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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 5-{4'-[(6"-ARYL)-2"-AMINO-3"-CYANO PYRIDINE-4"-YL] PHENYL CARBAMIDO}-DIBENZ [b,f] AZEPINES

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ABSTRACT

The titled compounds **(4a-4k)** have been synthesized by the condensation of 5-{4'-[(3"-aryl)-2"-propene-1"-one]-phenyl carbamido}-dibenz [b,f] azepines with malononitrile and ammonium acetate. The biological activities of these compounds have been determined against various Gram +ve, Gram –ve bacteria and fungi. The constitutions of the products are supported by IR, ^{1}H NMR, Mass spectra and elemental analysis.

Key words: Cyanopyridine derivaties, Antimicrobial, Azepines.

INTRODUCTION

Cyanopyridine derivative possess broad spectrum of pharmacological activities, which are reflected by their use as antihypertensive[1], antiepilective[2], anticovasant[3], antiinflemmatory[4], herbicidal[5], fungicide[6], etc. In view of getting potent therapeutic agents, titles compounds were synthesized.

5-{4'-[(6"-Aryl)-2"-amino-3"-cyno pyridine-4"-yl]-phenyl carbamido}-dibenz [b,f] azepines **(4a-4k)** have been synthesized by the condensation of 5-{4'-[(3"-aryl)-2"-propene-1"-one]-phenyl carbamido}-dibenz [b,f] azepines with malononitrile and ammonium acetate.

5-{4'-[(3"-Aryl)-2"-propene-1"-one]-phenyl carbamido}-dibenz [b,f] azepines **(3a-3k)** have been synthesized by the reaction of 5-(4'-acetyl phenyl carbamido)-dibenz [b,f] azepines with aromatic aldehyde in the present of aq. NaOH solution.

5-(4'-Acetyl phenyl carbamido)-dibenz [b,f] azepines **(2)** have been synthesized by the condensation of 5-dibenze[b,f] azepines methanonyl chloride **(1)** with 4-amino acetophenone in ethano and pyridine.

EXPERIMENTAL

Materials and methods

Antimicrobial activity

Cyano pyridine (**4a-4k)** were evaluated *in vitro* for antimicrobial activity against *B. Mega, S. aureus,*

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S. taphimarium, E. Coli and for antifungal activities against *A. niger* using DMF as solvent at 50 µg concentration by cup-plate method[7]. After 24 hrs of incubation at 37°C temp., the zone or inhibition were measured in mm. The activity was compared with the known antibiotics viz. Ampicillin chloramphenicol, Norfloaxacin, Greseofulvin at same concentration, which is represented in Table 1 and comparable anti microbial activity has been represented in Table 2.

All the melting points were taken in open glass capillaries and are uncorrected. IR absorption spectra were recorded on a Shimadza-FT-IR 8400 spectrophotometer using KBr pellet and ^{1}H NMR specra on a Bruker DPX-200 spectrometer (300 MHz) using DMSO as solvent and TMS as internal standard. Purity of the compounds was routinely checked by TLC using silica get G.

Experimental and spectral section

(A) 5-(4'–Acetyl phenyl carbamido)–dibenz [b,f] azepines (2)

A mixture of 5-dibenz [b,f] azepines methanoyl chloride (2.55 g, 0.01 m), 4-aminoacetophenone (1.35 g, 0.01 m) in ethanol (25 mL) and pyridine (5.0 mL) was refluxed on an oil bath at 120°C for 12 hrs. The content was poured into crushed ice, filltered and washed with water. The isolated product was crystallized from ethanol yield: 85.42%, MP. 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%).

