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Synthesis and biological screening of 1-(H)-3-N-{4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines and 2-amino-6-{4'-[(4'''-chloro phenyl) (phenyl) methyl amino] phenyl}-4 -aryl- 4H – pyran– 3- carbonitriles

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ABSTRACT

1-(H) 3-N-{4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (5a-5l) and 2-amino-6-{4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl}-4-aryl-4H–pyran–3-carbonitriles (6a-6l) have been synthesized. The products have been assayed for their biological activity against Gram +ve, Gram -ve bacteria and fungi. Some of the compounds showed moderate activity in concentration 50 µg/ml.

KEYWORDS

Pyrazolines;
Cyanopyranes.

INTRODUCTION

Pyrazolines and Cyanopyranes derivatives shows wide range of biological activities like analgesic[1], bactericidal[2,3], fungicidal[4,5], antiamoebic, antimicrobial[6], hypolipidemic[7] antipyretic[8] antiinvasive[9,10] etc. In view of getting we have synthesized Pyrazolines and Cyanopyranes derivatives. The product of Pyrazolines (5a-5l) and Cyanopyranes (6a-6l) have been synthesized and assigned the IR, ^{1}HNMR, Mass spectral data, and elemental analysis. The physical data and antimicrobial actitivities are represents in TABLE 1.

ANTIMICROBIAL ACTIVITY

1-(H)-3-N-{4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (5a-5l) and 2-amino-6-{4'-[(4'''-chlorophenyl)(phenyl) methyl amino] phenyl}-4-aryl-4H–pyran–3-carbonitriles (6a-6l) products were evaluated in vitro for their antimicrobial activities against *Bacillus Megatarium, Staphylococcus aureus, Escherichia coli, Salmonella typhy, and Aspergillus niger* using DMF as solvent at 50 µg / ml. concentration by cup plate method[11]. After 24 hrs of incubation at 37°C, the zones of inhibition were measured in mm. The activity of synthesized compounds were compared with the known antibiotic, viz, Ampicillin, Chloramphenicol, Norfloxacin, and Gresiofulvin at same concentration.

All the synthesized compounds **(5a-5l)** and **(6a-6l)** showed moderate to good and remarkable activities with known standard drugs at same concentration. The physical data and antimicrobial activities are represented in TABLE 1.

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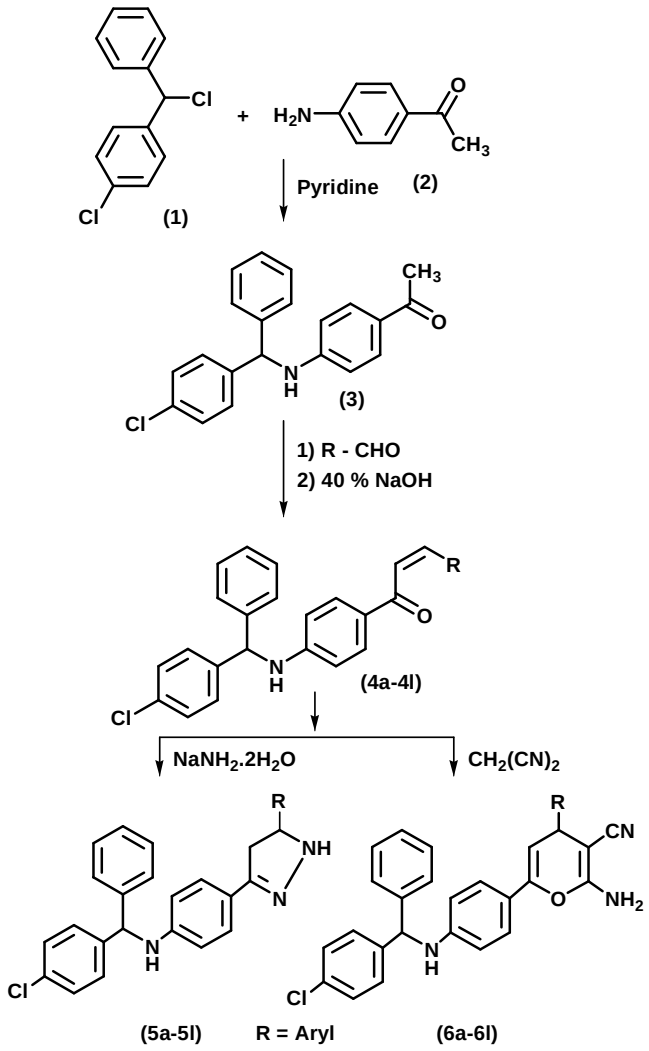

