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Synthesis and study of chlorosubstituted 4-aroyl/alkoyl pyrazoles and isoxazoles and their impact on phytotic growth of some vegetable crop plants

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ABSTRACT

Aroyl/alkoylacetophenones (2a-b) undergoes intramolecular claisen condensation to form 1-(2'-hydroxy-3',5'-dichlorophenyl)-3-aryl/alkyl-1,3-propanediones (4a-b) which on treatment with aromatic and aliphatic aldehydes in ethanol containing little piperidine forms 3-aroyl/alkoylchromanones (5a-b) subsequently 3-aroyl/ alkoylchromones (6a-b). 3-Aroyl/alkoylchromones (6a-b) on treatment with Ph.NH.NH$_2$.HCl in DMSO containing small amount of piperidine gave 4-aroyl/alkoylpyrazoles (7a-b).So also 3-aroyl/alkoylchromones (6a-b) on treatment with NH$_2$OH.HCl in DMSO containing a small amount of piperidine gave 4-aroyl/ alkoylisoxazoles (8a-b). The structures of newly synthesized chlorosubstituted 4-aroyl/alkoyl- pyrazoles (7a-b) and 4-aroyl/alkoylisoxazoles (8a-b) were elucidated on the basis of molecular weight, elemental analysis and their spectral data.

Keywords: Chromanones, Chromones, Pyrazoles, Isoxazoles.

INTRODUCTION

Pyrazoles and isoxazoles are well known and important nitrogen containing five membered hetero-cyclic compounds. Various methods have been worked out for their synthesis.[1-7] Derivatives of pyrazoles and isoxazoles have played a crucial role in the history of heterocyclic chemistry and have been extensively instrumental as pharmacophores and synthons in the field of organic chemistry and drug designing. Several pyrazole derivatives have been found to possess significant activities such as antimicrobial[8], antibacterial[9], 5-α-red-uctase inhibitor[10], antiproliferative[11], antiparasitic[12], herbicides[13]. A good number of pyrazoles have also been reported to have interesting biological activities like antiinflammatory[14], antimicrobial[15] and antiprotozoal[16-17] which render them valuable active ingredients of medicine and plant protecting agents.

MATERIALS AND METHODS

Synthesis of 2-hydroxy-3, 5-dichloroacetophenone (2b):
2-Hydroxy-5 chloroacetophenone (3g) was dissolved in acetic acid (5ml), sodium acetate (3g) was added to the reaction mixture and chlorine in acetic acid reagent (40ml) was added drop wise with constant stirring. The mixture was allowed to stand for 30 minutes. Then it was poured into cold water. A pale yellow solid product thus separated was filtered and crystallized from ethanol to get the compound (2b).

Synthesis of 2-benzoyloxy-3, 5-dichloroacetophenone (3a):
A mixture of 2-hydroxy-3, 5-dichloroacetophenone (0.04 mol) and bezoyl chloride (0.05 mol) was dissolved in NaOH (10%) (30 ml). The reaction mixture was shaken for half an hour, the product thus obtained then filtered, washed with $NaHCO_3$ (10%) and purified by recrystallization with ethanol to get 2-benzoyl-3, 5-dichloroacetophenone (3a).

Synthesis of 2-anisoyloxy-3, 5-dichloroacetophenone (3b):
A mixture of 2-hydroxy-3, 5-dichloroacetophenone (2b) (0.04 mol) and anisic acid (0.05) kept suspended in dry pyridine (30ml) for 30 min. To this $POCl_3$ (3ml) was added drop wise with constant stirring and occasional cooling. The reaction mixture was kept overnight and then worked up by dilution and acidification with ice cold HCl (50%) to neutralize pyridine. The solid product thus obtained then filtered and washed with $NaHCO_3$. It was purified by crystallization from ethanol to get 2-anisoyloxy-3, 5-dichloroacetopheonone (3b).

Synthesis of 1-(2-hydroxy-3, 5-dichlorophenyl)-3-phenyl-1, 3-propanedione (4a):
A mixture of 3a 1-(2-hydroxy, 3, 5-dichlorophenyl)-3-phenyl-1, 3-propanedione and dry pyridine was warmed up to 60 ^{0}C and pulverized KOH was added slowly with constant stirring and then kept it for overnight. After digestion the reaction mixture was acidified with cold 1:1 dil. HCl. The product thus obtained was filtered and washed with $NaHCO_3$ solution. Finally it was crystallized from ethanol.

