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SYNTHESIS, CHARACTERIZATION AND STUDY OF ANTIMICROBIAL ACTIVITY OF 2-HYDROXY 3-NITRO-5-METHYL-N-(SUBSTITUTED PHENYL) CHALCONE IMINES

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ABSTRACT: Chalcones and its derivatives show various biological activities. The present study deals with the synthesis of series of 2-hydroxy-3-nitro-5-methyl–N-substituted phenyl chalcone imines from 2-hydroxy-3-nitro-5-methylphenyl chalcone and different substituted aromatic animes in ethanol in presence of 2, 3 drops of Conc. H_2SO_4. Structures of synthesized compounds have been established by spectral (IR, NMR, etc.) and elemental analysis. In the present communication we report the synthesis substituted chalcone imines and its antimicrobial activity against pathogenic bacteria and fungi. The sensitivity carried out by disc diffusion method displayed significant antimicrobial activity.

INTRODUCTION: Chalcones and its derivatives show various biological activities. Chalcones are medicinally important class of compounds. It is also used as main intermediate for synthesis of heterocyclic compounds like pyrazolines[1], isoxazolines [2], flavonone[3], pyrimidines[4], etc. They have been reported to possess biological activities such as antioxidant[5], antimalarial,[6] anlgesic,[7] antiinflammatory,[8] anticancer [9] , insecticidal[10-11], antibacterial activity[12-13], fungicidal[14-15], activities. Chalcone imines are the phenolic Schiff bases, the present study deals with the synthesis of series of 2-hydroxy-3-nitro-5-methyl–N-substituted phenyl chalcone imines from 2-hydroxy-3-nitro-5-methylphenyl chalcone and different substituted aromatic animes.

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chalcone imines from chalcone and different substituted aromatic animes. Structures of synthesized compounds have been established by spectral (IR, NMR, etc.) and elemental analysis. The synthesized chalcone imines were screened for their antimicrobial activity against bacteria like *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* and antifungal activity against *Aspergillus niger*, *Aspergillus fumigates*, *Rhizopus* and *Candida albicans* carried out by disc diffusion method displayed significant antimicrobial activity.

Experimental

Synthesis of 1-(2'-hydroxy-3'-nitro-5'-methyl phenyl)-3-phenyl-2-propen-1-one(Chalcone) (Reaction Scheme1):

A mixture of equimolar quantities of 2'-hydroxy-3'-nitro-5'-methyl acetophenone (0.01 moles) and benzaldehyde (0.01 moles) were dissolved in ethanol and 40 % KOH was added in portions at 10^0C with stirring. The reaction flask was corked and kept at room temperature for 12hrs (overnight).

The contents of the flask were then acidified by dilute hydrochloric acid and poured over ice-cold water. Solid obtained was filtered, washed with water and crystallized from proper solvents.

Yield: 75%; colour: pale yellow crystalline solid; Melting point: 125^{o}C; Molecular formula: $C_{16}H_{13}O_4N$; Molecular weight: 283.

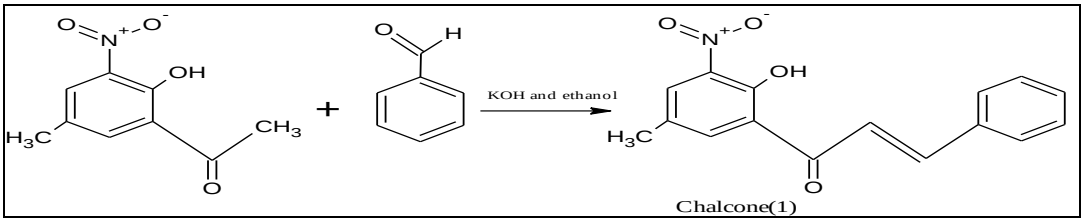
Spectral Data:
IR (KBr, cm^{-1}):3523(O-H), 1667(C=O), 1580 and 1450 (C=C, phenyl), 1614 (C=C, ethylenic). ^{1}H-NMR ($CDCl_3$ on Bruker Avance II 400 NMR Spectrometer using TMS as internal standard): 12.10 (s, 1H, -OH), 8.12(d, 1H, Ar-CH), 7.52(1H, Ar-CH), 6.99-6.93(m, 5H, Ar-H).

Synthesis of 2-hydroxy-3-nitro-5-methyl–N-substituted phenyl chalcone imines (2a-j) (Reaction Scheme 2):
The equimolar amount of 2-hydroxy-3-nitro-5-methylphenyl chalcne (0.01moles) and substituted aromatic amines (0.01moles) was dissolved in ethanol (20ml) and add 2, 3 drops of Conc. H_2SO_4 and refluxed for 4 hrs. Completion of reaction is monitor by TLC. After completion of reaction cool the reaction mixture dilute with ice cold water separated solid 2-hydroxy-3-nitro-5-methyl–N-substituted phenyl chalcone imines was obtained, these are filtered and purified.

