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Synthesis and Fungicidal Activities of Some 5-Aryl-2-(3,4-dimethyl phenyl)-amino-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles and 3-Aryl-6-mercapto-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles

Praveen Tripathi[1], Dharmendra Kumar Sahu[2] Monika Singh[3]

[1]Assistant Professor, [2]Assistant Professor, [3]Assistant Professor,

[1]Department of Chemistry, CMP Degree College, University of Allahabad, Prayagraj

Abstract

In this wok the compound 5-Aryl-2-(3,4-dimethyl phenyl)-amino-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles and 3-Aryl-6-mercapto-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles has been synthesized and applied to study of fungal activity. For that the methanolic solution of 4-Chlorobenzoyl hydrazine, KOH and CS_2 was stirred for 2 hours in ice water bath. This reaction mixture was cooled and poured into cold water and neutralised with dil. HCl. The compound 4-amino-5-(4-chlorophenyl)-3-mercapto-1,2,4-triazoles thus obtained was filtered and washed well with water and crystallised from aqueous ethanol. The compound 4-amino-5-(4-chlorophenyl)-3-mercapto-1, 2, 4-triazoles and 3,4-dimethyl phenyl Isocyanate was refluxed in DMF for 14 hours. After refluxing this mixture was poured into water. The compound 5-(4-chlorophenyl)-2-(3,4-dimethyl phenyl)-amino-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole thus precipitated out was filtered, washed with water dried and crystallised from aqueous ethanol. The final product have been characterized by spectral studies and screened for their fungicidal activities against two funguses *Aspergillusniger* and *Helminthosporiumoryzae*. The compound 3-(4-Chlorophenyl)-6-mercapto-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazolo was prepared by stirring 4-amino-5-(4-chlorophenyl)-3-mercapto-1,2,4-triazolo and carbon disulphide in methanol and KOH was added in this mixture and stirred for 6 hours. It was poured into water and neutralized by HCl. The compound has been screened for their fungicidal activity against four fungi *Aspergillusniger*, *Helminthosporiumoryzae*, *Rhizoctoniasolani* and *Penicilliumcitrinum*.

Keywords: 4-Chlorobenzoyl hydrazine, Synthesis, characterization, antifungal activity

INTRODUCTION

1,2,4-triazole (Amitrole) is a well-known commercial herbicide.[1] Similarly 1,2,4-triazole derivative have been reported to possess bactericidal[2-3], fungicidal[4-5], herbicidal[6-7] and insecticidal[8-9] activities 1,3,4-thiadiazole ring is associated with broad spectrum of biological activities.[10-11] This led to bring the two biolabile rings (triazolo, thiadiazole) in the molecular framework to achieve compact and planar system, with a hope to get compounds of better biocidal choice. The compound was synthesised which contain polar groups like-NH. The compound 3-Aryl-6- mercapto-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles was synthesized which contain-SH group adjacent to N- atom in 1,2,4- triazole may serve as a suitable ligand to form a chelate like hydroxyquinoline which displays diverse biocidal activities.

EXPERIMENTAL

(i) 4-Amino-5-(4-chlorophenyl)-3-mercapto-1,2,4triazoles.

(i) This compound has been prepared according to the method of Hoggrathet al[12]. A methanolic solution of 4-Chloro benzoyl hydrazine (0.05M, 8.5 g.), KOH (0.06M, 3.3g) and CS_2 (5.04ml) was stirred for 2 hrs in ice water bath. A solid mass was obtained. It was refluxed with excess of hydrazine hydrate (0.2M, 10ml) for 4 hours. This reaction mixture was cooled and poured into cold water and neutralised with dil. HCl. Products thus obtained was filtered and washed well with water and crystallised from aq. ethanol M.P.169^{0}C.

(ii) 5-(4-Chlorophenyl)-2-(3,4-dimethyl phenyl)-amino-1,2,4-triazolo-[3,4,-b]-1,3,4-thiadiazole.

The compound 4-amino-5-(4-chlorophenyl)-3-mercapto-1,2,4-triazoles (.005M, 1.12g) and 3,4-dimethyl phenyl Isocyanate (.005M, 0.7ml) was refluxed in DMF for 14 hours. After refluxing this mixture was poured into water. The compound thus precipitated out was filtered, washed with water, dried and crystallised from aq. ethanol. M.P. 145^{0}C, yield (50% of theory) (Scheme-I).

