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Synthesis and Antifungal Activity of Some Bis-(2-arylimino-3-yl-thiazolidinones) and Bis-(1-aryl-3-yl-2-thiohydantoins)

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Some *bis*-(2-arylimino-3-yl-4-thiazolidin-4-ones) and *bis*-(1-aryl-3-yl-2–thiohydantoins) were synthesised from *bis*-(4-aryl–3-thiocarbamides) and screened for their antifungal activity against *Aspergillus flavus*, *Helminthosporium tetramera* and *Pennicillium decombens*.

INTROUCTION

Some *bis*-thiazolidinones have been found to be associated with a wide variety of pharmacological activities[1–5]. The presence of N—C—S linkage has been postulated to account for the antifungal activity of 4-thiazolidinones.[6] Thiohydantoins are also associated with a broad biocidal spectrum[7] and some of them have been reported to possess antifungal properties.[8] The above observations led to the synthesis of *bis*-(4-aryl-3-thiocarbamides) (II), which on cyclisation with monochloro acetic acid/sodium acetate and monochloro acetic acid/pyridine were converted to *bis*-(2-arylimino-3-yl-thiazolidin-4-ones) (III) and *bis*-(1-aryl-3-yl-2-thiohydantoins) (IV) respectively. The steps involved in the synthesis are shown in scheme 1.

All these compounds II, III and IV were screened for their antifungal activity against *A. flavus*, *H. tetramera* and *P. decombens*.

EXPERIMENTAL

Melting points were taken in open capillaries in an electric melting point apparatus and are uncorrected. Infrared spectra of the compounds were recorded in KBr pellets, while pmr spectra were recorded on a 60 MHz and 90 MHz spectrometer using TMS as internal standard. Terephthaloyl chloride was prepared by the reported procedures[9].

Terephthaloyl bis-(4-aryl-3-thiocarbamides) II :

A mixture of ammonium thiocyanate (0.11 mole) and acetone (50 ml) was placed in a flask and solution of terephthaloyl chloride (0.05 mole) in acetone (50 ml) was added through a dropping funnel with stirring. Arylamine (0.1 mole) in acetone (50 ml) was then added to the reaction mixture in small portions when the addition was over, the reaction mix-

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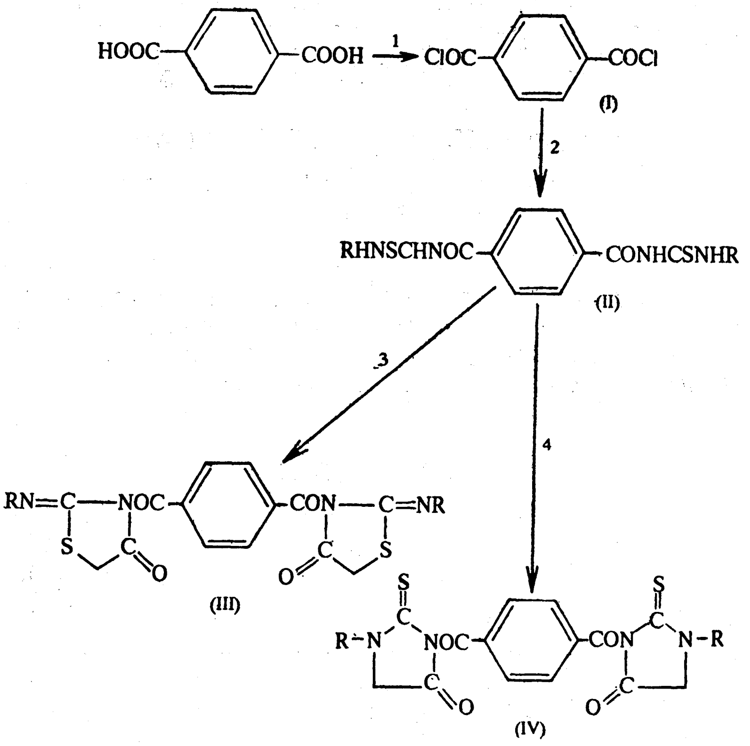

1. PCl_5 2. NH_4CNS/RNH_2 3. $ClCH_2COOH/CH_3COONa$ 4. $ClCH_2COOH$/PYRIDINE

ture was refluxed for 2 hrs., cooled, and poured into ice cold water. The resulting precipitate was filtered, washed with water, crystallised from ethanol. Various terephthaloyl *bis*-(4-aryl-3-thiocarbamides) thus prepared are recorded in Table 1.

