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Synthesis of 3-(2-hydroxy substituted phenyl)-4-(o-methyl benzoyl)-5-(substituted chloro aldehyde) -1-pyridyol pyrazoles

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ABSTRACT

Some new 3-(2-hydroxy substituted phenyl)-4-(*o*-methyl benzoyl)-5-(substituted chloro aldehyde) -1-pyridyol-pyrazoles (3) have been synthesized by the action of isoniazid on 3-aroyl flavones (2) in pyridine medium. Structures of these compounds have been established by spectral (IR, NMR and UV) and elemental analysis. The compounds were tested for their antimicrobial activities and because of electronegative fluorine atom the compounds showed enhanced antimicrobial activities. Heterocyclic compounds are well known for their wide range of biological applications out of which pyrazoles occupy unique position due to dominant applications. Pyrazoles are important nitrogen-containing five-member ring heterocyclic compounds.

I. INTRODUCTION

In the same way substituted pyrazoles constitute in the field of agricultural and medicinal chemistry because of their broad spectrum biological activities[1-3]. They are widely used as fungicide,[4] insecticide,[5] herbicide,[6,7] and antitumor agent.[8] Pyrazoles are anti-diabetic[9], anti-inflammatory[10], anti-parasitic[11], anti-oxidant[12], anti-cancer agents[13], anti-microbial[14], anti-depressant[15] and anti-protozoa[16].

II. REVIEW OF LITERATURE

Pyrazoles have been synthesized by different workers, 3-substituted 1-phenyl-1H-pyrazole-4-carbaldehydes and the corresponding ethanones by Pd-catalyzed cross-coupling reactions were synthesized by EgleArbaciauskiene[17].

R.S. Abdel Hameed had synthesized Pyrazole as corrosion inhibitor pyrazole derivatives for C- Steel in hydrochloric acid medium[18].

R. Mallikarjuna Rao had reported pyrazolo[3,4-c]pyrazole derivatives bearing indole moiety showing antimicrobial activity[19].

Anticancer and antimicrobial activities of some synthesized pyrazole and triazole derivatives had been reported by Eman M. Flefel[20].

Cyanopyridone derivatives pyrazole showing antimicrobial activity had been reported by Shridhar Malladi[21].

B. Chandrakantha had reported T3P mediated quinoline substituted pyrazole derivatives showing antibacterial[22].

III. EXPERIMENTAL

1. Preparation of flavanones (Ia-f):

1,3 diaryl-1,3- propanedione (0.01M) and fluoro substituted aldehyde (p-chloro- benzaldehyde, m-chloro-benzaldehyde, o-chloro-benzaldehyde) (0.01M) were reflux in ethanol (25-30 ml) for about 1 hour containing few drops of piperidine. The reaction mixture was cooled and the product separated was crystallized from ethanol-acetic acid mixture. List of the 3-aroyl flavanones (Ia-f) synthesized is as.

Ia) 2-(4′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-7-methyl flavanone.
Ib) 2-(3′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-7-methyl flavanone.
Ic) 2-(2′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-7-methyl flavanone.
Id) 2-(4′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-6-methyl flavanone.
Ie) 2-(3′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-6-methyl flavanone.
If) 2-(2′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-6-methyl flavanone.

2. Oxidation of flavanones:

The substituted flavanones (Ia-f) were oxidized by DMSO-I_2 to obtain substituted flavones. Physical characterization and data of synthesized flavones (II a-f) is given in table 1.

IIa) 2-(4′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-7-methyl flavone.
IIb) 2-(3′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-7-methyl flavone.
IIc) 2-(2′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-7-methyl flavone.
IId) 2-(4′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-6-methyl flavone.
IIe) 2-(3′- chloro benzaldehyde)-3-(2′-methyl) benzoyl-6-methyl flavone.
IIf) 2-(2′- chloro benzaldehyde)-3-(2′-methyl) benzoyl 6-methyl flavone.

3. Preparation of 3-(2-hydroxy substituted phenyl)-4-(o-methyl benzoyl)-5-(chloro substituted aldehyde) -1-pyridyol-pyrazoles (IIIa-f):

3-aroyl flavone. (IIa-f) (0.1M) were refluxed with isoniazid (0.2M) for 8-10 hours in pyridine solvent. The reaction mixture was decomposed by acidified water, filtered and wash with sufficient water. It was crystallized from ethanol-acetic acid mixture to obtain white crystalline product, yield 60-70%. Physical characterization and data of synthesized 3-(2-hydroxy substituted phenyl)-4-(o-methyl benzoyl chloride)-5-(chloro substituted aldehyde) -1-pyridyol-pyrazoles (IIIa-f) is given in table 2. List of the pyrazoles synthesized is as,

