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Sixteen new 3-arylaminoethyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thione and six 3-alkyl aryl alkyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thiones were synthesised and characterised by their sharp melting points, elemental analysis, ir, <sup>1</sup>H nmr and mass spectra. These substituted oxadiazolethiones were screened for their fungitoxic properties. Most of the compounds showed toxicity against two test organisms, *Curvularia verruciformis* and *Alternaria tenuis*. The degree of inhibition ranged from 38-100% for a few compounds.

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1,3,4-Oxadiazole-2-thione derivatives are reported to show a broad spectrum of biological activities [1,2]. These oxadiazoles have been shown to exhibit analgesic, muscle relaxant and tranquilising properties [5a]. It is also reported in the literature that some Mannich bases of 5-substituted phenyl-1,3,4-oxadiazole-2-thione possess central nervous system depressant activity [5b]. These observations prompted the synthesis of elsewhere unreported a series of Mannich bases, 3-arylaminoethyl-, **4a-19a** and 3-alkyl-arylalkyl- **4b-9b** derivatives of 5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thiones as possible fungicides.

The 5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thiones **3** required as starting material was prepared [3] by reaction of 2,4-dichlorobenzoylhydrazide (**2**) with potassium hydroxide and carbon disulphide under reflux in ethanol followed by the acidification with dilute hydrochloric acid.

The 2,4-dichlorobenzoylhydrazide (**2**) was prepared [4] by reaction of hydrazine hydrate (89%) and the 2,4-dichlorobenzoyl ester **1** in ethanol under reflux for 8 hours (mp 163° lit [4] mp 163-164°). The 5-substituted 3-arylaminoethyl derivatives **4a-19a** were prepared by the reaction of thione **3**, formaldehyde (35%) and appropriate alkyl/aryl amines in ethanol [5]. The physical properties and yields are given in Table 1. *N*-Alkyl or arylalkyl derivatives **4b-9b** were prepared [6] by reaction of thione **3** and appropriate alkyl or arylalkyl halides in presence of anhydrous potassium carbonate in dry acetone. The physical properties and yields for these compounds are given in Table 2.

All the newly synthesized compounds gave satisfactory spectral data and the structures were assigned on the basis of elemental analysis, mass, ir (potassium bromide) and <sup>1</sup>H

Table 1

Physical Data of 3-Arylaminoethyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thione

