Synthesis and characterization of some new heterocyclic chalcones and their derivatives

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ABSTRACT
Some new chalcones, 2-(4'-Chlorophenylamino)-4-(4'-fluorophenylamino)-6-[4'-{(3'-phenyl/substituted phenyl)-2''-propenon-1''-yl} phenylamino]-s-triazines (6a-e) have been synthesized by the Claisen-Schmidt condensation between ketone (5) based on s-trizine nucleus and different aromatic aldehydes. These chalcones (6a-e) on cyclisation with guanidinenitrate give aminopyrimidines (7a-e) and also on cyclisation with hydrazine hydrate in presence of glacial acetic acid give pyrazolines (8a-e). The structures of newly synthesized compounds have been characterized on the basis of elemental analysis,IR and 1H NMR spectra.

INTRODUCTION
Chalcone is known as α,β-unsaturated ketone. Chalcones[1-3] are very reactive compounds and increase their reactivity due to ketoenic(O=C-CH=CH) type of conjugated double bond system present in the molecule. Chalcones are useful intermediates in the synthesis of various heterocyclic compounds such as pyrazolines, isoxazolines, pyrimidines, flavones and flavonols. Chalcones have been found to possess many biological activities like analgesic[4] and anthelmintic[5]. Now a days, a number of drugs containing simple heterocyclic or a combination of different heterocyclic moieties have been used.

The synthesis of pyrimidine derivatives have attracted the attention of chemists because of their potential pharmacodynamic properties[6-8]. Pyrimidine derivatives play a vital role in many biological processes and in synthesis of drugs. Many pyrimidine derivatives can be used as therapeutic agents in treatment of AIDS[9] and tumor[10]. Synthesis and characterization of pyrazoline derivatives have been a developing field within the realm of heterocyclic chemistry for the past several decades because of their ready accessibility through synthesis and wide range of chemical reactivity. Pyrazoline derivatives have been found to possess wide range of therapeutic activities such as anticonvulsant[11], analgesic[12] and anticancer[13].

Earlier, we have reported synthesis of various derivatives of s-triazine based chalcones[14-16]. Claisen-Schmidt condensation of 2-(4'-chlorophenylamino)-4-(4'-fluoro phenylamino)-6-(4'-acetylphenylamino)-s-triazine (5) with different aromatic aldehydes gives chalcones (6a-e). Compound (5) was prepared by the condensation of cyanuric chloride and 4-chloroaniline at 0-5°C to form (3) which further reacts with 4-fluoroaniline at room temperature to form (4), which is treated with 4-amino acetophenone to form compound...
Chalcones (6a-e) on cyclisation with guanidine nitrate in presence of alkali it give aminopyrimidines (7a-e) and also on cyclisation with hydrazine hydrate in presence of glacial acetic acid it give acetyl pyrazolines (8a-e) (SCHEME 1).

**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 300MHz spectrometer with CDCl$_3$ as a solvent and TMS as internal reference. Purity of the compounds were checked on TLC using silica gel-G.

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

4-Chloroaniline (0.01 mole, 1.275 g in 10 ml acetone) was added slowly to cyanuric chloride (0.01 mole, 1.845 g in acetone 30 ml) with constant stirring for 4 hours at 0 to 5°C. Periodically sodium carbonate solution (0.005 mole, 0.53 g in 10 ml water) was added dropwise to neutralize HCl evolved during the reaction. Finally the contents was poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallised from alcohol to give (3). Yield 90% ; mp. 220°C.

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

4-Fluoroaniline (0.01 mole, 1.11 g in 10 ml acetone) was added slowly to compound (3) (0.01 mole, 2.75 g in 35 ml acetone) with constant stirring for 6 hours at room temperature. Periodically sodium carbonate solution (0.005 mole, 0.53 g in 10 ml water) was added dropwise to neutralize HCl evolved during the reaction. Finally the contents was poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallised from alcohol to give (4).
Preparation of 2-(4'-chlorophenylamino)-4-(4'-fluorophenylamino)-6-[4'-{2'-amino-6'-methoxyphenyl}-pyrimidine-4'yl]-phenylaminos-triazine (5)

4-Aminoacetophenone (0.01 mole, 1.35 g) and compound (4) (0.01 mole, 3.50 g) 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, 0.53 g in 10 ml water) was added to neutralize HCl evolved during the reaction. The solid separated out was filtered, washed with water, dried and recrystallised from alcohol to give (5).

Yield 79%; m.p. 208 °C; IR (KBr, cm⁻¹) 1658 (-C=O), 1020 (C-F), 800(C-N, s-triazine), 786(C=H); ¹H NMR (CDCl₃): δ 2.6 (s, 3H, -CO-CH=), 6.9 - 8.2 (m, 15H, 12 Ar-H and 3 NH).

