*Available online www.jocpr.com*

**Journal of Chemical and Pharmaceutical Research, 2014, 6(8):333-337**

**Research Article**

**ISSN : 0975-7384**
**CODEN(USA) : JCPRC5**

# Synthesis and characterization of some new 3, 5-disubstituted pyrazoline and isoxazoline derivatives

**Nilesh R. Thakare* and Amol K. Dhawas[#]**

**Department of Chemistry, Shri Shivaji Science College, Sant Gadge Baba Amravati University, Amravati(MS) India*
*[#]Department of Chemistry, Janata College, RTM Nagpur University, Nagpur (MS) India*

---

**ABSTRACT**

*Base catalyzed condensation of 4–chloroacetanilide (1) with different aromatic aldehyde (2a-c) gives N-(4-chlorophenyl)-3-(4-substitutedphenyl)-acryl amide (3a-c). These acryl amides(3a-c) on treatment with hydrazine hydrate and hydroxylamine hydrochloride in the presence of ethanol/glacial acetic gives 3, 5-disubstituted pyrazolines (4a-c) and 3, 5-disubstituted isoxazoline (5a-c) respectively. 1-Benzoyl-3, 5 disubstituted pyrazolines (6a-c) has been synthesized by the treatment of (4a-c) with benzoyl chloride in pyridine. All the newly synthesized compounds were characterized by analytical and spectral studies.*

**Keywords:** Pyrazolines, Isoxazolines, hydrazin hydrate, hydroxylamine hydrochloride, 4- chloro acetanilide, acryl amide, benzoyl chloride.

---

## INTRODUCTION

The development of simple, facile and efficient synthetic methods for the synthesis of five member heterocycles from readily available reagents is one of the major challenges in organic synthesis. Among five member heterocycles**,** pyrazoline and isoxazoline are represents a class of compounds of great importance in biological chemistry. For instance, pyrazoline derivatives posses the biological activities like, antidepressant[1], anticonvulsant[2], antimicrobial[3], analgesic[4] and antitumour[5] activity.

Isoxazoline derivative are known to exhibit analgesic[6], anti-inflammatory[7], antimicrobial[8] and HIV-inhibitory activity[9]. Some isoxazole derivatives display agrochemical properties namely herbicidal and soil fungicidal activity[10]. Therefore pyrazoline, isoxazolines and their derivatives are used as medicaments.

The starting 4-chloroacetanilide (1) on base catalyzed condensation with different aromatic aldehyde (2a-c) yielded chalcones (3a-c) when substituted chalcones (3a-c) treated with hydrazine hydrate and hydroxylamine hydrochloride in ethanol or acetic acid was refluxed for 5– 6 hrs gives pyrazolines (4a-c) & isoxazolines (5a-c) derivative respectively. The constitution of all the compounds synthesized was established by spectral study.

## EXPERIMENTAL SECTION

**Materials :** hydrazin hydrate, hydroxylamine hydrochloride, 4- chloro acetanilide, benzoyl chloride, vaniline, p-hydroxyl benzaldehyde, p- chloro benzaldehyde, ethanol, glacial acetic acid.

All the melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr using Perkin Elmer model 2000 spectrophotometer. H-NMR spectra were recorded in CDCl3 on a Brucker AC II

400 $MH_Z$ spectrophotometer using TMS as an internal standard. Chemical shift values are shown in δ ppm. The purity of all the synthesized compounds was checked by TLC on silica gel plates by using appropriate solvents.

**Synthesis of N-(4-chlorophenyl)-3-(4-substitutedphenyl)-acryl amide (3a-c).**
The mixture of 4–Chloroacetanilide (1) (0.01mole) and different aromatic aldehyde like vaniline, p-hydroxy benzaldehyde, 4-chlorobenzaldehyde (2a-c)(0.01 mole) in ethanol (20ml) added drop wise 2.5ml NaOH (20%) solution with stirring. It was then decomposed with ice cold water to obtained the crude product. It was then washed with water, filtered, dried and crystallized from ethanol to get (3a-c).

