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Synthesis and Antimicrobial Activity of 5-{4'-[(4"-aryl)- -3"-cyano 2"-ethoxy pyridine-6"-yl] phenyl carbamido}-dibenz [b,f] azepines derivatives

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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 Sodium ethoxide. 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.

1. Introduction

Cyano pyridine derivative possess broad spectrum of pharmacological activities which are reflected by their use as antidepressant[1], antipychotics[2], anticancer[3,4], herbicidal[5], antiinflemmatory[6], Fungicide[7], antileishmanial[8], etc. In view of getting potent therapeutic agents to synthesized titles compounds 5-{4'-[(4"-aryl)- 3"-cyno-2"-ethoxy- pyridine-6"-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 sodium ethoxide. 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.

2. Materials and Method

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 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.

2.1 Reaction Schemes

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

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 for 12 hrs °C. The content was poured into crushed ice, filltered and washed with water. The isolated product was crystallized from ethanol.

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

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.

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

A mixture of 5-{4'-[3"-(4"'-methoxy phenyl)-2"-Propene-1"-one]-Phenyl carbamido}-dibenz [b,f] azepines**(3g) (** (4.72 gm, 0.01 M); malononitrile (0.66 gm; 0.01 M) and sodium ethoxide as solvent was refluxed for 10 hrs. at 100° C. temp. The reaction mixture poured into crushed ice, filtered, dried and crystallized from dioxane.

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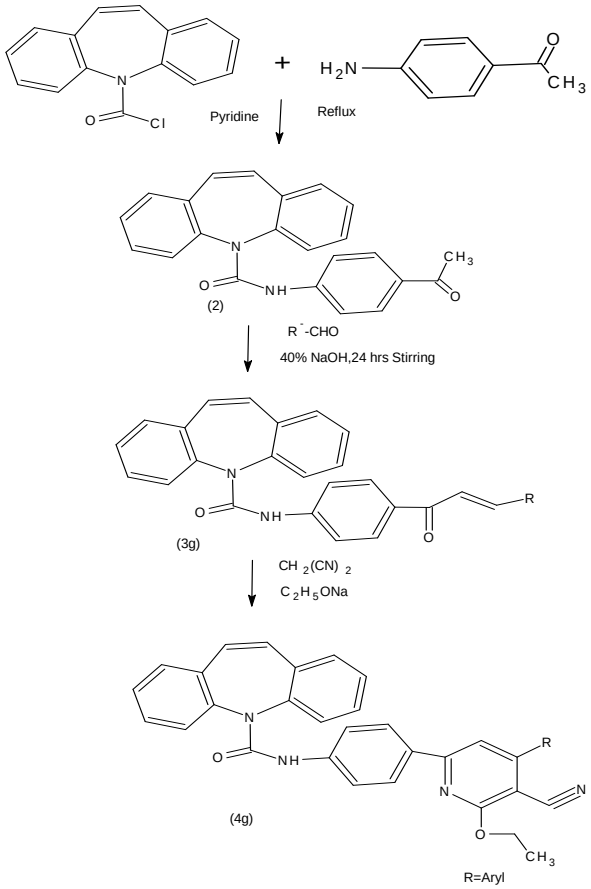

3. Results and Discussion

3.1 Structural determination and characterization of synthesized compounds

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

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%). **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

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.

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

Yield : 81.10 % ; M.P. 82° C. (Found : C : 76.52; H : 4.80; N : 9.80, $C_{36}H_{28}O_3N_4$ required C : 76.59; H : 4.96; N : 9.92 %). **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.), 1210 (C–O– C str. asym.), 1047 (C–O– C str. sym.), 2220 (C≡N str.), 1676 (C–N str.),1724 (C=O str),1298 (C–N ben.).**^{1}H NMR** : 3.71-3.86 (s, 3H, Ar–OCH_{3a}), 6.3 (s, 1H, N-H_b),3.44(t,3H,Ar-OCH_{3c}),6.9-7.3 (m, 16H, Ar-H_d), 6.8 (d, 2H, Ar–H_c), , 6.4 (s, 1H, -Ar-H_f), 6.1 (s, 1H, Ar–N_g), 3.31(q,2H,-OCH_{2h}) **Mass** : (m/z) 105, 211, 220, 458, 465, 464, 510, 534, 540, 564. Similarly other (4a – 4k) have been synthesized and their physical data represented in Table No. 1.

3.2 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 °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 antimicrobial activity represented in Table No. 2.

Table No. 1: The physical data and antimicrobial activity of compounds (**4a -4k)**

Compound R		Molecular Formula	M.P. (°C)	Yield (%)	N (%)		Antibacterial activity				Antifungal Activity
					Calc.	(Found)	*B. Mega*	*S. Auaras*	*S.taphimariu*	*E. Coli*	*A. nigar*
4a	C_6H_5	$C_{35}H_{26}N_4O_2$	180	70.20	10.48	10.40	19	20	15	11	15
4b	2-OH C_6H_4	$C_{35}H_{26}N_4O_3$	207	67.71	10.18	10.09	18	17	16	18	17
4c	3-OH C_6H_4	$C_{35}H_{26}N_4O_3$	98	71.80	10.18	10.08	16	16	18	12	21
4d	4-OH C_6H_4	$C_{35}H_{26}N_4O_3$	120	62.82	10.18	10.10	14	14	15	10	22
4e	4-OH,3-$OCH_3C_6H_4$	$C_{36}H_{28}N_4O_4$	79	74.10	9.65	9.60	12	12	13	11	19
4f	2-OCH_3 C_6H_4	$C_{36}H_{28}N_4O_3$	80	82.11	9.92	9.82	20	10	26	13	16
4g	4-OCH_3 C_6H_4	$C_{36}H_{28}N_4O_3$	82	81.10	9.92	9.80	11	11	11	11	14
4h	2-NO_2 C_6H_4	$C_{35}H_{25}N_5O_4$	180	59.60	12.08	11.26	13	17	14	12	21
4i	3-NO_2 C_6H_4	$C_{35}H_{25}N_5O_4$	115	65.64	12.08	11.27	16	16	15	10	16
4j	4-N,N$(CH_3)_2$ C_6H_4	$C_{37}H_{31}N_5O_2$	82	71.11	12.13	12.04	21	16	18	18	17
4k	C_4H_3O (Furfuryl)	$C_{33}H_{24}N_4O_3$	58	58.10	10.68	10.48	10	20	13	17	16

* Zone of inhibition in mm.

Table No. 2: Comparable antimicrobial activity

S. No.	Compound	*B. Mega*	*B. aureus*	S.taphimarium	*E. Coil*	*A. nigar*
	4a-4k	4c, 4f, 4j	4a, 4b, 4k	4c, 4f, 4j	4b, 4j, 4k	4c, 4d, 4h
1.	Ampicillin (50 µg)	30	29	30	32	-
2.	Chloramphenicol (50 µg)	30	32	29	28	-
3.	Norfloxacin (50 µg)	35	31	27	30	-
4.	Greseofulvin (50 µg)	-	-	-	-	27

Conclusion

The compounds 4a,4b, 4c, 4f, 4j,4k showed moderate antimicrobial activity then other synthesized compounds, compare with known standard drugs.

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