SYNTHESIS, CHARACTERIZATION AND EVALUATION OF FUNGITOXICITY OF 2, 5-DIARYL-1, 3, 4-THIADIAZOLO [3, 2-a]-s-TRIAZINE-7-THIONES

RAKESH MANI MISRA

Department of Chemistry, Harishchandra Post Graduate College, Maidagin, Varanasi (U.P.) -221001

RECEIVED : 24 April, 2017

Twelve title compounds 2, 5-diaryl-1, 3, 4-thiadiazolo [3, 2-a]-s-triazine-7-thiones (IV*a-l*) were synthesized from N^1-(5-aryl-1, 3, 4-thiadiazole-2-yl)-N^3-aroyl thioureas (III*a-l*) by refluxing 6 hours with $POCl_3/PCl_5$ in ethanol. These aroyl thioureas (III*a-l*) were prepared from 2-amino-5-aryl-1, 3-4-thiadiazole (II*a-d*) aroyl chloride and ammonium thiocyanate by heating in acetone-2-amino-5-substitued phenyl-1, 3, 4-thiadiazoles (II*a-d*) were obtained from cyclodehydration of corresponding benzoyl thiosemicarbazide (I*a-d*) with conc. H_2SO_4 as shown in scheme I. All the synthesized compounds were well characterized by their m.p., elemental analysis, I.R. and N.M.R spectral data. Synthesized compounds were screened for their fungitoxicity against two fungal species i.e. *Aspergillous niger* and *Fusarium oxysporium*. The screening data have been correlated with the structural features of the synthesized compounds.

KEYWORDS: Thiadiazoles, Dithane M-45, Semicarbazide.

INTRODUCTION

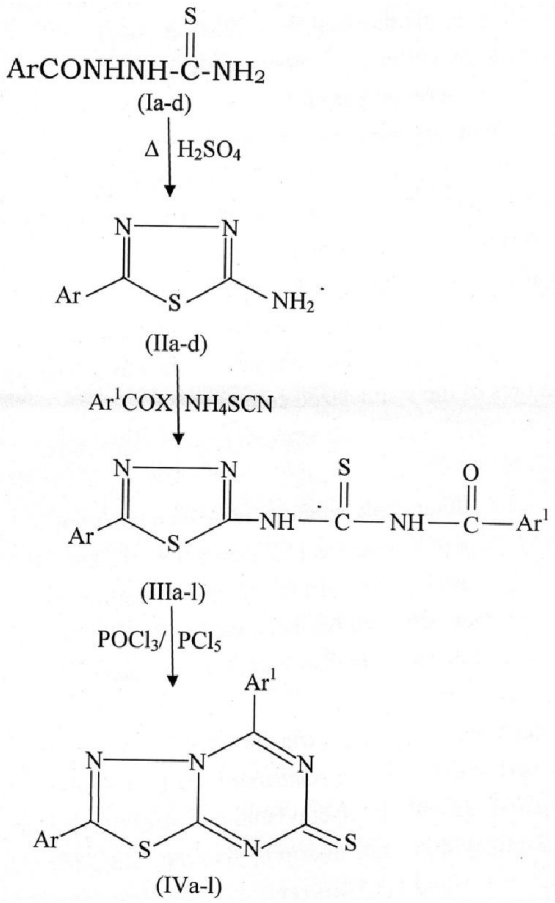
1, 3, 4-Thiadiazole nucleus is associated with a broad spectrum of biocidal activity for *e.g.* fungicides [1, 2], insecticides [3, 4], bactericides [5, 6] and herbicides [7, 8]. Possibly by virtue of incorporating >N–C–S–moiety. The toxophoric importance of which has been well stressed in many pesticides [9, 10]. The presence of =C=S group is also known to enhance the fungicidal activity of heterocyclic compounds [11].

Many derivatives of 1, 3, 5 triazines have significance in agriculture as fungicide and herbicides of these *Simazine* [2-chloro 4, 6-bis (ethyl amino) 1, 3, 5 triazine], *Atrazine* [2-chloro 4-ethylamino 6-isopropylamino 1, 3, 5-triazine], *Prometryne* [2-methylthio 4, 6-bisisopropylamino 1, 3, 5-triazine], *Dyrene* [2, 4 dichloro-6 (2-chloroanilino 1, 3, 5-triazine)] and *Methoprotryne* [2-methylthio 4-iso propylamino 6-3-methoxy propyl amino) 1, 3, 5-triazine] are more outstanding.

