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RESEARCH ARTICLE

SYNTHESIS AND SPECTRAL CHARACTERIZATION OF SOME SUBSTITUTED DERIVATIVES OF 4-CHLORO-PYRAZOLINES

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ABSTRACT:

The present investigation deals with the synthesis of some chloro-pyrazolines from substituted pyrazolines. The synthesized chloro pyrazolines were characterized by elemental analysis, IR and NMR spectral analysis; the result of spectral analysis reveals presence of hydroxyl, methoxy, methyl and chloro functional groups along with the presence of aromatic ring which was also evident in the ^{1}H-NMR spectra which suggest successful synthesis of desired compounds.

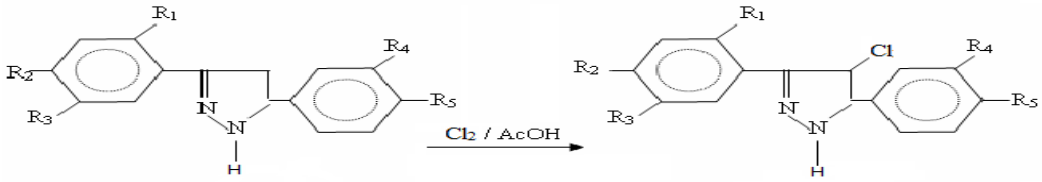
Keywords: 4-Chloro-Pyrazolones, elemental analysis, IR, NMR

INTRODUCTION

Pyrazoline are prominent nitrogen containing heterocyclic compounds play important role in medicinal chemistry[1] and various methods have been worked out for their synthesis[2]. In view of the influence of halogen atoms on the biological activity of organic compounds, Ankhiwala [3]synthesized some nuclear halogenated pyrazolines and their derivatives and screened them for their biological activity. These compounds were found to be active against *Staphylococcus aureus* and *Escherichia coli*. Wolf [4] synthesized N1- Aryloxyacetal-3-methyl-5-pyroziline. Reactions with these pyrazolines gave monoaryllidene derivatives along with bis-pyrazolone. Monoarylidine compounds were brominated with bromine in acetic acid. All these compounds were screened for their antifungal activity against *Aspergillus niger* and *Aspergillus flavus*. In general, antifungal activity[5] was found to increase. The different groups of the aldehyde moiety did not show any significant effect towards the antifungal activity. Keeping in mind the biological and clinical activity of pyrazolines [6]; the present study aimed to synthesize some new chloro-pyrazolines in order to study the further effect of chlorine on their biological activity.

EXPERIMENTAL

All the Chemicals and solvents used in the present investigation were BDH products. Melting points were determined in open capillary tube and are uncorrected. IR spectra of the synthesized compounds were recorded in KBr on Perkin Elmer 1600 (Japan) and NMR spectra on an AC 300F spectrophotometer with $CDCl_3$ using TMS as internal reference (chemical shift in d ppm).



S. No.	Compound code	Substituent				
		R1	R2	R3	R4	R5
1	P1	OH	H	CH_3	H	H
2	P2	OH	H	OCH_3	H	H
3	P3	H	CH_3	H	H	OCH_3
4	P4	H	OCH_3	H	H	H
5	P5	H	Cl	H	H	H

Scheme for the synthesis of substituted 4-chloro-pyrazolines derivatives

1. Synthesis of 3-(2-hydroxy-5-methylphenyl)-5-phenyl-4-chloropyrazoline (P1)

3-(2-hydroxy-5-methylphenyl)-5-phenyl-pyrozoline (0.66 g) was dissolved in hot acetic acid (40 ml). After cooling thionylchloride (0.8 ml) in acetic acid (10 ml) was added drop wise with constant shaking to ensure thorough mixing. The reaction mixture was then allowed to stand at room temperature overnight. The solid thus separated was filtered, washed with water and dried. Crystallization from a mixture of chloroform and alcohol (2:1) afforded light yellow crystals (0.58 g.).

IR: nmax (KBr): 3400, 2940, 1600, 1550, 1490, 1460, 1430, 1330, 1270, 1210, 1140, 1070, 900, 850, 830, 760, 700, 660, 570 and 550 cm^{-1}.

NMR ($CDCl_3$): d 2.20 (6H, dd, 2 -CH3), d 3.30 (1H, dd, CH), d 5.70 (1H, d, CH), d 6.90 to7.5 (11H, m, ArH), d 10.60 (1H, OH).

2. Synthesis of 3-(2‑hydroxy-5-methoxylphenyl)-5-phenyl-4-chloropyrazoline (P2)

3-(2‑hydroxy-5‑methoxylphenyl)-5-phenyl pyrozoline (0.68 g) was dissolved in hot acetic acid (40 ml). After cooling thionylchloride (0.8 ml) in acetic acid (10 ml) was added drop wise with constant shaking to ensure thorough mixing. The reaction mixture was occasionally shaken and was allowed to stand at room temperature overnight. The solid thus separated was filtered, washed with water and dried. Crystallization from a mixture of chloroform and alcohol (2:1) afforded pale yellow crystals (0.66 g.).

