International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.5, No.2, pp 420-425, April-June 2013

Synthesis, Characterization Of Some Novel Heterocycles And Their Growth Promoting Effect On Some Flowering Plants

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Abstract: The synthesis, spectral analysis and biological activities of some 4-phenyl-2-hydroxy-chlorosubstituted-2-imino-1, 3-thiazine with thiourea, phenyl thiourea and diphenyl thiourea have been carried out in three series. In series I we got 4-(2-hydroxy-3,5-dichlorophenyl)-6-(4-chlorophenyl)-2-imino-3,6-dihydro-1,3-thiazine (4a), 4-(2-hydroxy-3,5-dichlorophenyl)-6-(4-chlorophenyl)-2-imino phenyl -3,6-dihydro-1,3-thiazine (5a) and 4-(2-hydroxy-3,5-dichlorophenyl)-6-(4-chlorophenyl)-2-iminophenyl-6-hydro-3-phenyl-1,3-thiazine (6a) from 2-hydroxy-3,5-dichlorolphenyl-4-(4-chlorophenyl)-chalcone (3a) by the action of thiourea, phenylthiourea, diphenylthiourea. Initially the compound (3a) was synthesis from 2-hydroxy-3,5-dichloroacetophenone (2a) by the action of p-chlorobenzaldehyde in ethanol and 40% NaOH. Similarly (4b), (4c), (5b), (5c), (6b), and (6c) compounds were synthesized from the compounds (3b), and (3c) respectively. The compounds (3b) and (3c) were synthesized by the action of p-nitrobenzaldehyde and valeraldehyde respectively. All these compounds have been analyzed by UV, IR and NMR for structure assignment. The titled compounds were evaluated for their growth promoting activity on some flowering plants viz. *Papaver rhoeas, Dianthus chinensis, Candy tuft, Calendula officinalise, Gladiola tristis, Gaillardia.*
Keywords: Chalcone, thiazines, thiourea, phenyl thiourea, diphenyl thiourea, growth promoting activities.

Introduction:

Thiazine is a six member ring system, which contains two heteroatom (N & S) placed in the heterocyclic ring at 1, 3 positions. Many workers have synthesized different 1, 3-thiazines[1-6]. Thiazines are very useful units in the fields of medicinal and pharmaceutical chemistry and have been reported to exhibit a variety of biological activities such as blood platelet aggregation inhibitors[7], antipsychotic[8], antiviral and antimicrobial[9],. Moreover, thiazine nucleus is a pharmacophore of cephalosporin that occupy a very important place in the field of antibiotics and antifungal activity of thiazine nucleus is due to the presence of thiourea linkage in its structure. Chalcones and their analogues having α, β- unsaturated carbonyl system are very versatile substrates for the evolution of various reactions and physiologically active compounds. The reaction of thiourea with α, β- unsaturated ketones results in 1, 3- thiazine. It has been well focused that the presence of 4-phenyl chlorosubstituted moieties as well as 2-substituted amino group present in thiazine ring is an important structural feature, and the resulting molecule would exhibit promising biological activities[10]. In the present study, various 4-phenyl-2-substituted-imino-thiazines have been synthesized from Chalcones by using thiourea, phenylthiourea and diphenyl thiourea. The synthesized compounds were evaluated for their growth promoting activity on some flowering plants viz *Poppy, Pink, Candy tuft, Gaillardia Calendula, Gladiolus.*

Experimental:

All the glassware's used in the present work were of Pyrex quality. Melting points were determined in hot paraffin bath and are uncorrected. Purity of compounds was monitored on silica gel coated TLC plate. I.R. spectra were recorded on Perkin-Elmer spectrophotometer in KBr pellets, H^1NMR spectra on spectrometer in acetone with TMS as internal standard. U. V. spectra were recorded in nujol medium, on spectrophotometer. The analytical data of compounds were highly satisfactory. All the chemicals used were of analytical grade. All the solvents used were purified by standard methods. Physical characterization data of all the compounds are given in Table 1.

2'-Hydroxy 3', 5'-dichloroacetophenone (2a):

2'-Hydroxy 5'-chloroacetophenone (3g) was dissolved in acetic acid (5ml). Sodium acetate (3g) was added to the reaction mixture and then chlorine in acetic acid reagent (40ml, 7.5 w/v) was added drop wise with stirring. The temperature of the reaction mixture was maintained below 20°C. The mixture was allowed to stand for 30 minutes. It was poured into water with stirring. A pale yellow solid then obtained was filtered, dried and crystallized from ethanol.

