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Synthesis of Some Dihydropyridino Azitidinones and Their Antimicrobial Activity

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Hydrazides of substituted 1,4-dihydropyridines have been synthesised by condensing substituted dihydropyridine dicarboxylic acid ester with hydrazine hydrate. Hydrazides were condensed with different aromatic aldehydes to give different Schiff bases. These schiff bases on treatment with chloroacetyl chloride gave azitidinones. Teh synthesised compounds were screened for antimicrobial activity.

INTRODUCTION

2-Azitidinones and 4-thiazolidinone derivative are associated with diverse pharmacological and biological activities[1-3]. These observations prompted us to synthesise some azitidinones incorporating substituted dihydro pyridino[4] moiety and to study their biological activity. The 1,4-dicarboxylic acid hydrazide (I) on condensing with aldehydes gives schiff bases. The Schiff bases on treatment with chloroacetyl chloride gives 2-azitidinones 1–20. (Table-I). The steps involved in the synthesis are shown in Scheme-I.

All the compounds were screened for their antimicrobial activity against *Alternaria brassicicola*, *Fusarium udam*, *Staphylococcus* gram(+ve) and *Lactobacillus* gram(–ve). The activities are disccused in experimental part.

EXPERIMENTAL

All melting points were taken in open capillary in a liquid paraffin bath and the uncorrected. The purity of all compounds was checked by TLC. IR sepctra were recorded in nujol on Perkin-Elmer 1420 spectrophotometer while PMR spectra in $CDCl_3$ using TMS as an internal standard.

3,5-Bis(3′-chloro-4′-aryl-2′-azitidino-1′-yl carbonyl)-2,6-dimethyl-4-phenyl-1,4,-dihydro pyridine (1)

Schiff base of the hydrazide (I) was prepared by known procedure. The prepared Schiff base (0.01 M), chloroacetyl chloride (0.2 M) and triethanolamine (0.03 M) were refluxed in dioxane for 3 h. The reaction mixture was cooled and poured over crushed ice. The solid separated was filtered and crystallised from methanol. Yield: 75%; m.p.: 178°C (Compd No. 1,) (Table-I); IR: ν_{max} 3320 cm^{-1} (—NH), 1670 cm^{-1} (C=O), 1620 cm^{-1} (C=N), 1605 cm^{-1} (C=C).

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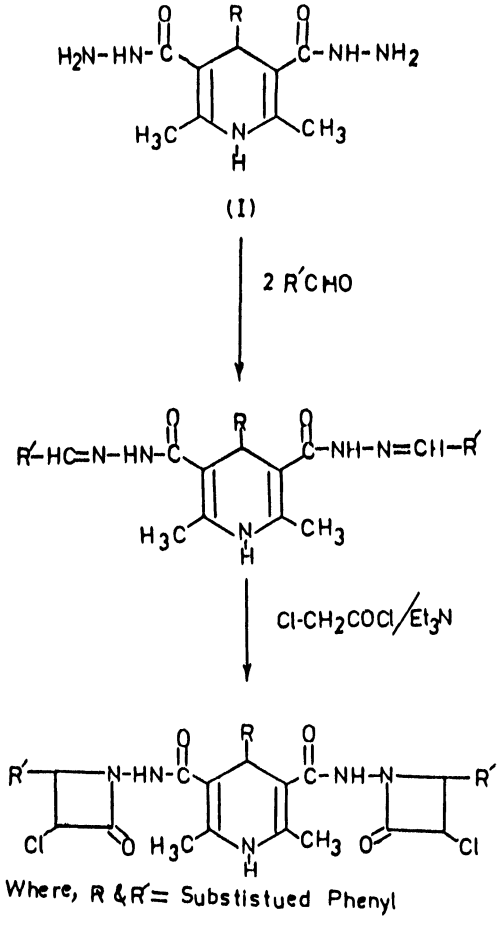

SCHEME-I

PMR δ 2.23 (S, 6H, —CH_3), 3.59 (S, 2H, Ar—CH), 4.74 (S, 2H, 2 × CH—Cl), 5.75 (S, CH pyridyl); 7.1–7.5 (m, 15 aromatic proton), 8.2 (S, 2H, 2 × CO—NH) and 8.5–9.5 (S, 1H, —NH pyridyl).

