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NOTE

Synthesis and Antibacterial Activity of 1-H-3-(2′-Hydroxy-4′-Ethoxy-5′-Nitro Phen-1′-yl)-5-Substituted Phenyl-2-Pyrazolines and their Related Compounds

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In the present note some biologically active 1-H-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-substituted phenyl-2-pyrazolines and their related compounds were synthesized characterized.

Several related 1-H-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-substituted phenyl-2-pyrazolines and their related compounds are prepared in view of the fact that a number of related compounds are known to possess biological activities[1].

2′-Hydroxy-4′-ethoxy-5′-nitro-chalcones have been prepared through the reaction of 2-hydroxy-4-ethoxy-5′-nitro acetophenone and aryladehyde by the Claisen-Schmidt condensation[2] Previous acetophenone was prepared by the reported method[3].

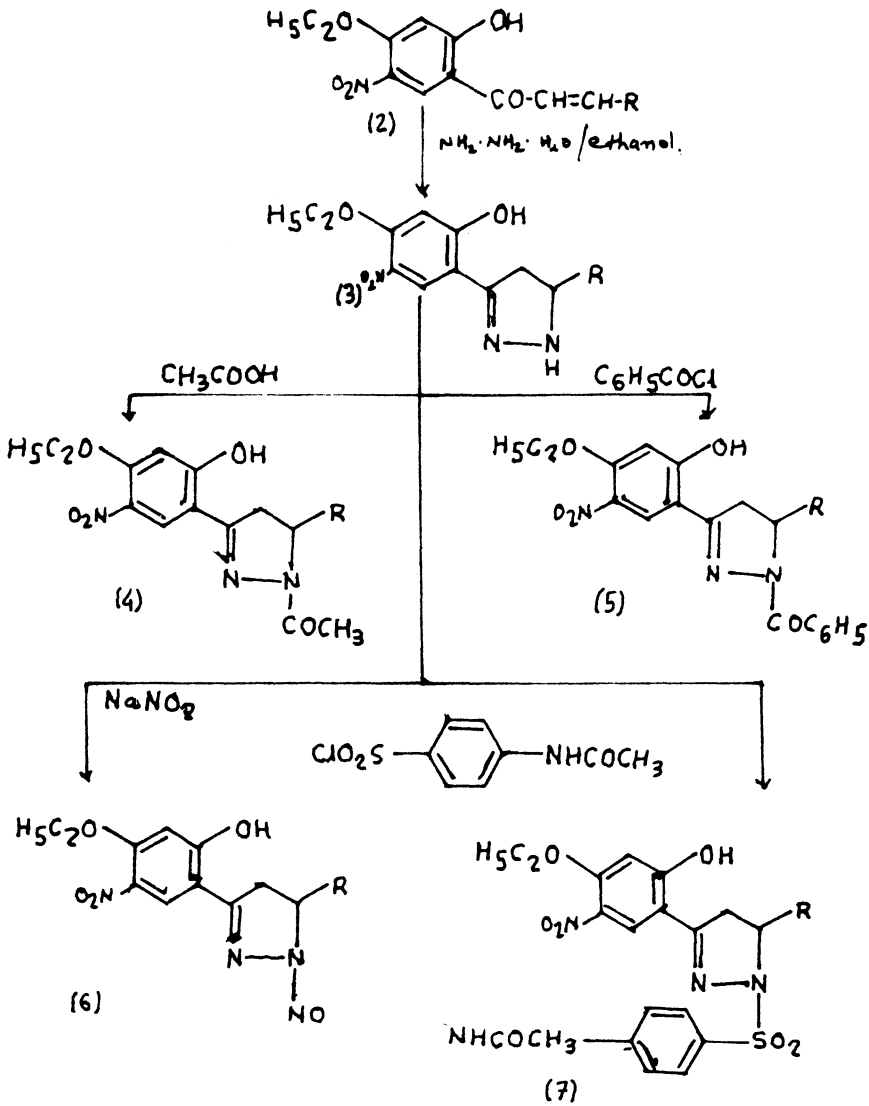
2′-hydroxy-4′-ethoxy-5′-nitro-chalcones on condensation with hydrazine hydrate in ethanol gave 1-H-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-substituted phenyl-2-pyrazolines[4] (2). The reaction of 2 with acetic acid gave acetyl derivatives (3) by direct method. Similarly, the reaction of 2 with benzoyl chloride gave benzoyl derivatives (4). Reaction of 2 with nitrous acid gave nitroso derivatives (5) and reaction of pyrazolines (2) with 4-acetamido sulphonyl chloride gave sulphonyl derivatives (6) (Scheme-I).

