Asian Journal of Chemistry Vol. 19, No. 5 (2007), 3511-3514

Synthesis and Antifungal Activity of Some Novel 1-Phenyl-3-methyl-4-substituted phenyl-6-imino-4,7-dihydro-1,3-thiazino(5,4-d)pyrazoles

A.K. YADAV, VANDANA SINGH and DAROGA SINGH*
Department of Chemistry, Synthetical Organic Research Laboratory
T.D. Postgraduate College, Jaunpur-222 002, India
E-mail: yadav_ajay002@rediffmail.com

1-Phenyl-3-methyl-4-substituted phenyl-6-imino-4, 7-dihydro-1,3-thiazino(5,4-d)pyrazoles (**3**) have been synthesized by the reaction of 1-phenyl-4-arylidene-3-methyl pyrazolo-5-ones (**2**) and thiourea in methanolic KOH. The synthesized compounds have been screened for their antifungal activity against *P. graminis tritici* and *P. recondita*.

Key Words: Thiazino pyrazoles, Pyrazoles, Antifungal activity.

INTRODUCTION

Several pyrazolone derivatives[1-5] have been reported as antifungal, antimalarial, antibacterial, insecticidal, herbicidal, anticonvulsive and antiinflammatory agents. The importance of pyrazolones have promoted us to synthesize some novel 1-phenyl-3-methyl-4-substituted phenyl-6-imino-4,7-dihydro-1,3-thiazino(5,4-d)pyrazoles. The antifungal activity of synthesized compounds have been screened against fungi *P. graminis tritici* and *P. recondita*.

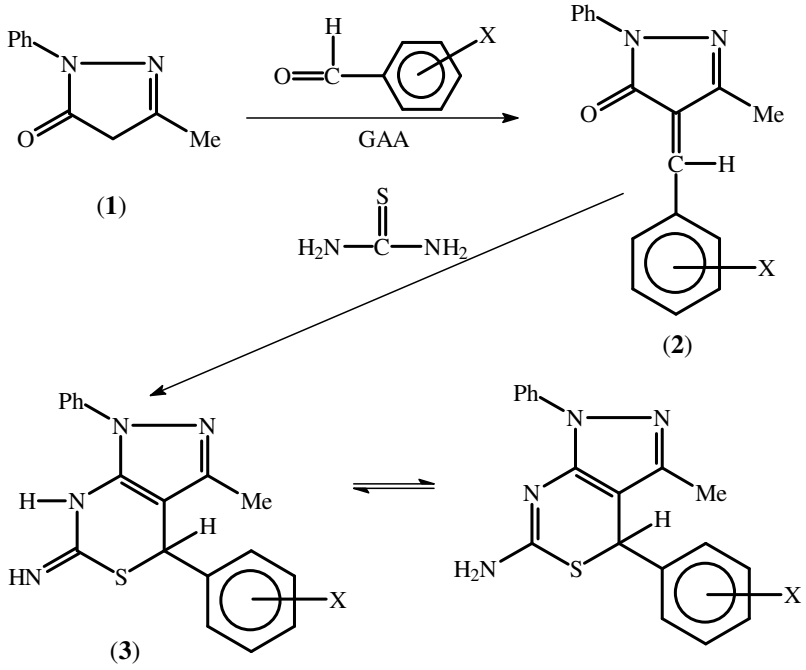
1-Phenyl-3-methyl pyrazol-5-one (**1**) was prepared by the known method[6]. The compound **1** condensed with substituted aromatic aldehyde in glacial acetic acid to yield 1-phenyl-4-arylidene-3-methyl pyrazolo-5-ones (**2**). The compound **2** was refluxed with thiourea and KOH in ethanol for 3-4 h to give the present compound **3** (**Scheme-I**).

EXPERIMENTAL

Melting points were taken in an open capillary tubes and are uncorrected. The IR spectra were recorded in KBr on Perkin-Elmer-720 spectrophotometer. The ^{1}H NMR spectra were recorded in $CDCl_3$ on Varian A-60D spectrophotometer. The chemical shifts are recorded in δ ppm downfield from TMS which are used as an internal standard.

1-Phenyl-4-arylidene-3-methyl pyrazolo-5-one (2): A mixture of **1** (0.01 mol) and substituted aromatic aldehyde (0.01 mol) in glacial acetic

acid (15 mL) was taken into a beaker. The reaction mixture was heated on sand bath for 15 min and left overnight at room temperature. The compound **2** was separated as coloured crystals, filtered, dried and recrystallized from benzene.



X = H, *o*-CH_3, *p*-NO_2, *m*-NO_2, *p*-OCH_3 and *p*-$N(CH_3)_2$

Scheme-I

1-Phenyl-3-methyl-4-substituted phenyl-6-imino-4,7-dihydro-1,3-thiazino(5,4-d)pyrazoles (3a-f): A mixture of compound **2** (0.01 mol), thiourea (0.01 mol) and KOH (0.02 mol) was refluxed in ethanol for 3-4 h. The reaction mixture was cooled at room temperature, it was acidified with dil. HCl and diluted it by addition of 20-30 mL water to get solid material. It was filtered, dried and recrystallized from ethanol. The physical data of all the synthesized compounds are given in Table-1. All the compounds gave satisfactory elemental analyses.

