Synthesis and Charactrization of New 3, 5 Disubstituted Pyrazoline

N. R. THAKARE

Department of Chemistry, Shri Shivaji Science College,Amravati (MS), India.
Corresponding author: tnilesh@gmail.com

Abstract

A series of N-(4-chlorophenyl)-3-(4-substitutedphenyl)-acryl amide (3a-c) and N-(4-chlorophenyl)-3-furan acryl amide(3d) were synthesized by the simple condensation of 4-chloroacetanilide(1) with aromatic aldehydes (2a-c) and (2d) in presence of 20% NaOH as a catalyst. These synthesized acryl amides then treated with phenyl hydrazine and 2,4-dinitrophenyl hydrazine in the alcoholic medium to give 3,5-disubstituted pyrazolines (4a-f) and (5d-6d) in a good to excellent yields using a facile approach.
These newly synthesized 3, 5-disubstituted pyrazolines have been characterized on the basis of spectral studies.

Keywords : Pyrazolines, 4-Chloroacetanilide, Acrylamide, 3, 5-Disubstituted Pyrazolines

Introduction

Pyrazolines are well known and important nitrogen contaning 5-membered heterocyclic compounds and various methods have been worked out for their synthesis. Numerous pyrazoline derivatives have been found to posses considerable biological activities which stimulated the research activity in this field. These are antidepressant [1,2], anticonvulsant[3],antifungal[3], antimicrobial[4], analgesic[5,6]and antitumor[7,8] activity. Pyrazolines also have antiviral [9], anti-inflammatory [10,11,] anti-tuberculosis [12], and anti-amoebic[13] activity. These compounds are usually prepared from cyclization of chalcones with hydrazine and its derivatives under alcoholic conditions. The major inventive behind the synthesis of these compounds was the immense biological activities associated to these heterocyclic derivatives

Materials and Methods

4-chloroacetanilide, hydroxylamine hydrochloride, hydrazine hydrate,4-chlorobenzaldehyde,4-hydroxy benzaldehyde,ethanol, sodiumhydroxide, vaniline, ferfuraldehyde. Melting points of all synthesized compounds were determine in open capillaries and are uncorrected. The proton NMR spectra were recorded in Bruker AC-II 400 NMR spectrometer in CDCl3 using TMS as a standered. IR spectra were recorded in KBr pallets using IR spectrometer. The chemicals used were of laboratory reagent grade and the purity of the compounds was checked by TLC

Synthesis of N-(4-Chlorophenyl)-3-Substituted Acryl Amide (3a-d)

The mixture of 4-chloroacetanilide(1) (0.01 mole) and different aromatic aldehydes like vaniline, p-chloro benzaldehyde, p-hydroxyl benzaldehyde, ferfuraldehyde (0.01 mole) in ethanol(20 mL) added drop wise to 2.5 mL NaOH(20 %) with stirring. It was then decomposed with ice cold water to obtain the crude product. It was then washed with water, filtered, dried and crystallized from ethanol to get (3a-d)

Characteristics

NMR (**δ**) : 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($\mathbf{V}_{max}$)cm^{-1} :-3352(O-H),3085(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-d) given in table no. 1

Synthesis of 3,5-Disubstituted Pyrazolines (4a-f)

A mixture of N-(4-chlorophenyl)-3-(4-substituted phenyl) acryl amide (0.01 moles) and phenyl hydrazine/2,4 dinitrophenyl hydrazine (0.01 mole) in ethanol was refluxed for 5-6 hours. The resulting mixture was concentrated and allowed to cool. The resulting solid was filtered, washed, dried and recrystallized from ethanol to get (4a-f).

