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Synthesis and antibacterial evaluation of some novel chalcones and their derivatives

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ABSTRACT

Chalcones (6a-e) have been prepared by the condensation of ketone (5) and different aromatic aldehydes. These chalcones (6a-e) on treatment with hydrazine hydrate, guanidine hydrochloride and malononitrile give acetylpyrazolines (7a-e) aminpyrimidines (8a-e) and cyanopyridines (9a-e) respectively. All the newly synthesized compounds have been characterized on the basis of IR, 1H NMR Spectral data as well as physical data. The compounds were tested for their antibacterial activity by uing agar diffusion method.

Key words: Chalcones, acetylprazolines, aminopyrimidines, cyanopyridines, spectral data.

INTRODUCTION

The variety of heterocyles has been explored for developing pharmaceutically important molecules like chalocones and its derivatives[1]. Chalcones have occupied unipue place in medicinal chemistry due to their diverse pharmacological properties such as antitumor[2]. Antiproliferatives[3] etc. Pyrazoline derivatives have been found to posses wide range of therapeutic activities such as antifungal[4], antitubercular[5] etc..... Pyrimidine derivatives play a vital role in many biological processes and can be used as therapeutic agents in treatment of anti HIV[6] and anticancer[7].

Cyanopyridine derivatives have attracted considerable attention as they possess analgesic[8], anti-inflammatory[9], etc. . activities. In view of the above and in continuation of our work[10-12] on chalcones and its derivatives, we herein report a new series of chalcones (6a-e), acetylpyrazolines (7a-e) aminopyrimidines (8a-e) and cyanopyridines (9a-e), the newly synthesized compounds were evaluated for their antibacterial activity.

EXPERIMENTAL

All the melting points were determined in an open capillary and are uncorrected. The IR spectra were recorded in KBr disc using, FTIR – 8400 specttrphotometer. 1H NMR spectra on a Bruker avance DPX 400 MHz spectrometer with CDCI3 AND DMSO as a solvents and TMS as internal reference. Purity of the compounds was checked on TLC using silica gel-G.

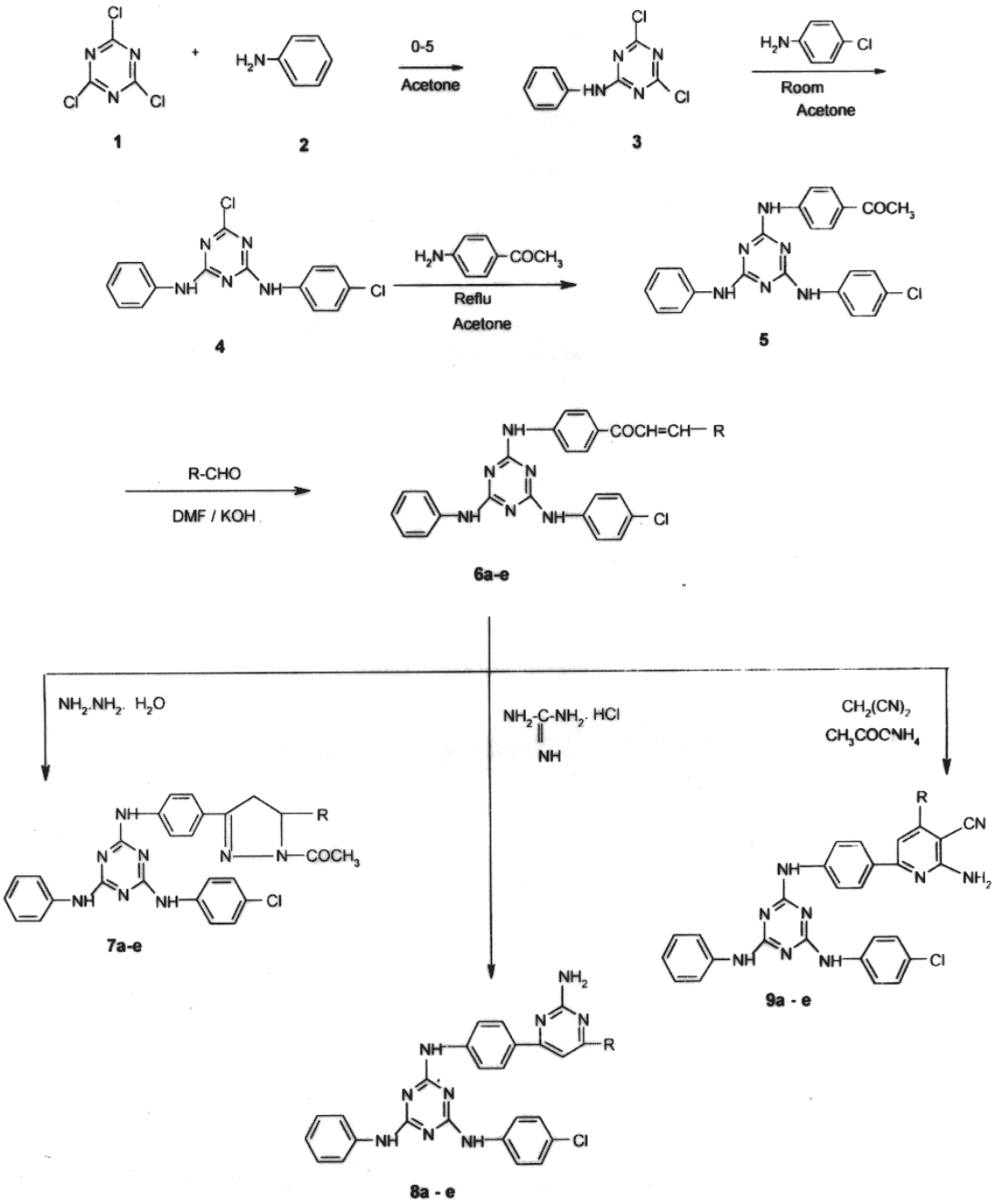
Prepration of compounds (3), (4), & (5)