Reaction scheme

EXPERIMENTAL

All the melting points were measured in open glass capillary method and are uncorrected. I.R. absorption spectra (in cm^{-1}) were recorded on a shimadzu FT-IR 8400-spectrophotometer using KBr pallet method and ^1H NMR spectra on BRUKER spectrometer (300 MHz) using TMS as internal standard (chemical shifts in δ ppm) and compounds were routinely checked by TLC using silica gel G.

4'-[(4'''-Chlorophenyl) (phenyl)-methyl-amino] phenyl-1-yl ethanone (3)

A mixture of (4'-Chlorophenyl) (phenyl)-methyl) chloride in methanol (2.37 gm, 0.01 M), p-amino acetophenone (1.47 gm, 1.2 M) and methanol (20ml) was refluxed in the presence of basic catalyst as pyridine for 8 hrs. The completion of the reaction is checked by TLC. The reaction mixture poured in to crushed ice, filter it and wash with water and dry it. The yield is 65 %, m.p.134 °C.

4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl-3-(4''''-methoxy phenyl) prop-2-en-1-one (4h)

A mixture of 4'-[(4'''-Chlorophenyl) (phenyl)-methyl-amino] phenyl-1-yl} - ethanone (3.35 gm, 0.01 M). 4-methoxy benzaldehyde (1.36 gm, 0.01 M) and methanol (25 ml). The reaction mixture stirred at room temperature for 24 hrs. in presence of catalytic amount

TABLE 1 : The physical data and antimicrobial activity of compounds (5a-5l) and (6a-6l)

Comp.	R	Molecular Formula	M.P. °C	Antibacterial activity				Antifungal activity	% of Nitrogen	
				B.Mega	*S.aureus*	*E.Coli*	*S.typhi*	*A.niger*	Calcd.	Found.
5a	C_6H_5-	$C_{28}H_{24}ClN_3$	112	11	16	14	11	17	9.60	9.55
5b	4-Cl-C_6H_4-	$C_{28}H_{23}Cl_2N_3$	208	15	11	17	13	13	8.89	8.87
5c	4-F-C_6H_4-	$C_{28}H_{23}ClFN_3$	125	16	14	16	10	18	9.22	9.20
5d	4-Br-C_6H_4-	$C_{28}H_{23}BrClN_3$	131	18	18	18	11	12	8.13	8.11
5e	2-OH-C_6H_4-	$C_{28}H_{24}ClN_3O$	188	17	14	9	14	20	9.26	9.25
5f	3- OH-C_6H_4-	$C_{28}H_{24}ClN_3O$	174	14	16	17	12	16	9.26	9.24
5g	4-OH-C_6H_4-	$C_{28}H_{24}ClN_3O$	233	14	13	16	13	15	9.26	9.23
5h	4-OCH_3-C_6H_4-	$C_{29}H_{26}ClN_3O$	156	18	10	19	11	18	8.98	8.95
5i	3-OCH_3-4-OH-C_6H_4-	$C_{29}H_{26}ClN_3O_2$	202	17	14	8	13	14	8.68	9.66
5j	4-N-$(CH_3)_2$-C_6H_3-	$C_{30}H_{29}ClN_4$	178	19	17	17	14	21	11.65	11.63
5k	$C_{10}H_7$-(Naphthayl)	$C_{32}H_{26}ClN_3$	166	15	15	16	14	19	8.61	8.60
5l	$C_{14}H_9$-(Anthranyl)	$C_{36}H_{28}ClN_3$	136	14	16	16	12	14	7.81	7.78
6a	C_6H_5-	$C_{31}H_{24}ClN_3O$	292	11	14	11	13	17	8.58	8.55
6b	4-Cl-C_6H_4-	$C_{31}H_{23}Cl_2N_3O$	184	14	15	16	11	12	8.01	8.00

