Note

Fungicidal Activity of Oxadiazolyl Sulfides

S. P. SUMAN and S. C. BAHEL

Chemistry Department, University of Gorakhpur, Gorakhpur (U. P.), India

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5-Substituted 1, 3, 4-oxadiazol-2-thiones and their derivatives have been found effective against *Mycobacterium tuberculosis*[1] and also possess higher hypoglycemic activity.[2] The oxoanalogs of 5-substituted-1, 3, 4-oxadiazoles are reported to exert adverse effect against several pathogenic fungi.[3] The -SH group is an important essential toxophore for the pesticidal activity. A comparative study of mercapto compounds and their sulphides[4] has revealed that the sulphides are relatively more active than the parent mercapto groups. The heterocyclic sulphides[4] have been found to have antitubercular, anticancer and antifungal properties. With this in view the title compounds have been prepared.

EXPERIMENTAL

All melting points are uncorrected.

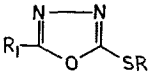
Aroyl/aryloxyacetyl hydrazines. These were prepared by the method of L. Conti.[5]

5-Aryl/aryloxymethyl-1, 3, 4-oxadiazol-2-thiones. These were prepared by the method of Young and Wood.[6]

2-Alkyl/allyl/benzyl/carboxy Alkyl-thio-5-aryl/aryloxymethyl-1, 3, 4-oxadiazoles. To an 4% ethanolic sodium hydroxide (10 ml) solution of 5-aryl/aryloxymethyl-1, 3, 4-oxadiazol-2-thione (0.01 M), alkyl/allyl/benzyl/carboxyalkyl chloride (0.01 M) was added. The resulting solution was refluxed for 3 hr and then poured into cold water. The precipitate thus obtained was filtered, washed and recrystallised. The compounds thus prepared are listed, in Table I.

Bis-(5-aryl/aryloxymethyl-1, 3, 4-oxadiazol-2-yl)-disulphides. To an ice cold ethanolic solution (15 ml)

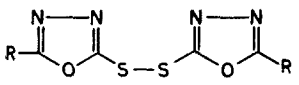
TABLE I. 2-ALKYL/ALLYL/BENZYL/CARBOXYALKYL-THIO-5-ARYL/ARYLOXYMETHYL-1, 3, 4-OXADIAZOLES



No.	R	R_1	mp (°C)	Yield (%)	Molecular formula	N %	
						Found	Calcd.
1	Methyl	*o*-Tolyl	142	80	$C_{10}H_{10}N_2OS$	13.47	13.59
2	Methyl	*m*-Tolyl	160	70	$C_{10}H_{10}N_2OS$	13.48	13.59
3	Allyl	*o*-Tolyl	S[a]	60	$C_{12}H_{12}N_2OS$	—	12.07
4	Allyl	*m*-Tolyl	S[a]	60	$C_{12}H_{12}N_2OS$	—	12.07
5	Benzyl	*o*-Tolyl	105	72	$C_{16}H_{14}N_2OS$	9.82	9.93
6	Benzyl	*m*-Tolyl	110	70	$C_{16}H_{14}N_2OS$	9.80	9.93
7	Benzyl	*p*-Tolyl	118	78	$C_{16}H_{14}N_2OS$	9.85	9.93
8	Benzyl	*m*-Nitrophenyl	83	78	$C_{15}H_{11}N_3O_3S$	13.33	13.42
9	Benzyl	*p*-Nitrophenyl	110	95	$C_{15}H_{11}N_3O_3S$	13.29	13.42
10	Benzyl	*p*-Chloro-*m*-tolyloxymethyl	94	80	$C_{17}H_{15}ClN_2O_2S$	7.92	8.00
11	Carboxymethyl	*o*-Tolyl	114	78	$C_{11}H_{10}N_2O_3S$	11.03	11.20
12	Carboxymethyl	*m*-Tolyl	127	80	$C_{11}H_{10}N_2O_3S$	11.11	11.20
13	Carboxymethyl	*m*-Nitrophenyl	76	70	$C_{10}H_7N_3O_5S$	14.81	14.95
14	Carboxymethyl	*p*-Nitrophenyl	90	75	$C_{10}H_7N_3O_5S$	14.87	14.95
15	Carboxymethyl	*p*-Chloro-*m*-tolyloxymethyl	93	80	$C_{12}H_{11}ClN_2O_4S$	8.79	8.90
16	Carboxyethyl	*o*-Tolyl	130	80	$C_{12}H_{12}N_2O_3S$	10.58	10.69
17	Carboxyethyl	*m*-Tolyl	142	76	$C_{12}H_{12}N_2O_3S$	10.58	10.69
18	Carboxyethyl	*m*-Nitrophenyl	92	72	$C_{11}H_9N_3O_5S$	14.20	14.33
19	Carboxyethyl	*p*-Nitrophenyl	115	74	$C_{11}H_9N_3O_5S$	14.26	14.33
20	Carboxyethyl	*p*-Chloro-*m*-tolyloxymethyl	96	82	$C_{13}H_{13}ClN_2O_4S$	9.47	8.52