Compounds (3), (4), & (5). Were prepared by reported method[13].

Preparation of 2-phenylamino -4 –(4'-cholrophenylamino)-6-[4-{3"-(3"4"-dimethoxyphenyl)-2"-propenon-1"-yl} phenyl amino] –s-triazine (6a)

Compounds (5) (0.01mol) was dissolved in DMF (30 ml) and 3,4-dimethoxybenzaldehyde (0.01 mol) was added to it. Then solution of KOH (5 ml of 40%) was added to the reaction mixture with constant stirring at room temperature after 24 hours

the reaction mixture was poured into crushed ice and neutralized with HCL. The product separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give (6a). Yield 70% m.p.165oC. IR (KBr) cm-1 1649(-C=0), 806 (C-N, s-striazine), 786 (C-Cl), 1H NMR ($CDCl_3$): δ6.88(D, IH, -CO-CH=), δ 7.0 – 8.1 (M, 18H, Ar-h AND NH), δ 8.05(D, 1H, Ar-CH=).



Scheme 1:

Similarly the remaining compounds (6b-e) were prepared by this method their physical data are given in Table – 1

Preparation of 2-phenylamino -4 –(4'-cholrophenylamino)-6-[4-{1acetyl-5"-(3"4"-dimethoxyphenyl)-2"-pyrazolin -3"- yl} phenyl amino] –s-triazine (7a)

Compound (6a) (0.01 mol) was dissolved in glacial acetic acid (25 ml) and hydrazine hydrate (0.01 mol) was added to it and refluxed for 6 hrs. the reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and crystallized from ethyl alcohol to give (7a.). Yield 65% m.p. 137oC IR (KBr) cm^{-1}: 1570 (-C=N), 1230 (C-O-C),808 (C-N, s-triazine). 777 (C-Cl),^{1}H NMR ($CDCl_3$): δ3.22 (dd, 1H,-CH_A) δ3.38 (dd, 1H,-CH_b) δ3.80 (s, 3H,m-OCH_3), δ3.86 (s, 3H,P-OCH_3) δ5.6 (dd, 1H,-CH), δ6.7-7.7 (m, 19H,- Ar-CH=).and NH).

Similarly the remaining compounds (7b-e) were prepared by this method their physical data are given in Table 1.

Preparation of 2-phenylamino -4-(4'cholrophenylamino)-6-[4-{2'-amino-6'-(3"',4"'-dimethoxyphenyl)-pyrimidin-4"-yl}-phenylamino]-s-triazine (8a)

Compound (6a) (0.01 mol) was dissolved in ethyl alcohol (25 ml) and guanidine hydrochloride (0.01 mol) was added to it. Then solution of KOH (5ml of 40%) was added to the reaction mixture and refluxed for 10 hours The reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and crystallized from ethyl alcohol to give (8a.). Yield 62% m.p. 189°C IR (KBr) cm^{-1}: 3470(-NH_2), 1576 (C=N), 1228 (C-O-C),803 (C-N, s-triazine). 780 (C-Cl),^{1}H NMR ($CDCl_3$): δ3.78 (s, 3H,m-OCH_3), δ3.84 (s, 3H,m-OCH_3), δ5.6 (s, 2H,-NH_3), δ6.9-8.2 (m, 21H,Ar-H and 3NH),

Preparation of 2-phenylamino -4 –(4'-cholrophenylamino)-6-[4-{2"-amino-3"-cyano-4"(3"4"-dimethoxyphenyl)-pyrimidin-6"-yl} phenylamino] –s-triazine (9a)

