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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3-(2'-HYDROXY-3'-NITRO-5'-METHYLPHENYL)-5-(ARYL/HETERYL) PYRAZOLES

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ABSTRACT: Heterocyclic compounds are well known for their different biological activities like anti-inflammatory, antibacterial, antifungal, anticancer, insecticidal, pecticidal, antibiotic, etc. the versatile applications of oxygen, nitrogen and sulphur containing heterocyclic compounds have made this area of extensive research. The present study deals with the synthesis of some new 3-(2'-hydroxy-3'-nitro-5'-methylphenyl)-5-(aryl/heteryl) pyrazoles synthesis from 1-(2'-hydroxy-3'-nitro-5'-methylphenyl) – 3 - aryl/heteryl - 2-propen-ones i.e. chalcone by reaction with hydrazine hydrate in ethanol and synthesized compounds screening for antimicrobial activity.

INTRODUCTION: Heterocyclic compounds are well known for their different biological activities. The versatile applications of oxygen, nitrogen and sulphur containing heterocyclic compounds have made this area of extensive research. Pyrazoles have been studied because of their wide range biological and pharmacological activities. These compounds have been found to be effective as antimicrobial, antiinflamatoryl [1], herebicidals [2], antibacterial [3] etc. The diverse properties of pyrazoles have promoted to synthesis some new pyrazoles. The synthesized3-(2'-hydroxy-3'-nitro-5'-methylphenyl)-5-(aryl/heteryl) pyrazoles were screened for their antimicrobial activity against bacteria like *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi, Proteus vulgaris* and antifungal activity against *Aspergillus niger, Aspergillus fumigates, Rhizopus* and *Candida albicans* carried out by disc diffusion method displayed significant antimicrobial activity.

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Experimental:

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 $CDCl_3$ on Bruker Avance II 400 NMR Spectrometer using TMS as internal standard. Purity of compounds was checked by TLC.

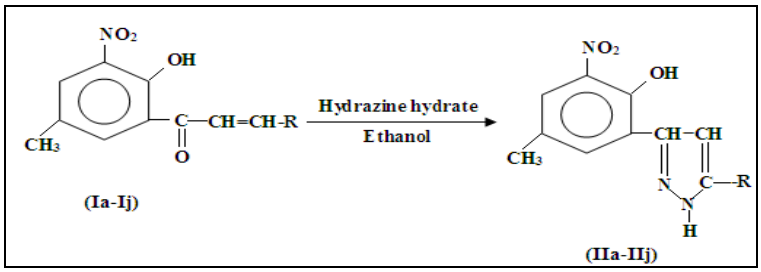
Synthesis-3-(2-Hydroxy - 3 – Nitro – 5 - Methyl Phenyl) – 5 - (Aryl/Heteryl)-2-Pyrazoles:

1-(2'-hydroxy-3'-nitro-5'-methylphenyl)- 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 recrystallized 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-nitro-5-methyl phenyl)-5-(p-dimethylamino phenyl)-2–pyrazole exhibited signals at δ NMR (δ ppm): The 6 protons of dimethylamino [-N $(CH_3)_2$] were observed at 3.06δ. 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).

Reaction



SCHEME: 1

TABLE 1: DIFFERENT SUBSTITUTION OF BENZALDEHYDE IN CHALCONE PREPARATION (I.E. R)

Sr. No.	Compounds	R
1	IIa	p-N, N- dimethyl amino phenyl
2	IIb	pheny
3	IIc	o-Nitro phenyl
4	IId	p-methoxy phenyl
5	IIe	o-Chloro phenyl
6	IIf	p-Chloro phenyl
7	gII	Furfuryl
8	IIh	Methylenedioxy phenyl
9	IIi	p-hydroxy phenyl
10	IIj	m-hydroxy phenyl

TABLE 2: CHARACTERIZATION DATA OF 3-(2'-HYDROXY-3'-NITRO-5'-METHYLPHENYL)-5-(ARYL/HETERYL) -2-PYRAZOLES

Comp. No.	M. P. ^0C	Yield %	Molecular formula	Anal. found (Calcd) % Nitrogen
IIa	270	80	$C_{18}H_{18}O_3N_4$	9.20 (9.42)
IIb	280	70	$C_{16}H_{13}O_3N_3$	6.05 (6.75)
IIc	240	75	$C_{16}H_{12}O_5N_4$	12.05 (12.21)
IId	221	72	$C_{17}H_{15}O_3N_3$	9.80 (9.85)
IIe	116	76	$C_{16}H_{12}O_3N_3Cl$	7.20 (7.37)
IIf	180	66	$C_{16}H_{12}O_3N_3Cl$	7.20 (7.37)
IIg	153	72	$C_{14}H_{11}O_4N_2$	8.20 (8.37)
IIh	285	56	$C_{17}H_{14}O_6N_2$	8.28 (8.35)
IIi	145	62	$C_{16}H_{13}O_4N_3$	5.48 (5.87)
IIj	132	78	$C_{16}H_{13}O_4N_3$	5.48 (5.87)