**Spectral interpretation of(3c)**

**NMR $\delta_{ppm}$ :** 3.87-3.82(S,3H,Ar-OCH3),7.35-3.33(S,1H,-OH),9.99-9.95(S,1H,-NH),7.91-7.74(M,7H,-Ar-H)

**IR**($v_{max}$)$cm^{-1}$**:** 3352 v(O-H),3085v(N-H),2857(C-H Aliphatic),1697(C=O),1587(C=C),1289(C-N),1204(C-O),833(p-sub Benzene),682(C-Cl)

Physical data of synthesized compounds (3a-c) given in Table no.1

**Synthesis of 3,5-disubstituted pyrazolines. (4a-c)**
A mixture of N–(4–chlorophenyl)-3–(4-substitutedphenyl)-acryl amide (0.01 mole) and hydrazine hydrate (0.01 mole) in ethanol was refluxed for 5 – 6 hours. The resulting mixture was concentrated and allow to cool. The resulting solid was filtered, washed and dried crystallized from ethanol to get (4a-c)

**Spectral interpretation of (4a)**

**NMR $\delta_{ppm}$ :**2.51(S,1H,-N-H),4.49-4.47(d,2H,C-H),7.51-7.43(dd,1H,-CH),7.63(S,1H,-OH),7.61-7.52(m,8H,-H)

**IR**($v_{max}$)$cm^{-1}$**:** 3388 v(O-H),3047 v(N-H),1585 v(C=N),1482 v(C=C),1294 v(C-O),1206 v(C-N),808 (p-sub benzene), 627(C-Cl)

Physical data of synthesized compounds (4a-c) given in Table no.1

**Synthesis of 3,5disubstituted isoxazolines. (5a-c).**
A mixture of N–4–(chlorophenyl)-3–(4-substitutedphenyl)-acryl amide (3a-c) (0.01mole) and hydroxyl amine hydrochloride in ethanol / acetic acid was refluxed for 5–6 hour. The resulting mixture was concentrated and allowed cool. The resulting solid was filtered, washed, dried & crystallized from ethanol to get(5a-c).

**Spectral interpretion of(5b):**

**NMR**$\delta_{ppm}$ **:** 2.5(s,1H,-N-H),7.32(d,2H,-C-H),7.4-7.6(dd,1H,-CH),8.O-8.1(m,8H,Ar-H)

**IR($v_{max}$)**$cm^{-1}$**:** 3298v(N-H), 3051v(Ar-CH), 1647v(-C=N), 1587v(-C=C), 1210v(-C-N), 1157v(-C-O), 819v(p-sub. benzene), 688v(-C-Cl)
Physical data of synthesized compounds (5a-c) given in Table no.

