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Synthesis and antimicrobial activity of 5-{4'-[(6"-aryl)-2"-amino-3",4"-dihydro pyrimidine-4"-yl]phenyl carbamido}-dibenz[b,f]azepines

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ABSTRACT

5-{4'-[(6"-aryl)-2"-amino-3",4"-dihydro pyrimidine-4"-yl] phenyl carbamido}-dibenz [b,f] azepins. **(4a-4n)** have been synthesized. The product have been assayed for their antimicrobial activity against Gram+ve bacteria and Gram-ve bacteria and fungi. The product have been characterised by IR, ^{1}HNMR, Mass spectra and TLC.

INTRODUCTION

Dibenz [b,f] azepines derivatives are known as a antitumor[1], carcinostatic[2], antiinflammatory[3], antimalarial[4], antimicrobial[5] activity etc. 5-{4'-[(6"-aryl)-2"-amino-3",4"-dihydro pyrimidine-4"-yl] phenyl carbamido}-dibenz [b,f] azepins. **(4a-4n)** have been synthesized by chemoselective cyclisation of 5-{4'-[(3"-aryl)-2"-propene-1"-one]-phenyl carbamido}-dibenz [b,f] azepines with guanidine hydrochloride and alcoholic KOH.

The products **(4a-4n)** were assigned by IR, ^{1}HNMR, mass spectral data, TLC and elemental analyses the physical data and antimicrobial activity represented in TABLE 1 and comparable anti antimicrobial activity represented in TABLE 2.

Antimicrobial activity

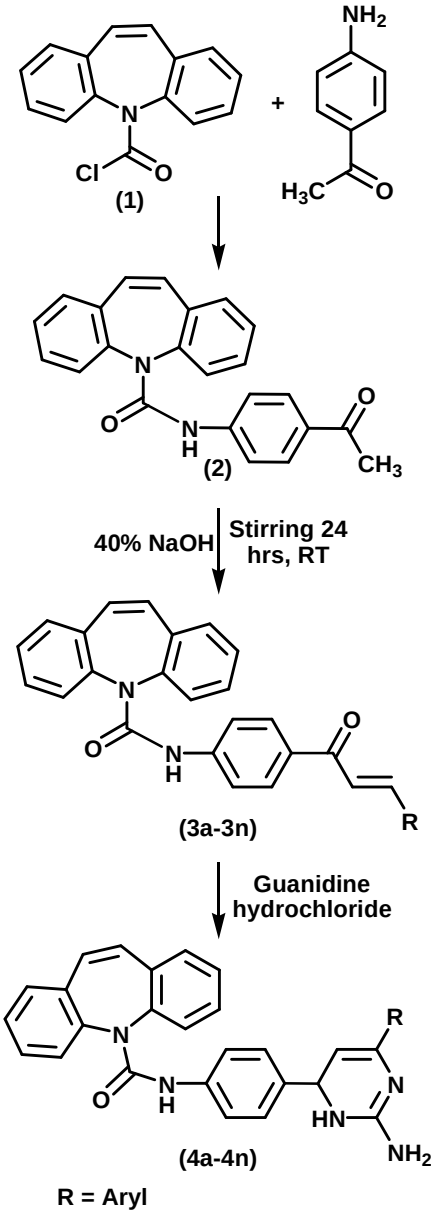
The antimicrobial activity was determined by cup plate method[6] at a concentration of 50 mg/ml using DMF as a solvent. The activity was taken by Gram positive bacteria *B.megaterium, B.aureus,* Gram negative bacteria *S. staphimarium, E.coli* and antifungal activity against *A.niger.* The zone of inhibition were measured in mm. The activity was compared with the known antibiotics, viz, ampicillin, chloramphenicol, norfloxacin, gresiofulvin at same concentration 50mg/ml. Which is represented in TABLE 1.

Comparable antimicrobial activity represented in TABLE 2.

Dibenz [b,f] azepines 5-carbonyl chloride **(1)**; 5-(4'-acetyl phenyl carbamido)-dibenz [b,f] azepines **(2)** and 5-{4'-[(3"-aryl)-2"-propene-1"-one]-phenyl carbamido}- dibenz [b,f] azepines **(3a-3n)** have been synthesised and their physical data and antimicrobial activities are published in another journal for our continuous publication.

