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Synthesis and Antibacterial Activity of Chalcone and 2-Amino Pyrimidine and Their Related Compound

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In the present work some biologically active substituted chalcone prepared through the reaction of 1-acetyl-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline with aldehyde and ethanol to give various chalcone and biologically active 4-[3′-(4″-nitro phenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-amino pyrimidine was prepared from chalcone, guanidine nitrate and ethanol, which reacts with *p*-acetyl amino benzene sulphonyl chloride with dry pyridine; it gives 4-[3′-(4″-nitro phenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-(4′-acetyl amino benzene sulphonamide).

Key words: Chalcome, 2-Amino pyrimidine, Antibacterial activity.

INTRODUCTION

4-[3′-(4″-Nitro phenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-amino pyrimidine and their related compounds are prepared in view of the fact that a number of related compounds are known to possess biological activity[1]. 1-Substituted-chalcone-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline (A_1) have been prepared through the reaction of 1-acetyl-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline and aryl aldehyde by the Claisen-Schmidt condensation[2]. Previous ketone was prepared by this method[3, 4].

1-Substituted-chalcone-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline on condensation with guanidine nitrate in ethanol gave 4-[3′-(4″-nitro phenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-amino pyrimidine[5] (A_2). The reaction of (A_2) with *p*-acetyl amino benzene sulphonamide gave *p*-acetanilide sulphonyl derivatives (A_3).

RESULTS AND DISCUSSION

The products were screened for antibacterial activity by paper-disc method at a concentration of 10 μg using gram positive bacteria *Staphylococcus aureus* and gram negative bacteria *Escherichia coli.* The compounds possess moderate to good activity against both strains in comparison with ampicillin, pennicillin and tetracycline. The standard antibiotics showed zone of inhibition as under:

	S. aureus	*E. coli*
Ampicillin (10 μg)	12.0 mm	6.0 mm
Penicillin (10 units)	10.0 mm	6.0 mm
Tetracycline (10 μg)	18.0 mm	16.0 mm

EXPERIMENTAL

All melting points were taken in open capillary tubes and are uncorrected. IR spectra in KBr were recorded on Perkin-Elmer-377 spectrophotometer. NMR spectra were recorded on Hitachi NMR-300 using TMS as an internal standard. All compounds gave satisfactory elemental analysis.

General method for the preparation of 1-substituted-chalcone-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline [A_1]

A mixture of 1-acetyl-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline (0.01 mol) and aromatic aldehyde (0.01 mol) in ethanol (30 mL) and KOH solution (40%, 25 mL) was kept overnight at room temperature. The content was than poured over crushed ice and acidified with dil. HCl. The solid separated was filtered, washed with distilled water, dried and crystallised from glacial acetic acid. IR (KBr): 3210 ν(—NH), 1320 ν(CH_2 pyrazoline), 1625 ν(C=N), 1260 cm^{-1} ν(C—N).

General method for the preparation of 4-[3′-(4″-nitro phenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-amino-pyrimidine [A_2]

A mixture of 1-substituted chalcone-3-(4′-nitro phenyl)-5-(4′-methoxy phenyl)-2-pyrazoline (0.01 mol), guanidine nitrate (0.015 mol) and sodium hydroxide (0.045 mol in 2 mL water) in ethanol (50 mL) was refluxed for 6 h. The content was than poured over crushed ice and acidified with dil. HCl. The solid separated was filtered, washed with distilled water, dried and crystallized from ethanol. IR (KBr): 1530 ν(C—NO_2), 1356 ν(—CH_2 pyrazoline), 1588 ν(—C=N), 1664 ν(—N—H bend), 3360 ν(NH), 1320 ν(—C—N), 2800 ν(—O—CH_3). NMR spectra: The PMR spectra of **2c**, 7.2–8.0 (13H, Ar—H), 5.8 (2H, —NH_2), 3.1 (1H, —CH), 2.5 (2H, —CH_2), 2.3 (3H, —OCH_3).

