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SYNTHESIS AND CHARACTERIZATION OF 2, 6, 7-TRIARYL-6, 7-DIHYDRO-1, 3, 4-THIADIAZOLO [3, 2-A]-S-TRIAZINE 5-THIONES AS FUNGICIDES

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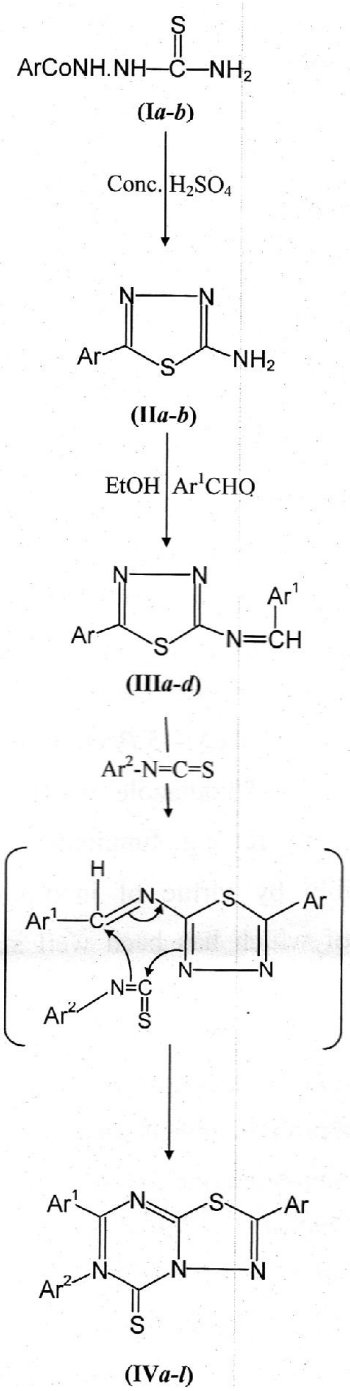
Twelve title compounds 2, 6, 7-triaryl 6, 7-dihydro-1, 3, 4-thiadiazolo [3, 2-a]-s-triazine 5-thiones [IV*a-l*] have been synthesized from their requisite 2-arylidine amino-5-aryl-1, 3, 4-thiadiazoles (III*a-d*) which were prepared from corresponding 2-amino-5-aryl 1, 3, 4-thiadiazoles (II*a-b*). These starting material 2-amino-5aryl-1, 3, 5-thiadiazoles were obtained from their corresponding aroyl thiosemi carbazides [I*a-b*]. All the synthesized compounds [IV*a-l*] were characterized by their molecular formula, elemental analysis I.R. and ^{1}HNMR spectral data. Fungicidal activity of the synthesized compounds was evaluated against *Phytophthora infestans* and *Aspergillus niger*. Fungicidal screening data correlated with the structural features of the tested compounds.

KEY WORDS: Thiadiazoles, Dithane M-45, *Phytophthora infestans* and *Aspergillus niger*.

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]. Many s-triazine derivative have attained significance in agriculture as herbicides [11] and fungicides [12]. Of these, *Simazine* 1 (2-chloro 4, 6-bis-(ethylamino)-s-triazine), *Atrazine* 2 (2-chloro-4-ethylamino-6-isopropylamino-s-triazine), *Prometryne* 3 (2-methylthio-4, 6-bis (isopropyl amino)-s-triazine, *Ametryne* 4 (2-methylthio-4-ethylamino-6-isopropylamino-s-triazine), *Dyrene* 5 (2, 4-dichloro-6-(2-chloroanilino)-s-triazine) and *Methoprotryne* 6 (2-methylthio-4-isopropylamino-6-(3-methoxy propylamino)-s-triazine) are more outstanding. >C=S group has also been reported to be responsible for the fungicidal activity [13]. The biologically versatile-s-triazine ring was fused with 1, 3, 4-thiadiazole nuclei to yield the planar ring system, viz. thiadiazolo-s-triazines ring systems (IV*a-l*), which might be expected to exhibit potential fungicidal action. The reaction sequence leading to the formation of title compounds is given in the Scheme-I and fungicidal screening data are given in the experimental section.



Ar : a-d = C_6H_5; e-h=2-$CH_3C_6H_4$; i-l = 4-$CH_3C_6H_4$

Ar^1 : a, c, e, g, i, k = 4-ClC_6H_4; b, d, f, h, j, l = 4-$OCH_3C_6H_4$

Ar^2 : a, b, e, f, i, j = C_6H_5; c, d, g, h, k, l = 4-ClC_6H_4

Scheme-I

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 360L (60 MHz) NMR spectrometer in $CDCl_3$ or $DMSOd_6$ with TMS as internal reference. Chemical shifts are expressed in δ ppm.

2-Arylideneamino-5-aryl-1, 3, 4-thiadiazoles (III*a-d*).

