Synthesis and Antimicrobial Activity of Some Iodo-Substituted 3,5-Diaryl Pyrazolines and Pyrazoles

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Some iodo-substituted *ortho*-hydroxy chalcones, flavanones and iodo-substituted 3,5-diaryl pyrazolines and pyrazoles were synthesized and tested for antibacterial activities against *Staphylococcus aureus*, *Escherichia coli*, *Proteus mirabilis*, *Enterobacter aerogenes*, *Pseudomonas aeruginosa* and antifungal activities against *Curvularia* and *Colletotrichum*. Title compounds were found effective against both bacteria (MIC 25–400 μg/mL) and fungal species (58–100% spore germination inhibition).

INTRODUCTION

Pyrazolines and substituted pyrazolines attracted considerable attention due to their bactericidal[1], fungicidal[2, 3], insecticidal[4] and anti-inflammatory[5] properties. Similarly substituted pyrazoles have been reported to possess antimicrobial, insecticidal antiinflammatory and antidiabetic activities[6, 7]. Pyrazolines and pyrazoles have been reported to be synthesized usually by the action of nucleophiles such as hydrazine, phenylhydrazine, etc. on chalcones, flavanones, β-diketones and flavones in pyridine solvent[8, 9].

Literature survey showed that iodo-substituted 3,5 diarylpyrazolines and pyrazoles have not been so far synthesized. With this background, it was thought interesting to synthesize iodo-substituted, 3,5-diarylpyrazolines and 3,5-diaryl pyrazoles and to study their antimicrobial activities.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 557 spectrophotometer. ^{1}H NMR spectra ($CDCl_3$) were recorded on Perkin-Elmer R-32 spectrophotometer. Purity of the compounds was checked on silica gel-G TLC plates. 2-hydroxy-3-iodo-5-methyl acetophenone, chalcone, 1,3-propanediones, flavones and flavanones were synthesised using known methods[10, 11]. These compounds were then used for the synthesis of various 3,5-diarylpyrazolines and 3,5-diarylpyrazoles.

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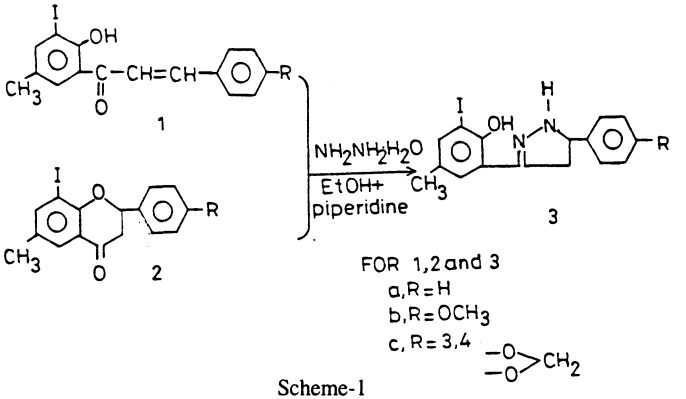
3,5-Diarylpyrazolines (3)

A mixture of chalcone (1) or flavanone (0.01 mol) (2) and hydrazine hydrate (0.02 mol) was refluxed in ethanol (25 mL) and piperidine (1 mL) for about 1.5–2 h. After cooling, the reaction mixture was acidified with dilute hydrochloric acid. The product was crystallised from ethanol (70%) (Scheme-1).



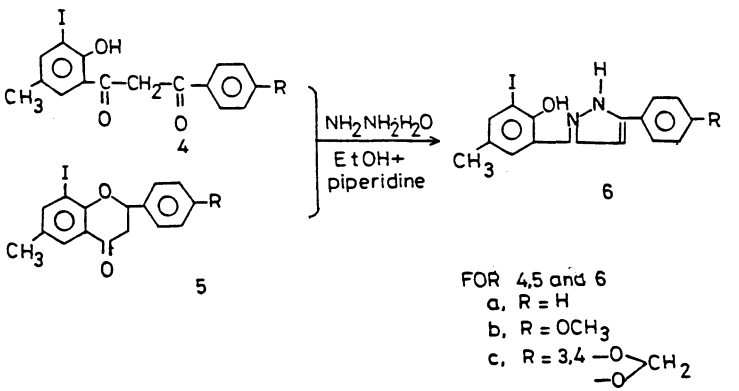
Scheme-1

(3b) IR: ν_{max} (Nujol) 3400 (broad) ν(O—H); 1600(s) ν(C=N); 1250(m) ν(Ar—H); 1180(m) ν(C—O stretching in phenols); 950 (m) ν(—N—O) and 700 (m) cm^{-1} ν(C—I); 1060(m) ν(CH_3—O stretching in ether).