Characteristics

NMR(**δ**) :-7.45(s,1H,-OH), 3.5(s,1H,N-H), 7.51-7.45(m,12H,Ar-H), 5.5(d,2H,-CH), 7.1(dd,1H,-CH).
IR ($\mathbf{V}_{max}$)cm^{-1}:- 3304(O-H),3024(N-H),1588(C=N),1485(C=C),1262(C-O),1203(C-N),816(P-sub.benzine ring),625(C-Cl).
Physical data of synthesized compounds given in table 1

Table 1 Physical Data of Synthesized Compounds

S.N	Compound	R	R1	R2	M.Pt(C)	Yield(%)	Mole. weight	Mole. Formula
1	3a	-Cl	-	-	140-145	65	257	$C_{15}H_{11}NOCl$
2	3b	-OH	-	-	170-172	68	272	$C_{15}H_{11}NOCl_2$
3	3c	-	-OH	-OCH3	160-165	70	261	$C_{14}H_{12}NO_2Cl$
4	4a	-Cl	-	-	180-185	65	347	$C_{21}H_{17}N_3Cl$
5	4b	-OH	-	-	180-185	66	364	$C_{21}H_{18}NOCl$
6	4c	-Cl	-	-	215-220	50-55	458	$C_{21}H_{15}N_5O_4Cl_2$
7	4d	-OH	-	-	175-180	55	454	$C_{21}H_{16}N_5O_5Cl$
8	4e	-	-OH	$-OCH_3$	185-190	55-60	382	$C_{21}H_{20}N_3ClO_2$
9	4f	-	-OH	$-OCH_3$	210-215	50	483.5	$C_{22}H_{18}N_5O_6Cl$
10	5d	-	-	-	170-175	65	337.5	$C_{19}H_{16}N_3ClO$
11	6d	-	-	-	175-180	57	426.5	$C_{19}H_{13}N_5O_5Cl$

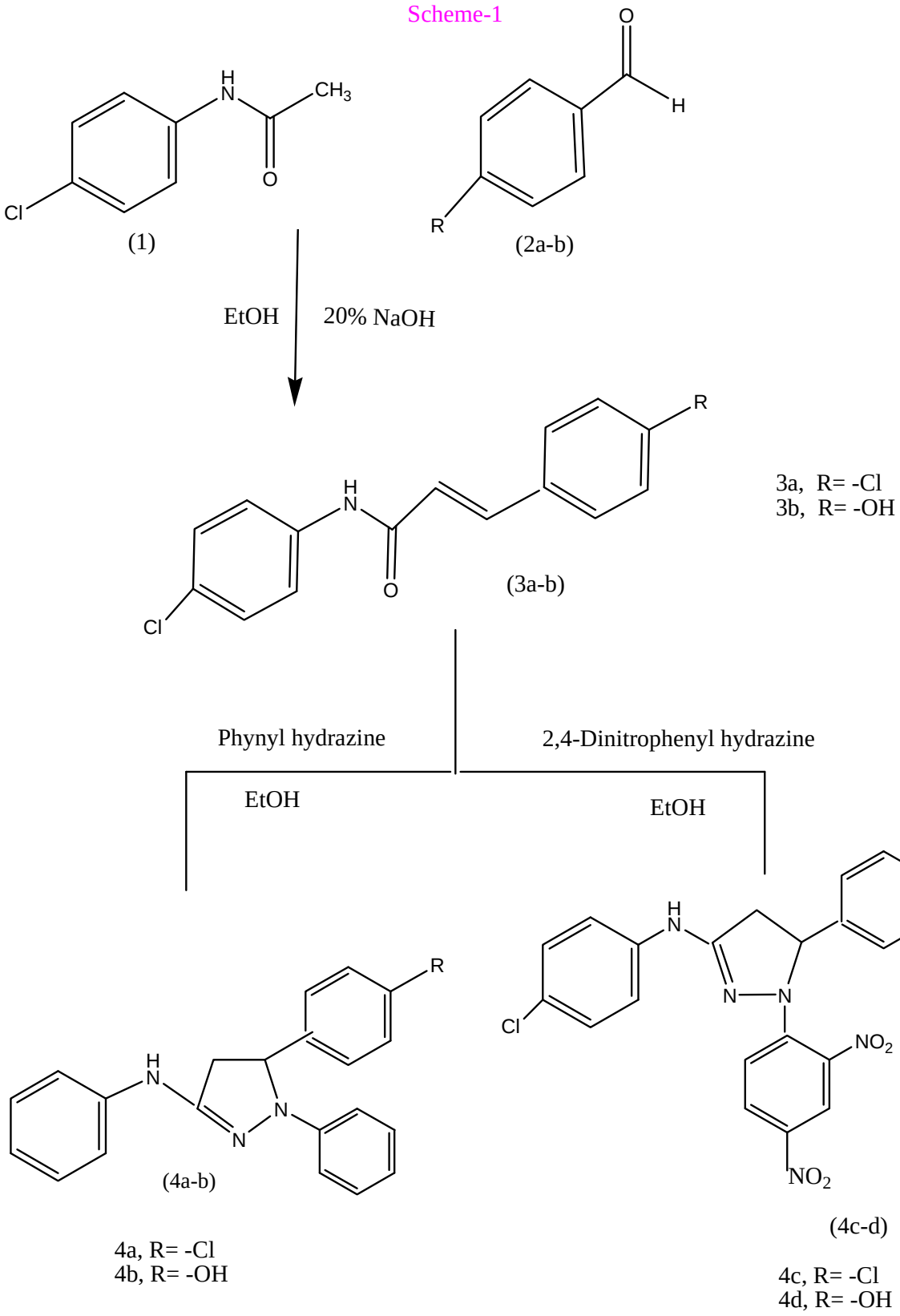
3-(4-Chlorophenyl)-5-Furan-N-Substituted Pyrazolines (5d-6d)

