ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Research Paper

Solvent Free Synthesis and Antibacterial Studies of Some Heterocyclic Compounds

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A Chalcones having an α,β -unsaturated carbonyl system is one of the most useful Michael acceptor and undergo Michael type nucleophillic addition followed by intramolecular cyclization and aromatization resulting a large number of heterocyclic and cyclic potentially useful system. The synthetic heterocyclic chalcones have been determined by IR spectroscopy, 1H-NMR spectroscopy. The antibacterial activity of the novel products was evaluated against bacteria such as *Staphylococcus aureus*, *streptococcus fecalis*, *Protius mirabiles*, *Escherichea coli.*

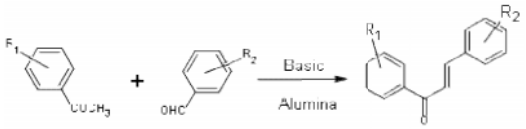
Keywords: Heterocyclic chalcone, Antibacterial agents, intramolecular cyclization, aromatization, nucleophillic addition.

INTRODUCTION

Biological properties are exhibited by chalcones and their derivatives including some of the heterocyclic analogues, which are determined by the growth of microbes,[2] malarial parasites, schistoma and intestinal worms. [3] Chalcones constitute an important group of natural products and natural biocides. The presence of α,β-unsaturated carbonyl group in the chalcone molecules confirm antibiotic activity upon it. Profound influence on the cardiovascular, neuromuscular and cerebrovascular system is shown by the compound of chalcone series.

Results and Discussions

Claisen-Schmidt condensation between acetophenone with benzaldedyde is a valuable C-C bond forming reaction, which allows α,β-unsaturated ketones[4-10] called chalcone (α,β-unsaturated carbonyl system) to be obtained **(1).**



Scheme 1:-The chemical reactivity of synthesized chalcones have been utilized for the synthesis of 2-(4-morpholinyl)-4,6-diaryl pyrimidines by the reaction with SBT in presence of organic bases morpholine under both conventional and microwave assisted dry media (basic Al2O3). From the comparative study it was observed that one pot synthesis of 2-(4-morpholinyl)-4,6-diaryl pyrimidines under solvent free microwave irradiation resulted enhanced reaction rates with improved yields (II).

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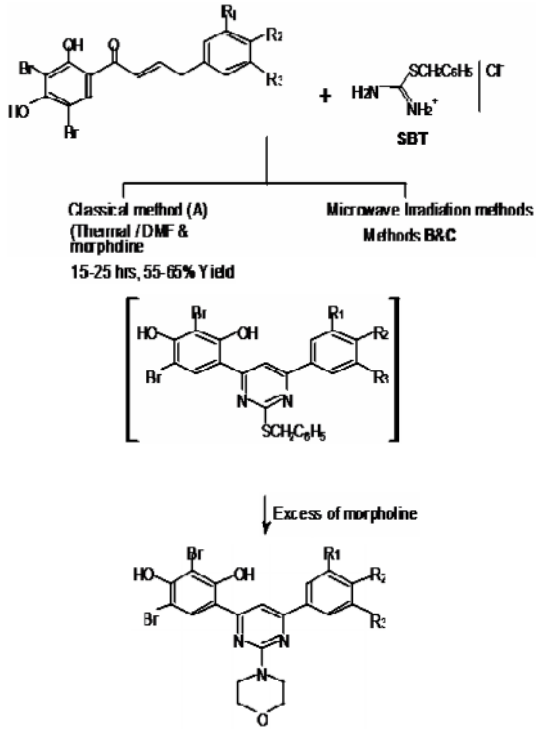
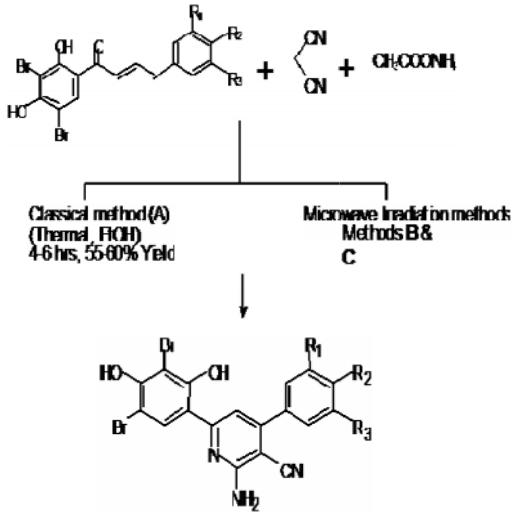
Scheme 1	Scheme 2
	
