INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH & DEVELOPMENT

ISSN 2278 – 0211 (Online)

Study of Some New Substituted Thiadiazole Derivatives as Fungicides

Dr. Shailendra Yadav
Guest Lecturer, Department of Chemistry, Shibli National College, Azamgarh, Uttar Pradesh, India

Abstract:
A number of 5-Aryl-2-(5-arylamino-1, 3, 4-thiadiazol-2-yl amino) -1, 3, 4-thiadiazole (3) have been prepared by the cyclo dehydration of 1-Aryl-6-(5-aryl-1, 3, 4-thiadiazol-2-yl) -2-thioureas (2) which was prepared by the reaction of 4-(5-Aryl-1, 3, 4-thiadiazol-2-yl)- semicarbazides (1) phenyl isothiocynate in presence of ethanol. These compounds have been evaluated for their fungicidal activity against Pyricularia oryzae, Sphaeotheca fuliginea, Phytopthora infestans and Pseudopernospora cubensis.

1. Introduction

A thiadiazole nucleus acknowledge with a broad spectrum of biological activities like pesticidal[1-4], hypoglycemic[5], anti-tubercular[6], antihypertensive[7], antimicrobial[8,9] anticonoulsant[10], bactericidal[11-13], herbicidal[14-19], fungicidal[20-23], acarcidal[24], algicidal[25] insecticidal[26-28] and biological[29-33] properties. Arylamino heterocycles have showed the diverse pesticidal[34-39] activities. A perusal of literature reveals that when a thiadiazole ring is coupled with other heterocyclic system compounds of better biological activities[40-42] were obtained.

Therefore, it is thought of interest to unite two thiadiazole rings and arylamino group together in a molecular framework to see the additive effect of these rings towards the biological activities. The investigation was found to be of further interest because of compactness and planarity of such ring systems may be an additive factor for enhancing activities as it does with algicidal, herbicidal, fungicidal and inflammation inhibitory activities.

The required 4-(5-Aryl-1, 3, 4-thiadiazol-2-yl)- semicarbazides (1) were prepared following the literature method[43]. Reaction of these semicarbazides with phenyl isothiocynate in ethanol furnished 1-Aryl-6-(5-aryl-1, 3, 4-thiadiazol-2-yl) -2-thioureas (2), which on cyclo- dehydration furnished the title compounds (3). The details of which are given in Figure-1 and Table-1.

2. Materials and Method

Procedure for one typical case for each step has been discussed. Melting points were taken in open capillaries and were uncorrected. IR spectra were recorded in KBr on a Perkin –Elmer 881 Spectrophotometer (υ_{max} in cm^{-1}), ^1H NMR spectra in DMSO-d6 on a Perkin-Elmer R-32(400 MHz) Spectrophotometer using TMS as internal reference (chemical shifts in δ, ppm).

2.1. 4-(5-Aryl-1, 3, 4-thiadiazol-2-yl)- semicarbazides (1a)

This compound was prepared following the literature method[43]. The mixture of 2-carbothoxyamino-5-(2-methyl phenyl)-1,3,4-thiadiazole(0.01M) and hydrazine hydrate(0.01M) were refluxed for 6 hours on water bath. The excess of hydrazine hydrate was removed under reduced pressure and the clear solution thus found was allowed to stand overnight. The solid mass thus formed washed, dried and re-crystallized from aqueous ethanol, mp 187^0C, yield 76%.

Other compounds of this type were prepared similarly and recorded in Table-1

2.2. 1-Aryl-6-(5-aryl-1, 3, 4-thiadiazol-2-yl) -2-thioureas (2a)

It was prepared by refluxing a mixture of 4-(5-Aryl-1, 3, 4-thiadiazol-2-yl) semicarbazides (1a) (0.01M) and phenyl isothiocynate (0.01M) in ethanol (200ml) on water bath for 3 hours. The solvent was removed and the solid thus obtained was filtered, washed, dried and re-crystallized from aqueous ethanol.mp 170^0C, yield 74%.

Analysis: $C_{17}H_{16}N_6OS_2$

Calcd: N 20.50; S16.33 %.

Found: N 21.87; S16.66 %.

^{1}HNMR:2.3(s,3H, CH_3), 7.2-7.7(m,9H,ArH), 8.6 (s,1H,NH).

Other compounds of this type were prepared similarly and recorded in Table-1

2.3. 5-Aryl-2-(5-arylamino-1, 3, 4-thiadiazol-2-yl amino) -1, 3, 4-thiadiazole (3a)

These compounds were prepared by making slurry of 1-Aryl-6-(5-aryl-1, 3, 4-thiadiazol-2-yl) -2-thiourea (2a) (0.01M) in sulphuric acid(0.01M) and leaving the reaction mixture overnight and then poured into cold water. The well stirred solution was neutralized with ammonia solution; the resulting precipitate was washed with water, dried and re-crystallized from aqueous ethanol. mp162^{0}C, yield 68%.