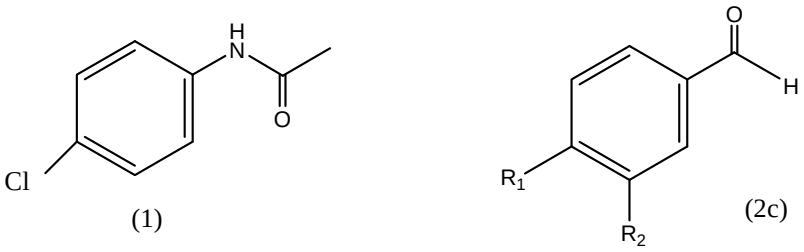
A mixture of N-(4-chlorophenyl)-3-furan acryl amide (0.01 mole) and 2,4-dinitrophenyl hydrazine/phenyl hydrazine(0.01 mole) in ethanol was refluxed for 5-6 hours. The mixture was concentrated and allows to cool. The resulting solid was filtered, washed, dried and crystallized to get (5d) and (6d).

Characteristics

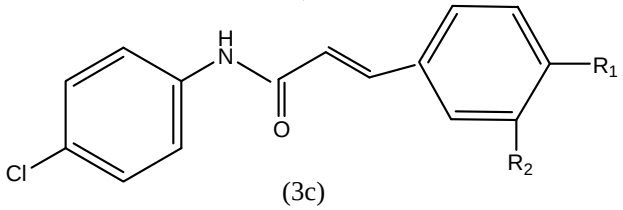
NMR(**δ**) :-3.35(d,2H,-CH),2.58(s,-NH),7.6(dd,1H,-CH),7.9-8.9(m,Ar-H),11.7(s,1H,Ar-H).
IR ($\mathbf{V}_{max}$)cm^{-1} :-3286(N-H), 3088(Ar C-H), 1580(C=N), 1615(C=C), 1513(-NO2,), 1220(C-N), 1136 (C-O), 833 (p-sub benzene).