Preparation of 2'-hydroxy 3', 5'-dichlorophenyl-4-(4-chlorophenyl)chalcone (3a):

2'-Hydroxy 3', 5'-dichloro acetophenone (3a), (0.1mol) was dissolved in ethanol (50 ml) and p-chlorobenzaldehyde (0.1mol) was added to the above solution and the mixture was heated to boiling aqueous sodium hydroxide solution (40%, 40 ml) was added drop wise with constant stirring. The mixture was stirred mechanically at room temperature for about half an hour and kept overnight. It was then acidified by hydrochloric acid solution (10%). The solid product separated was filtered, acid washed with sodium bicarbonate (10%) followed by water. The crude product was crystallized from ethanol acetic acid mixture (4a).

Similarly compounds 2'-hydroxy 3', 5'-dichlorophenyl-4-(4''-nitrophenyl)-chalcone (3b) and 2'-hydroxy 3', 5'-dichlorophenyl-4-butyl-chalcone (3c) were synthesized from the compound (2a) by the action of p-nitrobenzaldehyde and valeraldehyde respectively.

Preparation of 4-(2'-hydroxy-3'5'-dichlorophenyl)-6-(4''-chlorophenyl)-2-imino-3,6-dihydro-1, 3-thiazine (4a) :

2'-Hydroxy 3', 5'-dichlorophenyl-4-(4-chlorophenyl)-chalcone (3a**)** (0.01mol) dissolved in ethanol (25 ml) were added to thiourea (0.01M).To this aq. KOH solution (0.02mol) was added (prepared from KOH in small amount of distilled water). The reaction mixture was refluxed for 2.5 hours, cooled, diluted with water and acidified with conc. HCl. The product was filtered, dried and crystallized from ethanol (4a).

Similarly compounds 4-(2'-hydroxy-3'5'-dichlorophenyl)-6-(4''-nitrophenyl)-2-imino-3,6-dihydro-1,3-thiazine 4b and 4-(2'-hydroxy-3'5'-dichlorophenyl)-6-butyl-2-imino-3,6-dihydro-1, 3-thiazine (4c) were synthesized separately from the compounds (3b) and (3c) by the action of thiourea.

Preparation of 4-(2'-hydroxy-3',5'-dichlorophenyl)-6-(4''-chlorophenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine (5a) :

Synthesis of the compound (5a) was similar in manner as the compound (4a), but difference is that instead of thiourea, phenylthiourea was used.

Similarly compounds 4-(2-hydroxy-3',5'-dichlorophenyl)-6-(4''-nitrophenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine(5b) and 4-(2'-hydroxy-3',5'-dichlorophenyl)-6-butyl-2-iminophenyl-3,6-dihydro-1,3-thiazine (5c) were synthesized from the compounds (3b) and (3c) respectively by the action of phenylthiourea.

Preparation of 4-(2'-hydroxy-3',5'-dichlorophenyl)-6-(4''-chlorophenyl)-2-iminophenyl-6-hydro-3-phenyl -1,3-thiazine (6a) :

Synthesis of the compound (6a) was similar in manner as the compound (4a), but difference is that instead of thiourea, diphenylthiourea was used.

Similarly compounds 4-(2'-hydroxy-3',5'-dichlorophenyl)-6-(4''-nitrophenyl)-2-iminophenyl-6-hydro-3-phenyl-1,3-thiazine(6b) and4-(2'-hydroxy-3',5'-dichlorophenyl)-6-butyl-2-iminophenyl-6-hydro-3-phenyl-1,3-thiazine (6c) were synthesized from the compounds (3b) and (3c) respectively by the action of diphenylthiourea.

The newly synthesized compounds were characterized on the basis of elemental analysis, molecular determination, U.V., I.R., N.M.R. spectral data.

