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Synthesis and antimicrobial activity of (1-acetyl/1-phenyl)-3-{4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazoline

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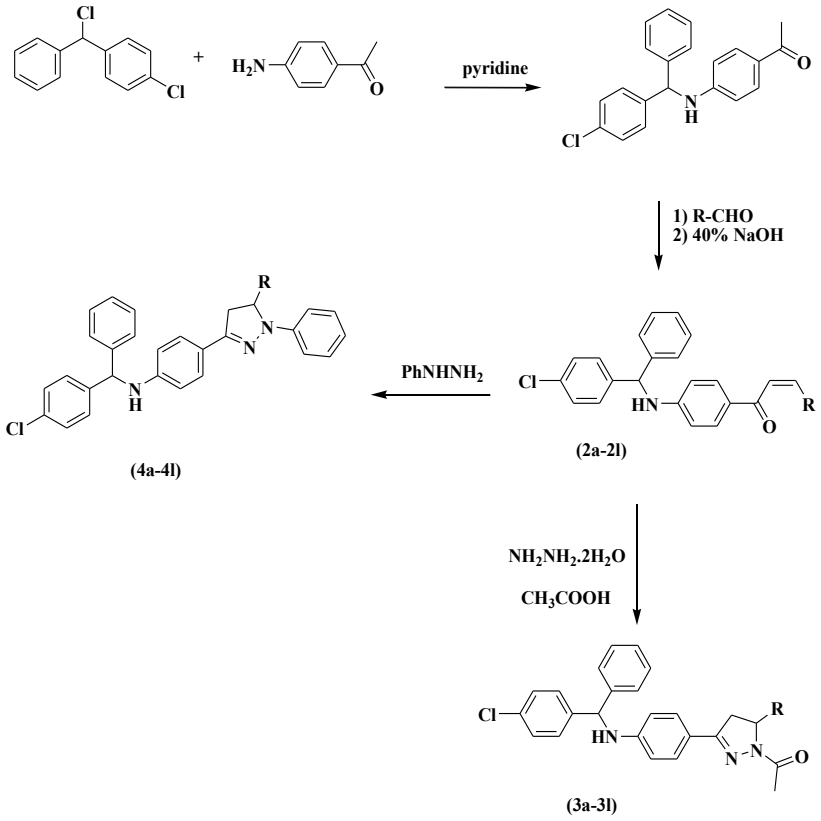
ABSTRACT

1-Acetyl-3-{4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (**3a-3l**) and 1-Phenyl-3-{4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (4a-4l) 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. The structure of the products have been elucidated by IR, ^{1}H-NMR, mass spectral data elemental analysis and Thin layer chromatography.

1. INTRODUCTION

Acetyl pyrazolines and phenyl pyrazolines derivatives shows wide range of biological activities like, antiallergic[1], fungicidal[2], antidiabetic[3], antiimplantation[4], antiinflammatory[5], antitumor[6], antineoplastic[7], analgesic[8], bactericidal[9], herbicidal[10], cardiovascular[11], diuretic[12], antiamoebic[13] etc. In view of getting to synthesized acetyl pyrazoline and phenyl pyrazoline derivatives. The products of acetyl pyrazolines (**3a-3l**) and phenyl pyrazolines (**4a-4l**) have been synthesized and assigned the IR, ^{1}H-NMR, mass spectral data, and elemental analysis. The physical data and antimicrobial activities are represents in Table-I.

Reaction Scheme



2. ANTIMICROBIAL ACTIVITY

1-Acetyl-3-{4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (**3a-3l**) and 1-Phenyl-3-{4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl}-5-aryl-pyrazolines (**4a-4l**) products were evaluated in vitro for their antimicrobial activities against *Bacillus megatarium, Staphylococcus aureus, Escherichia coli, Salmonella typhy* and *Aspergillus nige*r using DMF as solvent at 50 µg / ml. concentration by cup plate method[14]. After 24 hrs of incubation at 37°C, the zones of inhibition were measured in mm. The activity was compared with the known antibiotic, viz., ampicillin, chloramphenicol, norfloxacin, and gresiofulvin at same concentration.

All the synthesized compounds (**3a-3l**) and (**4a-4l**) showed moderate to good and remarkable activities with known standard drug at same concentration. The physical data and antimicrobial activities are represented in Table-I. The comparable antimicrobial activity represented in Table-II.

3. 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 ^{1}H-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.

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

A mixture of (4'-Chlorophenyl) (phenyl) methyl chloride in methanol (2.37 gm, 0.01 M) and p-amino acetophenone (1.47 gm, 1.2 M) is heated in the presence of basic catalyst pyridine (2 ml) for 8 hrs at 120°C. The completion of the reaction is checked by TLC and poured the reaction in to ice cold water, filter, wash with water and dry it. Yield is 65 %; m.p.134 °C.