TABLE 1

ANALYTICAL AND SPECTRAL DATA OF TEREPHTHALOYL BIS-(4-ARYL-3-THIOCARBAMIDES) II

Compd. No.	R	M. pt. °C	Yield %	Molecular Formula	Analysis (%) Found/(Calculated)	
					N	S
$\mathrm{II_a}$	C_6H_5	240	79.55	$C_{22}H_{18}N_4O_2S_2$	12.77 (12.90)	14.31 (14.75)
$\mathrm{II_b}$	p-ClC_6H_4	230	90.83	$C_{22}H_{16}N_4O_2S_2Cl_2$	11.24 (11.13)	12.60 (12.72)
$\mathrm{II_c}$	p-BrC_6H_4	200	65.52	$C_{22}H_{16}N_4O_2S_2Br_2$	9.55 (9.46)	10.92 (10.81)

TABLE 1 (cont.)

Compd. No.	R	M. pt. °C	Yield %	Molecular Formula	Analysis (%) Found/(Calculated)	
					N	S
II$_d$	p-IC$_6$H$_4$	225	68.26	$C_{22}H_{16}N_4O_2S_2I_2$	8.24 (8.16)	9.45 (9.36)
II$_e$	p-OCH$_3$C$_6$H$_4$	220	87.00	$C_{24}H_{22}N_4O_4S_2$	11.23 (11.34)	12.61 (12.94)
II$_f$	p-CH$_3$C$_6$H$_4$	170	72.72	$C_{24}H_{22}N_4O_2S_2$	12.00 (12.12)	13.41 (13.85)
II$_g$	p-NO$_2$C$_6$H$_4$	180	98.57	$C_{22}H_{16}N_6O_2S_2$	15.97 (16.03)	12.33 (12.21)
II$_h$	o-ClC$_6$H$_4$	215	89.07	$C_{22}H_{16}N_4O_2S_2Cl_2$	11.24 (11.13)	12.60 (12.72)
II$_i$	o-CH$_3$C$_6$H$_4$	240	87.26	$C_{24}H_{22}N_4O_2S_2$	12.00 (12.12)	13.72 (13.85)
II$_j$	o-OCH$_3$C$_6$H$_4$	200	78.59	$C_{24}H_{22}N_4O_4S_2$	11.23 (11.34)	12.61 (12.94)
II$_k$	o-NO$_2$C$_6$H$_4$	120	55.83	$C_{22}H_{16}N_6O_6S_2$	15.95 (16.03)	12.33 (12.21)
II$_l$	m-ClC$_6$H$_4$	240	68.28	$C_{22}H_{16}N_4O_2S_2Cl_2$	11.24 (11.13)	12.60 (12.72)
II$_m$	m-CH$_3$C$_6$H$_4$	220	64.64	$C_{24}H_{22}N_4O_2S_2$	12.01 (12.12)	13.72 (13.85)
II$_n$	m-OCH$_3$C$_6$H$_4$	210	81.62	$C_{22}N_4O_4S_2$	11.24 (11.34)	12.62 (12.94)
II$_o$	m-NO$_2$C$_6$H$_4$	>250	74.13	$C_{22}H_{16}N_6O_6S_2$	15.93 (16.03)	12.34 (12.21)

II$_a$: ν_{max} (cm^{-1}) (KBr) : 3100 (N—H, stretch), 1657 (CONH)
1552 (C=C, aromatic), 1340 (CN, stretch)
1260 (NHCHNH).
ppm(δ) : 7.1–7.7 (m, 10H, ArH) (b)
8.1 (s, 4H, ArH) (a), 11.4 (s, 2H, 2CONH)
12.4 (s, 2H, 2 CSNH)

Terephthaloyl bis-(2-arylimino-3-yl-thiazolidin-4-ones) II

A mixture of terephthaloyl *bis*-(4-aryl-3-thiocarbamides) (0.01 mole), monochloro acetic acid (0.02 mole) and anhydrous sodium acetate (0.02 mole) was refluxed in dimethyl formamide (50 ml) for 8–10 hrs. The reaction mixture was cooled, poured into ice cold water and kept over night. The precipitate thus obtained was filtered, dried and crystallised from ethanol. Analytical and spectral data of these compounds are recorded in Table 2.