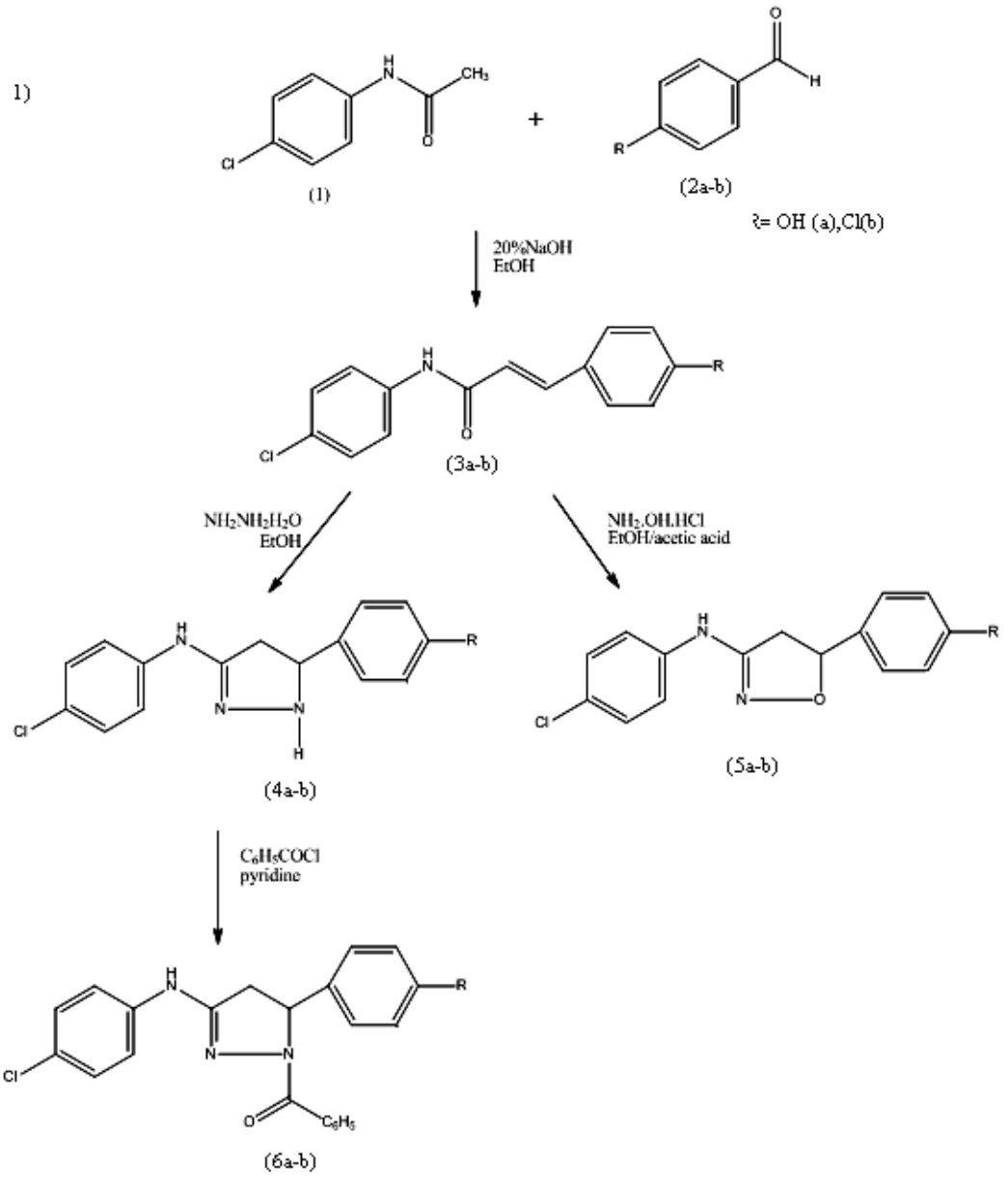
**Synthesis of 1-Benzoyl-3,5 disubstituted pyrazolines. (6a-c)**
A mixture of 3,5-disubstituted pyrazolines(4a-c) (0.01mole) and benzoyl chloride(0.01mole)in pyridine was stirred, for 1hr. The resulting solid was filtered, washed and dried, crystallized from ethanol to get(6a-c).

