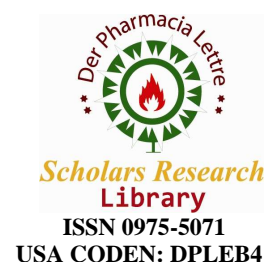




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### Synthesis and biological activity of 3-(2-(5-Benzoyl-1h-Benzo[d] Imidazol-1-Yl) Acetyl)-5-Benzylidene-2-Alkylthiazolidin-4-One

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#### Abstract

2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetohydrazide (3) undergoes facile condensation with aromatic aldehydes to afford the corresponding 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl)-N'-alkylidene aceto hydrazide (4a-h) in good yields. Cyclocondensation of compounds (4a-h) with thioglycolic acid yields 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-2-alkylthiazolidin-4-one (5a-h). These (5a-h) compounds are for the reacted with benzaldehyde in the presence of sodium ethanolate affords, giving 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-5-benzylidene-2-alkylthiazolidin-4-one (6a-h). The structures of these compounds were established on the basis of analytical and spectral data. All the newly synthesized compounds were evaluated for their antibacterial and antifungal activities.

**Key words:** 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) aceto hydrazide, thiazolidine, antibacterial activity.

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#### INTRODUCTION

Hydrazide and their heterocyclised products display diverse biological activities including antibacterial, antifungicidal, analgesic, anti-inflammatory properties [1-15]. These heterocyclic systems find wide use in medicine, agriculture and industry. One of the hydrazides, 2-hydroxy benzoic acid hydrazide (i.e. salicylhydrazide) and their condensed products play a vital role in medicinal chemistry [16-18]. 4-Thiazolidinones and its arylidene compounds give good pharmacological properties [19-23]. 4-thiazolidinones are also known to exhibit antitubercular [24], antibacterial [25], antifungal [26] and anticonvulsant activities. Hence, it was thought of interest to merge both of thiazolidinone and hydrazide moieties which may enhance the drug activity of compounds to some extent, or they might possess some of the above mentioned biological activities. From this point of view, the objective of the present work is to prepare new derivatives of benzimidazoleacetohydrazide containing thiazolidinone moiety. Many derivatives of benzimidazole show antiparasitic [27] and antiprotozoal [28] activities. Hence the present

communication comprises the synthesis of 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-5-benzylidene-2-alkylthiazolidin-4-one. The synthetic approach is shown in scheme-1.

## MATERIALS AND METHODS

Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively. LC-MS of selected samples taken on LC-MSD-Trap-SL\_01046.

### **Preparation of 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl)-N'-alkylidene aceto hydrazide (4a-h)**

**General procedure:** – An equimolar mixture of 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetohydrazide (3), (0.01mole) and the aromatic aldehydes (a-h) in ethanol (15ML) was refluxed on a water bath for 1-2 h. The solid separated was collected by filtration, dried and recrystallized from ethanol. The yields, melting points and other characterization data of these compounds are given in Table -1.

### **Preparation 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-2-alkylthiazolidin-4-one (5a-h)**

**General procedure:** A mixture 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl)-N'-alkylidene aceto hydrazide (4a-h) (0.01 mole) in THF (30ML) and mercapto acetic acid (thioglycolic acid) (0.01 mole) with a pinch of anhydrous ZnCl<sub>2</sub> was refluxed for 12 h. The solvent was then removed to get a residue, which was dissolved in benzene and passed through a column of silica gel using benzene: chloroform (8:2; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-2-alkylthiazolidin-4-one (5a-h), which were obtained in 52-66% yield. The yields, melting points and other characterization data of these compounds are given in Table -2.

### **Preparation of 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-5-benzylidene-2-alkylthiazolidin-4-one (6a-h).**

An equimolar solution of 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetyl)-2-alkylthiazolidin-4-one (5a-h) and benzaldehyde in dioxane (50ML) in the presence of C<sub>2</sub>H<sub>5</sub>ONa were refluxed for about 3 h. The solvent was removed in vacuo. The resulting product was recrystallized from methanol to yield compound (6a-h).