Analysis**:** Found % C57.41;H4.35;N19.85; $C_{17}H_{14}N_5SCl$

Required % C57.22;H4.20;N19.63.

The other such compounds were prepared by similar method and are recorded along with their Characterisation data.

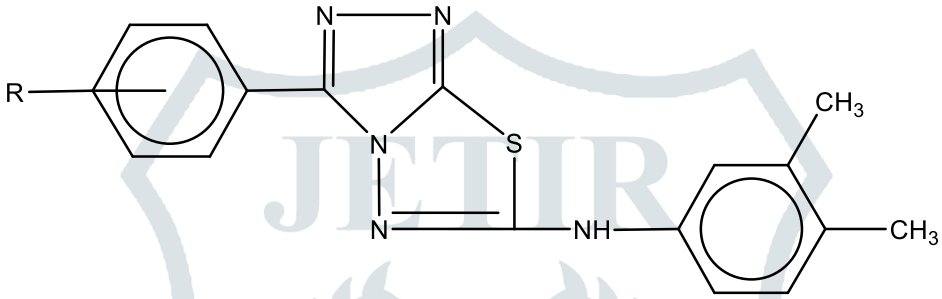


Table-I

S.No.	R	M.P. ºC	yield	Mol. Formula	Analysis Found (Calc) %		
					C	H	N
1.	2-Cl	150	52	$C_{17}H_{14}N_5SCl$	57.45 (57.22)	3.98 (4.20)	19.84 (19.63)
2.	2,4-Cl_2	135	46	$C_{17}H_{13}N_5SCl_2$	52.11 (52.30)	3.14 (3.33)	17.75 (17.94)
3.	2-CH_3	146	42	$C_{18}H_{17}N_5S$	64.64 (64.47)	5.25 (5.07)	20.98 (20.89)
4.	3-CH_3	125	52	$C_{18}H_{17}N_5S$	64.68 (64.47)	5.23 (5.07)	21.05 (20.89)
5.	4-CH_3	162	70	$C_{18}H_{17}N_5S$	64.71 (64.47)	5.27 (5.07)	21.12 (20.89)

All melting points were taken in open capillary tubes and are uncorrected. IR Spectra were recorded on Perkin-Elmer-710 Spectrophotometer in nujol and PMR spectra on Perkin-Elmer R-32 at 90 MHz. The completion of the reaction and purity of the synthesized compounds were checked by TLC.

The spectral data of one representative final compound is given below (R=Cl)

IR (KBr) : 1600(C=N); 1540, 1500, 1460 (C=C Ar-H); 2960(C-H);3300(N-H)cm^{-1}

^{1}HNMR (DMSO-d_6) : 2.1 (S,6H,CH_3); 6.2-7.8 (m,7H,Ar-H); 8.7 (S,1H,NH)

(iii) 3-(4-Chlorophenyl)-6-mercapto-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole (Ar=4-Chlorophenyl). It was prepared by stirring 4-amino-5-(4-chlorophenyl)-3-mercapto- 1,2,4-triazoles (1.12 g, 0.005M) and carbon disulphide (4.0 ml, 0.005 M) in methanol (15.0 ml) and KOH (0.3 g, 0.005 M) was added in this mixture and stirred for 6 hours. It was poured into water and neutralized by HCl. M.P. 132 ºC, yield (77% of theory). **(Scheme I).**

Analysis: Found % C39.95; H 1.68; N 20.65; $C_9H_5N_4S_2Cl$

Required % C40.22; H 1.86; N 20.85

Other such compounds prepared by similar procedure are recorded in Table II along with their characterization data.