General method for the preparation of 4-[3′-(4″-nitro phenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-(4′-acetyl amino benzene sulphonamide) [A_3]

A mixture of 4-[3′-(4″-nitrophenyl)-5′-(4″-methoxy phenyl)-2′-pyrazoline]-6-aryl substituted-2-amino pyrimidine (0.01 mol) and *p*-acetyl amino benzene sulphonyl chloride (0.012 mol) in dry pyridine (20 mL) was heated to 70–75°C on a water bath for 4 h. The content was than poured over crushed ice and acidified with dil. HCl. The solid separated was filtered, washed with hot water, dried and crystallized from acetic acid. IR ν(KBr): 1530 ν(—C—NO_2), 1360 ν(—CH_2 pyrazoline), 1588 ν(—C=N), 1325 ν(—NH), 3215 ν(—CONH), 2810 ν(—OCH_3), 1182 ν(—SO_2NH). NMR spectra: The PMR spectra of **3d**, 7.3–8.2 (17H, Ar—H), 6.3 (1H, —NH), 3.1 (1H, —CH), 2.4 (2H, —CH_2), 2.1 (3H, —CO—CH_3).

Reaction:

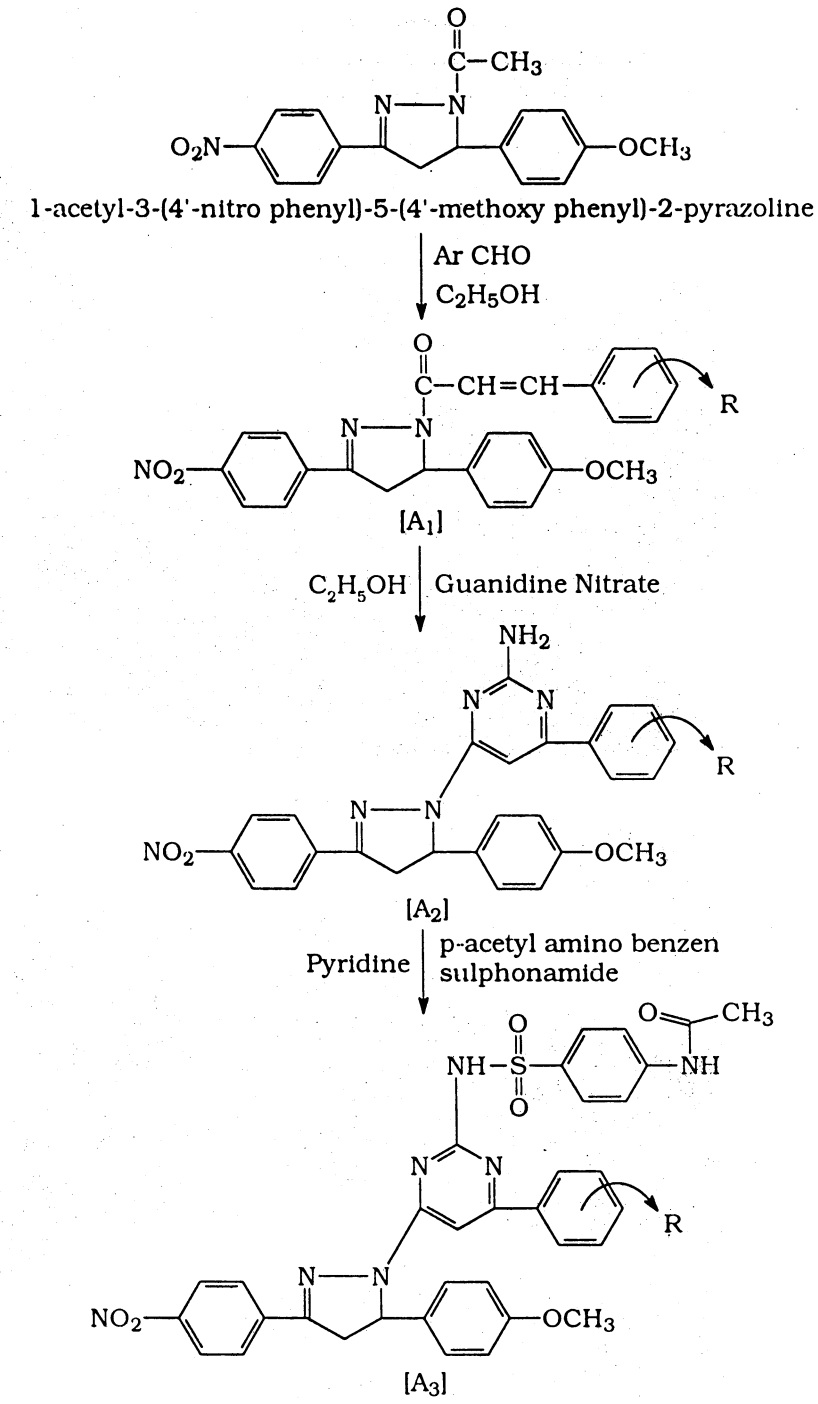
O
C–CH3
N–N
O2N
OCH3
1-acetyl-3-(4'-nitro phenyl)-5-(4'-methoxy phenyl)-2-pyrazoline
Ar CHO
C2H5OH
C–CH=CH
R
NO2
OCH3
[A1]
C2H5OH
Guanidine Nitrate
NH2
[A2]
Pyridine
p-acetyl amino benzen sulphonamide
NH–S
NH
CH3
[A3]

