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NOTE

Synthesis and Antimicrobial Activity of New 1H-3-(2-Acetoxy-4-Methoxy) Phenyl-5-Substituted-Phenyl-Pyrazolines and Their Derivatives

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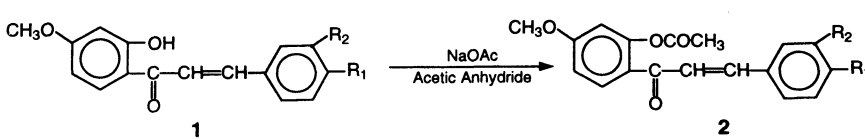
Condensation of 2-acetoxy-4,4′-dimethoxy chalcone with hydrazine hydrate either in ethanol or ethylene glycol medium gave the title compounds (3). Their N-substituted derivatives 4 and 5 have been obtained by acetylation and benzoylation. The compounds 3, 4 and 5 have been screened for antimicrobial activity.

Pyrazolines are important nitrogen containing heterocycles possesing diverse biological activity[1, 2]. In view of potential pharmacological values, the new pyrazoline derivatives are designed to contain —$COCH_3$/COC_6H_5 groups at position 1 and [2-acetoxy-4-methoxy] phenyl group at position 3. 2-Hydroxy-4-methoxy-acetophenone (paenol) was condensed with various aromatic aldehydes to obtain chalcones (1), which on acetylation give 2′-acetoxychalcones (2). The 2′-acetoxy-chalcones (2) on treatment with hydrazine hydrate in either ethanol or ethylene glycol medium give the pyrazolines (3). The pyrazolines (3) were N-acetylated by their reaction with acetic acid to obtain N-acetyl derivatives (4) and N-benzoylated with benzoyl chloride to obtain N-benzoyl derivatives (5).

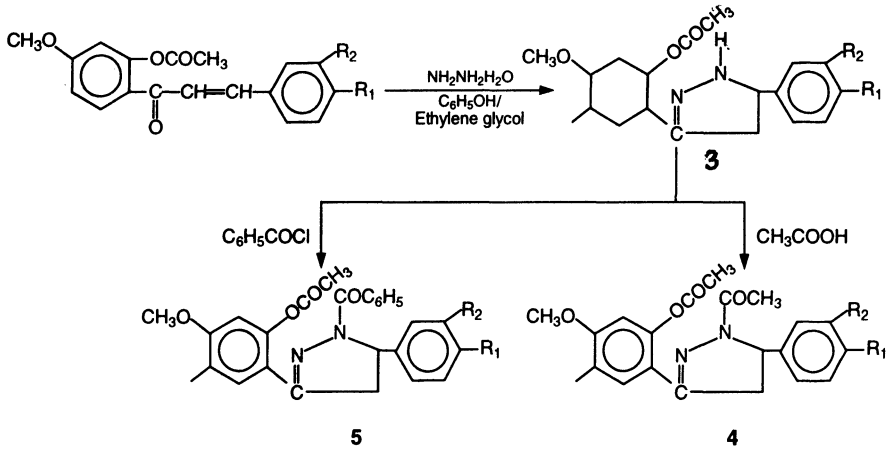
The compounds 3, 4 and 5 have been screened for their antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Aerobacter aerogenes*, *Vibrio cholerae*, *Klebsiella pneumoniae*, *Proteus vulgris* and *Shigella dysentery* at a concentration of 50 μg/mL by agar cup method[3].

Compounds 5a–c showed higher activity against all the bacteria studied except *V. cholerae*. Compound 4a was effective against *S. aureus*, *P. aeruginosa* and *S. typhi*. Compounds 3a and 3c were effective only against *P. aeruginosa* and *S. typhi*.

All the melting points have been determined in open capillaries and are uncorrected. IR spectra were taken on a Perkin-Elmer spectrophotometer and NMR on Jeol-90 spectrometer. Compounds were routinely checked for their purity on silica gel-G TLC plates.



Scheme 1



Scheme 2

(a) $R_1 = OCH_3$, $R_2 = H$; (b) $R_1 = H$, $R_2 = H$; (c) $R_1R_2 = —O—CH_2—O—$

Formation of 1H-3-(2-Acetoxy-4-Methoxy) Phenyl-5-Anisyl-Pyrazoline (3a)

2-Acetoxy-4,4′-dimethoxy-chalcone (2a), (0.01 mol, 3.2 g) and 99% hydrazine hydrate (0.015 mol, 0.6 mL) in ethanol (50 mL) was refluxed for 2 h. The reaction mixture was then concentrated and allowed to cool. The resulting solid was filtered, washed with ethanol and crystallised from ethanol to obtain yellow solid (3a). m.p. 142°C, yield 80%. Found: C 70%, H 5%, N 9.03%. Calculated for $C_{18}H_{17}O_3N_2$: C 69.9%, H 5.5%, N 9.06%. IR (nujol) (cm^{-1}): 3380 ν(—NH); 1540–1550 ν(C=N); 1620 ν(O—$COCH_3$); 1050 (O—CH_3 str.); 1310–1320 (O—CH_3 deformation). PMR ($CDCl_3$): δ 2.35 (s, 3H, —$COCH_3$); 3.25 (dd, 1H, >CHH_A-, J_{AB} = 18 Hz, J_{AX} = 4 Hz); 3.52 (dd, 1H, >CHH_B–, J_{AB} = 18 Hz, J_{BX} = 11 Hz); 3.8 (s, 6H, —OCH_3); 4.8 (dd, 1H, >CH_X-, J_{AX} = 4 Hz, J_{BX} = 11 Hz); 6.5 to 7.4 (m, 7H, Ar–H).

