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Synthesis, Characterization and Fungitoxicity of 3,4,6-triayl-s-triazolo [3,4-b]-1,3,4-thiadiazolo [1,3,5]-triazine-5-thiones

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ABSTRACT

In the present work 3,4,6-triayl-s-triazolo [3,4-b]-1,3,4-thiadiazolo [1,3,50-triazine-5-thiones (IVa-n) were synehsized by 4+2 cycloaddition of 6-arylidine amino-3- aryl-s-triazolo [3,4-b]-1,3,4-thiadiazoles (IIIa-n) are arylisothiocynate in dry tolune as solvent. 6-Arylidine amino-3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazoles (IIIa-n) were prepared from aromatic aldehyde refluxing in absolute ethanol with 6-amino-3-aryl-s-triazole [3,4-b]-1,3,4-thiadiazoles (IIa-g), which are prepared from 3-aryl, 4-amino-5- mercapto-s-triazole (Ia-g) by treating it with cyanogen bromide in ethanol. Starting material 3-aryl, 4-amino-5-mercapto-s-triazoles (Ia-g) wre prepred in excellent yield following the method of Ried and Heindel[1]. The reaction sequence leading to the formation of titled compounds are given in the scheme 1. All the synthesized fourteen titled compounds were well characterized by their analytical and spectral data. Fungitoxicity of titled compounds (IVa-n) have been evaluated against two fungal species i.e. *Helminthosporium orayzee* and *Alternaria solanai*.

Key words: Fungitoxicity, *Helminthosporium orayzae*, *Alternaria solanai*, Dithane M-45.

INTRODUCTION

Many 1,3,4-thiadiazole nucleus is associated with broad spectrum of biocidal activities for example fungicides[2-3], insecticides[4-5], bactercides[6-7] and herbicides[8-9] possibly by virtue of incorporating >N-C-S- moiety. The toxophoric importance of which has been well stressed in many pesticides[10]. The presence of >C=S group is also known to enhance the fungicidal activity of heterocyclic compounds[11]. 1,2,4-triazole derivatives are known to exhibit various type of useful biological activities. 1,2,4- Triazole derivatives have been reported as various pesticides[12-13].

Perusal of the above reports prompted aa to fuse the biolabile 1,2,4-triazole nucleus, 1,3,4-thiadiazole nucleus and 1,3,5-triazine nucleus to prepared the title compounds 3,4,6-triayl-s-triazolo [3,4-b]-1,3,4-thiadiazolo [1,3,5]-triazine-5-triones (IVa-n) with the hope that presence of above biolabile nucleus in the title compounds results a fungicides of enhanced potency.

Fungitoxicity

Synthesized fourteen titled compounds (IIIa-n) were evaluated for their fungitoxicity against two fungal species i.e. Helminthosporium oryzae and Alternaria solanai by Agar Plate Technique[14] at 1000, 100 and 10 ppm concentrations. It is apparent from the screening results that all the tested compounds (IIIa-n) displayed significant fungitoxicity at 1000 ppm against both the fungal species but their activity decreased markedly at lower concentration (100 and 10 ppm). The compound III*b*, III*c*, III*i* and III*l* exhibited antifungal activity of the order of Dithane M-45 at 1000 ppm and inhibited 53.6 to 55.6 growth of both the test fungi even at 10 ppm however overall results are not so encouraging one would expect from combined performance of the three biolable nucleus viz. 1,2,4-triazole, 1,3,4-thiadiazole and 1,3,5-triazine ring system.

Persuals of the screening data clearly indicates that three was significant altertation in the fungitoxicity with the change in the relative position of the substituent on phenyl ring. For example the compounds bearing o-chloro group were more toxic than the corresponding compounds with p-fluoro group. Similarly 2-chloro group was more effective then the 4-chloro group. It was noted that the introduction of chloro group is more effective than methyl or methoxy group.

EXPERIMETNAL

Melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on a Jasco FT/IR-460 plus Fourier transform infrared spectrometer. ^{1}HNMR spectra were scanned on a bruker ultraspec 500 MHz/AMX 400MHz spectrometer using DMSO as solvent (chimical shift in δ ppm). Mass spectra were recorded on JOEL Sx 102/DA-6000 mass spectrophotometer using Argon/Xenon (60KV, 10mA) as the FAB gas with in nitrobenyl alcohol as the matrix.

