International Journal for Pharmaceutical Research Scholars (IJPRS)

V-2, I-4, 2013 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Synthesis of 1,2,3,5- Thiatriazines, their Antimicrobial Screening and their Isomerization into 1,2,3,5-Tetrazines

Deshmukh PN*[1], Gaidhane MK[1], Berad BN[2]

[1]*Assistant Professor, Smt. Radhikatai Pandav, College of Engineering, Nagpur, India.*

[2]*P.G. Department of Chemistry, RTM Nagpur University, Nagpur, Maharashtra, India.*

Manuscript No: IJPRS/V2/I4/00226, Received On: 06/12/2013, Accepted On: 13/12/2013

ABSTRACT

Series of new heterocyclic compounds 2H-4-(pyrid-4yl)-5-arylidene / alkylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8a-f) have been synthesized by the basification of 2H-4-(pyrid-4yl)-5-arylidene / alkylidene – amino – 6- phenylimina-5,6-dihydro-1,2,3,5-thiatriazine hydrochloride (7a-f). The later were synthesized by the interaction of 1-aryl / alkylidene-3-(pyrid-4y) – dihydro formazan (5a-f) with N-phenyl-S-chloroisothiocarbamoyl chloride. The synthesized compounds were further isomerised into 1 phenyl –4-(pyrid-4yl)-5-aryldene / alkyldene amino –6-thio-1,2,3,5-tetrazines (9a-f) by using 5 % ethanolic sodium hydroxide. Compound (8) on benzalyation with excess 10 % sodium hydroxide and benzoyl chloride afforted corresponding benzoyl derivatives (10 a-f). The structures of newly synthesized compounds were confirmed on the basis of their elemental IR ^{1}H-NMR and mass spectral analysis. The title compounds were assayed for both antifungal and antibacterial activity against gram positive and gram negative micro-organisms.

KEYWORDS

Synthesis, 1,2,3,5-thiatriazines, antibacterial and antifungal activity, isomerization into 1,2,3, 5-tetrazines

INTRODUCTION

Synthesis of thiatriazines having hetero atoms at different positions has been reported in the literature[1,3]. The cycloaddition of diazoazoles with acylisothiocyanates has been found to result in the formation of a 1,2,3,5-thiatriazine ring[2]. Recently the synthetic applications of N-phenyl-S-chloroisothiocarbamoyl chloride have been investigated[4-7]. Synthesis and fungicidal activity of some 6-aryl-2-(-β-D-glucopyranosyl)-3-oxo-2,3-dihydro-1,2,4-oxadiazole [3,2-*b*]-1.2.4.6- thiatriazine-1,1-dioxides[8].

***Address for Correspondence:**
Priyadarshani N. Deshmukh
Assistant Professor,
Smt. Radhikatai Pandav, College of Engineering, Nagpur, India.
E-Mail Id: preetiingole@gmail.com

The reagent potentiality in the synthesis of Nitrogen and sulphur containing 5 & 6 membered heterocyclic compounds. In view of our interest in heterocyclic synthesis, we are reporting the novel synthesis of 1,2,3,5-thiatriazine by direct condensation method in the present communication.

MATERIALS AND METHOD

The melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Shimadzu FT-IR-8400 spectrophotometer using KBr disc and ^{1}H NMR spectra in DMSO- d6 or in CDCl3 (Chemical shift in δ ppm) on Bruker spectrometer (400 MHz) using TMS as an internal standard. The results are in good agreement with the structure

assigned. The purity of all compounds was checked by thin layer chromatography using TLC plates of silica gel (E.Merck G254) using Ethyl acetate: Hexane solvent system (7:3). Physical Constants and Spectral data of synthesized compounds (8a-8f), (9a-9f) and (10a-10f), are recorded in Table- 1, 2 and 2 respectively.

RESULTS AND DISCUSSION

The parent compounds 3-(pyrid-4 yl) –dihydroformazan (3) was prepared by known method, refluxing the mixture of isoniazide (1) and hydrazine hydrate (2) in 1:1 ratio in ethanolic medium for 1 hr. on completion of reaction and distilling off the solvent golden yellow crystals of compound (3) appeared. The compound (3) was then refluxed with different aryl / alkyl aldehydes (4a-f) in 1:1 ratio in ehtanolic medium for 1 hr. on cooling the reaction mixture and distilling off solvent the solid products were separated out. They were crystallised from ethanol and identified as 1-alkylidene / arylidene –3 (pyrid –4yl) –dihydroformazans (5a-f).

