02 (s, 1H, N*H* of benzimidazole ring, exchangeable with D_2O), 7.81 (brs, 2H, N*H*N*H,* exchangeable with D_2O), 7.70-7.45 (m, 5H, Ar-*H*), 6.40 (s, 2H, N*H*$_2$, exchangeable with D_2O). MS: $[M]^+$ at *m/z* 246.

Synthesis of 2-[2′-(benzylidenylimino-1′,3′-thiazol-4′-yl)hydrazido]benzimidazole (5a).

To the solution of compound **4** (0.01 mole) in methanol (75 mL), benzaldehyde (0.01 mole) with few drops of glacial acetic acid was added, and then reaction mixture was heated under reflux for 10 hours, while completion of the reaction was monitored by TLC. After distillation of the solvent, the reaction mixture was cooled, diluted with cold water and filtered. The solid thus collected was recrystallized from ethanol.

Yield 62%, m.p.132 ºC, Compound **5a** (Found: C, 61.25; H, 4.02; N, 25.33; Calc. for $C_{17}H_{14}N_6S$. C, 61.08; H, 4.19; N, 25.15 %). IR (KBr) ν in cm^{-1}: 3380.143 (N-H), 3043.328 (C-H aromatic), 2945.432 (C-H aliphatic), 1621.029 (C=N), 1580.384 (C⎓C of aromatic ring), 1229.083 (C-N), 678.243 (C-S-C). ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.62 (s, 1H, =C*H*-Ar), 8.05 (s, 1H, N*H* of benzimidazole ring, exchangeable with D_2O), 7.83 (brs, 2H, N*H*N*H*, exchangeable with D_2O), 7.68-7.05 (m, 10H, Ar-*H*). MS: $[M]^+$ at *m/z* 334.

Rest compounds of this series i.e. **5b**, **5c**, **5d**, **5e** and **5f** were prepared from compound **4** by the reaction with vanillin, *o*-methoxybenzaldehyde, anisaldehyde, *p*-hydroxybenzaldehyde and *p*-aminodimethylbenzaldehyde, respectively, and their physical and analytical data are given in Table I.

Synthesis of 2-{[2′-(3″-chloro-2″-oxo-4″-phenyl-1″-azetidinyl)-1′,3′-thiazol-4′-yl]hydrazido} benzimidazole (6a).

To a solution of compound **5a** (0.01 mole) in ethanol (70 mL), chloroacetyl chloride (0.02 mole) and triethylamine (0.02 mole) were added dropwise, and this heterogeneous mixture was refluxed for 8 hours. The solvent was evaporated, cooled and it was then poured over crushed ice with stirring. The product obtained after filtration was recrystallized from methanol.

Yield 55%, m.p.120 ºC, Compound **6a** (Found: C, 55.32; H, 3.77; N, 20.25; Calc. for $C_{19}H_{15}N_6OSCl$. C, 55.54; H, 3.65; N, 20.46 %). IR (KBr) ν in cm^{-1}: 3366.213 (N-H), 3023.134 (C-H aromatic), 1728.601 (C=O), 1618.241 (C=N), 1572.243 (C⎓C of aromatic ring) 1230.062 (C-N), 719.723 (C-Cl). ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.02 (s, 1H, N*H* of benzimidazole ring, exchangeable with D_2O), 7.85 (brs, 2H, N*H*N*H*, exchangeable with D_2O), 7.75-6.92 (m, 10H, Ar-*H*), 5.10 (d, *J* = 8.0 Hz, 1H, C*H*-Cl), 4.92 (d, *J* = 9.0 Hz, 1H, C*H*-Ar).

Compounds **6b**, **6c**, **6d**, **6e** and **6f** were synthesized from compounds **5b**, **5c**, **5d**, **5e** and **5f**, respectively, by employing identical method as described for compound **6a**. Physical and analytical data of compounds **6a-6f** are mentioned in Table II.

Synthesis of 2-{[2′-(2″-phenyl-4″-thiazolidinon-3″-yl)-1′,3′-thiazol-4′ yl] hydrazido} benzimidazole (7a).

A mixture of compound **5a** (0.01 mole), thioglycolic acid (0.01 mole) and anhydrous $ZnCl_2$ (2 gm) in absolute ethanol (50 mL) was refluxed for 10 hours. The progress and completion of reaction was checked by TLC. After refluxing, excess of solvent was distilled off and residue was poured in cold water, filtered, dried and finally product was recrystallized from benzene to give compound **7a**: m. p. 158 ^{0}C; yield 50 %; molecular formula $C_{19}H_{16}N_6OS_2$.

Yield 50%, m.p.158 ºC, Compound **7a** (Found: C, 56.15; H, 3.65; N, 20.72; Calc. for $C_{19}H_{15}N_6OSCl$. C, 55.88; H, 3.92; N, 20.59 %). IR (KBr) ν in cm^{-1}:

3334.138 (N-H); 3028.243 (C-H aromatic); 2935.263 (C-H aliphatic), 1692.321 (C=O), 1618.523 (C=N), 1575.362 (C⩦C of aromatic ring), 1225.621 (C-N), 688.052 (C-S-C).^{1}H-NMR ($CDCl_3$) δ in ppm: 8.06 (s, 1H, N*H* of benzimidazole ring, exchangeable with D_2O), 7.83 (brs, 2H, N*H*N*H*, exchangeable with D_2O), 7.74-6.95 (m, 10H, Ar-*H*), 4.95 (s, 1H, C*H*-Ar), 4.05 (s, 2H, CH_2 of thiazolidinone ring).MS: $[M]^+$ at *m/z* 408.

Compounds **5b**, **5c**, **5d**, **5e** and **5f** were utilized to procure compounds **7b**, **7c**, **7d**, **7e** and **7f**, respectively, using foregoing methodology for synthesis of compound **7a**, and physical and analytical data of compounds **7a-7f** are given in Table III.

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