TABLE-1
ANALYTICAL AND PHYSICAL DATA OF COMPOUNDS
1(a–d), 2(a–d) AND **3(a–d)**

Compd.	m.p. (°C)	m.f.	% Analysis, Found (Calc.)		
			C	H	N
1a	135	$C_{25}H_{21}N_3O_4$	70.25 (70.62)	4.91 (4.59)	13.83 (13.81)
1b	127	$C_{25}H_{21}N_4O_6$	53.40 (5.80)	4.43 (4.23)	11.80 (11.50)
1c	115	$C_{27}H_{27}N_3O_6$	56.25 (56.28)	5.52 (5.62)	11.00 (11.62)
1d	128	$C_{25}H_{21}N_3O_4Cl$	54.90 (54.92)	4.54 (4.34)	9.03 (9.50)
2a	142	$C_{26}H_{21}N_6O_3$	57.09 (57.10)	4.51 (4.60)	18.05 (18.00)
2b	172	$C_{26}H_{21}N_7O_5$	51.05 (51.10)	4.10 (4.12)	19.35 (19.22)
2c	122	$C_{28}H_{27}N_6O_5$	53.75 (53.62)	5.12 (5.10)	15.93 (16.00)
2d	162	$C_{26}H_{21}N_6O_3Cl$	52.33 (52.44)	4.19 (4.20)	16.73 (16.60)
3a	124	$C_{32}H_{29}N_7O_6S$	50.03 (50.12)	4.50 (4.60)	15.43 (15.40)
3b	154	$C_{32}H_{29}N_8O_8S$	58.11 (58.10)	4.20 (4.22)	18.15 (18.16)
3c	135	$C_{34}H_{35}N_7O_8S$	58.20 (58.23)	4.99 (4.92)	13.98 (13.90)
3d	127	$C_{32}H_{29}N_7O_6SCl$	56.97 (56.98)	4.22 (4.21)	14.26 (14.27)

Where, a = -H, b = 3-NO_2, c = 3,4-$(OCH_3)_2$, d = 3-Cl

TABLE-2
ANTIBACTERIAL ACTIVITY OF COMPOUNDS

Compd.	Zone of inhibition		Compd.	Zone of inhibition	
	Staphylococcus aureus	*Escherichia coli*		*Staphylococcus aureus*	*Escherichia coli*
1a	7	6	**2c**	7	6
1b	10	6	**2d**	12	10
1c	8	6	**3a**	7	6
1d	6	10	**3b**	12	6
2a	8	7	**3c**	12	9
2b	12	6	**3d**	8	6

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