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

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). Stirr the content at room temperature for 24 hr. in presence of catalytic amount of 40% NaOH. The reaction mixture was poured in to crush ice, thus the solid separated was filtrated, dried and crystallized from ethanol.

Yield 52%; M.P.102ºC; Anal. Calcd. For $C_{29}H_{24}ClNO_2$: Required C: 76.73; H:5.33; N:3.09% found C:76-71.H:5, 31; N, 3.07%.

Similarly others chalcones were prepared. The Physical data antimicrobial activity were published in our continuous publication.

(C) 1-Acetyl-3-4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl-5-(4''''-methoxy phenyl) pyrazoline (3h)

A mixture of 4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl-3-(4''''-methoxyphenyl) prop-2-ene-one (4.53 gm, 0.01 M), hydrazine hydrate (0.5 ml, 0.04 M) in 30 mL glacial acetic acid was refluxed for 12 hrs. The solution was poured into crushed ice. Filtered, dried the product and crystallized from DMF - Methanol. Yield 58%, m.p. 156 ^{0}C. Anal. Calcd. For $C_{31}H_{28}ClN_3O_2$; Requires C, 73.00; H, 5.53; N, 8.24%; found: C, 72.98; H, 5.51; N, 8.20%. IR (KBr, cm^{-1}); 2964 (C-H str.; asym.); 2869 (C-H str.; sym.); 1346 (C-H def.; sym.); 3050 (C-H aromatic); 1525(C=C str.; aromatic); 3352 (N-H str.), 752 (C-Cl str.); 1598 (C=N str.); 1184 (C-N str.); 1258 (C-O-C str.); 1658 (C=O str.); ^{1}H-NMR (DMSO-d6, δ ppm)**;** 2.40 (3H, s, -$COCH_3$); 2.70-2.79 (1H, dd, C-H); 3.93 (3H, s, Ar-OCH_3); 3.54-3.59 (1H, dd, C-H); 3.22 (1H, s, N-H); 5.00-5.08 (1H, dd, C-H); 5.62-5.63 (1H, d, C-H); 6.61-6.63 (2H, d, Ar-H); 6.77-6.78(2H,d,Ar-H); 7.24-7.34 (9H,m,Ar-H);7.67-7.69 (2H,d,Ar-H);7.80-7.89(2H,d,Ar-H)**.** m/z: 107, 136, 149, 154, 231, 258, 307, 336, 365, 375, 438, 467, 510.

Similarly, other acetyl pyrazoline (**3a-3l**) has been synthesized. The physical data are recorded in Table No. I.

(D) 1-Phenyl-3-4'-[(4'''-chlorophenyl) (phenyl) methyl amino] phenyl-5-(4''''-methoxy phenyl) pyrazoline (4h)

A mixture of 4-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl-3-(4''''-methoxyphenyl) prop-2-ene-1-one (4.53 gm, 0.01 M), Phenyl hydrazine (1.08 gm, 0.01 M) and 10 ml. glacial acetic acid. The reaction mixture refluxed for 12 hrs. The reaction mixture was poured into crushed ice. Product was isolated and crystallized from DMF - Methanol. Yield 58%; m.p.144ºC. Ana. Calcd. for $C_{35}H_{30}ClN_3O$; Requires C, 77.26; H, 5.56; N, 7.72%; found: C, 77.24; H, 5.54; N, 7.71%. IR (KBr, cm^{-1}); 2960 (C-H str.; asym.); 2852 (C-H str.; sym.); 1381 (C-H def.; sym.); 3048(C-H; aromatic); 1492(C=C str.; aromatic); 3318 (N-H; Str.), 706 (C-Cl; str.). 1638 (C=N; Str.), 1108 (C-N; Str.), 1250 (C-O-C; Str.). ^{1}H-NMR (DMSO-d6, δ ppm); 2.21-2.40 (1H, dd, C-H); 2.53-3.30 (1H, dd, C-H); 3.27-3.31 (1H, t, C-H); 3.34-3.85 (3H, s, Ar-OCH_3); 5.68-5.70 (1H, d, C-H); 6.64-6.66 (2H, d, Ar-H); 6.67-7.08 (4H, d, Ar-H);7.14-7.43 (10H, m, Ar-H); 7.54-7.57 (2H, d, Ar-H); 7.58-7.59 (2H, d, Ar-H); 8.07(1H, s, N-H). m/z**:** 78, 174, 201, 218, 246, 274, 274, 302, 318, 330, 353, 381, 387, 391, 417, 419, 433, 463, 509, 520, 521, 544.

Similarly, other compounds (**4a-4l**) were prepared. The physical data are recorded in Table-I.