EXPERIMENTAL

All the melting points were measured by open glass capillary method and are uncorrected. IR absorption spectra (in cm^{-1}) were recorded on a shimadzu IR-435 spectrophotometer using KBr pellet method, ^{1}H NMR



Scheme 1

spectra on Hitachi R-1200 (300-mHz) spectrometer using DMSO-d6 method, as internal standard (chemical shift in,dppm) and mass spectra on a Joel 300 ev. The purity of the compounds were routinely checked by TLC using silica gel-G.

5-(4'-acetyl phenyl carbamido)-dibenz [b,f] azepine (2)

A mixture of 5-dibenz [b,f] azepine methanoyl chloride (2.55g, 0.01M), 4-amino acetophenone (1.35g, 0.01M) in ethanol (25ml) and pyridine (5.0ml) was refluxed on a oil bath at 120°C for 12hrs. The products was cooled; poured into crushed ice, filtered, dried and crystallized from ethanol; yield 85.42%, M.P 170°C (Found; C, 77.85; H, 5.02; N, 7.82, $C_{23}H_{18}N_2O_2$ required C, 77.96; H, 5.08; N, 7.90%) IR (KBr): 2958 (C-H str. asym); 2829 (C-H str. sym,); 1467, (C-H def. asym); 1388 (C-H def. sym); 3065 (C-H str. aromatic); 801 (C-H; str. o.p.p def.); 1488 (C=C str.); 1350 (C-N str.); 1691 (>C=O str.) ^{1}H NMR; 2.5 (S, 3H, -$COCH_3$); (6-7.2) (m, 14H, Ar-H).

5-{4'-[3"-(4"'-methoxy phenyl)-2"-propene-1"-one]-phenyl carbamido}-dibenz [b,f] azepine; (3g)

A mixture of 5-(4'-acetyl phenyl carbamido) dibenz [b,f] azepine (3.54g, 0.01M) and 4-methoxy benazaldehyde (1.36g, 0.01M) in methanol 25 ml and 40% NaOH solution was stirring vigorously at 24hrs. The contents were poured into crushed ice, acidified, filtered, dried, and crystallized from ethanol. yield; 79.86%, M.P, 105^{o}C (Found; C, 75.80; H, 5.01; N,5.80; $C_{31}H_{24}N_2O_3$ required C, 75.86; H, 5.08 N, 5.93%) IR (KBr): 2952 (C-H str. asym): 2815 (C-H str. sym.) 1462 (C-H def. asym): 1380 (C-H def. Sym.): 3051 (C-H str. aromatic): 805 (C-H o.p.p def.): 1480 (C=C str.): 1351(C-N str.): 1592 (>C=O str.); 1501 (C=C str.); 1151 (C-O-C str) ^{1}H NMR: 3.8 (S, 3H,-OCH_3); 6.2-7.4 (m.18H, Ar-H). m/z: 472, 457, 448, 441, 372, 363, 35, 310, 287, 252, 238, 219, 209, 204, 196, 180, 161, 109, 102.

Similarly others compounds **(3a-3n)** were synthesised. The data were published in our contineous publication.

5-{4'-[6"-(4"'-methoxy phenyl)-2"-amino 3"-4"-dihydro pyrimidine-4"-yl]phenyl carbamido}-dibenz [b,f] azepine (4g)

A mixture of 5-{4'-[3"-(4"'-methoxy phenyl)-2"-propene-1"-one] phenyl carbamido}-dibenz [b,f]-azepine. (4.72g, 0.01M) and guanidine hydrochloride (0.95g, 0.01M) was refluxed at 110°C for 12 hrs. in presence of alcoholic KOH in methanol. The reaction mixture was poured into crushed ice, filtered and dried. The product was isolated, crystallised from dioxane: yield :69.71 % M.P. 89°C (Found: C:74.62; H: 5.40; N:13.44; $C_{32}H_{27}N_5O_2$ Required: C:74.70; H:5.44; N: 13.61 %) IR (KBr): 2958 (C-H str. asym): 2953 (C-H str.asym): 1440 (C-H def. bending); 3047 (C-H str

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TABLE 1 : The physical data and antimicrobial activities of compounds (4a-4n). Zone of inhibition in m.m.

