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A convenient synthesis of chalcones, acetylpyrazolines and aminopyrimidine

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ABSTRACT

Base catalysed condensation of 2-phenylamino-4-(4¹-chlorophenylamino)-6-(4¹-acetylphenylamino)-*s*-triazine (5) with different substituted aromatic aldehydes give chalcones (6a-e). These Chalcones (6a-e) on cyclisation with hydrazine hydrate in the presence of glacial acetic acid give acetylpyrazolines (7a-e) and with guanidine hydrochloride in the presence of alkali give aminopyrimidines (8a-e). All the synthesised compounds were characterized by IR, ^{1}H NMR and physical data.

Key words: Chalcones, acetylpyrazolines, aminopyrimidines, spectral data

INTRODUCTION

Commonly α,β-unsaturated ketone is known as chalcone. Chalcones[1,2] are very reactive compounds and increase their reactivity due to keto-ethylinic type of conjugated double bond system present in the molecule. Chalcones have occupied unique place in medicinal and biological chemistry due to their diverse pharmacological properties such as anticancer[3], anti-inflammatory[4], antiviral[5] and antibacterial[6]. Five membered heterocycles like pyrazolines have found wide application as pharmaceutical and agrochemical agents. Pyrazoline derivatives have been found to possess wide range of therapeutic activities such as diuretic[7], antifungal[8] and analgesic[9]. It has been reported that introduction of acetyl group at 1st position enhances the mollucicidal[10] activity as well as increases the stability of pyrazolines. Pyrimidine derivatives play a vital role in many biological processes and in synthesis of many drugs. Many pyrimidine derivatives have displayed diverse biological activities such as antitumor[11], hypnotensive[12], antiulcer[13] and anticonvulsant[14].

In view of the above and in a continuation of our work[15-18] on chalcones and its derivatives, we herein report a new series of chalcones (6a-e), pyrazolines (7a-e) and aminopyrimidines (8a-e).

EXPERIMENTAL

All the melting points were determined in an open capillary and are uncorrected. The IR spectra were recorded on Perkin-Elmer 237 spectrophotometer. ^{1}H NMR spectra on a Bruker Avance DPX 300 MHz spectrometer with $CDCl_3$ as a solvent and TMS as internal reference. Purity of the compounds was checked on TLC using silica gel-G.

Preparation of 2-(phenylamino)- 4, 6-dichloro-*s*-triazine (3)

Aniline (0.01 mol in 10ml acetone) was added slowly to cyanuric chloride (0.01 mol in 30 ml acetone) with constant stirring for 4 hours at 0 to 5 °C. Periodically, sodium carbonate solution (0.005 mol, 0.53g in 10ml water) was added dropwise to neutralized HCl evolved during the

reaction. Finally the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give (3). Yield 89 %, m.p. 196 °C.

Preparation of 2-(phenylamino)-4-(4'-chlorophenylamino)-6-chloro-*s*-triazine (4)

4-Chloroaniline (0.01 mol in 10ml acetone) was added slowly to compound (3) (0.01 mol in 35 ml acetone) with constant stirring for 6 hours at room temperature. Periodically, sodium carbonate solution (0.005 mol in10ml water) was added dropwise to neutralized HCl evolved during the reaction. Finally the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol to give (4). Yield 84%, m.p. 190°C.

Preparation of 2-(phenylamino)-4-(4'-chlorophenylamino)-6(4'-acetylphenylamino)-*s*-triazine (5)

4-Aminoacetophenone (0.01mol) and compound (4) (0.01 mol) were dissolved in acetone (40 ml). The reaction mixture was refluxed for 6 hours, cooled and poured into crushed ice. Periodically, sodium carbonate solution (0.005 in 10 ml water) was added to neutralize HCl evolved during the reaction. The solid separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give (5). Yield 79%, m.p. 208°C; IR (KBr) cm^{-1}: 1660 (-C=O), 806 (C-N, *s*-triazine), 784 (C-Cl). ^1H NMR ($CDCl_3$): δ 2.6 (s, 3H, $-COCH_3$), δ 6.9 - 8.8 (m, 16H, Ar-H and NH).

Preparation of 2-(phenylamino)-4-(4'-chlorophenylamino)-6-[4'-{3''-(4'''-methoxy phenyl)-2''-propenon-1''-yl } phenyl amino]-*s*-triazine (6a)

Compound (5) (0.01mol) was dissolved in DMF (30 ml) and 4-methoxybenzaldehyde (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 71%, m.p.185°C; IR (KBr) cm^{-1}: 1649 (-C=O), 803 (C-N, *s*-triazine), 776 (C-Cl). ^1H NMR ($CDCl_3$): δ 3.80 (s, 3H, OCH_3), δ 6.9 (d, lH, -CO-CH=), δ 7.0 – 8.0 (m, 19H, Ar-H and NH), δ 8.3 (d, 1H, Ar-CH=).

