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Synthesis and biological evaluation of s-triazine based chalcones and its aminopyrimidine and cyanopyridine derivatives

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ABSTRACT

Chalones, 2,4-bis-(4'-flurophenylamino)-6-[4'-{3"-(substituted phenyl/2"'-furanyl)-2"-propenon-1"-yl} phenylamino] s-triazine (6a-e) have been prepared from ketone (5) on treatment with different aromatic/hetarocyclic aldehydes. These chalcones on cyclisation with guandiine nitrate in presence of alkali and malononitrile in presence of ammonium acetate give the corresponding aminopyrimidine (7a-e) and cyanopyridine (8a-e) derivatives respectively. All the synthesized compounds have been screened for their antibacterial activity against *S. aureus* (MTCC 96), *B. subtilis* (MTCC 441), *E. coli* (MTCC 443) and *S. paratyphi*-B. (MTCC 733). The structure of the synthesized compounds have been established on the basis of their elemental analysis and spectral studies.

Key words: s-triazine, aminopyrimidine, cyanopyridine derivatives.

INTRODUCTION

The s-triazine and their derivatives have their own importance in heterocyclic chemistry due to their good biological activities[1-2]. Pyrimidine and pyridine derivatives[3-6] also plays a vital role in many biological processes and in synthesis of many drugs. These observations led us to synthesize some new s-triazinyl based chalcones and its corresponding aminopyrimidine[7] and cyanopyridine derivatives[8].

In the present work, herein we report the reaction of cyanuric chloride (1) with 4-fluoroaniline (2) at 0-5°C to give (3), which reacts with 4-fluoroaniline at room temperature to give (4). Compounds(4) is further treated with 4-aminoacetophenone to give 2,4-bis-(4'-fluorophynylamino)-6-(4-acetylphenyl amino)-s-triazine (5). Compound (5) on reaction with different aromatic and heterocyclic aldehydes to give chalcones (6a-e). Further these chalcones (6a-e) on reaction with guanidine nitrate in the presence of alkali and with malononitrile in the presence of ammonium acetate to give aminopyrimidines (7a-e) and cyancopyridines (8a-e) respectively (Scheme 1). The structure of the newly synthesised compounds have been identified on the basis of their elemental analysis, IR spectra and ^{1}H NMR spectra.

EXPERIMENTAL

All the melting points were taken 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 400 MHz spectrometer with $CDCl_3$ as a solvent and TMS as internal reference. TLC was performed on precoated Merck Silica Gel 60 F_{254} Aluminiuum foil.

Preparation of 2,4-bis-(4'-flurophenylamino)-6-(4'-acetylphenylamino)-s-triazine (5)

4-Aminoacetophenone (0.01 mol, 1.35g) and 2,4-bis-(4'-flurophenylamino)-6-(4'-acetylp henylamino)-s-triazine (4) (0.01 mol, 3.335g) were dissolved in 40ml acetone. The reaction mixture was refluxed for 6hrs. Periodically, sodium carbonate solution (0.005 mol, 0.53g in 20ml water) was added drop wise to neutralized HCl evolved during the reaction. Finally, the reaction mixture was cooled and poured into crushed ice. The solid separated

out was filtered, washed with water and recrystallised from alcohol to give (5), m.p. 195°C. IR(KBr) cm^{-1}, 1662 (C=O), 1055 (C-F), 805 (C-N, s-triazine). ^1H NMR ($CDCl_3$) δ ppm, 2.6 (s, 3H, -$COCH_3$), 7.20 to 7.90 (m, 13Ar-H and 3-NH).

Preparation of 2,4-bis-(4'-flurophenylamino)-6-[4'-{3"-(2'''-methoxyphenyl(-2"-propenon-1"-yl}phenylamino]-s-triazine(6c)

2,4-bis-(4'-flurophenylamino)-6-(4'-acetylphenylamino)-s-triazine) (5) (0.01mol), 4.32g)

Table 1: Physical data of compound 6 a-e, 7a-e and 8a-e

Comp.	R	MP (°C)	Yiled (%)
6a	2-NitroPhenyl	216	87
6b	2-Nitrophenyl	210	89
6c	2-Methoxyphenyl	98	90
6d	2,3-Dichlorophenyl	106	79
6e	2-Furanyl	116	78
7a	3-Nitrophenyl	204	72
7b	4-Nitrophenyl	198	69
7c	2-Methoxyphenyl	185	74
7d	2,3-Dichlorophenyl	174	70
7e	2-Furanyl	166	68
8a	2-NitroPhenyl	184	72
8b	2-NitroPhenyl	226	66
8c	2-Methoxyphenyl	257	68
8d	2,3-Dichlorophenyl	167	70
8e	2-Furanyl	170	63

