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Synthesis and Characterization of Some New Imidazo [2,1-a] Pyrazolo [3,4-d] Thiazoles as Potentials Fungicide

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ABSTRACT

The new cis-3,3a-imidazo[2,1-a]-pyrazolo[3,4-d] thiazoles (II*a-l*) have been synthesized by refluxing a mixture of 2-(p-ethoxy arylidene-5,6-dehydro imidazo [2,1-a]-thiazolidene-3-one(II*a-f*) with hydrazine hydrate or 2,4-di-nitro phenyl hydrazine and anhydrous sodiumacetate in glacial acetatic acid. All the synthesized compounds have been characterized by elemental analysis & spectral data and also screened for their fungicidal activity against two fungal species that is *Alternaria solanai* & *Puccinia recondita*. Screening data have been co-related with the structural feature of the tested compounds.

Key words: *Alternaria solanai*, *Puccinia recondita*, Agar plate technique, Thiazoles, imidazoles and spectral analysis.

INTRODUCTION

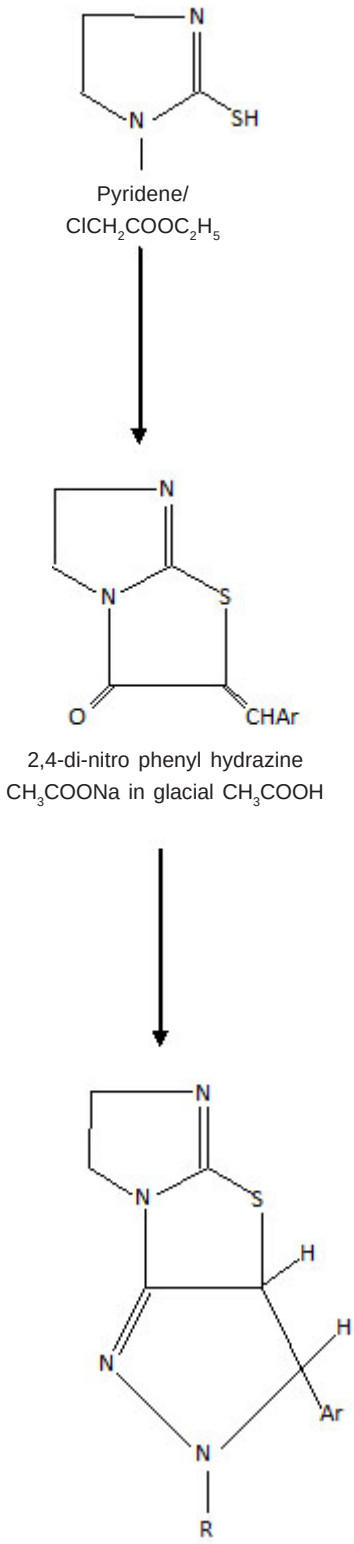
Many imidazoles have been reported to exhibit antibacterials[1], herbicidal[2,3], insecticidal[4], fungicidal activity[5-7]. The importance of some thiazoles prompted us to synthesized some novel imidazo [2,1-a] pyrazolo [3,4-d] thiazoles derivatives with a view to studying their antifungal activity. 2-Mercapto imidazoline was prepared following the method[8] which well agreed with their analytical data already reported in the literature[8]. 2-[p-Ethoxy arylididene]-5,6-dihydroimidazo [2,1-a] thiazolidine-3-ones (II*a-f*) was synthesized by a mixture of 2-mercapto imidazoline, pyridine and ethyl chloroacetate in dry ethanol. The reaction of (II*a-f*) with hydrazine hydrate or 2,4-dinirophenyl hydrazine and anhydrous sodium acetate in glacial acetic acid to give 3-(p-Ethoxy aryl)-cis-3,3a, imidazo [2,1-a] pyrazolo [3,4-d] thiazoles (III*a-l*). All the prepared (II*a-f*) and (III*a-l*) compounds were characterized with their m.p., yield, molecular formula and elemental analysis, I.R. and ^{1}HNMR spectral data of the representative compounds are also given as footnote in the Table-1.