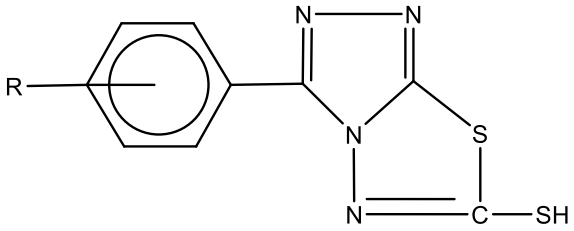


Table-II

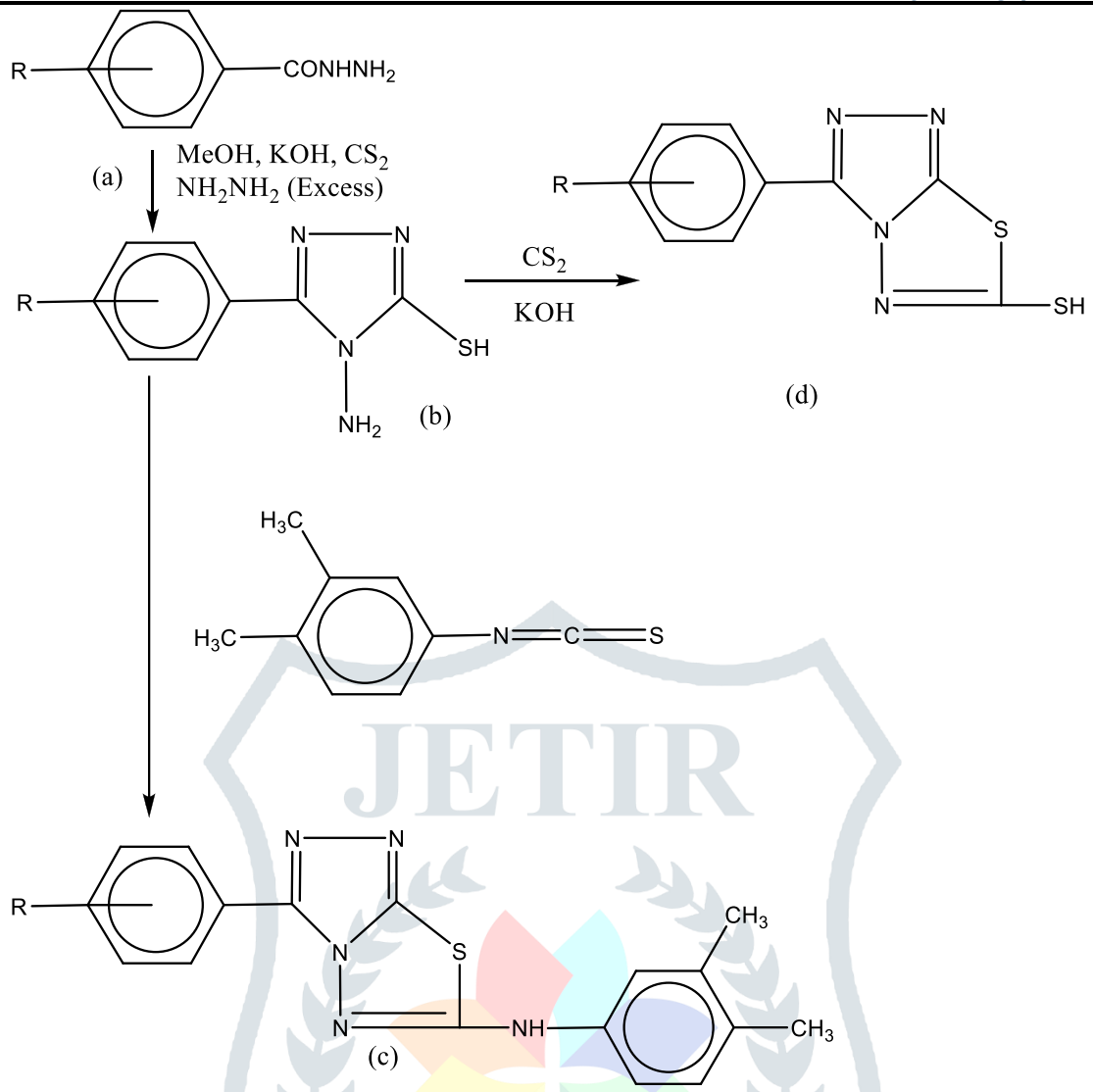
S.No.	R	MP °C	Yield	Mol. Formula	Analysis Found (Calc.)%		
					C	H	N
1.	2-Cl	125	66	$C_9H_5N_4S_2Cl$	40.03 (40.23)	1.65 (1.89)	20.63 (20.85)
2.	2,4-Cl_2	135	71	$C_9H_4N_4S_2Cl_2$	35.84 (35.64)	1.54 (1.32)	18.27 (18.48)
3	4-CH_3	165	69	$C_{10}H_8N_4S_2$	48.58 (48.38)	3.45 (3.22)	22.38 (22.57)
4.	3-CH_3	140	62	$C_{10}H_8N_4S_2$	48.60 (48.38)	3.47 (3.22)	22.35 (22.85)

All melting points were taken in open capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer-710 spectrophotometer in nujol and PMR spectra on Perkin-Elmer R-32 at 90 MHz. The completion of the reaction and purity of the synthesized compounds were checked by TLC.

