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Synthesis and Study of Antimicrobial Activity of 3-(2'-hydroxy-3'-nitro-5'-methylphenyl)-5-(Aryl/Heteryl)-2-Pyrazoles

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Abstract:
The present study deals with the synthesis and study of antimicrobial characteristics of 3-(2'-hydroxy-3'-nitro-5'- methylphenyl)-5-(aryl/heteryl) pyrazoles synthesized from 1-(2'-hydroxy-3'-nitro-5'-methylphenyl)-3- aryl/heteryl-2-propen-1-ones by reaction with hydrazine hydrate in ethanol. The structures of synthesized compounds have been established by spectral (IR, NMR, etc.) and elemental analysis. Pyrazoles and its derivatives have been studied because of their wide range biological and pharmacological activities. They have been demonstrated to posses many biological and pharmacological activities such as antibacterial, antifungal, antiviral, antioxidant, antiinflammatory, antimutagenic and antiallergic activities and inhibitory activities on several enzymes. The synthesized compounds were tested against the pathogenic bacteria using cup-plate method and their minimum inhibitory concentrations (MIC) were determined using broth macro dilution method

Keywords: Synthesis, Pyrazoles, and Antimicrobial activity

Introduction:

Pyrazoles constitute an essential class of natural and synthetic products, many of which exhibit flexible biological activity. Antitumor, herbicides, antibacterial, antifungal, hypoglycemic, antidepressant, analgesic, anti-inflammatory, anti-cancer, enzyme inhibitor activity are shown among the pyrazoles. As represented by the molecular formula, Pyrazole is a five membered ring structure consisting of three carbon atoms and two nitrogen atoms in adjacent positions. The word pyrazole was first coined by Ludwig Knorr in 1883. They are known as alkaloids because of their structures and unique pharmacological effects on human beings. 1-pyrazolylalanine was the first natural pyrazole isolated from watermelon seeds in the year 1959. In organic chemistry, the chemistry of heterocyclic compounds remains a blossoming field. One of the heterocyclic compounds is Pyrazole. In the history of heterocyclic chemistry, pyrazole derivatives have played a crucial role and have been extensively studied due to their ready accessibility, diverse chemical reactivity, and extensive biological activity. Pyrazole derivatives are widely applicable in different areas, i.e. Industry, rehabilitation and cultivation in medicine.

Pyrazoles have been studied because of their wide range biological and pharmacological activities. They have been demonstrated to posses many biological and pharmacological activities such as antibacterial, antifungal, antiviral, antioxidant, antiinflammatory, antimutagenic and antiallergic activities and inhibitory activities on several enzymes.

Methods and Materials:

The diverse properties of pyrazoles have promoted to synthesis some new pyrazoles. Melting points are uncorrected. The IR spectra of some of the representative compounds from the series were recorded on PERKIN ELMER IR Spectrometer -450. The NMR spectra of few representative compounds were studied in CDCl3 on Bruker Avance II 400 NMR Spectrometer using TMS as internal standard. Purity of compounds was checked by TLC.

Synthesis-3-(2-Hydroxy-3-Nitro-5-MethylPhenyl)-5-(Aryl/Heteryl)-2-Pyrazoles.-

1-(2'-hydroxy-3'-nitro-5'-methyl phenyl)-3-phenyl-2-propen-1-one (0.01 mole) treated with hydrazine hydrate (0.012 mole) in 25 ml of ethanol and reaction mixture was refluxed for 2-3 hours. Then reaction mixture was cooled, poured in ice cold water. The separated solid product was filtered washed with water, dried and recrystalized from proper solvent. Similarly all the other compounds of the series were also prepared by the above procedure. The IR spectra shows the presence of absorption band in the region 3600-3300 cm-1 for (N-H) stretching vibrations characteristic band of pyrazole ring. The absorption at 1600 cm-1 is due to C=N stretching. The absorption in the region 3360- 3380 cm-1 is due to –OH group. The NMR spectra of 3-(2-hydroxy-3-nitro5-methyl phenyl)-5-(p-dimethylamino phenyl)-2– pyrazole exhibited signals at δ NMR (δ ppm): The 6 protons of dimethyl amino [-N (CH3)2] were observed at 3.06 δ. The aromatic protons were absorbed at 6.81-7.91 δ and the signal due to phenolic (-OH) proton was seen at 9.82δ (s).

Result and Discussion:

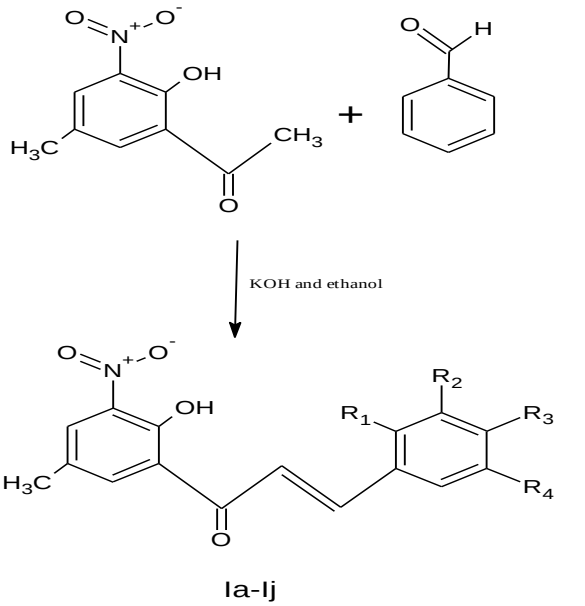
Pyrazole and its derivatives synthesized (IIa, IIb, IIc, IId, IIe, IIf, IIg, IIh, IIi, IIj) were studied for their antimicrobial activities against pathogenic bacteria causing variety of infections in human being and the inhibitory effects were recorded.

