RESEARCH PAPER

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Studies on Pyrazolines : Preparation and Antimicrobial Activity of 3-(3'(P-Chlorophenylsulphonamidophenyl)-5 aryl- 1H/Acetyl Pyrazolines

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Substituted chalcones (IIa-j), prepared by the treatment of 3'(p- chlorophenylsulphonamido) acetophenone (I) with araldehyde, on condensation with hydrazine hydrate in ethanol furnished desired pyrazolines of the type (IIIa-j) and (IVa-j) respectively. The structure of the products have been assigned on the basis of elemental analyses and spectral data. The products were evaluated for their *in-vitro* growth inhibiting activity against several microbes. Some of the compounds showed significant antimicrobial activity.

PYRAZOLINE derivatives possess a broad spectrum of pharmacological action which are reflected by their use as analgesics,[1] antiinflammatory,[2,7] anticonvulsant,[3] insecticidal,[4] herbicidal,[5] antimicrobial,[6] anticarcinogenic[8] and antidiabetic.[9] In the light of these interesting biological activities, it appeared of interest to synthesize some new pyrazoline derivatives bearing 3'(p-chlorophenylsulphonamido) acetophenone moiety and assess their biopotential.

The starting compound m-aminoacetophenone was condensed with p- chlorobenzene sulphonylchloride to yield 3'-(p- chlorophenylsulphonamido) acetophenone, which was further treated with various aromatic aldehydes to get 3'-(p-chlorophenylsulphonamido) chalcones (IIa-j). Compounds (IIa-j) on treatment with hydrazine hydrate in ethanol and in acetic acid afforded corresponding 3-(3'-p chlorophenyl sulphonamidophenyl)- 5 aryl- 1H/acetyl pyrazolines (IIIa-j, IVa-j).

The structure of the compounds synthesized were assigned on the basis of elemental analyses, IR and NMR spectral data. The antimicrobial potential of the compounds synthesized has been studied against several microbes.

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EXPERIMENTAL

Preparation of 3'-p-Chlorophenylsulphonamido chalcones (IIf)

To an efficiently stirred solution of 3'(p-chlorophenylsulphonamido) acetophenone (3.09 gm, 0.01 mole) and p- anisaldehyde (1.36 gm, 0.01 mole) in ethanol 20-25 ml was added 40% KOH (3ml). The reaction mixture was heated for 10 minutes and left overnight, poured into ice water, acidified, filtered and crystallized from ethanol to give (IIf). Yield 70%, m.p. 170°. Anal.calcd. for $C_{22}H_{18}NO_4SCl$: C,61.75; H,4.21; N,3.27 mol. wt. 427.5. Found : C,61.75; H,4.20; N,3.25.

IR(KBr) : 3200 cm^{-1} (N-H), 1635 cm^{-1} (C=O), 1315 cm^{-1} (S=O), 1145 cm^{-1} (S-O), 690 cm^{-1} (C-C1).[1] H NMR (TFA) : δ (ppm 4.0 (S,3H,OCH_3), 6.96(S,2H, 2 x C = CH) and 7.2 to 8.1 (m, 12H, ArH).

Similarly other members of (II) were prepared and their physical data are presented in the table 1.

Preparation of 3-[3'-(p-Chlorophenylsulphonamidophenyl)]-5-(4''- methoxyphenyl)-1-H pyrazoline (IIIf)

A mixture of (IIIf) (4.28 gm, 0.01 mole) in 20-25 ml ethanol, hydrazine hydrate (10.5 gm, 0.01 mole) and piperidine (1 ml) was refluxed on a boiling water bath for 8-10 hours. The product was isolated and crystallised from ethanol to give (IIIf). Yield 70%, m.p. 161°. Anal. calcd. for $C_{22}H_{20}N_3O_3SCl$, C,59.79; H, 4.53; N, 9.51 mol. wt. 441.5 Found : C, 59.72 H, 4.52;N, 9.49;

IR(KBr) : 3200 cm^{-1} (N-H), 1565 cm^{-1} (C=N), 1310 cm^{-1} (S=O), 1250 cm^{-1} (C-N), 1140 cm^{-1} (S=O), 680 cm^{-1} (C-Cl). ^1H NMR (TFA) : 3.02 (dd, 1H, > CH_A), 3.3-4.5 (m, 4H, $>CH_3$ + OCH_3).

Similarly other members of (III) were prepared and their physical data are presented in the Table - 1.

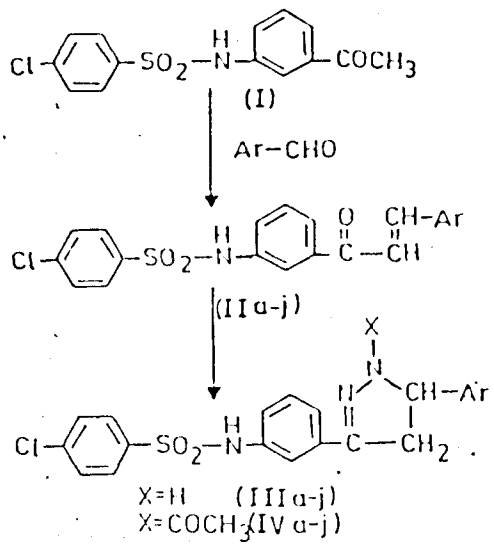
Preparation of 3-[3'-(p-Chlorophenylsulphonamidophenyl)]-5-(4''- methoxyphenyl)-1 acetyl pyrazoline (IVf)

A mixture of (IIf) (4.27 gm, 0.01 mole) in 20-25 ml ethanol, hydrazine hydrate (0.5 gm, 0.01 mole) and acetic acid (10 ml) was refluxed for 8-10 hours. The product was Isolated and crystallised from ethanol to give (IVf). Yield 72%, m.p. 249°, Anal. calcd. for $C_{24}H_{22}N_3O_4SCl$ C, 59.56; H, 4.50, N, 8.67 mol. wt. 4835 Found : C, 59.56; H, 4.55; N, 8.68.