Comp[d]	R	Mole. For.	m.p. °C	Antibacterial activity				Antifungaractivities	%of Nitogen	
				B.megaterium	*S. aureus*	*S.taphimarium*	*E. coli*	*A. niger*	Calcd.	Found
4a	C_6H_5 -	$C_{31}H_{25}N_5O$	120	19	19	21	20	18	14.49	14.23
4b	2-OHC_6H_4 -	$C_{31}H_{25}N_5O_2$	135	23	17	19	25	18	14.02	13.93
4c	3-OHC_6H_4 -	$C_{31}H_{25}N_5O_2$	115	13	13	18	23	18	14.02	13.98
4d	4-OHC_6H_4 -	$C_{31}H_{25}N_5O_2$	97	21	19	19	13	11	14.02	13.93
4e	3 - OCH_3, 4-OHC_6H_3 -	$C_{32}H_{27}N_5O_3$	95	25	20	21	11	21	13.23	13.11
4f	2-OCH_3, C_6H_4 -	$C_{32}H_{27}N_5O_2$	98	20	17	19	14	18	13.61	13.50
4g	4-OCH_3, C_6H_4 -	$C_{32}H_{27}N_5O_2$	89	25	20	19	12	21	13.61	13.44
4h	2-NO_2 C_6H_4 -	$C_{31}H_{24}N_6O_3$	145	21	23	19	11	19	15.90	15.85
4i	3-NO_2 C_6H_4 -	$C_{31}H_{24}N_6O_3$	198	19	17	23	12	12	15.90	15.70
4j	2-Cl C_6H_4 -	$C_{31}H_{24}N_5OCl$	160	18	23	13	13	17	13.53	13.40
4k	4 - N, $N(CH_3)_2$ C_6H_4 -	$C_{33}H_{30}N_6O$	200	18	13	21	14	20	15.96	15.88
4l	C_4H_3O (Furfuryl) -	$C_{29}H_{23}N_5O_2$	85	19	21	25	10	17	14.79	14.60
4m	$C_{10}H_7$ (Napthyl) -	$C_{35}H_{27}N_5O$	240	21	23	20	14	19	13.13	13.10
4n	$C_{14}H_9$ (Authryl) -	$C_{39}H_{29}N_5O$	170	19	25	25	21	18	12.00	11.96

TABLE 2 : Compounds showing compareble antimicrobial activity with known standard drugs

Compound	*B.mega*	*S.aureus*	*S. taph.*	*E.coli*	*A. niger*
(4a-4n)	4c,4e,4g	4h,4j,4m,4n	4i,4j,4n	4b,4c,4n	4e,4g

TABLE 3 : Activity of standared drugs

No.	Drugs	*B. megaterium*	*S. aureus*	*S. taphimarium*	*E. coli*	*A. nige*
1	Ampicillion 50µg/ml	22	18	19	27	--
2	Chloramphenicol "	24	19	25	26	--
3	Norfloxacin "	24	19	25	26	--
4	Griseofulvion "	--	--	--	--	23

aromatic): 800 (C-H str. o.o p def.): 1523 (C=C str.) 1332 (C-N str.), 3583 (N-H str.): 1714 (>C=0)str.): 1180 (C-O-C str.), ^{1}H NMR 3.79(S, 3H, -OCH_3) 7.1-7.5 (m, 16H, Ar-H): m/z; 535, 520, 511, 505, 481, 435, 428, 405, 344, 311, 105, 108.

similarly others compounds **(4a-4n)** were synthesed and their physical data are represented in TABLE 1.

CONCLUSION

5-{4'-[6"-(4'"-aryl)-2"-amino 3",4"-dihydro pyrimidine -4"-yl] phenyl carbamido}-dibenz [b,f] azepine **(4a-4n)** have been synthesised. Compounds **(4c)**, **(4e)**, **(4g)**, **(4j)**, **(4n)** shows good remarkable antimicrobial activity compare with known standard drugs.

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