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Study of Some New Substituted Pyrazoline Derivatives As Fungicides

KEYWORDS

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ABSTRACT *A number of 7-Aroyl-4-methyl coumarino-[7,8-c]-1H-pyrazoline (3) have been prepared by the cyclo dehydration of 8-(Aroyl-hydrazino methyl)-7-hydroxy-4-methyl coumarin (2) which was prepared by the reaction of 7-hydroxy-4-methyl coumarin (1) , aroyl hydrazide and formaldehyde in presence of methanol. The title compounds have been evaluated for their anti fungal activity against Pyricularia oryzae, Sphaeotheca fuliginea, Phytopthora infestans and Pseudopernospora cubensis*

Introduction- Coumarin derivatives have been found to possess a wide range of biological properties[1-3]. A number of other coumarin derivatives have been synthesized as rodenticides[4-6], insecticides[7] and fungicides[8,9].

Similarly pyrazoline and its derivatives have been reported to exhibit fungicidal[10], bactericidal[11], herbicidal[12] and other biological activities[13-16].

Therefore it is thought of interest to combine the two above mentioned biolabile rings together in a molecular framework to see the additive effect of these rings towards the biological activities. The investigation was found to be of further interest because of compactness and planarity of such ring systems may be an additive factor for enhancing activities as it does with algicidal, herbicidal, fungicidal and inflammation inhibitory activities.

The required 7-hydroxy-4-methyl coumarins (1) were prepared following the literature method[17]. Reaction of these coumarins with aroyl hydrazide and formaldehyde in methanol furnished 8-(Aroyl-hydrazino methyl)-7-hydroxy-4-methyl coumarin (2), which on cyclo- dehydration furnished the title compounds (3). The details of which are given in Scheme-I and Table-I.

Materials and method- Procedure for one typical case for each step has been discussed. Melting points were taken in open capillaries and were uncorrected. IR spectra were recorded in KBr on a Perkin –Elmer 881 Spectrophotometer (υ_{max} in cm^{-1}), ^1H NMR spectra in DMSO-d6 on a Perkin-Elmer R-32(400 MHz) Spectrophotometer using TMS as internal reference (chemical shifts in υ, ppm).

7-Hydroxy-4-methyl coumarin (1a)- This compound was prepared following the literature method16 by the condensation of ethyl acetoacetate (0.01 M) and resorcinol(0.01 M) in the presence of concentrated sulphuric acid (150ml). The solid mass thus formed washed, dried and re-crystallized from aqueous ethanol, mp 187^{0}C, yield 66%.

8-(Aroyl-hydrazino methyl)-7-hydroxy-4-methyl coumarin(2a)- It was prepared by refluxing a mixture of 7-hydroxy-4-methyl coumarin (1a (0.01M), aroyl hydrazide (0.01M) and formaldehyde (0.012M) in methanol (50ml) for 3 hours. The solvent was removed and the reaction mixture was cooled and poured into water. The solid thus obtained was filtered, washed, dried and re-crystallized from aqueous ethanol, mp 120^{0}C, yield 69%.

Analysis: $C_{18}H_{16}N_2O_4$

Calcd: C 68.78; H 3.82; N 8.91 %.

Found: C 68.46; H 3.50; N 8.74%.

IR(KBr):3490(-OH), 3130(NH), 1660,1600(>C=O), 1570, 1430, 1380, (Aromatic ring);

^{1}HNMR:2.3(s,3H, CH_3), 3.8(s,2H, CH_2),5.9 (s,IH,CH),6.4-6.8(m,7H,ArH), 7.1-7.4 (b,1H,NH).

Other compounds of this type were prepared similarly and recorded in Table-1

7-Aroyl-4-methyl coumarino-[7,8-c]-1H-pyrazoline (3a)- These compounds were prepared by making slurry of 8-(aroyl-hydrazino methyl)-7-hydroxy-4-methyl coumarin(2a) (0.01M) in sulphuric acid(0.01M) and leaving the reaction mixture overnight and then poured into cold water. The well stirred solution was neutralized with ammonia solution; the resulting precipitate was washed with water, dried and re-crystallized from aqueous ethanol, mp165^{0}C, yield 68%.