Similarly 4b was also synthesized.

1-(2-Hydroxy-3, 5-dichlorophenyl)-3-(4'-methoxyphenyl)-1,3-propanedione (4b):

Synthesis of 3-benzoyl-2-(2'-propoyl)-6, 8-dichlorochromanone (5a):
A mixture of 1-(2-hydroxy-3, 5-dichlorophenyl-3-phenyl-1,3-propanedione (4a) (0.01 mol) and propionaldehyde (0.02 mol) was refluxed in DMSO (25 ml) and piperidine (0.5ml) for 15-20 minutes. After cooling the reaction mixture was acidified with dil. HCl (1:1) and the product thus separated was crystallized from ethanol to get the compound 5a.

Synthesis of 3-anisoyl-2-(2'-propoyl)-6, 8-dichlorochromanone (5b):
Similarly 5b was synthesized with minor changes in the reaction conditions i.e. reflux time, amount of solvent etc.

Synthesis of 3-benzoyl-2-(2'-propoyl)-6, 8-dichorochromone (6a):
3-Benzoyl-2-(2'-propyl)-6,8-dichlorochromanone (5a) (0.01 mol) was refluxed for 10 min. with a crystal of Iodine in DMSO (20ml). After cooling the reaction mixture was diluted with water. The solid product thus separated, filtered, washed with sodium thiosulphate solution and crystallized with ethanol.

Synthesis of 3-anisoyl-2-(2'-propoyl)-6,8-dichlorochromone (6b):
Compound 6b was synthesized in similar way as 6a.

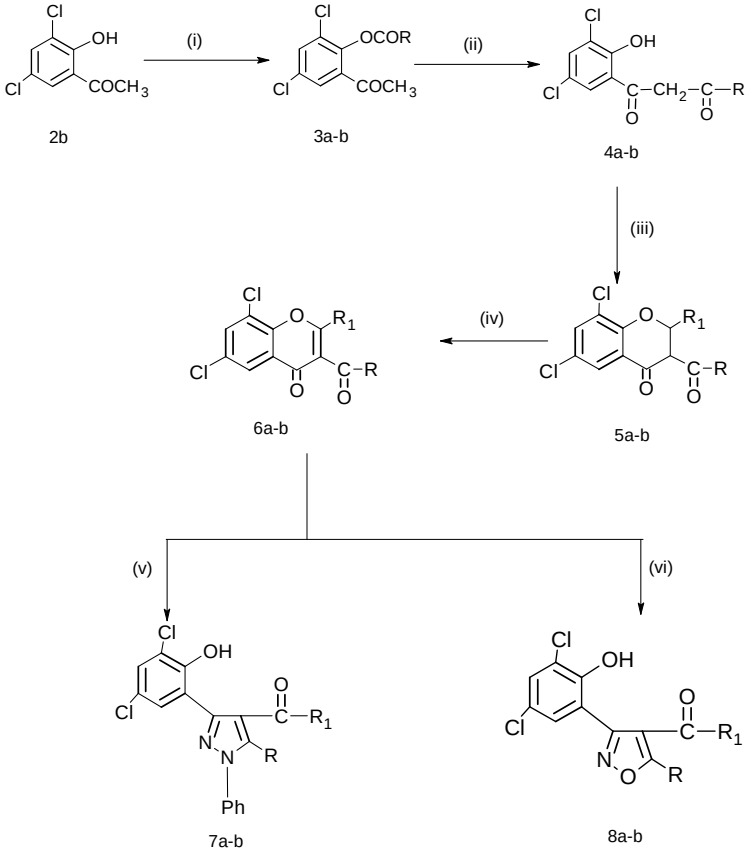
Synthesis of 3-(2-hydroxy-3,5-dichlorophenyl)-4-benzoyl-5-(2'-propoyl)-1-phenylpyrazole (7a):
A mixture of 3-benzoyl-2-(2'-propyl)-6,8-dichlorochromanone (6a) (0.01 mol) and Ph.NHNH$_2$HCl (0.02 mol) was refluxed in DMSO (20ml) containing 1 ml piperidine for 1.5 hours. After cooling, the reaction mixture was acidified with dil. HCl. The solid product thus obtained was filtered and washed with sodiumbicarbonate (5%) solution. It was crystallized from ethanol to get the compound 7a.

