JOURNAL OF CRITICAL REVIEWS

ISSN-2394-5125 VOL 7, ISSUE 3, 2020

NOVEL SYNTHESIS OF CHLOROSUBSTITUTEDPYRAZOLINESAND ITS ANTIBACTERIAL ACTIVITIES.

S. P. Rathod*[1]and R.T.Parihar[2]

[1*]Department of Chemistry, G. S. G. College, Umarkhed (MS), India.
[2]Department of Chemistry, Vidnyan College,Malkapur (MS), India.
email:rathodsp.gsg@gmail.com

***Corresponding Author:** S. P. Rathod
*Department of Chemistry, G. S. G. College, Umarkhed (MS), India.

Abstract:
The synthesis, spectral analysis and effect on some crop plants by some 4-Aroylpyrazolineswith 3- aroylflavone on treatment with phenylhydrazinehydrochloride in presence of peridine.We got two series while carried out in different aromatic acids. In series, we got 3-(2-hydroxy-3,5-dichlorophenyl)-4-anisoyl-5-(3-nitro phenyl) pyrazoline and 3-(2-hydroxy-3,5-dichlorophenyl)-4-benzoyl-5-(3'-nitrophenyl) 1-phenyl pyrazoline. It has been revealed that, the use of piperidine in DMSO as the solvent in the above reaction influences the rate of the reaction and also the yield of the products.. All these compounds have been analyzed by UV, IR and NMR for structure. The newly synthesized chlorosubstituted pyrazoline were studied.

Kewords; Pyrazoline, Antibacterial activities, 3- Aroylflavone .

INTRODUCTION:

Pyrazolines is a five membered heterocyclic compound containing both N nitrogen atoms in the 1,3 positions placed in the heterocyclic ring. Many workers have synthesized different Pyrazoline[1-7]. Heterocyclic compounds are very useful units in the fields of medicinal and pharmaceutical chemistry and have been reported to exhibit a variety of biological activities [8-13]. 3-aroylflavone on treatment with phenylhydrazinehydrochloride. It has been revealed that, the use of piperidine in DMSO as the solvent in the above reaction influences the rate of the reaction and also the yield of the products. 3-aroylflavone on treatment with $NH_2OH.HCl$ to gives final product. It has been well focused that, the presence of chlorosubstituted moieties is an important structural feature also, the present work deals with the study of microbial activitieson crops and Human pathogens.

Experimental:

All the glassware's used in the present work were of Pyrex quality. Melting points were determined in open capillary and are uncorrected. Purity of compounds was monitored on silica gel coated TLC plate. The IR spectra were recorded on `Perkin-Elmer 202` Infra red spectrophotometer 1310. The UV-VIS spectra were recorded on Systronics 119 spectrophotometer. The PMR spectra were recorded on Varian Mercury YH - 300 spectrometer in $CDCl_3$.. 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.
The synthetic methods used in present work are given below along with their UV, IR and NMR data.

2-Hydroxyacetophenones (2) :

2-Hydroxy-5-chloroactophenon(2a), m.p.56^{o}C and2-hydroxy-3, 5-dichloroacetophenone, (2b), m.p. 53^{o}C were used as starting materials. The former was prepared by known method while the later was prepared by a new method invented by Rajput et al.

Preparation of 2-hydroxy-3,5-dichloroacetophenone (2b):

2-Hydroxy-5-choloroacetophenone (3g) was dissolved in acetic acid (5ml). Sodium acetate (3g) was added to the reaction mixture and then chlorine in acetic acid reagent (20ml) (7.5 w/v) was added drop wise with stirring. The temperature of the reaction mixture was maintained below 20^{o}c. The mixture was allowed to stand for about 30 minutes. Finally it was poured into water with stirring. The pale yellow solid product thus separated was filtered and crystallized from ethanol, m.p. 53^{o}C yield 1.5g.

IR (KBr): 3040 (-OH phenolic stretching); 1660 (>C=O stretching); 1345 (-OH bending in phenol); 650 (C-Cl stretching).

PMR: 2.60 (s, 3H, -ArOCH$_3$); 7 to 8 (s,2H, -ArH); 12.11 (s, 1H, Ar-OH).