A mixture of 2-amino-5-phenyl-1, 3, 4-thiadiazole 3.5 g (0.02 mol) and 4-chloro benzaldehyde 2.8 g (0.02 mol) in absolute ethanol (35 ml) was refluxed for 4 hour and filtered while hot, the filtrate upon cooling furnished the desired product which was recrystallized from ethanol as yellowish needles M.P. 224°C, yield 2.2g (78% of the theory).

Analysis : Found C, 60.10; H, 3.28; N, 14.10; S, 10.72; $C_{15}H_{10}ClN_3S$

Requires C, 60.00, H, 3.33; N, 14.02; S, 10.68%

IR (KBr) : 1665 (exocyclic C=H), 1615 (cyclic C=N) cm^{-1}

The other Schiff's bases prepared in the same way and recrystallized from ethanol are given below-

(i) 2-(4-Methoxybenzylidene) amino-5-phenyl-1,3,4-thiadiazole; M.P. 229^{0}C; yield (85% of theory)

Analysis : Found C, 68.85; H, 4.62; N, 10.07; S, 11.56; $C_{16}H_{13}ClN_3S$

Requires C, 68.81, H, 4.65; N, 15.05; S, 11.46%

IR (KBr) : 1660 (exocyclic C=H), 1610 (cyclic C=N) cm^{-1}

^{1}HNMR ($CDCl_3$-DMSO-d_6) δ : 3.76 (3H, OCH_3); 7.50–8.00 (9H, m, Ar-H) and N=CH

(ii) 2-(4-Chlorobenzylidene) amino-5-(4-chlorophenyl)-1, 3, 4-thiadiazole; M.P. 208°C; yield (80% of theory)

Analysis : Found C, 53.78; H, 2.62; N, 12.46; S, 9.46; $C_{15}H_9Cl_2N_3S$

Requires C, 53.89, H, 2.69; N, 12.37; S, 9.58%

(iii) 2-(4-Chlorobenzylidene) amino-5-(4-methoxyphenyl)-1, 3, 4- thiadiazole; M.P. 230^{0}C; yield (82% of theory)

Analysis : Found C, 61.34; H, 3.75; N, 13.48; S, 10.32; $C_{16}H_{12}ClN_3S$

Requires C, 61.24, H, 3.82; N, 13.39; S, 10.20%

2, 6, 7-Triaryl-6, 7-dihydro-1, 3, 4-thiadiazolo [3,2-a]-s-triazine-5-thiones (IV*a-l*).

A mixture of 2-(4-chlorobenzylideneamino-5-pheynyl-1, 3, 4-thiadiazole 3.0 g (0.01 mol) and Phenyl isothiocyanate 1.4 g (0.01 mol) was refluxed in dry toluene for six hour and the solvent was distilled off under reduced pressure. The residue thus obtained was washed with small amount of ethanol followed by water, and the product was recrystallized from ethanol as shining yellowish needles. Yield, melting point, molecular formula and elemental analysis of this as well as that of the other compounds of this class are recorded in Table-1.

Table-1. Characterization data of 2, 6, 7-Triaryl-6, 7-dihydro-1, 3, 4-thiadiazolo [3, 2-a]-s-triazine-5-thiones (IV*a-l*).

Compd. No.	Ar^2	Ar^1	Yield (%)	M.P. (^{0}C)	Molecular Formula	Analysis (Calcd.)% Found		
						C	N	S
Ar = C_6H_5								
IVa	C_6H_5	4-ClC_6H_4	74	234	$C_{22}H_{15}ClN_4S_2$	60.72 (60.75)	12.82 (12.88)	14.62 (14.72)
b*	C_6H_5	4-$OCH_3C_6H_4$	77	252	$C_{23}H_{18}N_4OS_2$	64.05 (64.18)	13.22 (13.02)	14.82 (14.88)
c	4-ClC_6H_4	4-ClC_6H_4	69	219	$C_{22}H_{15}Cl_2N_4S_2$	56.27 (56.17)	12.00 (11.91)	13.51 (13.61)
d	4-ClC_6H_4	4-$OCH_3C_6H_4$	71	231	$C_{23}H_{17}ClN_4OS_2$	59.52 (59.41)	12.00 (12.05)	13.72 (13.77)
					Ar=2-$CH_3C_6H_4$			
e	C_6H_5	4-ClC_6H_4	73	237	$C_{23}H_{17}ClN_4S_2$	61.48 (61.53)	12.47 (12.48)	14.22 (14.26)
f	C_6H_5	4-$OCH_3C_6H_4$	70	245	$C_{24}H_{20}ClN_4OS_2$	64.85 (64.86)	12.62 (12.61)	14.50 (14.41)
g	4-ClC_6H_4	4-ClC_6H_4	72	192	$C_{23}H_{18}Cl_2N_4S_2$	56.92 (56.90)	11.55 (11.54)	13.29 (13.19)
h**	4-ClC_6H_4	4-$OCH_3C_6H_4$	68	215	$C_{24}H_{19}ClN_4OS_2$	60.15 (60.18)	11.73 (11.70)	13.45 (13.37)
Ar = 4-$CH_3C_6H_4$								
i	C_6H_5	4-ClC_6H_4	74	233	$C_{23}H_{17}ClN_4S_2$	61.42 (61.53)	12.45 (12.48)	14.35 (14.26)
j***	C_6H_5	4-$OCH_3C_6H_4$	78	241	$C_{24}H_{20}N_4OS_2$	64.82 (64.86)	12.63 (12.61)	14.44 (14.41)
k	4-ClC_6H_4	4-ClC_6H_4	73	198	$C_{23}H_{18}Cl_2N_4S_2$	56.97 (56.90)	11.53 (11.54)	13.29 (13.19)
l	4-ClC_6H_4	4-$OCH_3C_6H_4$	75	221	$C_{24}H_{19}ClN_4OS_2$	60.28 (60.18)	11.55 (11.70)	13.35 (13.37)