The pyrazoles were active towards S. aureus , S. typhi, E.coli. P. pneumoniae and P. mirabilis in the MIC range of 62 to 500 µg / ml. However, it was inactive towards S. dysentariae at 1000 µg / ml, the highest concentration tested . The inhibitory action was lower towards E.coli, S. aureus, P.mirabilis, moderate active towards K. pneumoniae with MIC 125 µg / ml and higher towards S. typhi with MIC of 62µg /ml.

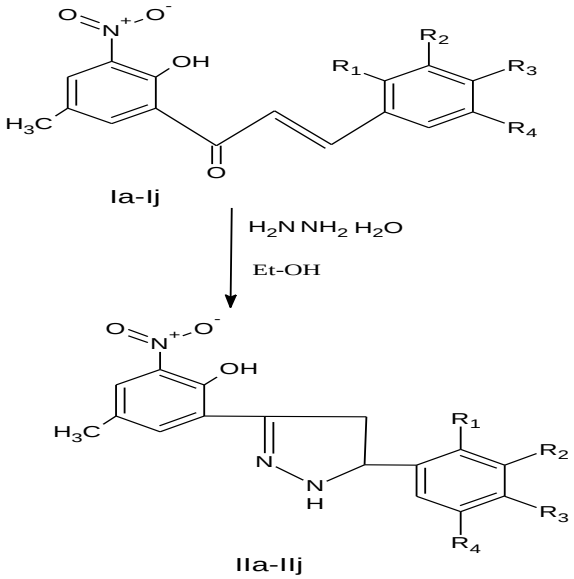
The compounds IIb to IIe were found to be more active against S. dysentariae with MIC value 62 µg / ml. Similarly, Compound IIa also showed increase activity against S. aureus and P. mirabilis.

Although pyrazole and its derivatives were less active than standard drug Chloramphenicol, but they may find some uses in chemotherapy of certain infection of bacterial origin after studying their pharmacological, biochemical and other properties Studies on non toxicity of human body and bactericidal effects at therapeutic doses, their metabolism in human body will further help to understand various hidden useful characteristics of these pyrazoles and their derivatives.

REACTION SCHEME-1



REACTION SCHEME-2



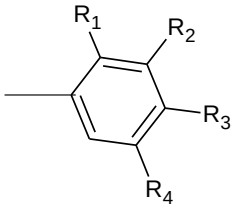


Table 1: Substituent's in the position of R_1, R_2, R_3, and R_4 are as given below

Sr. no.	Compounds	R_1	R_2	R_3	R_4
1	IIa	-H	-H	-H	-H
2	IIb	-Cl	-H	-H	-H
3	IIc	-H	-H	-Cl	-H
4	IId	-H	-H	-OH	-H
5	IIe	-H	-OH	-H	-H
6	IIf	$-NO_2$	-H	-H	-H
7	IIg	-H	-H	$-OCH_3$	-H
8	IIh	-H	-H	$-O-CH_2-O-$	
9	IIi	-H	-H	$-CH_3$	-H
10	IIj	-H	-H	$-N(CH_3)_2$	-H

Table 2: Characterization data of 3-(2'-hydroxy-3'- nitro-5'-methylphenyl)-5-(Aryl/Heteryl)-2-Pyrazoles

Sr. No.	Comp. No.	M. P. ^0C	Yield %	Molecular formula	Anal. found (Calcd) %Nitrogen
1	IIa	570	80	$C_{18}H_{18}O_3N_4$	9.20 (9.42)
2	IIb	280	70	$C_{16}H_{13}O_3N_3$	6.05 (6.75)
3	IIc	240	75	$C_{16}H_{12}O_5N_4$	12.05 (12.21)
4	IId	221	72	$C_{17}H_{15}O_3N_3$	9.80 (9.85)
5	IIe	116	76	$C_{16}H_{12}O_3N_3Cl$	7.20 (7.37)
6	IIf	180	66	$C_{16}H_{12}O_3N_3Cl$	7.20 (7.37)
7	IIg	153	72	$C_{14}H_{11}O_4N_2$	8.20 (8.37)
8	IIh	285	56	$C_{17}H_{14}O_6N_2$	8.28 (8.35)
9	IIi	145	62	$C_{16}H_{13}O_4N_3$	5.48 (5.87)
10	IIj	132	78	$C_{16}H_{13}O_4N_3$	5.48 (5.87)

Table 3-Antimicrobial activity of some of 3-(2-hydroxy-3-nitro5-methyl phenyl)-5-(p-dimethylamino phenyl)-2– pyrazole (Zone of inhibition measure in mm).

Name of compounds	E.coil	S. aureus	*S. typhi*	*Staph. albas*	*Shigella dysenterty*	*B. subtilis*	*Vibro Cholerae*	*Kl. pneumoniae*
IIa	13	10	16	10	14	06	12	14
IIb	13	12	14	08	08	10	10	10
IIc	14	12	13	10	10	08	08	10
IId	12	10	14	08	09	05	-	08
IIe	16	15	12	-	10	12	12	09
IIf	13	09	10	-	12	09	10	11
IIg	13	12	12	-	11	10	09	08
IIh	12	11	14	06	13	-	11	12
IIi	16	10	10	10	10	06	08	12
IIj	10	14	08	-	08	10	09	08

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