UV: 346nm.
Scheme-1
Preparation of 2-benzoyloxy -3, 5-dichloroacetophenone (3a) :
2-Hydroxy-3,5-dichloroacetophenone (0.04 mol) and benzoyl- chloride (0.05mol) were dissolved in NaOH (10%) (30ml). The reaction mixture was shaken for about half an hour. The product thus separated was filtered, washed with water followed by sodium bicarbonate (10%) washing and then again with water. The solid product was crystallized from ethanol to obtain 2-benzoyloxy-3,5-dichloroacetophenone (3a), m.p.66^{o}C, yield 76%.

IR (KBr): 3040 (-OH phenolic stretching); 1660 (>C=O stretching); 1345 (-OH bending in phenol); 650 (C-Cl stretching).

PMR: 2.60 (s, 3H, -ArOCH$_3$); 6.8 to 7.64 (m,2H, -ArH); 12.7 (s, 1H, Ar-OH).
UV: 346 nm.

Preparation of 1-(2-hydroxy-3,5-dichlorophenyl)-3-phenyl-1,3-propane-dione (4a):
2-Benzoyloxy-3,5-dichloroacetophenone (3a) (0.05 mol) was dissolved in dry pyridine (40ml). The solution was warmed up to 60^{o}C and pulverized KOH (15g) was added slowly with constant stirring. After 4 hours of heating the reaction mixture was acidified by adding ice cold dil. HCl (1:1). The brownish yellow solid product thus separated was filtered, washed with sodium bicarbonate solution (10%) and finally again with water. It was then crystallized from ethanol acetic acid mixture to get 1-(2-hydroxy-3-dichloro-phenyl)-3-phenyl-1,3-propanedione(4a),m.p.110^{o}C yield 75%.

IR (KBr): 3030 (-OH phenolic stretching); 1600 (>C=O stretching); 1170 (-OH bending in phenol); 790 (C-Cl stretching).

PMR: 3.60 (s, 3H, -ArOCH$_3$); 4.56 (s,2H –due to dione) 6.6 (s,6H, -ArH);
12.75 (s, 1H, Ar-OH)
UV: 359 nm.

Preparation of 3-benzoyl-2-(3'-nitrophenyl)-6,8-dichloroflavanone(5a):
A mixture of 1-(2-hydroxy-3,5-dichlorophenyl)-3-phenyl-1,3 propanedione (4a) (0.01mol) and 3-nitrobenzaldelyade (0.012 mol) was refluxed in ethanol (25ml) and piperidine (0.5 mol) for 15-20 min. After cooling, the reaction mixture was acidified with dil HCl (1:1) and the product thus separated, was crystallized from ethanol-acetic acid mixture to get the compound(5a), m.p.187^{o}C yield 80%.

Action of PhNHNH$_2$.HCl on 3-benzoyl-2-(3nitrophenyl)-6,8-dichloro-flavanone (5a) :
Formation of 3-(2-hydroxy-3,5-dichlorophenyl)-4-benzoyl,5-(3-nitro phenyl)-1-phenyl- Δ^2-pyrazoline (6a) :
A mixture of 3-benzoyl-6,8-dichloroflavanone (5a) (0.01mol) and phenylhydrazinehydrochloride (0.02 mol) was refluxed in DMSO (20 ml) containing a few drops of piperidine for 1.5 hrs. After cooling the mixture was diluted with water,the product thus separated was filtered and crystalised from ethanol-acetic acidto get crystals of the compound (6a), m.p.162^{o}C, yeild 72%.

IR (KBr):3415 (-OH phenolic stretching); 1602 (>C=O stretching); 1168 , (C-Cl stretching): 808 (C-H stretching aliphatic): 1444 (NO_2 stretching)

PMR: 3.07 (s, 3H, -ArOCH$_3$); 6.66 to 8.08(m,10H, -ArH); 11.3 (s, 1H, Ar-OH)
UV: 449.6 nm
Scheme-2

Preparation of 2-anisoyloxy-3, 5-dichloroacetophenone (3b) :
2-Hydroxy-3,5-dichloroacetophenone (2b) (0.04mol) and anisic acid (0.05mol) were suspended in dry pyridine (30ml) and to this $POCl_3$ (3ml) was added drop wise with constant stirring and cooling. The reaction mixture was kept for overnight and then worked up by dilution and acidification with ice cold HCl (50%) to neutralize pyridine. The solid product thus obtained was filtered washed with water followed by sodium carbonate (10%) washing and finally again with water. It was crystallized from ethanol to obtain 2-anisoyloxy-3,5-dichloroacetophenone (3b), m.p. 111^{o}C and yield 74%.