IR: nmax (KBr): 3300, 2900, 1600, 1570, 1530, 1490, 1450, 1330, 1270, 1210, 1180, 1140, 1060, 1040, 890, 850, 830, 800, 760, 700, 660, 600 and 560 cm^{-1}.

NMR (CDCl3): d 3.30 (1H, dd, CH), d3.80 (3H, s, OCH3), d 6.90 to 7.70 (10H, m, Ar), d 10.75 (1H, s, OH)

3. Synthesis of 3-(4‑methylphenyl)-5-(4-methoxyphenyl)-4- chloropyrazoline (P3)

3-(4-methylphenyl)-5-(4-methoxyphenyl) pyrazoline (0.67 g) was dissolved in hot acetic acid (40 ml). After cooling thionylchloride (0.8 ml) in acetic acid (10 ml) was added drop wise with constant shaking to ensure thorough mixing. The reaction mixture was occasionally shaken and was allowed to stand at room temperature overnight. The solid thus separated was filtered, washed with water and dried. Crystallization from a mixture of chloroform and alcohol (2:1) afforded pale yellow crystals (0.55 g.).

IR: nmax (KBr): 3300, 2900, 1600, 1530, 1520, 1460, 1420, 1320, 1300, 1270, 1250, 1230, 1160, 1140, 1110, 1030, 930, 910, 840, 800, 760, 680, 630, 560 and 540 cm^{-1}.

NMR (CDCl3): d 3.30 (1H, dd, CH), d3.80 (3H, s, OCH3), d 6.90 to 7.70 (10H, m, Ar).

4. Synthesis of 3-(4‑methoxyphenyl)-5-phenyl-4-chloropyrazoline (P4)

3-(4-methoxyphenyl)-5-phenyl pyrazoline (0.62 g) was dissolved in hot acetic acid (40 ml). After cooling thionylchloride (0.8 ml) in acetic acid (10 ml) was added drop wise with constant shaking to ensure thorough mixing. The reaction mixture was occasionally shaken and was allowed to stand at room temperature overnight. The solid thus separated was filtered, washed with water and dried. Crystallization from a mixture of chloroform and

alcohol (2:1) afforded brick orange crystals (0.55 g.).

IR: nmax (KBr): 2940, 1600, 1540, 1500, 1460, 1370, 1300, 12240, 1200, 1170, 1110, 1060, 1030, 960, 890, 860, 830, 800, 760, 700, 690, 660 and 550 cm-1.

5. Synthesis of 3-(4-chlorophenyl)-5-phenyl-4-chloropyrazoline (P5)

3-(4‑chlorophenyl)-5-phenyl-pyrazoline (0.65 g) was dissolved in hot acetic acid (40 ml). After cooling bromine (0.3 ml) thionylchloride (0.8 ml) in acetic acid (10 ml) was added drop wise with constant shaking to ensure thorough mixing. The reaction mixture was occasionally shaken and was allowed to stand at room temperature overnight. The solid thus separated was filtered, washed with water and dried. Crystallization from a mixture of chloroform and alcohol (2:1) afforded pale yellow crystals (0.63 g.).

IR: nmax (KBr): 1600, 1530, 1500, 1440, 1390, 1350, 1330, 1300, 1270, 1210, 1180, 1150, 1090, 1030, 990, 970, 920, 870, 810, 760, 690, 640, 600, 590, and 550 cm^{-1}.

NMR (CDCl3) d 3.20 (1H, dd, C-H), d 5.80 (1H, dd, CH), d 7.20 to 7.8 (10H, m, ArH)

RESULTS AND DISCUSSION

Structure of all the synthesized derivatives have been established on the basis of their consistent IR and ^{1}H-NMR spectral analysis. The synthesized derivatives showed the presence of hydroxyl, methoxy, methyl and chloro functional groups along with the presence of aromatic ring which was also evident in the ^{1}H-NMR spectra.

FTIR spectra of the compounds showed the characterstic peak of O-H stretching. The stretching vibration at 1483 cm^{-1} indicates the presences of aromatic C=C. The characteristic peak of C-H group indicated at 800-1200cm^{-1} . The characteristic peak at 3000-3700 cm^{-1} indicates the presence of N-H group. IR spectra of compounds also showed stretching band and $-CH_3$ deformation at 1330 cm^{-1}. It also exhibits an intense sharp band at 1171 cm^{-1} due to C-N stretch vibration. It was also observed that $-CH_2$ ring stretching at 2857 cm^{-1}. There is also -CH deformation at 681 cm^{-1}.

NMR spectra of pyrazolines also exhibits double doublets for each $–CH_2$ proton between d 3.25 and 3.60 and d 3.90 and 4.00, and double doublets between d 5.25 and d 6.20 for –CH proton. However, in NMR spectra the signal in range of d 3.90 to d 4.00 is absent (d 3.14). This provides the conclusive evidence that electrophilic attack of chlorine takes place at C-4 of the pyrazoline nucleus.

Thus spectral analysis confirmed the synthesis of desired compounds which suggests that adopted scheme for the synthesis of substituted derivatives of 4-chloro-pyrazolines was appropriate and can be utilized at large scale also.

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