Fungicidal Activity

The compounds (II*a-f*) and (III*a-l*) were screened for their antifungal activity against *Alternaria solanai* and *Puccina recondita* at 1000, 100 and 10 ppm concentration following the agar plate technique[9]. It is appeared from the screening data that all the compounds were more active against *Alternaria solanai* as compared with *Puccinia recondita* but their difference was marginal

most of the compound showed the significant anti-fungal activity at 1000 ppm against both the fungal species but their toxicity decreased markedly at lower concentration (100 & 10 ppm). The compounds (III*c* & III*i*) exhibited fungitoxicity of the order of Dithane M-45 at 1000 ppm against both the test fungi. However, their activity decreased markedly at lower concentration (100 ppm & 10 ppm) except in the case of the compounds III*c* & III*i* which inhibited 50-53% growth of the both the fungi species even at 10 ppm.

It is however, noteworthy that the introduction of chloro and methoxy group in the aryl moiety of these compounds tend to enhance the fungitoxicity, and that the introduction of chloro group at ortho position is more effective than that of para position, likewise, the introduction of methoxy group that at ortho position is more also noted that the compounds bearing 2,4-dinetro phenyl moiety are more active. The overall results are not so encouraging as one would expert from combined performance of the two biolabile nuclei viz. imidazole and thiazole. the fungicidal activity of (III*a-l*) compounds were screened and the fungicidal data are recorded in table-2.



(IIa-l)

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. The IR spectra in KBr were recorded on a Jasco FT/IR-460 plus Fourier Transform infrared specro photometer. ^{1}HNMR spectra were scanned on a bruker ultraspec 500 MHz/ AMX spectrometer using Dinso as solvent chemical shifts are expressed in d ppm spectra were recorded on JEO2 SX 102/DA-6000 mass spectrophotometer using argon/Xenon (6KV, 10mA) as the FAB gas with m-nitrobenzylalcohol as the matrix.

Synthesis of 2-(p-Ethoxy arylidine)-5,6-dihydro imidazo [2,1-a]-thiazolidine-3-ones (II*a-f*)

The corresponding 2-(p-Ethoxy arylidene)-5,6-hydroimidazol [2,1-a] thiazolidine -3-ones were synthesized by condensation of 2-mercapto imidazolene. Pyridine and ethyl chloroacetate in dry ethanol was refluxed on a stem bath for 4 hrs. there after suitable ethoxy aromatic aldehyde and piperidine was added and the

reaction mixture was refluxed further for 1 hr. cooled, filtered, washed well with water and the product was recrystallized from glacial acetic to give cream colour crystals. The structure was assigned on the basis of analytical data and spectral data which are given in the table-1.

Synthesis of 3-(p-ethoxyaryl)-cis-3,3a,6,7-tetrahydro-2H-Imidazo[2,1-a] pyrazolo [3,4-d]-thiazoles (III*a-l*)

A mixture of 2-(p-ethoxy arylidene-5,6-dihydro imidazo [2,1-a]-thiazoledine-3-ones (0.0025 mol), hydrazine hydrate (0.0025 mol) or 2,4-di-nitro phenyl hydrazine (0.0025 mol) and anhydrous sodium acetate (0.0025 mol) in glacial acetic acid (50 ml) was heated under refluxes for 6 hrs., cooled to room temperature, filtered, washed will with water and recrystallized from acetic acid as light yellow crystals. All the prepared title compounds with their characterization data m.p., yield, molecular formula, elemental analysis and spectral data as footnote are recorded in table-1.