TABLE 2

ANALYTICAL AND SPECTRAL DATA OF TEREPHTHALOYL BIS-(2-ARYLIMINO-3-YL-THIAZOLIDIN-4-ONES) III

Compd. No.	R	M. pt. °C	Yield %	Molecular Formula	Analysis (%) Found/(Calculated)	
					N	S
III$_a$	C_6H_5	115	31.51	$C_{26}H_{18}N_4O_4S_2$	10.99 (10.89)	12.56 (12.45)
III$_b$	p-ClC_6H_4	100	42.80	$C_{26}H_{16}N_4O_4S_2Cl_2$	9.53 (9.61)	10.81 (10.98)
III$_c$	p-BrC_6H_4	160	52.32	$C_{26}H_{16}N_4O_4S_2Br_2$	8.41 (8.33)	10.01 (9.52)
III$_d$	p-IC_6H_4	120	36.89	$C_{26}H_{16}N_4O_4S_2I_2$	7.42 (7.35)	8.46 (8.38)
III$_e$	p-$OCH_3C_6H_4$	140	26.87	$C_{28}H_{22}N_4O_6S_2$	9.67 (9.76)	11.04 (11.15)
III$_f$	p-$CH_3C_6H_4$	165	22.14	$C_{28}H_{22}N_4O_4S_2$	10.23 (10.33)	11.70 (11.81)
III$_g$	p-$NO_2C_6H_4$	205	43.04	$C_{26}H_{16}N_6O_8S_2$	14.02 (13.90)	10.69 (10.59)
III$_h$	o-ClC_6H_4	125	6.86	$C_{26}H_{16}N_4O_4S_2Cl_2$	9.52 (9.61)	10.82 (10.98)
III$_i$	o-$CH_3C_6H_4$	160	57.19	$C_{28}H_{22}N_4O_4S_2$	10.22 (10.33)	11.71 (11.81)
III$_j$	o-$OCH_3C_6H_4$	155	55.74	$C_{28}H_{22}N_4O_6S_2$	9.67 (9.76)	11.00 (11.15)
III$_k$	o-$NO_2C_6H_4$	>250	38.05	$C_{26}H_{16}N_6O_8S_2$	14.00 (13.89)	10.67 (10.54)
III$_l$	m-ClC_6H_4	180	79.07	$C_{26}H_{16}N_4O_4S_2Cl_2$	9.50 (9.61)	10.83 (10.98)
III$_m$	m-$CH_3C_6H_4$	140	46.12	$C_{28}H_{22}N_4O_4S_2$	10.22 (10.33)	11.67 (11.81)
III$_n$	m-$OCH_3C_6H_4$	120	50.52	$C_{28}H_{22}N_4O_6S_2$	9.69 (9.76)	11.01 (11.15)
III$_o$	m-$NO_2C_6H_4$	>250	38.07	$C_{26}H_{16}N_6O_8S_2$	14.02 (13.90)	10.69 (10.59)

III$_a$: ν_{max}(cm^{-1}) (KBr) : 1670 (C = O, exocyclic), 1585 (C = O, endocyclic),
1550 (C = C, aromatic & C = N stretch),
1250 (C—S—C, thiazolidinone)

III$_f$: ppm(δ) : 1.9 (s, 6H, $2CH_3$), 4.0 (s, 4H, $2CH_2$),
7.1–7.5 (m, 12H ArH).

Terephthaloyl bis-(1-aryl-3-yl-2-thiohydantoins) IV

Terephthaloyl *bis*-(4-aryl-3-thiocarbamides) (0.0025 mole) was dissolved in a mininum amount of pyridine. To this mixture was added chloroacetic acid (0.005 mole) and 15 ml of a mixture of ethanol and dioxan (1 : 1). This mixture was refluxed for 12 hrs. On cooling it was poured into ice cold water. Solid mass that seperated out was filtered, dried and crystallised from dimethyl sulfoxide. Analytical and spectral data of these compounds are recorded in Table 3.

