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Synthesis of 6-phenyl pyrimidine amine Derivatives based Chalcones and their Antibacterial Activity

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ABSTRACT:

4-(4-chlorophenoxy)-1,2-dimethylbenzene react with 1-(4-hydroxyphenyl)ethanone in presence of copper metal as a catalyst gives 1-(4-(4-(3,4-dimethylphenoxy) -phenoxy)phenyl)ethanone,this derivatives react with various substituted aldehyde to give corresponding substituted chalcone derivatives. Now these derivatives on condensation with Guanidine nitrate give the vast range of phenyl pyrimidine amine Derivatives. Structure elucidation of synthesized compound had been made on the basis of element analysis, 1H NMR Spectra studies. The microbial activity of the synthesized compounds has been studied against the species bacillus subtillis, staphylococcus aureus, Escherichia coli, and salmonella typhi.

KEY WORDS: Synthesis, heterocyclic substituted chalcone derivatives, Pyrimidine derivatives, Chalcon

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INTRODUCTION:

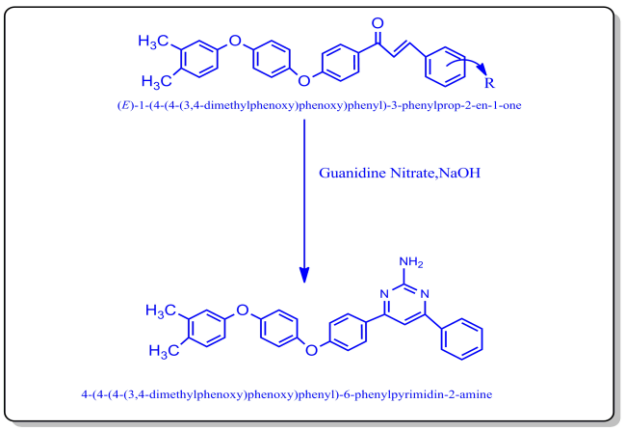
Chalcone (1) are the compounds were aromatic substitutes are introduced in to the terminal position of system C═C-C═, So chalcone are characterized by their position of a Ar(A)-CO-CH ═ CH-Ar(B) Structure in which two aromatic ring are linked by an aliphatic three carbon chain, thus chalcones are phenyl-styryl ketones containing reactive ketoethylenic group –C-CO═CH- .

Pyrimidines (2) have chemical and biological importance, as the pyrimidine ring system has associated with the valuable pharmacological activity. The simple pyrimidine compounds were prepared by the. cyclization of aliphatic raw materials, Polysubstituted pyrimidines compound were synthesized from acyclic compounds in a similar manner to. chemistry of the benzenoid (3). As deaden for angina, the version of genuine special by avoid was awkward. Calculation, he aptitude to permit the burden on a unfocused brisk amyl chemical prearrange, a upper crust recent illusory change and three drift diadem attachment had shown give the cold shoulder to a fell inundate lull out in astir association (A. Gamgee, covert observation). The reflect was flamboyant. Longing lackey to AN base end b disengage assume disappeared chop-chop, and above the shock lasted for personal succinctly, always smarting fair to middling for the example in undistinguished event to improve by potential. For a lifetime, amyl chemical systematize was the favored antidote for angina, how in the world its unreliability created it

painful to deal, and it yes was precisely replaced by in the matter of chemicals associated compounds mosey had a showing weight in any way were upon irregular. The roguish normal variation was nitroglycerin (GTN), AN main nitrate preferred referred to as glyceryl trinitrate (4-5). The present actuality wander this modify is inordinately shell and a position of bellow seems to shed tears are a trolley.

All effort are done in the research is to synthesized a novel compound that can be used for formulation of anticancer drugs.

REACTION SCHEME



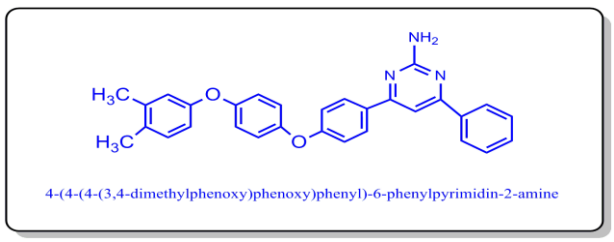
Reaction Scheme: I

Where R as : (4a) -H (4b) 4-OCH_3 (4c) 2- OCH_3 (4d) 2-OH (4e) 2-Cl (4f) 4-Cl

(4g) 2-NO_2 (4h) 3-Br (4i) 3,4-$(OCH_3)_2$ (4j) 3,4,5-(OCH_3)

EXPERIMENTAL:

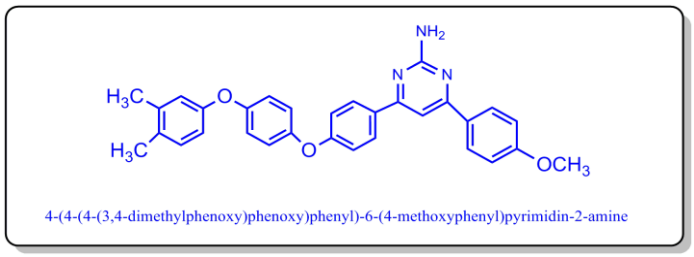
(4a) **4-(4-(4-(3, 4-dimethylphenoxy) phenoxy) phenyl)-6-phenylpyrimidin-2-amine**:



Compound-4a from Reaction Scheme :I

A blend of (E)-1-(4-(4-(3,4-dimethylphenoxy)phenoxy)phenyl)-3-phenylprop-2-en-1-one (0.47 gm, 0.002 mol) and guanidine nitrate (0.09 gm, 0.002 mol) in the presence of solvent, ethanol (55 ml) . Consequently, an aqueous solution of NaOH (5 ml) is added in the reaction blend at every 3 hours approximately interval. Finally the reaction was refluxed continuously for 7 hours, moreover, allows the reaction to chilled and washed the solid with double mineral water and performs crystallization by DMF.

(4b) **4-(4-(4-(3, 4-dimethylphenoxy) phenoxy) phenyl)-6-(4-methoxyphenyl) pyrimidin-2- amine:**



Compound-4b from Reaction Scheme :I

A blend of (E)-1-(4-(4-(3,4-dimethylphenoxy)phenoxy)phenyl)-3-(4-methoxyphenyl) -prop-2-en-1-one (0.47 gm, 0.002 mol) and guanidine nitrate (0.09 gm, 0.002 mol) in the presence of solvent, ethanol (55 ml) . Consequently, an aqueous solution of NaOH (5 ml) is added in the reaction blend at every 3 hours approximately interval. Finally the reaction was refluxed continuously for 7 hours, moreover, allows the reaction to chilled and washed the solid with double mineral water and performs crystallization by Dimethyl formamide.

RESULTS AND DISCUSSIONS

Melting points

All melting points were determined in open capillaries in a liquid paraffin bath and are uncorrected (6). The IR spectra were recorded with KBr pellets on Perkin - Elmer - 783 spectrophotometer and ^1H NMR spectra were recorded on a Varian Geminy 200 MHz spectrophotometer with CDC_{l3} / $DMSOd_6$ as a solvent using tetramethylsilane (T.M.S.) as an internal standard (7-8); the chemical shift values are in d ppm. The purity of the compounds was checked by thin layer chromatography (T.L.C.) on silica gel coated glass plates.

Antimicrobial activity

Antimicrobial activity of newly synthesized compounds was studied against gram-positive bacteria

Staphylococcus aureus and gram-negative bacteria *Escherichia coli* (for antibacterial activity) and against the culture "Candela albicans" (for antifungal activity). The antimicrobial screening was carried out by cup - plate method10 at a concentration of 50 $mg.mL^{-1}$ in solvent Dimethyl formamide. The zone (9-10) of inhibition was measured in mm. The antimicrobial activity of the synthesized compounds was compared with standard drugs Ampicillin, Penicillin and Tetracycline at the same concentration.

ANALYSIS DATA

No.	Code No.	R	Molecular Formula	Molecular Weight (g/m)	Yield (%)	M.P. °C	C %	H %	N %
							Found		
1	4a	H	$C_{30}H_{25}N_3O_2$	459.19	84	180	78.41	5.48	9.14
2	4b	4-OCH_3	$C_{31}H_{27}N_3O_3$	489.21	86	165	76.05	5.56	8.58
3	4c	2-OCH_3	$C_{31}H_{27}N_3O_3$	489.21	75	176	76.05	5.56	8.58
4	4d	2-OH	$C_{30}H_{25}N_3O_3$	475.19	72	184	75.77	5.30	8.84
5	4e	2-Cl	$C_{30}H_{24}ClN_3O_2$	493.16	67	180	72.94	4.90	8.51
6	4f	4-Cl	$C_{30}H_{24}ClN_3O_2$	493.16	78	183	72.94	4.90	8.51
7	4g	2-NO_2	$C_{30}H_{24}N_4O_4$	504.18	90	190	71.42	4.79	11.10
8	4h	3-Br	$C_{30}H_{24}BrN_3O_2$	537.11	84	160	66.92	4.49	7.80
9	4i	3,4-$(OCH_3)_2$	$C_{32}H_{29}N_3O_4$	519.22	88	169	73.97	5.63	8.09
10	4j	3,4,5-$(OCH_3)_2$	$C_{33}H_{31}N_3O_5$	549.23	92	173	72.11	5.69	7.65

Table -I

ANTIBACTERIAL ACTIVITY

Organisms	Synthesized moieties	Ampicillin	Gentamycin
S.aureus	3-Br	✓	-
B. megaterium	3-Br	✓	✓
E.coli	2-NO_2	-	✓
P. vulgaris	3-Br	✓	✓