The yields, melting points and other characterization data of these compounds are given in Table -3.

## **Biological Screening**

### **Antibacterial activities**

The antibacterial activities of all the compounds were studied against gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and gram-negative bacteria (*E.coli*, and *klebsiella promioe*) at a concentration of 50µg/ML by agar cup plate method. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds 5d, 5f, 5g, 6c, 6f and 6g were found more toxic for microbes. Other compounds found to be less or moderate active than tetracycline Tables -4 & 5.

### **Antifungal Activities**

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *Nigrospora Sp*, *Aspergillus niger*, *Botrydepladia*

*thiobromine, and Rhizopus nigricum, Fusarium oxysporium.* The antifungal activity of all the compounds (5a-h) & (6a-h) were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200g, dextrose 20g, agar 20g and water 1c. Five days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120° C for 15 min. at 15atm. pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

$$\text{Percentage of inhibition} = 100(X-Y) / X$$

Where, X = Area of colony in control plate  
Y = Area of colony in test plate

The fungicidal activity displayed by various compounds (5a-h) and (6a-h) is shown in Tables-6 and 7.

## RESULTS AND DISCUSSION

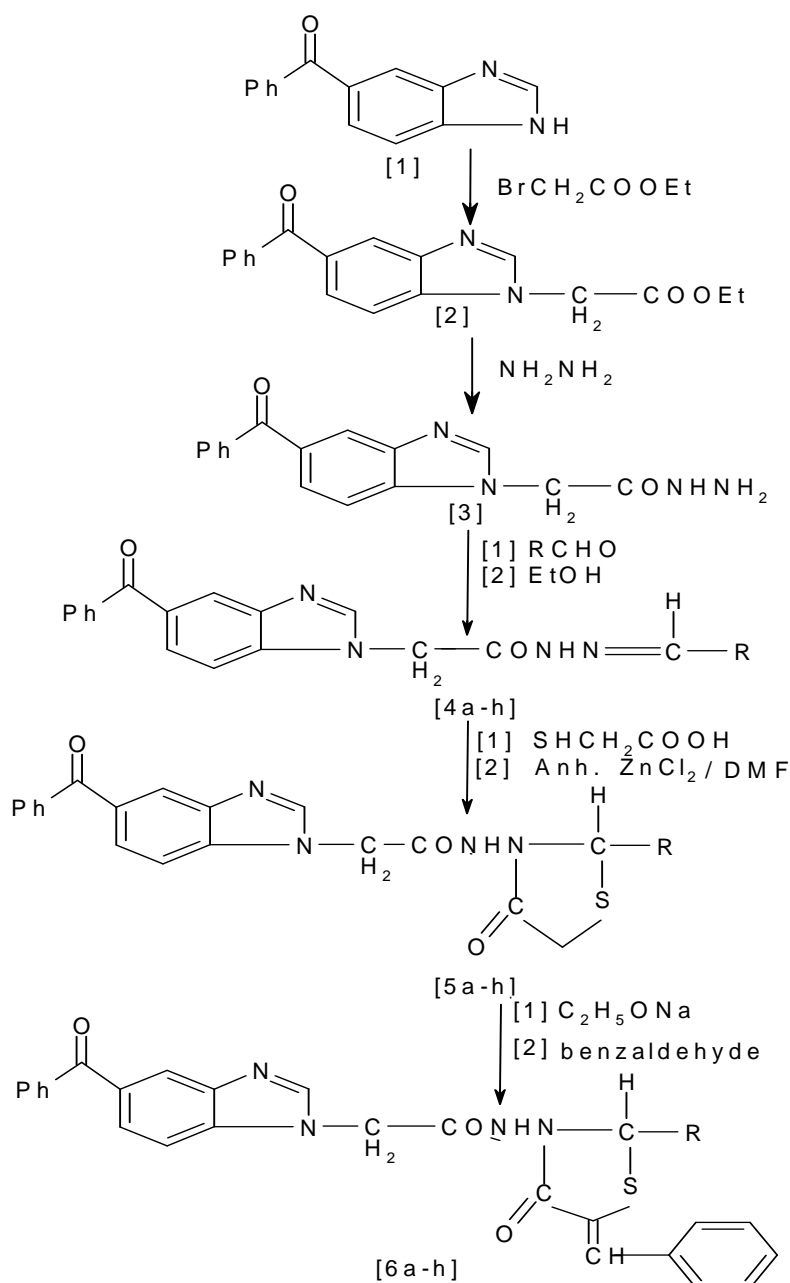
It was observed that 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetohydrazide (3), on condensation with aromatic aldehydes, yields 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl)-N'-alkylidene aceto hydrazide (4a-h). The structures of (4a-h) were confirmed by elemental analysis and IR spectra showing an absorption band at 1620-1640 (C=N), 3030-3080 cm<sup>-1</sup> (C-H, of Ar.), 1720-1750 cm<sup>-1</sup> (-CO), 2815-2850 cm<sup>-1</sup> (-OCH<sub>3</sub>), 2950, 1370 cm<sup>-1</sup> (-CH<sub>3</sub>). <sup>1</sup>H NMR : 6.95 – 7.91 (9H, m) (Ar - H), 11.800-11.809 (1H, s) (-CONH), 8.43-8.80 (1H, s) (-N=CH), 4e; 2.41 (3H, s) (-CH<sub>3</sub>), 4b, 4g; 3.90 (3H, s) (-OCH<sub>3</sub>), 4h; 4.09 (4H, q) (CH<sub>2</sub>), 1.33 (6H, t) (CH<sub>3</sub>), 4f; 6.09 (2H, s) (-OCH<sub>2</sub>O- cyclic). <sup>13</sup>C NMR:117.9-118.1, 118.2-118.4, 121.8-122.0, 128.9-129.1, 129.2-129.4, 129.5-130.0, 131.2-131.5, 133.6-133.8, 133.9-134.3, 159.6-160.0 (Ar-10C), 163.5-163.8 (-CONH), 146.9-150.4 (-CH); (4b,4g): 55.5-56.7 (-OCH<sub>3</sub>); (4e): 22.5 (CH<sub>3</sub>); (4f): 103.5 (OCH<sub>2</sub>O cyclic); (4h): 65.3 (OCH<sub>2</sub>), 15.0 (CH<sub>3</sub>). The C, H, N analysis data of all compounds are presented in Table -1.

