

Synthesis and Characterization of triaryl-s-triazolo-[3,4-b]-1,3,4-thiadiazolo [3,2-b]-s-triazine-5-thiones as fungicides

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Abstract

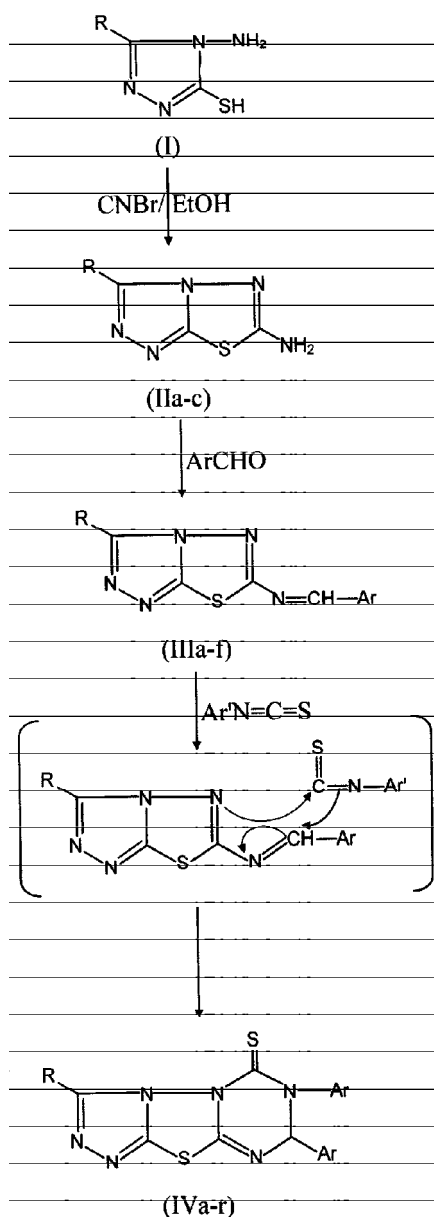
6-Amino-3-aryl-s-triazolo [3,4-b]-1,3,4-thiadiazoles (IIa-c) were obtained from 3-aryl-4-amino-5-mercapto-s-triazoles (Ia-c) by treating it with cyanogen bromide in ethanol. Which in turn were treated with aromatic aldehydes to give 3-aryl-6-(arylideneamino)-s-triazole-[3,4-b]-1,3,4-thiadiazoles (IIIa-f). Compounds III were further treated with aryl isothiocyanates to yield 3,4,6-triaryl-s-triazolo [3,4-b]-1,3,4-thiadiazolo-[3,2-b]-s-triazine-5-thiones (IVa-r). Structure of all these unknown compounds were confirmed by their spectral studies and elemental analysis. The compounds (IVa-r) were screened for their antifungal activity against *Phytophthora infestans* and *Aspergillus niger*.

Key words : *Phytophthora infestans* and *Aspergillus niger*, Dithane M-45, s-triazole, 1,3,4-thiadiazoles, Agar Plate Technique.

Introduction

In continuation of our research work on the synthesis of bridgehead nitrogen heterocyclic system as pesticides herein we report the synthesis and antifungal activity of 3,4,6-triaryl-s-triazolo-[3,4-b]-1,3,4-thiadiazolo [3,2-b]-s triazine-5-thiones (IVa-r). These compounds were synthesized in view of literature because 1,2,4-triazole derivatives possess fungicidal¹, bactericidal^{2,3} and insecticidal^{4,5} activities. Recently some 1,3,4-thiadiazole derivatives were reported to possess fungicidal^{6,7},

herbicidal⁸ and bactericidal⁹ activity. Similarly 1,3,5-triazine derivatives were also reported as fungicides^{10,11}. In view of these reports in the present investigation we have fused 1,2,4-triazole and 1,3,4-thiadiazole nucleus with 1,3,5-triazine ring to synthesise the title compounds and fungicidal activity have been evaluated and co-related with the substituents to probe how for these combinations could enhance the fungicidal action^{12,13}. The reaction sequence leading to the formation of the title compounds is given in the Scheme-1.



R : C_6H_5 , 2- FC_6H_4 , 2- $\text{OCH}_3\text{C}_6\text{H}_4$

Ar : 2- ClC_6H_4 , 4- $\text{OCH}_3\text{C}_6\text{H}_4$

Ar' : a-f= C_6H_5 , g-l=2- BrC_6H_4 , m-r=4- BrC_6H_4

SCHEME-I

3-aryl-4-amino-5-mercapto-s-triazoles (I) were synthesized by known procedure and converted to 6-amino, 3-aryl-s-triazolo-[2,4-b]-1,3,4-thiadiazoles (II) by one step reaction compounds (II) on treated with aromatic aldehydes gave (III), which on treatment with aryl-isothiocyanates yielded 3,4,6-triaryl-s-triazolo(3,4-b)-1,3,4-thiadiazolo(3,2-b)-s-triazolo(3,4-b)-1,3,4-thiadiazolo(3,2-b)-s-triazine-s-thiones (IVa-r).

