SYNTHESIS AND CHARCTERISATION OF SOME NEW PYRAZOLINE DERIVATIVES AS ANTIMICROBIAL AGENTS

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Abstract:
Heterocyclic nitrogenous compounds and their fused analogues represent an important class of heterocyclic compounds. They exist in numerous natural products, display a wide range of biological and pharmaceutical activities. Pyrazolines are well known important nitrogen containing five member heterocyclic compounds Some new pyrazolines have been synthesized by the action of isoniazid on 3-aroyl flavanones in pyridine medium. In this synthesis p-cresol and m-cresol are used as starting material. Isoniazid is use as anti tuberculosis drug. Structures of this compound have been established by spectral and elemental analysis.
Keywords: Chalcones, Isonizid Pyrazolines, Antimicrobial activities

Introduction:

Heterocyclic compounds are well known for their wide range of biological applications out of which pyrazolines occupy unique position due to dominant applications. Pyrazolines are known to possess antimicrobial, ant tubercular, antiviral, anti HIV, molluscicidal and cerebroprotective properties . Pyrazolines are and important nitrogen-containing five-member ring heterocyclic compounds. Pyrazoline derivatives have been found to possess a broad spectrum of biological activities such as tranquillizing, muscle relaxant, psychoanaleptic, anti-convulsant, antihypertensive, and antidepressant activities[1,2]Pyrazolines derivatives are also used as Anesthetics [3], Analgesic [4],Antitubercular [5], Antitumor [6], Immunosuppressive [7], Antidepressant [8, 9], Cerebroproctive[10], Antidiabetic[11-12], Anticancer [13], Antiviral [14], anticonvulsant [15], molluscicidal [16], Insecticides [17,18], Fungicides[19], Antiinflammatory[20,21], Herbicides[22], Antiimplanatory[23], Antimicrobial and antibacterial [24&19]

One of the important applications of pyrazoline is the use of pyrazolines as a fluorescent brightening agent[25]. They can absorb light of 300-400 nm and emit blue fluorescence. Pyrazolines are also acting as whole transporting material in OELD (organic electroluminescent device) because of formation of p-π conjugated system due to one of the nitrogen atom. Bleaching Agents, Luminescent, Fluorescent [26].

The literature survey clearly indicates that 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ^2- pyrazolines are not yet synthesized. It was, therefore thought of interest to synthesize 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ^2- pyrazolines from 3-aroyl flavanones.
Thus the present work deals with synthesis of 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ^2- pyrazolines from 3-aroyl flavanones (scheme) and Isoniazid in pyridine medium . Structures of this compound have been established by spectral and elemental analysis.

Experimental

Melting points are uncorrected. IR spectra in KBr were recorded on PE-983/PE-781IR spectrophotometer. NMR in DMSO on Varian EM 390-cw NMR spectrophotometer and UV on Varian Cary 239 OUV spectrophotometer.

(1) Preparation of 1,3-diaroyl-1,3 propadione (1a – 1f)

2-benzoyloxy acetophenone was dissolved in dry pyridine. The solution was warmed up to 60^{o}C and pulverized KOH was added slowly with constant stirring. After about 4 hours the reaction mixture was acidified by adding ice cold HCl. The brownish yellow product obtained was filtered, wash with sodium bicarbonate solution and sufficient water. The product obtain was crystallized from ethanol-acetic acid mixture.

(2) Preparation of 3-aroyl flavanones (2a-2f)

1,3-diaroyl-1,3 propadione (1a – 1f) and aromatic aldehydes (p-chlorobenzaldehyde, m-chlorobenzaldehyde and o-chlorobenzaldehyde) where reflux for about 1 hours in ethanol containing a few drops of piperidine. The resulting mixture was cool and the product separated was crystallized from ethanol-acetic acid mixture. The structure of this compound where confirm by spectral analysis.

Spectral interpretation of 3a:

IR (νmax):1650 cm^{-1} ν(C=O); 1615 cm^{-1} ν(C=O);1590-1585 cm^{-1} ν(C=C);1245 cm^{-1} ν(C-O-C).

^{1}H NMR: δ2.30(S, 3H, Ar-CH_3); 3.80(S,3H Ar-O-CH_3);6-7-8.3(m,11HAr-H)

UV(λ max):322nm.

(3) Preparation of 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ^{2}- pyrazolines (4a-4f)

3-aroyl flavanones where reflux with isoniazid for 8 to 10 hours in pyridine solvent. The reaction mixture was decomposed by acidified water, filtered and wash with sufficient water. The product obtain was crystallized from ethanol-acetic acid mixture. To obtain a crystalline solid. Yield 60 – 80%.

Spectral interpretation of 4a:

IR(νmax):1625cm^{-1} ν(C=O);3350 cm^{-1} ν(OH);1620 cm^{-1} ν(C=N);1500 cm^{-1} ν(C=C);1390 cm^{-1} ν(C-N);1035 cm^{-1} ν(C-O)(Phenol)

^{1}H NMR: δ1.9(S, 3H,-CH_3); 7.2-7.6(m,17H,-Ar-H); 12(S,1H,-OH).