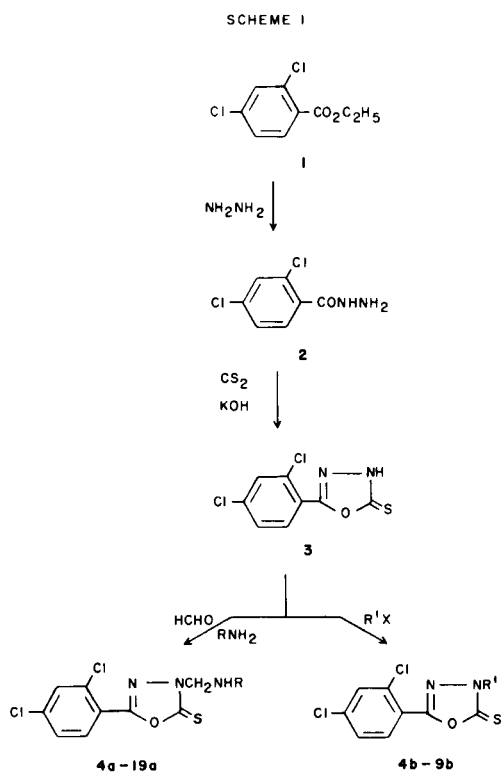
Compound No.	R [a]	Yield % [b]	Mp, °C	Molecular Formulae	Microanalysis Found (Calcd.)			
					C	N	(C)	(N)
<b>3</b>	H	96	171	C <sub>8</sub> H <sub>4</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	38.75	11.40	(38.86)	(11.33)
<b>4a</b>	C <sub>6</sub> H <sub>5</sub>	95	125	C <sub>15</sub> H <sub>11</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	51.15	11.88	(51.13)	(11.93)
<b>5a</b>	2-ClC <sub>6</sub> H <sub>4</sub>	94	182	C <sub>15</sub> H <sub>10</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>2</sub> S	46.60	10.80	(46.57)	(10.86)
<b>6a</b>	3-ClC <sub>6</sub> H <sub>4</sub>	92	146	C <sub>15</sub> H <sub>10</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>2</sub> S	46.42	10.90	(46.57)	(10.86)
<b>7a</b>	4-ClC <sub>6</sub> H <sub>4</sub>	90	151	C <sub>15</sub> H <sub>10</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>2</sub> S	46.40	10.82	(46.57)	(10.86)
<b>8a</b>	4-BrC <sub>6</sub> H <sub>4</sub>	95	146	C <sub>15</sub> H <sub>10</sub> BrCl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	41.90	9.72	(41.76)	(9.74)
<b>9a</b>	2-COOHC <sub>6</sub> H <sub>4</sub>	90	200	C <sub>16</sub> H <sub>11</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	48.50	10.57	(48.48)	(10.60)
<b>10a</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	85	152	C <sub>15</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>3</sub> S	45.52	14.20	(45.34)	(14.10)
<b>11a</b>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	87	190	C <sub>15</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>3</sub> S	45.52	14.15	(45.34)	(14.10)
<b>12a</b>	2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	86	180	C <sub>15</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>3</sub> S	45.42	14.08	(45.34)	(14.10)
<b>13a</b>	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	95	141	C <sub>16</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	52.52	11.50	(52.45)	(11.47)
<b>14a</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	93	137	C <sub>16</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	52.50	11.42	(52.45)	(11.47)
<b>15a</b>	4-COOHC <sub>6</sub> H <sub>4</sub>	89	181	C <sub>16</sub> H <sub>11</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	48.54	10.58	(48.48)	(10.60)
<b>16a</b>	2-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	91	140	C <sub>16</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	50.32	10.91	(50.26)	(10.99)
<b>17a</b>	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	92	156	C <sub>16</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	50.40	10.94	(50.26)	(10.99)
<b>18a</b>	-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	90	155	C <sub>16</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	52.40	11.50	(52.45)	(11.47)
<b>19a</b>	<i>n</i> -(CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub>	92	141	C <sub>12</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	56.62	16.60	(56.69)	(16.53)

[a] The ms showed correct M<sup>+</sup>. [b] Crude product.

Table 2  
Physical Data of 3-Alkyl/arylalkyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thione

Compound No.	R' [a]	Yield % [b]	Mp, °C	Molecular Formulae	Microanalysis Found (Calcd.)			
					C	N	(C)	(N)
<b>4b</b>	-CH <sub>3</sub>	95	78	C <sub>9</sub> H <sub>8</sub> Cl <sub>2</sub> N <sub>2</sub> OS	41.52	10.64	(41.37)	(10.72)
<b>5b</b>	-CH <sub>2</sub> CH <sub>3</sub>	92	70	C <sub>10</sub> H <sub>8</sub> Cl <sub>2</sub> N <sub>2</sub> OS	43.62	10.19	(43.63)	(10.18)
<b>6b</b>	<i>n</i> -(CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub>	94	138	C <sub>12</sub> H <sub>12</sub> Cl <sub>2</sub> N <sub>2</sub> OS	47.41	9.30	(47.52)	(9.24)
<b>7b</b>	-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	90	105	C <sub>15</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>2</sub> OS	53.43	8.30	(53.41)	(8.30)
<b>8b</b>	-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub> [4]	85	107	C <sub>16</sub> H <sub>12</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	52.39	7.63	(52.31)	(7.62)
<b>9b</b>	-CH <sub>2</sub> COOEt	90	75	C <sub>12</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	43.30	8.45	(43.24)	(8.40)

[a] The ms showed correct M<sup>+</sup>. [b] Crude product.



nmr spectral data, given in Table 3.