Analysis: $C_{18}H_{14}N_2O_3$

Calcd: C 70.58; H 4.57; N 9.15 %.

Found: C 70.90; H 4.29; N 9.02 %.

IR(KBr):3120 (NH), 1660,1600(>C=O), 1550,1500,1430,1380(Aromatic ring);

^{1}HNMR:2.3(s,3H, CH_3), 2.6(s,2H, CH_2),5.9 (s,IH,CH),6.5-6.8(m,7H,ArH), 7.3 (b,1H,NH).

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TABLE (1) Characterization data of the compounds (2) and (3)

Compd	R	Mp ^{0}C	Yield (%)	Mol. Formula	Analysis					
					Carbon (%)		Hydrogen (%)		Nitrogen (%)	
					Found	Calcd	Found	Found	Calcd	Found
2a	2-Cl	150	70	$C_{18}H_{15}N_2O_4Cl$	61.10	61.32	4.52	4.41	7.92	7.50
2b	4-Cl	165	67	$C_{18}H_{15}N_2O_4Cl$	61.10	61.32	4.52	4.41	7.92	7.50
2c	2,4-Cl_2	180	66	$C_{18}H_{14}N_2O_4Cl_2$	55.67	55.78	3.86	3.65	7.21	7.50
2d	3-CH_3	128	64	$C_{19}H_{18}N_2O_4$	67.52	67.75	5.32	5.54	8.13	8.35
2e	2-OH	170	67	$C_{18}H_{16}N_2O_5$	63.45	63.85	4.70	4.92	8.23	8.50
2f	4-OCH_3	135	66	$C_{19}H_{18}N_2O_5$	62.33	62.50	5.45	5.70	7.27	7.54
2g	4-NO_2	185	70	$C_{18}H_{15}N_3O_6$	57.00	57.42	4.50	4.72	10.50	10.40
3a	2-Cl	170	71	$C_{18}H_{13}N_2O_3Cl$	64.38	64.52	4.17	4.32	8.34	8.51
3b	4-Cl	178	66	$C_{18}H_{13}N_2O_3Cl$	64.38	64.52	4.17	4.32	8.34	8.51
3c	2,4-Cl_2	195	73	$C_{18}H_{12}N_2O_3Cl_2$	58.37	58.52	3.51	3.65	7.58	7.70
3d	3-CH_3	153	71	$C_{19}H_{16}N_2O_4$	71.25	71.50	5.00	5.20	8.75	8.90
3e	2-OH	140	67	$C_{18}H_{14}N_2O_4$	67.08	67.20	4.34	4.50	8.69	8.85
3f	4-OCH_3	148	64	$C_{19}H_{15}N_2O_4$	65.39	65.50	5.17	5.40	7.62	7.75
3g	4-NO_2	198	70	$C_{18}H_{13}N_3O_5$	59.68	59.76	4.18	4.35	10.98	10.72

Evaluation of fungicidal activity-The anti fungal activity was evaluated by agar plate technique against *Pyricularia oryzae, , Sphaeotheca fuliginea, Phytopthora infestans* and *Pseudopernospora cubensis* at concentrations 500 ppm and 100 ppm. The replications in each case were three. On the basis of growth recorded on 7th day of incubation the fungicidal activity of test compounds was calculated in terms of present inhibition of mycelial growth using the following formula.

$$\text{Present inhibition of mycelial growth} = \frac{c-t}{c}\times 100$$

Where c =Average diameter growth of the colony in control sets on 7th day of incubation.

t = Average diameter growth of the colony in treatment set on 7th day of incubation

Diameter growth=apparent diameter of the colony–diameter of colony of the inoculums

The percentage inhibitions of various compounds are recorded in table -2

TABLE (2) Anti Fungal Activity Data for Compounds (3)

Compd.	Average % inhibition after 7 days							
	Pyricularia oryzae		Sphaerotheca fuliginea		Phytoptho-ra infestans		Pseudoper-nospora cubensis	
	500 ppm	100 ppm	500 ppm	100 ppm	500 ppm	100 ppm	500 ppm	100 ppm
3a	82	68	83	69	82	68	84	69
3b	90	74	90	72	91	72	90	73
3c	93	76	92	75	93	76	93	76
3d	95	74	96	78	95	75	94	74
3e	93	72	94	76	94	77	93	72
3f	81	70	84	72	82	71	83	71
3g	90	78	88	72	87	70	89	72
Carben-dazim	100	89	100	88	100	89	100	88