The UV, IR and NMR spectral data:

Compound (3a): I.R. (KBr): 3022 cm^{-1} (-OH phenolic), 2404.6(aliphatic –CH stretching). 1642 cm^{-1} (>C=O in ketone), 1574 cm^{-1} (-C-CH=CH asymmetric stretching), 1335.7 cm^{-1} (-OH bending in phenol) 766.4 cm^{-1} (C-Cl stretching), PMR δ 7.020 (d, 1H, -CH=C**H**-C_6H_5Cl); δ(acetone solvent) 7.050 (d,1H, -CO-C**H**=CH-); 7.5 to 8.348 (m, 6H, Ar-H); δ12.779 (s, 1H, Ar-OH); U.V.: 342 nm[11-12]

Compound (4a): I.R (KBr): 3317.7 (-OH phenolic), 3198.2 (N-H stretching); 1418 (OH bending in phenol); 758 (C-Cl stretching). PMR: δ 2.895 (d, 1H, >CH-S); δ 4.9 (s, 1H, Cyclic >NH) δ 5.318 (s, 1H, =NH), δ 5.4 (d, 1H, >C=CH), δ 7.377 to 8.101(m, 6H, Ar-H). UV: 230 nm

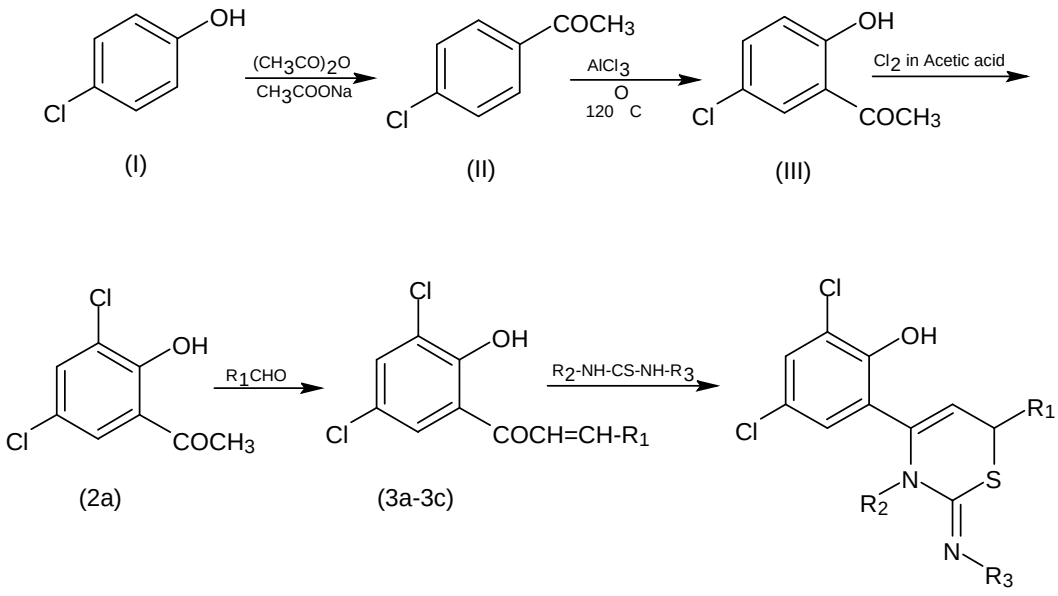
Compound (5a): IR (KBr): 3668 (-OH phenolic stretching); 2967 (-NH stretching); 1596.7(-C=N stretching); 1272 (-CN stretching); 768.6 (C-Cl stretching). PMR: δ 3.599 (d, 1H, >CH-S), δ 3.66 (s, 1H, Cyclic >NH), δ 5.4 (d, 1H, >C=CH), δ 6.908 to7.976 (m, 11H Ar-H). UV: 331 nm

Compound (6a): IR (KBr): 3026.7 (-OH phenolic stretching); 2925 (-NH stretching); 1642.9 (-C=N stretching); 1273(-CN stretching); 761.5 (C-Cl stretching). PMR: δ 2.9 (d, 1H, >CH-S), δ 5.739 (d, 1H, >C=CH),l δ 7.1 to 8.137(m, 16H, Ar-H); UV: 355 nm

Table No. 1: Characterization data of newly synthesized compounds:

Compound.	Molecular formula	M. P. in ^0C	% of Yield	% of element			
				C	H	N	S
2a	$C_8H_6O_2Cl_2$	54	75	46.75/46.82	2.85/2.93	-	-
3a	$C_{15}H_9O_2Cl_3$	170	80	54.80/54.97	2.60/2.75	-	-
4a	$C_{16}H_{11}OCl_3N_2S$	100	75	49.80/49.93	2.50/2.60	7.10/7.28	8.00/8,32
5a	$C_{22}H_{15}OCl_3NS$	110	80	57.28/57.32	3.00/3.04	6.00/6.08	6.78/6.95
6a	$C_{28}H_{19}OCl_3N_2S$	140	75	62.40/62.63	3.29/3.35	2.54/2.60	5.86/5.96
3b	$C_{15}H_9O_4NCl_2$	180	70	53.10/53.25	2.40/2.66	3.98/4..14	-
4b	$C_{16}H_{11}O_3N_3Cl_2S$	220	80	48.50/48.60	2.35/2.53	10.4/10.6	8.00/8.10
5b	$C_{22}H_{15}O_3N_3Cl_2S$	160	75	55.85/56.05	2.85/2.97	8.86/8.92	6.50/6.80
6b	$C_{28}H_{19}O_3N_3Cl_2S$	180	70	61.28/61.42	2.98/3,29	7.48/7.68	5.67/5.85
3c	$C_{13}H_{14}O_2Cl_2$	102	80	57.00/57.14	5.00/5,13	-	-
4c	$C_{14}H_{15}ON_2Cl_2S$	90	80	50.68/50.90	4.35/4.54	8.30/8.48	9.50/9.69
5c	$C_{20}H_{20}OCl_2N_2S$	126	80	59.09/59.11	4.50/4.67	6.58/6.89	769/7.88
6c	$C_{26}H_{23}OCl_2N_2S$	92	70	64.62/64.73	4.63/4.77	5.69/5.80	6.38/6.63

Scheme



Where R= C_6H_5-NO_2, C_6H_5-Cl, $(CH_2)_3$-CH_3

1. For 4a,4b and 4c : R_2=R_3= H
2. For 5a,5b and 5c : R_2= H, R_3=C_6H_5-
3. For 6a, 6b and 6c: R_2=R_3= C_6H_5-

Growth Promoting Effect On Some Flowering Plants:

The experimental set up of the study was divided into, i) Seed Treatment ii) Field Experiment

i) Seed Treatment:

With a view to safeguard dormant seed's potential from harmful external agencies, the seed of the test plants were treated by test compounds before sowing.

ii) Field Experiment:

Pre-germinated quality seeds of *Poppy, Pink, Candy tuft, Gaillardia Calendula, Gladiolus* were procured from genuine agricultural agencies.

The beds of black cotton soil, 2.5 x 2.5m size were prepared on an open field. The sowing of seeds of all six flowering plants under examination were done in beds and in earthen pots separately by conventional methods and irrigated as and when required.

The plants from each bed and pot were divided into two groups i.e. A and B which were designated as *'control'* and *'treated'* group plants respectively.

The plants from group B were sprayed with the solution of test compounds at fortnightly intervals. The field experiments were conducted to compare the treated plants of group B with untreated plants of controlled group A. In this context, the observation were recorded on 15, 30, 45, 60, 75 and 90 days after sowing; corresponding to early vegetative, late vegetative, flowering, pod filling and pod maturation stages, with special reference to number of leaves and height of shoots,

The results of field's experiments with test compounds are tabulated in the following tables 2.

Table 2. Activity of the test compounds (3b), (4b), (5b), (6b)

