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Synthesis and Antifungal Activity of Some 3-[5′-Aryl-3′-Mercapto-1′, 2′, 4′-Triazol-4′-yl]-2-Aryl-4-Thiazolidinones

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A number of [3-5′-aryl-3′-mercapto-1′, 2′, 4′-triazol-4′-yl]-2-aryl-4-thiazolidinones have been synthesised by the cyclocondensation of mercapto acetic acid and anlls. Their antifungal activities have been screened against *A. niger* and *H. oryzae*.

INTRODUCTION

The 4-amino-3-mercapto-1,2,4-triazoles often display interesting physiological activities[1–3]. Further, 4-thiazolidinones possessing heterocyclic moieties or other aromatic systems possess significant biocidal activities like bactericidal[4], fungicidal[5], cysticidal[6], antileukemic[7], antiinflammatory[8], anticonvulsants[9] and others[10,11]. Keeping these in the view some triazolyl-4-thiazolidinones have been synthesised and studied their fungicidal activity.

The required 4-amino-3-mercapto-1,2,4-triazoles (II) were prepared essentially by the condensation of mercapto oxadiazoles (I) with hydrazine hydrate following the method of Reid and Heindel[12]. The condensation of (II) with aromatic aldehydes in methanol furnished the compounds (IIIa-j), which were converted into title compounds (IVa-j) by cyclocondensation with mercaptoacetic acid in dioxane (Scheme 1). The structure of these products were established by elemental analysis, IR and PMR spectra. Spectrally, the compounds (III) displayed IR bands at *ca.* 3240 cm^{-1} (—NH of the ring) and *ca* 1630 cm^{-1} due to $\nu_{(C=N)}$ stretching vibrations characteristic of azomethine structure and PMR resonances in the region of δ 7–8.2 ppm representing the aromatic protons. The compounds (IV) displayed IR absorption peak in the region of *ca* 1670 cm^{-1} (—N—C—) bond and PMR resonances at δ 3.1 (s, 1H, —SCH—) and

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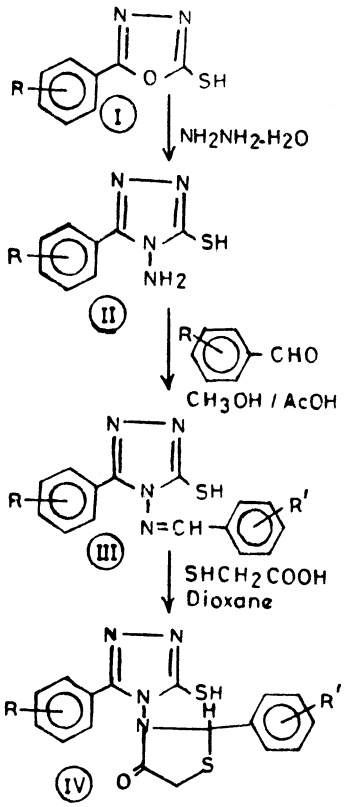
3.4 (*s*, 2H, CH_2) ppm.

EXPERIMENTAL

Procedure for one representative case for each step has been described. Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer 157 spectrophotometer in KBr pellets (ν_{max} in cm^{-1}) and PMR spectra on a Varian EM-360 (60 MHz) spectrometer in DMSO-d_6 (Chemical shifts in δ ppm).

SCHEME 1



III and IV

	R	R'
a.	4-Cl	4-Cl
b.	2-Cl	4-Cl
c.	2-Cl	3,4(OCH_3)$_2$
d.	4-Cl	2-Cl
e.	2,4-Cl_2	4-Cl
f.	2-CH_3	4-Cl
g.	4-NO_2	3,4(OCH_3)$_2$
h.	4-OH	2-Cl
i.	4-OH	3,4-(OCH_3)$_2$
j.	2-CH_3	3,4-(OCH_3)$_2$

4-Amino-5-(4-Chlorophenyl)-3-Mercapto-1,2,4-Triazole (II)

It was prepared by the action of hydrazine hydrate on 2-mercapto-5-(4-chlorophenyl)-1,3,4-oxadiazole following the method of Reid and Heindel[12].

4-(4-Chlorobenzylidene) amino-5-(4-chlorophenyl)-3-mercapto-1,2,4-triazole (IIIa)

A mixture of 4-amino-5-(4-chlorophenyl)-3-mercapto-1,2,4-triazole (0.01 mol) and 4-chlorobenzaldehyde (0.01 mol) in methanol using glacial acetic acid as a catalyst was refluxed for 4 hrs. The excess of methanol was distilled off and the residue was poured into water and recrystallised from aqueous ethanol to give (IIIa). Mpt. 179°C, yield 76%.

Analysis: Found C; 51.43; H, 2.98; N, 16.20: $C_{15}H_{10}N_4SCl_2$

requires C, 51.58; H. 2.87; N, 16.05%.

Significant bands (cm^{-1}) in IR spectra (KBr) were 3240 (NH), 1630 (C=N), 1605, 1510 (aromatic ring) and PMR : δ, 7.0–8.2 (m, 9H, 8 ArH + 1H azomethine) 10.2 (s, 1H, NH).

Other compounds prepared similarly, are recorded in Table 1.

