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Synthesis and Antimicrobial Activity of 2-(Methyl Amino)-4-(4′-Ethoxy Anilino)-6-(Substituted Dihydrodino)-S-Triazines

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Cyanuric chloride and methyl amine in equimolar proportion were condensed and then treated with *p*-phenitidine in equimolar proportion to get the corresponding intermediate (I) which was further treated with various substituted dihydropyridines to get the corresponding 1,3,5-triazines (II). The compounds were tested for their antimicrobial activity. Some of the compounds show remarkable activity.

INTRODUCTION

Although a large number of S-triazines[1, 2] analogues have been synthesized, there exists much scope for the synthesis of S-triazine derivatives possessing different pharmocophores[3, 4]. Dihydropyridines[5] are known to exhibit antihypertensive, antimicrobial and calcium channel blocking activity[6] and one of the starting material required for the preparation of target compounds was prepared from 'Hantzsch synthesis'.

Literature survey reveals that various 2,4,6-substituted S-triazines have resulted in many potential drugs[7]. These observations prompted us to synthesize some new S-triazinyl derivatives with a view to studying their pharmacological profile.

EXPERIMENTAL

The melting points were taken in open glass capillary using liquid paraffin bath and are uncorrected. IR spectra were recorded on Perkin-Elmer 1420 spectrophotometer using nujol mull. The NMR spectra were recorded on FT-80A spectrometer in $CDCl_3$ using TMS as internal standard (chemical shift in δ ppm). The purity of the compounds was checked on TLC.

2-(Methylamino)-4-(4′-ethoxy anilino)-6-chloro-S-triazines (I)

It was prepared according to reported methods in literature[8, 9].

2-(Methyl amino)-4-(4′-ethoxy anilino)-6-substituted-S-triazines (II)

Cyanuric chloride and methyl amine stirred at 0°C for 2 h and the product so obtained was treated with *p*-phenitidine in equimolar proportion and condensed. The intermediate compound (II) so obtained was treated with various substituted dihydropyridines giving (III) (cf. Scheme-I) and was confirmed by IR and NMR spectroscopy and yielded a single product (TLC). These compounds were tested against *Alternaria brassicicola*, *Fusarium udam*, *Esch. coli* (gram –ve) and *Staphylococuus* (gram +ve) bacteria.

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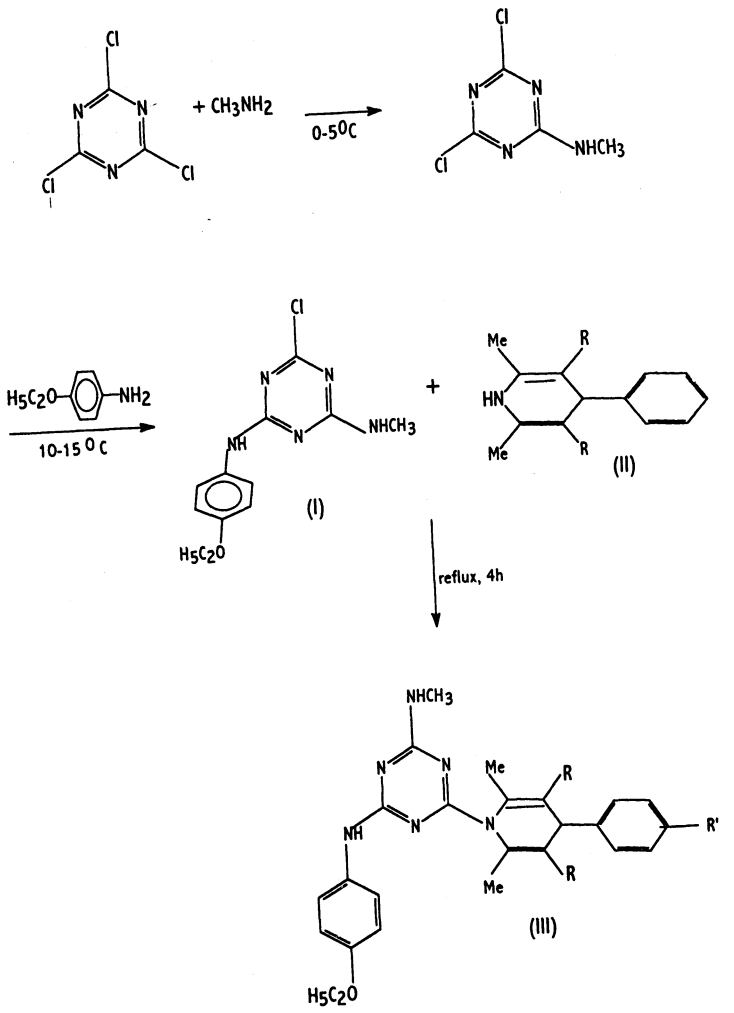
TABLE-1
PHYSICAL CHARACTERISATION DATA OF SYNTHESISED COMPOUNDS (1–32)

