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Synthesis of Some 2-Arylimino-3,4-Diaryl-6-Imino Thiazolo [5,4-d] [1,3] Thiazines as Potential Fungicides

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Thiazolidinones (II) prepared by condensing sym. diarylthioureas with chloroacetylchloride, were converted into (III) under Knoevenagel conditions. The latter reacted with thiourea in methanolic KOH to furnish 2-arylimino-3,4-diaryl-6-imino thiazolo [5,4-d] [1,3] thiazines(IV).

INTRODUCTION

Thiazole derivatives are well known for their diverse biological activities like insecticidal[2], fungicidal[1] and bactericidal[3]. Likewise, 1,3-thiazine ring which incorporates thiourea linkage in its structure is also associated with various biological activities[4–6]. Further, the compounds (IV) by virtue of incorporating a suitable site for metal chelation may serve as a suitable ligand to chelate the essential metals which fungus needs in its metabolism[7–10]. In view of these facts and in the hope of achieving compounds of enhanced biocidal properties, it was decided to design the title compounds involving the fusion of thiazole and thiazine moieties.

The required thiazolidinones (II) were readily formed by the reaction of sym. diarylthioureas with chloroacetyl chloride following the method of Okawara *et al.*[11] These were characterised on the basis of their IR spectra and elemental analyses. The condensations of (II) with aromatic aldehydes under Knoevenagel conditions gave (III). The IR spectra of compounds (III) showed a band *ca.* 1670 cm^{-1} which indicated $-C=C-C=O$ stretching frequency. The condensations of (III) with thiourea in alcoholic KOH furnished the title compounds (IV) (Scheme 1).

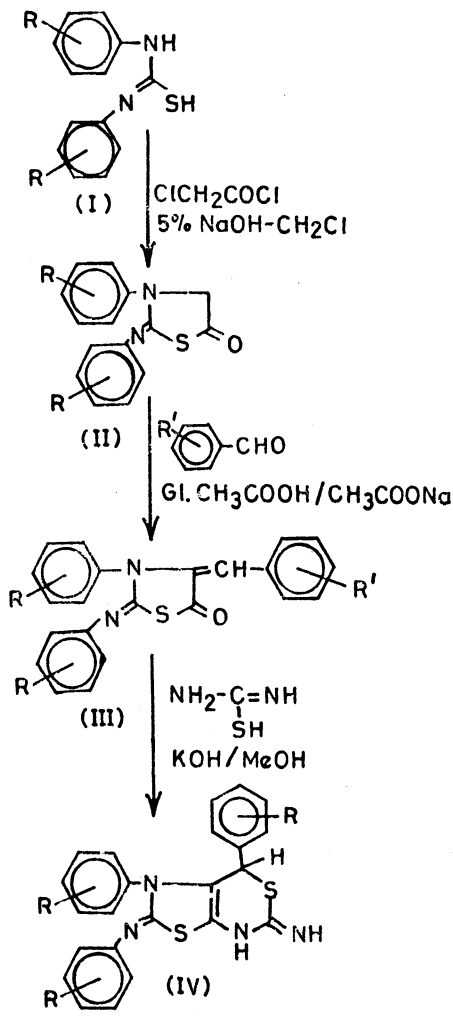
EXPERIMENTAL

The melting points were determined 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 (90 MHz) spectrometer in $CDCl_3$ (chemical shifts in δ_{ppm}). The characterisation data of the compounds prepared are given in Tables 1–3.

2-(p-Tolyl)Imino-3-(p-Tolyl)-5-Thiazolidinone (IIc)

Sym. di-(*p*-tolyl) thiourea (0.01 mol) was treated with chloroacetyl chloride (0.01 mol) in dichloromethane (30 ml) and 5% NaOH (30 ml) as

SCHEME 1



II		III & IV			
R	R	R	R′	R	R′
a-2-CH_3	e-4-Cl	a-2-CH_3	4-Cl	e-4-Cl	4-Cl
b-3 CH_3		b-2-CH_3	2-Cl	f-4-OCH_3	4-Cl
c-4 CH_3		c-3-CH_3	4-Cl	g-4-OCH_3	2-Cl
d-4 OCH_3		d-4-Cl	2-Cl	h-4-CH_3	3,4 $(OCH_3)_2$

usual and the compound was purified by recrystallisation from aqueous ethanol to give (IIc). M.pt. 110°C, yield 72%.

