P: ISSN NO.: 2394-0344 RNI No.UPBIL/2016/67980 VOL-3* ISSUE-9*(Part-2) December- 2018
E: ISSN NO.: 2455-0817 *Remarking An Analisation*

Synthesis and Characterization of Some Novel Heterocyclic Compounds Containing Pyrazole Derivatives as Their Medicinal Importance

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Abstract

Pyrazole condense with substituted aromatic aldehydes in acidic medium. The reaction when carried out in acetic acid yields 4-arylmethylene pyrazolones. Further these derivatives of pyrazolone reacts with substituted thiourea to give thiazinopyrazoles. The synthesized compound thiazinopyrazoles have been screened against test bacteria S. aureus and B. subtilis at 100 µg ml $^{-1}$ and 10 µg ml $^{-1}$.

Keywords: Pyrazolone, Thiazinopyrazole.

Introduction

Heterocyclic compounds are those cyclic compounds in which one or more of the ring carbons are replaced by another atom. The most common hetero atoms are nitrogen, oxygen and sulphur. Pyrazole is well known heterocyclic compound with two hetero atoms nitrogen at position 1 and 2. Pyrazoles are aromatic molecules due to their planar conjugated ring structures with six delocalized π-electrons. Pyrazole is a colourless solid m.p.70^{0}C. Pyrazole is a tautomeric substance because its position 3 and 5 must be equivalent.

Pyrazole derivatives have been found to be active as pathogenic agents. These derivatives may be used as bactericides, fungicides, insecticides, herbicides. These derivatives also show antitubercular, antitumor, antipyretic, antidiabetic, analgesic, antimicrobial, antimalerial anticancer properties.

Experimental

Melting points were taken in an open capillary tube and are uncorrected. The IR spectra were recorded in KBr on Perkin Elmer-720 spectrophotometer. The ^{1}H-NMR spectra were recorded in $CDCl_3$ on varian A-60 D spectrophotometer. The chemical shifts are recorded in ppm downfield from TMS, which are used as an internal standard.

Preparation of 2,4-dihydro-2,5-disubstituded-3H-pyrazol-3-ones

0.1 mol of appropriate β-keto ester in 20-30 ml of 95% ethanol was placed in a 100 ml round bottom flask equipped with a reflux condenser to this 0.1 mol of substituted hydrazine hydrate in 20-30 ml of 95% ethanol was added in one lot. The reaction started immediately with evolution of heat. It was refluxed for an additional one hour. The 2, 4-dihydro-2,5-disubstituded-3H-pyrazol-3-one, were separated in the reaction mixture, filtered and washed with a little 95% ethanol (2 × 10 ml) and recrystallised from 95% ethanol. The solution was concentrated under reduced pressure on rotary evaporator, the residue treated with ether, the solid, thus obtained was filtered under suction, washed with a little ether and recrystallised from ethanol-water mixture (50:50).

Preparation of 4-Arylmethylene-2,4- dihydro-2,5-disubstituded-3H-pyrazol-3-ones

A mixture of 0.01 mol of appropriate 2,4- dihydro-2,5-disubstituded-3H-pyrazol-3-one and 0.01 mol of benzaldehyde were dissolve in 10-15 ml glacial acetic acid into a flask. The reaction mixture was heated for 15 minutes and left overnight at room temperature. Colour crystals of 4-Arylmethylene-2,4- dihydro-2,5-disubstituded-3H-pyrazol-3-one were separated, filtered, dried and recrystallised from benzene. At this stage, if no crystals separated, a small amount of water was added till slight turbidity appeared and the mixture was allowed to stand to get coloured crystals of 4-Arylmethylene-2,4- dihydro-2,5-disubstituded-3H-pyrazol-3-ones, filtered, dried and recrystallised from ethanol: water.

Preparation of 1,3-disubstituted-4-substituted phenyl-4,5-dihydro pyrazolo [4,3-e] [1,3]-thiazin-6-imine

A mixture of 0.01 mol of appropriate 4-Arylmethylene-2,4- dihydro-2,5-disubstituded-3H-pyrazol-3-one and 0.01ml of thiourea/phenyl thiourea were dissolved in 20 ml of glacial acetic acid into a flask. The mixture was refluxed for 3-5 hours, it was allowed to cool and the solid obtained was separated, filtered, dried and recrystallised from ethanol: water.

Result and discussion

Pyrazole (1) condense with substituted aromatic aldehydes (2) in acidic medium. The reaction when carried out in acetic acid yields 4-arylmethylene pyrazolones (3) further this derivatives of pyrazolone reacts with substituted thiourea to give thiazinopyrazoles (4) (scheme-1).