UV(λ max):256nm.

TABLE 1

Physical Characterization data of Synthesized Compound 3-Aroyl flavanones (3a-3f)

Compound	R_1	R_2	R_3	R_4	R_5	R_6	Yield (%)	M.P.(^{o}C)	Molecular Formula
3a	H	H	CH_3	H	H	Cl	85	132	$C_{23}H_{17}O_3Cl$
3b	H	H	CH_3	Cl	H	H	85	138	$C_{23}H_{17}O_3Cl$
3c	H	H	CH_3	H	Cl	H	85	148	$C_{23}H_{17}O_3Cl$
3d	H	CH_3	H	H	H	Cl	75	135	$C_{23}H_{17}O_3Cl$
3e	H	CH_3	H	Cl	H	H	90	145	$C_{23}H_{17}O_3Cl$
3f	H	CH_3	H	H	Cl	H	85	136	$C_{23}H_{17}O_3Cl$

TABLE 2

Pyrazolines derivatives (4a-4f)

Compound	R_1	R_2	R_3	R_4	R_5	R_6	Yield (%)	M.P.(^{o}C)	Molecular Formula
4a	H	H	CH_3	H	H	Cl	65	252	$C_{29}H_{21}O_3N_3Cl$
4b	H	H	CH_3	Cl	H	H	75	250	$C_{29}H_{21}O_3N_3Cl$
4c	H	H	CH_3	H	Cl	H	80	249	$C_{29}H_{21}O_3N_3Cl$
4d	H	CH_3	H	H	H	Cl	75	254	$C_{29}H_{21}O_3N_3Cl$
4e	H	CH_3	H	Cl	H	H	80	252	$C_{29}H_{21}O_3N_3Cl$
4f	H	CH_3	H	H	Cl	H	80	253	$C_{29}H_{21}O_3N_3Cl$

SCHEME

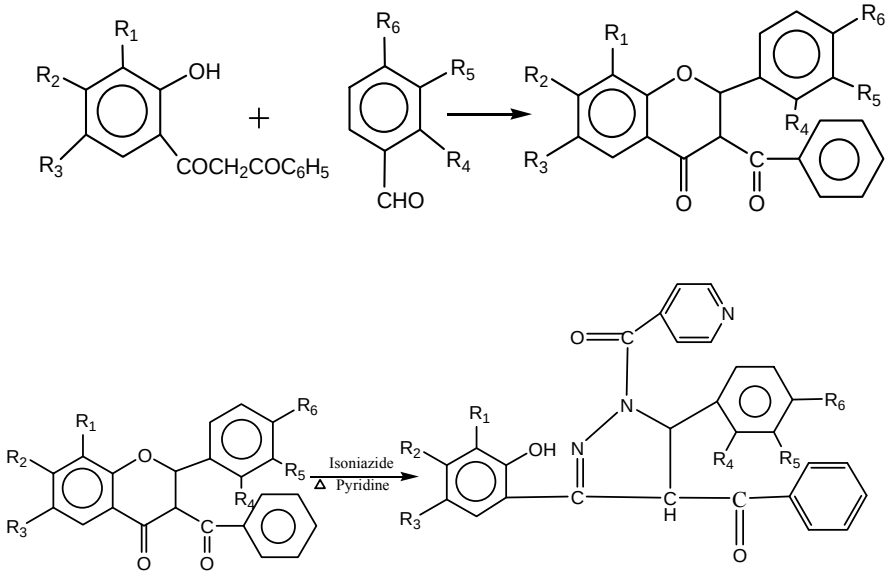

Table:-Antimicrobial activity of synthesized pyrazoline derivatives

Bacteria (zone of inhibition)						Fungi (zone of inhibition)			
Entry	**A**	**B**	**C**	**D**		**A**	**B**	**C**	**D**
4a	**13**	**17**	**20**	**14**		**-ve**	**RG**	**RG**	**-ve**
4b	**16**	**13**	**21**	**12**		**RG**	**RG**	**-ve**	**RG**
4c	**-**	**21**	**17**	**16**		**RG**	**-ve**	**-ve**	**RG**
4d	**-12**	**15**	**16**	**17**		**-ve**	**RG**	**RG**	**ve**
4e	**13**	**-**	**-**	**-**		**RG**	**-ve**	**RG**	**-ve**
4f	**16**	**-**	**20**	**15**		**RG**	**-ve**	**-ve**	**RG**

(Zone of Inhibition in mm)

A= Escherichia coli, B=Salmonella typhi, C= Staphylococcus aureus, D=Bacillus subtilis
E= Aspergillusniger F=penicilliumchrysogenum, G=Fusariummoneliforme,
H=Aspergillusflavus
- = No Antibacterial activity, RG= Reduced Growth (Moderate Activity)
-ve = Growth (Antifungal Activity Observed)

Conclusions:-

In conclusion, we have reported an efficient procedure for the synthesis of pyrazolines in pyridine medium. The major advantage of this method is that the ease of work-up. This method also offers some other merits such as pure synthesis, high yields of products, and use of various substrates, which make it useful and attractive procedure for the synthesis pyrazolines.

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