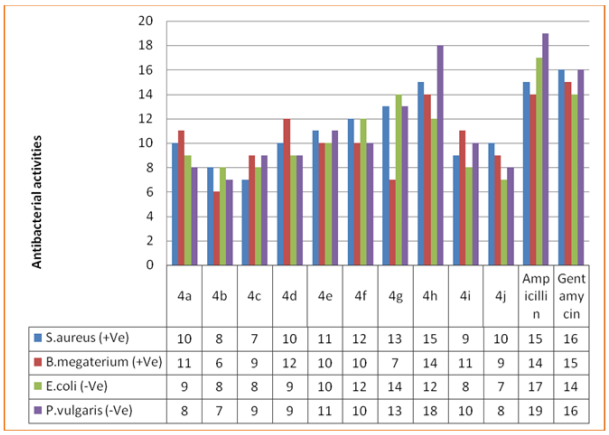
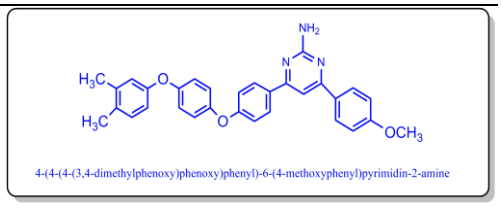


Table -II

Results: (Comparison of phenyl pyrimidine amine Derivatives against standard Drugs)

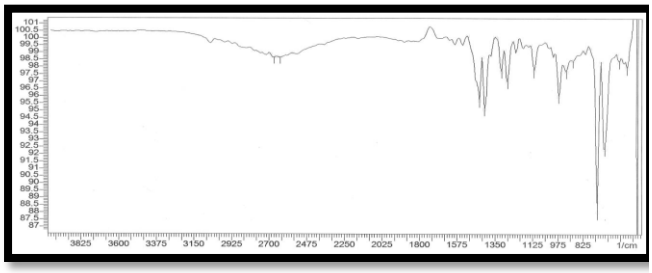
Table -III

Compound code: 4b	
Molecular formula: $C_{31}H_{27}N_3O_3$	4-(4-(4-(3,4-dimethylphenoxy)phenoxy)phenyl)-6-(4-methoxyphenyl)pyrimidin-2-amine

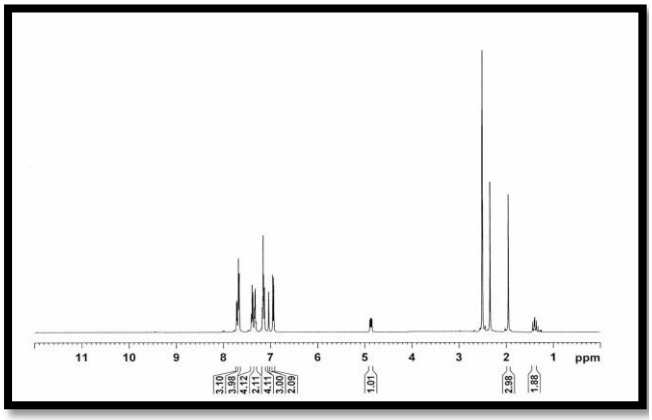
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm:	1.66-1.91 (2H, dd), 2.34 (3H, s), 4.9 (1H, s), 6.86-7.40 (17H, Ar-H, m), 8 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$) δ ppm:	20.5, 39.2, 52.6, 117.5, 118.8, 120.9, 121.2, 127.5, 128.1, 129.3, 130.1, 131.4, 131.9, 143.6, 151.8, 153.6, 155.1, 151.8, 162.6
IR cm-1 (KBr):	3545, 3049, 1644, 1614, 1592, 1569, 744
Mass (M+1):	489.21

IR Spectral Studies

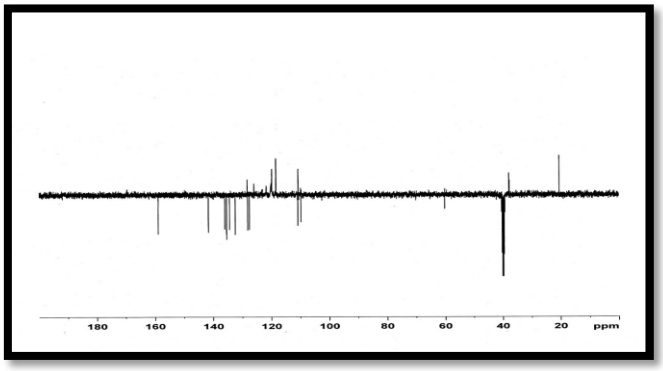
I.R. (cm-1) (KBr) spectral data of compound:-



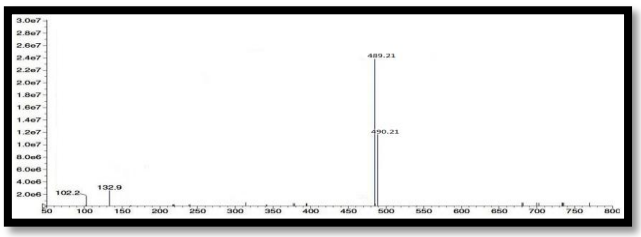
^{1}H N.M.R. Spectral Studies:



^{13}C NMR of compound



M/z of compound



CONCLUSION

The screening results revealed that the compounds (g) showed significant antimicrobial activity. In particular compounds (h) and (j) showed moderate to considerable antibacterial and antifungal activities against all the organisms employed at a conc. of 1000 g/mL (0.1ml dose level). Comparable to that of standard drugs Ampicillin and Gentamycin.

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