Initially, the mixture of 1-arylidene / alkilidene – 3- (pyrid-4yl) –dihydroformazans (5a-f) (0.01mole) was refluxed with N-phenyl –S-Chloroisothiocarbamoyl chloride (0.01 mole) (6) in chloroform medium for 4 hrs. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixture and distilling off chloroform afforded sticky masses which on trituration with petroleum ether gave granular solids. It was found acidic to litmus and on determination of equivalent weight, was found to be monohydrochloride of 2H-4-(pyrid-4yl)-5-arylidene / alkylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5- thiatriazines (7a-f), The salts on basification with dilute ammonium hydroxide afforted a free bases 2H-4-(pyrid-4yl)-5-arylidene / alkyldene-amino-6-phenylimino-5-6-dihydro-1,2,3,5-thiatriazine (8a-f). The results are presented in Table 1.

These compounds were boiled for 1.5 hr with 5 % aqueous ethanolic 1:1 sodium hydroxide solution (25.0 ml) on water bath. The reaction mixture was cooled and solids obtained were filtered, washed and crystallized from ethanol. The obtained compounds (9a-f) were found to be de-sulphurizable with hot alkaline plum bite solution indicating presence of >C = S linkage. The results are presented in Table 2.

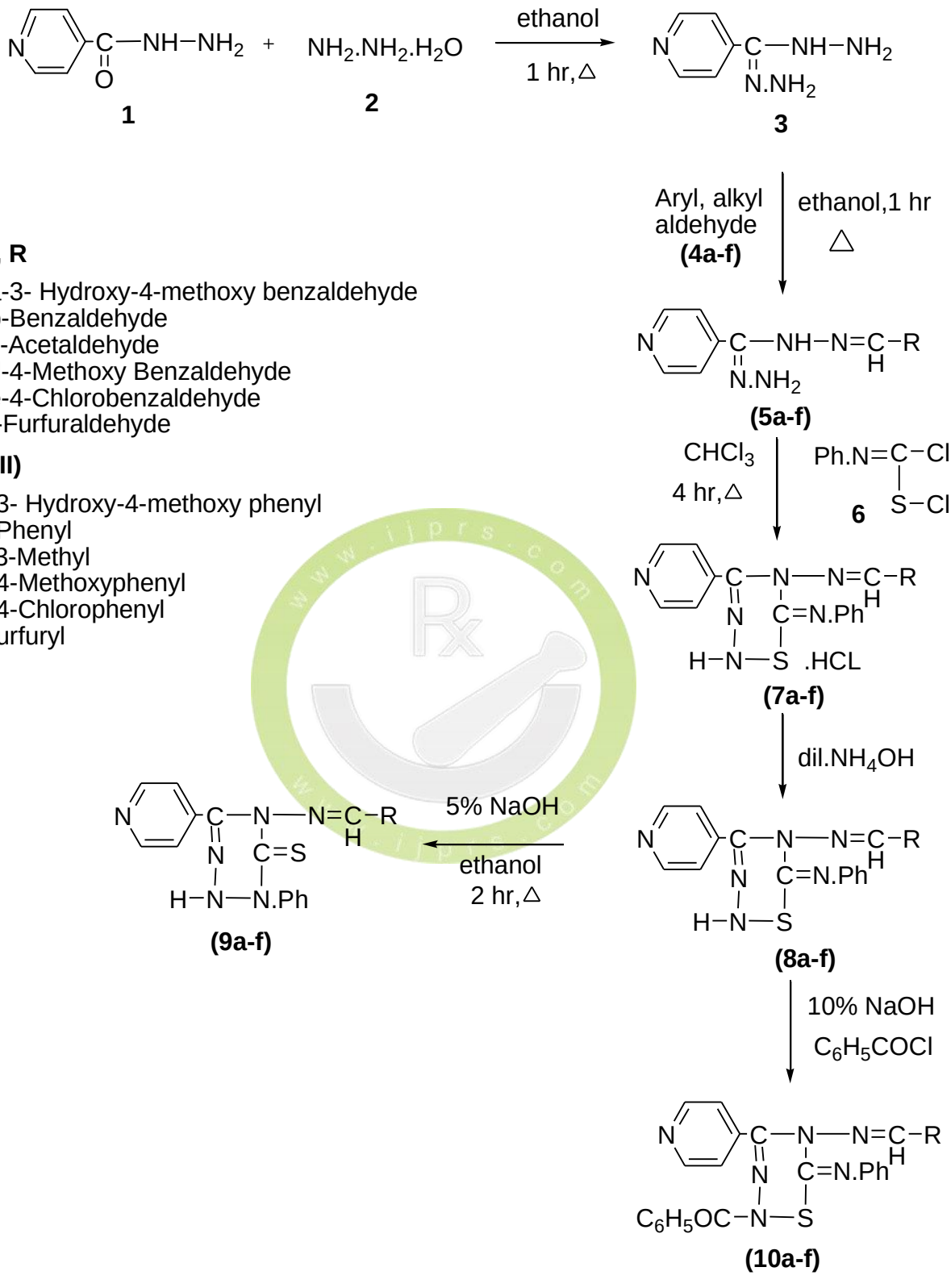
On the other hand, the compounds (8a-f) were placed in excess 10 % sodium hydroxide solution. To this dropwise addition of benzoyl chloride (0.01 mole) was made with a constant stirring. The compounds get slowly benzolyated and solids were separated out which on crystallization with ethanol afforded benzoyl derivatives (10a-f). The results are presented in Table 3. The formation of products 3-7 has been shown in scheme 1.