Biological Evaluation:
Antibacterial activity of synthesized compounds (2a-j):
Antibacterial test sample solution was prepared by dissolving 100mg of sample in 1ml of DMF. All the synthesized compounds (2a-j) were tested by disc diffusion method against the bacteria as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi*. The antibacterial activities of all compounds are compared against Amplicilline as a standard drug as shown in **Table 2.**

Antifungal activity synthesized compounds (2a-j):
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 as shown in **Table 3.**

Reaction Scheme 1:



Reaction Scheme 2:

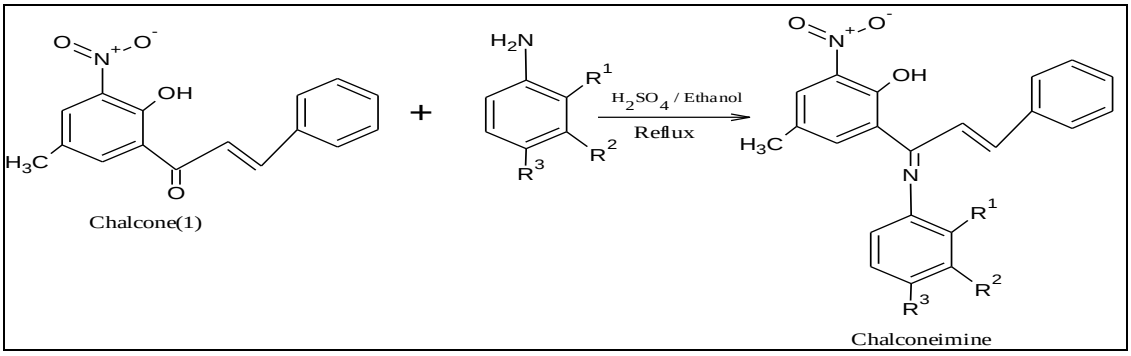


TABLE 1: THE OTHER CHALCONE IMINES PREPARED ARE TABULATED

Sr. No.	Compounds	R^1	R^2	R^3	M.P. (^{0}C)	Yield (%)
1	2a	H	H	H	86	76
2	2b	NO_2	H	H	102	60
3	2c	H	NO_2	H	98	58
4	2d	H	H	NO_2	82	65
5	2e	OH	H	H	72	52
6	2f	H	OH	H	164	74
7	2g	H	H	OH	142	72
8	2h	CH_3	H	H	127	78
9	2i	H	CH_3	H	112	74
10	2j	H	H	CH_3	94	70

TABLE 2: ANTIBACTERIAL ACTIVITY OF CHALCONEIMINES (2a-j)

Sr. No.	Compounds	*Escherichia coli*	*Staphylococcus aureus*	*Pseudomonas aeruginosa*	*Salmonella typhi*
1	**2a**	16	10	17	10
2	**2b**	15	14	16	12
3	**2c**	13	11	16	10
4	**2d**	12	12	14	18
5	**2e**	14	13	16	15
6	**2f**	13	10	15	14
7	**2g**	18	13	18	13
8	**2h**	17	12	21	19
9	**2i**	18	14	19	18
10	**2j**	16	10	17	16
11	**Amplicilline**	22	23	22	20

Zone of inhibition measure in mm

TABLE 3: ANTIFUNGAL ACTIVITY OF CHALCONEIMINES (2a-j)

Sr. No.	Compounds	*Aspergillus niger*	*Aspergillus fumigates*	*Candida albicans*	*Rhizopus*
1	2a	--	12	14	10
2	2b	16	14	13	12
3	2c	12	10	15	14
4	2d	--	14	13	16
5	2e	14	16	15	10
6	2f	12	--	15	14
7	2g	11	12	17	15
8	2h	10	14	20	11
9	2i	--	11	18	18
10	2j	16	14	17	16
11	Greseofulvin	22	22	26	28

Zone of inhibition measure in mm

RESULT AND DISCUSSION

In present study new 2-hydroxy-3-nitro-5-methyl–N-substituted phenyl chalcone imines have been synthesized by the reaction of 2-hydroxy-3-nitro-5-methylphenyl chalcone and aromatic substituted amines at reflux using ethanol as solvent in presence of conc. H_2SO_4 in 52-78% yield. Structures of all these synthesized compounds were established on the basis of spectral data (IR, NMR) and elemental analysis.

All the compounds (2a-j) were tested for their antimicrobial activity against the bacteria *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa*, *Salmonella typhi* and *Aspergillus niger, Aspergillus fumigates, Rhizopus, Candida albicans.* The results were compared with the standard antibacterial drug Amplicilline and standard antifungal drug Greseofulvin. The Zones of inhibition for antibacterial activity were summarized in **Table 2** and for antifungal activity

were summarized in **Table 3**. Some compounds as 2g, 2h, 2i, and 2j shows higher activity against the microorganism. While other shows moderate activity against the microorganism.

CONCLUSION: In present study new 2-hydroxy-3-nitro-5-methyl–N-substituted phenyl chalcone imines have been synthesized with percentage yield range 52-78%. Structures of all these synthesized compounds were established on the basis of spectral data (IR, NMR) and elemental analysis. From the antimicrobial activity it has been interesting to note that the chalconeimines were more active against the microorganism.

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