Method B: Solvent phase method (DMF), 8-11 min, 55-66% Yield **Method C**: Solid phase method (basic Al_2O_3), 9-10 min, 78-85% Yield	**Method B:** Solvent phase (Ethanol), 4-8 min. 70-60% yield **Method C:** Solid phase (basic Al_2O_3), 3-7 min. 85-95% yield

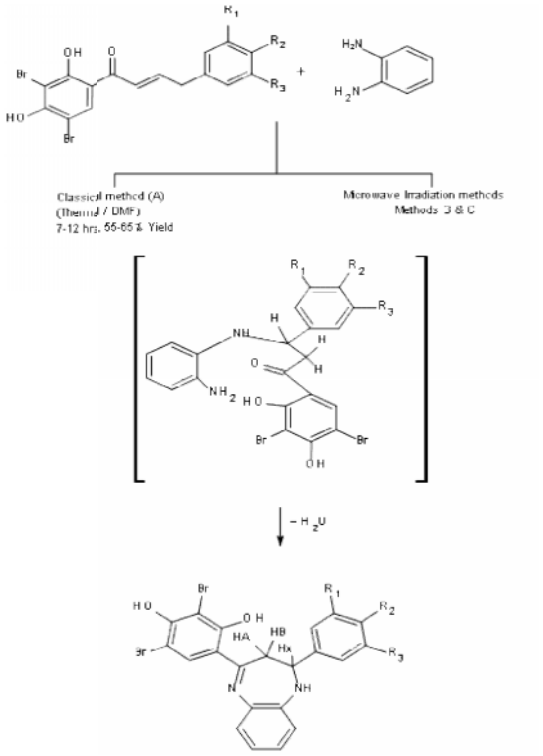
Scheme 2: Pyridines heterocycles and their derivatives represent one of the most active classes of nitrogen containing heterocycles possessing a wide spectrum of biological properties. 2-amino-3-cyano-4,-6-diarylpyri -dines are obtained by refluxing chalcones with malononitrile in presence of ammonium acetate under both conventional and microwave assisted dry media (basic Al_2O_3) **(III).**

Scheme 3:-Benzodiazepines and its derivatives constitute an important class of heterocyclic compounds which possess a wide range of therapeutic and pharmacological properties**.** The synthesis of 1,5 benzodiazepines has been reported by the reaction of α,β-unsaturated carbonyl compounds such as chalcones with o-phenylenediamin **(1V).**

Biological evaluation

The screening data indicated that among the all synthesized compound shows moderate to good activity against the used microorganisms. The compound **(I)** exhibited the excellent activity against *E.coli* and exhibited the good activity against gram positive bacteria.2- (4-morpholinyl)-4, 6-diarylpyrimidine compounds **(II)** shows

Scheme 3



Method B: Solvent phase method (DMF), 12-18 min, 60-65% Yield

Method C: Solid phase method (basic Al_2O_3), 5-8 min, 70-80% Yield

shows moderate activity against used microorganism except *E.coli.* 2-amino-3-cyano-4,6-diarylpyridine **(III)** shows good to excellent activity against the all used microorganism. Diazepine compounds **(IV)** shows moderate activity against the all used microorganism.

On the basis of structural activity relationship at can de concluded that the presence of hydroxyl, bromo and other substituted group in the heterocyclic system exhibited the excellent activity against used bacterial strain.