Synthesis of 3-aryl-4-amino-5-mercapto-triazoles(Ia-g)

3-Aryl-4-amino-5-mercapto-triazoles were prepared in excelleng yield following the method of Reid and Heindel[1] following seven (Ia-g) mercapto triazoles were prepared which well agreed with their analytical data already reported in literature[1-15].

Synthesis of 6-amino-3-aryl-s-triazolo-[3,4-b],1,3,4-thiadiazoles (IIa-g)

A mixture of 3-aryl-4-amino-5-mercapto-triazoles 5.0 gm (0.22 mol) and cyanogen bromide 2.31 gm (0.022 mol) in ethanol (150ml) was heated under reflux on a water bath for 6 hours concentration to one fourth of its original volume and neutralized with saturated aqueous solution of K_2CO_3. The white precipitate thus obtained was filtered and recrystallized from ethanol to give colourless shiny crystals of titled compounds, which are given in table 1 with their characterization data.

Synthesis of 6-arylidine amino-3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazoles (IIIa-n)

A mixture of 6-amino-3-aryl-s-triaolo [3,4-b]-1,3,4-thiadiazoles (0.02 mol) and aromatic aldehdyde (0.02 mol) in absolute ethanol (40ml) was refluxed and filtered while hot a filtrate upon cooling, furnished the desired product, which was recrystallized from ethanol as yellowish needles. All the prepared fourteen compounds (III a-n) are given in table 1 with their characterization data.

Synthesis of 3,4,6-triaryl-s-triazolo-[3,4-b]1,3,4-thiadiazolo [1,3,5]-triazine-5-thiones (IVa-n)

A mixture of 6-arylidine amino -3-aryl-s-triazolo [3,4-b]-1,3,4-thiadi-azoles (0.01 mol) and phenyl isothiocynanate 1.4 gm (0.01mol was refluxed in dry toluene for 6 hours and the solvent was distilled of 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. All the compounds synthesized (IVa-n) are given in table 2 with their characterization data.

Table 1: Characterization data of 6-amino-3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazoles (IIa-g) and 6-arylidine amino -3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazoles (IIIa-n)

Compd. No.	R	Molecular formula	m.p. (°C)	Yield (%)	Found (Calculated) %		
					C	N	S
IIa	C_6H_5	$C_9H_7N_5S$	238	57	49.74 (49.76)	32.26 (32.25)	17.76 (14.74)
b	2-C_6H_4Cl	$C_9H_6N_5SCl$	242	58	43.03 (43.02)	27.85 (27.88)	12.70 (12.74
c*	2-$C_6H_4CH_3$	$C_{10}H_9N_5S$	244	56	51.95 (51.94)	30.28 (30.30)	13.86 (13.85)
d	2-$C_6H_4OCH_3$	$C_{10}H_9N_5SO$	243	58	48.57 (48.58)	28.31 (28.34)	12.93 (12.95)
e	4-C_6H_4Cl	$C_9H_6N_5SCl$	241	59	43.03 (43.02)	27.90 (27.88)	12.76 (12.74)
f	4-$C_6H_4CH_3$	$C_{10}H_9N_5S$	243	57	51.96 (51.94)	30.34 (30.30)	13.82 (13.85)
g	4-$C_6H_4OCH_3$	$C_{10}H_9N_5SO$	244	60	48.59 (48.58)	28.38 (28.34)	12.98 (12.98)
		Ar-4-FC_6H_4					
IIIa	C_6H_5	$C_{16}H_{10}N_4SF$	208	72	62.15 (62.13)	18.13 (18.12)	10.33 (10.35)
b	2-C_6H_4Cl	$C_{16}H_9N_4SF$	213	70	55.94 (55.97)	16.31 (16.31)	09.35 (09.32)
c**	2-$C_6H_4CH_3$	$C_{17}H_{12}N_4SF$	207	74	63.13 (63.15)	17.30 (17.33)	06.92 (09.90)
d	2-$C_6H_4OCH_3$	$C_{17}H_2N_4OSF$	209	76	60.18 (60.17)	16.53 (16.51)	09.40 (09.32)
e	4-C_6H_4Cl	$C_{16}H_9N_4SClF$	213	71	55.96 (55.97)	16.35 (16.32)	09.35 (09.32)
f	4-$C_6H_4CH_3$	$C_{17}H_{12}N_4SF$	216	78	63.13 (63.15)	17.31 (17.33)	09.94 (09.90)
g	4-$C_6H_4OCH_3$	$C_{17}H_{12}N_4OSF$	217	77	60.19 (06.17)	6.50 (16.51)	09.41 (09.43)
		[Ar=4-P-F-$OCH_3C_6H_5$]					
h	C_6H_5	$C_{17}H_{12}N_4SF$	211	72	63.14 (63.17)	17.31 (17.33)	09.91 (09.90)
i	2-C_6H_4Cl	$C_{17}H_{11}N_4SClF$	220	76	57.15 (57.14)	15.69 (15.68)	08.95 (08.95)
j	2-$C_6H_4CH_3$	$C_{18}H_{14}N_4SF$	222	75	64.10 (64.09)	16.62 (16.61)	09.46 (09.49)
k**	2-$C_6H_4OCH_3$	$C_{18}H_{14}M_4SF$	219	75	61.20 (61.18)	15.85 (15.86)	09.10 (09.06)
l	4-C_6H_4Cl	$C_{17}H_{11}N_4SClF$	214	77	57.15 (57.14)	15.69 (15.68)	08.94 (08.96)