On the basis of properties, chemical reactions and spectral data, 3a was considered to be 1H-3 (2-acetoxy-4-methoxy) phenyl-5-anisyl pyrazoline (3a). Similarly 3b and 3c were prepared.

Formation of 1-Acetyl-3-(2-Acetoxy-4-Methoxy) Phenyl-5-Anisyl-Pyrazoline (4a)

A mixture of 3a (0.001 mol, 0.34 g) and acetic acid (20 mL) was refluxed for 2 h. The solution was then concentrated. On cooling the solid separated was filtered, washed with water and recrystallised from ethanol to obtain white crystalline compound (4a). Yield 80%, m.p. 158°C. Found: C 68, H 5.5, N 7%. Calculated for $C_{20}H_{20}O_4N_2$: C 68.18, H 5.68, N 7.95%), IR (nujol) cm^{-1}: 1665 ν(N—$COCH_3$); 1615 ν(C=O); 1515 ν(C=N); 1215 ν(C—N). PMR ($CDCl_3$): δ 2.35 (s, 6H, —$COCH_3$); 3.25 (dd, 1H, >CHH_A–J_{AB} = 18 Hz, J_{AX} = 4 Hz); 3.52 (dd, 1H, >CHH_B-, J_{AB} = 18 Hz, J_{BX} = 11 Hz); 5.5 (dd, 1H, CH_x-, J_{AB} = 4 Hz, J_{BX} = 11 Hz); 3.8 (s, 6H, —OCH_3) 6.3 to 7.4 (m, 7H, Ar—H).

On the basis of properties, chemical reactions and spectral data, 4a was considered to be 1-acetyl-3-(2-acetoxy-4-methoxy) phenyl-5-anisyl-pyrazoline (4a). Similarly 4b and 4c were prepared.

Formation of 1-Benzoyl-3-(2-Acetoxy-4-Methoxy) Phenyl-5-Anisyl-Pyrazoline (5a)

A mixture of 3a (0.001 mol, 0.3 g) and benzoyl chloride (0.002 mol) was dissolved in dry pyridine (10 mL) and stirred at room temperature for 1 h, after which the reaction mixture was treated with cold dil. HCl. The resulting solid was filtered, washed successively with water, cold NaOH (2%) and water and recrystallised from glacial acetic acid to get compound (5a); yield 85%, m.p. 120°C. (Found: C 72, H 5.6, N 6.00%; Calculated for $C_{25}H_{21}O_4N_2$: C 72, H 5.09, N 6.79%). IR (nujol) cm^{-1}: 1660 ν(C=O, N—C=O); 1610 ν(C=N); 1600 (benzene ring); 1210 ν(C—N); 1750 (—$OCOCH_3$); 1350 (—OCH_3 str.); 1040 (—OCH_3 deformation). PMR ($CDCl_3$): δ 3.35 (dd, 1H, >CHH_A-, J_{AB} = 16 Hz, J_{AX} = 4 Hz) 3.55 (dd, 1H, >CH_BA, J_{AB} = 16 Hz, J_{BX} = 11 Hz); 3.75 (s, 3H, —$COCH_3$); 4.1 (s, 6H, —OCH_3); 5.85 (dd, 1H, >CH_x-, J_{AX} = 4 Hz, J_{BX} = 11 Hz); 6.5 to 8.3 (m, 12H, Ar—H).

On the basis of properties, chemical reactions and spectral data, 5a, was considered to be 1-benzoyl-3(2-acetoxy-4-methoxy) phenyl-5-anisyl-pyrazoline. Similarly 5b and 5c were prepared.

TABLE-1
PHYSICAL DATA OF THE COMPOUNDS

S.No.	R_1	R_2	m.p. (°C)	Yield in alcohol (%)	Yield in ethylene glycol (%)	Molecular formula
3a	—OCH_3	H	142	80	85	$C_{18}H_{17}O_3N_2$
3b	H	H	105	85	88	$C_{19}H_{20}O_4N_2$
3c	—O—CH_2—O—		130	78	80	$C_{19}H_{19}O_5N_2$
4a	—OCH_3	H	130	75	76	$C_{25}H_{21}O_4N_2$
4b	H	H	135	82	84	$C_{26}H_{24}O_5N_2$
4c	—O—CH_2—O—		165	80	85	$C_{26}H_{23}O_6N_2$
5a	—OCH_3	H	158	76	80	$C_{20}H_{20}O_4N_2$
5b	H	H	178	74	78	$C_{20}H_{20}O_4N_2$
5c	—O—CH_2—O—		182	78	85	$C_{21}H_{21}O_6N_2$

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