Table 1 : Characterization data of 2-(p-Ethoxy arylidene-5,6-dihydro imidazo [2,1-a] thiazolidine –3-ones (II*a-f*) and 3-(p-ethoxy aryl) cis–3,3a, 6,7-tetrahydro-2H-imidazo [2,1-a] pyrazolo [3,4-d] thiazoles (III*a-l*)

Compd. No.	R	Ar	Molecular formulae	M.P. (°C)	Yield (%)	Analysis,Found (Calculated) C	N	S
IIa*		C_6H_5	$C_{14}H_{15}N_2O_2S$	245	62	61.20 (61.09)	10.28 (10.18)	11.72 (11.63)
b		m-$NO_2C_6H_4$	$C_{14}H_{14}N_3O_4S$	255	35	52.62 (52.50)	13.22 (13.12)	10.10 (10.00)
c		o-ClC_6H_4	$C_{14}H_{14}N_2O_2SCl$	196	49	54.17 (54.28)	09.15 (09.04)	10.44 (10.33)
d		p-ClC_6H_4	$C_{14}H_{14}N_2O_2SCl$	201	52	54.25 (54.28)	09.02 (09.18)	10.35 (10.33)
e		o-$H_3COC_6H_4$	$C_{15}H_{17}N_2O_3S$	198	56	59.10 (59.01)	09.28 (09.18)	10.50 (10.49)
f		p-$H_3COC_6H_4$	$C_{15}H_{17}N_2O_3S$	203	58	59.25 (59.01)	09.25 (09.18)	10.48 (10.49)
IIIa*0	H	C_6H_5	$C_{14}H_{17}N_4OS$	245	58	58.25 (58.13)	19.28 (19.26)	11.20 (11.07)
b	H	m-$NO_2C_6H_4$	$C_{14}H_{16}N_5OS$	250	35	50.30 (50.29)	21.00 (20.95)	09.49 (09.45)
c	H	o-ClC_6H_4	$C_{14}H_{16}N_4OSCl$	215	49	52.00 (51.93)	17.40 (17.20)	09.45 (09.43)
d	H	p-ClC_6H_4	$C_{14}H_{16}N_4OSCl$	230	52	52.10 (52.08)	17.40 (17.31)	09.91 (09.88)
e**	H	o-$H_3COC_6H_4$	$C_{15}H_{19}N_4O_2S$	248	56	56.54 (56.42)	17.60 (17.55)	9.98 (10.03)
f	H	p-$H_3COC_5H_4$	$C_{15}H_{19}N_4O_2S$	251	60	56.38 (56.42)	17.52 (17.55)	10.21 (10.03)
g	2,4-di-nitro-phenyl	C_6H_5	$C_{20}H_{19}N_6O_6S$	246	70	51.02 (50.94)	17.79 (17.83)	06.58 (06.79)
h	2,4-di-nitro-phenyl	m-$NO_2C_6H_4$	$C_{20}H_{18}N_7O_7S$	252	45	48.15 (48.00)	19.55 (19.60)	06.52 (06.40)
i	2,4-di-nitro-phenyl	o-ClC_6H_4	$C_{20}H_{18}N_6O_5SCl$	245	48	49.17 (49.02)	17.25 (17.16)	06.48 (06.53)
j	2,4-di-nitro-	p-ClC_6H_4	$C_{20}H_{18}N_6O_5SCl$	230	42	49.18	17.30	06.55

	phenyl					(49.02)	(17.16)	(06.53)
k	2,4-di-nitro-	o-$H_3COC_6H_4$	$C_{21}H_{21}N_6O_6S$	242	41	52.02	17.28	06.46
	phenyl					(51.95)	(17.31)	(06.59)
l	2,4-di-nitro-	p-$H_3COC_5H_4$	$C_{21}H_{21}N_6O_6S$	247	46	52.05	17.41	06.60
	phenyl					(51.95)	(17.31)	(06.59)

*IIa. IR (KBr); 840 (1,4-disubstituted benzene ring) 1520 (C-N-Stretching), 1590 (>C=C<), 1610 (>C=N), 1680 (>C=O), 3050 (Ar-C-H Stretching) cm^{-1}

^{1}HNMR ($DMSOd_6$) δ : 3.4 (2H, t, C_5 Methylene proton), 3.8 (2H, t, C_6 methylene proton) 1.4 (3H, t, CH_3 proton), 3.8 (3H, s, OCH_3), 7.0-8.1 (7H, m, Ar-H)