Scheme-1


(1)
(2a-b)
EtOH
20% NaOH
(3a-b)
3a, R= -Cl
3b, R= -OH
Phynyl hydrazine
2,4-Dinitrophenyl hydrazine
EtOH
EtOH
(4a-b)
(4c-d)
4a, R= -Cl
4b, R= -OH
4c, R= -Cl
4d, R= -OH



(1) (2c)

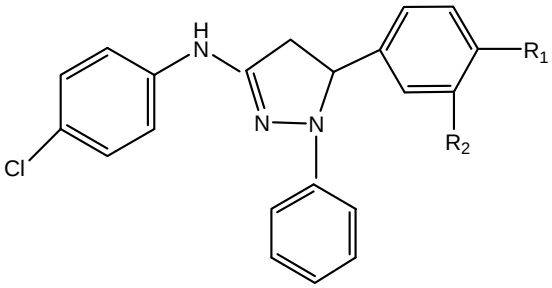


(3c)

R_1= -OH
R_2=-OCH_3

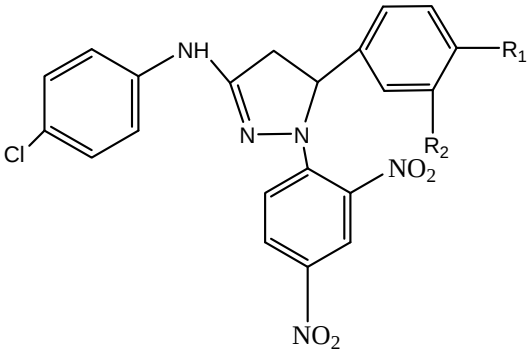
Phenyl hydrazine
EtOH

2,4-Dinitrophenyl hydrazine
EtOH



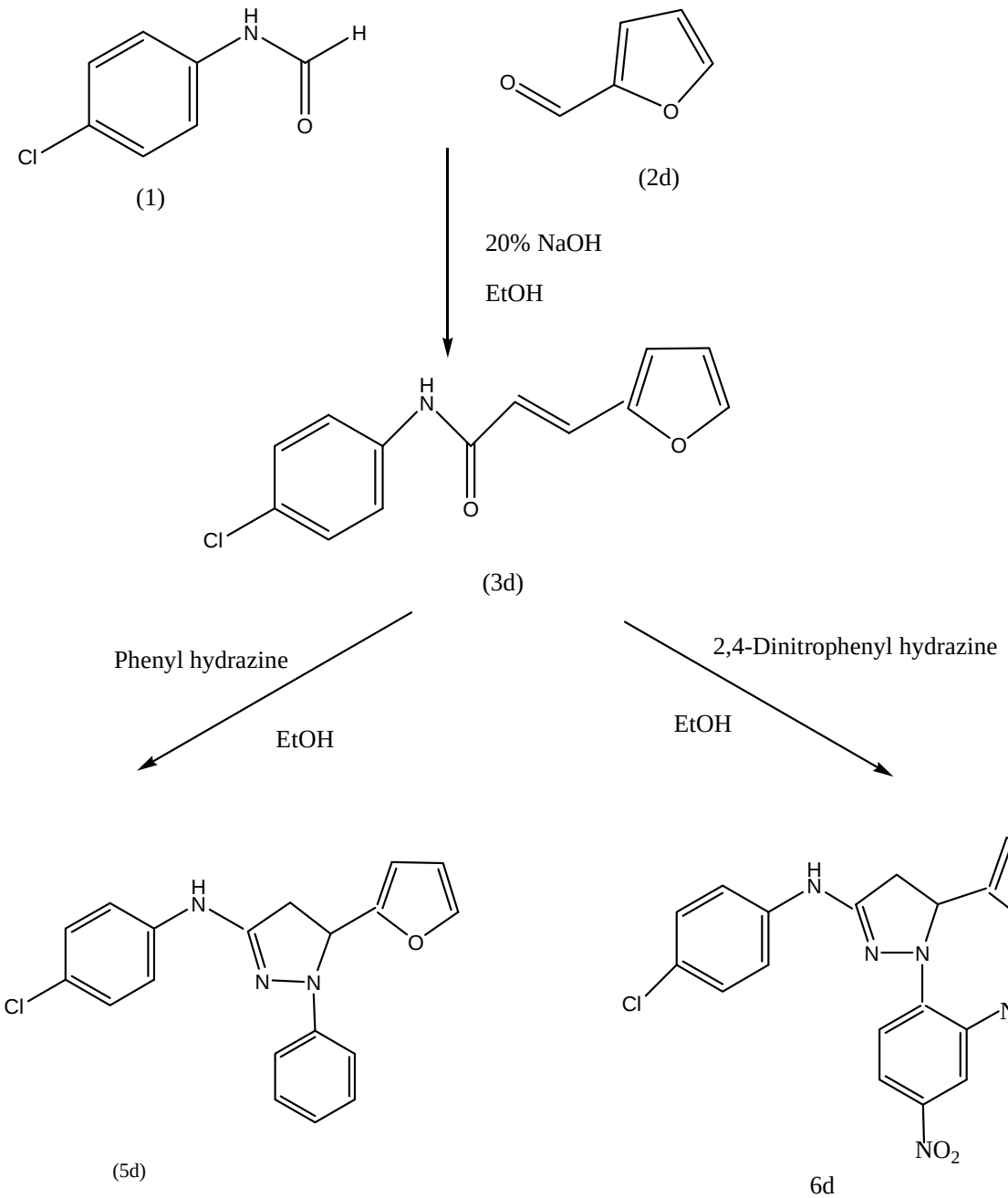
R_1= -OH
R_2= -OCH_3

(4e)



(4f)

Scheme-2



Observations

The spectral studies of synthesized compounds were carried out. The IR spectrum of compound (3c) shows the characteristic band at 1600-1700 cm^{-1} which confirms the -C=O group and band at 1587cm-1 for C=C shows the formation of chalcone. The IR spectra of (4e) shows band at 1500-1600 cm-1 of C=N and H-NMR spectra shows the dd of –CH at 7.1 ppm which confirms the formation of pyrazoline ring. The spectral interpretation of (6d) also shows dd of –CH at 7.6 ppm in H-NMR

spectrum, confirms the formation of pyrazoline and IR spectra shows presence of band at 1580 cm-1 of C=N group.

Conclusion