Antimicrobial Activity

Compounds 1, 8, 10, 11 and 17 from Table-I were screened for their antifungal activity against *Alternaria brassicicola* and *Fusarium udam*, while for antibacterial activity against *Lactobacillus* and *E. coli* by paper disc method[5] at 250 ppm and 500 ppm concentration in dimethyl sulfoxide. Standard Zapkes medium was used. Filter paper discs of 5 mm size were used and the diameters of zones of inhibition formed around each disc after incubating for a period of 48 h at 30°C were recorded. Results were compared with reference to fungicide (carbendiazium) and bactericide (streptomycine). The compounds 10 and 17 were showing good activity when compared with standards because these two nuclei were incorporated with more percentage of chlorine atom which is known for its toxicity.

TABLE-I
CHARACTERISATION DATA OF AZITIDINONES (1–20)

Comp No.	R	R′	Yield (%)	m.p.* (°C)	Mol. Formula	% N	
						Found	(Calcd)
1	C_6H_5	C_6H_5	75	178	$C_{31}H_{29}N_5O_4Cl_2$	11.25	(11.55)
2	C_6H_5	4-Cl C_6H_4	73	169	$C_{31}H_{27}N_5O_4Cl_4$	20.60	(20.88)
3	C_6H_5	4-CH_3 C_6H_4	74	163	$C_{33}H_{33}N_5O_4Cl_2$	11.00	(11.19)
4	C_6H_5	4-OH_3 C_6H_4	76	171	$C_{33}H_{33}N_5O_6Cl_2$	10.40	(10.66)
5	2-Cl C_6H_4	C_6H_5	80	178	$C_{31}H_{28}N_5O_4Cl_3$	16.50	(16.62)
6	2-Cl C_6H_4	4-Cl C_6H_4	68	168	$C_{31}H_{26}N_5O_4Cl_5$	24.90	(25.01)
7	2-Cl C_6H_4	4-CH_3 C_6H_4	71	157	$C_{33}H_{32}N_5O_4Cl_3$	15.70	(15.93)
8	2-Cl C_6H_4	4-OCH_3 C_6H_4	78	148	$C_{33}H_{32}N_5O_6Cl_3$	15.00	(15.20)
9	4-Cl C_6H_4	C_6H_5	73	139	$C_{31}H_{28}N_5O_4Cl_3$	16.02	(16.22)
10	4-Cl C_6H_4	4-Cl C_6H_4	78	175	$C_{31}H_{26}N_5O_4Cl_5$	24.70	(25.01)
11	4-Cl C_6H_4	4-CH_3 C_6H_4	70	153	$C_{33}H_{32}N_5O_4Cl_3$	15.70	(15.93)
12	4-Cl C_6H_4	4-OCH_3 C_6H_4	76	172	$C_{33}H_{32}N_5O_6Cl_3$	14.90	(15.20)
13	4-OCH_3 C_6H_4	C_6H_5	75	158	$C_{32}H_{31}N_5O_5Cl_2$	19.82	(20.14)
14	4-OCH_3 C_6H_4	4-Cl C_6H_4	78	152	$C_{32}H_{29}N_5O_5Cl_4$	18.10	(18.34)
15	4-OCH_3 C_6H_4	4-CH_3 C_6H_4	71	162	$C_{34}H_{35}N_5O_7Cl_2$	11.70	(11.91)
16	4-OCH_3 C_6H_4	4-OCH_3 C_6H_4	73	165	$C_{34}H_{35}N_5O_7Cl_2$	11.10	(11.30)
17	3-Cl C_6H_4	C_6H_5	76	162	$C_{31}H_{28}N_5O_4Cl_3$	16.25	(16.62)
18	3-Cl C_6H_4	4-Cl C_6H_4	78	170	$C_{31}H_{26}N_5O_4Cl_5$	24.55	(25.01)
19	3-Cl C_6H_4	4-CH_3 C_6H_4	72	179	$C_{33}H_{32}N_5O_4Cl_3$	15.72	(15.93)
20	3-Cl C_6H_4	4-OCH_3 C_6H_4	73	168	$C_{33}H_{32}N_5O_6Cl_3$	15.00	(15.20)

*All compounds were crystallised from methanol.

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