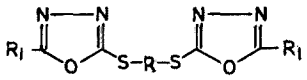
[a] Semi solid.

TABLE II. BIS-(5-ARYL/ARYLOXYMETHYL-1, 3, 4-OXADIAZOL-2-YL)-DISULFIDES



No.	R	mp (°C)	Yield (%)	Molecular formula	N %	
					Found	Calcd.
21	*m*-Tolyl	130	60	$C_{18}H_{14}N_4O_2S_2$	14.55	14.66
22	*p*-Tolyl	126	71	$C_{18}H_{14}N_4O_2S_2$	14.53	14.66
23	*p*-Fluorophenyl	115	60	$C_{12}H_8F_2N_4O_4S_2$	14.05	14.14
24	*p*-Chloro-*m*-tolyloxymethyl	125	65	$C_{20}H_{16}Cl_2N_8O_8S_2$	10.84	10.96
25	*o*, *p*-Dimethylphenoxymethyl	67	60	$C_{22}H_{22}N_4O_4S_2$	11.75	11.91

TABLE III. BIS-(5-ARYL/ARYLOXYMETHYL-1, 3, 4-OXADIAZOL-2-YL)-METHYLENE/ ETHYLENE DISULFIDES



No.	R	R_1	mp (°C)	Yield (%)	Molecular formula	N %	
						Found	Calcd.
26	Methylene	*o*-Tolyl	92	80	$C_{19}H_{16}N_4O_2S_2$	14.00	14.15
27	Methylene	*m*-Tolyl	85	74	$C_{19}H_{16}N_4O_2S_2$	14.03	14.15
28	Methylene	*m*-Nitrophenyl	122	70	$C_{17}H_{10}N_8O_6S_2$	18.20	18.34
29	Methylene	*p*-Nitrophenyl	96	72	$C_{17}H_{10}N_8O_6S_2$	18.24	18.34
30	Methylene	*p*-Chloro-*m*-tolyloxymethyl	140	75	$C_{21}H_{18}Cl_2N_4O_4S_2$	10.62	10.67
31	Ethylene	*o*-Tolyl	112	76	$C_{20}H_{18}N_4O_2S_2$	—	13.66
32	Ethylene	*m*-Tolyl	80	72	$C_{20}H_{18}N_4O_2S_2$	13.54	13.66
33	Ethylene	*m*-Nitrophenyl	100	65	$C_{18}H_{12}N_8O_6S_2$	—	17.80
34	Ethylene	*p*-Nitrophenyl	105	68	$C_{18}H_{12}N_8O_6S_2$	17.70	17.80
35	Ethylene	*p*-Chloro-*m*-tolyloxymethyl	120	70	$C_{22}H_{20}Cl_2N_4O_4S_2$	10.21	10.37

of 5-aryl/aryloxy-methyl-1, 3, 4-oxadiazol-2-thione (0.01 M), a cold ethanolic solution of bromine (0.005 M) was added dropwise with swirling The precipitate thus obtained was filtered, washed with ethanol and recrystallised. The compounds thus prepared are listed in Table II.