Compd. No.	Substitutents R	Substitutents R′	Yield (%)	m.p. (°C)	m.f.	% N, found	% N, (calcd.)
1.	-Me	H	65	120	$C_{32}H_{38}N_6O_3$	15.02	15.16
2.	-Me	2-Me	61	130	$C_{33}H_{40}N_6O_3$	14.61	14.78
3.	-Me	4-Me	68	122	$C_{33}H_{40}N_6O_3$	14.61	14.78
4.	-Me	2-OMe	70	118	$C_{33}H_{40}N_6O_4$	14.20	14.38
5.	-Me	4-OMe	65	128	$C_{33}H_{40}N_6O_4$	14.20	14.38
6.	-Me	2-Cl	62	124	$C_{32}H_{37}N_6O_3Cl$	14.07	14.27
7.	-Me	4-Cl	68	131	$C_{32}H_{37}N_6O_3Cl$	14.07	14.27
8.	-Me	2-NO_2	72	140	$C_{32}H_{37}N_7O_3$	16.11	16.36
9.	-Me	4-NO_2	68	136	$C_{32}H_{37}N_7O_3$	16.11	16.36
10.	-Me	4-Br	67	132	$C_{32}H_{37}N_6O_3Br$	13.04	13.27
11.	-Me	4-OH	69	125	$C_{32}H_{38}N_6O_4$	14.60	14.70
12.	-OMe	H	65	127	$C_{32}H_{38}N_6O_5$	14.13	14.33
13.	-OMe	2-Me	70	124	$C_{33}H_{40}N_6O_5$	13.84	14.00
14.	-OMe	4-Me	65	109	$C_{33}H_{40}N_6O_5$	13.84	14.00
15.	-OMe	2-OMe	59	114	$C_{33}H_{40}N_6O_6$	13.49	13.63
16.	-OMe	4-OMe	66	156	$C_{33}H_{40}N_6O_6$	13.84	14.00
17.	-OMe	2-Cl	71	171	$C_{32}H_{37}N_6O_5Cl$	13.34	13.53
18.	-OMe	4-Cl	70	135	$C_{32}H_{37}N_6O_5Cl$	13.34	13.53
19.	-OMe	4-Br	60	172	$C_{32}H_{37}N_6O_5Br$	12.49	12.69
20.	-OMe	2-NO_2	69	128	$C_{32}H_{37}N_7O_7$	15.39	15.53
21.	-OMe	4-NO_2	72	110	$C_{32}H_{37}N_7O_7$	15.39	15.53
22.	-OMe	2-OH	77	98	$C_{32}H_{38}N_6O_6$	13.83	13.53
23.	-OMe	4-OH	73	126	$C_{32}H_{38}N_6O_6$	13.83	13.63
24.	-OEt	H	80	108	$C_{34}H_{42}N_6O_5$	13.44	13.68
25.	-OEt	4-Me	70	144	$C_{35}H_{44}N_6O_5$	13.18	13.37
26.	-OEt	2-OMe	68	130	$C_{35}H_{44}N_6O_6$	12.89	13.04
27.	-OEt	4-OMe	71	152	$C_{35}H_{44}N_6O_6$	12.68	13.04
28.	-OEt	2-Cl	67	132	$C_{34}H_{41}N_6O_5Cl$	12.83	12.95
29.	-OEt	4-Cl	69	138	$C_{34}H_{41}N_6O_5Cl$	12.86	12.95
30.	-OEt	3-Br	80	170	$C_{34}H_{41}N_6O_5Br$	12.09	12.28
31.	-OEt	4-NO_2	80	148	$C_{34}H_{41}N_7O_7$	12.67	12.74
32.	-OEt	4-OH	81	144	$C_{34}H_{42}N_6O_6$	13.15	13.31

*All the compounds recrystallised from aq. ethanol and give satisfactory C and H analysis.