#### Biological Studies.

The new synthetic compounds were screened for fungitoxic properties. The method of American Phytopathological Society [7] modified by Horsfall and Rich [8] was used for screening on two test organisms, *Curvularia verruciformis*, Agarwal and Sahni and *Alternaria tenuis*, Nees.

#### Determination of Fungi Toxic Activity.

The test compounds were dissolved in acetone, 1.00 g per litre and a 0.2 ml aliquote was taken with a graduated syringe in microscopic grooved (15 mm diameter, 3 mm deep) slides. The solvent was allowed to evaporate leaving a deposit of the test compound in the bottom of the de-

pression and then 0.4 ml of spore suspension was taken with a separate syringe. Suitable controls in sterilized distilled water were also used. The spore suspension was adjusted to give 40-50 conidia per low power field of microscope. The slides were incubated in moist chambers at 20-25° for a period of 24 hours. The percentage germination of treated slides with the control and is shown in Table 4.

Table 3

#### IR and <sup>1</sup>H NMR Spectral Data of Compounds 4a-19a and 4b-9b

Compound No.	IR (Potassium bromide) (cm <sup>-1</sup> )	<sup>1</sup> H NMR (Solvent) (TMS = 0 ppm)
<b>3</b>	3100 (NH), 2520 (SH), 1600 (C=N), 1345 (C=S), 1275 (C-O-C)	(Acetone-d <sub>6</sub> ), 6.8-7.4 (m, 3H-Ar, NH)
<b>4a</b>	3300 (NH), 1600 (C=N), 1370 (C=S), 1260 (C-O-C)	(Acetone-d <sub>6</sub> ), 4.9 (s, 2H), 6.2-6.6 (m, 5H-Ar), 6.8-7.4 (m, 3H-Ar, NH)
<b>5a</b>	3410 (NH), 1600 (C=N), 1370 (C=S), 1260 (C-O-C)	(DMSO-d <sub>6</sub> ), 5.7 (m, 2H), 7.1-7.3 (m, 4H-Ar), 7.4-7.9 (m, 3H-Ar, NH)
<b>6a</b>	3300 (NH), 1600 (C=N), 1375 (C=S), 1260 (C-O-C)	(Acetone-d <sub>6</sub> ), 5.6 (s, 2H), 6.4-6.8 (m, 4H-Ar), 7.4-7.8 (m, 3H-Ar, NH)
<b>7a</b>	3380 (NH), 1600 (C=N), 1360 (C=S), 1260 (C-O-C)	(Acetone-d <sub>6</sub> ), 5.0 (s, 2H), 6.3-6.6 (m, 4H-Ar), 7.0-7.4 (m, 3H-Ar, NH)
<b>8a</b>	3320 (NH), 1600 (C=N), 1360 (C=S), 1260 (C-O-C)	(Acetone-d <sub>6</sub> ), 4.9 (s, 2H), 6.2-6.8 (m, 4H-Ar), 7.0-7.4 (m, 3H-Ar, NH)
<b>9a</b>	3320 (NH), 1700 (C=O), 1600 (C=N), 1370 (C=S), 1270 (C-O-C)	(Acetone-d <sub>6</sub> ), 4.9 (s, 2H), 6.4-6.8 (m, 4H-Ar), 6.9-7.2 (m, 3H-Ar, NH), 9.3 (s, 1H)
<b>10a</b>	3350 (NH), 1600 (C=N), 1375 (C=S), 1270 (C-O-C)	(Acetone-d <sub>6</sub> ), 4.9 (s, 2H), 6.6-7.4 (m, 7H-Ar, NH)
<b>11a</b>	3310 (NH), 1600 (C=N), 1375 (C=S), 1270 (C-O-C)	(Acetone-d <sub>6</sub> ), 5.0 (s, 2H), 6.7-7.4 (m, 7H-Ar, NH)
<b>12a</b>	3420 (NH), 1600 (C=N), 1375 (C=S), 1270 (C-O-C)	(Acetone-d <sub>6</sub> ), 5.0 (s, 2H), 7.1-7.8 (m, 7H-Ar, NH)
<b>13a</b>	3410 (NH), 1600 (C=N), 1370 (C=S), 1260 (C-O-C)	(Deuteriochloroform), 1.9 (s, 3H), 5.0 (s, 2H), 6.4-6.8 (m, 4H-Ar), 7.2-7.6 (m, 3H-Ar, NH)
<b>14a</b>	3320 (NH), 1600 (C=N), 1375 (C=S), 1265 (C-O-C)	(Deuteriochloroform), 1.7 (s, 3H), 5.1 (s, 2H), 6.3-6.8 (m, 4H-Ar), 6.9-7.6 (m, 3H-Ar, NH)

