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Synthesis and Antimicrobial Activities of 3-(2-Hydroxy-3-substituted-5-methyl phenyl)-5-(3,4-methylenedioxyphenyl)-2-pyrazoline and Its Derivatives

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2-Hydroxy-3-substituted-5-methyl acetophenone **(Ia–c)** condenses with 3,4-methylenedioxy benzaldehyde in ethanol medium in presence of NaOH to give chalcones **(IIa–c)**. Chalcones **(IIa–c)** react with hydrazine hydrate in ethanol to give I-H pyrazolines **(IIIa–c)**. Chalcones **(IIa–c)** react with phenyl hydrazine in ethanol to give 1-phenyl pyrazolines **(IVa–c)**. Similarly, chalcones **(IIa–c)** react with 2,4-dinitrophenyl hydrazine in ethanol to give 1-2,4-dinitrophenyl pyrazolines **(Va–c)**. The structures were established on the basis of spectral data, IR and NMR. Antimicrobial activities of these compounds assayed against test organisms *S. aureus, S. dysentariae, S. typhi, E. coli, K. pneumonie* and *P. mirabilis*. The activities of these compounds were compared with standard drug chloram phenicol.

Key Words: Synthesis, Chalcones, Substituted pyrazoline, Antimicrobial activity.

INTRODUCTION

Pyrazolines are known to have bacterial[1], fungicidal[2] and insecticidal[3] properties. Some pyrazolines are also reported to have anti-inflammatory, antidiabetic, anaesthetic and analgesic properties[4–7]. Pyrazolines and their derivatives have been reported to have biological activities[8–10]. Recently, Ali *et al.*[11] have reported the synthesis of isomeric pyrazolines and their derivatives. Chalcones react with hydrazine hydrate in ethanol to give 1-H pyrazolines[12–16]. Chalcones react with phenyl hydrazine in ethanol in presence of KOH to give 1-phenyl pyrazolines[12–16]. Literature survey indicates that pyrazolines have not been prepared from 2-hydroxy-3-substituted-5-methylphenyl-3′,4′-methylenedioxy chalcones. Hence, chalcones were prepared by known method[17, 18]. It was thought of interest to prepare some new pyrazolines from 2-hydroxy-3-substituted-5-methylphenyl-3′,4′-methylenedioxychalcones. The present work deals with the synthesis of pyrazolines from chalcones and phenyl hydrazine and 2,4-dinitrophenyl hydra-