Keeping the above observation in view 1, 3, 4-thiadiazolo [3, 2-a]-s-triazine-7-thiones have been synthesized with the hope that fusion of the bio-labile 1, 3, 4-thiadiazole and 1, 3, 5-triazine nuclei might result in the fungicides of enhanced potency.

EXPERIMENTAL

Melting points were determined in open glass capillaries and are uncorrected. The IR Spectra in KBr were recorded either on Perkin-Elmer 157 or Hitachi 295 Infrared spectrophotometer. ^{1}HNMR spectra were recorded on a EM 360 L (60 MHz) NMR spectrometer in $CDCl_3$ or $DMSOd_6$ with TMS as internal reference. Chemical shifts are expressed in δ ppm.



Ar : (a, e, i) = C_6H_5, (b, f, j) = 4-ClC_6H_4, (c, g, k) = 2-$CH_3C_6H_4$; (d, h, l) = 4-$CH_3C_6H_4$.

Ar^1 = (a-d) = 4-ClC_6H_4; (e-h) = 4-$CH_3C_6H_4$; (i-l) = 4-$CH_3OC_6H_4$.

(i) 2-Amino-5-aryl-1, 3, 4-thiadiazoles (I*a-d*).

These were prepared by cyclodehydration of aroylthio-semicarbazide with conc. H_2SO_4. Following the method of Maffi *et al* [12]. All the compounds agreed well with their analytical data already reported in literature [13, 14].

(ii) N^1-(5-Aryl-1, 3, 4-thiadiazole-2-yl)-N^3-aroylthioureas (II*a-d*).

This was prepared by following the method of Silberg *et al* [15]. Thus a mixture of NH_4SCN (0.12 mol) and aroyl chloride (0.12 mol) in acetone (160 ml) was heated under reflux for 0.5 hr. followed by addition of 2-amino-5-aryl-1, 3, 4-thiadiazole (0.12 mol) and mixture was further refluxed for 2 hrs. The excess of acetone was removed and ice-cold water

was added to it. The precipitated product washed with ammonium hydroxide followed by water and recrystallized from ethanol. Yield, melting points, molecular formula and spectral data of representative compounds, thus synthesized are recorded in Table-1.

Tabel-1. Characterization data of N^1-(5-aryl-1, 3, 4-thiadiazole-2-yl)-N^3 -aroylthioureas.

Comp. No.	Ar	Molecular Formula	M.P. (°C)	Yield (%)	Found (Calculated)%		
					C	N	S
		Ar^1=4-ClC_6H_4					
Ia*	C_6H_5	$C_{16}H_{11}N_4S_2OCl$	208	65	51.32 (51.33)	14.95 (14.97)	17.10 (17.11)
B	4-ClC_6H_4	$C_{16}H_{10}N_4S_2OCl_2$	190	70	46.94 (46.94)	13.68 (13.69)	15.62 (15.64)
C	2-$CH_3C_6H_4$	$C_{17}H_{13}N_4S_2OCl$	165	74	52.56 (52.55)	14.41 (14.43)	16.48 (16.49)
D	4-$CH_3C_6H_4$	$C_{17}H_{13}N_4S_2OCl$	162	75	52.58 (52.55)	14.45 (14.43)	16.50 (16.49)
		Ar^1=4-$CH_3C_6H_4$					
E	C_6H_5	$C_{16}H_{14}N_4S_2O$	186	73	56.12 (56.14)	16.35 (16.37)	18.70 (18.71)
F	4-ClC_6H_4	$C_{16}H_{13}N_4S_2OCl$	163	74	51.04 (51.06)	14.90 (14.89)	17.04 (17.02)
G	2-$CH_3C_6H_4$	$C_{17}H_{16}N_4S_2O$	188	68	57.28 (57.30)	15.75 (15.73)	17.95 (17.97)
H	4-$CH_3C_6H_4$	$C_{17}H_{16}N_4S_2O$	185	66	57.32 (57.30)	15.71 (15.73)	17.98 (17.97)
		Ar^1=4-$CH_3OC_6H_4$					
I	C_6H_5	$C_{17}H_{14}N_4S_2O_2$	182	72	55.13 (55.13)	15.15 (15.15)	17.30 (17.29)
j**	4-ClC_6H_4	$C_{17}H_{13}N_4S_2O_2Cl$	160	74	55.15 (55.13)	15.17 (15.15)	17.28 (17.29)
K	2-$CH_3C_6H_4$	$C_{18}H_{16}N_4S_2O_2$	186	76	56.26 (56.25)	14.60 (14.58)	16.68 (16.66)
1	4-$CH_3C_6H_4$	$C_{18}H_{16}N_4S_2O_2$	183	68	56.24 (56.52)	14.57 (14.58)	16.65 (16.66)