Synthesis of 3-(2-hydroxy-3,5-dichlorophenyl)-4-anisoyl-5-(2'-propoyl)-1-phenylpyrazole (7b):
Compound 7b was synthesized in similar way as 7a.

Synthesis of 3-(2-hydroxy-3,5-dichlorophenyl)-4-benzoyl-5-(2'-propoyl)isoxazole (8a):
The mixture of 6a (0.01 mol) and NH$_2$OH.HCl (0.02 mol) was refluxed in DMSO (20ml) containing 0.5ml of piperidine for 1.5 hours. After cooling the reaction mixture was acidified with dil. HCl. The solid product was washed with NaHCO$_3$ and then crystallized from ethanol to get 8a.

Synthesis 3-(2-hydroxy-3,5-dichlorophenyl]-4-anisoyl-5-(2'-propoyl) isoxazole (8b):
Compound 8b was synthesized in similar way as 8a.

The synthetic route for obtaining the final products is presented in **scheme-I**.



Scheme – I

Physical and analytical data of the newly synthesized compounds are summarized in the following table 1.

Table 1. Physical and analytical data of the newly synthesized compounds

Compounds	Mol. Fourmula	Mol Wt.	R	R'	Yield %	M.P. ^{0}C	Found (Calcd.)%	
							C	N
2b	$C_8H_6Cl_2O_2$	205			75	53		
3a	$C_{15}H_{10}O_3Cl_2$	308	$-C_6H_5$		75	65	58.44	
3b	$C_{16}H_{12}O_4Cl_2$	338	$-C_6H_5$-OCH_3		75	113	56.80	
4a	$C_{15}H_{10}O_3Cl_2$	308	$-C_6H_5$		75	113	58.44	
4b	$C_{16}H_{12}O_4Cl_2$	338	$-C_6H_5$-OCH_3		60	113	56.80	
5a	$C_{19}H_{16}O_3Cl_2$	362	$-C_6H_5$	$-CH_2-CH_2-CH_3$	70	110	70.00	
5b	$C_{20}H_{18}O_3Cl_2$	376	$-C_6H_5$-OCH_3	$-CH_2-CH_2-CH_3$	60	112	61.22	
6a	$C_{19}H_{14}O_3Cl_2$	360	$-C_6H_5$	$-CH_2-CH_2-CH_3$	60	110	63.33	
6b	$C_{20}H_{16}O_3Cl_2$	374	$-C_6H_5$-OCH_3	$-CH_2-CH_2-CH_3$	60	90	64.66	
7a	$C_{25}H_{20}O_2N_2Cl_2$	450	$-C_6H_5$	$-CH_2-CH_2-CH_3$	60	147	66.66	6.22
7b	$C_{26}H_{22}O_3N_2Cl_2$	480	$-C_6H_5$-OCH_3	$-CH_2-CH_2-CH_3$	60	210	65.00	5.83
8a	$C_{19}H_{15}O_3NCl_2$	375	$-C_6H_5$	$-CH_2-CH_2-CH_3$	62	180	60.80	3.73
8b	$C_{20}H_{17}O_4NCl_2$	406	$-C_6H_5$-OCH_3	$-CH_2-CH_2-CH_3$	60	196	59.11	3.44

Growth promoting effect of the titled compounds on some *vegetable crops* –

Pregerminated seeds of some vegetable crop plants viz. *Momordica charantia L, Lagenaria Siceraria, Luffa Cylindrica L, Benincasa hispida* have procured from Horticulture Department of PKV, Amravati. The beds of black cotton soil 2.5 x 2.5 meter size were prepared on an open field.