Comp.	R	Molecular Formula	M.P. °C	Antibacterial activity				Antifungal activity	% of Nitrogen	
				B.Mega	*S.aureus*	*E.Coli*	*S.typhi*	*A.niger*	Calcd.	Found.
6c	4-F-C_6H_4-	$C_{31}H_{23}ClFN_3O$	180	11	19	11	10	20	8.27	8.25
6d	4-Br-C_6H_4-	$C_{31}H_{23}BrClN_3O$	130	13	12	15	14	11	7.39	7.36
6e	2-OH-C_6H_4-	$C_{31}H_{24}ClN_3O_2$	178	17	15	13	13	12	8.30	8.29
6f	3- OH-C_6H_4-	$C_{31}H_{24}ClN_3O_2$	136	11	14	10	11	16	8.30	8.28
6g	4-OH-C_6H_4-	$C_{31}H_{24}ClN_3O_2$	144	14	10	16	11	19	8.30	8.27
6h	4-OCH_3-C_6H_4-	$C_{32}H_{26}ClN_3O_2$	192	15	13	14	12	13	8.08	8.07
6i	3-OCH_3-4-OH-C_6H_4-	$C_{32}H_{26}ClN_3O_3$	170	12	11	15	15	19	7.84	7.82
6j	4-N-$(CH_3)_2$-C_6H_3-	$C_{33}H_{29}ClN_4O$	120	11	14	10	13	17	10.51	10.50
6k	$C_{10}H_7$-(Naphthayl)	$C_{35}H_{26}ClN_3O$	146	14	15	16	11	12	7.78	7.75
6l	$C_{14}H_9$-(Anthranyl)	$C_{39}H_{28}ClN_3O$	192	11	19	17	10	20	7.12	7.10

Zones of inhibition in mm

TABLE 2 : Comparable antimicrobial activity with known standard drugs

Compounds (50 µg/ml)	*B.mega*	*S. aureus*	*E.Coli*	*S. typhi*	*A.niger*
Ampicillin	21	19	19	21	-
Chloramphanicol	24	20	25	23	-
Norfloxacin	25	20	25	24	-
Greseofulvin	-	-	-	-	25
Maximum antimicrobial activity of synthesized products					
(5a-5l)	5c, 5d, 5e, 5h, 5i, 5j	5a, 5d, 5f, 5j, 5l	5b, 5d, 5f, 5h, 5j	5b, 5e, 5g, 5i, 5j, 5k	5a, 5c, 5e, 5h, 5k, 5j
(6a-6l)	6b, 6e, 6g, 6h, 6k	6b, 6c, 6e, 6k, 6l	6b, 6g, 6d, 6k, 6l	6d, 6e, 6i, 6j	6a, 6c, 6f, 6g, 6i, 6j, 6l

of 40% NaOH. The reaction mixture was poured on to crush ice, filter it, dry it and crystallized from ethanol, Yield 52 %, m. p.102° C. ($C_{29}H_{24}ClNO_2$). Required C,76.73; H,5.33; N,3.09 found C,76.71; H,5.31; N,3.07%.

Similarly other compounds (4a-4l) have been synthesed. The physical data and antimicrobial activity published in other journal.