The IR (KBr) and ^{1}H NMR ($CDCl_3$-DMSO-d_6) spectra of the representative compounds are also given as the footnote of this table.

*IR (KBr) : 1605, 1635 (>C=N), 1195 (>C=S) cm^{-1}

^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ : 3.74 (3H, s, OCH_3), 6.74 (1H, s, NCH)
7.46–7.96 (14H,m,aromatic H)

** IR (KBr) : 1610, 1630 (>C=N), 1195 (>C=S) cm^{-1}

^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ : 3.64 (3H, s, OCH_3), 6.74 (1H, s, NCH)
2.32 (3H, s, CH_3) 7.44–7.94 (12H, m, aromatic H)

*** IR (KBr) : 1615, 1635 (>C=N), 1200 (>C=S) cm^{-1}

^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ : 3.44 (3H, s, OCH_3), 6.64 (1H, s, NCH)

2.22 (3H, s, CH_3), 7.20–8.00 (13H, m, aromatic H)

FUNGICIDAL ACTIVITY : The fungicidal activity of such twelve compounds (IV*a-l*) were evaluated against *Phytophthora infestans* and *Aspergillus niger* at 1000, 100 & 10 ppm concentration following the Agar Plate Technique [14] and the results are summarized in Table-2.

Table-2. Fungicidal screening data of 2, 6, 7-Triaryl, 6, 7-dihydro-1, 3, 4-thiadiazolo [3, 2-a] -s-triazine-5-thiones (IVa-l).

Compd. No.	Average % inhibition against.					
	Phytophthora infestans at			Aspergillus niger at		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
IVa	84	41	28	85	42	25
b	86	42	26	87	44	27
c	98	62	42	99	65	44
d	87	38	32	86	40	31
e	76	36	30	75	35	28
f	82	38	31	80	36	29
g	98	61	40	99	62	41
h	86	37	38	84	38	36
i	85	34	30	86	32	29
j	77	35	29	78	36	28
k	99	37	32	98	38	30
l	84	44	30	82	43	31
Dithane M-45	100	85	68	100	80	66

RESULTS AND DISCUSSION

Persual of the screening results indicates that all the tested compounds (IV*a-l*) inhibited more than 75% growth of both the test fungi i.e. *Phytophthora infestans* and *Aspergillus niger* at 1000 ppm concentration. Of these the most active compounds (IV*c*, IV*g* and IV*k*) exhibited fungicidal activity almost equivalent to that of **Dithane M-45** at 1000 ppm concentration and inhibited 30-44% growth of both the fungal species even at 10 ppm concentration.

Although some of the screened compounds IV*c*, IV*g* and VI*k* were highly toxic to *Phytophthora infestans* and *Aspergillus niger* at higher concentration (1000 ppm) the overall results are not so encouraging as one would expect from the combined performance of the two biolabile nuclei *i.e.* 1, 3, 4-thiadiazole and -s-triazine. This might be attributed to the partial saturation in the -s-triazine ring system. This presumption is supported by the earlier observations that compact size and planarity of molecule often enhance its pesticidal activity [15, 16].

It is however, noteworthy that the introduction of chloromethoxy and methyl groups in the aryl moiety. The fungal activity varied but marginally with the fungal species.

Conclusions

The comparison of antifungal activity of the title compounds IV*a-l* with their precursors clearly shows that the former incorporating different toxophoric groups are more active. The screening data (Table-2) clearly indicates that there was significant alteration in the fungitoxicity with the change of the toxophoric group. For example introduction of chloro groups in the aryl moiety of these compounds tends to augment the fungitoxicity. The fungal activity varied but marginally with the fungal species.

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