



## SYNTHESIS AND THEIR POSSIBLE BIOLOGICAL ACTIVITIES OF FEW FORMAZANS OF 3-AMINO-2-SULPHANYL-2,3,4,5,6,7,8-HEXA HYDRO(1) BENZOTHIENO(2,3-d)PYRIMIDIN-4(1H)-ONE

N. Lakshmi, V. Haritha, V. Sreeram, D. Rajalakshmi, N. Sindhura and  
D. Visagaperumal\*

Department of Pharmaceutical Chemistry, Bapatla College of pharmacy, Bapatla(AP)

E mail : vis\_realab1@yahoo.co.in

### ABSTRACT

3-amino-2-sulfanyl-2,3,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-4(1H)-one **1** was diazotized to give the diazonium salt of 3-amino-2-sulfanyl-2, 3, 5, 6, 7, 8-hexahydro [1] benzothieno [2, 3-d] pyrimidin-4(1H)-one **2**. Various Schiff bases are then treated with **2** to give 3-[(phenyl hydrazono)(substituted phenyl)methyl]diazonyl-2-sulfanyl-2,3,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-4(1H)-one **4a-i**. The structures of the compounds were confirmed by IR and <sup>1</sup>H NMR spectra. The synthesized compounds were screened for antibacterial and antifungal activities. All the compounds have shown promising antibacterial and antifungal activities.

**Keywords:** Thienopyrimidines, Formazans, antibacterial, antifungal

### INTRODUCTION

Thienopyrimidines and its analogs constitute the active class of the compounds possessing wide spectrum of biological activity<sup>1</sup> and gastric antisecretory activity<sup>2</sup>. Further formazans are well famed for their antiviral<sup>3, 4</sup>, antimicrobial<sup>5</sup>, anticonvulsants<sup>6</sup> and antifertility<sup>7</sup>. In the light of the above fact we have synthesized some new formazans with the hope to possess better antimicrobial activity. All the synthesized compounds were screened for their antibacterial and antifungal activities against some selected microbes. 3-[(phenyl hydrazono)(substituted phenyl) methyl] diazenyl-2-sulfanyl-2,3,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-4(1H)-one **4a-i** was synthesized from the diazonium salt of 3-amino-2-sulfanyl-2, 3, 5, 6, 7, 8-hexahydro [1] benzothieno [2, 3-d] pyrimidin-4(1H)-one **2** when it was treated with different Schiff bases **3a-i**. The diazonium salt was synthesized from of 3-amino-2-sulfanyl-2, 3, 5, 6, 7, 8-hexahydro [1] benzothieno [2, 3-d] pyrimidin-4(1H)-one **1** on diazotization. 3-amino-2-sulfanyl-2, 3, 5, 6, 7, 8-hexahydro [1] benzothieno [2, 3-d] pyrimidin-4(1H)-one **1** was synthesized according to reported method<sup>8</sup>.

### EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. TLC was performed on the silica gel G and spotting was found using iodine vapours. IR spectra were recorded on JASCO FT IR-40 spectrophotometer (cm<sup>-1</sup>) using KBr disc. <sup>1</sup>H NMR spectra were recorded on a Perkin Elmer (model RB-12) spectrometer using CDCl<sub>3</sub> as solvent and TMS as an internal standard. All chemical shift values are recorded in δ scale downfield from TMS.

**Synthesis of 3-{ [(phenyl hydrazono)(substituted phenyl)methyl]diazanyl}-2-sulfanyl-2,3,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-4(1H)-one (4a-i):**

3-amino-2-sulfanyl-2,3,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-4(1H)-one (0.01 mol) was dissolved in aqueous hydrochloric acid (10 ml). It was cooled and aqueous sodium nitrite was slowly added to get 2. 1-phenyl-2-(substituted phenyl methylidene) hydrazine **3a-i** (0.01 mol) was dissolved in dry pyridine (10 ml) and sodium acetate (0.03g) was added. The contents were cooled in ice-bath and stirred. To it a clear and cold solution of diazonium salt of 3-amino-2-sulfanyl-2, 3, 5, 6, 7, 8-hexahydro [1] benzothieno [2, 3-d] pyrimidin-4(1H)-one was added dropwise for 1 hour at low temperature (0-5<sup>o</sup>C). The reaction mixture was kept in ice-bath for 3 hours and then poured into ice water. The resulting dark coloured mass was filtered, washed with water till it was free from pyridine and dried. The product was recrystallized from a suitable solvent. **4a**. Yield 74.2%, m.p. 140<sup>o</sup>C. IR (KBr, cm<sup>-1</sup>): 3308 (N-H str), 3137 (C-H str in aromatic), 2997.02 (C-H str in aliphatic), 1694 (C=O str), 1613.05 (C=N str), 1508.9 (C-S str). <sup>1</sup>H NMR: δ 3.22 (s, 1H, SH), 3.511-3.705 (m, 8H, tetrahydrobenzo ring), 7.6-8.1(m, 10H, ArH) The physical data for the synthesized compounds were given in Table-1.

