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Synthesis and Antibacterial Activity of 1-H-3-(2′-Hydroxy-4′-ethoxy-5′-bromo phen-1′-yl)-5-substituted Phenyl-2-pyrazolines and Their Related Compounds

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In the present note the author describes the synthesis and antibacterial activity of 1-H-3-(2′-Hydroxy-4′-ethoxy-5′-bromo phen-1′-yl)-5-substituted phenyl-2-pyrazolines and their related compounds.

INTRODUCTION

Several related 1-H-3-(2′-hydroxy-4′-ethoxy-5′-bromo phen-1′-yl)-5-sustituted 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′-bromo chalcones have been prepared through the reaction of 2-hydroxy-3-ethoxy-5′-bromo acetophenone and arylaldehyde by the Claisen-Schmidt condensation[2]. Previous acetophenone was prepared by the reported method[3]. 2′-Hydroxy-4′-ethoxy-5′-bromo-chalcones on condensation with hydrazine hydrate in ethanol to give 1-H-3-(2′-hydroxy-4′-ethoxy-5′-bromo 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].

RESULTS AND DISCUSSION

Antibacterial activity

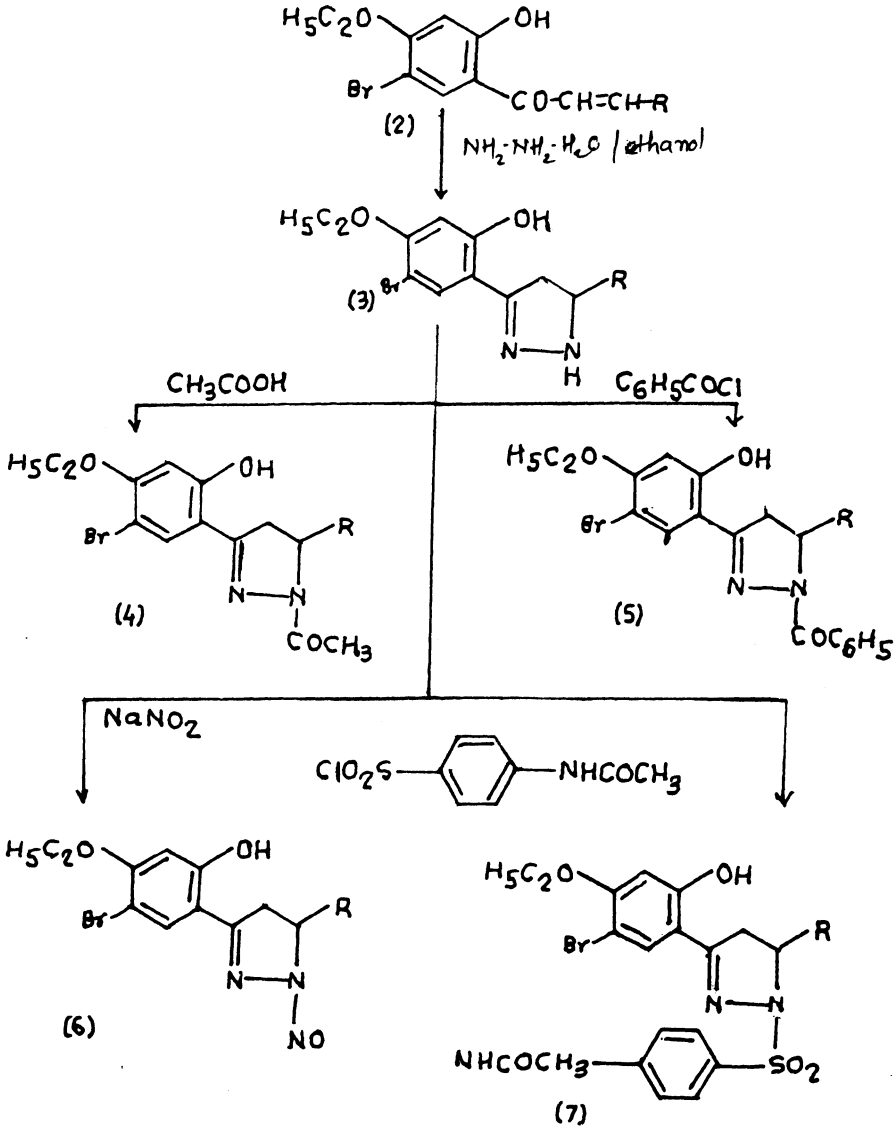
The antibacterial screening of all the compounds was carried out by paper-disc method, at a concentration of 50 μg. using gram-negative bacteria *Escherichia coli* and gram-positive bacteria *Staphylococus aureus*. The compounds possess moderate to good activity.

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 sulphonamide derivatives (**7**) of pyrazoline

are more active against both bacteria than the pyrazolines (**3**) and their acetyl (**4**), benzoyl (**5**) and nitroso (**6**) derivatives. The presence of bromine/ chlorine atom in the nucleus is responsible for the increase of antimicrobial activity.

EXPERIMENTAL

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.



