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Synthesis of Some 3,5-*Bis*-1,4-dihydro-4-phenyl 2,6-Dimethyl pyridino-2′-amino-6′-phenyl Pyrimidines

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1,4-Dihydro-4-phenyl-2,6-dimethyl-3,5-diacetyl pyridine were converted into chalcone by Claisen-Schmidt condensation with aldehydes. These chalcones were cyclized with guanidine hydrochloride to give pyrimidines.

Key Words: 1,4-Dihydropyridine, Chalcone, Guanidine, Pyrimidine.

INTRODUCTION

Pyrimidine derivatives have received attention due to their applications in physiology[1,2] and derivatives of pyrimidine like phenobarbital, mysoline, *etc.* are well known in pharmacology. Various aminopyrimidines were found effective as antimalarial[3] agents. Dihydropyridines[4] are known to exhibit antihypertensive[5,6] properties. These findings prompted us to synthesise some pyrimidines incorporating 1,4-dihydropyridino moiety and to study their biological activity. 1,4-Dihydro-4-phenyl-2,6-dimethyl-3,5-diacetyl pyridines were converted into chalcones by Claisen-Schmidt condensation with aldehydes. The chalcones were cyclized with guanidine to give aminopyrimidines.

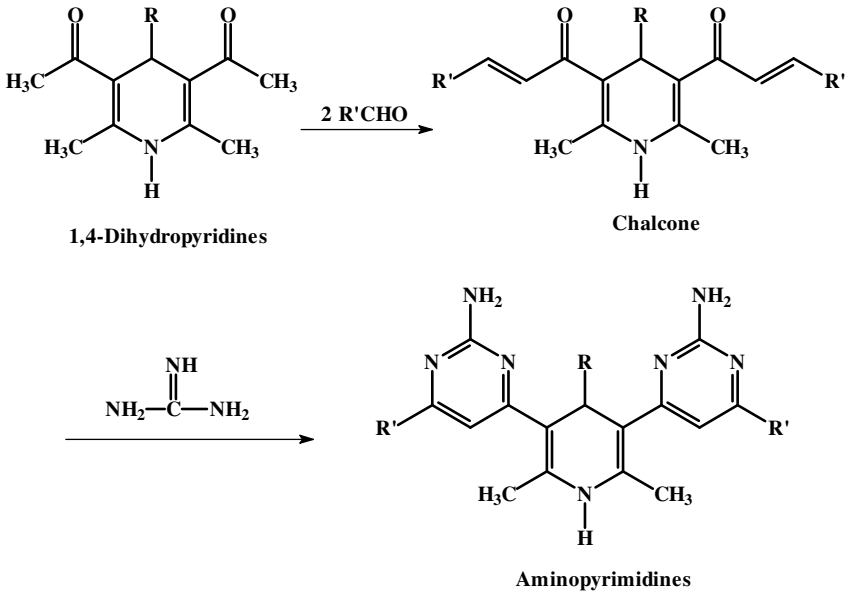
EXPERIMENTAL

All melting points were taken in open capillary in liquid paraffin bath and are uncorrected. Purity of all compounds were checked by TLC. IR spectra were recorded in nujol on Perkin-Elmer 1420 spectrophotometer while PMR spectra in $CDCl_3$ using TMS as an internal standard (chemical shifts in ppm).

3,5-*Bis*-1,4-dihydro-4-phenyl 2,6-dimethyl pyridino-2'-amino-6' phenyl pyrimidine (1): A mixture of chalcone (0.01 M) in dioxane and guanidine hydrochloride (0.02 M) were refluxed for 4 h. The reaction mixture was cooled and acidified with acetic acid. The solid was filtered, washed with water and crystallized from ethanol to give compound no. **1**. IR (KBr, cm^{-1}): 3320-3300 ν(-NH), 1620 ν(C=N), 1605 ν(C=N). PMR: 2.23 δ (S,6H-CH_3), 5.17 δ (S, 1H), 5.5 δ (S,NH_2), 5.75 δ (S,-NH pyridyl), 7.0-8.0 d (m, 15H, aromatic proton). Similarly, other compounds **2-20** were synthesized.