**Biological activity:**

The antimicrobial activity was assayed by the cup-plate agar diffusion method<sup>9, 10</sup> at the concentration of 500 µg/ml. All the synthesized compounds were tested *in vitro* for their antibacterial activity against various microbes such as *Bacillus subtilis* NCIM 2063, *Escherichia coli* NCIM 2118, *Pseudomonas auroginosa* NCIM 2036 and antifungal activity against *Candida albicans* NCIM 3102. Plates incubated 24 hr for bacterial and 48 hr for fungicidal activities. The inhibition zone of the testing compounds was measured in mm. Ciprofloxacin (10µg/disc) and Fluconazole (2µg/disc) were used as standard. (Table-2)

**RESULTS AND DISCUSSION**

The data in **Table 1** and **2** represent the data for Physical and Antimicrobial activity. It has shown all prepared compounds have significant effect. It can be concluded from the **Table II** that compounds **3c, 3d, 3i, 4a, 4c, 4g, 4h, 4i** were active against *Bacillus subtilis* and **3b, 3c, 3d, 3e, 3f, 3g, 3h, 4b, 4d, 4e, 4h, 4i** showed significant activity against *Escherichia coli*. **3a, 3b, 3c, 3d, 3e, 3f, 3g, 4a, 4c, 4d, 4e, 4g, 4h, 4i** showed activity against *Pseudomonas aeruginosa*. The compound **3a, 3b, 3c, 4a, 4b, 4c, 4f, 4g, 4h, 4i** were found active against *Candida albicans*. The other compounds were resistant to the selected microbial strains.

**ACKNOWLEDGMENT**

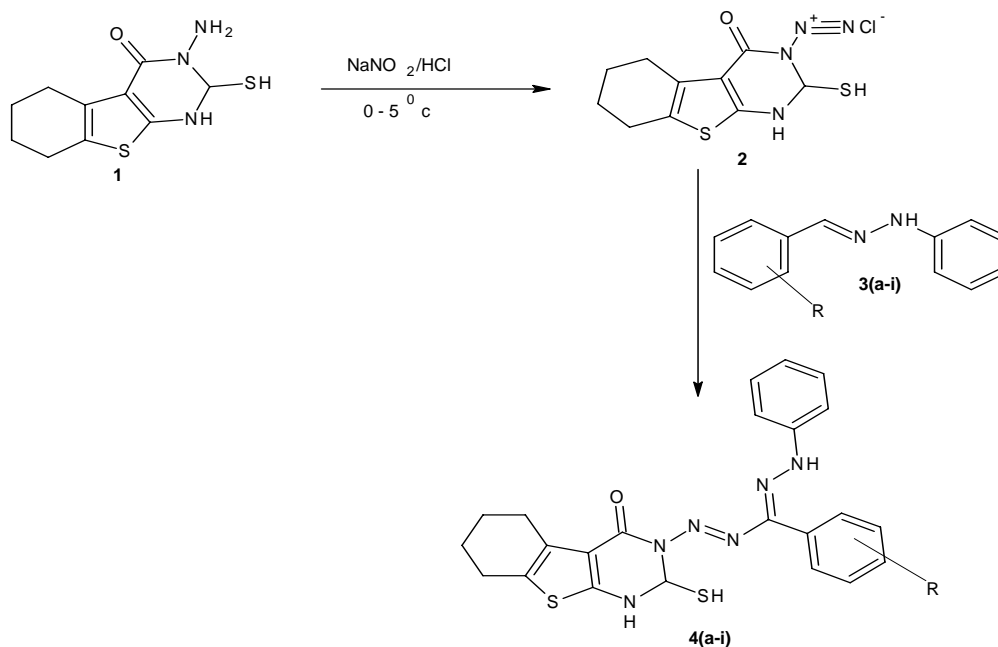
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**Table-1:** Physical data

Compound code	R	Molecular formula	Molecular weight	Melting point ( <sup>o</sup> C)	% Yield
4a	H	C <sub>23</sub> H <sub>22</sub> N <sub>6</sub> OS <sub>2</sub>	462	140	74.2
4b	2-Cl	C <sub>23</sub> H <sub>21</sub> N <sub>6</sub> O <sub>3</sub> S <sub>2</sub> Cl	497	95	59.1
4c	4-NO <sub>2</sub>	C <sub>23</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> S <sub>2</sub>	508	100	46.3
4d	3,4,5-OCH <sub>3</sub>	C <sub>26</sub> H <sub>22</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub>	553	91	47.6
4e	2-NO <sub>2</sub>	C <sub>23</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> S <sub>2</sub>	508	105	56.3
4f	4-N (CH <sub>3</sub> ) <sub>2</sub>	C <sub>25</sub> H <sub>27</sub> N <sub>7</sub> O <sub>3</sub> S <sub>2</sub>	506	101	75
4g	3,4-OCH <sub>3</sub>	C <sub>25</sub> H <sub>26</sub> N <sub>6</sub> O <sub>3</sub> S <sub>2</sub>	523	110	63
4h	4-OCH <sub>3</sub>	C <sub>24</sub> H <sub>24</sub> N <sub>6</sub> O <sub>2</sub> S <sub>2</sub>	493	98	71.2
4i	4-CH <sub>3</sub>	C <sub>24</sub> H <sub>24</sub> N <sub>6</sub> O <sub>2</sub> S <sub>2</sub>	476	95	79.2

Table-2: Antimicrobial activity

Compound	Antibacterial			Antifungal
	<i>B. subtilis</i>	<i>E. coli</i>	<i>P. aureginosa</i>	<i>C. albicans</i>
3a	00	00	10	08
3b	16	10	10	08
3c	11	11	10	10
3d	12	10	11	00
3e	00	12	13	00
3f	00	10	12	00
3g	00	10	14	00
3h	00	10	00	00
3i	13	00	00	00
4a	11	00	15	10
4b	00	10	00	14
4c	12	00	12	12
4d	00	14	13	00
4e	00	10	11	00
4f	00	00	00	12
4g	14	00	14	11
4h	12	10	12	13
4i	14	11	12	12
Ampicillin	15	18	20	--
Fluconazole	--	--	--	15



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