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Synthesis and Reactions of 2-Amino-4,6-Diaryl Pyrimidine Derivatives

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Variously substituted chalcones(I) were prepared by the Claisen-Schmidt condensation of substituted acetophenones with aromatic aldehydes which on treatment with guanidine nitrate (II) in presence of base furnished 2-amino-4,6-diaryl pyrimidines (III). The reactions of these compounds have been carried out with aromatic aldehydes, acetic anhydride, phenyl isothiocyanate and benzoyl isothiocyanate. Structures of the resultant compounds (IV), (V), (VI) and (VII) have been confirmed on the basis of elemental analysis and spectral data. Antibacterial activity of some of these compounds has also been carried out.

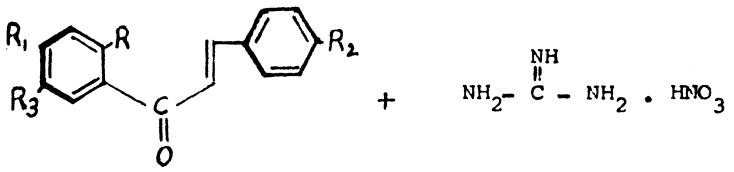
INTRODUCTION

Pyrimidine and its derivatives form a component in a number of useful drugs and are associated with many biological, pharmaceutical and therapeutical activities[1-4]. Therefore, pyrimidine derivatives are important synthons to the synthetic organic chemists as is evident from the work of different workers[5-9].

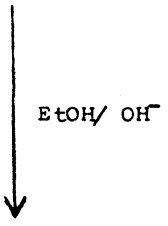
In view of significant biological activities of substituted amino-pyrimidines[5, 6, 10] we have synthesised some new 2-amino-4,6-diaryl pyrimidines (IIIa–j) (Scheme I) which on treatment with aromatic aldehydes in presence of neutral alumina and toluene furnished the corresponding Schiff's bases (IVa–j).

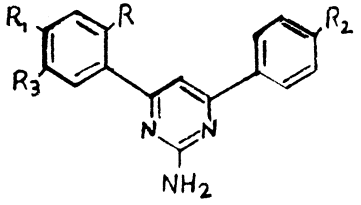
Compound (III) on treatment with acetic anhydride and pyridine gave acetyl derivatives (Va–c). Similarly the reaction of (III) with aryl and aroyl isothiocyanate afforded the pure thiourea derivatives (VIa–i) and N-benzoyl-N'-pyrimidyl thiourea derivatives (VIIa–f) (Scheme II).

The antibacterial activity was determined by following the paper disc diffusion[11] plate method against the following strains of micro-organisms: *S. albus, S. aureus, E. coli, K. oxytoca* and *P. Aeruginosa* at maximum concentration of 100 μg/mL of ethyl alcohol. Compounds (IIIa–d), (IVa, c, d, e, h & i), (Va) and (VIIa and c) were screened for their antibacterial activity, out of which compound (IIId) showed moderate activity against *S. albus* whereas IVa, IVe and Va showed significant activity against this strain, while rest of the compounds did not show any activity against the tested micro-organisms.



(I) (II)





(III)