All compounds gave satisfactory %C and %N analysis

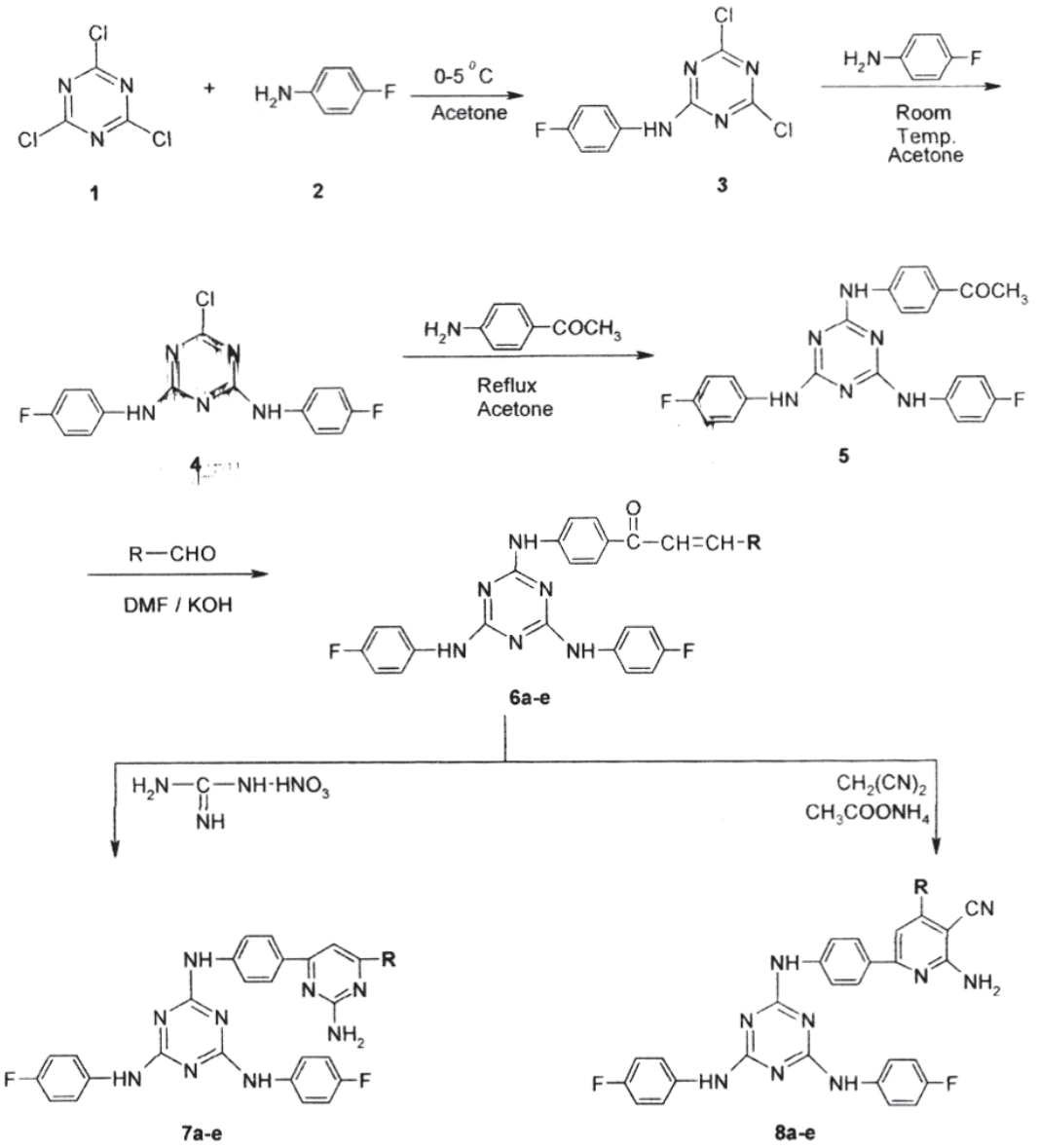
Table 2: Antibacterial activity data of compound 6a-e, 7a-e, and 8a-e