Antibacterial Activity

The title compounds (8a-f) were screened for their antibacterial activity using cup-plate diffusion method[9-10]. The bacterial organisms used included both gram positive and gram negative strains like E. coli, S. Aureus, B. Subtilis, A. aerogenes, P. Vulgaris. Sensitivity plates were seeded with a bacterial inoculum of 1 x 106 CIU / ml and each well diameter (10 mm) So that concentration of each test compounds was 100 µg/ml. The zones of inhibition were recorded after incubation for 24 hrs using vernier caliper. Inhibition zones record of the compounds clearly indicated that 5b, 5c, 5d and 5e were highly active against B. Subtitles, 5d and 5e were highly active against E. coli whereas 5a, 5c were moderately active against E.coli. Majority of the compounds were found to be resistant against A. aerogenes and P. vulgaris. The results are presented in Table 4.

Experimental

All melting points were recorded using hot paraffin bath and are uncorrected. Chemicals used were of A.R grade. IR spectra (4000 – 400 cm^{-1}) were recorded on Perkin-Elmer spectrophotometer in N. nujol mull and as KBr pellets. PMR spectra were recorded with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as solvents[11-12]. Purity of the compounds was checked on silica gel-G plates by TLC.



1 **2** **3**

(5a-f) **(7a-f)** **(8a-f)** **(9a-f)** **(10a-f)**

Where, R

IIa-3- Hydroxy-4-methoxy benzaldehyde
IIb-Benzaldehyde
IIc-Acetaldehyde
IId-4-Methoxy Benzaldehyde
IIe-4-Chlorobenzaldehyde
IIf-Furfuraldehyde

R-(III-VII)

a-3- Hydroxy-4-methoxy phenyl
b-Phenyl
c-3-Methyl
d-4-Methoxyphenyl
e-4-Chlorophenyl
f-furfuryl

Scheme

The parent compound 3-(pyrid-4yl) –dihydroformazon **(I)** was prepared by known method, refluxing the isoniazide and hydrazine hydrate in 1:1 ratio in ethanol for 1 hr. The mixture of 3 (pyrid-4yl) –dihydroformazan (I) (0.01 mole) and vanillin **(II a)** (0.01 mole) in ethanol was refluxed for again 1 hr. on completion of reaction, the reaction mixture was cooled and solvent was distilled off, when a solid residue was obtained. It was crystallized from ethanol to yield 1- (3-hydroxy-4-methoxy)-benzylidene-3-(pyrid-4yl) –dihydroformazan (3a), m.p. 111^0C.

Synthesis of 2H-4-(pyrid-4yl)-5-(4-hydroxy-4-methoxy)-benzylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8a)

1-(3-hydroxy-4-methoxy)-benzylidene-3-(pyrid-4yl) –dihydroformazan (**5a**) (0.01 mole) was suspended in chloroform (0.01 mole). To this was added a chloroformic solution of N-phenyl-S-chloroisothiocarbamoyl chloride (**6**) (0.01 mole in 10.0 ml). The reaction mixture was refluxed over a water bath for 4 hrs. The evolution of hydrogen gas was clearly noticed. After completion of reaction, the reaction mixture was cooled and chloroform was distilled off when a solid mass was obtained. It was crystallized from ethanol and identified as monohydrochlorides os 2H-4-(pyrid-4yl) –5-(3-hydroxy-4 methoxy)-benzylideneamino –6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine **(7a)**, yield 68 %, m.p. 152^0C. Compound (**7a**) on basification with dilute ammonium hydroxide solution afforded a free base **(8a)**.

Analytical Data of the Compounds 8a-8f

Synthesis of 2H-4-(pyrid-4yl)-5-(4-hydroxy-4-methoxy)-benzylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8a)

^{1}H-NMR ($CDCl_3$) δppm : 11.89 (1H, s, OH), 9.44 (1H, s, N-H), 7.80-8.66 (4H, m, Pyridyl – protons), 8.35 (1H, s, N=CH-Ar), 6.69 –7.91 (9H, m, Ar-H), 3.84 (3H, s, Ar-O-CH_3).