The seeds of all four species under examination were sowed in these beds separately by conventional methods. Beds were irrigated as and when required by tap water. The plants of each bed were divided into to two groups (A) and (B). The group (A) plants were kept unsprayed and termed as control group whereas the plants from group (B) designated as treated group. The plants were sprayed with the test compounds before sowing [Seed treatment] and after germination to screen their growth promoting impact on the test plants.

Table 2: Effect of newly synthesized compound (7a) on growth of vegetable crops

Name of test compound	Periodicity of the observation (days)	Vegetable Crops															
		Momordica charantia Bitter gurad - (Karela)				*Lagenaria Siceraria Snake guard - (Lavki)*				*Luffa cylindrica Sponge guard - (Gilke)*				*Benincasa hispida Pumpkin - (Kohle)*			
		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves	
		C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
3-(2-Hydroxy 3,5-dichlorophenyl)-4-benzoyl-5-(2'-propyl)-1-phenyl pyrazole (7a)	15	5	6	5	7	3	5	3	6	4	3	4	5	7	7	4	3
	30	6	8	6	8	4	6	4	7	5	4	5	8	8	8.2	5	6
	45	7.2	8.5	7	9	5	8	6	9	7	6	6	10	10	12	6	8
	60	8.5	10	10	12	8	10	8	12	10	10	8	12	11	13	8	10
	75	8.7	12	12	13	9	10.2	9	13	10.5	10.3	9	13	11.2	13.7	10	11
	90	9.2	14	14	15	10	11	12	15	11	12.5	10	15	12.6	15.2	12	14

The spraying solution of newly synthesized chlorosubstituted heterocyclic compounds pyrazoles and isoxazoles have been prepared in dioxane (0.01 dilution) separately and sprayed at fortnightly intervals [15,30,45,60,75 and 90 days] on vegetable crop plants. The plants were carefully examined and number of leaves and heights of their shoot were recorded. The data obtained subjected to analysis of growth parameter.

Table 3: Effect of newly synthesized compound (7b) on growth of vegetable crops

Name of test compound	Periodicity of the observation (days)	Vegetable Crops															
		Momordica charantia Bitter gurad - (Karela)				*Lagenaria Siceraria Snake guard - (Lavki)*				*Luffa cylindrica Sponge guard - (Gilke)*				*Benincasa hispida Pumpkin - (Kohle)*			
		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves	
		C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
3-(2-Hydroxy 3,5-dichlorophenyl)-4-anisoyl-5-(2'-propyl)-1-phenyl pyrazole (7b)	15	6	7	3	5	3	5	3	7	3	5	4	4	3	6	2	4
	30	8	9	5	7	5	7	5	9	4	6	5	5	4	7	4	6
	45	10	12	8	9	7	8	6	10	5	8	6	8	5	8	8	10
	60	12	15	10	13	8	10	8	12	8	10	9	10	6	10	9	12
	75	13	16	11	14	9	11	9	13	9	11	10	11	7	12	10	14
	90	15	17	13	15	10	13	10	15	10	14	11	13	9	14	12	16

Table 4: Effect of newly synthesized compound (8a) on growth of vegetable crops

Name of test compound	Periodicity of the observation (days)	Vegetable Crops															
		Momordica charantia Bitter gurad - (Karela)				*Lagenaria Siceraria Snake guard - (Lavki)*				*Luffa cylindrica Sponge guard - (Gilke)*				*Benincasa hispida Pumpkin - (Kohle)*			
		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves	
		C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
3-(2-Hydroxy 3,5-dichlorophenyl)-4-benzoyl-5-(2'-propyl) isoxazole (8a)	15	5	6	4	7	4	5	4	6	4	4	3	4	7	6.5	4	4
	30	6	12	7	10	12.5	15	5	8	12	14	7	9	20	24.5	5	6
	45	10	15	10	14	14	19	8	11	14	18	9	11	24	28	9	10
	60	40	45	15	24	15	18	8	10	18	20	8	9	25	32	8	9
	75	42	46	17	27	17	20	10	15	22	25	10	12	27	35	10	14
	90	44	48	18	30	18	22	12	19	25	30	12	15	30	37	12	18