The structures assigned to 3-(2-(5-benzoyl-1H-benzo[d]imidazol-1-yl)acetyl)-2-alkylthiazolidin-4-one (5a-h) were supported by the elemental analysis and IR spectra showing an absorption bands at 1690cm<sup>-1</sup> (C=O of thiazolidinone ring), 718cm<sup>-1</sup> (C-S-C of thiazolidinone ring), 3075-3095cm<sup>-1</sup> (CH<sub>2</sub> of thiazolidinone ring), 3030-3080 cm<sup>-1</sup> (C-H, of Ar.), 3450-3550 cm<sup>-1</sup> (-OH), 1660-1670 cm<sup>-1</sup> (-CONH) for (5a) compound.

<sup>1</sup>H NMR: 3.85-3.95 (2H, s) (-CH<sub>2</sub> of the ring), 5.950-5.959 (1H, s) (-CH), 6.90-7.95 (9H, m) (Ar-H), 8.20-8.22 (1H, s) (-CONH), 11.200-11.209 (1H, s) (-OH), 5e; 2.43 (3H, s) (-CH<sub>3</sub>), 5b,5g; 3.91 (3H, s) (-OCH<sub>3</sub>), 5h; 4.07 (4H q) (CH<sub>2</sub>), 1.33 (6H, t) (CH<sub>3</sub>), 5f; 6.09 (2H, s) (-OCH<sub>2</sub>O- cyclic). <sup>13</sup>C NMR:115.9-116.2, 121.3-121.5, 126.9-127.3, 127.4-127.6, 128.3-128.5, 128.6-128.8, 128.9-129.2 139.2-139.4, 156.9-157.5, 168.9-169.3 (Ar-10C), 38.9-39.5 (-CH<sub>2</sub> of the ring), 67.8-68.3 (-CH), 164.8-165.9 (-CONH), 168.9-169.9 (-CO of the ring), (5b,5g): 56.0-56.4 (-OCH<sub>3</sub>); (5e): 22.9 (CH<sub>3</sub>); (5f): 102.2 (OCH<sub>2</sub>O cyclic); (5h): 65.8 (OCH<sub>2</sub>), 15.5 (CH<sub>3</sub>). The C, H, N, S analysis data of all compounds are presented in Table-2.