IR(KBr)υcm^{-1} 3410-3570 (Ar-OH), 3225 (NH), 1593 (C=N), 1288 (C=N), 1222 (Ar-O), 1066 (CH_3-O), 748 (C-S), MS (m/z): 418 (M+, 0.1), 419 (M+ +1, 11.02), 327 (0.3), 268 (0.2), 363 (0.2), 150 (10.2), 136 (65.10).Elemental analysis: Calculated for ($C_{21}H_{18}N_6O_2S_1$): C: 60.28; H: 4.71; N: 20.24; S: 7.13; found: C: 60.52; H: 4.71, N: 20.24; S: 7.13. %. m.p. 134^0C; Yield 78 %

Synthesis of 2H-4-(pyrid-4yl)-5)-benzylidene-amino-6-phenylimino-5, 6-dihydro-1,2,3,5-thiatriazine (8b)

^{1}H-NMR : δ 9.35 (1H, s, N-H), 7.86-8.65 (4H, m, Pyridyl – protons), 8.43 (1H, s, N=CH-Ar), 6.78 –8.15 (10H, m, Ar-H).

IR(KBr)υcm^{-1} 3220 (NH), 1620 (C=N), 1275 (C=N), 745 (C-S), MS (m/z): 372.45 ; Elemental analysis: Calculated for ($C_{20}H_{16}N_6S$): C: 66.28; H: 4.71; N: 22.24; S: 8.13; found: C: 64.50; H: 4.33; N: 22.56; S: 8.61 %. m.p. 214^0C; Yield; 74 %.

Synthesis of 2H-4-(pyrid-4yl)-5-methyl-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8c)

^{1}H-NMR : δ 9.35 (1H, s, N-H), 7.82-8.60 (4H, m, Pyridyl – protons), 8.12 (1H, s, N=CH-Ar), 6.75 –8.10 (4H, m, Ar-H) 1.03 (3H, s, CH_3).

IR(KBr)υcm^{-1} 3235 (NH), 2915 (CH in CH_3), 1615 (C=N), 1245 (C=N), 757 (C-S), ; MS (m/z): 310. ; Elemental analysis: Calculated for ($C_{15}H_{14}N_6S$): C: 58.08; H: 4.56; N: 27.20; S: 10.23; found: C: 58.05; H: 4.55; N: 27.08; S: 10.33 %. m.p. 197^0C; Yield 80%

Synthesis of 2H-4-(pyrid-4yl)-5-(4-methyl)-benzylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8d)

^{1}H-NMR : δ 9.32 (s, 1H, N-H), 7.80-8.63 (m, 4H, Pyridyl – protons), 8.25 (s, 1H, N=CH-Ar), 6.80 –8.35 (m, 9H, Ar-H), 2.25 (s, 3H, Ar-CH_3).

IR(KBr)υcm^{-1} 3230 (NH), 2912 (CH in CH_3), 1625 (C=N), 1265 (C=N), 740 (C-S). MS (m/z): 386 ; Elemental analysis: Calculated for ($C_{21}H_{18}N_6S$): C: 65.38; H: 4.65; N: 21.84; S: 8.23; found: C: 65.26; H: 4.69; N: 21.75; S: 8.30 %. m.p. 182^0C; Yield 79 %.

Synthesis of 2H-4-(pyrid-4yl)-5-(4-chloro)-benzylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8e)

^{1}H-NMR : δ 9.25 (1H, s, N-H), 7.68-8.80 (4H, m, Pyridyl – protons), 8.45 (1H, s, N=CH-Ar), 6.75 –8.25 (9H, m, Ar-H).

IR(KBr)υcm^{-1} 3245 (NH), 1648 (C=N), 1235 (C=N), 755 (C-S), MS (m/z): 406; Elemental analysis: Calculated for ($C_{20}H_{15}ClN_6S$): C: 65.38; H: 4.65; N: 21.84; S: 8.23; found: C: 59.04; H: 3.72; Cl: 8.71; N: 20.65; S: 7.88 %. m.p. 168^{0}C; Yield 77 %.

Synthesis of 2H-4-(pyrid-4yl)-5-(2-methylfuran)-benzylidene-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (8f)

^{1}H-NMR : δ 9.45 (1H, s, N-H), 7.65-8.82 (4H, m, Pyridyl – protons), 8.35 (1H, s, N=CH-Ar), 6.63 –8.35 (8H, m, Ar-H).

IR(KBr)υcm^{-1} 3210 (NH), 1650 (C=N), 1255 (C=N), 725 (C-S), MS (m/z): 362 ; Elemental analysis: Calculated for ($C_{18}H_{14}N_6OS$): C: 59.58; H: 3.75; N: 23.04; O, 4.32; S: 8.43; found: C: 59.65; H: 3.89; N: 23.19; O: 4.41; S: 8.85 %. m.p. 178^{0}C; Yield 80%.