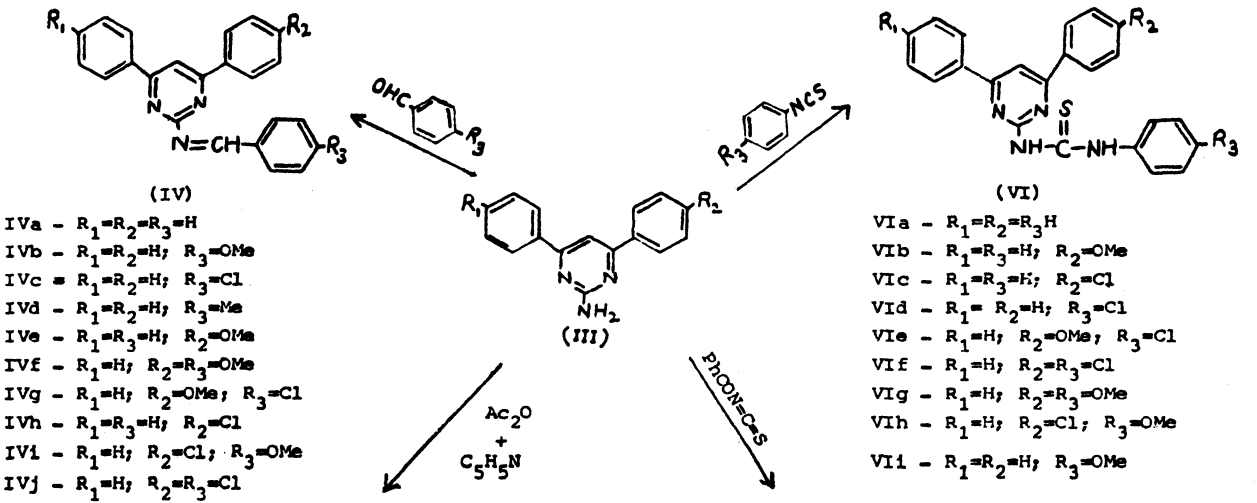
III-a	$R = R_1 = R_2 = R_3 = H$	III-f	$R = OH; R_1 = H, R_2 = OMe, R_3 = Cl$
III-b	$R = R_1 = R_3 = H; R_2 = OMe$	III-g	$R = OH, R_1 = H; R_2 = R_3 = Cl$
III-c	$R = R_1 = R_3 = H; R_2 = Cl$	III-h	$R = R_2 = R_3 = H; R_1 = OMe$
III-d	$R_1 = R_2 = R_3 = H; R = OH$	III-i	$R = R_3 = H; R_1 = OMe; R_2 = Cl$
III-e	$R_1 = R_3 = H; R = OH; R_2 = OMe$	III-j	$R = R_3 = H; R_1 = R_2 = OMe$

SCHEME I

EXPERIMENTAL

The structure of these compounds was established by elemental and spectral analysis. All the melting points were taken in open capillaries and are uncorrected. Purity of the compounds was checked by TLC on silica gel. IR spectra were recorded on Perkin-Elmer-881, 557 spectrophotometer, and mass spectra on Jeol D-300 (EI/CI) spectrometer.

The chalcones (I) used for the synthesis of (III) were synthesised by condensing the appropriate aromatic aldehydes and substituted acetophenones in ethanol at room temperature using sodium hydroxide solution as reported in literature[12, 13].



(IV)

IVa - $R_1=R_2=R_3=H$
IVb - $R_1=R_2=H$; $R_3=OMe$
IVc - $R_1=R_2=H$; $R_3=Cl$
IVd - $R_1=R_2=H$; $R_3=Me$
IVe - $R_1=R_3=H$; $R_2=OMe$
IVf - $R_1=H$; $R_2=R_3=OMe$
IVg - $R_1=H$; $R_2=OMe$; $R_3=Cl$
IVh - $R_1=R_3=H$; $R_2=Cl$
IVi - $R_1=H$; $R_2=Cl$; $R_3=OMe$
IVj - $R_1=H$; $R_2=R_3=Cl$

(III)

(VI)

VIa - $R_1=R_2=R_3H$
VIb - $R_1=R_3=H$; $R_2=OMe$
VIc - $R_1=R_3=H$; $R_2=Cl$
VId - $R_1=R_2=H$; $R_3=Cl$
VIe - $R_1=H$; $R_2=OMe$; $R_3=Cl$
VIf - $R_1=H$; $R_2=R_3=Cl$
VIg - $R_1=H$; $R_2=R_3=OMe$
VIh - $R_1=H$; $R_2=Cl$; $R_3=OMe$
VIi - $R_1=R_2=H$; $R_3=OMe$

(V)

Va - $R_1=R_2=H$
Vb - $R_1=H$; $R_2=OMe$
Vc - $R_1=H$; $R_2=Cl$

(VII)