Antifungal activity :

The fungicidal activity of the compound (IVa-r) was evaluated against *P. infestans* and *A. niger* by the usual Agar plate technique¹², at 1000, 100 and 10 ppm conc. **Dithane M-45** a standard commercial fungicide was also tested under similar conditions for comparing the results.

It is evident from the screening data that all the tested compounds (IVa-r) inhibited more than 65% growth of both the test fungi at 1000 ppm conc. of these compounds IVb, IVf, IVj and IVp exhibited the fungicidal action almost-equivalent to **Dithane M-45** at 1000 ppm conc. and inhibited 42.5-46.5% growth of both fungal species even at 10 ppm concentration.

Although some of the screened compounds (IVb, IVf, IVj and IVp) were highly toxic to *P. infestans* and *A. niger* at higher concentration (1000 ppm) the over all results are not so encouraging.

Experimental

Melting points were determined in open glass capillaries and are uncorrected. Infrared spectra (KBr disk) were recorded, on a Perkin-Elmer 157 spectrophotometer.

Table 1. Characterization data of compounds (IVa-r)

Compd. No.	R	Ar	Ar'	Yield (%)	M.P. (°C)
IVa	C ₆ H ₅	2-ClC ₆ H ₄	C ₆ H ₅	60	247
b	2-FC ₆ H ₄	2-ClC ₆ H ₄	C ₆ H ₅	67	250
c	2-CH ₃ OC ₆ H ₄	2-ClC ₆ H ₄	C ₆ H ₅	58	248
d	C ₆ H ₅	4-CH ₃ OC ₆ H ₄	C ₆ H ₅	65	246
e	2-FC ₆ H ₄	4-CH ₃ OC ₆ H ₄	C ₆ H ₅	60	251
f	2-CH ₃ OC ₆ H ₄	4-CH ₃ OC ₆ H ₄	C ₆ H ₅	70	246
g	C ₆ H ₅	2-ClC ₆ H ₄	2-BrC ₆ H ₄	59	252
h	2-FC ₆ H ₄	2-ClC ₆ H ₄	2-BrC ₆ H ₄	68	253
i	2-CH ₃ OC ₆ H ₄	2-ClC ₆ H ₄	2-BrC ₆ H ₄	72	249
j	C ₆ H ₅	4-CH ₃ OC ₆ H ₄	2-BrC ₆ H ₄	67	246
k	2-FC ₆ H ₄	4-CH ₃ OC ₆ H ₄	2-BrC ₆ H ₄	66	250
l	2-CH ₃ OC ₆ H ₄	4-CH ₃ OC ₆ H ₄	2-BrC ₆ H ₄	70	247
m	C ₆ H ₅	2-ClC ₆ H ₄	4-BrC ₆ H ₄	65	248
n	2-FC ₆ H ₄	2-ClC ₆ H ₄	4-BrC ₆ H ₄	62	252
o	2-CH ₃ OC ₆ H ₄	2-ClC ₆ H ₄	4-BrC ₆ H ₄	66	250
p	C ₆ H ₅	4-CH ₃ OC ₆ H ₄	4-BrC ₆ H ₄	63	249
q	2-FC ₆ H ₄	4-CH ₃ OC ₆ H ₄	4-BrC ₆ H ₄	70	247
r	2-CH ₃ OC ₆ H ₄	4-CH ₃ OC ₆ H ₄	4-BrC ₆ H ₄	62	246

IVa, IR (KBr) : 1610 (>C=N), 1990 (>C=S) cm⁻¹.

¹HNMR (DMSO-d₆)=7.14-8.16 (15H, m, Ar-H).

IVr, IR (KBr) : 1080 (>C=S),

¹HNMR (DMSO-d₆) : 3.81 (6H, s, OCH₃), 7.20-8.25 (13H, m, Ar-H).

¹HNMR spectra were recorded on a EM-360L (60MHz) NMR spectrophotometer in DMSO-d₆ using TMS as an internal reference, chemical shift are expressed in δ ppm.