R = Phenyl, 4-Methyl phenyl, 4-Chlorophenyl, 4-Methoxy phenyl, 4-N,N'-Dimethyl aminophenyl, 2-Furfuryl

1-H-3-(2')-Hydroxy-4'-ethoxy-5'-bromo phen-1'-yl)-5-substituted phenyl-2-pyrazoline (General)

A mixture of 2'-hydroxy-4'-ethoxy-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 cooled. The resulting solid was filtered, washed with ethanol and recrystallized from ethanol to give **2** (Table-1).

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

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

A mixture of pyrazoline (**2**) (0.001 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) ν_{max} (cm^{-1}): 3400–3350 ν(OH), 1680–1650 ν(N—C=O, C=O), 1610–1590 ν(C=N), 1370–1360 cm^{-1} ν(CH_2 of pyrazoline).

1-Benzoyl-3-(2'-hydroxy-4'-ethoxy-5'-bromo 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 recrystallized from glacial acetic acid to give **4** (Table-1).

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

1-Nitroso-3-(2'-hydroxy-4'-ethoxy-5'-bromo phen-1'-yl)-5-substituted 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 and recrystallised from ethanol to give **5** (Table-1).

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

1-*p*-acetamido phenyl sulphonyl-3-(2'-hydroxy-4'-ethoxy-5'-bromo 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 cooled in an ice bath and to it *p*-acetamido phenyl sulphonyl chloride (0.0011 mol) was added. The mixture was stirred for 1 h 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) ν_{max} (cm^{-1}): 3500–3350 ν(OH), 1610–1590 ν(C=N), 1160–1140, 1330–1290 ν(S=O, asym. and sym.)

TABLE-1
PHYSICAL DATA OF COMPOUNDS

Sr. No.	R	m.p. (°C)	Mol.formula
2a	Phenyl	152	$C_{17}H_{15}O_3Br$
2b	4-Methyl phenyl	175	$C_{18}H_{17}O_3Br$
2c	4-Chloro phenyl	179	$C_{17}H_{14}O_3ClBr$
2d	4-Methoxy phenyl	164	$C_{18}H_{17}O_4Br$
2e	4-N-N′-Dimethyl amino phenyl	75	$C_{19}H_{20}O_3NBr$
2f	2-Furfuryl	97	$C_{15}H_{13}O_4Br$
3a	Phenyl	110	$C_{17}H_{17}O_2N_2Br$
3b	4-Methyl phenyl	114	$C_{18}H_{19}O_2N_2Br$
3c	4-Chloro phenyl	98	$C_{17}H_{16}O_2N_2ClBr$
3d	4-Methoxy phenyl	100	$C_{18}H_{19}O_3N_2Br$
3e	4-N-N′-Dimethyl amino phenyl	122	$C_{19}H_{22}O_2N_3Br$
3f	2-Furfuryl	113	$C_{15}H_{15}O_3N_2Br$
4a	Phenyl	176	$C_{19}H_{19}O_3N_2Br$
4b	4-Methyl phenyl	156	$C_{28}H_{21}O_3N_2Br$
4c	4-Chloro phenyl	189	$C_{19}H_{18}O_3N_2ClBr$
4d	4-Methoxy phenyl	167	$C_{20}H_{21}O_4N_2Br$
4e	4-N-N′-Dimethyl amino phenyl	164	$C_{21}H_{24}O_3N_3Br$
4f	2-Furfuryl	179	$C_{17}H_{17}O_4N_2Br$
5a	Phenyl	84	$C_{24}H_{21}O_3N_2Br$
5b	4-Methyl phenyl	74	$C_{25}H_{23}O_3N_2Br$
5c	4-Chloro phenyl	98	$C_{24}H_{20}O_3N_2ClBr$
5d	4-Methoxy phenyl	98	$C_{25}H_{23}O_4N_2Br$
5e	4-N-N′-Dimethyl amino phenyl	139	$C_{26}H_{26}O_3N_3Br$
5f	2-Furfuryl	101	$C_{22}H_{21}O_4N_2Br$
6a	Phenyl	116	$C_{17}H_{16}O_3N_3Br$
6b	4-Methyl phenyl	112	$C_{18}H_{18}O_3N_3Br$
6c	4-Chloro phenyl	109	$C_{17}H_{15}O_3N_3ClBr$
6d	4-Methoxy phenyl	139	$C_{18}H_{18}O_4N_3Br$
6e	4-N-N′-Dimethyl amino phenyl	100	$C_{19}H_{21}O_3N_4Br$
6f	2-Furfuryl	97	$C_{15}H_{14}O_4N_3Br$

7a	Phenyl	88	$C_{25}H_{24}O_5N_3SBr$
7b	4-Methyl phenyl	98	$C_{26}H_{26}O_5N_3SBr$
7c	4-Chloro phenyl	114	$C_{25}H_{23}O_5N_3SClBr$
7d	4-Methoxy phenyl	110	$C_{26}H_{26}O_6N_3SBr$
7e	4-N-N'-Dimethyl amino phenyl	154	$C_{27}H_{29}O_5N_4SBr$
7f	2-Furfuryl	142	$C_{23}H_{22}O_6N_3SBr$

All compounds gave satisfactory elemental analysis

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