(B) 5-{4'-[3"-(4"'-Methoxy phenyl)-2"-Propene-1"-one]-Phenyl carbamido}-dibenz [b,f] azepines (3g)

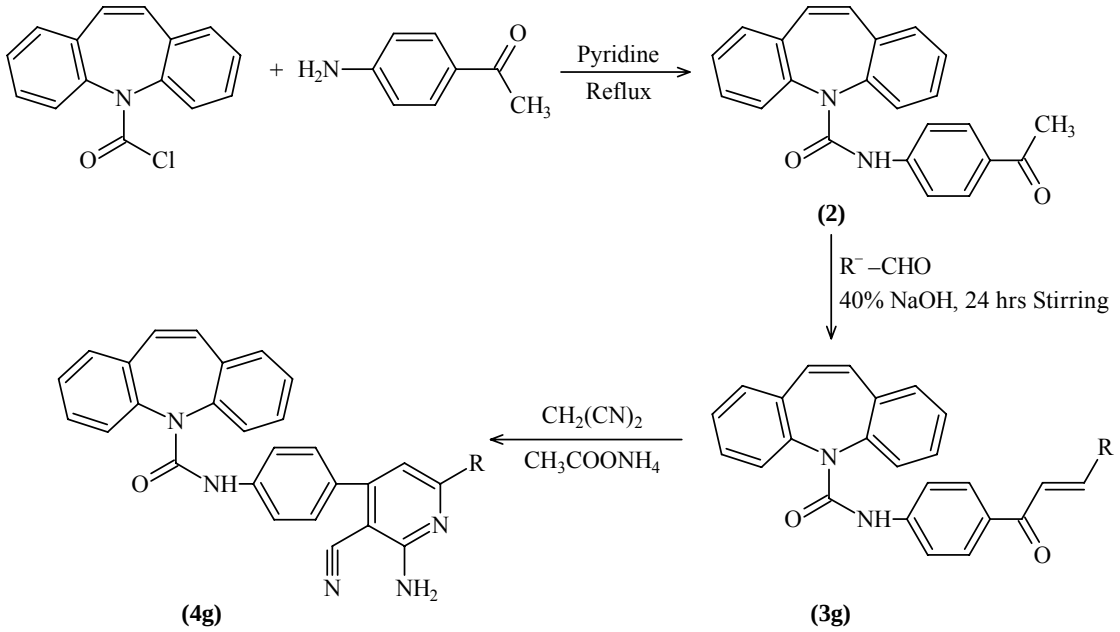
A mixture of 5-(4'-acetyl phenyl carbamido)-dibenz [b,f] azepines (3.54 g, 0.01 m), 4-methoxy benzaldehyde (1.36 g, 0.01 m), methanol (25 mL) and 40% aq. NaOH solution till becomes basic medium. The reaction mixture was stirred 24 hrs at room temp. The contents were poured into crushed ice, acidified, filltered and crystalized from dioxane. Yield 79.86%, M. P.: 105°C. (Found C, 75.80, H, 5.01, N, 5.80, $C_{31}H_{24}O_3N_2$ required C, 75.86, H, 5.08, N, 5.93%) IR: 2958 (C–H str. asym.), 2870 (C–H Str. Sym), 1420 (C–H def.), 3056 (C–H str. aromatic), 801 (C-H;str.o.p.p def.) 1509 (C=C str.), 1118 (C–N str.), 1620 (N–H bend), 1700 (C=O str.) ^{1}H NMR: 3.65 (s, 3H Ar–OCH_{3a}); 6.33 (s, 1H, $CONH_{2b}$), 6.96 (s, 2H, $CH{=}CH_c$), 16 H (m, Ar-H_d), 6.97 (d, 2H). Mass: (m/z), 103, 180, 196, 252, 238, 287, 441, 457.

Similarly other chalcones **(3a-3k)** were prepared and their physical data and antimicrobial activities have been evaluated.

(C) 5-{4'-[6"-(4"'-Methoxy phenyl)-2"-amino-3"-cyno pyridine-4"-yl]-phenyl carbamido}-dibenz [b,f] azepines (4g)

