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Studies on Some New Thiazolidones as Potential Fungicides

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There are several reports on 2,3-(disubstituted)-4-thiazolidones as local anaesthetics,[1] antibacterials[2] and antifungal agents.[3] Bhargava *et al.* have shown some thiazolidones and their derivatives screened as fungicides.[4,5] Antifungal activity against *Alternaria tenuis* and *Botrytis allii* by Matolcsy *et al.*[6] and against *Helminthosporium euphorbiae* by Srivastava[7] was tested for thiazolidones and found to be sufficient active.

On the basis of the above findings we have synthesized some 3-benzyl-(or *p*-tolyl)-5-methyl-2-(substituted-benzothiazol-2′-ylimino)-4-thiazolidones by the interaction of N-benzyl (or *p*-tolyl)-N′-(substituted)benzothiazol-2-yl thiocarbamides with α-chloropropionic acid in anhydrous condition. These thiazolidones were screened against the fungus *Alternaria tenuis* by Agar-growth method at concentrations 1: 1000, 1: 5000 and 1: 10,000. The percentage inhibition in growth by an inhibitor at a particular concentration is determined by comparison with the growth in controls (*i.e.*, untreated petridishes) and the results are recorded in Table II.

TABLE II. FUNGICIDAL ACTIVITY OF 3-BENZYL (OR *p*-TOLYL)-5-METHYL-2-(SUBSTITUTED-BENZOTHIAZOL-2′-YLIMINO)-4-THIAZOLIDONES

Control: 42 mm, 44.5 mm and 45.5 mm at concentrations 1: 1,000, 1: 5,000 and 1: 10,000 respectively. Temperature, 25~30°C; Fungus, *Alternaria tenuis*; Time, 6 days; Medium, Czapek's agar.

S.No.[a]	Percentage inhibition of concentration		
	1: 1,000	1: 5,000	1: 10,000
1	28.6	40.5	42.9
3	100	100	100
4	100	49.5	7.7
5	17.9	35.9	38.5
6	76.4	23.8	7.7
8	93.1	88.1	37.1
9	100	90.1	40.9

[a] S.No. corresponds to the serial number of the compounds in Table I.

It is evident that the compound 3-benzyl-5-methyl-2-(4′-chlorobenzothiazol-2′-ylimino)-4-thiazolidone inhibits 100% spore germination of the fungus at all the three concentrations. Antifungal potency is being found to be increased by halogen substituents. It is also evident that the activity is being decreased with the increase in dilution.

All melting points were taken by the capillary method and are uncorrected. The purity of the compounds was tested by thin-layer chromatography. A Varian A60D model was used for recording of NMR spectra, Perkin Elmer-257 for IR and a Coleman Analyzer for analyses.

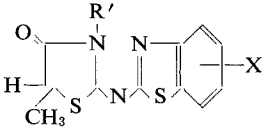
N-Benzyl-N′-5-methylbenzothiazol-2-yl thiocarbamide. A mixture of 5-methyl-2-aminobenzothiazole (4.1 g), benzyl isothiocyanate (3.7 ml) and dry benzene (40 ml) was refluxed on a water-bath with occasional shaking for about 5 hr at 80~90°C. The residue was filtered under suction and washed successively with ether and 40% HCl solution. The product was crystallised from ethanol, yield 76%, mp 192°C. TLC: Rf=0.82 (benzene-ether, 3: 1). *Anal.* Calcd. for $C_{16}H_{15}N_3S_2$: N, 13.42; S, 20.45. Found: N, 13.39; S, 20.56. IR ν_{max}^{nujol} cm^{-1}: 3175s (>NH), 3075 (>NH), 1565s (>C=N- or >C=C<), 1210 (>C=S). NMR ($CDCl_3$) δ (J=Hz): 2.48 (3H, s) for benzene ring methyl protons, 5.08 (2H, d, J=5.0) for aromatic protons, 7.80 (1H, broad) and 10.95 (1H, broad) for two >NH bonds.

Similarly, other 2-amino-(substituted)benzothiazoles were converted into their respective thiocarbamides by treating with benzyl isothiocyanate and *p*-tolyl isothiocyanate.