Synthesis of 6-amino-3-aryl-s-triazolo-(3,4-b)-1,3,4-thiadiazoles (IIa-c):

A mixture of 3-aryl-4-amino-5-mercapto-s-triazole¹³, (0.22 mol) and cyanogens bromide

was heated under reflux on a water-bath for 6 hr. concentrated to one-fourth of its original volume and neutralized with saturated aq. solution of K₂CO₃. The white precipitate thus obtained was filtered and recrystallized from ethanol.

IIa. R=C₆H₅, m.p. 240⁰, Yield 60%. IR (KBr): 835 (1,4-disubstituted benzene ring), 1520 (C-N stretching), 1615 (cyclic > C=N),

3140, 3310 (N-H stretching) cm^{-1} . ^1H NMR (DMSO- d_6): 2.40 (3H, s, CH_3), 5.25 (2H, s, NH_2), 7.00-7.80 (4H, m, Ar-H). [F found C, 49.74, N, 32.28, S, 14.76, $\text{C}_9\text{H}_7\text{N}_5$ requires C, 49.75, N, 32.27, S, 14.75%].

IIb. $\text{R}=2\text{-FC}_6\text{H}_4$, m.p. 235° , Yield 58%. [Found C, 46.16, N, 29.90, S, 13.65, $\text{C}_9\text{H}_6\text{N}_5\text{S}$ required C, 46.15, N, 29.91, S, 13.67%].

IIc. $\text{R}=2\text{-OCH}_3\text{C}_6\text{H}_4$, m.p. 242° , yield 56%. [Found: C, 48.9, N, 28.3, S, 13.88, $\text{C}_{10}\text{H}_9\text{N}_5\text{S}$ requires C, 48.59, N, 28.35, S, 13.87%].

Synthesis of 3-aryl-6-(arylidene amino)-s-triazolo (3,4-b)-1,3,4-thiadiazoles (IIIa-f) :

A mixture of 6-amino-3-aryl-s-triazolo (3,4-b)-1,3,4-thiadiazoles (0.02 mol.) and appropriate aromatic aldehyde (0.02 mol.) in absolute ethanol (35 ml) was refluxed for 4 hours and filtered while hot. The filtrate upon cooling furnished the desired product, which was recrystallized from ethanol as yellowish needles and were directly proceeds for the synthesis of the title compounds.

Synthesis of 3,4,6-triaryl-s-triazolo (3,4-b)-1,3,4-thiadiazolo (3,2-b)-s-triazine-5-thiones (IVa-r):

An equimolar mixture of 3-aryl-6-(arylidene amino)-s-triazolo (3,4-b)-1,3,4-thiadiazoles (III) and appropriate isothiocyanates was refluxed for 4-6 hr. in dry toluene and the solvent was distilled off under reduced pressure. The residue was washed with small amount of ethanol followed by water and the product was recrystallized from ethanol as shining yellowish needles. Compounds (IVa-r) thus synthesized are recorded in Table 1.

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References

1. Patel, K., *et al.*, *Indian J. Chem. Soc.* 29b(2): 135 (1990).
2. Hallo, B., *et al.*, *Heterocycle*, 32, 96 (1991). *Chem. Abstr.* 115: 183246y (1991).
3. Dandia, *et al.*, *Relat. Elem.* 97(1-4), 27033 (1994); *Chem. Abstr.*; 123, 228077z (1995).
4. Fuzaka, *et al.*, *PCT Int. Appl. WO.* 97, 11 075; *Chem. Abstr.*; 126: 293354p, (1997).
5. Arundt, *et al.*, U.S.U.S., 5614, 469, *Chem. Abstr.* 126, 33592e, (1997).
6. Zhag Zigi, *et al.*, *Rep. China.* 14(1), 78-80 (1994), *Chem. Abstr.* 121, 9267s (1994).
7. Patel, K., Himat, *et al.*, *Indian J. Chem.* 29B(2), 135, (1990).
8. Yukimasa, *et al.*, *Jpn Kokai Tokkyo Koho J.P.* 08, 20, 584 [9620, 584]; *Chem. Abstr.* 124: 243297d, (1996).
9. Mohan J. and Rothee A., *Indian J. Heterocyclic Chem.*, 15, 77 (2005).
10. Mishra, R.M., Singh, D.V., and Mishra, A.R., *Indian J. Heterocyclic Chem.*, 14, 85 (2004).
11. Mishra, A.R., *et al.*, *Indian J. of Heterocyclic Chem.* 10, 279, (2001).
12. Horsefall, J.G., *Bot. Rev.*, 11, 357 (1945).
13. Reid, J.R. and Heindel, N.D., *J. Heterocyclic Chem.* 13, 925 (1976).