The IR spectra of (6a-h) are almost resemble those of the corresponding (5a-h) only discernable difference observed that the new band (but not strong) at 1625cm<sup>-1</sup> (-C=CH-Ar) is observed in all the spectra of (6a-h) Which might be responsible.

$^1\text{H}$  NMR: 7.762 (1H, s) (-CH), 6.90-7.98 (9H, m) (Ar-H), 8.20-8.28 (1H, s) (-CONH), 5.350-5.359 (1H, s) (-OH), 6e; 2.41 (3H, s) (-CH<sub>3</sub>), 6b, 6g; 3.92 (3H, s) (-OCH<sub>3</sub>), 6h; 4.04, (4H, q) (-CH<sub>2</sub>), 1.33 (6H, t) (-CH<sub>3</sub>), 6f; 6.09 (2H, s) (-OCH<sub>2</sub>O cyclic).  $^{13}\text{C}$  NMR: 117.9-118.2, 118.5-119.9, 121.6-121.9, 125.9-126.3, 127.3-127.6, 128.7-128.8, 128.9-129.1, 133.8-134.0, 141.9-142.3, 159.5-160.8 (Ar-10C), 143.4-143.7 (-C- of the ring), 73.1-73.4 (-CH of the ring), 114.9-115.3 (-CH<sub>2</sub>), 166.5-166.7 (-CO), 166.8-166.9 (-CONH), (6b,6g): 55.9-56.7 (-OCH<sub>3</sub>); (6e): 21.8 (CH<sub>3</sub>); (6f): 102.8 (OCH<sub>2</sub>O); (6h): 66.1 (OCH<sub>2</sub>), 14.9 (CH<sub>3</sub>). The C, H, N, S analysis data of all compounds are presented in Table-3.



### SCHEME - 1

Where, R = (a) C<sub>6</sub>H<sub>5</sub>; (b) 4-OCH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>; (c) 4-OH-C<sub>6</sub>H<sub>4</sub>; (d) 2-OH-C<sub>6</sub>H<sub>4</sub>; (e) 4-CH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>; (f) 3,4-CH<sub>2</sub>O<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>; (g) 4-OH-3-OCH<sub>3</sub>-C<sub>6</sub>H<sub>3</sub>; (h) 3,4-C<sub>2</sub>H<sub>5</sub>-C<sub>6</sub>H<sub>4</sub>