1-(H)-3-N-{4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl}-5-(4''''-methoxy phenyl) pyrazoline (5h)

A mixture of 4'-[(4'''-chlorophenyl) (phenyl) methyl amino] Phenyl-1'-yl-3-(4''''-methoxy phenyl) -2-propene-1-one (4.53 gm, 0.01 M), hydrazine hydrate (0.5 ml, 0.01 M) in 30 ml methanol was refluxed for 12 hrs. The reaction mixture poured into crushed ice filtered, washed with water and crystallized from dioxane. Yield: 64%, m.p.156°C. ($C_{29}H_{26}ClN_3O$; Requires: C, 74.43; H, 5.56; N, 8.98%; found: C, 74.41; H, 5.55; N, 8.95%).

IR (KBr); 2958 (C-H str. asym); 2865 (C-H str. sym); 1378 (C-H def.sym); 3039 (C-H aromatic); 1439(C=C str. aromatic); 3397 (N-H Str.), 690 (C-Cl str.). 1605 (C=N Str.), 1058 (C-N Str.), 1279 (C-O-C Str.). ^{1}HNMR (DMF); 3.83 (3H,s,Ar- OCH_3); 4.19 (1H,s,N-H);5.19-5.27 (1H,t,C-H); 6.34-6.38(2H,d,Ar-H);6.50-6.53(2H,d, Ar-H); 7.13(1H,s,N-H); 7.15-7.17 (2H,d,Ar-H):7.21-7.25(5H,m,Ar-H);7.26-7.35 (4H,d,Ar-H);7.54-7.57(2H,d,Ar-H). m/z: 43, 78, 133, 174, 205, 218, 249, 253, 268, 293, 310, 321, 336, 375, 401, 437, 467.

Similarly other Pyrazolines have been synthesized. The physical data and antimicrobial activity are represented in TABLE 1

2-Amino-6-{4'-[(4'''-chlorophenyl)(phenyl) methyl amino]phenyl}-4-(4''''-methoxy phenyl)-4H-pyran-3-carbonitrile (6h)

A mixture of 4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl-1'-yl-3-(4''''-methoxy phenyl)-2-propene-1-ones (4.53 gm, 0.01 M), malononitrile (0.66 g, 0.01 M) dissolved in pyridine (20 ml). The reaction mixture was refluxed for 12 hrs. The product was isolated and crystallized from absolute ethanol. Yield, 58%,

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m.p. 192°C. ($C_{32}H_{26}ClN_3O_2$); requires C, 73.91; H, 5.04; N, 8.08; found: C, 73.91; H, 5.02; N, 8.07 %).

IR-(KBr); 2969 (C-H str. asym); 2821 (C-H str. sym); 1378 (C-H def.sym); 3075 (C-H aromatic); 1600(C=C str. aromatic); 3375 (N-H Str.), 754 (C-Cl str.). 1600 (C=N Str.), 1058 (C-N Str.), 1101 (C-O-C Str.), 3425 (NH_2 Str.), 2221 (CN Str.). ^{1}HNMR (DMF); 3.85 (3H,s,Ar- OCH_3); 4.60 (1H,s,N-H); 5.58-5.90 (1H,d,C-H); 6.65-6.69 (4H,d,Ar-H); 6.95-7.01 (10H,m, Ar-H); 7.09-7.13 (4H,d,Ar-H); 7.24 (2H,s,Ar-NH_2): 7.35-7.37 (2H,d,Ar-H). m/z: 174, 201, 203, 204, 234, 278, 287, 289, 290, 325, 347, 361, 417, 419, 453, 506, 521.

Similarly, other compounds **(6a-6l)** have been synthesized. The physical data and antimicrobial activity are represented in TABLE 1.

SUMMARY

1-(H)-3-N-{4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (5a-5l) and 2-amino-6-{4'-[(4'''-chlorophenyl)(phenyl) methyl amino] phenyl}-4-aryl-4H–pyran–3-carbonitriles (6a-6l) have been synthesized.

Compounds containing **(5d)**, **(5h)**, **(5e)**, **(5j)**, and **(6b)**, **(6e)**, **(6g)**, **(6k)**, **(6l)** showed more comparable antimicrobial activity compare to other compounds. Antimicrobial activity compared with known standard drugs.

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