TABLE-1
CHARACTERIZATION DATA OF PYRIMIDINES

Compd.	R	R′	Yield (%)	m.p. (ºC)	m.f.	N Found (Calcd.) %
1	C_6H_5	C_6H_5	74	114	$C_{33}H_{29}N_7$	18.50 (18.73)
2	C_6H_5	2-ClC_6H_4	72	120	$C_{33}H_{27}N_7Cl_2$	16.21 (16.55)
3	C_6H_5	3-ClC_6H_4	70	124	$C_{33}H_{27}N_7Cl_2$	16.25 (16.55)
4	C_6H_5	4-ClC_6H_4	68	119	$C_{33}H_{27}N_7Cl_2$	16.20 (16.55)
5	C_6H_5	4-$NO_2C_6H_4$	66	99	$C_{33}H_{27}N_9O_4$	20.15 (20.55)
6	2-$NO_2C_6H_4$	C_6H_5	68	109	$C_{33}H_{28}N_8O_2$	19.62 (19.71)
7	2-$NO_2C_6H_4$	2-ClC_6H_4	68	103	$C_{33}H_{26}N_8O_2Cl_2$	16.42 (16.74)
8	2-$NO_2C_6H_4$	3-ClC_6H_4	66	107	$C_{33}H_{26}N_8O_2Cl_2$	16.35 (16.74)
9	2-$NO_2C_6H_4$	4-ClC_6H_4	70	109	$C_{33}H_{26}N_8O_2Cl_2$	16.39 (16.74)
10	2-$NO_2C_6H_4$	4-$NO_2C_6H_4$	72	115	$C_{33}H_{26}N_{10}O_6$	21.00 (21.27)
11	2-ClC_6H_4	C_6H_5	74	117	$C_{33}H_{28}N_7Cl$	17.32 (17.54)
12	2-ClC_6H_4	2-ClC_6H_4	68	103	$C_{33}H_{26}N_7Cl_3$	15.31 (15.64)
13	2-ClC_6H_4	3-ClC_6H_4	68	111	$C_{33}H_{26}N_7Cl_3$	15.19 (15.64)
14	2-ClC_6H_4	4-ClC_6H_4	62	118	$C_{33}H_{26}N_7Cl_3$	15.24 (15.64)
15	2-ClC_6H_4	4-$NO_2C_6H_4$	64	112	$C_{33}H_{26}N_9O_4Cl$	19.20 (19.48)
16	2-ClC_6H_4	C_6H_5	70	119	$C_{33}H_{28}N_7Cl$	17.25 (17.54)
17	2-ClC_6H_4	2-ClC_6H_4	70	113	$C_{33}H_{26}N_7Cl_3$	15.35 (15.64)
18	2-ClC_6H_4	3-ClC_6H_4	72	118	$C_{33}H_{26}N_7Cl_3$	15.30 (15.64)
19	2-ClC_6H_4	4-ClC_6H_4	74	121	$C_{33}H_{26}N_7Cl_3$	15.26 (15.64)
20	2-ClC_6H_4	4-$NO_2C_6H_4$	66	114	$C_{33}H_{26}N_9O_4Cl$	19.25 (19.42)



Scheme-I

RESULTS AND DISCUSSION

Few of the representative compounds from the synthesized series were screened against fungi *viz.*, *Alternaria brassicicola*, *Aspergillus niger* and bacteria *viz.*, *Lactobacillus* gram (-ve) and *E. coli*, using cup plate method[7,8] at 500 and 250 ppm concentrations using 5 mm size filter paper disc. At similar conditions standard drugs carbendazim and streptomycine were

TABLE-2
ACTIVITY DATA OF PYRIMIDINES

Compd.	R	R′	AB	AN	L	EC
2	C_6H_5	3-ClC_6H_4	+8	+10	+11	+10
5	C_6H_5	4-$NO_2C_6H_4$	–	+9	+8	–
7	2-$NO_2C_6H_4$	2-ClC_6H_4	+9	+11	+6	+8
10	2-$NO_2C_6H_4$	4-$NO_2C_6H_4$	+6	+7	+9	+7
14	2-ClC_6H_4	4-ClC_6H_4	+16	+15	+10	+14
15	2-ClC_6H_4	4-$NO_2C_6H_4$	+8	+10	+9	+11
19	4-ClC_6H_4	4-ClC_6H_4	+15	+14	+13	+14
20	4-ClC_6H_4	4-$NO_2C_6H_4$	+13	+12	+10	+11
Carbendazim (bavistin)	–	–	+17	+18	–	–
Streptomycine	–	–	–	–	+18	+16

AB = *A. brassicicola*; AN = *A. niger*; L = *Lactobacillus*; EC = *E. coli*

used. The czapeks medium was used as a basal solution for the growth of microbials. All the experiments were carried out twice and average values were calculated. The data is recorded in Table-2. Compound nos. 14, 19 and 20 showed good activity. It seems that the introduction of –Cl and $–NO_2$ group in the aryl moiety increases fungitoxicity of the compounds.

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