4-substituted benzyliden-2,4-dihydro-2-phenyl-5-methyl-3H-pyrazol-3-one

The reaction of 2,4-dihydro-2-phenyl-3-methyl-3H-pyrazol-3-one with substituted benzaldehyde in equimolar proportion in presence of glacial acetic acid was heated for 15 minutes and left over night at room temperature yielded crystals of 4-substituted benzylidene-2,4-dihydro-2-phenyl-5-methyl-3H-pyrazol-3-one, filtered dried and recrystallised from ethanol: water. The elemental analysis of this compound corresponds to molecular formula $C_{17}H_{14}N_2S$. The IR spectrum of this compound shows characteristic absorption bands at 1523 cm $^{-1}$,1650 cm $^{-1}$, 3510 cm $^{-1}$ and 3050 cm $^{-1}$ for C=C, C=O, NH and Ar-CH group respectively. PMR spectrum exhibits singlet (3H) at δ 1.8 for CH_3 proton, singlet (1H) at δ 2.5 for CH proton and multiplet (10H) at δ 7.0 – 8.0 for aromatic protons.

4-substituted benzyliden-2,4-dihydro-2,5-diphenyl -3H-pyrazol-3-one

The reaction of 2,4-dihydro-2,5-diphenyl -3H-pyrazol-3-one with substituted benzaldehyde in equimolar proportion in presence of glacial acetic acid was heated for 15 minutes and left over night at room temperature yielded crystals of 4-substituted benzylidene-2,4-dihydro-2,5-diphenyl -3H-pyrazol-3-one, filtered dried and recrystallised from ethanol: water. The elemental analysis of this compound corresponds to molecular formula $C_{22}H_{16}N_2O$. The IR spectrum of this compound shows characteristic absorption bands at 1515 cm $^{-1}$ 1655 cm $^{-1}$ and 3530 cm $^{-1}$ for C=C, C=O and NH group respectively. PMR spectrum exhibits singlet (1H) at δ 2.6 for CH proton and multiplet (15H) at δ 7.10 – 8.15 for aromatic protons.

1-phenyl-3-methyl-4-substituted phenyl-4,5-dihydropyrazolo [4,3-e] [1,3] thiazin-6-imine

The reaction of 4-substituted benzyliden-2,4-dihydro-2-phenyl-5-methyl-3H-pyrazol-3-one with thiourea in equimolar proportion in presence of glacial acetic acid was heated and cooled at room temperature yielded crystals of1-phenyl-3-methyl-4-substituted phenyl-4,5-dihydropyrazolo [4,3-e] [1,3] thiazin-6-imine,filtered dried and recrystallised from ethanol: water. The elemental analysis of this compound corresponds to molecular formula $C_{18}H_{16}N_4S$. The IR spectrum of this compound shows characteristic absorption bands at 3410 cm $^{-1}$ and 1590 cm $^{-1}$ for NH and C=N group respectively. PMR spectrum exhibits singlet (3H) at δ 1.8 for CH_3 proton, singlet (1H) at δ 3.8 for CH proton ,multiplet (10H) at δ 7.0 – 8.0 for aromatic protons and singlet (2H) at δ 9.5 for NH proton.

1,3-diphenyl-4-substituted phenyl-4,5-dihydropyrazolo [4,3-e] [1,3] thiazin-6-imine

The reaction of 4-substituted benzyliden-2,4-dihydro-2,5-diphenyl -3H-pyrazol-3-one with thiourea in equimolar proportion in presence of glacial acetic acid was heated and cooled at room temperature yielded crystals of1,3-diphenyl-4-substituted phenyl-4,5-dihydropyrazolo [4,3-e] [1,3] thiazin-6-imine,filtered dried and recrystallised from ethanol: water. The elemental analysis of this compound corresponds to molecular formula $C_{23}H_{18}N_4S$.The IR spectrum of this compound shows characteristic absorption bands at 3440 cm $^{-1}$ and1556cm $^{-1}$ for NH and C=N group respectively. PMR spectrum exhibits singlet (1H) at δ 3.5 for CH proton, multiplet (15H) at δ 7.10 – 8.15 for aromatic protons and singlet (2H) at δ 9.5 for NH proton.

Antibacterial Activity

1,3-disubstituted-4-substituted phenyl-4,5-dihydropyrazolo [4,3-e] [1,3] thiazin-6-imines have been screened for their antibacterial activity against S. aureus and B.subtilis at two concentrations viz 100 μ g ml $^{-1}$ and 10 μ g ml $^{-1}$.

Aim of Study

Pyrazole Derivatives are extensively employed in photography as colour couplers, sensitizers, supersensitizers, colour filter, antihalation agents. For its medicinal activities several research workers synthesized these compounds.

Conclusion

The antibacterial activity of synthesized thiazinopyrazoles have been screened against test

bacteria S. aureus and B. subtilis at 100 μg ml-1 and 10 μg ml-1 concentration. Thus nitrogen and sulphur containing heterocyclic conpounds have antibacterial activity.

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