TABLE 3

ANALYTICAL AND SPECTRAL DATA OF TEREPHTHALOYL BIS-(1-ARYL-3-YL-2-THIOHYDANTOINS) IV

Compd. No.	R	M. pt. °C	Yield %	Molecular Formula	Analysis % Found/(Calculaled)	
					N	S
IV_a	C_6H_5	215	42.37	$C_{26}H_{18}N_4O_4S_2$	10.97 (10.89)	12.55 (12.45)
IV_b	p-ClC_6H_4	215	68.49	$C_{26}H_{16}N_4O_4S_2Cl_2$	9.52 (9.61)	10.82 (10.08)
IV_c	p-BrC_6H_4	145	70.58	$C_{26}H_{16}N_4O_4S_2Br_2$	8.42 (8.33)	10.00 (9.52)
IV_d	p-IC_6H_4	220	42.32	$C_{26}H_{16}N_4O_4S_2I_2$	7.41 (7.35)	8.46 (8.38)
IV_e	p-$OCH_3C_6H_4$	>250	75.86	$C_{28}H_{22}N_4O_6S_2$	9.67 (9.76)	11.03 (11.15)
IVf	p-$CH_3C_6H_4$	210	59.70	$C_{28}H_{22}N_4O_4S_2$	10.22 (10.33)	11.72 (11.81)
IV_g	p-$NO_2C_6H_4$	200	33.11	$C_{26}H_{16}N_6O_8S_2$	14.00 (13.90)	10.68 (10.59)
IV_h	o-ClC_6H_4	250	66.66	$C_{26}H_{16}N_4O_4S_2Cl_2$	9.51 (9.61)	10.81 (10.98)
IV_i	o-$CH_3C_6H_4$	>250	42.85	$C_{28}H_{22}N_4O_4S_2$	10.21 (10.33)	11.72 (11.81)
IV_j	o-$OCH_3C_6H_4$	>250	39.73	$C_{28}H_{22}N_4O_6S_2$	9.67 (9.76)	11.01 (11.15)
IV_k	o-$NO_2C_6H_4$	>250	26.63	$C_{26}H_{16}N_6O_8S_2$	13.89 (13.83)	10.61 (10.56)
IV_l	m-ClC_6H_4	>250	73.33	$C_{26}H_{16}N_4O_4S_2Cl_2$	9.50 (9.61)	10.81 (10.98)
IV_m	m-$CH_3C_6H_4$	200	28.57	$C_{28}H_{22}N_4O_4S_2$	10.22 (10.33)	11.70 (11.81)
IV_n	m-$OCH_3C_6H_4$	240	39.73	$C_{28}H_{22}N_4O_6S_2$	9.69 (9.76)	11.00 (11.15)
IV_o	m-$NO_2C_6H_4$	>250	26.66	$C_{26}H_{16}N_6O_4S_2$	14.00 (13.90)	10.66 (10.59)

IV_a : ν_{max} (cm^{-1}) (KBr) ; 1605 (C=O, exocyclic), 1620 (C=O endocyclic) 1535 (C=C, aromatic), 1330 (C=S).

Screening for antifungal activity

Compounds II, III and IV were screened for their antifungal activity against *A. flavus*, *H. tetramera* and *P. decombens* as the test fungi by paper disc plate method[10] at concentration levels of 2.0 and 0.2% (w/v) in dimethyl sulfoxide. Standard PDA medium was used. Filter paper disc of diameter 12 mm were used and the diameter of zones of inhibition formed around each disc after incubating for a period of 48 hrs. at 25–30°C were recorded. Results were compared with reference fungicides, Dithane z-78 and Thiram-75 W. The compounds III and IV were found to be less fungicidal than that of their precursors II. On comparison with reference fungicides, they were found to be less effective.

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CORRIGENDUM

Paper entitled "Complexation Behaviour of Some 3d-Metal Ions with Aminobenzoic Acids".

In the title of this paper please read 3d-Metal instead of 3d-Metals; In abstract, line no. 2, please read Ni(II) instead of Nd(II); In abstract, line no. 5, the stability order is Cu(II) > Ni(II) > Co(II) > Zn(II). On page 934, line no. 9, please omit pH.