Table-I

The physical data and antimicrobial activity of compounds (**3a-3l**) and (**4a-4l**). [Zone of Inhibition in mm]

Comp. Id	R	Molecular Formula	M.P. ° C	Antibacterial activity				Antifungal activity	% of Nitrogen	
				B.mega	*S.aureus*	*E.Coli*	*S.typhi*	*A.niger*	Calcd.	Found
3a	C_6H_5-	$C_{30}H_{26}ClN_3O$	142	14	13	10	11	15	8.75	8.74
3b	4-Cl-C_6H_4-	$C_{30}H_{25}Cl_2N_3O$	144	13	12	13	10	11	8.17	8.15
3c	4-F-C_6H_4-	$C_{30}H_{25}ClFN_3O$	218	19	12	10	13	17	8.44	7.50
3d	4-Br-C_6H_4-	$C_{30}H_{25}BrClN_3O$	151	17	16	14	12	19	7.52	8.40
3e	2-OH-C_6H_4-	$C_{30}H_{26}ClN_3O_2$	166	15	10	12	14	12	8.47	8.44
3f	3- OH-C_6H_4-	$C_{30}H_{26}ClN_3O_2$	212	12	11	16	15	11	8.47	8.41
3g	4-OH-C_6H_4-	$C_{30}H_{26}ClN_3O_2$	106	14	12	11	10	15	8.47	8.43
3h	4-OCH_3-C_6H_4-	$C_{31}H_{28}ClN_3O_2$	156	14	10	11	13	20	8.24	8.20
3i	3-OCH_3-4-OH-C_6H_4-	$C_{31}H_{28}ClN_3O_3$	206	11	13	12	14	16	7.99	7.97
3j	4-N-$(CH_3)_2$-C_6H_3-	$C_{32}H_{31}ClN_4O$	181	14	12	11	10	15	10.71	10.70
3k	$C_{10}H_7$-(Naphthayl)	$C_{34}H_{28}ClN_3O$	162	16	17	12	17	20	7.93	7.90
3l	$C_{14}H_9$-(Anthranyl)	$C_{38}H_{30}ClN_3O$	186	14	13	10	11	15	7.24	7.22
4a	C_6H_5-	$C_{34}H_{28}ClN_3$	140	17	15	12	14	17	8.17	8.16
4b	4-Cl-C_6H_4-	$C_{34}H_{27}Cl_2N_3$	112	16	10	17	11	12	7.66	7.60
4c	4-F-C_6H_4-	$C_{34}H_{27}ClFN_3$	102	11	13	14	12	15	7.90	7.90
4d	4-Br-C_6H_4-	$C_{34}H_{27}BrClN_3$	130	15	14	16	11	14	7.09	7.08
4e	2-OH-C_6H_4-	$C_{34}H_{28}ClN_3O$	190	14	16	15	13	17	7.93	7.91
4f	3- OH-C_6H_4-	$C_{34}H_{28}ClN_3O$	148	18	15	17	11	18	7.93	7.92
4g	4-OH-C_6H_4-	$C_{34}H_{28}ClN_3O$	96	16	10	11	15	20	7.93	7.90
4h	4-OCH_3-C_6H_4-	$C_{35}H_{30}ClN_3O$	144	17	15	16	10	19	7.72	7.71
4i	3-OCH_3-4-OH-C_6H_4-	$C_{35}H_{30}ClN_3O_2$	188	16	10	15	12	15	7.50	7.49
4j	4-N-$(CH_3)_2$-C_6H_3-	$C_{36}H_{33}ClN_4$	98	12	13	12	14	18	10.06	10.04
4k	$C_{10}H_7$-(Naphthayl)	$C_{38}H_{30}ClN_3$	126	17	15	16	10	10	7.45	7.44
4l	$C_{14}H_9$-(Anthranyl)	$C_{42}H_{32}ClN_3$	150	16	11	15	12	15	6.84	6.80

Table – II
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
Remarkable antimicrobial activity					
(3a-3l)	3c,3d,3e,3k	3a,3d,3i,3k	3b,3d,3e,3f,3i,3k	3e,3f,3i,3k	3c,3d,3h,3k
(4a-4l)	4a,4b,4f,4h,4k	4a,4e,4f,4h,4k	4b,4d,4f,4h,4k	4a,4e,4g,4j	4f,4g,4h,4j

4. CONCLUSION

1-Acetyl-3-4'-[(4'''-Chlorophenyl) (phenyl) methyl amino] phenyl-5-aryl-pyrazolines (**3a-3l**) and 1-Phenyl-3-4'-[(4'''-chlorophenyl)(phenyl) methyl amino] phenyl-5-aryl-pyrazolines (**4a-4l**) have been synthesized. Compounds containing **3c, 3d, 3e, 3k, 3j** and **4a, 4d, 4g, 4h, 4k** showed moderate comparable antimicrobial activity compare with known standard drugs.

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