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Synthesis and fungitoxicity of 3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazolo [3,2-b] imidazo [4,5-b] quinoxalines

ATMA RAM MISHRA, KASHI NATH TRIPATHI and H.C. MISHRA

Department of Chemistry,
Shri Durga Ji P.G. College, Chandeswhar Azamgarh, and
R. P.G. College, Jamuhai, Jaunpur, U.P. (INDIA)

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Abstract

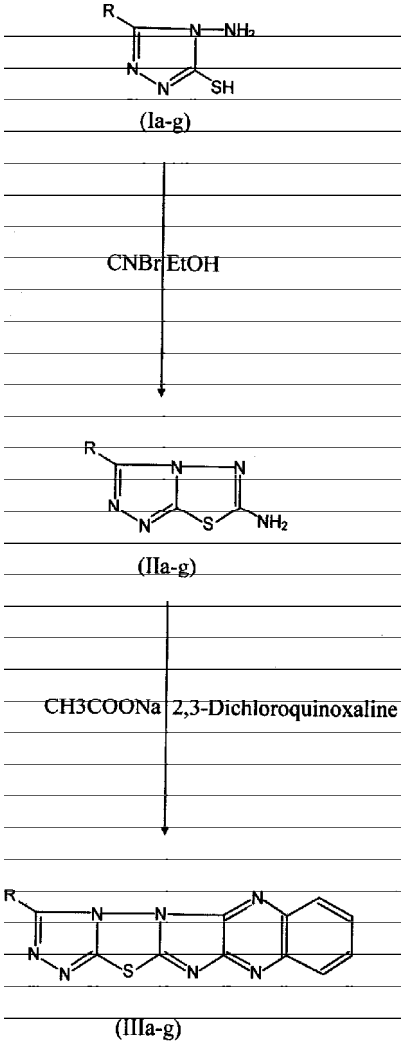
3-Aryl-4-amino-5-mercapto-s-triazoles (Ia-g) were prepared in excellent yield. These compounds further treating with equimolar mixture of cyanogen bromide in ethanol yielded 6-amino-3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadizoles (IIa-g) which on further treating with 2,3-dichloroquinoxaline in the presence of anhydrous sodium acetate gives the title compound 3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazolo [3,2-b] imidazo [4,5-b] quinoxalines (IIIa-g). All the synthesize compounds were well characterized by their elemental and spectral studies. Fungitoxicity of the synthesized compounds were evaluated against *Phytophthora infestans* and *Aspergillus niger*.

Key words : s-triazoles, Thiadiazoles, Imidazoles quinoxalines *Phytophthora infestans* and *Aspergillus niger*.

Introduction

Nitrogen containing heterocyclic compounds are present in all the living beings where these performs important biological functions. Nitrogenous heterocyclic compounds occurred widely in roast food and drugs and posses different pharmacological properties due to oxidation of nitrogen in molecule[1]. s-Triazole nucleus is associated with broad spectrum of pesticidal activities like fungicides[2,3], bactericides[4,5], herbicides[6,7], insecticides[8,9] *etc.* Similarly 1,3,4-thiadiazole nucleus is also possesses a large number of biological activities viz. fungicidal[10,11], insecticidal[12,13], herbicidal[14,15]. In association quinoxaline derivatives shows medicinal properties[16,17].

Considering the above facts we have fused biolabile 1,2,4-triazole, 13,4-thiadiazole and quinoxaline nucleus to prepare the title compounds 3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazolo [3,2-b] imidazo [4,5-b] quinoxalines (Scheme-1) and hope that these compounds may be suitable fungicides of enhanced potency.



R : a=C_6H_5, b=2-ClC_6H_4, c=2-$CH_3C_6H_4$, d=2-$OCH_3C_6H_4$, e=4-ClC_6H_4, f=4-$CH_3C_6H_4$, g=4-$OCH_3C_6H_4$

Scheme-I

Experimental

(i) 3-Aryl-4-amino-5-mercapto-s-triazoles (Ia-g):

3-Aryl-4-amino-5-mercapto-s-triazoles were prepared in excellent yield following the method of Reid and Heindel following seven mercapto triazoles were prepared which well agreed with their analytical data already reported in litrature.