2-(Methyl amino)-4-(4′-ethoxy anilino)-6-(N-1,4-dihydro-4′-(4″-hydroxy phenyl)-3′,5′-diacetyl-2′,6′-dimethyl pyridino)-S-triazine (II)

A mixture of (I) (0.01 mol) and 1,4-dihydropyridino-4-(4′-hydroxy phenyl)-



Scheme-1

3,5-diacetyl-2,6-dimethyl pyridine (0.01 mol) on acetone was refluxed for 4 h on a boiling water bath. It was then cooled and poured on crushed ice and the resulting solid was filtered, washed, dried and recrystallised from aq. alcohol.

Yield 69%; m.p. 125°C.IR: 3340 ν(—NH), 1695 ν(C=O), 1630 ν(C=N), 1605 cm^{-1} ν(C=C).

PMR: δ 1.20–1.25 (t, 3H, CH_2—CH_3), 2.20 (s, 6H, —CH_3), 3.56 (s, 6H, CO—CH_3), 3.60 (s, 3H, —OCH_3), 3.74–3.96 (q, 2H, —OCH_2—CH_3), 5.70 (s, 1H, pyridyl H-4), 6.40–7.26 (m, 9H, Ar—H and —NH).

All the synthesized compounds were tested for their antifungal activity against *Alternaria brassicicola*, *Fusarium udam*, while antimicrobial activity were tested against *E. coli* (gram –ve) and *Staphylococcus aureus* (gram + ve) bacteria (Table-2).

TABLE-2
ANTIMICROBIAL ACTIVITY OF THE SYNTHESISED COMPOUNDS

Compound No.	*Alternaria brassicicola*	*Fusarium udam*	*Staphylococcus aureus* (gr + ve)	*Esch. coli* (gr –ve)
1.	++	++	++	–
2.	++	++	–	++
3.	++	++	++	–
4.	++	++	–	–
5.	++	++	–	++
6.	++	++	–	++
7.	+++	+++	+++	++
8.	++++	++++	+++	+++
9.	++++	++++	++++	++++
10.	++	++	++	++
11.	++	+++	++	++
12.	++	++	++	+
13.	–	++	++	++
14.	++	+	+	+
15.	+	+	+	++
16.	++	++	++	++
17.	++++	++++	+++	+++
18.	+++	+++	++	++
19.	++	++	++	++
20.	++++	++++	++	+++
21.	++	++	++	++
22.	++	++	++	++
23.	++	++	++	+
24.	++	+	++	+
25.	++	++	++	++
26.	++	++	++	+
27.	++	++	+	+
28.	++	++	++	++
29.	++++	+++	++	++
30.	++	++	++	++
31.	++++	++++	+++	+++
32.	++	++	++	++
Standard	Carbendazim		Taracyclin	
	++++	++++	++++	++++
Solvent	–	–	–	–

+mm Antagonistic Zones of inhibition in mm; –mm Nil zone of inhibition
\+ 8–12 mm Inactive ++ 12–18 mm Slightly active
+++ 18–21 mm Moderately active ++++ 21–25 mm Highly active

The activity of these compounds was tested using filter paper disc method[10] at 500 ppm concentration using 5 mm size filter paper in similar conditions; the standard *i.e.*, control drugs used were carbendazim and tetracycline. The zones of inhibition were measured in mm.

From the activity data it was found that compound Nos. **6, 7, 8, 9, 17, 21, 28, 29** and **31** showed good activity against fungi while compound Nos. **8, 17, 28, 29** and **31** were found active against bacteria too. S-triazines having —Cl and —NO_2 group substituted in the dihydropyridines moiety were showing good antimicrobial activity while groups such —Br, —OCH_3, —CH_3 and —H were showing moderate activity against fungi and bacteria. The most active compounds of the series were found to be compound Nos. **9, 17** and **31.**

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