**Table:-1 Analytical Data and Elemental Analysis of Compounds (4a-h)**

Compd.	Molecular formula (Mol.wt.)	LC-MS Data	Yield	M.P.* °C	Elemental Analysis					
					%C		%H		%N	
					Found	Calcd.	Found	Calcd.	Found	Calcd.
4a	C <sub>23</sub> H <sub>18</sub> N <sub>4</sub> O <sub>2</sub> (382)	395	88	237- 239	72.1	72.25	4.6	4.71	14.5	14.65
4b	C <sub>24</sub> H <sub>20</sub> N <sub>4</sub> O <sub>3</sub> (412)	427	84	242- 244	69.8	69.90	4.8	4.85	13.5	13.59
4c	C <sub>23</sub> H <sub>18</sub> N <sub>4</sub> O <sub>3</sub> (398)	414	82	237- 239	69.3	69.34	4.4	4.52	14.0	14.07
4d	C <sub>23</sub> H <sub>18</sub> N <sub>4</sub> O <sub>3</sub> (398)	416	85	230- 234	69.3	69.34	4.4	4.52	14.0	14.07
4e	C <sub>24</sub> H <sub>20</sub> N <sub>4</sub> O <sub>2</sub> (396)	419	84	236- 238	72.6	72.72	4.9	5.05	14.0	14.14
4f	C <sub>24</sub> H <sub>19</sub> N <sub>4</sub> O <sub>4</sub> (427)	442	86	241- 243	67.3	67.44	4.4	4.44	13.0	13.11
4g	C <sub>24</sub> H <sub>21</sub> N <sub>4</sub> O <sub>4</sub> (429)	438	83	241- 244	67.0	67.13	4.8	4.89	13.0	13.05
4h	C <sub>27</sub> H <sub>26</sub> N <sub>4</sub> O <sub>2</sub> (438)	452	76	252- 255	73.9	73.97	5.8	5.93	12.7	12.78

\* Uncorrected

**Table:-2 Analytical Data and Elemental Analysis of Compounds (5a-h)**

Compd.	Molecular formula (Mol.wt.)	LC-MS Data	Yield	M.P.* °C	Elemental Analysis							
					%C		%H		%N		%S	
					Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
5a	C <sub>24</sub> H <sub>20</sub> N <sub>4</sub> O <sub>3</sub> S (444)	459	69	210-212	64.83	64.86	4.46	4.50	12.54	12.61	7.17	7.20
5b	C <sub>25</sub> H <sub>22</sub> N <sub>4</sub> O <sub>4</sub> S (474)	49	62	206-208	63.26	63.29	4.60	4.64	11.76	11.81	6.71	6.75
5c	C <sub>24</sub> H <sub>20</sub> N <sub>4</sub> O <sub>4</sub> S (460)	476	58	155-158	62.57	62.60	4.28	4.34	12.12	12.17	6.93	6.95
5d	C <sub>24</sub> H <sub>20</sub> N <sub>4</sub> O <sub>4</sub> S (460)	477	64	130-134	62.54	62.60	4.27	4.34	12.13	12.17	6.91	6.95
5e	C <sub>25</sub> H <sub>22</sub> N <sub>4</sub> O <sub>3</sub> S (458)	472	67	167-170	65.47	65.50	4.76	4.80	12.08	12.12	6.96	6.98
5f	C <sub>25</sub> H <sub>21</sub> N <sub>4</sub> O <sub>5</sub> S (489)	504	58	181-183	61.28	61.34	4.24	4.29	11.39	11.45	6.48	6.54
5g	C <sub>25</sub> H <sub>22</sub> N <sub>4</sub> O <sub>5</sub> S (490)	507	52	154-156	61.19	61.22	4.45	4.48	11.36	11.42	6.47	6.53
5h	C <sub>28</sub> H <sub>28</sub> N <sub>4</sub> O <sub>3</sub> S (500)	513	64	190-194	67.17	67.20	5.56	5.60	11.15	11.20	6.37	6.40

\* Uncorrected

Table:-3 Analytical Data and Elemental Analysis of Compounds (6a-h)