IIIa) 3-(2′-hydroxy-4′-methyl phenyl)-4-(o-methyl benzoyl)-5-(4′- chloro benzaldehyde) -1-pyridyol-pyrazole.
IIIb) 3-(2′-hydroxy-4′-methyl phenyl)-4-(o-methyl benzoyl)-5-(3′- chloro benzaldehyde) -1-pyridyol-pyrazole.
IIIc) 3-(2′-hydroxy-4′-methyl phenyl)-4-(o-methyl benzoyl)-5-(2′- chloro benzaldehyde) -1-pyridyol-pyrazoles.
IIId) 3-(2′-hydroxy-5′-methyl phenyl)-4-(o-methyl benzoyl)-5-(4′- chloro benzaldehyde) -1-pyridyol-pyrazoles.
IIIe) 3-(2′-hydroxy-5′-methyl phenyl)-4-(o-methyl benzoyl)-5-(3′- chloro benzaldehyde) -1-pyridyol-pyrazole.
IIIf) 3-(2′-hydroxy-5′-methyl phenyl)-4-(o-methyl benzoyl)-5-(2′- chloro benzaldehyde) -1-pyridyol-pyrazole.

Spectral determination of IIIb

IR (V_{max}): 3400 cm^{-1}v(C-OH); 550 cm^{-1}v(C-Br); 1550 cm^{-1}v(C=N); 1200 cm^{-1}v(C-N);
1150cm^{-1}v (C-O);1150 cm^{-1}v

NMR : δ 2.4(s, 3H, -CH_3); δ 3.6(d, 1H, -CH); δ 6.8(d, 1H, -CH); δ 8 to8.5 (m,15H, Ar-H);
δ 11.8(s, 1H, -OH).

UV (λ_{max}): 280 nm

Table 1. Physical Characterization and data of synthesized flavones

Compound	R_1	R_2	R_3	R_4	R_5	Molecular Formula	Molecular Weight	MP^{O}C	%Yield
IIa	CH_3	H	Cl	H	H	$C_{24}H_{17}O_3Cl$	388.5	173	65
IIb	CH_3	H	H	Cl	H	$C_{24}H_{17}O_3Cl$	388.5	162	65
IIc	CH_3	H	H	H	Cl	$C_{24}H_{17}O_3Cl$	388.5	183	60
IId	H	CH_3	Cl	H	H	$C_{24}H_{17}O_3Cl$	388.5	189	65
IIe	H	CH_3	H	Cl	H	$C_{24}H_{17}O_3Cl$	388.5	160	65
IIf	H	CH_3	H	H	Cl	$C_{24}H_{17}O_3Cl$	388.5	185	60

Table 2. Physical Characterization and data of synthesized 3-(2-hydroxy substituted phenyl)-4-(o-methyl benzoyl)-5-(chloro substituted benzaldehyde) -1-pyridyol-pyrazoles

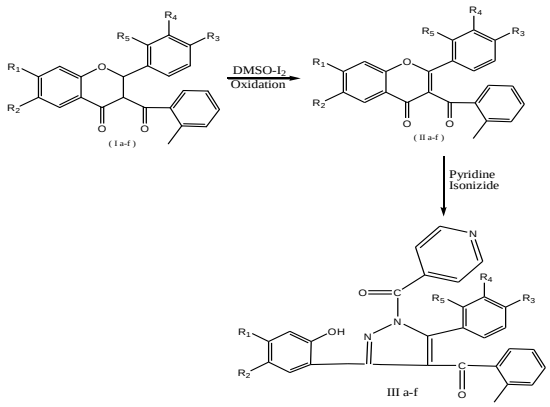
Compound	R_1	R_2	R_3	R_4	R_5	Molecular Formula	Molecular weight	MP^{O}C	%N Cal. (Found)
IIIa	CH_3	H	Cl	H	H	$C_{30}H_{21}O_3N_3Cl$	506.5	360	8.51 (8.50)
IIIb	CH_3	H	H	Cl	H	$C_{30}H_{21}O_3N_3Cl$	506.5	368	8.53 (8.48)
IIIc	CH_3	H	H	H	Cl	$C_{30}H_{21}O_3N_3Cl$	506.5	379	8.50 (8.49)
IIId	H	CH_3	Cl	H	H	$C_{30}H_{21}O_3N_3Cl$	506.5	378	8.57 (8.52)
IIIe	H	CH_3	H	Cl	H	$C_{30}H_{21}O_3N_3Cl$	506.5	362	8.58 (8.52)
IIIf	H	CH_3	H	H	Cl	$C_{30}H_{21}O_3N_3Cl$	506.5	350	8.59 (8.50)

Antimicrobial activities of synthesized pyrazoles

Antimicrobial screening was done by using cup plate method at a concentration of 100µg/ml. The compounds were evaluated for antimicrobial activity against P. aeruginosa, S. aureus, C. frundii, E. coli, P. mirabilis and S. typhi. The results of antimicrobial data are summarized in table 1. All compounds show the moderate to good activity. (Zone of inhibitions in mm).

Organisms	IIIa	IIIb	IIIc	IIId	IIIe	IIIf
P. aeruginosa	10	12	14	12	13	10
S. aureus	15	14	10	11	13	14
C. frundii	13	12	10	11	14	13
E. coli	12	12	11	10	15	14
P. mirabilis	13	13	10	10	14	12
S. typhi	14	12	12	12	14	13

Strongly active range; >12 mm, moderately active range: 8-12 mm, weakly active range: < 8 mm. inactive —



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