Analysis: $C_{17}H_{14}N_6S_2$

Calcd: N 22.92; S17.68 %.

Found: N 22.95; S17.49 %.

IR(KBr):3350 (NH), 1640(>C=N), 1520,1500,1430 (Aromatic ring), 1260,1060 (C-O-C);

^{1}HNMR: 2.5(s,3H, CH_3), 7.2-7.5(m,9H, ArH), 8.6 (b,2H, NH).

Other compounds of this type were prepared similarly and recorded in Table-1

Compd	R	R'	Mp ^{0}C	Yield (%)	Mol. Formula	Analysis					
						Carbon (%)		Hydrogen (%)		Nitrogen (%)	
						Found	Calcd	Found	Found	Calcd	Found
1a	H	-	178	63	$C_9H_9N_5OS$	46.01	45.96	3.69	3.83	29.23	29.79
1b	2-CH_3	-	179	64	$C_{10}H_{11}N_5OS$	48.01	48.19	4.51	4.42	28.23	28.11
1c	4-CH_3	-	192	71	$C_{10}H_{11}N_5OS$	48.29	48.19	4.33	4.42	28.01	28.11
1d	2-OCH_3	-	154	69	$C_{10}H_{11}N_5O_2S$	45.39	45.28	4.05	4.15	26.31	26.42
1e	4-OCH_3	-	169	67	$C_{10}H_{11}N_5O_2S$	45.03	45.28	4.23	4.15	26.53	26.42
2a	H	H	164	69	$C_{16}H_{14}N_6OS_2$	50.99	51.35	4.01	3.78	22.41	22.70
2b	2-CH_3	H	170	75	$C_{17}H_{16}N_6OS_2$	53.42	53.12	4.01	4.17	20.50	21.87
2c	2-CH_3	4-OCH_3	197	82	$C_{18}H_{18}N_6O_2S_2$	52.13	52.43	4.03	4.38	20.41	20.39
2d	4-OCH_3	H	238	84	$C_{17}H_{16}N_6O_2S_2$	50.29	50.00	4.18	4.00	20.85	21.00
2e	4-OCH_3	4-OCH_3	187	80	$C_{18}H_{18}N_6O_3S_2$	50.89	50.23	4.49	4.18	19.36	19.53
3a	H	H	159	69	$C_{16}H_{12}N_6S_2$	54.89	54.55	3.79	3.41	24.11	23.86
3b	2-CH_3	H	162	70	$C_{17}H_{14}N_6S_2$	56.01	55.74	4.13	3.83	22.92	22.95
3c	2-CH_3	4-OCH_3	168	65	$C_{18}H_{16}N_6OS_2$	54.92	54.55	4.19	4.04	21.12	21.21
3d	4-OCH_3	H	175	78	$C_{17}H_{14}N_6OS_2$	52.99	53.40	4.01	3.66	22.58	21.99
3e	4-OCH_3	4-OCH_3	167	75	$C_{18}H_{16}N_6OS_2$	52.63	52.43	4.12	3.88	20.16	20.39

Table 1: Characterization data of the compounds (1), (2) and (3)

2.4. Evaluation of Fungicidal Activity

The anti fungal activity was evaluated by agar plate technique against *Pyricularia oryzae, Sphaeotheca fuliginea, Phytopthora infestans* and *Pseudopernospora cubensis* at concentrations 500 ppm and 100 ppm. The replications in each case were three. On the basis of growth recorded on 7th day of incubation the fungicidal activity of test compounds was calculated in terms of present inhibition of mycelial growth using the following formula.

Present inhibition of mycelial growth $= \frac{c-t}{c} \times 100$

Where c = Average diameter growth of the colony in control sets on 7th day of incubation.

t = Average diameter growth of the colony in treatment set on 7th day of incubation.

- Diameter growth=apparent diameter of the colony–diameter of colony of the inoculums

The percentage inhibitions of various compounds are recorded in table -2

Compd.	Average % inhibition after 7 days							
	Pyricularia oryzae		*Sphaerotheca fuliginea*		*Phytopthora infestans*		*Pseudopernospora cubensis*	
	500 ppm	100 ppm	500 ppm	100 ppm	500 ppm	100 ppm	500 ppm	100 ppm
3a	71	52	70	51	71	53	70	50
3b	82	68	83	69	82	68	84	69
3c	94	75	93	76	94	76	94	76
3d	90	73	89	70	89	71	90	74
3e	90	76	91	75	90	74	90	77
Carbendazim	100	89	100	88	100	89	100	88

Table 2: Anti Fungal Activity Data Compounds (3)

3. Results and Discussion

It is evident from the activity data that the all of the tested compounds have significant fungitoxicity at 500 ppm against all the fungi but their toxicity decreased considerably at lower concentration, although compounds having serial number 3b, 3c, 3d and 3e show greater fungicidal activity against all the organisms but the result are not very spectacular except for compounds 3c, 3d and 3e.