VIIa - $R_1=R_2=H$
VIIb - $R_1=H$; $R_2=OMe$
VIIc - $R_1=H$; $R_2=Cl$
VIId - $R_1=OMe$; $R_2=H$
VIIe - $R_1=OMe$; $R_2=Cl$
VIIf - $R_1=R_2=OMe$

SCHEME II

2-Amino-4-phenyl-6-(4-chlorophenyl) pyrimidine (IIIc)

A mixture of 4-chlorochalcone (2.4 g; 0.01 mole), guanidine nitrate (1.22 g; 0.01 mole) and sodium hydroxide (40%, 2 mL) in ethanol (30 mL) was refluxed for 20 h. Completion of the reaction was judged by TLC. The resultant mixture was cooled to room temperature. Separated compound was filtered, washed with water, dried and recrystallised from ethanol to give white needles (2.3 g; 64%) m.p. 168°C (Found: C, 68.32; H, 4.37; N, 14.25; $C_{16}H_{12}N_3Cl$ requires: C, 68.35; H, 4.27; N, 14.94%); IR (Nujol) cm^{-1} 3460, 3250 (—NH_2), 1630, 1590 (—NH); m/z: 281 [M^+], 240, 205, 104, 76 and 52.

Similarly, other compounds were prepared. IIIa (47%), 142°; IIIb (52.7%), 175°C; IIId (24%), 184°C; IIIe (26%), 202°C; IIIf (30%), 223°C; IIIg (32%), 235°C; IIIh (46%), 155°C; IIIi (35%), 170°C; and IIIj (36%), 177°C.

2-(Benzylideneamino)-4,6-diphenyl pyrimidine (IVa)

A mixture of IIIa (2.4 g; 0.01 mole), benzaldehyde (1.0 g; 0.01 mole) and alumina (0.5 g) in toluene (50 mL) was refluxed for 10 h. The reaction mixture was filtered and the filtrate on concentration gave a white coloured solid. It was filtered, dried and crystallised from toluene (1.4 g; 58%); m.p. 217°C. (Found: C, 83.00; H, 4.99; N, 12.3°C; $C_{23}H_{17}N_3$ requires C, 82.30; H, 5.07; N, 12.50%); IR (Nujol) cm^{-1}: 1600, 1580 (>C=N); m/z: 335 [M^+], 247, 233, 205, 191, 130, 103, 78 and 54.

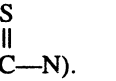
Similarly, other compounds were prepared in 26%–64% yield. IVb, 190°C; IVc, 236°C; IVd, 205°C; IVe, 120°C; IVf, 150°C; IVg, 204°C; IVi, 155°C; and IVj, 202°C.

2-Acetylamino-4,6-diphenyl pyrimidine (Va)

A mixture of compound IIIa (2.4 g; 0.01 mole) in pyridine (10 mL) and acetic anhydride (10 mL) was kept overnight. The reaction mixture was refluxed for 10–15 min on water bath, cooled, poured into cold water and filtered. The product separated was crystallised from ethanol as white needles (2.0 g; 83.3%); m.p. 218°. (Found: C, 75.0; H, 5.19; N, 14.28; $C_{18}H_{15}N_3O$ requires: C, 74.7; H, 5.19; N, 14.53%); IR (Nujol) cm^{-1}: 3010 (—NH), 1660 (>C=O). Following the above procedure compounds Vb, 209°C and Vc, 240°C were also prepared.

1-Phenyl-3-(4,6-diphenyl pyrimidine-2-yl)-2-thiourea (VIa)

To a solution of 2-amino-4,6-diphenyl pyrimidine (IIIa) (2.4g; 0.01 mole) in dry benzene (80 mL) was added phenyl isothiocyanate (1.35 g; 0.01 mole). The reaction mixture was refluxed for 20 h. The solid separated was filtered, washed with benzene and crystallised from chloroform to give white needles (1.2 g; 32.4%), m.p. 224°C. (Found: C, 71.94; H, 4.63; N, 14.23; $C_{23}H_{18}N_4S$ requires: C, 72.25; H, 4.71; N, 14.6%); IR (Nujol) (cm^{-1}); 1250, 1360, 1375 (>C=S),



1250, 1180 (—N—C—N).