Results and discussion-It is evident from the activity data that the all of the tested compounds have significant fungitoxicity at 500 ppm against all the fungi but their toxicity decreased considerably at lower concentration, although compounds having serial number 3b, 3c, 3d, 3e and 3g show greater fungicidal activity against all the organisms but the result are not very spectacular except for compounds 3c, 3d and 3e.

It is also evident from the fungicidal screening data of the tested coumarino-pyrazoline derivatives showed that, the most active compounds were 3c, 3d and 3e (>90%).

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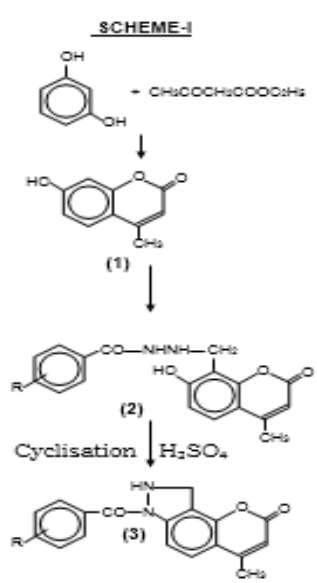

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References-

1. T.O. Soine, **J. Pharm. Sci.** 1964, **53**, 231.
2. T.R. Sechadri, **Proc. Nat. Int, Sci, India**, 1968, **35**, 94.
3. A.A. Dean, **J. Med. Chem.** 1983, **26**, 580.
4. J.A.O. Connor, **Use of blood anticogulants for rodent control, Research, London,** 1948, **1**, 334.
5. R.S.Overman and M.A.Stalmann, **J. Priol. Chem.**, 1944, **221**, 5.
6. M. Reiff and W. Weerman, **Acta Tropica**, 1957, **8**, 97.
7. E.Nerger **USP, 4, 078, 079** (1976); **Chem. Abstr.** 1978, **89**, 43114.
8. S. Giri and Y. Singh, **Bokin Bobai**, 1978, **6**, 340.
9. S. Nakajima and S. Sughyama, **Org. Prep. Proced, Int,** 1979, **11**, 77.
10. G. Kleefeld and Stefan Dutzmam (Bayer. A.G.) **Eur. Pat. Appl., EP 409, 026 (Cl, Co; D231/06)**, 1991; **Chem. Abstr.**, 1991, **115**, 29317n.
11. L.M. Pulido and J.G. Fenyer, **(Buckman Laboratories International Inc.); Chem. Abstr.**, 1997, **116**, 146150j).
12. F. Coderbaum, H.G. Bruner and M. Boeger (Ciba-Geigy AG) PTC. **Int. Appl. WO 9216, 510 (Cl,077,231/32)** 1992; **Chem. Abstr.**, 1993, **118**, 38935b.
13. H. Suzuki, T. Takeyama, M. Hanaue, H. Oye, M. Nakayama and T. Its (Neran Chemical Industries Ltd.) **Jpn. Kokai Tokkyo Koho JP 04/316559, 92, 316, 559)** Cl (07 D231/14) 1992; **Chem. Abstr.**, 1993, **118**, 213066t.
14. R.I. Al-Bayati, A. A. H. Al-Aminery and Y.K. Al-Majedy, **African J. of Pure & Appl. Chem.**, 2010, **4(6)**, 74-86.
15. C.P.K. Reddy, V.M. Gond, N. Sreenivasulu and R. Prasad, **Int. J. of Pharm, World Res.**, 2010, **1(2)**, 1-19.
16. J. Huang, H.M. Ayad and P R Temmons (Rhone Poulene Agrochemic) **Eur. Pat. Appl. EP, 511, 845** (Cl, Co7D231/44) 1992; **Chem. Abstr.**, 1993, **118**, 101949b.
17. Pechmann and Dueberg, **Ber.**, 1883, **16**, 2119