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Antioxidant Activity and Isomerisation: Synthesis of 1,2,3,5- Thiatriazines

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ABSTRACT

Synthesis of thiatriazines having hetero atoms at different positions has been reported in the literature. The cycloaddition of diazoazoles with acylisothiocyanates has been found to result in the formation of a 1,2,3,5-thiatriazine ring. Recently the synthetic applications of N-phenyl-S-chloroisothiocarbamoyl chloride have been investigated. 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 antioxidant activity compared with standard ascorbic acid

KEYWORDS: Synthesis, 1,2,3,5-thiatriazines, antioxidant 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]. 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.

Material And Methods

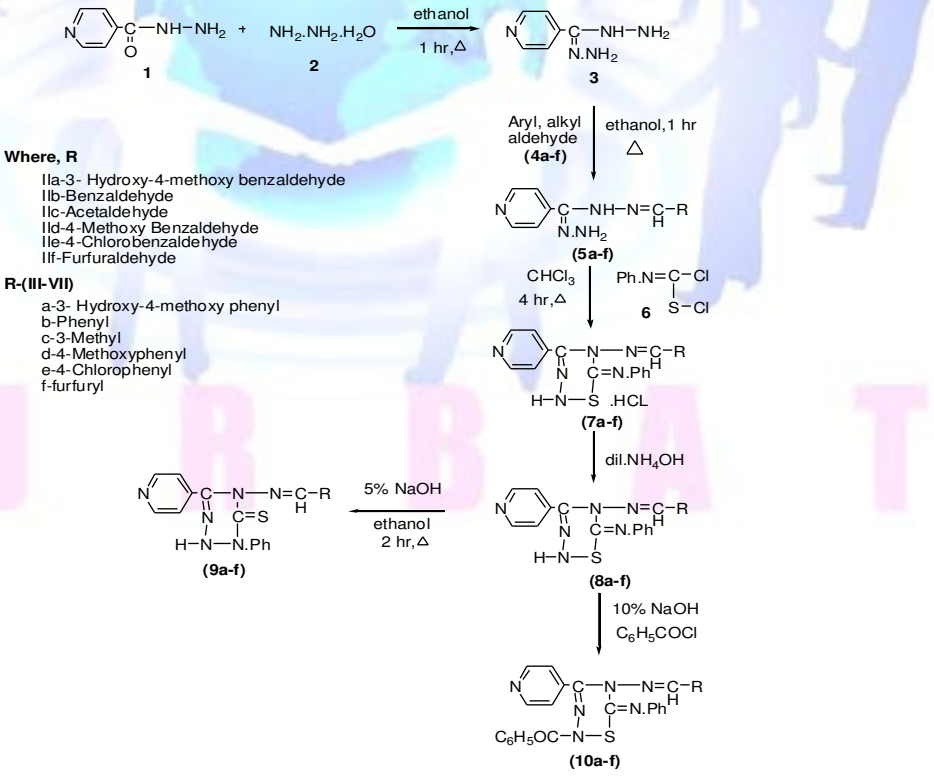
The melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Shimadzu FT-IR-8400 spectrophotometer using KBr disc and

^{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.

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[9-10]. Purity of the compounds was checked on silica gel-G plates by TLC.

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^{0}C.



Scheme

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^{0}C. 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^{0}C; 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^{0}C; 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^{0}C; 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^{0}C; 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).

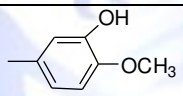
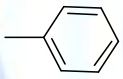
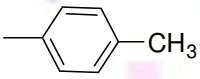
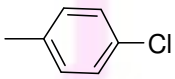
IR(KBr)ucm^{-1} 3245 (NH), 1648 (C=N), 1235 (C=N), 755 (C-S), MS (m/z): 406; Elemental analysis: Calculated for ($C_{20}H_{15}ClN_6S$): C: 65.38; H: 4.65; N: 21.84; S: 8.23; found: C: 59.04; H: 3.72; Cl: 8.71; N: 20.65; S: 7.88 %. m.p. 168^{0}C; Yield 77 %.