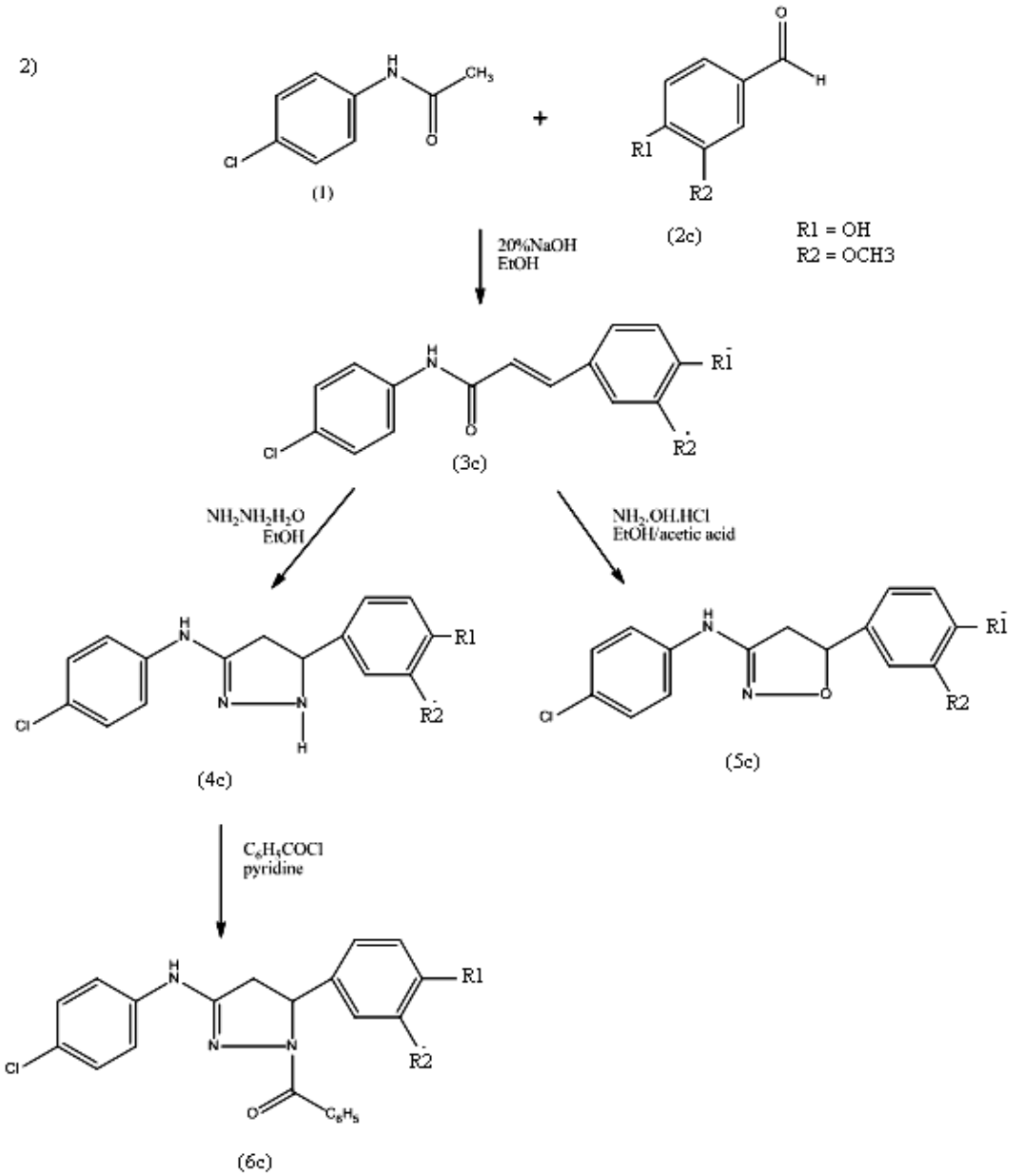
**Spectral interpretation of (6a)**

**NMR $\delta_{ppm}$ :** 4.49-4.47(d,2H,C-H),7.51-7.43(dd,1H,2CH),7.63(S,1H,-OH),7.61-7.52(m,8H,Ar-H),7.29(m,5H,Ar-H)

**IR($v_{max}$)$cm^{-1}$:** 3388 v(O-H),1585 v(C=N),1482 v(C=C),1294 v(C-O),1206 v(C-N),808 (p-sub benzene),627(C-Cl),1720v(C=O).

Physical data of synthesized compounds (6a-c) given in Table no.1


1)
(1)
(2a-b)
R= OH (a),Cl(b)
20%NaOH
EtOH
(3a-b)
NH2NH2H2O
EtOH
NH2.OH.HCl
EtOH/acetic acid
(4a-b)
(5a-b)
C6H5COCl
pyridine
(6a-b)




## RESULTS AND DISCUSSION

The structures of the synthesized compounds were characterized with the help of IR and NMR . The IR spectrum of compound (3c) shows characteristics band at 1600-1700cm-1 due to the C=O group. The IR spectrum of compounds (4a) and (5b) shows the characteristic band at 1500-1600cm-1 due to the C=N group. There are no absorption in the region of 1600-1700cm-1 indicating the absence of C=O group in 4a and 5b.

