J. Indian Chem. Soc.,
Vol. LXI, May 1984, pp. 434-435

Synthesis and Antifungal Activity of Some New 1-Phthalimidoacetyl Thiosemicarbazides/Thiazolidones**

P. C. JOSHI, JR*. and P. C. JOSHI, SR.

Department of Chemistry, Kumaun University Constituent College, Almora-263 601

Some 1-phthalimidoacetyl-4-aryl thiosemicarbazides and their corresponding 3-phthalimidoacetylamino-2-arylimino-4-thiazolidones were synthesised and screened for their antifungal activity against *Alternaria alternata*, *Drechslera papendorfii* and *Helminthosporium oryzae*. Only thiosemicarbazides showed measurable activity against all the test fungi.

A large number of phthalimide derivatives having trichloromethylthio[1], trifluoromethylthio[2], aryl sulphonyl[3], and amino[4] substituents attached to N-atom of phthalimido group have been reported to possess antifungal activity. Various 4-substituted thiosemicarbazides[5] and their cyclised products, thiazolidones[6-8] have also been reported to possess antifungal and antibacterial activity.

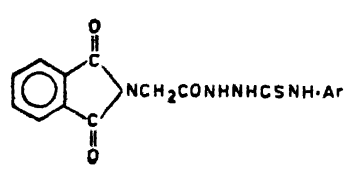
These facts induced us to synthesise some 1-phthalimido acetyl-4-aryl thiosemicarbazides and their corresponding 3-phthalimidoacetylamino-2-arylimino-4-thiazolidones with a view to evaluate their antifungal activity against *Alternaria alternata*, *Drechslera papendorfii* and *Helminthosporium oryzae*. The efficacy of these compounds was ascertained by comparing them with the reference fungicide, Thiram 75W.

Experimental

The melting points were taken in H_2SO_4 bath and are uncorrected. The ir spectra were determined in KBr pellets on Perkin Elmer infrared spectrophotometer.

1-Phthalimidoacetyl-4-aryl thiosemicarbazides: A mixture of 4-aryl thiosemicarbazide[9-11] (0.01 mol), phthalimidoacetyl chloride[12] (0.01 mol) and triethylamine (0.01 mol) was refluxed in dioxan (80 ml) for 4-6 h. The reaction mixture was then poured into cold water (500 ml). The precipitated product obtained was filtered, washed with a saturated solution of sodium bicarbonate followed by water, dried and recrystallised from aqueous dimethylformamide. These compounds (Table 1) were characterised by analysis, melting points, and

TABLE 1—ANALYTICAL DATA AND ANTIFUNGAL ACTIVITY OF 1-PHTHALIMIDOACETYL-4-ARYL THIOSEMICARBAZIDES



Ar	m.p °C	Yield %	Molecular† formula	Inhibition zone dia.* (mm) of fungi at concn. (%, w/v)					
				A. alternata		*D. papendorfii*		*H. oryzae*	
				2	0.2	2	0 2	2	0.2
C_6H_5	>320	72	$C_{17}H_{14}N_4O_3S$	18	–	20	17	17	15
p-$CH_3C_6H_4$	>320	70	$C_{18}H_{16}N_4O_3S$	18.5	–	17	–	16	–
p $OCH_3C_6H_4$	>320	75	$C_{18}H_{16}N_4O_4S$	17	15.5	23	16	21	17
p-ClC_6H_4	>320	71	$C_{17}H_{13}ClN_4O_3S$	17	14 5	16	–	18	16
p-BrC_6H_4	304	73	$C_{17}H_{13}BrN_4O_3S$	16.5	–	18	–	19	14
Thiram 75 W‡				40	28	40	32	36	28

* Three replicates averaged; no zone of inhibition at 0.02 and 0.002 concn. for all the compounds, except for Thiram 75 W at 0.02 (25 mm).

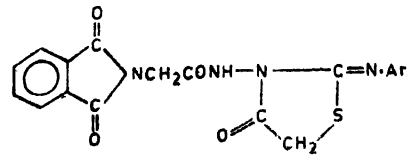
‡ Reference fungicide.

† Analysis for C, H and N found within ±0.5%.

– No inhibition.

**Paper presented at the 'Annual Convention of Chemists', Kurukshetra, 1979.

TABLE 2—ANALYTICAL DATA OF 3-PHTHALIMIDOACETYLAMINO-2-ARYLIMINO-4-THIAZOLIDONES



Ar	m. p. °C	Yield %	Molecular formula	Analysis ; Found/(Calcd.) C	H	N
C_6H_5	245	48	$C_{19}H_{14}N_4O_4S$	57.48 (57.86)	3.13 (3.55)	13.98 (14.21)
p-$CH_3C_6H_4$	232	44	$C_{20}H_{16}N_4O_4S$	58.51 (58.82)	3.63 (3.92)	13.47 (13.72)
p $OCH_3C_6H_4$	212	49	$C_{20}H_{16}N_4O_5S$	56.16 (56.60)	3.43 (3.77)	12.87 (13.20)
p-ClC_6H_4	262	43	$C_{19}H_{13}ClN_4O_4S$	52.85 (53.20)	2.95 (3.03)	12.73 (13.06)
p-BrC_6H_4	274	45	$C_{19}H_{13}BrN_4O_4S$	47.75 (48.20)	2.36 (2.74)	11.48 (11.83)