The structural assignments of the compounds were based on their elemental analysis and IR spectral data. The antibacterial activity of 1–7 has been studied by paper-disc method[5].

Antibacterial activity: The anti-bacterial screening of all the compounds was carried out using paper-disc method, at a concentration of 50 g using gram-negative bacteria *Escherichia coli* and gram-positive bacteria *Staphylococus aureus*. The compounds possess moderate to good activity.

Most of the compounds showed activity against different strains of bacteria and the (7–24 mm, zone of inhibition) compounds 3–7 were found to be active against *S. aureus* and *E. coli*. It was observed that sulphonimide derivatives (7) of pyrazoline are more active against both bacteria than pyrazolines (3) and their acetyl (4), benzoyl (5) and nitroso (6) derivatives. The presence of chlorine atom in the nucleus is responsible for the increase of antimicrobial activity.

Melting points were taken in open capillary tubes and are uncorrected. The purity of the synthesised compounds was checked by TLC. Infrared spectra (KBr) were recorded on Perkin-Elmer 377 Spectrophotometer.



1-H-3-(2′)-Hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-substituted phenyl-2-pyrazoline (general)

A mixture of 2′-hydroxy-4′-ethoxy-5′-nitro-4-substituted phenyl chalcone, (0.01 mol and 99% hydrazine hydrate (0.015 mole) in ethanol (20 mL) was refluxed gently for 2 h. The mixture was then concentrated and cool. The resulting solid was filtered, washed with ethanol, and recrystallised from ethanol to give 2 (Table-1).

IR (KBr): 3500–3400 cm^{-1} (OH), 3100–3000 cm^{-1} (NH), 1370–1360 cm^{-1} (CH_2 of pyrazoline), 1610–1590 cm^{-1} (C=N), 1225–1215 cm^{-1} (—C—O—N).

TABLE-1
PHYSICAL DATA OF COMPOUNDS

S. No.	R	m.p. (°C)	Mol. formula
2a	Phenyl	149	$C_{17}H_{15}O_5N$
2b	4-Methyl phenyl	175	$C_{18}H_{17}O_5N$
2c	4-Chloro phenyl	163	$C_{17}H_{16}O_5NCl$
2d	4-Methoxy phenyl	143	$C_{18}H_{17}O_6N$
2e	4-N-N-dimethyl amino phenyl	193	$C_{19}H_{20}O_5N$
2f	2-Furfuryl	134	$C_{15}H_{13}O_6N$
3a	Phenyl	118	$C_{17}H_{17}O_4N_3$
3b	4-Methyl phenyl	133	$C_{18}H_{19}O_4N_3$
3c	4-Chloro phenyl	108	$C_{17}H_{18}O_4N_3Cl$
3d	4-Methoxy phenyl	118	$C_{18}H_{19}O_5N_3$
3e	4-N-N-dimethyl amino phenyl	132	$C_{19}H_{22}O_4N_3$
3f	2-Furfuryl	149	$C_{15}H_{15}O_5N_3$
4a	Phenyl	139	$C_{19}H_{19}O_5N_3$
4b	4-Methyl phenyl	162	$C_{18}H_{21}O_5N_3$
4c	4-Chloro phenyl	132	$C_{19}H_{18}O_5N_3Cl$
4d	4-Methoxy phenyl	159	$C_{20}H_{21}O_6N_3$
4e	4-N-N-dimethyl amino phenyl	184	$C_{21}H_{24}O_5N_3$
4f	2-Furfuryl	157	$C_{17}H_{17}O_6N_3$
5a	Phenyl	101	$C_{24}H_{21}O_5N_3$
5b	4-Methyl phenyl	97	$C_{25}H_{23}O_5N_3$
5c	4-Chloro phenyl	94	$C_{24}H_{20}O_5N_3Cl$
5d	4-Methoxy phenyl	122	$C_{25}H_{23}O_6N_3$
5e	4-N-N-dimethyl amino phenyl	96	$C_{26}H_{26}O_5N_3$
5f	2-Furfuryl	69	$C_{22}H_{19}O_6N_3$
6a	Phenyl	119	$C_{17}H_{16}O_5N_4$
6b	4-Methyl phenyl	165	$C_{18}H_{18}O_5N_4$
6c	4-Chloro phenyl	157	$C_{17}H_{15}O_5N_4Cl$
6d	4-Methoxy phenyl	138	$C_{18}H_{18}O_6N_4$
6e	4-N-N-dimethyl amino phenyl	108	$C_{19}H_{21}O_5N_5$
6f	2-Furfuryl	118	$C_{15}H_{14}O_6N_4$
7a	Phenyl	131	$C_{25}H_{24}O_7N_4S$
7b	4-Methyl phenyl	154	$C_{26}H_{26}O_7N_4S$
7c	4-Chloro phenyl	138	$C_{25}H_{23}O_7N_4SCl$
7d	4-Methoxy phenyl	121	$C_{26}H_{26}O_8N_4S$
7e	4-N-N-dimethyl amino phenyl	98	$C_{27}H_{29}O_7N_4S$
7f	2-Furfuryl	161	$C_{23}H_{22}O_8N_4S$