Synthesis of 1-phenyl-2H-4-(pyrid-4yl)-5-(3-hydroxy-4-methoxy)-benzgli-deneamino-6-thio-5,6-dihydro-1,2,3,5-tetrazine (9a)

2H-4-(pyrid-4yl)-5-(3-hydroxy-4-methxoy)-benzylideneamino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine **(8a)** (0.01 mole) was boiled for 1.5 hr. with 5 % aqueous ethanolic 1:1 sodium hydroxide solution (25.0ml) on water bath. The reaction mixture was cooled and the solid obtained **(9a)** was filtered, washed and crystallized from ethanol. The compound was identified as 1-phenyl-2H-4-(pyrid-4yl)-5-(3-hydroxy-4-methoxy)-benzylideneamino-6-thio-5,6-dihydro-1,2,3,5-tetrazine **(9a).**

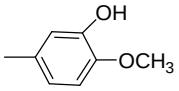
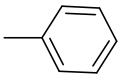
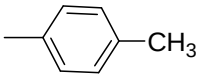
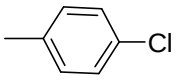
Analytical Data of the Compounds 9a-9f

Synthesis of 1-phenyl-2H-4- (pyrid-4yl)- 5-(3-hydroxy-4-methoxy) –benzgli -deneamino-6-thio-5, 6-dihydro-1,2,3,5-tetrazine (9a)

^{1}H-NMR : δ 9.52 (s,1H, NH), 8.74-8.55 (m, 4H, pyridyl protons), 8.37 (s,1H, CH – Ar), 6.64-7.93 (m, 8H, Ar-H).

.

Table 1: Formation of 2H-4(pyrid-4yl)-5-arylidene / alkylidene amino-6-phenylimino-5,6-dihydro – 1,2,3,5 – thiatriazines (8 a-f)

Compd.	R	Yield (%)	m.p. (^{0}C)	Elemental Analysis: Found (Calcd.) %	
				N	S
8a		68	134	20.24 (29.09)	7.13 (7.65)
8b		74	214	21.90 (22.58)	8.32 (8.60)
8c		80	197	27.39 (27.09)	10.10 (10.32)
8d		79	182	20.21 (20.84)	7.72 (7.94)
8e		77	168	20.53 (20.68)	7.42 (7.88)
8f		80	178	23.68 (23.14)	8.92 (8.81)

IR (KBr): $V_{max}cm^{-1}$ 3324-3600 (OH), 3154 (NH), 1577 (C=N), 1483 (Ar. C = C), 1287 (C.N), 1071 (CH_3-O), 1140 (Ar-O), 754 (C=S). MS (m/z): 418. Elemental analysis: Calculated for ($C_{21}H_{18}N_6O_2S_1$); C: 60.49; H: 4.21; N: 20.30; S: 7.26, found C: 60.28, H: 4.30; N: 20.09; S: 7.65%. m.p. 350^0C, Yield 70%

Synthesis of 1-phenyl-2H-4-(pyrid-4yl)-5-benzylidene amino-6-thio-5,6-dihydro-1,2,3,5-tetrazine (9b)

^{1}H-NMR : δ 9.38 (1H, s, N-H), 7.82-8.56 (4H, m, Pyridyl – protons), 8.35 (1H, s, N=CH-Ar), 6.75 –8.07 (10H, m, Ar-H).

IR(KBr)υcm^{-1} 3236 (NH), 1628 (C=N), 1265 (C=N), 755 (C-S). MS (m/z): 372. Elemental analysis: Calculated for ($C_{20}H_{16}N_6S$): C: 64.78; H: 4.21; N: 22.26; S: 8.43; found: C: 64.50; H: 4.33; N: 22.56; S: 8.61 %. m.p. 293^0C; Yield 82%.

Synthesis of 1-phenyl-2H-4-(pyrid-4yl)-5-methyl amino-6-thio-5,6-dihydro-1,2,3,5-tetrazine (9c)

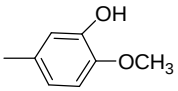
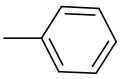
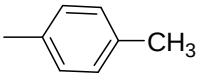
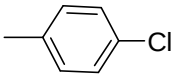
^{1}H-NMR : δ 9.38 (1H, s, N-H), 7.88-8.64 (4H, m, Pyridyl – protons), 8.16 (1H, s, N=CH-Ar), 6.56 –8.13 (9H, m, Ar-H) 1.12 (3H, s, CH_3).

IR(KBr)υcm^{-1} 3245 (NH), 2925 (CH in CH_3), 1645 (C=N), 1240 (C=N), 752 (C=S). MS (m/z): 310. Elemental analysis: Calculated for ($C_{15}H_{14}N_6S$): C: 57.75; H: 4.36; N: 26.80; S: 10.03; found: C: 58.05; H: 4.55; N: 27.08; S: 10.33 %. m.p. 322^0C; Yield 85%

Synthesis of 1-phenyl-2H-4-(pyrid-4yl)-5-(4-methyl)- benzylidene amino-6-thio-5,6-dihydro-1,2,3,5-tetrazine (9d)

^{1}H-NMR : δ 9.42 1H, (s, N-H), 8.56-7.85 (4H, m, Pyridyl – protons), 8.35 (1H, s, N=CH-Ar), 6.82–8.38 (9H, m, Ar-H), 2.18 (3H, s, Ar-CH_3).