Table 5: Effect of newly synthesized compound (8b) on growth of vegetable crops

Name of test compound	Periodicity of the observation (days)	Vegetable Crops															
		Momordica charantia Bitter gurad - (Karela)				*Lagenaria Siceraria Snake guard - (Lavki)*				*Luffa cylindrica Sponge guard - (Gilke)*				*Benincasa hispida Pumpkin - (Kohle)*			
		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves		Shoot Height		No. of Leaves	
		C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
3-(2-Hydroxy 3,5-dichlorophenyl)-4-anisoyl-5-(2'-propyl) isoxazole (8b)	15	6	7	4	5	3	5	3	7	3	5	4	4	4	6	5	6
	30	5	9	8	10	11	12	5	8	11.2	13.2	5	6	11	13	5	6
	45	9	10	9	11	12	14	6	9	13	15	6	8	12.5	14	6	8
	60	14	18	12	15	14	16	8	10	15	18	8	12	13	15	8	12
	75	16	20	14	18	17	20	10	14	16	20	10	15	15	17	10	14
	90	18	22	16	20	19	24	12	18	18	22	12	17	18	22	12	18

RESULTS AND DISCUSSION

When the first comparison of morphological character was made between those of treated and controlled group plants, it was interesting to note that all the treated plants exhibited remarkable shoot growth and considerable increase in the number of leaves as compared to the untreated ones. When all the treated plants were compared among themselves, it was distinctly observed that the change which is dominant in *Momardica charantia L.* than *Benincasa hispida*. In the

first interval of 15 to 30 days the growth gradually increases but after 30 days it shows a considerable increase.

REFERENCES

[1] E. Herman, and J. Gablis, *Cancer Chemother Rept*., **1961**, 14, 85.
[2] I. I. Grandberg, S. N. Milovanovan, A. N. Kost, and I.T. Netto, *Chem. Abstr*., **1962**, 56, 1968.
[3] R.H. Wiley, Ed. *Pyraozles, Pyrazolines, Pyrazolidines, Indazoles* and *Condensed Rings*; In *The Chemistry of Heterocyclic Compounds*; Weiss- berger, A., Ed. Interscience publishers; New York, **1967**, Vol. 22, p 180.
[4] T Norris, R Colon-Cruz and D.H.B. Ripin *Org Biomol Chem.*, **2005**, 3, 1844.
[5] J. Elguero, In *Comprehensive Heterocyclic Chemistry II*, Katritzky, A.R., Ress, C.W., Seriven, E.F. Eds; Pergamon Press: Oxford, **1996**; Vol. 3, p.1.
[6] A.J. Levai, *Heterocycl. Chem.*, **2002**, 39, 1.
[7] O. Ruhoglu, Z. Ozdemir, U.Calis, B.Gumusel and A.A. Bilgin, *Arzneim Forsch.*, **2005**, 55 (8), 431.
[8] K. Ramalingham, G.X. Thyvekikakath, K.D. Berlin, R.W. Chestnut, R.A. Brown, N. N.Durham, A.E. Ealick, D.Vander Helm, *J. Med. Chem.* **1977**, 20847.
[9] D. Azarifar and S.Maseud, *Molecules*, **2002**, 7, 85.
[10] Amr AEI GES, N. A. Abdel-Latif and M. M. Abdlla, *Acta Pharm*, **2006**, 56, 1203.
[11] S. Chimichi, M.Boccalini, M.M.M. Hassan, G.Viola, Dall' Acqua F & M.Curini, *Tetrahedron* **2006**, 62, 90.
[12] T.A. Henry, *The Plant Alkoloids*, Anmol Publicaion Pvt. Ltd., **1999**.
[13] Kobayashi, Hisafumi, Kato, Motto; Nitani, Fumio, *Chem, Abstr* 1989, 106 297008/g.
[14] A. Nugent Richard, Marphy Meghan et. al., *J. Med. Chem.* **1993**, 36 (1) 134.
[15] S.B. Bhawasar, V.P. Chavan, A.S. Mane and M.S. Shingare, *Indian J. Heterocycl. Chem.* **1999**, 9, 135.
[16] M.A. Hantoon, Minnesota *Medicine*, **2001**, 84, 102.
[17] X. Zhang, Li X., G.F. Allan and T. Sbriscia, *J. Med. Chem*. **2007**, 50 (16), 3857.