Compd.	Molecular formula (Mol.wt.)	LC-MS Data	Yield	M.P. °C	Elemental Analysis							
					%C		%H		%N		%S	
					Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
6a	C <sub>31</sub> H <sub>24</sub> N <sub>4</sub> O <sub>3</sub> S (532)	548	72	215-217	69.86	69.92	4.47	4.51	10.45	10.52	5.97	6.01
6b	C <sub>32</sub> H <sub>26</sub> N <sub>4</sub> O <sub>4</sub> S (562)	576	63	222-223	68.27	68.32	4.56	4.62	9.93	9.96	5.64	5.69
6c	C <sub>31</sub> H <sub>25</sub> N <sub>4</sub> O <sub>4</sub> S (549)	562	65	202-205	67.71	67.75	4.49	4.55	10.17	10.20	5.76	5.82
6d	C <sub>31</sub> H <sub>25</sub> N <sub>4</sub> O <sub>4</sub> S (549)	564	57	205-206	67.70	67.75	4.46	4.55	10.18	10.20	5.75	5.82
6e	C <sub>32</sub> H <sub>26</sub> N <sub>4</sub> O <sub>3</sub> S (546)	569	52	192-196	70.29	70.32	4.70	4.76	10.21	10.25	5.83	5.86
6f	C <sub>32</sub> H <sub>25</sub> N <sub>4</sub> O <sub>5</sub> S (577)	590	58	204-209	66.48	66.55	4.28	4.33	9.66	9.70	5.49	5.54
6g	C <sub>32</sub> H <sub>27</sub> N <sub>4</sub> O <sub>5</sub> S (579)	592	55	194-196	66.26	66.32	4.62	4.66	9.62	9.67	5.47	5.52
6h	C <sub>35</sub> H <sub>33</sub> N <sub>4</sub> O <sub>5</sub> S (589)	601	54	216-218	71.27	71.30	5.55	5.60	9.46	9.50	5.38	5.43

\*Uncorrected

\*

**Table:-4 Antibacterial Activity of Compounds (5a-h)**

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiella promioe
5a	51	51	60	48
5b	56	54	54	57
5c	62	57	57	64
5d	67	66	76	46
5e	55	57	66	63
5f	65	72	76	77
5g	73	66	65	65
5h	58	58	57	45
Tetracycline	55	79	74	84

**Table:-5 Antifungal Activity of Compounds (5a-h)**

Zone of Inhibition at 1000 ppm (%)					
Compounds	Nigrospora Sp.	Aspergillus Niger	Botrydepladia Thiobromine	Rhizopus Nigricum	Fusarium oxyporium
5a	67	68	64	56	70
5b	58	51	60	65	64
5c	71	68	73	62	77
5d	66	66	67	73	61
5e	64	63	60	78	74
5f	62	51	63	65	72
5g	61	65	67	57	72
5h	58	70	72	74	66

**Table:-6 Antibacterial Activity of Compounds (6a-h)**

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiella promioe
6a	50	55	67	65
6b	60	59	56	62
6c	78	77	81	79
6d	68	72	79	43
6e	55	58	67	50
6f	63	67	58	41
6g	73	78	70	70
6h	58	60	58	60
Tetracycline	55	79	72	84

**Table:-7 Antifungal Activity of Compounds (6a-h)**

Compounds	Zone of Inhibition at 1000 ppm (%)				
	Nigrospora Sp.	Aspergillus Niger	Botrydepladia Thiobromine	Rhizopus Nigricum	Fusarium oxyporium
<b>6a</b>	68	72	68	62	63
<b>6b</b>	65	66	59	63	58
<b>6c</b>	77	58	76	67	69
<b>6d</b>	63	70	67	63	68
<b>6e</b>	68	48	70	58	71
<b>6f</b>	64	70	62	73	66
<b>6g</b>	70	58	63	63	53
<b>6h</b>	72	53	67	70	60

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure. The final structure of all compounds is confirmed by LC-MS. LC-MS data of all compounds are presented in Tables-1, 2, 3.