Table 3, Continued

Compound No.	IR (Potassium bromide) (cm <sup>-1</sup> )	<sup>1</sup> H NMR (Solvent) (TMS = 0 ppm)
<b>15a</b>	3320 (NH), 1710 (C=O), 1600 (C=N), 1365 (C=S)	(Acetone-d <sub>6</sub> ), 4.9 (s, 2H), 6.4-6.8 (m, 4H-Ar), 7.4-8.0 (m, 3H-Ar, NH), 9.3 (s, 1H)
<b>16a</b>	3420 (NH), 1600 (C=N), 1370 (C=S), 1260 (C-O-C)	(Deuteriochloroform), 3.5 (s, 2H), 5.2 (s, 2H), 6.4-7.6 (m, 7H-Ar, NH)
<b>17a</b>	3320 (NH), 1600 (C=N), 1370 (C=S), 1260 (C-O-C)	(Deuteriochloroform), 3.5 (s, 3H), 5.2 (s, 2H), 6.3-6.8 (m, 4H-Ar), 6.9-7.6 (m, 3H-Ar, NH)
<b>18a</b>	3310 (NH), 1600 (C=N), 1370 (C=S), 1260 (C-O-C)	(Deuteriochloroform), 4.0 (s, 2H), 5.0 (s, 2H), 6.8-7.6 (m, 8H-Ar, NH)
<b>19a</b>	3200 (NH), 1600 (C=N), 1375 (C=S), 1260 (C-O-C)	(Deuteriochloroform), 0.7 (t, 3H), 1.4 (q, 2H), 2.8 (q, 2H), 5.2 (s, 2H), 7.1-7.8 (m, 3H-Ar, NH)
<b>4b</b>	1600 (C=N), 1360 (C=S), 1190	(Carbon tetrachloride), 2.6 (s, 3H), 7.2-7.5 (m, 2H), 7.8 (d, J = 2.7 Hz)
<b>5b</b>	1600 (C=N), 1370 (C=S), 1260	(Deuteriochloroform), 2.6 (s, 3H), 3.6 (s, 2H), 7.2-7.5 (m, 2H), 7.8 (d, 1H, J = 2.7 Hz)
<b>6b</b>	1600 (C=N), 1360 (C=S), 1190	(Deuteriochloroform), 0.6 (t, 3H), 1.2 (qq, 4H), 2.9 (q, 2H), 7.0-7.3 (m, 3H), 7.6 (d, 1H, J = 2.7 Hz)
<b>7b</b>	1600 (C=N), 1365 (C=S), 1190	(Deuteriochloroform), 4.2 (s, 2H), 6.9-7.4 (m, 7H-Ar), 7.7 (d, 1H, J = 2.7 Hz)
<b>8b</b>	1610 (C=N), 1380 (C=S), 1260, 1190	(Deuteriochloroform), 3.1 (s, 3H), 3.9 (s, 2H), 6.4 (d, 2H, J = 2.8 Hz), 6.9-7.2 (m, 4H-Ar), 7.6 (d, 1H, J = 2.7 Hz)
<b>9b</b>	1750 (C=O), 1600 (C=N), 1310 (C=S), 1190	(Deuteriochloroform), 0.9 (t, 3H), 3.7 (s, 2H), 3.9 (q, 2H), 7.0-7.4 (m, 2H), 7.7 (d, 1H, J = 2.7 Hz)

## EXPERIMENTAL

Melting points were determined with a Buchi oil heated apparatus and are uncorrected. Infrared (ir) spectra were recorded with a Perkin Elmer 237B spectrophotometer using potassium bromide discs, unless otherwise stated. Nuclear magnetic resonance (nmr) spectra were determined in solutions stated, with tetramethylsilane as the internal reference and recorded in 60 MHz on a Varian T60 spectrometer and in 90 MHz on a Varian EM-300 X spectrometer. Mass spectra were recorded on an AEI-MS 30 instrument operating at 70 eV.