Table 2 : Formation of 2-benzoyl -4(pyrid-4yl)-5-arylidene / alkylidene amino-6-phenylimino-5,6-dihydro – 1,2,3,5 – thiatriazines (9a-f)

Compd.	R	Yield (%)	m.p. (^{0}C)	Elemental Analysis : Found (Calcd.) %	
				N	S
9a		70	350	20.30 (29.09)	7.26 (7.65)
9b		82	293	22.14 (22.58)	8.40 (8.60)
9c		85	322	27.43 (27.09)	10.30 (10.32)
9d		76	214	20.30 (20.84)	7.83 (7.94)
9e		73	246	20.62 (20.68)	7.50 (7.88)
9f		80	256	23.47 (23.14)	8.90 (8.81)

IR(KBr)υcm^{-1} 3235 (NH), 2945 (CH in CH_3), 1630 (C=N), 1268 (C=N), 745 (C=S), MS (m/z): 386. Elemental analysis: Calculated for ($C_{21}H_{18}N_6S$): C: 65.18; H: 4.34; N: 21.32; S: 8.03; found: C: 65.26; H: 4.69; N: 21.75; S: 8.30 %. m.p. 214^{0}C; Yield 76%.

Synthesis of 1-phenyl-2H-4-(pyrid-4yl)-5-(4-chloro)- benzylidene amino-6-thio-5,6-dihydro-1,2,3,5-tetrazine (9e)

^{1}H-NMR : δ 9.43 (1H, s, N-H), 7.78-8.89 (4H, m, Pyridyl – protons), 8.58 (1H, s, N=CH-Ar), 6.83 –8.58 (9H, m, Ar-H).

IR(KBr)υcm^{-1} 3255 (NH), 1628 (C=N), 1265 (C=N), 775 (C=S), MS (m/z): 406 ; Elemental analysis: Calculated for ($C_{20}H_{15}ClN_6S$): C: 59.30; H: 3.60; N: 20.14; S: 7.43; found: C: 59.04; H: 3.72; Cl: 8.71; N: 20.65; S: 7.88 %. m.p. 246^{0}C; Yield 73%.

Synthesis of 1-phenyl-2H-4-(pyrid-4yl)-5-(2-methylfuran)- benzylidene amino-6-thio-5,6-dihydro-1,2,3,5-tetrazine (9f)

^{1}H-NMR : δ 9.41 (1H, s, N-H), 7.65-8.86 (4H, m, Pyridyl – protons), 8.62 (1H, s, N=CH-Ar), 6.61–8.38 (7H, m, Ar-H).

IR(KBr)υcm^{-1} 3223 (NH), 1650 (C=N), 1275 (C=N), 745 (C=S), MS (m/z): 362 ; Elemental analysis: Calculated for ($C_{18}H_{14}N_6OS$): C: 59.35; H: 3.35; N: 23.12; O, 4.02; S: 8.23; found: C: 59.65; H: 3.89; N: 23.19; O: 4.41; S: 8.85%. m.p. 256^{0}C. Yield 80%.

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-(3-hydroxy-4-methoxy)-benzylideneamino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (10a)

2H-4-(pyrid-4yl)-5-(3-hydroxy-4-methoxy)-benzyldeneamino-6-phenylimino 5, 6-dihydro-1,2,3,5-thiatriazine. (8a) (0.01 mole) was placed in excess 10 % sodium hydroxide solution. To this the dropwise addition of benzoyl chloride (0.01 mole) was made with a constant stirring. The compound (8a) got slowly benzoylated and solid was separated out (10a). It was crystallized from ethanol and identified as 2-benzoyl-4-(pyrid-4yl) –5-(3-hydroxy-4-methoxy)-benzylideneamino-6-phenylimino-5, 6-dihydro-1,2,3,5-thiatriazine (10a).

Analytical Data of the Compounds 10a-10f

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-(3-hydroxy-4-methoxy)-benzylideneamino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (10a)

^{1}H-NMR : δ 11.13 (1H, s, OH), 9.35 (1H, s, N-H), 7.75-8.62 (4H, m, Pyridyl – protons), 8.45 (1H, s, N=CH-Ar), 6.75 –8.85 (13H, m, Ar-H), 3.85 (3H, s, Ar-O-CH_3). IR(KBr)υcm^{-1} 3468 (OH), 1597 (C=N), 1551 (Ar C = C), 1328 (C-N), 1228 (Ar – O), 1067 (CH_3-O), 709 (C-S); MS (m/z): 522. Elemental analysis: Calculated for ($C_{28}H_{22}N_6O_3S_1$): C, 64.12; H, 4.68; N, 16.28; S, 6.82. found: C: 64.35; H: 4.24; N: 16.08; O: 9.18; S: 6.14 %. m.p. 222^{0}C. Yield 78 %.