Biological evaluation:

Antibacterial activity of synthesized compounds (IIa-IIj): For antibacterial test sample solution of all synthesized 3-(2' – hydroxyl - 3' - nitro-5'-methylphenyl)-5-(aryl/heteryl) pyrazoles was prepared by dissolving 100mg of sample in 1ml of DMF. All the synthesized compounds (IIa-IIj) were tested by disc diffusion method [9] against the bacteria as *Escherichia coli, Staphylococcus*

aureus, Salmonella typhi, Pseudomonas aeruginosa, and *Proteus vulgaris.*

Antifungal activity synthesized compounds (IIa-IIj):

The antifungal activity of all synthesized compounds was studies at 1000ppm concentration in vitro. Plant pathogenic organisms were *Aspergillus niger, Aspergillus fumigates, Rhizopus* and *Candida albicans.* The antifungal activity of all the compounds was measured on each of these plants pathogenic strains on potato dextrose agar (PDA), 5-6 day old cultures were employed. The inhibition for fungi was calculated after five days using the formula as Percentage of inhibition = 100(x-y) / x, where, x= area of colony in control plate. And y= area of colony in test plate.

TABLE 3: ANTIBACTERIAL ACTIVITY OF 3-(2'-HYDROXY-3'-NITRO-5'-METHYLPHENYL)-5-(ARYL / HETERYL) -2-PYRAZOLES (IIa-IIj)

Compounds	*Escherichia coli*	*Staphylococcus aureus*	*Salmonella typhi*	*Pseudomonas aeruginosa*	*Proteus vulgaris*
IIa	16	14	10	-	06
IIb	14	12	11	06	12
IIc	12	11	08	06	-
IId	08	-	-	-	07
IIe	16	-	-	06	06
IIf	12	12	-	-	10
IIg	14	12	10	08	08
IIh	10	10	-	12	10
IIi	12	08	-	10	06
IIj	10	06	-	07	08
DMF solvent control	-	-	-	-	-

Range: Strongly active: >12mm; Moderate active: 8-12 weakly active: <8mm; - inactive

TABLE 4: ANTIFUNGAL ACTIVITY OF 3-(2'-HYDROXY-3'-NITRO-5'-METHYLPHENYL)-5-(ARYL / HETERYL) -2-PYRAZOLES (IIa-IIj)

Compounds	*Aspergillus niger*	*Aspergillus fumigates*	*Rhizopus*	*Candida albicans*
IIa	18	20	14	12
IIb	16	17	12	16
IIc	14	16	14	12
IId	18	20	18	17
IIe	22	18	16	19
IIf	20	22	18	14
IIg	12	14	16	12
IIh	16	20	22	20
IIi	22	16	18	17
IIj	14	14	10	12
Greseofulvin	24	26	22	26

Zone of inhibition measure in mm

RESULT AND DISCUSSION: In present study new 3-(2'-hydroxy-3'-nitro-5'-methylphenyl)-5-(aryl/heteryl) pyrazoles have been synthesized by the reaction of 1-(2'-hydroxy-3'-nitro-5'-methylphenyl)-3-aryl/heteryl-2-propen-ones i.e. chalcone by reaction with hydrazine hydrate in ethanol. Structures of all these synthesized compounds were established on the basis of spectral data (IR, NMR) and elemental analysis. All the compounds (IIa-IIj) were tested for their antimicrobial activity against the bacteria *Escherichia coli, Staphylococcus aureus, Salmonella typhi, Pseudomonas aeruginosa, and Proteus vulgaris.* Some of the compounds showed remarkable zone of inhibition i.e. strongly active IIa, IIb, IIe, IIg, some of them moderate active IIc, IIf, IIh, IIj and other are weakly active IId, as shown in **Table 3.**

In case of antifungal activity against the *Aspergillus niger, Aspergillus fumigates, Rhizopus, Candida albicans.* All synthesizes compounds are strongly active; the results were compared with the standard antifungal drug Greseofulvin and were summarized in **Table 4**.

CONCLUSION: In present study 3-(2'-hydroxy-3'-nitro-5'-methylphenyl)-5-(aryl/heteryl) pyrazoles have been synthesized with percentage yield range 56-80%. Structures of all these synthesized compounds were established on the basis of spectral data (IR, NMR) and elemental analysis. The screening results revealed that the near about all compounds showed significant antimicrobial activity and antifungal activity. The screening results of all compounds against all the micro-organisms are comparable to that of standard drugs.

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