2,4-Dichlorobenzoyl ethyl ester (**1**) was prepared by esterification of 2,4-dichlorobenzoic acid as usual.

2,4-Dichlorobenzoyl Hydrazide (**2**).

Ethyl 2,4-dichlorobenzoate (0.5 mole) was dissolved in ethanol (200 ml) and hydrazine hydrate (25 ml, 89%) was added. The mixture was refluxed on a water bath for 8 hours. The solution was cooled and kept overnight at room temperature. The solid which separated was filtered, washed

Table 4

Percentage Inhibition of Conidial Germination in the Test Solutions

Compound No.	Test Organisms	
	<i>Curvularia verruciformis</i>	<i>Alternaria tenuis</i>
<b>3</b>	38.31	39.16
<b>4a</b>	86.49	33.22
<b>5a</b>	62.80	26.31
<b>6a</b>	4.92	18.26
<b>7a</b>	+	+
<b>8a</b>	92.82	86.17
<b>9a</b>	+	+
<b>10a</b>	10.95	23.83
<b>11a</b>	8.85	2.83
<b>12a</b>	+	+
<b>13a</b>	1.92	-
<b>14a</b>	0.25	-
<b>15a</b>	8.61	7.54
<b>16a</b>	9.50	7.08
<b>17a</b>	10.62	50.30
<b>18a</b>	40.47	80.17
<b>19a</b>	+	+
<b>4b</b>	65.16	76.26
<b>5b</b>	61.97	75.85
<b>6b</b>	58.21	74.24
<b>7b</b>	52.42	73.55
<b>8b</b>	0.93	5.33
<b>9b</b>	16.49	6.78

"+" = Complete (100%) inhibition. "-" = No inhibition.

with cold ethanol and dried, mp 163°, lit [4] mp 163-164°, yield 60%.

5-(2,4-Dichlorophenyl)-1,3,4-oxadiazole-2-thione (**3**).

The method of Young and Wood [3] was used for the preparation of the thione. A mixture of 2,4-dichlorobenzoylhydrazide **2** (0.1 mole), potassium hydroxide (0.1 mole), carbon disulfide (20 ml) and ethanol (100 ml) was heated under reflux until the evolution of hydrogen sulfide had nearly stopped. The excess solvent was removed by distillation and the residue was dissolved in water and acidified with dilute hydrochloric acid. The resulting oxadiazolyl thione was collected by filtration, washed with water and dried. The product was recrystallized from ethanol, mp 171°, yield 96%.

3-Arylaminoethyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thiones (**4a-19a**).

Utilizing the method of Ram, *et al.* [5b] a mixture of ethanolic solution of 5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thione (0.01 mole) and formaldehyde (1.5 ml, 35%) was treated with ethanolic solution of suitable amine (0.01 mole) with stirring by slow addition. The solution was stirred for an hour and left overnight in a refrigerator. The solid mass obtained was filtered, washed with cold ethanol and dried. The various 3-arylaminoethyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thiones are reported in Table 1 and characterised by their sharp melting points, elemental analysis, ir, <sup>1</sup>H nmr and mass spectra.

3-Alkyl/arylalkyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thiones **4b-9b**.

A mixture of 5-(2,4-dichlorophenyl)-1,3,4-oxadiazole-2-thione (0.01 mole), anhydrous potassium carbonate (1 g), dry acetone (30 ml) and the appropriate alkyl/arylalkyl halide (0.01 mole) was refluxed for 4-6 hours on a water bath. After completion of the reaction acetone was distilled off and solid poured in water, stirred well and kept overnight. The residue was filtered, dried and recrystallized from suitable solvent. The yield and physical data are given in Table 2.

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