A mixture of 5-{4'-[3"-(4"'-methoxy phenyl)-2"-propene-1"-one]-phenyl carbamido}-dibenz [b,f] azepines **(3 g)** (4.72 g, 0.01 M); malononitrile (0.66 g; 0.01 M) and ammonium acetate (0.77 g; 0.01 M) the reaction mixture was refluxed of 10 hrs at 120°C. The reaction mixture was poured into crushed ice, filtered, dried and crystallized from dioxane, Yield: 66.75%; M.P. 85°C. (Found : C : 76.16; H : 4.61; N : 12.98, $C_{34}H_{25}O_2N_5$ required C : 76.26; H : 4.67; N : 13.08%). IR (KBr): 2985 (C–H str. asym), 2853 (C–H str. sym.) 1440 (C–H def. asym), 1322 (C–H def. sym.), 3047 (C–H str. aromatic) 1101 (C–H i. p. def.), 800 (C–H o.o.p. def.), 1450 (C=C str), 1332 (C–N str.), 1581 (C=N str.), 3413 (N–H str.), 1550 (N–H ben.), 1215 (C–O–C str. asym.), 1047 (C–O–C str. sym.), 2220 (C≡N str.), 1676 (C–N str.), 1714 (C=O str), 1298 (C–N ben.). NMR: 3.90 (s, 3H, Ar–OCH_{3a}), 6.9-7.3 (m, 16H, Ar-H_d), 3.44 (s, 3H, Ar–OCH_{3c}),6.3 (s, 1H, N-H_b),

6.8 (d, 2H, -Ar-H_e), 6.1 (s, 1H, Ar–N_f). Mass: (m/z) 108, 105, 311, 344, 405, 428, 435, 481, 505, 511, 520, 535. Similarly, other compounds **(4a-4k)** have been synthesized and their physical data are represented in Table 1.



Scheme 1

RESULTS AND DISCUSSION

The physical data and antimicrobial activity of compounds **(4a-4k)** have been reported in Table 1.

Table 1

Compd.	R	Mol. formula	M.P. (°C)	Yield (%)	N (%)		Antibacterial activity				Antifungal activity
					Calc.	Found	*B. Mega*	*B. Subtil*	*E. Coli.*	*S. Taphimariu*	*A. nigar*
4a	C_6H_5	$C_{33}H_{23}N_5O$	114	79.70	13.86	13.40	16	17	14	19	20
4b	2-OHC_6H_4	$C_{33}H_{23}N_5O_2$	190	71.60	13.43	13.32	15	19	17	20	17
4c	3-OHC_6H_4	$C_{33}H_{23}N_5O\ O_2$	130	78.52	13.43	13.32	20	14	23	18	21
4d	4-OHC_6H_4	$C_{33}H_{23}N_5O\ O_2$	102	59.75	13.43	13.32	18	20	22	23	19
4e	4-OH, 3-$OCH_3C_6H_4$	$C_{34}H_{25}N_5O_3$	110	80.12	12.70	12.57	19	12	13	20	19
4f	2-$OCH_3C_6H_4$	$C_{34}H_{25}N_5O_2$	120	81.65	13.08	13.01	19	15	18	18	16
4g	4-$OCH_3C_6H_4$	$C_{34}H_{25}N_5O_2$	85	80.23	13.08	13.02	16	14	17	17	14
4h	2-$NO_2C_6H_4$	$C_{33}H_{22}N_6O_3$	105	83.56	15.27	15.13	23	17	15	19	21
4i	3-$NO_2C_6H_4$	$C_{33}H_{22}N_6O_3$	130	65.70	15.27	15.13	24	21	14	21	16
4j	4-N,N$(CH_3)_2C_6H_4$	$C_{35}H_{28}N_6O$	85	72.72	15.32	15.23	15	15	19	18	17
4k	C_4H_3O (Furfuryl)	$C_{31}H_{21}N_5O_2$	90	85.11	14.14	14.10	13	17	18	17	22

Zone of inhibition in mm

Table 2: Comparable antimicrobial acivity

Compd.	*B. Mega*	*B. Subtillis*	*E. Coil*	*S. Taphimarium*	*A. nigar*
4a-4k	**4c, 4h, 4i**	**4b, 4d, 4i**	**4c, 4d, 4j**	**4b, 4d, 4i**	**4c, 4h, 4k**
Ampicillin (50 µg)	23	18	17	27	-
Chloramphenicol (50 µg)	24	19	25	26	-
Norfloxacin (50 µg)	24	19	25	26	-
Greseofulvin (50 µg)	-	-	-	-	23

CONCLUSION

The compounds **(4b)**, **(4c)**, **(4d)** and **(4i)**, showed moderate antimicrobial activity than other synthesized compounds, compared with known standard drugs.

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