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Synthesis, Analysis and Antibacterial Evaluation of Pyrazole Derivative

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Abstract

In the present study we had synthesised some pyrazole derivatives for finding potential antibacterial agents. Ethyl acetoacetate was reacted with benzene diazonium compound and the resulting compound was condensed with phenylhydrazine in presence of acetic acid to afford pyrazole compound. The synthesized compound was analyzed by physical and chromatography data. The presence of specific functional group in the product was confirmed by the IR spectroscopy and further structure determination by NMR and Mass spectroscopy is in progress. The *in vitro* antibacterial efficacy of synthesized compound was tested against Gram positive and Gram negative microorganisms by Cup and Plate method. The pyrazole derivative showed promising activity against Gram positive bacteria *Staphylococcus aureus*.

Key words: Pyrazole, Cup and plate method, Antibacterial.

Introduction

The worldwide use of antimicrobial compounds to treat infection leads to the evolution of microbes resistant to existing drugs. The emergence of resistance to the major classes of antibacterial agents is recognized as a serious health concern. The search for antibacterial agents with new mode of actions will always remain an important and challenging task.[1] The heterocyclic compounds particularly nitrogen containing heterocycles are synthetically challenging models for a number of physiological active natural products. One such class of compounds includes pyrazole.

Pyrazole and pyrazolones ring system represents important class of compounds possessing a wide spectrum of biological activities. The recent success of pyrazole COX-2 inhibitor has further highlighted the importance of these heterocycles in medicinal chemistry.[2] It is also showing angiotensin antagonists, antibacterial, sedative, antidiabetic and anticoagulant activities.[3] Recently some pyrazole are reported to have non-nucleoside HIV–1 reverse transcriptase inhibitory activities.[4] With this aim we made an attempt to synthesis heterocyclic derivatives of pyrazole to show the antibacterial activity.

Experimental Work

The chemicals used in the study were obtained from Nice chemicals. Melting points were determined in open glass capillary tubes and are uncorrected. Thin layer chromatography was used to find the purity of synthesized compounds. The IR spectra of compounds were recorded on Shimadzu FT-IR -8400S spectrometer using KBR pellet technique and are expressed in cm^{1}. Preparation of pyrazoles[5] was carried out as per scheme I. Aniline was dissolved in a mixture of conc. HCl (4ml) and water (5ml) and cooled to 0° to 5°C in ice bath. To this solution of Sodium nitrite (0.69g) in water was added. The diazonium compound so obtained was filtered into already ice cooled solution mixture of sodium acetate (10g) and ethyl acetoactate 1.2ml (0.01mol) in ethanol. The resulting product was added to a solution of phenyl hydrazine 0.5ml (0.002mol) in acetic acid (5 ml) and the mixture was warmed in water bath for 1hr. On cooling yellow crystals were obtained which were recrystallised from ethanol. Yield 61%, M.pt 114-116, Rf value: 0.3 {Mobile Phase – Ethyl acetate & Chloroform (8 : 2)}, IR (KBr, cm^{-1}): 3400- 3285 (NH), 3032 (ArC-H), 1660 (C=O), 1597 (C=C), 1245 (C-N).

Antibacterial activity

The compound was screened for their antibacterial activity by Cup plate method against Gram positive bacteria *Staphylococcus aureus* and Gram negative bacteria *Escherichia coli*. Sterile nutrient agar plates were prepared, by pouring the sterile agar into petri-dishes in aseptic conditions. About 0.1ml of each standardized test organism culture was spread on to agar plates. Cavity was done by using a sterile borer of diameter 6 mm. 100 µg/well of the test compounds as well as the standard drug solutions and DMSO solvent were placed in the cavity separately. Then the plates were maintained at +4 °C for 1 h to allow the diffusion

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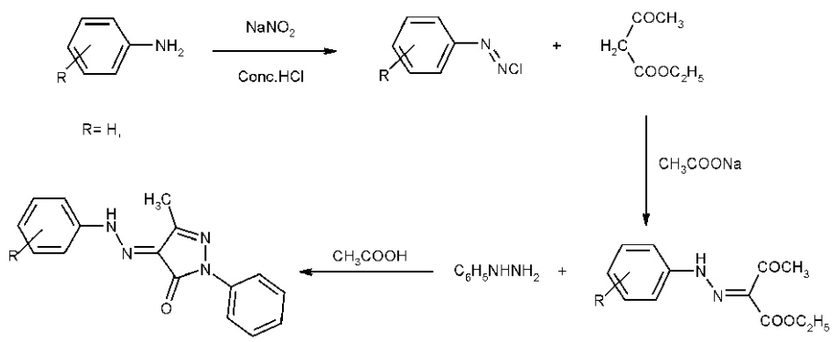
Scheme - I



of solution into the medium. Then the plates were incubated at 37 °C for 24 h. After the incubation period for 24 h, the zone of inhibition was measured.[6]

Results and Discussion

The result of antibacterial screening shows some promising activity against Gram positive bacteria *Staphylococcus aureus*. The synthesized compounds were analyzed mainly by IR spectral, physical and chromatography readings. Further analysis of structure by NMR, Mass spectrometer is in progress. In future, we will synthesis more pyrazole derivatives by taking different substituted anilines to find potential antibacterial agents.

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