It is also evident from the fungicidal screening data of the tested substituted thiadiazole derivatives showed that, the most active compounds were 3c, 3d and 3e (>89%).

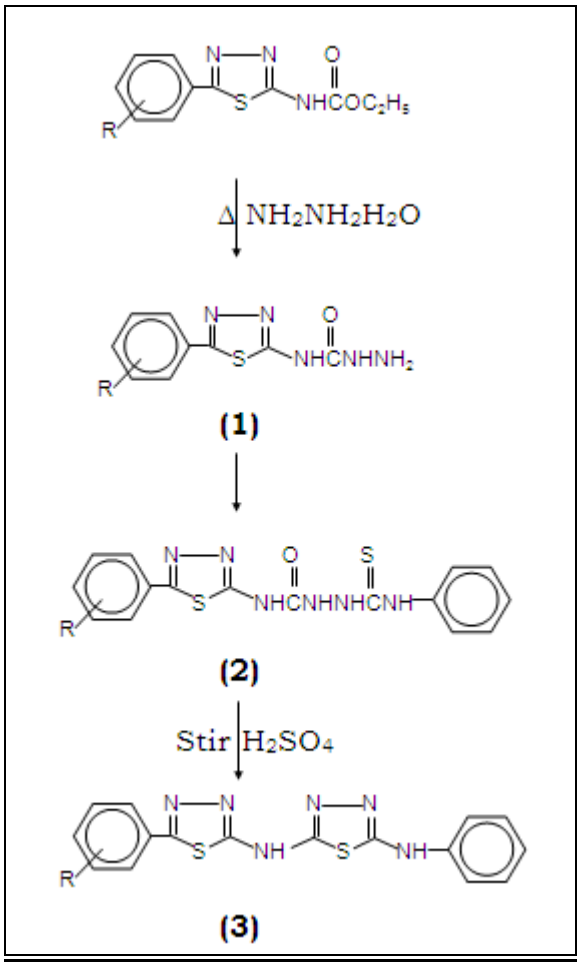

Figure 1

4. Acknowledgements

The authors are thankful to Head, Department of Chemistry, Principal, S. N. College, Azamgarh for providing necessary laboratory facilities and Director RSIC, CDRI, Lucknow for IR and NMR spectral analysis.

5. References

i. T.T. Rilor; Chem. Abstr., 1984, 100, 209832g
ii. E. Regel, P. Frahberger and P. Erust. Ger. Offen 2, 712630/ 1973; Chem. Abstr., 1979, 90, 6401m.
iii. Shi Hai-Jean, Youji Huxaxue, 1999, 19(2), 195-199; Chem. Abstr., 2000, 131, 44776k.
iv. R.H. Udapi, J. Indian Chem. Soc., 1999, 76(9), 461-462; Chem. Abstr., 1999, 131, 122562Z.
v. V.P. Cherryply and P.A. Beczyglub, Khim Farm. Zh., 1979, 13(9), 32-6.
vi. G.L. Maheshwari, R.P Mahesh and R. Singh, Curr. Sci, 1975, 44, 549.
vii. L.K. Chein and H.N. Kuan; Chem. Abstr., 1987, 107, 198229a.
viii. A. Omer, M.E. Mosen and A.E.M. Osmania, J. Heterocycle. Chem. Soc., 1986, 6(2), 1339-4.
ix. M.M. Yousef, A.M. Ismail, A.A. Euam and M.M. El Kerdauy, J. Chem. Soc. Pak., 1986, 6(2), 183-90.
x. B.C. Chepleop, L.P. Mayers, C.B.A. Smith, F. Ian Tulloch and D. Walters, J. Med. Chem., 1987, 30(5), 1.
xi. F. Russo and M. Sentagat, Farmaco Ed. Sci., 1976, 31(1), 41-8; Chem. Abstr., 1976, 84, 90080r.
xii. L. Orlikowski and C.C. Skrazyp. Agrodrilice 1981, 18, 47.
xiii. Jpn Kokai Tokkyo Koho JP 157, 570/1980; Chem. Abstr., 1981, 95, 71995.
xiv. S.C. Benur and V.B. Jigajinnai, Rev. Rou. Chem., 1976, 21(5), 757-62; Chem. Abstr., 1976, 84, 94306j.