Compound (6a) (0.01 mol) was dissolved in ethyl alcohol (25 ml) malanonitrile (0.01mol,

Table 1: Characterization data of compounds (6a-e), (7a0e), (8a-e) and (9a-e)

Compd.	R	m.p.°C	Yield (%)
6a	3,4-Dimethoxyphenyl	165	70
6b	4-Methyphenyl	154-156	73
6c	3,4,5- Trimethoxyphenyl	143-146	71
6d	4,N,N-Dimethylaminophenyl	138-141	68
6e	4,N,N-Dimethylaminophenyl	240	65
7a	3,4-Dimethoxyphenyl	136-139	65
7b	4-Methyphenyl	143-146	71
4c	3,4,5- Trimethoxyphenyl	126-129	63
7d	4,N,N-Dimethylaminophenyl	179	60
7e	4,N,N-Dimethylaminophenyl	160	58
7a	3,4-Dimethoxyphenyl	188-190	61
8b	4-Methyphenyl	156-158	64
8c	3,4,5- Trimethoxyphenyl	161-163	62
8d	4,N,N-Dimethylaminophenyl	105-108	58
8e	4,N,N-Dimethylaminophenyl	109-111	57
9a	3,4-Dimethoxyphenyl	124-126	67
9b	4-Methyphenyl	109-112	70
9c	3,4,5- Trimethoxyphenyl	139-142	64
9d	4,N,N-Dimethylaminophenyl	103-106	61
9e	4,N,N-Dimethylaminophenyl	91-94	59

Table 1: Characterization data of compounds (6a-e), (7a0e), (8a-e) and (9a-e)

S. No.	R	Antibacterial activity Diameter of zone of inhibition (in mm)			
		S. aureus **MTCC-96**	***B. subtilis*** **MTCC-441**	***E. coli*** **MTCC-443**	***S. paratyphi*-B** **MTCC-733**
6a	3,4-Dimethoxyphenyl	18	17	18	17
6b	4-Methyphenyl	19	17	18	18
6c	3,4,5- Trimethoxyphenyl	14	15	15	16
6d	4,N,N-Dimethylaminophenyl-	-	17	16	-
6e	4,N,N-Dimethylaminophenyl	16	16	17	17
7a	3,4-Dimethoxyphenyl	13	17	21	19
7b	4-Methyphenyl	18	17	18	18
4c	3,4,5- Trimethoxyphenyl	-	16	18	17
7d	4,N,N-Dimethylaminophenyl	-	-	19	15
7e	4,N,N-Dimethylaminophenyl	-	-	19	18
7a	3,4-Dimethoxyphenyl	-	17	14	16
8b	4-Methyphenyl	15	19	14	15
8c	3,4,5- Trimethoxyphenyl	15	14	20	13
8d	4,N,N-Dimethylaminophenyl	13	16	16	16
8e	4,N,N-Dimethylaminophenyl	18	15	15	18
9a	3,4-Dimethoxyphenyl	15	16	20	19
9b	4-Methyphenyl	17	13	17	18
9c	3,4,5- Trimethoxyphenyl	19	18	18	18
9d	4,N,N-Dimethylaminophenyl	19	19	17	15
9e	4,N,N-Dimethylaminophenyl	15	18	20	17
	Ciprofloxacin (Standard drug)	22	24	26	27

0.66g) and ammonium acetate (0.08 mol, 6.16g) was added to it and refluxed for 8 hours. The reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and crystallized from ethyl alcohol to give (9a.). Yield 67% m.p. 125oC IR (KBr) cm^{-1}: 3470(-NH_2), 2205 (C=N), 1230 (C-O-C),805 (C-N, s-triazine). 788 (C-Cl),^{1}H NMR(DSMO): δ3.80 (s, 3H,m-OCH_3), δ3.88 (s, 3H,m-OCH_3), δ5.7 (s, 2H,-NH_2), δ6.9-8.0 (m, 21H,Ar-H and NH),

Similarly the remaining compounds (9b-e) were prepared by this method their physical data are given in Table 1.

RESULTS AND DISCUSSION

Antibacterial activity

All the synthesized compounds were screened for their in vitro antibacterial activity S. aureus (MTCC-96). *B. subtilis* (MTCC-441) [GRAM-positive bacterial] and *E. coli* (MTCC-433), *S. paratyphi* - B(MTCC-733)[Gram-negative bacterial] by using agar diffusion method of Barry[14]. known antibiotic Ciprofloxacin was used as standard drug. The screening results indicate that the compound 6B, 9e, 9d, and 9e were active against *S. aureus* (MTCC-96) the compound 8b and 9d were active *B. subtilis* (MTCC-411). Compounds 7a was active against *E. coli* (MTCC-443), Where as remaining compounds were moderately active, less active and inactive against all bacterial stain.

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