S. No	R	Diameter of zone of inhibition (in mm)			
		S. aureus MTCC 96	*B. subtilis* MTCC 441	*E.coli.* MTCC 443	*S.parathyphi-B* MTCC 773
6a	2-NitroPhenyl	14	-	-	10
6b	2-Nitrophenyl	-	14	17	16
6c	2-Methoxyphenyl	13	-	13	17
6d	2,3-Dichlorophenyl	-	12	10	11
6e	2-Furanyl	-	-	12	-
7a	2-Nitrophenyl	-	-	11	-
7b	3-Nitrophenyl	-	-	18	12
7c	2-Methoxyphenyl	-	-	13	-
7d	2,3-Dichlorophenyl	-	12	-	-
7e	2-Furanyl	-	13	-	-
8a	2-NitroPhenyl	-	-	-	-
8b	3-NitroPhenyl	-	-	-	-
8c	2-Methoxyphenyl	-	-	-	11
8d	2,3-Dichlorophenyl	-	10	21	16
8e	2-Furanyl	-	12	14	17
Standard drug	Ciprofoxacin	22	20	24	25

was dissolved in DMF (30ml) and 2-methoxy benzaldehyde in DMF (0.01 mol, 1.36g) was added to reaction mixture with constant stirring at room temperature. Then 40% KOH solution was added to the reaction mixture with constant stirring. After 24 hrs the reaction mixture was poured into crushed ice and neutralized with HCl. The product separated out was filtered, washed with water and recrystallised from alcohol to give(6c), m.p. 98°C. Similarly, reamainig compounds were prepared by the above method. IR (Kbr): cm^{-1} 1664 (C=O), 1037 (C-F), 1033 (C-O-C), 804 (C-N, s-triazine). ^1H NMR ($CDCl_3$) δppm: 3.82 (s, 3H, o-OCH_3), 6.98 (d, 1H, -CO-CH=), 7.1 to 7.99 (m, 15 Ar-H and 3-NH), 8.2 (d, 1H, Ar-CH=).

Preparation of 2,4-bis-(4'-flurophenylamino)-6-[4'-{2"-amino-6"-(2"-methoxyphenyl) pyrimidine-4"-yl} phenylamino]-s-triazine (7c)

A mixture of 2,4-bis-(4'-flurophenylamino)-6-[4'-}3"-(2'"-methoxyphenyl) pyrimidine-4"-yl} phenylamino]-s-triazine (6c) (0.005 mol, 2.75g) in



Scheme 1:

50 ml alcohol, guanidine nitrate (0.01mol, 1.22g) and 40% KOH solution (2ml) were refluxed for 10hrs. Then the reaction mixture was cooled and poured into crushed ice. The product separated out was filtered, washed with water and recrystallised from alcohol to give (7c), m.p. 185°C. Similarly, remaining compounds were prepared by the above method. IR (KBr) cm^{-1}: 3410 (-NH_2), 1652(C=N), 804 (C-N s-triazine), 1075 (C-F), 1032 (C-O-C). ^1H NMR ($CDCl_3$): δppm, 3.91 (s, 3H, o-OCH_3), 5.15 (s, 2H,-NH_2), 7.01 to 8.15 (m, 17 Ar-H and 3-NH).

Preparation of 2,4-bis(4'-fluorophenylamino)-6-[4'-{2"-amino-3"-cyano-4"-(2'"-methoxyphenyl) pyridine-6"-yl} phenylamino]-s-triazine (8c)

A mixture of 2,4-bis(4'-fluorophenylamino)-6-[4"-{3"-(2'"-methoxyphenyl)-2"-Propenone-6'"-yl} phenylamino]-s-triazine (6c) (0.005mol, 2.75g) in 40ml alcohol, malanonitrile (0.005 mol, 0.33g) and ammonium acetate (0.005 mol, 3.08g) was refluxed for 8hrs. Then the reaction mixture was cooled and poured into crushed ice. The product separated out was filtered, washed with water and recrystallised from alcohol to give (8c) m.p. 257°C. Similarly, remaining compounds were prepared by the above method. IR (KBr) cm^{-1}: 3406 (-NH_2), 2200 (C=N), 1120 (C-F), 801 (C-N s-triazine), 1029 (C-O-C). ^1H NMR ($CDCl_3$) δppm: 3.89 (s, 3H, o-OCH_3), 5.23 (s, 2H,-NH_2), 7.10 to 8.11 (m, 17Ar-H and 3-NH).

RESULTS AND DISCUSSION

Antibacterial acitivity

All the synthesised compounds were screened for their antibacterial activity against *S. aureus* (MTCC 96), *B. subtilis* (MTCC 441) (Gram-positive) and *E. coli* (MTCC 443) *S. paratyphi* B. (MTCC 733) (Gram-negative) by agar-diffusion method[8] at conentration of 100 µg/ml in solvent DMF. The zone of inhibition was measured in mm. Under similar conditions controlled experiment was carried out using Ciprofloxacin as a standard durg for comparison and the results were collected in (Table 2). By the visualizing activity data, compound (6b) and (7b) were found moderately active against *E. coli* (MTCC 443), where as all the other compounds were found less active or inactive against all the bacteria.

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