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'-chlorophenylamino)-6-[4'-{1''-acetyl-5''- (4'''-methoxyphenyl)- 2''-pyrazolin- 3''-yl} phenylamino]-*s*-triazine (7a)

Compound (6a) (0.01mol) was dissolved in glacial acetic acid (30 ml) and hydrazine hydrate (0.01mol) was added to it. Then the reaction mixture was refluxed for 6 hours then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give (7a). Yield 67%, m.p. 240°C, IR (KBr) cm^{-1}: 1573 (-C=N), 1244 (C-O-C), 806 (C-N, *s*-triazine), 754 (C-Cl); ^1H NMR ($CDCl_3$): δ 2.44 (s, 3H, $-COCH_3$), 3.2 (dd, 1H, $-CH_A$), δ 3.4 (dd, 1H, $-CH_B$), δ 3.90 (s, 3H, OCH_3), δ 5.6 (dd, 1H, -CH), δ 6.8 - 7.6 (m, 20H, Ar-H 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'-chlorophenylamino)-6- [4'-{ 2''-amino-6''-(4'''-methoxyphenyl)- pyrimidine-4''-yl} phenylamino] -*s*-triazine(8a)

Compound (6a) (0.01 mol) was dissolved in alcohol (25ml), guanidine hydrochloride (0.01 mol) was added to it. Then solution of KOH (5 ml 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 recrystallized from ethyl alcohol to give (8a). Yield 64%, m.p. 158°C; IR (KBr) cm^{-1}: 3470 ($-NH_2$), 1234 (C-O-C), 805 (C-N, *s*-triazine), 753 (C-Cl), ^1H NMR ($CDCl_3$): δ 3.8 (s, 3H, OCH_3), 5.6 (s, 2H, $-NH_2$), 6.9 to 8.1 (m, 21H, Ar-H and NH).

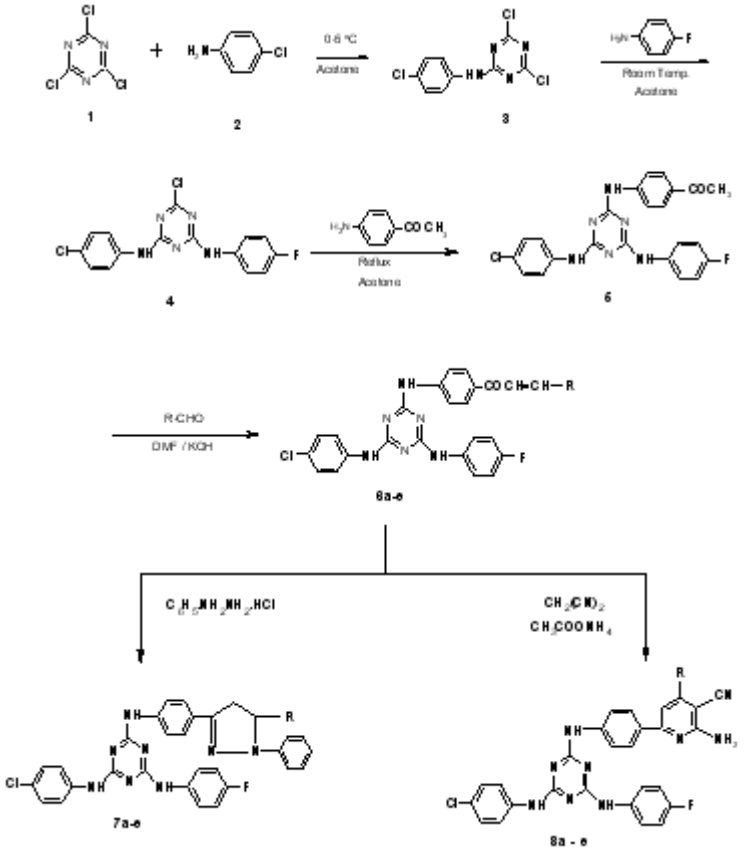
Similarly the remaining compounds (8b-e) were prepared by this method. Their physical data are given in Table 1.

RESULTS AND DISCUSSION

The IR spectrum of compound (6a) shows the characteristic band at 1649 cm^{-1} due to -C=O group. The IR spectrum of compound (7a) shows characteristic band at 1573 cm^{-1} due to –C=N group. The IR spectrum of compound (8a) shows the characteristic band at 3470 cm^{-1} which indicate the presence of (-NH_2) primary amine. The IR spectrum of compound (7a) and compound (8a) does not show any absorption band in the region of 1700 – 1600 cm^{-1} which indicate the absence of -C=O group. ^1H NMR spectrum of compound (6a) shows doublet at δ 6.9 due to (-CO-CH=). The ^1H NMR spectrum of compound (7a) shows a sharp singlet at δ 2.44 due to (-$COCH_3$). The ^1H NMR spectrum of compound (8a) shows singlet at δ 5.6 due to –NH_2 protons.

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

Compd	R	M.P °C °C	% Yield
6a	4-Methoxy phenyl	185	71
6b	2-Chloro phenyl	175	70
6c	3-Chloro phenyl	165	71
6d	4-Chloro phenyl	187	69
6e	2-Nitro phenyl	180	68
7a	4-Methoxy phenyl	240	67
7b	2-Chloro phenyl	180	61
7c	3-Chloro phenyl	160	62
7d	4-Chloro phenyl	201	63
7e	2-Nitro phenyl	158	63
8a	4-methoxy phenyl	158	67
8b	2-Chloro phenyl	155	61
8c	3-Chloro phenyl	183	58
8d	4-Chloro phenyl	180	60
8e	2-Nitro phenyl	190	61



Scheme 1

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