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#### REFERENCES

- [1] M. R. Shiradkar, K. K. Murahari, H. R. Gangadasu, T. Suresh, C. C. Kalyan, D. Panchal, R. Kaur, P. Burange, J.Ghogare, V.Mokale, M.Raut, *Bioorg.Med. Chem.*, **2007**, 15, 3997.
- [2] Y. Janin, *Bioorg. Med. Chem.***2007**, 15, 2479.
- [3] E. Gursoy, N. Guzeldemirci-Ulusoy, *Eur. J. Med. Chem.* **2007**, 42, 320.
- [4] M. R. Rao, K. Hart, N. Devanna and K. B. Chandrasekhar, *Asian J. Chem.* **2008**, 20, 1402.
- [5] K. B. Kaymakcioglu, E. E. Oruc, S. Unsalan, F. Kandemirli, N. Shvets, S. Rollas, D. Anatholy, *Eur. J. Med. Chem.***2006**,41, 1253.
- [6] R. Kalsi, M. Shrimali, T. N. Bhalla, J. P. Barthwal, *Indian J. Pharm. Sci.* **2006**, **41**, 353.
- [7] S. Gemma, G. Kukreja, C. Fattorusso, M. Persico, M. Romano, M. Altarelli, L. Savini, G. Campiani, E. Fattorusso, N. Basilio, *Bioorg. Med. Chem. Lett.* **2006**,16, 5384.
- [8] D. Sriram, P. Yogeewari, K. Madhu, *Bioorg. Med. Chem. Lett.* **2006**, 15, 4502.
- [9] A. Nayyar, R. Jain, *Curr. Med. Chem.* **2006**, 12, 1873.
- [10] R. M. Fikry, N. A. Ismael, A. A. El-Bahnasawy, A. A. Sayed El-Ahl., *Phosphorus Sulfur and Silicon.* **2006**, 179, 1227.
- [11] A. Walcourt, M. Loyevsky, D. B. Lovejoy, V. R. Gordeuk, D. R. Richardson,*Int. J. Biochem. Cell Biol.* **2004**, 36, 401 .
- [12] M. G. Mamolo, V. Falagiani, D. Zampieri, L. Vio, E. Banfi , G. Scialino,*Farmaco***2003**, 58, 631.
- [13] N. Terzioglu, A. Gursoy, *Eur. J. Med. Chem.*, **2003**, 38, 781.
- [14] S. G. Kucukguzel, E. E. Oruc, S. Rollas, F. Sahin, A. Ozbek, *Eur. J. Med. Chem.* **2002**,37, 197.
- [15] S. Rollas, N. Gulerman, H. Erdeniz, *Farmaco*, **2002**,57, 171.
- [16] Al- Mawsawi LQ, R. Dayam, L. Taheri, M. Witvrouw, Z. Debyser, N. Neamati, *Bioorg. Med. Chem. Lett.* **2007**, 17(23) 6472.

- [17] C. Plasencia, R. Daym, Q. Wang, J. Pinski, T. R. Jr. Burke, D. I. Quinn, and N. Neamati, *Mol. Cancer Ther.* **2005**, 4(7) 1105.
- [18] H. Zhao, N. Neamati, S. Sunder, H. Hong, S. wang; G. W. Milne, Y. Pommier, T. R. Jr. Burke, *J. Med. Chem.* **1997**,40(6) 937.
- [19] K C Asati, S K srivastava and S D Srivastava, *Ind.J.Chem.*, **2006**,45 (B), 526.
- [20] A Bishnoi, K Srivastava and C K M Tripathi, *Ind.J.Chem.*, **2006**,45(B), 2136.
- [21] N. P. Shetgiri and A. D. Chitre, *Ind .J .Chem.* **2006**,45(B), 1308.
- [22] R Jadav, S Srivastava and S D Srivastava, *Chemistry, An Indian Journal*, **2006**,1, 95.
- [23] S. Srivastava, A. Jain, and S. Srivastava, *J. Indian Chem. Soc.*, **2006**, 83, 1118.
- [24] K M Mistry and K R Desai, *E- Journal of Chem.*, **2004**,1(4), 189.
- [25] H. S. Patel, H. J. Mistry, *Phosphorous, Sulfur and Silicon*, **2004**,179, 1085.
- [26] J. J. Bhatt, B. R. Shah and N. C. Desai, *Ind .J. Chem.*,**1994**, 33B, 189.
- [27] J.Valdez, R.Cedillo,A.Hernandez-Campos, L. Yepez, F.Hernandez-Luis, G. Navarrete-Vazquez, A.Tapia, R. Cortes, M. R. Castillo Hernandez,*Bioorg. Med. Chem. Lett.*, **2002**,12 2221.
- [28] Z. Kazimierczuk, J.A., Upcroft, P., A.Gorska,B.Starosciak, Laudy, *Acta Biochim. Polon.*, **2002**,49(1)185.