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)ucm^{-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%

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)

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).

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^{0}C, 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)ucm^{-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^{0}C; 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)ucm^{-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^{0}C; 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).

IR(KBr)ucm^{-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).

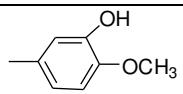
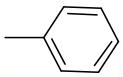
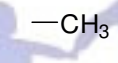
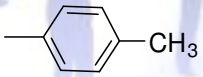
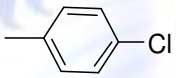
IR(KBr)ucm^{-1} 3255 (NH), 1628 (C=N), 1265 (C=N), 775 (C=S), MS (m/z): 406 ; Elemental analysis: Calculated for ($C_{20}H_{15}ClN_6S$): C: 59.30; H: 3.60; N: 20.14; S: 7.43; found: C: 59.04; H: 3.72; Cl: 8.71; N: 20.65; S: 7.88 %. m.p. 246^{0}C; Yield 73%.

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%.

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)

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)ucm^{-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)ucm^{-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)ucm^{-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)ucm^{-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)ucm^{-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 %.

Result and Discussion

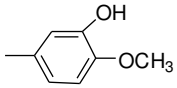
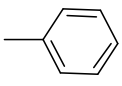
The parent compounds 3-(pyrid-4 yl) – dihydroformazan (**3**) was prepared by known method, refluxing the mixture of isoniazide (**1**) and hydrazine hydrate (**2**) in 1:1 ratio in ethanolic medium for 1 hr. on completion of reaction and distilling off the solvent golden yellow crystals of compound **(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).**

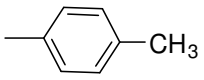
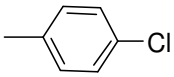
Initially, the mixture of 1-arylidene / alkilidene – 3- (pyrid-4yl) – dihydroformazans **(5a-f)** (0.01 mole) was refluxed with N-phenyl –S-Chloroisothiocarbamoyl chloride (0.01 mole) (**6**) in chloroform medium for 4 hrs. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixture and distilling off chloroform afforded sticky masses which on tituration 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 addtion 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**.

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)

Antioxidant Activity:

Free radical scavenging activity of the test compounds 3a-g, 4a-g, 5a-g and 6a-g were determined by the 1, 1- diphenyl picryl hydrazyl (DPPH) assay method[11]. Drug stock solution (1 mg mL–1) was diluted to final concentrations of 2, 4, 6, 8 and 10 mg mL–1 in methanol. DPPH methanol solution (1 mL, 0.3 mmol) was added to 2.5 mL of drug solutions of different concentrations and allowed to react at room temperature. After 30 min the absorbance values were measured at 518 nm and converted into the percentage antioxidant activity. Methanol was used as the solvent and ascorbic acid as the standard. Results are presented in **Table 4**. The standard drug used was ascorbic acid.

Table 4: Antioxidant activity of the compounds 8a-8f, 9a-9f, and 10a-10f.

% Inhibition					
Comp. Code	**20 µg**	**40 µg**	**60 µg/**	**80 µg**	**100 µg/ml**
8a	22	25	28	30	35
8b	18	30	32	33	37
8c	18	24	28	24	38
8d	28	35	42	35	36
8e	22	28	33	37	32
8f	22	25	28	30	35
9a	37	40	48	36	37
9b	36	40	47	52	54
9c	35	46	48	49	56
9d	18	20	21	33	46
9e	37	40	48	36	37
9f	20	23	33	35	34
10a	42	45	48	48	55
10b	30	35	42	52	53
10c	33	42	49	55	56
10d	38	42	42	52	56

10e	34	38	38	42	45
10f	38	42	45	52	55
Ascorbic acid	**2 µg/ml**	**4 µg/ml**	**6 µg/ml**	**8 µg/ml**	**10 µg/ml**
	12	18	22	42	62

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