The spectral data of one representative final compound is given below.

IR(KBr): Compound No. (C); (R=Cl, Ar=4ClC_6H_5); 1580(C=N); 1530, 1490, 1450(C=C, Ar-H); 2550(S-H)

^{1}HNMR(DMSO-d_6): 6.8-7.6(m,4H,Ar-H), Peak for -SH could not be observed.



Scheme I

Fungicidal Activity

The compound (c) has been screened for their fungicidal activity by agar growth technique[13] against two fungi *Aspergillusniger* and *Helminthosporiumoryzae*. The compound (d) has been screened for their fungicidal activity by agar growth technique[13] against four fungi. viz. *Aspergillusniger*, *Helminthosporiumoryzae*, *Rhizoctoniasolani* and *Penicilliumcitrinum*.

The fungus was planted in agar growth media mixed with test compounds. The diameter of the fungus colony was measured at three different concentrations viz, 1000,100 and 10ppm. The inhibition of the fungus growth was determined as the difference in growth between the control plate and those treated with the test compound. The activity of the test compounds was compared with commercial fungicide carbendazim under similar conditions. The activity of the test compounds was compared with commercial fungicide. Dithane M-45 under similar conditions. The percentage inhibition was calculated as:

Percentage inhibition = {(C-T)/C}×100

C = diameter of fungus colony (in mm) in the control plate after 96h.

T = diameter of fungus colony (in mm) in the treated plate after 96h.

Table-III: Antifungal activity of compound (c)

Compund No.	**R**	**Average Percentage Inhibition after 96 hour**					
		Organism- *A. niger* concentration used			**Organism-*H. oryzae* concentration used**		
		1000 ppm	100 ppm	10ppm	1000 ppm	100 ppm	10ppm
1.	2-Cl	66	57	48	65	56	46
2.	4-Cl	68	60	52	68	59	46
3.	2,4-Cl_2	70	62	54	70	59	48
4.	2-CH_3	65	58	53	62	52	45
5.	3-CH_3	66	58	56	65	57	54
6.	4-CH_3	70	64	55	71	66	56

A perusal of the fungicidal data indicates that compound No. 1-6 are fungitoxic. They inhibited 60-80% of the fungus growth at 1000ppm. Compound having 2,4-Cl_2 in Phenyl moiety works better than others. The most active compound of this series is No. 3.**Table-IV: Antifungal activity of Compound (d)**

Compound No.	R	Average Percentage Inhibition after 96 hours					
		Organism-A. niger concentration used			Organism- H. oryzae concentration used		
		1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
1	2-Cl	67	58	50	67	58	48
2	4-Cl	70	62	53	69	59	46
3	2,4-Cl_2	72	63	54	67	58	47
4	4-CH_3	70	64	55	71	66	56
5	3-CH_3	66	57	51	60	50	43

Table-V: Antifungal activity of Compound (d)

Compound No.	R	Average Percentage Inhibition after 96 hours					
		Organism-R. solani concentration used			Organism- P. citrinum concentration used		
		1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
1	2-Cl	69	60	51	70	59	50
2	4-Cl	72	63	54	71	61	47
3	2,4-Cl_2	74	65	56	70	59	46
4	4-CH_3	72	66	57	69	64	55
5	3-CH_3	68	58	50	62	51	46
Dithane M-45		98	94	90	99	97	93

In this series compound No. 1-5 have been tested for their antifungal screening. Compound No. 3 containing 2,4-Cl_2 in phenyl moiety shows strong activity. Compound No. 2 also shows better activity. These compounds have been also tested against the fungi R. solani and P. citrinum. Compound No. 2,3 and 4 shows strong activity. The commercial fungicide taken is Dithane M-45.

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