characteristic ir bands at 3220 and 3150 cm^{-1} (N-H stretching), 1780 and 1720 cm^{-1} (endocyclic C=O), 1620 cm^{-1} (-CONH-), 1580 cm^{-1} (aromatic C=C), 1510 and 1480 cm^{-1} (C-N stretching), 1345 cm^{-1} (NHCSNH) and 740 cm^{-1} (monosubstituted benzene).

3-Phthalimidoacetylamino-2-arylimino-4-thiazolidone: A mixture of 1-phthalimidoacetyl-4-aryl thiosemicarbazide (0.01 mol) and anhydrous sodium acetate (0.015 mol) was refluxed in glacial acetic acid (100 ml). After complete dissolution of thiosemicarbazide a solution of monochloro acetic acid (0.01 mol) in glacial acetic acid (10 ml) was added. The reaction mixture was further refluxed for 10-12 h and then poured into ice-cold water and kept overnight at room temperature. The crude product was filtered, washed several times with water and recrystallised from ethanol. The identity of these thiazolidones (Table 2), was established by their sharp melting points and analytical data and presence of characteristic ir bands at 3200 and 3000 cm^{-1} (N-H stretching), 1720 cm^{-1} (C=O), 1600 cm^{-1} (-CONH- and C=C aromatic), 1540 cm^{-1} (C=N), 1480 and 1440 cm^{-1} (C-N stretching), 1310 and 1250 cm^{-1} (C-S-C) and 750 cm^{-1} (monosubstituted benzene).

Antifungal activity: All these 1-phthalimidoacetyl-4-aryl thiosemicarbazides and their cyclised products, 3-phthalimidoacetylamino-2-arylimino-4-thiazolidones were screened for their antifungal activity against *Alternaria alternata*, *Drechslera papendorfii* and *Helminthosporium oryzae* as the test fungi by paper disc plate method[18] at concentrations 2, 0.2, 0.02 and 0.002% in dimethylformamide (w/v). Standard PDA medium was used. Filter paper discs of diameter 12 mm were used and the diameter of zones of inhibition formed around each disc after incubating for a period of 48 h at 25-28° was recorded.

All the thiosemicarbazides exhibited low antifungal activity against all the test fungi at concentration 2% (Table 2). Among these thiosemicarbazides maximum antifungal activity was observed with the compounds having methoxy group at *p*-position in the phenyl ring against *Drechslera papendorfii* and *Helminthosporium oryzae* at a concentration of 2%. Considerable change in the antifungal activity was not observed when methyl, chloro or bromo substituents were introduced at the *p*-position in the phenyl ring of these thiosemicarbazides. These compounds were found to be less effective as compared to Thiram 75W. Thiazolidones, the cyclised product of thiosemicarbazides were found to be completely devoid of antifungal activity against all the test fungi at all concentrations.

Acknowledgement

One of the authors (P.C.J., Jr.) is indebted to U.G.C., New Delhi for financial assistance.

References

1. A. R. KITTLESON, *Science*, 1952, **115**, 84.
2. E. KUEHLE, A. HAAS, W. KLUNG and F. GREWE, *Ger. Offen.*, 1, 908, 680, 1970 (*Chem. Abstr.*, **73**, 109522).
3. K. SHINODA, S. HAYASHI, K. SATAKE and S. YAMAZAKI, *Japan Kokai*, 7328, 639, 1973 (*Chem. Abstr.*, **79**, 88315).
4. P. MINIERI, *U.S.P.*, **3**, 798, 327, 1974 (*Chem. Abstr.*, **81**, 100717).
5. N. V. PHILLIPS, *Gloeilampenfabrieken Belg.*, 1961, 622, 688.
6. S. C. SHARMA, *Bull. Chem. Soc. Jpn.*, 1967, 40, 2422.
7. P. N. BHARGAVA and I. C. TIWARI, *Curr. Sci.*, 1973, 42, 717.
8. P. N. BHARGAVA and G. C. SINGH, *J. Indian Chem. Soc.*, 1968, 45, 32.
9. E. FROMM, R. KAPELLER, A. HAHN, LE PIRK and TH. LEIPERT, *Ann.*, 1926, 447, 259.
10. P. C. GUHA and H. P. RAY, *J. Am. Chem. Soc.*, 1925, 47, 385.
11. T. FROMM, *Ann.*, 1925, 442, 154.
12. J. C. SHEEHAN and V. S. FRANK, *J. Am. Chem. Soc.*, 1949, 71, 1856.
13. H. H. THORNBERRY, *Phytopathology*, 1950, 40, 419.