EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 10
Issue: 10
227-230
Year: 2023

# NOVEL SYNTHESIS AND CHARACTERIZATION OF SOME CHLOROSUBSTITUTED 4-AROYL/ALKOYL PYRAZOLES AS ANTIBACTERIAL AGENTS

**Chhaya D. Badnakhe***

Department of Chemistry, Dr. Manorama and Prof. H.S. Pundkar, Arts, Commerce and Science College, Balapur, Dist. Akola.

***Corresponding Author: Chhaya D. Badnakhe**
Department of Chemistry, Dr. Manorama and Prof. H.S. Pundkar, Arts, Commerce and Science College, Balapur, Dist. Akola.

**Article Received on 27/07/2023** **Article Revised on 18/08/2023** **Article Accepted on 08/09/2023**

## 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 (5ab) subsequently 3-aroyl/ alkoylchromones (6a-b). 3-Aroyl/alkoylchromones (6a-b) on treatment with Ph.NH.NH2.HCl in DMSO containing small amount of piperidine gave 4-aroyl/alkoylpyrazoles (7a-b). The structures of newly synthesized chlorosubstituted 4-aroyl/alkoyl- pyrazoles (7a-b) were elucidated on the basis of molecular weight, elemental analysis and their spectral data.The titled compounds were assayed for their antibacterial activity against some plant pathogens; Gram+ve bacteria viz. Staphylococcus pneumoniae, Staphylococcus aureus and Gram-ve bacteria viz. Escherichia coli and Pseudomonas fluorescens by using Agar disc diffusion method. The antibacterial activity is very encouraging.

## INTRODUCTION
Pyrazoles 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 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 anti-inflammatory[14], antimicrobial[15] and antiprotozoal[16] which render them valuable active ingredients of medicine and plant protecting agents.

In the present study, chlorosubstituted 4-aroyl/alkoyl-pyrazoles has been prepared along with their nanoparticles and screened them fortheir antibacterial activity against some plant pathogens; Gram+ve bacteria viz. Staphylococcus pneumoniae, Staphylococcus aureus and Gram-ve bacteria viz. Escherichia coli and Pseudomonas fluorescens by using Agar disc diffusion method.

## 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 NaHCO3 (10%) and purified by recrystallization with ethanol to get 2-benzoyl-3, 5-dichloroacetophenone (3a).

**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 0C 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

NaHCO3 solution. Finally it was crystallized from ethanol.