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-benzylideneamino- 6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (10b)

^{1}H-NMR : δ 9.30 (1H, s, N-H), 7.82-8.63 (4H, m, Pyridyl – protons), 8.45 (1H, s, N=CH-Ar), 6.70 –8.25 (15H, m, Ar-H).

IR(KBr)υcm^{-1} 3235 (NH), 1610 (C=N), 1255 (C=N), 725 (C-S), MS (m/z): 476 ; Elemental analysis: Calculated for ($C_{27}H_{20}N_6OS$): C: 67.88; H: 4.11; N: 17.24; O: 3.06; S: 6.13; found: C: 68.05; H: 4.23; N: 17.64; O: 3.36; S: 6.73 %. m.p. 146^{0}C; Yield 71%.

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-methyl-amino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (10c)

^{1}H-NMR : δ 9.30 (1H, s, N-H), 7.80-8.65 (4H, m, Pyridyl – protons), 8.24 (1H, s, N=CH-Ar), 6.70 –8.30 (10H, m, Ar-H) 1.10 (3H, s, CH_3).

IR(KBr)υcm^{-1} 3215 (NH), 2855 (CH in CH_3), 1645 (C=N), 1225 (C=N), 752 (C-S), MS (m/z): 414. ; Elemental analysis: Calculated for ($C_{15}H_{14}N_6S$): C: 63.58; H: 4.12; N: 20.12; O: 3.23; S: 7.23; found: C: 63.75; H: 4.38; N: 20.28; O: 3.86; S: 7.74%. m.p. 206^{0}C; Yield 67 %.

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-(4-methyl)-benzylideneamino-6-phenylimino-5, 6-dihydro-1,2,3,5-thiatriazine (10d)

^{1}H-NMR : δ 9.35 (1H, s, N-H), 7.85-8.70 (4H, m, Pyridyl – protons), 8.35 (1H, s, N=CH-Ar), 6.76 –8.45 (14H, m, Ar-H), 2.35 (3H, s, Ar-CH_3).

IR(KBr)υcm^{-1} 3235 (NH), 2908 (CH in CH_3), 1645 (C=N), 1245 (C=N), 748 (C-S), MS (m/z): 477 ; Elemental analysis: Calculated for ($C_{27}H_{21}N_6OS$): C: 67.56; H: 4.33; N: 17.45; O: 3.25; S: 6.71; found: C: 67.91; H: 4.43; N: 17.60; O: 3.35; S: 6.71 %. m.p. 187^{0}C; Yield 72%.

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-(-4-chloro)-benzylideneamino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (10e)

^{1}H-NMR : δ 9.35 (1H, s, N-H), 7.65-8.86 (4H, m, Pyridyl – protons), 8.40 (1H, s, N=CH-Ar), 6.85 –8.05 (14H, m, Ar-H).IR(KBr)υcm^{-1} 3235 (NH), 1625 (C=N), 1245 (C=N), 769 (C-S), MS (m/z): 511 ; Elemental analysis: Calculated for ($C_{27}H_{19}ClN_6OS$): C: 63.23; H: 3.45; Cl: 6.56; N: 16.24; O: 3.02; S: 6.09; found: C: 63.46; H: 3.75; Cl: 6.94; N: 16.45; O: 3.13; S: 6.27 %. m.p. 159^{0}C; Yield 77%.

Synthesis of 2-benzoyl –4-(pyrid-4yl)-5-(2-methylfuran)-benzylideneamino-6-phenylimino-5,6-dihydro-1,2,3,5-thiatriazine (10f)

^{1}H-NMR : δ 9.40 (s, 1H, N-H), 7.62-8.80 (m, 4H, Pyridyl – protons), 8.25 (s, 1H, N=CH-Ar), 6.60 –8.38 (m, 13H, Ar-H).

IR(KBr)υcm^{-1} 3225 (NH), 1645 (C=N), 1250 (C=N), 745 (C-S), MS (m/z): 466 ; Elemental analysis: Calculated for ($C_{18}H_{14}N_6OS$): C: 64.16; H: 3.45; N: 17.65; O: 6.45; S: 6.34; found: C: 64.36; H: 3.89; N: 18.01; O: 6.86; S: 6.87 %. m.p. 200^{0}C; Yield 69 %.

Antifungal Activity

All these synthesized compounds (8a-f) were also screened for their antifungal activity using cup-plate diffusion method. The fungi used were C. albicans, A. higer and A. flavus. The method is similar to the antibacterial activity.