Bis-(5-aryl/aryloxymethyl-1, 3, 4-oxadiazol-2-yl)-methylene/ethylene disulphides. To an ethanolic solution (20 ml) of 5-aryl/aryloxymethyl-1, 3, 4-oxadiazol-2-thione (0.01 M) methylene/ethylene dichloride (0.005 M) and fused sodium acetate (2.0 g) were added and the mixture refluxed for three hours. The reaction mixture was poured into cold water and the precipitate thus obtained was filtered, washed and recrystallized. The compounds thus prepared are listed in Table III.

Fungicidal activity. All the 35 compounds have been screened for their antifungal activity against '*Aspergillus niger*' and '*A. flavus*' by agar plate technique[7,8] at three different concentrations namely 1 : 1,000 1 : 10,000 and 1 : 1,00,000. A commercial fungicide Dithane M-45 was tested under similar conditions. The average percentage inhibitions of the compounds are recorded in Table IV.

$$\% \text{ Inhibition} = \frac{C-T}{C} \times 100$$

where C = diameter of the fungus colony in control plates after 96 hr. and T = diameter of the fungus colony in treated plates after 96 hr.

All the compounds display fungicidal activity. However, the highest level of fungicidal activity has been shown by compounds 29, 30, 33, 34 and 35.

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TABLE IV. NUMBER OF REPLICATIONS IN EACH CASE=3

Compound number	Average percentage inhibition after 96 hr					
	Organism- *A. niger* concentrations used			Organism- *A. flavus* concentrations used		
	1: 1,000	1: 10,000	1: 100,000	1: 1,000	1: 10,000	1: 100,000
1	80.2	45.2	33.0	82.4	48.0	36.0
2	77.5	45.0	32.1	80.5	47.1	35.5
3	77.4	41.5	31.0	81.5	46.5	34.8
4	72.1	40.1	30.2	78.4	44.0	33.1
5	84.5	48.5	36.0	90.5	50.4	40.5
6	82.2	47.9	35.4	88.2	49.5	39.4
7	89.4	49.2	36.5	93.2	51.5	42.5
8	100.0	61.0	46.7	100.0	65.9	50.4
9	100.0	62.0	46.5	100.0	64.7	52.5
10	100.0	60.0	45.0	100.0	63.5	48.9
11	84.0	48.1	35.7	88.2	50.4	37.8
12	82.0	47.5	23.1	85.3	50.0	36.1
13	100.0	59.0	46.0	100.0	64.5	49.8
14	100.0	61.7	47.1	100.0	63.1	48.0
15	100.0	58.0	44.7	100.0	63.9	48.0
16	81.5	47.4	35.0	83.4	49.2	37.0
17	80.4	46.0	34.0	83.0	48.5	35.4
18	100.0	58.2	45.1	100.0	63.5	47.0
19	100.0	60.0	46.5	100.0	65.4	49.2
20	100.0	58.7	44.0	100.0	60.2	46.4
21	78.0	44.3	31.2	80.2	48.0	35.4
22	80.0	48.0	37.2	85.4	50.0	38.3
23	100.0	64.5	48.0	100.0	66.3	54.0
24	95.2	62.1	47.2	100.0	66.3	54.0
25	84.5	50.1	39.2	90.5	55.2	49.5
26	83.4	55.2	44.5	85.4	58.4	48.0
27	82.5	52.7	40.5	84.2	54.3	45.0
28	87.5	67.7	53.2	89.2	67.0	55.9
29	100.0	68.0	53.7	100.0	72.0	58.0
30	100.0	67.5	53.0	100.0	69.5	55.2
31	82.5	53.8	42.7	83.5	55.5	46.0
32	78.4	50.0	39.7	82.2	52.3	44.3
33	100.0	66.3	51.7	100.0	66.8	55.6
34	100.0	67.2	52.0	100.0	70.4	56.5
35	100.0	65.9	51.2	100.0	65.4	54.2
Dithane M-45 (A commercial fungicide)	100.0	85.0	70.7	100.0	84.5	67.0

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