m	4-$C_6H_4CH_3$	$C_{18}H_{14}N_4SF$	217	73	64.06 (64.09)	16.63 (16.61)	09.50 (09.49)
n	4-$C_6H_4OCH_3$	$C_{18}H_{14}N_4OSF$	218	74	61.16 (61.18)	15.85 (15.86)	09.64 (09.66)

* IR (KBr) : 835 (1,4-disubstituted benzene ring), 1520 (CN stretching) 1620 (Cyclic C=N, 3310 (N-H stretching)

^{1}H NMR (DMSO-d_6) δ: 2-40 (3H, s, CH3), 5.25 (2H, br, s, NH_2), 7.00-7.80 (4H, m,Ar-H).

** IR (Kbr) : 1625 (Cyclic C=N), 1665 (exocyclic C=N) cm^{-1}

^{1}HNMR (CDMO-d_6) δ: 2.40 (3H, s, CH_3). 7.10-8.12 (9H, H, aromatic H)

*** IR (KBr) : 1620 (cyclic (C=N), 1670 (exocyclic C=N)

^{1}H NMR (DMSO-d_6) δ: 3.60 (3H, s, OCH3), 7.00-7.90 (11H, m, aromatic H)

Table 1: Characterization data of 6-amino-3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazoles (IIa-g) and 6-arylidine amino -3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazoles (IIIa-n)