Table 3: Formation of 1-phenyl -4(pyrid-4yl)-5-arylidene / alkylidene amino-6-thio-5,6-dihydro – 1,2,3,5 – thiatriazines (10a-f)

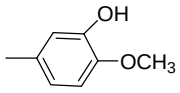
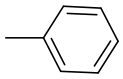
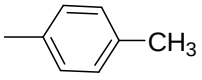
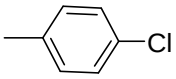
Compd.	R	Yield (%)	M.P. (^{0}C)	Elemental Analysis: Found (Calcd.) %	
				N	S
10a		78	222	16.28 (16.09)	6.82 (6.13)
10b		71	146	17.34 (17.64)	6.16 (6.75)
10c	—CH_3	67	206	17.52 (17.72)	7.22 (6.75)
10d		72	187	16.84 (16.60)	6.90 (6.32)
10e		77	159	16.59 (16.47)	6.26 (6.27)
10f		69	200	17.98 (18.02)	6.31 (6.86)

Table 4: Antibacterial activity of 2H-4(pyrid-4yl)-5-arylidene / alkyldene) amino-6-phenylimino-1,2,3,5- thiatriazine (5a-f).

	Organisms					
Entry	**Compd.**	**E.coli**	**S.Cureus**	**B.Sublilis**	**A.aerogenes**	**P.Vulgaris**
1	5a	++	+	-	-	+
2	5b	+	+	+++	++	-
3	5c	++	-	+++	-	++
4	5d	+++	+	+++	-	+
5	5e	+++	+	+++	+	-
6	5f	-	++	-	-	+

(Diameter of inhibition zone in mm)(Conc. 100 µg /ml)
(-) Resistant < 10.0 mm
(+) slightly active > 10.0 to 15.0 mm

Table 5: Antifungal activity of 2H -4(pyrid-4yl)-5-arylidene / alkyldene) amino-6-phenylimino-1,2,3,5-thiatriazine (5a-f)

	Organisms			
Entry	**Compd.**	**C.albicans**	**A.niger**	**A.fluvus**
1	5a	-	+	+
2	5b	-	+	+
3	5c	++	+++	-
4	5d	-	+	+
5	5e	-	+	++
6	5f	++	+++	+

(Diameter of inhibition zone in mm)(Conc. 100 µg /ml)
(-) Resistant < 10.0 mm (+) slightly active > 10.0 to 15.0 mm
(++) Moderately active > 15.0 to 20.0 mm (+++) highly active > 25.0 mm.

The zones of inhibition were recorded after incubation for 24 hrs using vernier calliper. Inhibition zones recorded of the compounds clearly indicated that 8a and 8e were highly active against A. niger, where as 8a, 8b and 8d were moderately active against C. albicans, 8b, 8c and 8e were moderately active against A. flavors the results are presented in table 5.

ACKNOWLEDGEMENT

The authors are very much thankful to the Prof. V. G. Thakare Principal, Shri Shivaji Science College, Amravati for providing necessary facilities Authors are also thankful to RSIC Punjab University, Chandigarh for elemental and NMR data while RSIC, CDRI, Lucknow for IR and mass data.

REFERENCES

1. Khare RK, Shrivastava AK, "Synthesis of thiatriazines", IPC. Int. C17 CO7D 285/00, 2.
2. Sadchikova EV, Bakulev VA, Dahaen W, Hecke KV, Rubeyns K, Meervelt LV, Mokrushin VS, Padwa A, "The cycloaddition of diazoazoles with acylisothiocyanates has been found to result in the formation of a 1,2,3,5-thiatriazine ring" *Synlett*, 2004, 2037-2039.
3. Butter RN, Shea DFO, "Synthesis of thiatriazines having hetero atoms", Journal of Chemical Research, 1994, 350.
4. Deshmukh RS, Berad BN, "Applications of N-phenyl-S-chloroisothiocarbamoyl chloride", Indian Journal of heterocyclic chemistry, 2002, 12, 153.
5. Deshmukh RS, Vidhale NN, Berad BN, "Applications of N-phenyl-S-chloroisothiocarbamoyl chloride", Asian Journal of Chemistry, 2002, 14 (1) 162.
6. Deshmukh RS, "Synthesis and applications of N-phenyl-S-chloroisothiocarbamoyl chloride" Thesis, Amravati University, Amravati, 2002.
7. Bhaskar CS, "Applications of N-phenyl-S-chloroisothiocarbamoyl chloride", Thesis, Amravati University, Amravati, 2002.
8. Khare RK, Shrivastava AK, Singh H, Indian Journal of Chemistry, 2005, 44B, 163-166.
9. Barry AL, "The Antimicrobial susceptibility test; principle and practices", eds. Illus Lea and Fibriger, Philaolelphia, PA, USA, 180.
10. Cavanagh F, "Analytical Microbiology", Academic Press, New York, 1963, 126.
11. Calthup NB, Daly LH, Wiberly SE, "Introduction to Infrared and Raman Spectroscopy", Academic Press, New York, 1964.
12. Silverstein RM, Bassler GC, Morril TC, "Spectrometric Identification of organic compounds" 4th ed., John wiply and sons. New York, 1981.