In conclusion, a simple protocol of synthesis of some novel pyrazoline-3,5 derivatives was developed. From the literature it was revealed that all these synthesized compounds posses good anti-microbial activities.

References

[1] R.Y. Prasad, L.L. Rao, K .Parsoona, Murli, Ravi Kumar, *Bioorg. Chem. Lett.*,2005,15,5030.
[2] E.Palaska, D.Erol, R. Deriradmar, *Eur.J.Med.Chem*,1996,31,43.
[3] O.Zuhal, K.H. Burak, G. Bulent, *Eur. J. Med. Chem.*,2007,42,403
[4] O. Ahmet, T.J.Gulhan, A.K. Jafer, *Eur. J. Med. Chem.* 2007,42,403.
[5] G.S. Aysel, Demirayak, C. Gultaze et.al., *Eur.J.Med.Chem* 2000,35,359.
[6] M.Amir, H. Kumar, S.A. Khan, *Bioorg.Med. Chem. Litt.*,2008,18,918
[7] Z. Brzozwski, F.S. Czewski, Gdaniec, *Euro. J. Med. Chem.*,2000,35,1053.
[8] B.f.Abdel-Wahab,H.A.Abdal Aziz,E.M.Ahmed,*Eur.J. Med. Chem.*
]9] M.I. Husaim, S.Shukla, *Indian J.Chem.*, 1986
[10] V.H.Babu, C.H.Sridevi, A. Joseph, K.K.Shrinivasan,*Ind. J. Pharm. Sci*. 2007,69,470
[11]F.F. Barsoum, H.M. Hosni, A.S. Girgis, *Bioorg.Med.Chem*, 2006,14,3929.
[12]Y.K.Agrawal, K.Munna, V.H. Babu, H.Bhatt, P.J.Gogoi, *Ind. J. Het.Chem*., 2007,16,263.
[13]M.Abid, A. azam, *Eur.J.Med.Chem*., 2005,40,935.