IR (KBr): 3045 (-OH phenolic stretching); 1680 (>C=O stretching); 1365 (-OH bending in phenol); 670 (C-Cl stretching).

ISSN-2394-5125 VOL 7, ISSUE 3, 2020

PMR: 2.65 (s, 3H, -ArOCH$_3$); 6 to 7.64 (m,2H, -ArH); 12.5 (s, 1H, Ar-OH)

Prepration of 1-(2-hydroxy-3,5-dichlorophenyl)-3-(4'-methoxypehnyl)-1,3-propanedione (4b) :
2-Anisoyloxy-3,5-dichloroacetophenone (3b) (0.05 mol) was dissolved in dry pyridine (40 ml). The solution was warmed at about 60^{o}C and pulverized KOH (0.15 mol) was added slowly with constant stirring. After 4 hours the reaction mixture was acidified with ice cold dil. HCl (1:1) and processed as described in (4a) to get the compound , 1-(2-hydroxy-3,5-dichlorophenyl)-3-(4'-methoxyphenyl)-1,3-propanedione (4b), m.p. 114^{o}C, yield 75%.

IR (KBr): 3045 (-OH phenolic stretching); 1650 (>C=O stretching); 1160 (-OH bending in phenol); 760 (C-Cl stretching).

PMR: 3.50 (s, 3H, -ArOCH$_3$); 4.35 (s,2H –due to dione) 6.3 (s,6H, -ArH); 12.6 (s, 1H, Ar-OH)
UV: 348 nm

Preparation of 3-anisoyl-2-(4'-N,N-dimethylaminophenyl)-6,8-dichloro flavanone (5b) :
A mixture of 1-(2-hydroxy-3,5-dichlorophenyl)-3-(4'-methoxy-phenyl)-1,3-propanedione (4b) (0.01 mol) and 4-N,N-dimethylamino- benzaldelyde (0.12 mol) was refluxed in ethanol and piperidine (0.5mol) for 15-20 min. After cooling, the reaction mixture was acidified with dil HCl (1:1) and the product thus separated, was crystallized from ethanol-acetic acid mixture to get the compound(5b), m.p. 190^{o}C yield 78%.

IR (KBr): 3065 (-OH phenolic stretching); 1645 (>C=O stretching); 1535 (-NO_2 stretching); 748 (C-Cl stretching).

PMR: 3.07 (s, 3H, -ArOCH$_3$); 6.66 (m,10H, -ArH); 12.6 (s, 1H, Ar-OH).

Preparation of 3-anisoyl-2-(4-N,N-dimethylaminophenyl)-6,8-dichloroflavone (6b) :
A mixture of 3-anisoyl-2-(4-N,N-dimethylaminophenyl)-6,8-dichloro-flavanone (5b) (0.01 mol) and iodine crystal was refluxed in DMSO (20ml) for 10 min. and processed as in experiment No. 12 to get the compound (6d), m.p.155^{0}C, yield 70%.

IR (KBr): 3076 (-OH phenolic stretching); 1641 (>C=O stretching); 1160 (-OH bending in phenol); 767 (C-Cl stretching):2906(C-H stretching aliphatic):1556(NO_2 stretching)

PMR: 3.07 (s, 3H, -ArOCH$_3$); 6.66 (m,10H, -ArH); 12.6 (s, 1H, Ar-OH)
UV: 269.6 nm

RESULTS AND DISCUSSION:
The compound (3a-7c) and (3b-7d) were studied the antibacterial activities against some human pathogens *S.aureus ,S.typhi ,C.gulkar ,A.niger* and crop pathogens *P. solanacearum, A. tumefacines x. camperstris* Species at 1000 µm gentamycine as a standard.DMF was used as solvent control using agar plate techniques. The zones of inhibition formed were measured in mm and are shown in Table. It gives following results. It was observed that, hetero atoms increase the antibacterial activity of compounds from (4a-6b) and (4b-6d).