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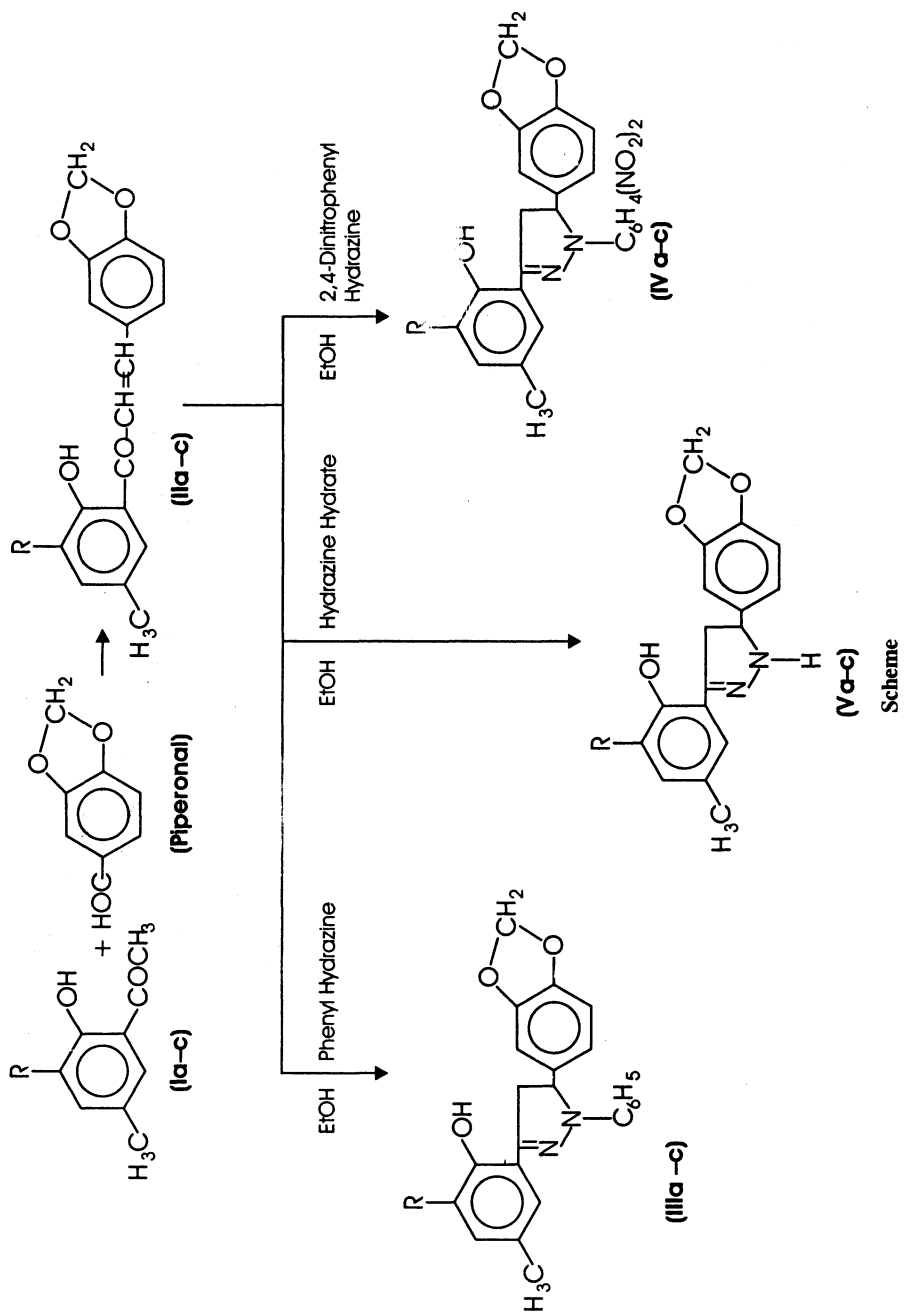
(Ia–c)
(Piperonal)
(IIa–c)
EtOH
Phenyl Hydrazine
Hydrazine Hydrate
2,4-Dinitrophenyl Hydrazine
(IIIa–c)
(Va–c)
(IVa–c)

Scheme

zine in alcoholic medium. The structures of these compounds have been established by elemental and spectral analysis.

Melting points were determined in open capillaries and are uncorrected. IR spectra in KBr were recorded on PE-983/PE-781 IR spectrophotometer. NMR in DMSO on DSX-300 MHz solid state FT-NMR spectrophotometer.

Antimicrobial activities of these compounds were assayed against test organisms *S. aureus, S. dysentariae, S. typhoid, E. coli, K. pneumoniae* and *P. mirabilis.* The minimum inhibitory concentration (MIC) values were determined by serial dilution method. Activities of these compounds were compared with standard drug chloramphenicol.

EXPERIMENTAL

Synthesis of 2-hydroxy-3-substituted-5-methyl phenyl-3′,4′-methylenedioxy chalcones (IIa–c)

2-Hydroxy-3-substituted-5-methyl acetophenone (0.01 mol) dissolved in ethanol and 3,4-methylenedioxybenzaldehyde (0.01 mol) was added to this solution and the solution was heated to near boiling. To this hot solution 40% aq. NaOH was added with vigorous stirring. After some time, a coloured solid was obtained, which was kept overnight and acidified by 10% HCl, washed by 10% $NaHCO_3$ followed by H_2O and crystallized from ethanol to give chalcones **(IIa–c).**

Synthesis of 1-phenyl-3-(2-hydroxy-3-substituted-5-methyl phenyl)-5-(3,4-methylenedioxyphenyl)-2-pyrazolines (IIIa–c)

2-Hydroxy-3-substituted-5-methyl phenyl-3′,4′-methylenedioxychalcones **(IIa–c)** (0.01 mol) and phenyl hydrazine (0.01 mol) in ethanol was refluxed for 1 h. The reaction mixture was concentrated and allowed to cool. The refluxing solid was filtered, washed with ethanol and crystallized from ethanol to obtain solid compounds **(IIIa–c).**

Properties of Compound IIIa

(a) It is yellow coloured crystalline compound with melting point 285°C.

(b) Alcoholic solution gives intense green colour with neutral $FeCl_3$ solution.