Antifungal activity

The compounds **3a-f** were screened for their antifungal activity against *P. graminis tritici* and *P. recondita* by known method[7] at the three concentrations *viz.*, 1000, 100 and 10 ppm. The screening data of compounds are listed in Table-2. Results were compared with commercial fungicide miconazole tested under similar conditions. The percentage inhibition has been calculated by the formula:

$$\text{Inhibition (\%)} = (C\text{-}T) \times 100/C$$

where C and T are diameter (in mm) of fungus colony in control and treated plates, respectively.

TABLE-1

Compd. No.	X	m.p. (ºC)/ Yield (%)	IR (KBr, ν_{max} cm^{-1})	^{1}H NMR ($CDCl_3$) δ (ppm)
3a	H	198/53	1690 (C=O), 1570 (C=N), 3395 (=NH)	1.8 (3H, s, CH_3), 3.8 (1H, s, S-CH), 7.0-7.8 (10H, m, Ar-H), 9.1 (2H, s, NH)
3b	*o*-CH_3	176/55	1690 (C=O), 1575 (C=N), 3400 (=NH)	2.6 (6H, s, 2XCH_3), 3.6 (1H, s, S-CH), 7.5-8.2 (9H, m, Ar-H), 9.0 (2H, s, NH)
3c	*p*-NO_2	165/60	1695 (C=O), 1560 (C=N), 3400 (=NH)	2.0 (3H, s, CH_3), 3.6 (1H, s, S-CH), 8.0-8.8 (9H, m, Ar-H), 9.3 (2H, s, NH)
3d	*m*-NO_2	145/58	1680 (C=O), 1570 (C=N), 3395 (=NH)	2.0 (3H, s, CH_3), 3.7 (1H, s, S-CH), 7.5-8.1 (9H, m, Ar-H), 9.2 (2H, s, NH)
3e	*p*-OCH_3	125/63	1700 (C=O), 1575 (C=N), 3390 (=NH)	2.2 (3H, s, CH_3), 3.7 (1H, s, S-CH), 3.9 (3H, s, OCH_3) 7.4-8.3 (9H, m, Ar-H), 9.3 (2H, s, NH)
3f	*p*-$N(CH_3)_2$	183/72	1695 (C=O), 1568 (C=N), 3390 (=NH)	1.8 (3H, s, CH_3), 2.8 (6H, s, $N(CH_3)_2$), 3.7 (1H, s, S-CH), 7.6-8.6 (9H, m, Ar-H), 9.2 (2H, s, NH)

TABLE-2

Compd. No.	X	Average % inhibition after 96 h					
		P. graminis tritici (ppm)			*P. recondita* (ppm)		
		1000	100	10	1000	100	10
3a	H	65	51	40	60	48	36
3b	*o*-CH_3	69	55	43	64	53	41
3c	*p*-NO_2	70	57	48	66	55	45
3d	*m*-NO_2	72	60	46	69	57	44
3e	*p*-OCH_3	75	62	50	71	60	47
3f	*p*-$N(CH_3)_2$	78	65	55	75	63	52
Miconazole		100	85	70	99	83	68

RESULTS AND DISCUSSION

It is observed from the antifungal screening data that results the most of the compounds have significant toxicity at 1000 ppm, but their toxicity decreaes upon dilution. The antifungal activity of the compounds is due to presence of biolabile groups N=C–S and N–N=C present in the nuclei of the compound and slight variation in antifungal activity is due to different group attached with benzene nucleus *i.e.*, the compound **3b-f** show more fungitoxicity than compound **3a** because they contains CH_3, NO_2, OCH_3 and NMe_2 group in the benzene nucleus. It is note worthy that the compound **3b** shows some what less toxicity than the compound **3c-f**. The less toxicity in compound **3b** is probably due to CH_3 group attached with benzene nucleus.

ACKNOWLEDGEMENTS

The authors are grateful to the Principal and Head, Department of Chemistry, T.D.P.G. College, Jaunpur for providing necessary facilities. Thanks are also due to Dr. M.S. Singh, Department of Chemistry, Banaras Hindu University, Varanasi for spectral analyses.

REFERENCES

1. H.A. Etman, E.G. Sadak and M.A. Metwally, *J. Indian Chem. Soc.*, **67**, 213 (1990).
2. R. Jain, P. Padmaja, J. Bhadauria and S. Tomar, *J. Indian Chem. Soc.*, **77**, 42 (2000).
3. R. Jain, P. Padmaja, S. Tomar and M.K. Shrivastava, *J. Indian Chem. Soc.*, **77**, 44 (2000).
4. K.G. Ojha, N. Jaisinghani and H. Tahiliani, *J. Indian Chem. Soc.*, **79**, 191 (2002).
5. B. Kaulluraya, J.K. John and B.S. Holla, *J. Indian Chem. Soc.*, **72**, 99 (1995).
6. R.B. Pathak, Ph.D. Thesis, Gorakhpur University (1979).
7. J.G. Horsfall, *Bot. Rev.*, **11**, 357 (1995).

(*Received*: 2 March 2006; *Accepted*: 24 February 2007) AJC-5438