(a) 3-(Phenyl)-4-amino-5-mercapto-1,24-triazoles; M.P. 243^{0}C, yield 50%.
(b) 3-(2-Chloropenyl)-4-amino-5-mercapto-1,2,4-triazoles; M.P. 239^{0}C, yield 53%.
(c) 3-(2-methylphenyl)-4-amino-5-mercapto-1,2,4-triazoles; M.P. 240^{0}C, yield 51%.
(d) 3-(2-methoxyphenyl)-amino-5-mercapto-1,2,4-triazoles; M.P. 243^{0}C, yield 50%.
(e) 3-(4-Chlorophenyl)-4-amino-5-mercapto-1,2,4-triazoles; M.P. 241^{0}C, yield 53%.
(f) 3-(4-methylphenyl)-4-amino-5-mercapto-1,2,4-triazoles; M.P. 244^{0}C, yield 52%.
(g) 3-(4-methoxyphenyl)-4-amino-5-mercapto-1,2,4-triazoles; M.P. 245^{0}C, yield 54%.

(ii) 6-Amino-3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazoles (IIa-g):

A mixture of 3-aryl-4-amino-5-mercapto-s-triazole 5.0 gm (0.022 mol) and cyanogen bromide 2.31 gm (0.022 mol) in ethanol (150 ml) was heated under reflux on a water-bath for 6 hrs. concentrated to one fourth of its original volume and neutralized with saturated aq. solution of K_2CO_3. The white precipitate thus obtained, was filtered and recrystallized from ethanol to give colourless shiny crystals.

6-amino-3-aryl-s-triazolo-[3,4-b)-1,3,4-thiadiazoles thus synthesized in 55-60% yield of theory and recrystallized from ethanol which are given in Table 1 with their characterization data of M.P. yield, molecular formula, elemental analysis, IR and ^{1}H-NMR spectra of the representative compounds.

Table 1. Characterization data of 6-amino-3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazoles

Compd. No.	R	Yield (%)	M.P. (^{0}C)	Molecular Formula	Analysis Found (Calcd)% C	N	S
IIa	C_6H_5	58	239	$C_9H_7N_5S$	49.76 (49.75)	32.25 (32.27)	14.74 (14.75)
b	2-ClC_6H_4	56	241	$C_9H_6N_5SCl$	43.02 (43.05)	27.88 (27.87)	12.74 (12.72)
c*	2-$CH_3C_6H_4$	55	243	$C_{10}H_9N_5S$	51.94 (51.92)	30.30 (30.29)	13.85 (13.87)
d	2-$OCH_3C_6H_4$	59	244	$C_{10}H_9N_5SO$	48.58 (48.59)	28.34 (28.33)	12.95 (12.94)
e	4-ClC_6H_4	58	242	$C_9H_6N_5SCl$	43.02 (43.01)	27.88 (27.89)	12.74 (12.75)
f	4-$CH_3C_6H_4$	56	244	$C_{10}H_9N_5S$	51.94 (51.95)	30.30 (30.33)	13.85 (13.84)
g	4-$OCH_3C_6H_4$	60	245	$C_{10}H_9N_5SO$	48.58 (48.61)	28.34 (28.36)	12.95 (12.97)

* IR (KBr) : 835 (1,4-disubstituted benzene ring), 1520 (C-N stretching), 1615 (cyclic C=N), 3140, 3310 (N-H stretching).
^{1}HNMR (DMSO-d_6) δ : 2.40 (3H, s, CH_3), 5.25-(2H, br, s, NH_2), 7.00-7.80 (4H, m, Ar-H).