xv. C. Budeanu and T. Houga, Rev. Chem. 1979, 30(12), 1189-92; Chem. Abstr., 1980, 93, 26352m.
xvi. Velsicor Chem. Crop. Nath Appl. 7317, 578/1975; Chem. Abstr., 1976, 84, 164785v.
xvii. J. Krenzer, Brit. 1, 447, 182/1976; Chem. Abstr., 1977, 86, 72709n.
xviii. V.I. Timechnko, Visu sists, Koyospod. Nauki 526/1981; Chem. Abstr., 1981, 95, 75242.
xix. R.N. Campbell, Phytophatolgy, 1980, 70(12), 1190.
xx. Jag Mohan and Sangeeta Kataria, Indian J. Chem. Sec (B), 1998, 37 B(7), 713-714; Chem. Abstr., 1998, 129, 260398q.
xxi. Yan Zhang, Lanzhou Daxue Xuebao Ziran Kexueban, 2000, 133, 164(1), 53-57; Chem. Abstr., 2000, 133, 164026d.
xxii. Kyashi Kuroda, Toru, Uchikurohane, Tajima Sokichi and Kenji Tsubata, U.S. 456, 166, 054(CI, 514-361; A01N 43182/ 2000); Chem. Abstr., 2001, 134, 38255k.
xxiii. Chen Han-Song; Chem. Abstr., 2001, 134, 293635.
xxiv. A.N. Dhale, U.S. 453959, 301/1975; Chem. Abstr., 1976, 85, 46695p.
xxv. B. Bochner and D. Daiver, Ger. Offen, 2, 500, 485/1975; Chem. Abstr., 1976, 85, 46695p.
xxvi. T. Cebalo, Ger. Offen, 2, 050, 979/1971; Chem. Abstr., 1971, 75, 45094w.
xxvii. W. Mayer and B. Bochner. Ger Offen, 2, 418, 363/1974; Chem. Abstr., 1975, 82, 31328k.
xxviii. S.S. Tewari and A.K. Sengupta, Indian J. Appl. Chem. 1974, 33(4), 231-233.
xxix. Shi Hai-Tian Wang Zong Yi and Shi Hao Xin, Hecheng, Huzaue, 2000 8(3), 252-255; Chem. Abstr., 2001, 134, 17435d.
xxx. G. Heubach, B. Sachse and H. Buerstell, Ger. Offen. 2, 826, 760/1980; Chem. Abstr., 1980, 92, 181200h.
xxxi. Xiang Zhu, Na Mi, Zhejin Fan and Zhikun Yang, J. Agric. Food Chem., 2010, 58(5), 2755-2762.
xxxii. M. Vedavathi, A. Rajareddy, G.M. Sreenivasa and E. Jayachandran, Int. J. Ph. Sci., 2010, 2(1), 404-410.
xxxiii. Xiang Zhu, Na Mi, Zhejin Fan and Zhikun Yang, J. Agric. Food Chem., 2010, 58(5), 2755-2762.
xxxiv. C. Pakawatchai and S. Sailhong, Acta Crystallo. 2010, 66(9), 2195-2199.
xxxv. D.C.K. Chem., Belg, BE 891, 268, US Appl. 210, 919/1980; Chem. Abstr., 1982, 97, 23615w.
xxxvi. H. Singh and L.D.S. Yadav, Agric. Biol., Chem., 1976, 40(4), 759-64; Chem. Abstr., 1980, 93, 8097c.
xxxvii. S. Giri and H.G. Gupta, Bokin Bobai, 1979, 7(12), 447-560; Chem. Abstr., 1980, 93, 8097c.
xxxviii. Shi Haijian, Wang Zhongyi and Shi Haoxin, Synth. Commun. 1998, 28(21), 3973-982; Chem. Abstr., 1999, 130, 13957v.
xxxix. P.Y. Shirodakar and M.M. Vertek, Indian Drugs, 1998, 35(9), 597-599; Chem. Abstr., 1999, 130, 66463n.
xl. V. Dekic, N. Radulovic, R. Vukicevic, B. Dekic, Z.S. Radic and R. Palic, African J. of Pharm & Pharmacology, 2011, 5(3), 371-375.
xli. A.R.M. Alam and M. Nasrollahzadeh, Turk J. Chem., 2009, 33, 267-280.
xlii. C. Takayama, A. Fijinami, O. Kirino and T. Kato; Chem. Abstr., 1984, 100, 63375e.
xliii. M.Lora-Tomayo, G. Alonso and R. Madronero, Bull. Soc. Chem. France, 1962, 1020.