IR(KBr) : 3200 cm^{-1} (N-H), 1670 cm^{-1} (N-$COCH_3$) 1590 cm^{-1} (C=N), 1320 cm^{-1} (S=O), 1255 cm^{-1}(C-N), δ^1H NMR (TFA) : 2.72 (S, 3H, -$COCH_3$), 3.2(dd, 1H, $>CH_A$), 3.3-4.3 (4H, m, CH_B + OCH_3), 5.85 (1H, dd $>CH_x$) and 7.3-7.95 (12H, m, ArH).

Similarly other members of (IV) series were prepared and their physical data are presented in the table 1.

SCHEME-1



II,III,IV,a :	Ar	2Cl-C_6H_4
b :		4Cl-C_6H_4
c :		$N(CH_3)_2$ C_6H_4
d :		C_4H_3O
e :		2(OCH_3) C_6H_4
f :		4-(OCH_3) C_6H_4
g :		3-O_2N-C_6H_4
h :		3-Br-C_6H_4
i :		C_6H_5
j :		3-4(H3CO)2-C6H3

Biological Activity

The antimicrobial screening of the compounds synthesised was conducted using cup-plate agar diffusion technique at a concentration of 50 ug by measuring zone of inhibition in mm. All the compounds were screened **in vitro** for their antimicrobial activity against a variety of bacterial strains such as **Bacillus megaterium, Staphylococcus citrus, Escherichia coli, Salmonella typhosa Aspergillus niger.** Chloramphenicol, ampicillin, norfloxacin and griseofulvin were used as standard for comparing the products. The results for the antimicrobial screening is presented in (table 1).

RESULTS AND DISCUSSION

Synthesised Compounds of type II, III and IV were screened for antimicrobial activity against **B.mega, S.citrus, E.coli, S.typhosa** and antifungal activity against **A.niger** using cup-plate method, at

Table 1 : Physical data of 3-[3'(p-chlorophenylsulphonamidophenyl)]-5-aryl-1H/acetyl-pyrazoline

Compd No.	R	Yield %	M.P. °C	Molecular formula	% Nitrogen Calc/Found	Zone of inhibition in mm				
						E.coli	B.mega	S.typhosa	S.citrus	A.niger
IId	C_4H_3O	77	119	$C_{18}H_{14}NO_4SCl$	3.8/ 3.7	22	11	13	15	13
IIe	2-$(OCH_3)C_6H_4$	72	148	$C_{22}H_{18}NO_4SCl$	3.1/ 3.1	21	13	14	18	12
IIf	4-$(OCH_3)C_6H_4$	70	135	$C_{22}H_{18}NO_4SCl$	3.3/ 3.2	25	11	14	15	11
IIh	3-Br C_6H_4	79	150	$C_{21}H_{12}NO_3SCr$	3.6/ 3.5	17	13	16	17	13
IIi	C_6H_5	80	145	$C_{22}H_{15}N_2O_5SCl$	3.3/ 3.4	20	14	16	17	11
IIIe	2-$(OCH_3)C_6H_4$	72	162	$C_{22}H_{20}N_3O_3SCl$	9.6/ 9.5	23	13	13	16	12
IIIf	4-$(OCH_3)C_6H_4$	70	161	$C_{22}H_{20}N_3O_3SCl$	9.7/ 9.7	24	14	14	14	12
IIIg	3-$O_2NC_6H_4$	64	119	$C_{21}H_{17}N_4O_4SCl$	12.2/12.1	24	11	13	15	12
IIIh	3-Br C_6H_4	60	117	$C_{21}H_{17}N_3O_3SBr$	10.2/10.0	23	11	14	16	12
IIIj	3-4$(OCH_3)_2C_6H_3$	72	191	$C_{23}H_{23}N_4O_2SCl$	8.6/ 8.5	21	12	15	15	12
IVc	N-$(CH_3)_2C_2H_4$	82	168	$C_{25}H_{25}N_4O_3SCl$	11.3/11.1	19	14	15	16	13
IVd	C_4H_3O	80	130	$C_{21}H_{18}N_3O_4SCl$	9.5/ 9.4	22	11	14	17	13
IVf	4-(OCH_3) C_6H_4	72	249	$C_{24}H_{22}N_3O_4SCl$	8.9/ 8.6	24	12	16	14	11
IVi	C_6H_5	60	163	$C_{23}H_{20}N_3O_3SCl$	9.1/ 9.2	20	11	14	14	13
IVj	3-4$(OCH_3)_2C_6H_3$	70	129	$C_{22}H_{24}N_3O_3SCl$	8.0/ 8.0	19	13	16	15	12

a concentration of 50 µg/ml using DMF as a solvent. The plates were incubated at 37° for 24 hrs in case of antibacterial activity where as in case of antifungal activity at 30° for 48 hrs and the control was also maintained with 0.05 ml. of DMF in similar manner and the zone of inhibition of the growth were measured in mm. DMF (Control) exhibited activity in the range of 8-10 mm. against all bacterial strains. The activity was compared with that of Standard drugs Ampicillin, Chloramphenicol, Norfloxacin and Gresiofulvin at the same concentration.

All the compounds were screened for antimicrobial activity and displayed moderate activity, however most of the compounds were found to have significant activity against **E.coli** either equal to or slightly greater than the standard drug. Simple pyrazoline derivatives of the type II bearing R=2-Chloro, 4-Chloro, 4- methoxy, 3-nitro exhibited maximum activity.

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