2-(4-Chlorophenyl)-3-[5'(4-chlorophenyl)-3'-mercapto-1',2',4'-triazol-4'-yl]-4-thiazolidinone (IVa)

A solution of 4-(4-chlorobenzylidene) amino-5-(4-chlorophenyl)-3-mercapto-1,2,4-triazole (IIIa, 0.01 mol) and mercaptoacetic acid (0.012 mol) in dioxane was refluxed for 5 hrs. The excess of dioxane was distilled off and the residue was poured in to water. The thiazolidinone thus precipitated, was washed with 10% sodium bicarbonate solution and then with cold water. It was recrystallised from ethanol. M.pt. 195–6°C, yield 96%.

Analysis : Found C, 48.14; H, 2.77; N, 13.35; $C_{17}H_{12}N_4OS_2Cl$ requires C, 48.23; H, 2.84; N, 13.24%.

Significant bands (cm^{-1}) in IR spectra (KBr) were 3245 (NH), 3070 (C–H aromatic), 2940, 2840 (C–H aliphatic), 1670 (C=O), 1600 (C=N), 1585, 1515 (aromatic ring) and PMR (DMSO–d_6 + $CDCl_3$); δ 3.1 (*s*, 1H, SCH–), 3.4 (*s*, 2H, $-CH_2-$), 70–80 (m, 8H, Ar H), 10.2 (*s*, 1H, NH).

Other compounds prepared similarly, are recorded in Table 1.

Antifungal Activity

Some representative compounds of the type (IV) were screened for their antifungal activity by agar plate technique[13] against two test fungi viz. *A. niger* and *H. oryzae* at 1000 ppm, 100 ppm and 10 ppm concentrations. A commercial fungicide carbendazim was also tested under similar conditions for comparison. The percentage inhibitions of various compounds are recorded in Table 2.

RESULTS AND DISCUSSION

The fungicidal screening data indicate that most of the compounds had significant toxicity at 1000 ppm concentration against both the test fungi but their fungitoxicity decreased considerably upon dilution. The compound numbers IVc, IVe, IVg, IVh were found to have activity comparable to commercial fungicide carbendazim at 1000 ppm concentration. The presence of chlorosubstituents in the phenyl ring appear to enhance the toxicity of the compounds.

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TABLE 1
CHARACTERISATION DATA OF III AND IV

Compound No.	m.pt. °C	% Yield	Molecular formula	Analysis % Found (Calculated)		
				C	H	N
IIIb	108–9	70	$C_{15}H_{10}N_4Cl_2S$	51.40 (51.58)	2.90 (2.87)	16.20 (16.05)
IIIc	109–10	74	$C_{17}H_{15}N_4O_2ClS$	54.32 (54.47)	4.08 (4.00)	15.10 (14.95)
IIId	128–9	80	$C_{15}H_{10}N_4Cl_2S$	51.50 (31.58)	2.96 (2.87)	16.16 (16.05)
IIIe	122	72	$C_{15}H_9N_4Cl_3S$	46.80 (46.94)	2.50 (2.35)	14.83 (14.60)
IIIf	148	67	$C_{16}H_{13}N_4ClS$	58.28 (58.45)	4.10 (3.96)	17.12 (17.05)
IIIg	196	88	$C_{17}H_{15}N_5O_4S$	52.86 (52.99)	3.98 (3.90)	18.30 (18.18)
IIIh	194	91	$C_{15}H_{11}N_4OSCl$	54.36 (54.46)	3.40 (3.33)	17.00 (16.94)
IIIi	127–8	65	$C_{17}H_{16}N_4O_3S$	57.18 (57.30)	4.60 (4.49)	15.88 (15.73)
IIIj	167–8	78	$C_{18}H_{18}N_4O_2S$	60.95 (61.02)	5.12 (5.08)	15.96 (15.82)
IVb	182	80	$C_{17}H_{12}N_4OS_2ClS$	48.10 (48.23)	2.76 (2.84)	13.36 (13.24)
IVc	192	76	$C_{19}H_{17}N_4O_3S_2Cl$	50.76 (50.84)	3.70 (3.79)	12.62 (12.49)
IVd	137–8	90	$C_{17}H_{12}N_4OS_2Cl_2$	48.16 (48.23)	2.74 (2.84)	13.36 (13.24)
IVe	145–6	40	$C_{17}H_{11}N_4OS_2Cl_3$	44.50 (44.59)	2.36 (2.40)	12.36 (12.24)
IVf	134	55	$C_{18}H_{15}N_4OS_2Cl$	53.54 (53.66)	3.69 (3.73)	13.99 (13.91)
IVg	214–5	45	$C_{19}H_{17}N_5O_5S_2$	49.60 (49.67)	3.61 (3.70)	15.37 (15.25)
IVh	205	58	$C_{17}H_{13}N_4O_2S_2Cl$	50.29 (50.43)	3.17 (3.21)	13.97 (13.84)
IVi	220–21	65	$C_{19}H_{18}N_4O_4S_2$	53.00 (53.02)	4.20 (4.19)	13.07 (13.02)
IVj	163–4	60	$C_{20}H_{20}N_4O_3S_2$	56.00 (56.07)	4.62 (4.67)	13.17 (13.08)

TABLE 2

FUNGICIDAL SCREENING DATA

Compound No.	Average % inhibition after 7 days					
	Organism : *A. niger* Concentration used			Organism : *H. oryzae* Concentration used		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
IVa	84	63	34	87	64	43
IVb	81	59	33	82	59	38
IVc	93	76	37	96	80	46
IVd	82	59	30	86	55	39
IVe	95	79	37	98	81	53
IVf	79	53	27	80	60	32
IVg	94	78	32	98	63	35
IVj	92	76	29	97	59	35
Carbendazim	96	85	77	100	87	82

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