Experimental Section

General Method I: - In the determination of antibacterial activity "Peptone" nutrient broth was used. The media was prepared for gram-negative organisms by adding 2% mecconkey agar to the nutrient broth and for gram positive. It was prepared by adding 10% blood agar and 2% nutrient agar to the nutrient broth. Paper disc diffusion plate method was followed by special microbial filter paper disc. It consisted in impregnating small discs of standard filter paper with given quantity of compound, placing them on plate of culture media, inoculated with organism to be tested and after incubation, determining of degree of sensitivity by measuring easily

Table 1: Antibacterial screening results of synthesized compounds

Compd. and standard drugs	Zone of Inhibition (mm)/activity index			
	Gram positive		Gram negative	
	S. aureus	*S. fecalis*	*E. coli*	*P. mirabiles*
I	24/.85	23/.77	29/.96	25/.91
II	13/.46	11/.36	25/.86	14/.5
III	25/.89	24/.8	29/.96	26/.92
IV	15/.53	13/.43	20/.66	10/.35
Amicacin	28/1	30/1	-	-
Amoxyclav	26	25	-	-
Tobramycin	-	-	30/1	27
Amoxycillin	-	-	30	28/1

visible area of inhibition of growth produce by diffusion of compound from disc surrounding media. The compounds were screened at maximum concentration of 200□g/mL in DMF & compared with standard drugs Amicacin, Amoxyclav, Tobramycin and Amoxicillin. The zones of inhibition measured in millimeter

Method II

(I):- Synthesized 3,5-dibromo-2,4-dihydroxy substituted chalcones-

IR (KBr, □max, cm-1): 3360-3439 (-OH), 3020-3053 (Ar-H), 980-1050 (-CH=CH-trans), 1520, 1476, 1410 (C=C/Ar), 827, 739, 648 (substituted phenyl) 1H NMR □H (DMSO,ppm):3.05-3.18(m,Ar-H), 3.61-3.68 (d,1H,α-H), 6.77-7.95 (d,1H,β-H), 8.32, 13.40 (s.1H.OH)

(II):- Synthesis of 2-(4-morpholinyl)-4,6-diarylpyrimidines-

IR (KBr, vmax, cm-1): 3381-3339 (-OH), 3047-3153 (=C-H), 2918, 2851 (-C-H), 1620, 1596, 1489 (C=C/C=N), 877, 759, 688 (substituted phenyl) 1H NMR δH (DMSO,ppm):3.05-3.18(t,4H,CH_2-N-CH_2), 3.61-3.68 (t,4H,CH_2-O-CH_2), 6.77-7.95 (pyrimidine-H_5, Ar-H), 8.32, 13.40 (s.1H.OH)

(III):- Synthesis of 2-amino-3-cyano-4,6-diarylpyridines-

IR (KBr, vmax, cm-1): 3320-3460 (-OH,NH_2 (br)), 3016-3080(Ar-H), 2200-2215 (-CN), 1633, 1596, 1490 (C=C/C=N), 887, 769, 668 (substituted phenyl) 1H NMR δH (DMSO,ppm):6.85-7.20(br,2H,NH_2), 3.61-3.68 (t,4H,CH_2-O-CH_2), 7.18-8.26 (pyridine, Ar-H), 8.32, 13.40 (s.1H.OH).

(IV) :-Synthesis of 2,4-diaryl-2,3-dihydro-1*H*-1,5-benzodiazepine –

IR (KBr, vmax, cm-1): 3443-3333 (-NH str.), 3047-3072 (=C-H), 2918, 2851 (-C-H), 1623, 1586, 1499 (C=C/C=N), 897, 749, 678 (substituted phenyl) 1H NMR δH (DMSO,ppm):3.98(s, Ar-C-NH), 2.98 (dd, 1H, HA, methylene), 3.08 (dd, 1H, HB

methylene), 5.32 (dd, 1H, Ar-C-HX), 6.77-7.95 (m, broad and unresolved, Ar-H), 8.32, 13.40 (s.1H.OH)

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