(c) From analytical data, molecular formula was found to be $C_{17}H_{13}N_3O_5$.

(d) A soaked paper with the solution of compound in benzene turned bluish green when exposed to bromine vapours (Knorr's test for pyrazoline).

(e) It gives blue solution with conc. H_2SO_4.

(f) IR (KBr, cm^{-1}): 3300 ν(—OH), 1600 ν(C=N of pyrazoline), 1400 ν(—CH_2 of pyrazoline), 1250 ν(C—N stretching).

(g) NMR: δ 2.47 (s, —CH_2), 3.33 (s, 3H, —CH_3), 6.8–7.8 (m, 11H, Ar—H), 3.23 (dd, 1H, —CHH_A), 3.64 (dd, 1H, —CHH_B), 4.97 (dd, 1H, CH_X), 6.2 (s, 1H, —NH), 14, (s, 1H, —OH).

Synthesis of 1-2,4-dinitrophenyl-3-(2-hydroxy-3-substituted-5-methyl phenyl)-5-(3,4-methylenedioxyphenyl)-2-pyrazolines (IVa–c)

2-Hydroxy-3-substituted-5-methyl phenyl-3′,4′-methylenedioxychalcones **(IIa–c)** (0.01 mol) and 2,4-dinitrophenyl hydrazine (0.01 mol) in ethanol was refluxed for 1 h. The reaction mixture was concentrated and allowed to cool. The refluxing solid was filtered, washed with ethanol and crystallized from ethanol to obtain solid compound **(IVa–c).** (a) IR (KBr, cm^{-1}): 3400 ν(br, —OH), 3000 ν(Ar—H), 1450 ν(CH_2) pyrazoline 1570 ν(NO_2, Sym), 1250 ν(C—N Str). (b) NMR: δ 2.47 (s, —CH_2), 3.33 (s, 3H, —CH_3), 6.8–8.5 (m, 9H, Ar—H), 3.23 (dd, 1H, —CHH_A), 3.64 (dd,1H, —CHH_B), 4.91 (dd, 1H, CH_X), 12.6 (S, 1H, —OH).

Similarly, other compounds are prepared by the above methods listed in Table-1. These compounds were tested against test organisms. The MIC values of these compounds were determined by serial dilution method. The activities of these compounds were compared with standard drug chloramphenicol.

TABLE-1
PHYSICAL CHARACTERIZATION DATA OF SYNTHESIZED COMPOUNDS

Compound	R_1	R_2	m.f.	m.p. (°C)	m.w.	% N (Calcd.)	Yield (%)
IIa	H	—	$C_{17}H_{14}O_4$	216	282	—	72
IIb	Br	—	$C_{17}H_{13}O_4Br$	252	361	—	70
IIc	NO_2	—	$C_{17}H_{13}O_6N$	263	327	4.28 (5.24)	80
IIIa	H	C_6H_5	$C_{23}H_{20}O_3N_2$	305	372	7.43 (7.53)	68
IIIb	Br	C_6H_5	$C_{23}H_{19}O_3N_2Br$	325	451	5.98 (6.20)	70
IIIc	NO_2	C_6H_5	$C_{23}H_{19}O_5N_3$	265	417	9.91 (10.07)	72
IVa	H	$C_6H_4(NO_2)_2$	$C_{23}H_{19}O_7N_4$	348	463	11.97 (12.09)	78
IVb	Br	$C_6H_4(NO_2)_2$	$C_{23}H_{18}O_7N_4Br$	368	542	10.23 (10.33)	80
IVc	NO_2	$C_6H_4(NO_2)_2$	$C_{23}H_{18}O_9N_5$	372	508	13.57 (13.77)	68

TABLE-2
MINIMUM INHIBITORY CONCENTRATION VALUES IN μg/mL

Compound	Gram +ve			Gram –ve		
	S. aureus	*S. dysentariae*	*S. typhi*	*E. coli*	*K. pneumoniae*	*P. mirabilis*
IIa	250	125	125	500	250	250
IIb	250	62	125	500	250	250
IIc	62	31	31	62	125	250
IIIa	62	31	31	250	125	125
IIIb	125	62	62	500	125	125
IIIc	125	62	125	500	125	125
IVa	62	125	62	250	125	125
IVb	62	62	125	500	250	125
IVc	62	62	125	500	250	125
Standard drug chloramphenicol	**25**	**03**	**12**	**06**	**06**	**50**

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