Table (1): Characterization data of synthesized new compound

Compound	Molecular Formula	M.P. (^{o}C)	Yield (%)	Rf
2	$C_8H_6O_2Cl_2$	53	75	0.84
3a	$C_{15}H_{10}O_3Cl_2$	66	76	0.66
3b	$C_{16}H_{12}O_4Cl_2$	66	76	0.66
4a	$C_{15}H_{10}O_3Cl_2$	110	75	0.71
4b	$C_{16}H_{12}O_4Cl_2$	114	75	0.81
5a	$C_{22}H_{13}O_5Cl_2N$	187	80	0.45
5b	$C_{25}H_{21}O_4Cl_2N$	190	78	0.64
6a	$C_{28}H_{19}O_4N_3Cl_2$	162	72	0.66
6b	$C_{31}H_{27}O_3N_3Cl_2$	192	65	0.62

Table – 1 Effects of newly synthesized compounds on crop pathogens:

ISSN-2394-5125 VOL 7, ISSUE 3, 2020

S. N.	Test Compounds	Zones of inhibition (mm)		
		Plant Pathogens		
		P. sulanacearum	***A. tume faciens***	***X. Comperstris***
1	2a	+	+	++
2	2b	+	++	+
3	3a	++	+	+
4	3b	+	+	+
5	4a	+++	++	++
6	4b	++	+	++
7	5a	++	++	++
8	5b	++	+	++
9	6a	++	++	++
10	6b	++	++	++

Table-2 Effects of newly synthesized compounds on Human pathogens:

S. N.	Test Compounds	Zones of inhibition (mm)			
		Human Pathogens			
		S. aureus	***S. typhi***	***C. gulkar***	***A. niger***
1	2a	++	++	++	++
2	2b	++	++	+++	++
3	3a	+++	+++	++	++
4	3b	+++	++	++	++
5	4a	++	+++	+++	+++
6	4b	+++	++	+++	+++
7	5a	+++	++	+	++
8	5d	+	++	++	+++
9	6a	+++	++	+	++
10	6b	++	+++	+	++

++++ Very Strongly active range
+++ Strongly active range
++ Moderately active range
+ Weakly active range
- Inactive range

Acknowledgement
The authors are thankful to V.B.M.V. Amravati for providing all the facilities to carry out the work and and S. G. B. Amravati, University (M.S),India.

.**References:**

1. A .Castells., and A.D.Colombo,*J* ,*Chem.Soc*.18 ,(1969),1062
2. W.S.Johnson.,and W.E.Shelber, *J* , *AM Chem.Soc*.67 ,(1945),1745.
3. R.P.Barnes, and A.S.Spriggs, *J* , *AM Chem.Soc*.67 ,(1945),134.
4. R.V.Steven, and K.A Albizati *J* ,*Chem.Soc*.18 ,(1969),1062.
5. N.G.Malyula, and Khisamutdinov, *Chem.Abst*.108 ,(1988),150351 C.
6. 6 K.A.Thakar, and P.R.Muley, Indian J *Chem.14* ,(B),(1976),224.
7. S.B.Lohiya and B. J. Ghiya, *Indian J. Chem.*26 B, (1987), 873-76.
8. A.M.Osman, and K.M.Hasan, *Indian J. Chem.*14 B, (1954), 282.
9. Z.H.Khalil,and A.S.Yanni, *J Ind.*,*Chem.Soc*.58 ,(1981),168.
10. J.M.Rashdi,and N.S.Habib, ,*Chem.Abstr*.89 ,(1978),163490J.
11. N.K.Mandal and K.P.Banarjee, *Chem.Abstr*.104 ,(1986),34034V.
12. M.D.Ankhiwala and K.B.Naik, *Chem.Abstr*.112 ,(1990),5561.
13. S.V.Damle,and P.R.Muley, *Indian J. Heterocyclic Chem.*,9 (1999), 8.