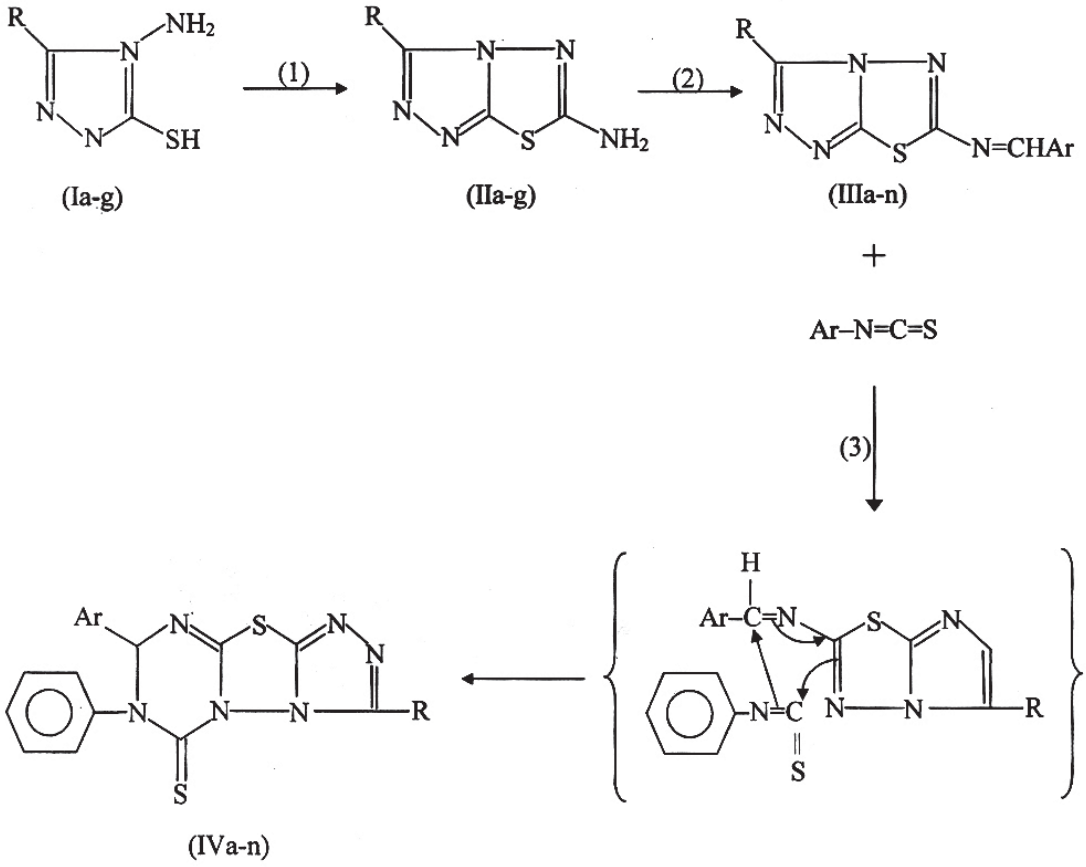
Compd. No.	R	Molecular formula	m.p. (°C)	Yield (%)	Found (Calculated) %		
					C	N	S
IVa	C_6H_5	$C_{23}H_{15}N_6S_2F$	181	69	60.22 (60.26)	18.35 (18.34)	13.99 (13.97)
b	2-ClC_6H_4	$C_{23}H_{14}N_6S_2ClF$	185	73	56.11 (56.09)	17.05 (17.07)	13.03 (13.00)
c*	2-$CH_3C_6H_4$	$C_{24}H_{17}N_6OS_2F$	183	66	56.06 (56.09)	17.10 (17.07)	13.04 (13.14)
d	2-$OCH_3C_6H_4$	$C_{24}H_{17}N_6ClS_2F$	186	67	59.00 (59.01)	17.20 (17.21)	13.14 (13.11)
e	4-ClC_6H_4	$C_{23}H_{14}N_6ClS_2F$	183	77	56.06 (56.09)	17.10 (17.07)	13.04 (13.00)
f	4-$C_6H_4CH_3$	$C_{24}H_{17}N_6S_2F$	187	71	61.04 (61.01)	17.68 (17.79)	13.57 (13.55)
g	4-$OCH_3C_6H_4$	$C_{24}H_{17}N_6OS_2F$	182	71	59.05 (59.01)	17.18 (17.21)	13.57 (13.11)
h	C_6H_5	$C_{24}H_{17}N_6S_2F$	184	68	61.03 (61.01)	17.80 (17.79)	13.50 (13.55
i	2-ClC_6H_4	$C_{24}H_{16}N_6S_2ClF$	187	66	56.93 (56.91)	16.65 (16.60)	12.68 (12.64)
j	2-$CH_3C_6H_4$	$C_{25}H_{19}N_6S_2F$	186	70	61.70 (61.72)	17.24 (17.28)	13.19 (13.16)
k**	2-$OCH_3C_6H_4$	$C_{25}H_{19}N_6ClS_2F$	182	73	59.73 (59.76)	16.75 (16.73)	12.70 (12.74)
l	4-ClC_6H_4	$C_{24}H_{16}N_6ClS_2F$	188	76	56.90 (56.91)	16.58 (16.60)	12.69 (12.64)
m	4-$C_6H_4CH_3$	$C_{25}H_{19}N_6S_2F$	185	70	61.70 (61.72)	17.30 (17.28)	13.12 (13.76)
n	4-$OCH_3C_6H_4$	$C_{25}H_{19}N_6OS_2F$	189	77	59.78 (59.76)	16.75 (16.73)	12.76 (12.74)

* IR (Kbr) : 1620(Cyclic C=N), 1090 (>C=S), 1370 (C=S=C) cm^{-1}

^{1}HNMR (CDMO-d_6) δ: 2.30 (3H, s, CH_3). 1.74 (1H, s, NCH), 7.40-7.90 (13H, m, aromatic H).

** IR (KBr) : 1620 (cyclic (C=N), 1100 (>C=S), 1370 (C=S=C) cm^{-1}

^{1}H NMR (DMSO-d_6) δ: 2.35 (3H, s, OCH3), 3.55 (3H, s, OCH_3), 6.68 (1H, s, NCH), 7.00-8.00 (12H, m, Ar-H).



Scheme 1.

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