*IIIa IR(KBr) : 820 (1,4-disubstituted benzene ring, 1510 (C-N-Stretching), 1600 (>C=C<). 1620 (>C=N), 3040 (Ar C-H) Stretching), 3280 (N-H Stretching) cm^{-1}

^{1}HNMR ($CDCl_3$) δ : 1.35 (2H, t, CH_3), 2.5 (1H, s, NH Exchangeable with D_2O), 3.38 (2H, t, C_7 methylene proton), 3.7 (2H, t, C_6 methylene proton), 4.1 (2H, q, CH_2 protons of ethoxy group), 7.57 (1H, d, J = 8.48, Hz, C_{3a}-H), 7.80 (H, d, J = 8.49 Hz, H-3 & H-5'), 7.88 (2H, d, J = 8.48, Hz, H-2', & H-6')

**IIIe IR (KBr) : 825 (1,4-disubstituted benzene ring), 1520 (C-N stretching), 1610 (>C=C>), 1625 (>C=N), 3030 (Ar C-H) stretching), 3260 (N-H Stretching) cm^{-1}

^{1}HNMR ($CDCl_3$) δ : 1.28 (3H, t, CH_3); 2.4 (1H, s, NH); 3.28 (2H, t, C_7 methylene proton) 3.7 (2H, q, t, C_6 methylene proton) , 4.2 (2H, q, CH_2, Proton of ethoxy group), 7.48 (1H, d, J = 8.49 H_Z, C3a-H), 7.80 (H, d, J = 8.50 H_Z, H-3' & H-5') , 7.85 (2H, d, J = 8.48, H_Z, H-2' & H-6')

Table 2: Fungicidal screening data of 3-(p-ethoxy)-cis-3.3a, 6.7-tetrahydro-2H-Imidazo[2,1-a] pyrazolo [3,4-d] thiazoles (III*a-l*)

Compd. No.	Average (%) inhibition against					
	Alternaria solanai at			*Puccinia recondita* at		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
IIIa	62	35	15	60	63	13
b	74	40	20	72	38	18
c	98	64	51	97	63	50
d	78	42	22	76	41	20
e	72	38	20	70	36	18
f	71	36	19	71	34	17
g	74	37	17	71	36	15
i	99	66	53	98	64	51
j	92	48	25	90	46	24
k	85	42	22	83	40	20
l	83	41	21	81	39	19
Dithane M-45	100	85	65	100	82	64

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REFERENCES

1. Hiral, Kenzi and Ucheda, Jpn Kokai Tokkyo Koho J.P. **264**: 888 (2002). *Chem. Abstr.,* **133**: 252452v (2000).
2. Li, Bin, Faming Zhugandi Shenging Gonghai Shuoming Shu, CNI, **325**: 849 (2001). *Chem. Abstr*., **138**: 153521s (2003).
3. Tinem Bart O.; Brand C. Hiden, Ceba Geigy, Switz A-G Ger. Offen (1996). *Chem. Abstr,* **125**: 142731n (1996).
4. Kuwano, Eiichi and Kamei Jpn Kokai Tokkyo Koho J.P. 1999, 158/56 (99, 758, 156), *Chem. Abstr.,* **131**: 58859s (1999).
5. Banoglu *et. al., J. Fac. Pharma.* **10**(1): (1993). *Chem. Abstr.,* **121**: 924 (1994).
6. Ding et al., Huaze Xuebao **60**(10): 1983-1898 (2002). (che) *Xexure Chubar, Chem. Abstr.,* **138**: 255166u (2003).
7. Yukimasa et al., Jpn Kokai Tokkyo koho J.P. 584 (9620, 684) (2002), *Chem. Abstr.,* **124**: 3432297d (1996).
8. Allan, C.F.H. Dens C.O., and J. Van Allan, *Org. Syn. Coll.*, **3**: 394 (1955).
9. Horsfall, J.G., *Bot. Rev.*, **357**: 11 (1945).