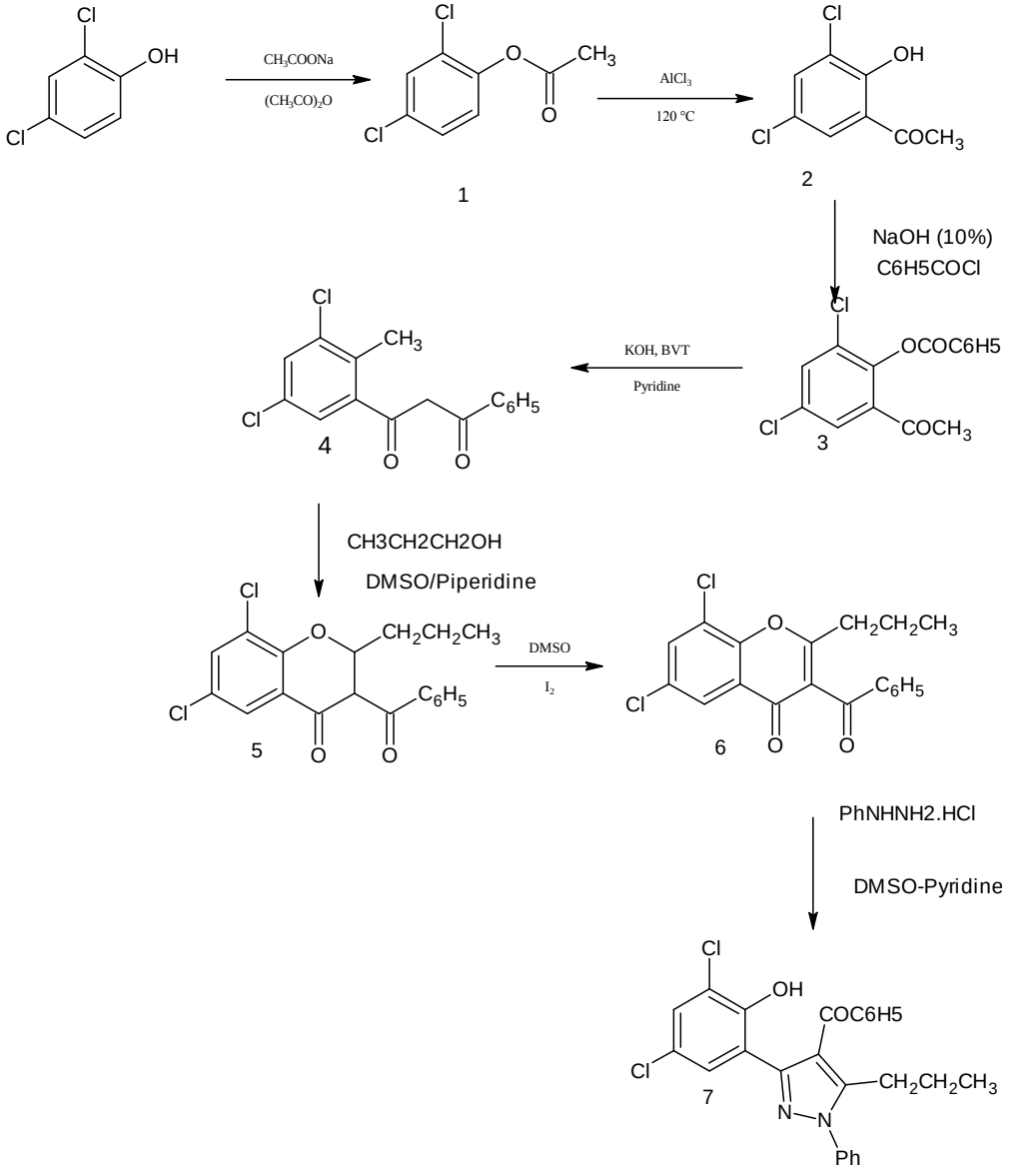
**Synthesis of 3-benzoyl-2-(2'-propoyl)-6, 8-dichlorochromanone (5a):** A mixture of 1-(2-hydroxy-3, 5-dichlorophenyl-3-phenyl-1,3-propanedione (4a) (0.01 mol) and propionaldehyde (0.02 mol) was refluxed in DMSO (25 ml) and piperidine (0.5ml) for 15-20 minutes. After cooling the reaction mixture was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

**Synthesis of 3-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-(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.NHNH2HCl (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-benzoyl-5-(2'-propoyl)isoxazole (8a):** The mixture of 6a (0.01 mol) and NH2OH.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 NaHCO3 and then crystallized from ethanol to get 8a.

The synthetic route for obtaining the final products is presented in 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 |

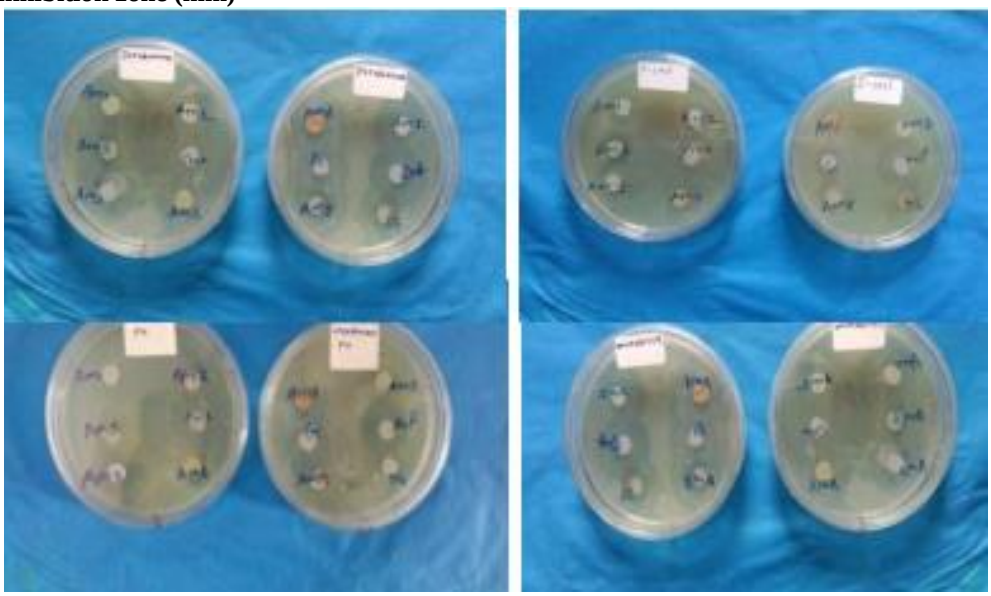
**Antibacterial Assay**

The compounds (2a-8a) were screened for their antibacterial activity against Gram+ve bacteria viz. Staphylococcus pneumoniae, Staphylococcus aureus and Gram-ve bacteria viz. Escherichia coli and Pseudomonas fluorescens at conc. of 1000 ppm by using Agar disc diffusion method. Ofloxacin used as a standard and chloroform as solvent control. The zones of inhibition formed were measured in mm and are shown in Table No.2.