3-Benzyl-5-methyl-2-(5′-methylbenzothiazol-2′-ylimino)-4-thiazolidone. N-Benzyl-N′-5-methylbenzothiazol-2-yl thiocarbamide (3.13 g) was dissolved in absolute alcohol (35 ml) and α-chloropropionic acid (1.5 ml) as well as anhydrous sodium acetate (2.5 g) were added to this. The mixture was refluxed on a water-bath for 8~10 hr and then poured into ice-cooled water. On keeping overnight, the solid mass was obtained. It was filtered and washed several times with hot water. The dried product was crystallised from ethanol into shining needles, yield 80%, mp 201°C. TLC: Rf= 0.84(benzene-ether, 3: 1). *Anal.* Calcd. for $C_{19}H_{17}N_3OS_2$: N, 11.44; S, 17.44. Found: N, 11.41; S, 17.56. IR ν_{max}^{nujol} cm^{-1}: 1720s (>C=O), 1552s (>C=N- or >C=C<). NMR ($CDCl_3$) δ (J=Hz): 2.75 (3H, s) for benzene ring methyl protons, 1.75 (3H, d, J=7.5) for thiazolidone ring methyl protons, 4.17 (1H, q, J=7.5) for thiazolidone ring single proton, 5.21 (2H, s) for benzyl methylene protons and 8.25 (8H, m) for aromatic protons.

Following the same procedure, other 3-benzyl (or *p*-tolyl)-5-methyl-2-(substituted benzothiazol-2′-ylimino)-4-thiazolidones were synthesized by condensing the respective thiocarbamides with α-chloropropionic acid. The structures and the purity of the compounds are recorded in Table I.

TABLE I. PHYSICAL DATA AND IR PEAKS OF 3-BENZYL(OR *p*-TOLYL)-5-METHYL-2-(SUBSTITUTED BENZOTHIAZOL-2′-YLIMINO)-4-THIAZOLIDONES



S. No.	Substituent X	Molecular formula	Yield (%)	mp(°C)	Nitrogen(%)		Sulphur(%)		Characteristic IR peaks (cm^{-1})	*Rf* values[a]
					Found	Calcd.	Found	Calcd.		
			R′=$-CH_2-C_6H_5$							
1	5–CH_3	$C_{19}H_{17}N_3OS_2$	80	201	11.41	11.44	17.56	17.44	1720s, 1572s, 1522m	0.84
2	6–CH_3	$C_{19}H_{17}N_3OS_2$	88	168	11.40	11.44	17.47	17.44	1710s, 1565s, 1535m	0.91
3	5–Cl	$C_{18}H_{14}N_3OS_2Cl$	64	221	10.83	10.84	16.59	16.52	1722s, 1650s, 1570m	0.73
4	6–Cl	$C_{18}H_{14}N_3OS_2Cl$	72	250	10.82	10.84	16.49	16.52	1725s, 1640s, 1600m	0.87
5	6–OCH_3	$C_{19}H_{17}N_3O_2S_2$	76	182	10.93	10.93	16.93	16.71	1612s, 1565s, 1530m	0.68
			R′=$-C_6H_4\cdot CH_3$(p)							
6	H	$C_{18}H_{15}N_3OS_2$	55	193	11.52	11.89	17.94	18.13	1670s, 1596s, 1575m	0.78
7	4–CH_3	$C_{19}H_{17}N_3OS_2$	67	221	11.03	11.44	17.21	17.44	1680s, 1570w, 1560m	0.77
8	4–Cl	$C_{18}H_{14}N_3OS_2Cl$	69	225	10.49	10.83	16.38	16.52	1655s, 1560s, 1525s	0.68
9	5–Cl	$C_{18}H_{14}N_3OS_2Cl$	53	232	10.76	10.83	16.29	16.52	1725s, 1550s, 1515m	0.67

[a] *Rf* values were measured on developing the TLC plates (adsorbent, silica gel BDH) in benzene-ether (3: 1) mixture. s=sharp, m=medium and w=weak.

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REFERENCES

1) A. R. Surrey, *J. Am. Chem. Soc.*, **71**, 3105 (1949).
2) M. K. Rout and H. K. Pujari, *J. Sci. Ind. Research (India)*, **14**, 448 (1955).
3) H. Tripathy, R. N. Dash, B. C. Dash and G. N. Mahapatra, *Indian J. Chem.*, **9**, 1232 (1971).
4) P. N. Bhargava and G. C. Singh, *J. Ind. Chem. Soc.*, **45**, 32 (1968).
5) P. N. Bhargava and M. R. Chaurasia, *J. Chem. UAR*, **12**, 149 (1969).
6) G. Matolcsy, B. Bordash and M. Hamran, *Acta Phytopathol.*, **4**, 345 (1969).
7) K. S. L. Srivastava, *Indian J. Appl. Chem.*, **32**, 369 (1969).