*All compounds gave satisfactory element analysis.

1-Acetyl-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen 1′-yl)-5-substituted phenyl-2-pyrazoline

A mixture of pyrazoline (2) (0.01 mol) and acetic acid (10 mL) was refluxed for 2 h. The solution was then concentrated. On cooling, the resulting solid was filtered, washed with water and recrystallised from ethanol (90%) to give 3 (Table-1).

IR (KBr): 3500–3400 cm^{-1} (OH), 1680–1650 cm^{-1} (N—C=O, C=O), 1610–1590 cm^{-1} (C=N), 1370–1360 cm^{-1} (CH_2 of pyrazoline).

1-Benzoyl-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-substituted phenyl-2-pyrazoline

A mixture of pyrazoline (2) (0.001 mol) and benzoyl chloride (0.0011 mol) was dissolved in dry pyridine (10 mL) and stirred at room temperature for 1 h. The resulting mixture was treated with cold HCl (2N). The resulting solid was filtered and washed successively with water, cold NaOH (2%) and water and recrystalline from glacial acetic acid to give 4 (Table-1).

IR (KBr): 3400–3350 cm^{-1} (OH), 1670–1650 cm^{-1} (N—C=O, C=O), 1610–1590 cm^{-1} (C=N), 1370–1360 cm^{-1} (CH_2 of pyrazoline), 1230–1220 cm^{-1} (C—N).

1-Nitroso-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-subtisuted phenyl-2-pyrazoline

A mixture of 2 (0.002 mol) was dissolved in 1 : 1 HCl (2 mL) and then cooled in an ice bath; cold 10% sodium nitrite solution (6 mL) was then added dropwise with constant stirring. The mixture was further stirred for 30 min at room temperature. The resulting solid was separated, recrystallised from ethanol to give 5 (Table-1).

IR (KBr): 3500–3350 cm^{-1} (OH), 1500 cm^{-1} (—N=O).

1-*p*-acetamido phenyl sulphonyl-3-(2′-hydroxy-4′-ethoxy-5′-nitro phen-1′-yl)-5-substituted phenyl-2-pyrazoline

A solution of 2 (0.001 mol) was dissolved in dry pyridine (10 mL). This solution was colled in an ice bath and to it *p*-acetamido phenyl sulphonyl chloride (0.0011 mol) was added. The mixture was stirred for an hour at room temperature and was then treated with cold dil. HCl (2N). The solid obtained was washed with water and recrystallised from ethanol to give 6 (Table-1).

IR (KBr): 3500–3350 cm^{-1} (OH), 1610–1590 cm^{-1} (C=N), 1160–1140 cm^{-1}, 1330–1290 cm^{-1} (S=O, asym. and sym.).

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