* IR (KBr); 3275 (NH), 1620 (>C=N), 1220 (>C=S) Cm^{-1}

** IR (KBr); 3280 (NH), 1625 (>C=N), 1225 (>C=S) Cm^{-1}

(iii) 2, 5-Diaryl-1, 3, 4-thiadiazolo [3, 2-a]-s-triazine-7-thiones (III*a-l*).

A mixture of N^1-(5-aryl-1,3,4-thiadiazole-2yl)-N^3-thio-ureas (0.01 mol), ethanol (40 ml) and PCl_3/$POCl_3$ (0.02 mol) was refluxed for 6 hours and concentrated to a small volume of the contents were poured into ice cold water and acidified with dilute HCl to get the desired product which was recryastallized from ethanol. Yield, melting points, molecular formula and spectral data of representative compounds are recorded in Table-2.

Table 2. Characterization data of 2, 5-diaryl-1, 3, 4-thiadiazolo [3, 2-a]-s-triazine-7-thiones.

Comp.	Ar	Molecular	M.P.	Yield	Anal. (%) found (Cald.)

No.		Formula	(°C)	(%)	C	N	S
		Ar^1=4-ClC_6H_4					
IIa*	C_6H_5	$C_{16}H_9N_4S_2Cl$	250	70	53.92 (53.93)	15.71 (15.73)	17.95 (17.97)
B	4-ClC_6H_4	$C_{16}H_8N_4S_2Cl_2$	265	65	49.12 (49.10)	14.30 (14.32)	16.35 (16.36)
C	2-$CH_3C_6H_4$	$C_{17}H_{11}N_4S_2Cl$	268	68	55.12 (55.13)	15.12 (15.13)	17.28 (17.29)
D	4-$CH_3C_6H_4$	$C_{17}H_{11}N_4S_2Cl$	260	71	55.15 (55.13)	15.15 (15.13)	17.30 (17.29)
		Ar^1=4-$CH_3C_6H_4$					
e**	C_6H_5	$C_{17}H_{12}N_4S_2$	170	66	60.70 (60.71)	16.65 (16.66)	19.02 (19.04)
F	4-ClC_6H_4	$C_{17}H_{11}N_4S_2Cl$	180	72	55.15 (55.13)	15.11 (15.13)	17.27 (17.29)
G	2-$CH_3C_6H_4$	$C_{18}H_{14}N_4S_2$	200	65	61.70 (61.71)	16.01 (16.00)	18.26 (18.26)
H	4-$CH_3C_6H_4$	$C_{18}H_{14}N_4S_2$	198	71	61.72 (61.71)	15.90 (16.00)	18.30 (18.28)
		Ar^1=4-$CH_3OC_6H_4$					
i***	C_6H_5	$C_{17}H_{12}N_4S_2O$	168	70	57.93 (57.95)	15.83 (15.90)	18.16 (18.18)
J	4-ClC_6H_4	$C_{17}H_{11}N_4S_2ClO$	178	76	52.82 (52.84)	14.52 (14.50)	17.50 (17.78)
K	2-$CH_3C_6H_4$	$C_{17}H_{11}N_4S_2O$	198	71	59.00 (59.01)	14.48 (14.50)	16.56 (16.58)
l	4-$CH_3C_6H_4$	$C_{18}H_{14}N_4S_2O$	169	65	59.03 (59.01)	14.52 (14.50)	16.60 (16.58)

* IR (KBr); 1080 (>C=S), 1620 (Cyclic>C=N) Cm^{-1}

^{1}HNMR ($CDCl_3$) δ=7.00-8.00 (9H, m, aromatic-H)

** IR (KBr); 1082 (>C=S), 1620 (Cyclic>C=N) Cm^{-1}

^{1}HNMR ($CDCl_3$) δ=7.07-8.15 (9H, m, Ar-H) 2.12 (3H, s, CH_3)

*** IR (KBr); 1085 (>C=S), 1625 (Cyclic>C=N) Cm^{-1}

^{1}HNMR ($CDCl_3$) δ=7.20-8.25 (9H, Ar-H) 3.66 (3H, s, OCH_3)

ANTIFUNGAL ACTIVITY

The fungicidal activity of such 24 compounds (III*a-l*) & (IV*a-l*) were evaluated against *Aspergillus niger* and *Fusarium oxysporium* at 1000, 100 & 10 ppm concentration following the Agar Plate Technique [16].