Periodicity of the observation (in days)	Poppy (*Papaver rhoeas)*				Calendula (*Calendula officinalise)*				Gladiolus (*Gladiola tristis)*				*Gaillardia (Gaillardia aristata)*				Pink (*Dianthus chinensis)*				Candytuft (*Iberis* sp)			
	Shoot height		No. of leaves		Shoot height		No. of leaves		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	C	T	C	T	C	T	C	T
Activity of the Test compound 2-Hydroxy-3', 5'-dichlorophenyl-4-(4''-nitrophenyl) chalcone (3b)																								
15	3	2	9	6	2	2	9	6	2	3	1	1	4	3	4	4	2	4	4	6	3	3	9	10
30	7	5	15	11	4	8	18	30	6	5	2	2	6	6	15	15	5	9	10	16	6	6	15	25
45	10	9	20	15	8	13	30	60	10	9	4	3	8	8	30	35	7	15	15	25	8	10	45	60
60	12	12	22	25	10	17	55	100	15	16	5	5	12	12	50	76	10	17	25	34	12	14	60	90
75	16	15	30	45	13	22	80	150	20	21	6	5	16	18	70	105	13	19	34	65	15	17	100	115
90	20	20	50	70	15	24	100	190	22	23	6	5	20	24	105	165	18	21	50	90	28	20	130	188
Activity of the compound 4-(2'-Hydroxy-3',5'-dichlorophenyl)-6-(4''-nitrophenyl)-2-imino-3,6-dihydro-1,3-thiazine (4b)																								
15	3	4	9	15	2	3	9	9	2	3	1	1	4	3	4	4	2	3	4	6	3	3	9	14
30	7	8	15	23	4	7	18	30	6	5	2	2	6	7	15	18	5	7	10	16	6	5	15	27
45	10	12	20	36	8	12	30	55	10	9	4	2	8	10	30	32	7	15	15	25	8	10	45	53
60	12	18	22	65	10	18	55	95	15	13	5	3	12	14	50	65	10	18	25	53	12	13	60	85
75	16	22	30	90	13	24	30	120	20	19	6	3	16	20	70	110	13	20	34	89	15	17	100	130
90	20	28	50	140	15	26	100	165	22	23	6	3	20	24	105	145	18	23	50	100	18	21	130	200
Activity of the compound 4-(2'-Hydroxy-3',5'-dichlorophenyl)-6-(4''-nitrophenyl)-2-imino-phenyl-3,6-dihydro-1,3-thiazine (5b)																								
15	3	5	9	7	2	4	9	10	2	3	1	2	4	4	4	6	2	3	4	5	3	5	9	6
30	7	6	15	13	4	6	18	20	6	5	2	3	6	8	15	15	5	6	10	11	6	8	15	13
45	10	10	20	20	8	10	30	38	10	9	4	4	8	12	30	38	7	9	15	20	8	12	45	38
60	12	15	22	54	10	13	55	67	15	16	5	5	12	14	50	50	10	13	25	36	12	15	60	60
75	16	20	30	80	13	17	80	150	20	21	6	5	16	18	70	95	13	16	34	59	15	20	100	95
90	20	24	50	130	15	23	100	206	22	23	6	5	20	23	105	160	18	21	50	93	18	21	130	160
Activity of the compound 4-(2'-Hydroxy-3',5'-dichlorophenyl)-6-(4''-nitrophenyl)-2-imino-phenyl-6H-3-phenyl-1,3-thiazine (6b)																								
15	3	2	9	8	2	3	9	11	2	2	1	2	4	3	4	5	2	1	4	6	3	4	9	8
30	7	4	15	12	4	5	18	20	6	7	2	3	6	5	15	13	5	3	10	15	6	6	15	25
45	10	10	20	25	8	13	30	30	10	13	4	3	8	7	30	20	7	6	15	30	8	10	45	60
60	12	15	22	35	10	18	55	50	15	17	5	4	12	12	50	40	10	9	25	50	12	13	60	100
75	16	18	30	48	13	20	80	80	20	22	6	4	16	16	70	74	13	11	34	70	15	18	100	169
90	20	20	50	60	15	22	100	120	22	24	6	4	20	21	105	125	18	14	50	96	18	24	130	210

Note: C= Control, T= Treated

Results And Discussion:

The synthesized compounds were screened for their growth promoting activity on some flowering plants. The plants used were *Poppy, Pink, Candy tuft, Gaillardia Calendula, Gladiolus.* The efforts have been made to examine and analyze the morphology of treated plants.

When the comparison of morphological characters was made between those of treated and control groups plants, it was interesting to note that all the plants exhibited significant shoot growth, and considerable increase in the number of leaves as compared to those of untreated ones.

Acknowledgement:

The authors are thankful to SAIF, CDRI, Lucknow for providing the spectral data. I am also thankful to the eminent faculty members of Dr. P. D. K. V. Akola, Dr. R. M. Gade, Professor, Department of Plant Pathology, Mrs. M. S. Gaikwad, Senior Research Asstt., Department of Plant pathology, Dr. Paithankar, Assit. Prof., Department of Horticulture, Dr. Ashish U. Nimkar Asst, Prof., Department of forestry for providing the necessary help for the completion of interdisciplinary part of the present work.

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