Preparation of 2-(4'′-chlorophenylamino)-4-(4'′-fluorophenylamino)-6-[4'′-[3'-{4'′′-methoxyphenyl}-2′′-propenon-1′′-yl]-phenylaminos-triazine (6e)

Compound (5) (0.01 mole, 4.48 g) was dissolved in DMF (30 ml) and 4-methoxy benzaldehyde (0.01 mole, 1.36 g) 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 neutralize with HCl. The product separated out was filtered, washed with water, dried and recrystallised from alcohol to give (6).

Yield 61%; m.p. 178 °C; IR (KBr, cm⁻¹) 3403 (-NH₂), 1578 (C=N), 1227 (C-O-C), 1013(C-F), 803(C-N, s-triazine); ¹H NMR (CDCl₃): δ 3.8 (s, 3H, -OCH₃), 6.7 - 8.2 (m, 20H, 17 Ar-H and 3 NH).

Similarly the remaining compounds (6a-d) were prepared by this method. Their physical and analytical data are given in TABLE.

Preparation of 2-(4'′-chlorophenylamino)-4-(4'′-fluorophenylamino)-6-[4'′-[2′′-amino-6′′-(4'′′-methoxyphenyl)-pyrimidine-4'′yl]-phenylaminos-triazine (7e)

Compound (6e) (0.01 mole, 5.66 g) was dissolved in alcohol (25 ml) and guanidine nitrate (0.01 mole, 1.22 g) 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 alcohol to give (7e).

Yield 61%; m.p. 178 °C; IR (KBr, cm⁻¹) 3403 (-NH₂), 1578 (C=N), 1227 (C-O-C), 1013(C-F), 803(C-N, s-triazine); ¹H NMR (CDCl₃): δ 3.8 (s, 3H, -OCH₃), 6.7 - 8.2 (m, 20H, 17 Ar-H and 3 NH). Anal. Calcd for C₃₂H₂₅N₂O₃Cl F: C, 63.41; H, 4.21; N, 14.80.

Similarly the remaining compounds (7a-d) were prepared by this method. Their physical and analytical data are given in TABLE.

**Preparation of 2-(4'-chlorophenylamino)-4-(4'-fluorophenylamino)-6-[4'-{5'-{(4'-methoxyphenyl)1'-acetylpyrazoline-3'-yl}-phenylamino]-s-triazine (8e)**

Compound (6e)(0.01mole,5.66g) was dissolved in glacial acetic acid (25ml) and hydrazine hydrate (0.01mole,0.5g) was added to it. Then the reaction mixture was refluxed for 6 hours. The reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and recrystallized from alcohol to give (8e).

Yield 62%; m.p. 185°C; IR(KBr,cm\(^{-1}\)) 1570(–C=N),1221(C-O-C), 1013(C-F), 809(C-N, s-triazine),785(C-Cl); \(\delta\)H NMR(CDCl\(_3\)): \(\delta\)2.5(s,3H,-COCH\(_3\)), \(\delta\)3.0(dd, 1H, -CH\(_A\)), \(\delta\)3.2(dd, 1H, -CH\(_B\)), \(\delta\)3.83(s,3H, -OCH\(_3\)), \(\delta\)5.7(dd, 1H, -CH), \(\delta\)6.8 - 7.7(m,19H,16H, Ar-H and 3NH). Anal. Calcd for C\(_{33}\)H\(_{28}\)N\(_8\)O\(_2\)ClF: C,63.61; H;4.49; N,17.99. Found: C,63.60; H;4.48; N,17.98.

Similarly the remaining compounds (8a-d) were prepared by this method. Their physical and analytical data are given in TABLE.

**RESULTS AND DISCUSSION**

The IR spectrum of (6e) shows the characteristic band at 1649cm\(^{-1}\) due to –C=O group. The IR spectrum of (7e) shows the characteristic band at 3403cm\(^{-1}\) which indicate the presence of primary amine. The IR spectrum of (7e) do not show any absorption bands in the region of 1700-1600cm\(^{-1}\) which indicate the absence of –C=O group. The IR spectrum of (8e) shows characteristic band at 1570cm\(^{-1}\) due to –C=N group. The NMR spectrum of (6e) shows a doublet at \(\delta\) 6.9 due to (-CO-CH=). The NMR spectrum of (7e) shows a singlet at \(\delta\) 5.7 due to -NH\(_2\) protons. The NMR spectrum of (8e) shows a sharp singlet at \(\delta\) 2.5 due to (-COCH\(_3\)).

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**REFERENCES**