**Table No. 2: Impact of test compounds against plant pathogens.**

| Sample Code | (Gram positive) | | (Gram Negative) | |
|---|---|---|---|---|
| | Staphylococcus pneumoniae | Staphylococcus aureus | Escherichia coli | Pseudomonas fluorescens |
| 2a | 17 | 15 | 12 | 12 |
| 2b | 15 | 13 | 15 | 12 |
| 3a | 17 | 14 | 12 | 15 |
| 4a | 15 | 12 | 12 | 25 |
| 5a | 14 | 12 | 15 | 12 |
| 6a | 14 | 15 | 15 | - |
| 7a | 12 | 13 | 12 | 18 |
| 8a | 12 | 15 | 14 | 25 |
| Reference Antibiotic | (Ofloxacin) | (Ofloxacin) | (Ofloxacin) | (Ofloxacin) |

**Diameter of inhibition zone (mm)**



## RESULT AND DISCUSSION

Most of the test compounds have shown remarkable and very encouraging antibacterial activities. A further detailed study in the light of plant pathology is advised.

## ACKNOWLEDGEMENTS

The authors are thankful to the Principal, Dr.D.H.Pundkar, Dr.Manorama & Prof.H.S.Pundkar, Arts, Commerce & Science College, Balapur, Dr.B.B.Wankhade, Principal, Malkapur Vidnyan Mahavidyalaya, Malkapur for providing necessary facilities to carry out the research work.

## REFERENCES

1. Swarnkar P.K., Kriplani B., Gupta G.N., Oijha K.G., synthesis and antimicrobial activity of some new phenothiazine derivatives, *E.J. Chem.*, Jan. 2007; 4(1): 14-20.
2. Kakade B.S., "Synthesis in heterocyclic compounds (Role of DMSO as a solvent," Ph.D. Thesis, Nagpur University, 1981.
3. Chincholkar M.M., and Ramekar M.A. *J. Ind. Chem. Soc.*, 1994; 71(4): 199.
4. S.P. Rathod, A.P. Charjan and P.R. Rajput, Rasayan*J. Chem.*, 2010; 3(2): 363-367.
5. Dabholkar V.V. and F.Y. Ansari, *Indian J. Chem.*, Nov. 2008; 47B: 1759–1761.
6. D.H. Morey and S.N. Patil *ori., J. Chem.*, Mar., 2002.
7. C.Brown and R.N.Davidson, *Adv. Heterocycl. Chem.*, 1985; 38: 135.
8. P. Descacq, A. Nubrich, M. Capdepuy and G. Devanuz, *Eur, J. Med. Chem.*, 1990; 25: 285.
9. M.I. Younes, H.H. Abbas, and S.A.M. Metwally, *Arch, Pharma*, 1987; 230.
10. D.T. Witiar, M.E. Wolff and R.C. Covestri, "In Berger", *S. Medicinal Chemistry"*, part III, Edi. Willey, Newyork, 1981; 603.
11. M. Crewzet and F. Helene, Eurpat App. Ep., 121, 489, *Chem. Abstr.*, 102, 1985, 787244, *Chem., Abstr.*, 1978; 89: 108943 m.
12. F.M. Dean, K.A. Thakur and C.H. Gill, "Naturally occuring oxygen ring compounds*", J. Indian Chem. Soc.*, 1983; 60: 668.
13. P. Valenti, A. Bisi, A. Rampa, F. Belluti, S. Gobbi, A. Zampiron, M. Carrara, Biosy, *Med. Chem.*, 2002; 239.
14. Y.Q. Shi, J. Fukai, H Sakagami, W.J. Chang, P.Q. Yang, F.P. Wang, T. Nomura, *J. Nat. Prod.*, 2001; 64: 181.
15. G.J. Reddy, D. Latha, K.S. Rao, *Heterocycl, Commun.*, 2004; 10: 279.
16. T. Ghosh, S. Saba, C. Bandyopadhya, *Synthesis*, 2005; 11: 1845.