The H NMR spectrum of compound (3c) showed singlet of –NH at 9.95ppm and multiplet of Aromatic protons at 7.91 to 7.94 ppm. The H- NMR spectrum of compounds (4a) and (5b) shows the dd of –CH at 7.4-7.6 ppm which confirms the formation of pyrazolines and isoxazoline rings.

**Table 1:-Physical data of synthesized compounds**

| Sr. No. | Compounds | R | $R_1$ | $R_2$ | M.P. ($^0$C) | Yeild (%) | Molecular Weight | Molecular Formula |
|---|---|---|---|---|---|---|---|---|
| 1 | 3a | OH | _ | _ | 170-172 | 68 | 272 | $C_{15}H_{11}NO_2Cl$ |
| 2 | 3b | Cl | _ | _ | 140-145 | 64 | 291 | $C_{15}H_{11}NOCl_2$ |
| 3 | 3c | _ | OH | $OCH_3$ | 160-165 | 70 | 261 | $C_{14}H_{12}NO_2Cl$ |
| 4 | 4a | OH | _ | _ | 180-185 | 65 | 287 | $C_{15}H_{14}N_3OCl$ |
| 5 | 4b | Cl | _ | _ | 160-162 | 66 | 305 | $C_{15}H_{13}N_3Cl_2$ |
| 6 | 4c | _ | OH | $OCH_3$ | 190-195 | 69 | 316 | $C_{16}H_{15}N_3O_2Cl$ |
| 7 | 5a | OH | _ | _ | 95-98 | 64 | 288 | $C_{15}H_{13}N_2O_2Cl$ |
| 8 | 5b | Cl | _ | _ | 150-155 | 70 | 305 | $C_{15}H_{11}N_2OCl_2$ |
| 9 | 5c | _ | OH | $OCH_3$ | 65-70 | 60 | 318 | $C_{16}H_{15}N_2O_3Cl$ |
| 10 | 6a | OH | _ | _ | 180-185 | 65 | 379 | $C_{21}H_{18}N_3O_2Cl$ |
| 11 | 6b | Cl | _ | _ | 196-198 | 64 | 397 | $C_{21}H_{17}N_3OCl_2$ |
| 12 | 6c | _ | OH | $OCH_3$ | 198-200 | 58 | 409 | $C_{22}H_{20}N_3O_3Cl$ |

## CONCLUSION

A series of 3,5- disubstituted Pyrazolines and Isoxazolines were synthesized and their structure was confirmed by spectral analysis. From the literature survey it was revealed that all these synthesized compounds possess wide range of antimicrobial activities and displays agrochemical properties.

**Acknowledgement**
The authors are grateful to the authorities of Shri Shivaji Science College, Amravati for providing necessary facilities.

## REFERENCES

[1] R. Y. Prasad; L.L. Rao; K. Prasoona; Murali; Ravi Kumar, *Bioorg. Med. Chem. Lett.*, **2005,(**15),5030.
[2] O. Zuhal; K. H. Burak; G. Bulent, *Euro. J. Med. Chem.*, **2007**,(42), 373.
[3] O. Ahmet; T. Z. Gulhan; A. K. Zafer, *Euro. J. Med.Chem*., **2007**, (42), 403.
[4] G. S. Aysel; Demirayak; C. Gultaze *et.al*, *Euro. J. Med. Chem*., **2000**, (*35*), 359.
[5] Z. Brzozwski; F. S. Czewski; Gdaniec, *Euro. J. Med. Chem*., **2000**,(35), 1053.
[6] T. V. Hansen; P. Wu; V. V. Fokin, *J. Org. Chem*., **2005**,(70),7761.
[7] A. Bhatt; H. Parekh; K. Parikh; A. R. Parikh, *Indian J. Chem*., **2001**,40(B), 57.
[8] D. N. Nagar; T. Mehta; V. H. Shah, *Indian J. Heterocyclic Chem*., **2003**, (13), 173.
[9] Chem. Abstr; **1983**, (98),16671.
[10] J. T. Strupezewski; R. C. Allen; R. W. Durm, *J. Med. Chem*., **1985**,(28), 761.