Survey of screening data clearly indicates that all the screened compounds inhibited the growth of both the fungal species *Aspergillus niger* and *Fusarium oxysporium* to some extent. Therefore they are fungicides. All the tested compounds are more active at 1000 ppm concentration but their toxicity decreased considerably at lower concentrations (100, 10 ppm)

compounds III*b*, III*f* & III*j* are more active and shows fungitoxicity of the order of Dithane M-45 at 1000 ppm concentration and also inhibited the growth of both the fungal species from 39-44% even at 10 ppm concentration.

The titled compounds (IV*a–l*) are more potent than their precursors thioureas (III*a–l*) due to the compact size and planarity of the molecule the observation is in conformity that reported earlier the compact size and planarity enhanced the fungicidal activity of the molecules [17, 18].

Introduction of chloro group and methoxy group in the phenyl moiety of these compounds tends to argument the fungitoxicity and that the introduction of chloro group is more effective than that of 4-methoxy group. Fungicidal activity varied marginally with the fungal species.

ACKNOWLEDGEMENT

The author expressed their deep gratitude to the Principal and HOD, Department of Chemistry of the respective institution for the constant research encouragement and providing necessary research facilities.

REFERENCES

1. Zhag, Zigi, *et al.*, *Youji Huaxure*, **14(1)**, 74-80 (1994); *Chem. Abstr.*, **121**, 9267s (1994).
2. Zhaohai and Houdin, *Nongyaexe, Xuebao.,* **2(3)**, 8-12 (2000); *Chem. Abstr.*, **135**, 107222g (2001).
3. John, Stanley, *Ger. Offen.,* 2704288 (1977); *Chem. Abstr.,* **87**, 201546 (1977).
4. Ramara, Khagyuani, Ashok, K. and Shukla, R.S., *J. Indian Chem. Soc.,* **57(8)**, 856-7 (1980).
5. Uragami, *et al*., *JPN. Kokai Tokkyo Koho JP,* **09**, 40, 675, *Chem. Abstr.,* **126**, 212149a (1997).
6. Haijoun, Shiv and Zhangyi, Zhenggue, Yoowni, *Nuaxue Zozni*, **11(3)**, 125-128, (2001); *Chem. Abstr.*, **136**, 279396d (2002).
7. Foerster, H., Hofer, V.W., Schmidt, R.R. and Eue, L., *Ger. Offen,* **DE 3**, 218, 482 (1983); *Chem. Abstr.,* **100**, 85705, (1984).
8. Zhag, Zigi, *et al.*, *Youji Huaxure*, **14(1)**, 74-80, (1994); *Chem. Abstr.,* **121**, 9267s (1994).
9. Quin, Z., *et al.*, Nongyaoxue Xuebao, **2(3)**, 8-12 (2000) (CH), Nongyaoxue Xuebao, *Chem. Abstr.,* **135**, 197222g (2001).
10. Donald, E.H. Frear, *Chemistry of the pesticide,* **3rd Ed.**, 295, D-Van Nostrand Co. Inc. Toronto-New York (1955).
11. Horsfall, J.G. and Rich, S., *Contribs.*, Boyce Thompson Inst., **16**, 361 (1951).
12. Maffi, G. Testa, E. and Ettore, R. II, *Farmaco (Pavia) Ed. Sci.,* **13**, 187, (1958); *Chem. Abstr.,* **53**, 2211c (1959).
13. Shukla, J.S. and Agrawal, K, *Curri. Sci.,* **51**, 817 (1982).
14. Rothwell, K. and Wain, R.L., *Ann. Appl. Biol.,* **51**, 161 (1963).
15. Silberg, A.L and Cosma, N., *Acad. Rep. Popular Romeni Lui Carceteri,* **10**, 151, *Chem. Abstr.,* **54**, 8794 (1960).
16. Horsefall, J.G., *Bot. Rev.*, **11**, 357 (1945).
17. Rothwell, K. and Wain, R.L., *Ann. Appl. Biol.*, **51**, 161, (1963)
18. Fischer, H. and Summers, L.A., *Tetrahedron*, **32**, 615 (1976)

❑