(3) 3-Aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazolo [3,2-b] imidazo [4,5-b] quinoxalines (IIIa-g) :

A solution of 6-amino-3-aryl-s-trizolo-[3,4-b]-1,3,4-thiadiazole 0.5 gm. (0.002 mol) 2,3-dichloroqunoxaline 0.398 gm (0.002 mol) and anhydrous sodium acetate 0.328 gm (0.004 mol) in ethanol (25 ml) was heated under reflux for 6 hrs. The reaction mixture was concentrated, cooled and poured into cold water. A yellow precipitate thus obtained was filtered off, dried and recrystallized from methanol to give yellow coloured crystals.

Similarly all the 3-aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazolo–[3,2-b] imidazo [4,5-b]-quinoxaline thus synthesized in 56-60% yield of theory and recrystallised from ethanol which are given in Table 2 with their characterization data of M.P., yield, molecular formula, elemental analysis, IR and 1H-NMR spectra of the representative compounds are given.

Table 2. Characterization data of 3-Aryl-s-triazolo-[3,4-b]-1,3,4-thiadiazolo [3,2-b] imidazo [4,5-b] quinoxalines (IIIa-g).

Compd. No.	R	Yield (%)	M.P. (^{0}C)	Molecular Formula	Analysis Found (Calcd)%		
					C	N	S
IIIa*	C_6H_5	58	86	$C_{17}H_9N_7S$	59.47 (59.49)	28.57 (28.55)	09.32 (09.31)
b**	2-ClC_6H_4	59	82	$C_{17}H_8N_7SCl$	54.11 (54.14)	25.99 (25.98)	08.48 (08.49)
c	2-$CH_3C_6H_4$	57	84	$C_{18}H_{11}N_7S$	60.50 (60.51)	27.45 (27.42)	08.96 (08.97)
d	2-$OCH_3C_6H_4$	58	85	$C_{18}H_{11}N_7OS$	57.90 (57.93)	26.27 (26.26)	08.57 (08.59)
e	4-ClC_6H_4	56	83	$C_{17}H_8N_7SCl$	54.11 (54.10)	25.99 (25.97)	08.48 (08.46)
f	4-$CH_3C_6H_4$	55	83	$C_{28}H_{11}N_7S$	60.50 (60.49)	27.45 (27.47)	08.96 (08.95)
g	4-$OCH_3C_6H_4$	60	86	$C_{18}H_{11}N_7OS$	57.90 (57.88)	26.27 (26.28)	8.57 (08.55)

* IR (KBr) : 760, 825 (1,2 and 1,4-disubstituted benzene ring), 1525 (C-N stretching), 1625 (cyclic C=N), 3020, 3055 (aromatic C-H stretching) cm^{-1}
^{1}H-NMR (DMSO-d_6) δ : 3.80 (3H, s, OCH_3), 7.073-7.94 (8H, m, Ar-H)

** IR (KBr) : 765, 830 (1,2 and 1,4-disubstituted benzene ring), 1525 (C-N stretching), 1625 (cyclic C=N), 3020, 3055 (aromatic C-H stretching) cm^{-1}
^{1}H-NMR (DMSO-d_6) δ : 2.40 (3H, s, OCH_3), 7.00-7.99 (8H, m, Ar-H)

Result and Discussion of Fungitoxicity

The screening data indicates that all the compounds were more active against *Aspergillus niger* as compared with *Phytophthora infestans* but the difference was marginal. Most of the compounds showed the significant antifungal activity at 1000 ppm against both the fungal species but their fungitoxicity decreased markedly on dilution (100 and 10 ppm) concentration out of these the compounds 3b and 3e exhibited fungitoxicity of the order of **Dithane M-45** at 1000 ppm against both the test fungi. However, their activity decreased markedly at lower concentration (100 ppm and 10 ppm) except in the compounds 3b and 3e which exhibited 50-53% growth of the both the fungi species even at 10 ppm.

It is, however, noteworthy that the introduction of chloro and methoxy group in the aryl moiety of these compounds tends to arguments the fungitoxicity, and that the introduction of chloro group at ortho position is more effective than that at para position. Likewise, the introduction of methoxy group at ortho position is more effective than para position. The overall results are not so encouraging as one would expect from combined performance of the two biolabile nuclei, viz. Triazole and Thiadiazole.

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