Analysis. Found C, 68.75; H, 5.30; N, 9.35; $C_{17}H_{16}N_2OS$; requires C, 68.92; H, 5.41; N, 9.46%.

TABLE 1

PHYSICIAL DATA OF THE COMPOUNDS II

S. No.	M.pt.	% Yield	Molecular formula	Analysis Found (Calc.) % of		
				C	H	N
IIa	128–30	78	$C_{17}H_{16}N_2OS$	68.80(68.92)	5.30(5.41)	9.40(9.46)
IIb	93	60	$C_{17}H_{16}N_2OS$	68.80(68.92)	5.35(5.41)	9.50(9.46)
IId	103–4	66	$C_{17}H_{16}N_2O_3S$	62.10(62.20)	4.70(4.88)	8.70(8.54)
IIe	155–6	74	$C_{15}H_{10}H_2OSCl_2$	53.30(53.41)	2.90(2.97)	8.30(8.31)

TABLE 2

PHYSICAL DATA OF THE COMPOUNDS III

S. No.	M.pt.	% Yield	Molecular formula	Analysis Found (Calc.)% of	
				N	S
IIIa	101–2	66	$C_{24}H_{19}N_2OSCl$	6.78(6.69)	7.76(7.65)
IIIb	146	65	$C_{24}H_{19}N_2OSCl$	6.80(6.69)	7.80(7.65)
IIId	123	86	$C_{22}H_{13}N_2OSCl_3$	6.20(6.09)	7.02(6.96)
IIIe	128	84	$C_{22}H_{13}N_2OSCl_3$	6.20(6.09)	7.08(6.96)
IIIf	175–6	60	$C_{24}H_{19}N_2O_3SCl$	6.38(6.22)	7.20(7.10)
IIIg	70–1	63	$C_{24}H_{19}N_2O_3SCl$	6.30(6.22)	7.18(7.10)
IIIh	178	48	$C_{26}H_{24}N_2O_3S$	6.46(6.31)	7.30(7.21)

TABLE 3

PHYSICAL DATA OF THE COMPOUND IV

S. No.	M.pt.	Yield %	Molecular formula	Analysis Found (Calc.) % of		
				C	H	N
IVa	144–5	80	$C_{25}H_{21}N_4S_2Cl$	62.82(62.96)	4.32(4.41)	11.80(11.75)
IVb	137–8	69	$C_{25}H_{21}N_4S_2Cl$	62.80(62.96)	4.32(4.41)	11.90(11.75)
IVc	146	73	$C_{25}H_{21}N_4S_2Cl$	62.80(62.96)	4.35(4.41)	11.80(11.75)
IVd	177	76	$C_{23}H_{15}N_4S_2Cl_3$	53.22(53.33)	2.80(2.90)	10.90(10.82)
IVe	168–9	81	$C_{23}H_{15}N_4S_2Cl_3$	53.20(53.33)	2.82(2.90)	10.95(10.82)
IVf	148	64	$C_{25}H_{21}N_4O_2S_2Cl$	58.90(59.00)	4.10(4.13)	11.10(11.01)
IVg	178	65	$C_{25}H_{21}N_4O_2S_2Cl$	58.87(59.00)	4.05(4.13)	11.13(11.01)

Significant bands (cm^{-1}) in IR spectra (KBr) were 3010 (C–H aromatic), 1710 (C=O), 1640 (–C=N–), 1610, 1585, 1510, 1480 (aromatic ring), 1370 (C–N), 1270, 1090 (C–S–C).

The other compounds of the type (II) prepared similarly and are recorded in Table 1.