Similarly, other compounds were prepared. VIb (70%), 206°C; VIc (80.4%), 228°C; VId (40.69%), 254°C; VIe (63.69%), 234°C; VIf (60%), 250°C; VIg (22.5%), 215°C; VIh (30%), 242°C; and VIi (35%), 230°C.

1-(4,6-Diphenyl pyrimidine-2-yl)-3-benzoyl-2-thiourea (VIIa)

Ammonium thiocyanate (0.92 g; 0.012 mole) was dissolved in dry acetone (40.0 mL). To it benzoyl chloride (1.40 g; 0.01 mole) was slowly added and the reaction mixture was refluxed for 15 min. A solution of 2-amino-4,6-diphenyl pyrimidine (2.4 g; 0.01 mole) in dry acetone was added to it and further refluxed for 1 h. The reaction was then cooled and poured into ice-cold water. The solid obtained was filtered, washed, dried and crystallised from benzene-petroleum ether (60– 80°C) to give pale yellow crystals (3.0 g; 63%); m.p. 198°C. (Found: C, 69.0; H, 4.98; N, 13.45; $C_{24}H_{18}N_4SO$ requires: C, 70.24; H, 4.39; N, 13, 6%); IR (Nujol) cm^{-1}; 1700 (>C=O), 1370, 1240 (>C=S), 1160, 1100 (—N—C—N).

Similarly other compounds were prepared. VIIb (50%), 194°C; VIIc (54%), 201°C; VIId (47.94%), 184°C; VIIe (69.44%), 204°C and VIIf (648%), 196°C.

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REFERENCES

1. S.N. Sawhney, A. Gupta and Dharamvir, *Indian J. Chem.*, **29B**, 1107 (1990).
2. U.S. Pathak, S. Singh and J. Padh, *Indian J. Chem.*, **30B**, 618 (1991).
3. K. Anoop, Ashok Sharma and K. Yadav, *Indian J. Chem.*, **34B**, 740 (1995).
4. M.A. El Hashash, M.R. Mahmoud and S.A. Madboli, *Indian J. Chem.*, **32B**, 449 (1993).
5. M. Seada, A.M. Abdel Halim, S.S. Ibrahim and M. *Abdel Megid, Asian J. Chem.*, **4**, 588, 591 (1992).
6. V.J. Ram, Navedul Haque and Mahendra Nath, *Indian J. Chem.*, **29B**, 1129 (1990); **30B**, 962 (1991); **32B**, 754 (1993).
7. V.K. Ahluwalia, Rachna Aggarwal, Shashibala and Ramesh Chandra, *Indian J. Chem.*, **28B**, 964, 1060 (1989).
8. V.K. Ahluwalia, A. Chauhan and Anju Khurana, *Indian J. Chem.*, **30B**, 1062 (1991).
9. A.S.R. Anjaneyulu, G. Sudha Rani, K. Gowri Annapura and Y.L.N. Murthy, *Indian J. Chem.*, **34B**, 933 (1995).
10. C.S. Andotra, Jatindra Khajuria, G.B. Singh and Surjeet Singh, *J. Indian Chem. Soc.*, **70**, 266 (1993).
11. S. Imai, Y. Kanai, A. Nohara, H. Oteuka and Y. Sanno, *Japan Pat.* 71, 43, 900 (1968); *Chem. Abstr.*, **76**, 103784 (1972).
12. A.I. Vogel, A Textbook of Practical Organic Chemistry, Orient Longman (ELBS ed.), p. 796 (1978).
13. F.Z. Saiyad, D.R. Nadkarni and T.S. Wheeler, *J. Indian Chem. Soc.*, **14**, 1737 (1937).

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