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Chemistry

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.

KEYWORDS : Cyano pyridine derivaties,Antimicrobial , Azepines.

INTRODUCTION :

Cyano pyridine derivative possess broad spectrum of pharmacological activities which are reflected by their use as antihypertensive[1], antiepilective[2],anti-microbial[3]. Cardiotonic[4],anti-inflammatory [5], anticancer[6], etc. In view of getting potent therapeutic agents to synthesized titles compounds.

5-{4'-[(6"-aryl)- 2"-amino-3"-cyano - 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 ethanol and pyridine.

MATERIALS AND METHODS

Antimicrobial activity :

Cyano pyridine (**4a -4k)** were evaluated in vitro for antimicrobial activity against *B. Mega,S.aureus,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 ^{0}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-I and comparable anti microbial activity represented in Table no. II

Method Section :

All the melting points were taken in open glass capillaries and are uncorrected. IR absorption spectra were recorded on a Shimadza-FT-IR 8400 spectro-photometer using KBr pellet and ^{1}H NMR spectra on a Bruker DPX-200 spectrometer (300 MHz) using DMSO as solvent and TMS as internal standard. Purity of the compounds were 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 gm, 0.01 m), 4-amino acetophenone (1.35 gm, 0.01 m) in ethanol (25 ml) and pyridine (5.0 ml) was refluxed on a oil bath at 120^{0}C for 12 hrs. The content was poured into crushed ice, filtered and washed with water. The isolated product was crystallized from ethanol yield : 85.42%, MP. 170 ^{0}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 : 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 : 2.5 (s, 3H Ar–$COCH_3$); 6.50–6.63 (m, 4H, Ar–H), 9.95 (s, 1H, N–H). Mass : (m/z), 103, 180, 196, 252, 238, 287, 441, 457.

(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 gm, 0.01 m), 4–methoxy benzaldehyde (1.36 gm, 0.01 m), methanol (25 ml). and 40% aq. NaOH solution till becomes basic medium. The reaction mixture was stirring 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 (KBr): 2923 (C–H str. asym.), 2852 (C–H str. sym), 1436 (C–H str. asym), 1371 (C–H str. sym) 3097 (C–H str. aromatic) 1276 (C–H i.p. def.), 821 (C–H, o.o.p. def.), 1677 (C=O str.), 1118 (C–N Str.), 3311 (N–H str.) 3045 (C=C str.), 1245 (C–O–C Str.), ^{1}H NMR : 3.62–3.86 (s, 3H, Ar-OCH_3), 7.01–7.03 (m. 18H, Ar–H), 8.08–8.72 (D. D. 4H, Ar– Hc), 4.79–4.80 (t, 4H, CH_2–Cl), 2.50–2.51 (t, 4H, -NCH_2), 9.95 (s, 1H, –NHf), 4.80–4.83 (s, 2H, CH=CH) Mass : (m/z) 102, 109, 161, 219, 238, 252, 287, 310, 363, 372, 441, 448, 457, 472.

Similarly other chalcones (**3a -3k)** where prepared and their physical data and antimicrobial activities data published in other journal.

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

A mixture of 5-{4'-[3"-(4"'-methoxy phenyl)-2"-Propene-1"-one]-Phenyl carbamido}-dibenz [b,f] azepines**(3g)** (4.72 g, 0.01 M); malononitrile (0.66 gm; 0.01 M) and ammonium acetate(0.77g;0.01 M) the reaction mixture was refluxed for 10 hrs. at 120º C. temp. The reaction mixture poured into crushed ice, filtered, dried and crystallized from dioxane, Yield : 66.75 % ; M.P. 85º 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 (CN 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_b), 3.44 (s, 3H, Ar–OCH_{3c}),6.3 (s, 1H, N-H_d), 6.8 (d, 2H, -Ar-H_c), 6.1 (s, 1H, Ar–N_f), Mass : (m/z) 108,105, 311, 344,405, 428, 435,481,505, 511, 526, 520, 535.

RESULTS AND DISCUSSION :

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

Table-I

Compd	R	Mol. Formula	M.P. ^{0}C	Yield (%)	N(%)		Antibacterial activity				Antifungal Activity
					Calc.	(Found)	*B. Mega*	*S. Subtil*	*E. Coli.*	S.taphimari	*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-OH C_6H_4	$C_{33}H_{23}N_5O_2$	190	71.60	13.43	13.32	15	19	17	20	17
4c	3-OH C_6H_4	$C_{33}H_{23}N_5O_2$	130	78.52	13.43	13.32	20	14	23	18	21
4d	4-OH C_6H_4	$C_{33}H_{23}N_5O_2$	102	59.75	13.43	13.32	18	20	22	23	19

4e	4-OH, 3-OCH_3 C_6H_4	$C_{34}H_{25}N_5O_3$	110	80.12	12.70	12.57	19	12	13	20	19
4f	2-OCH_3 C_6H_4	$C_{34}H_{25}N_5O_2$	120	81.65	13.08	13.01	19	15	18	18	16
4g	4-OCH_3 C_6H_4	$C_{34}H_{25}N_5O_2$	85	80.23	13.08	13.01	16	14	17	17	14
4h	2-NO_2 C_6H_4	$C_{33}H_{22}N_6O_3$	105	83.56	15.27	15.13	23	17	15	19	21
4i	3-NO_2 C_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 $(CH_3)_2$ C_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

Similarly other (4a – 4k) have been synthesized and their physical data represented in Table no. I.

Reaction scheme

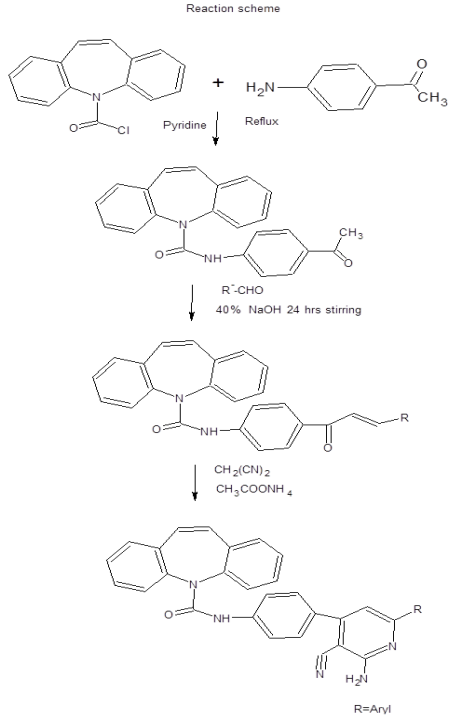

Table-II Comparable antimicrobial acivity.

	Compd	*B. Mega*	*B.aur es*	*E. Coil*	S.taphi marium	*A.niger*
	4a-4k	4c,4h, 4i	4b, 4d, 4i	4c, 4d, 4j	4b, 4d, 4e,4i	4c, 4h, 4k
1	Ampicillin (50 µg)	30	29	32	30	-
2	Chloramphenicol (50 µg)	30	32	28	29	-
3	Norfloxacin (50 µg)	35	31	30	27	-
4	Greseofulvin (50 µg)	-	-	-	-	27

CONCLUSION :

The compounds 4b,4c, 4d, 4i showed good antimicrobial activity then other synthesized compounds compare with known standard drugs.

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