2-(*m*-Tolyl) Imino-3-(*m*-Tolyl)-4-(*p*-Chlorobenzylidene)-5-Thiazolidinone(IIIc)

A mixture of 2-(*m*-tolyl) imino-3-(*m*-tolyl)-5-thiazolidinone (IIb, 0.01 mol), *p*-chlorobenzaldehyde (0.01 mol) and anhydrous sodium acetate (0.015 mol) was refluxed in glacial acetic acid for 4 hrs. The reaction mixture was cooled, poured into water and filtered. The filtrate was washed with water, dried and recrystallised from aqueous ethanol to give (IIIc). M.pt. 109–10°C, yield 79%.

Analysis. Found N, 6.75; S, 7.60; $C_{24}H_{19}N_2OSCl$; requires N, 6.69: S, 7.65%.

The IR absorption of (IIIc) showed a band *ca.* 1660 cm^{-1} assignable to the α,β-unsaturated ketone. PMR in $CDCl_3$; δ, 2.26, 2.32 (s, 6H, each $-CH_3$), 3.4 (s, 2H, $-CH_2$), 6.7–7.3 (m, 12H, Ar H).

The other compounds of the type (III) prepared similarly and are recorded in Table 2.

2-(*p*-Tolyl) Imino-3-(*p*-Tolyl)-4-(3,4-Dimethoxyphenyl)-6-Imino Thiazolo [5,4-d] [1,3] Thiazine (IVh)

A mixture of 2-(*p*-tolyl) imino-3-(*p*-tolyl)-4-(3,4-dimethoxybenzylidene)-5-thiazolidinone (IIIh, 0.01 mol), thioureas (0.012 mol) and KOH (0.015 mol) was refluxed in methanol for 4 hrs. The excess of methanol was evaporated. The residual liquid was acidified with dilute hydrochloric acid. The product thus precipitated was recrystallised from aqueous ethanol to give (IVh). M.pt. 173°C, yield 54%.

Analysis. Found C, 64.45; H, 5.10; N, 11.30; $C_{27}H_{26}N_4O_2S_2$ requires, C, 64.54; H 5.18; N 11.16%.

Significant bands (cm^{-1}) in IR spectra (KBr) were 3000 (C–H aromatic), 2900, 2840 (C–H aliphatic), 1655 (C=NH), 1640 (–C=N–), 1585, 1505, 1460 (aromatic ring), 1240, 760 (C–S–C) and PMR in $CDCl_3$: δ, 2.2 (s, 1H, –SCH–), 2.25, 2.3 (s, 6H, each $-CH_3$), 3.74, 3.76 (s, 6H, each $-OCH_3$), 6.7–7.3 (m, 11H, Ar H), 7.65 (s, 2H, NH).

The other compounds of the type (IV) prepared similarly and are recorded in Table 3.

Fungicidal Activity

All the compounds of the type (IV) were evaluated for their antifungal

activity by agar plate technique[12], against two fungi viz. *A. niger* and *H. oryzae* at 1000 ppm and 100 ppm concentrations. A commercial fungicide carbendazim was also tested under similar conditions for comparison. The percentage inhibitions of various compounds are recorded in Table 4.

TABLE 4
FUNGICIDAL SCREENING DATA

Compounds	Average % inhibition after 7 days			
	Organism—*A. niger* Concentration used		Organism—*H. Oryzae* Concentration used	
	1000 ppm	100 ppm	1000 ppm	100 ppm
IVa	75	56	79	58
IVb	73	52	74	55
IVc	73	53	75	56
IVd	81	67	85	71
IVe	83	68	89	73
IVf	79	67	88	73
IVg	78	61	84	69
IVh	87	63	88	72
Carbendazim	96	87	95	81

RESULTS AND DISCUSSION

It is evident from the fungicidal data that all the compounds showed antifungal activity > 70% against both the test fungi at 1000 ppm concentration but their toxicity against both the test fungi decreased markedly with dilution. None of these compounds exhibited fungitoxicity comparable to the commercial fungicide at a concentration of 100 ppm.

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