UV-Vis (Chloroform): λ_{max} 255 and 320 nm corresponding to n → π* transition. PMR ($CDCl_3$): δ 2.20 (3H, s, Ar—CH_3); 3.58 (3H, s, O—CH_3); 2.96 (1H, dd, CHH_A); 3.40 (1H, dd, CHH_B); 4.70 (1H, t, C—H); 5.75 (broad, 1H, N—H); 6.6–7.3 (7H, m, Ar—H).

3,5-Diaryl pyrazoles (6)

Mixture of 1,3-propanedione (4) or flavone (5) (0.01 mol) and hydrazine hydrate (0.02 mol) was refluxed in ethanol (25 mL) containing piperidine (1 mL) for about 1 h. After cooling, the reaction mixture was acidified with dilute hydrochloric acid and the product was crystallised from ethanol (70%) (Scheme-2). The physical data of the sythesized compound are presented in Table-1.



Scheme-2

TABLE-1
PHYSICAL DATA OF COMPOUNDS*

Compound No.	R	m.p. (°C)	Yield %	m.f.
3a	H	194	67	$C_{16}H_{15}ON_2I$
3b	OCH_3	156	80	$C_{17}H_{17}O_2N_2I$
3c	3,4 	212	85	$C_{17}H_{17}O_3N_2I$
6a	H	152	75	$C_{16}H_{13}ON_2I$
6b	OCH_3	181	65	$C_{17}H_{15}O_2N_2I$
6c	3,4 	202	75	$C_{17}H_{13}O_3N_2I$

*All compounds gave statisfactory elemental analyses.

(6b) IR: ν_{max} (Nujol): 3400–3460 (br), ν(O—H) (br), 1585–1600 (m), ν(C=C and C=N); 1260 ν(Ar—O), 750 cm^{-1}.

UV-Vis (Chloroform): λ_{max} 367.7 nm (OD. 1.942) corresponding to $n \rightarrow \pi^*$ transition. PMR ($CDCl_3$): δ 2.6 (3H, s, Ar—CH_3); 3.1(1H, m, OH); 3.4 (1H, m, N—H, pyrole); 4.0 (3H, S, O—CH_3); 6.9–7.1 (1H, m, =CH—); 7.2–8.10 (7H, m, Ar—H).

Antibacterial Activity

The antibacterial activity of title compounds (minimum inhibitory concentration) was tested against *S. aureus*, *E. coli*, *Pr. mirabilis*, *E. aerogenes* and *Ps. aeruginosa* using known methods[10, 11]

Antifungal Activity

Antifungal activity of the compounds was evaluated by testing spore germination inhibition percentage of two fungal oraganisms, *viz.*, *Colletotrichum* and *Curvularia* using the method described earlier[10, 11].

RESULTS AND DISCUSSION

Antibacterial activity of iodo-substituted 3,5-diaryl pyrazoles and 3,5 pyrazolines is shown in Table-2. Table-3 shows the percentage inhibition of fungal spore germination by the title compounds.

The pyrazolines (3) were found effective towards both gram positive and gram negative bacteria while pyrazoles (6) were found to be effective towards only gram negative bacteria but inactive against gram positive *Staphylococci* up to 400 μg/mL, the highest concentration tested. The compounds were active in the MIC range of 50–200 μg/mL (*E. coli, E. aerogenes*), 50–100 μg/mL (*P. aeruginosa*), and 50–400 μg/mL (*Pr. mirabilis*).

The fungal species used in the present investigation are known plant pathogens. The compounds were more effective against *Colletotrichum* sp. than against *Curvularia* sp. All the compounds were effective in inhibiting 62–100% *Colletotrichum* spore germination and 57–75% *Curvularia* spore germination.

TABLE-2
ANTIBACTERIAL ACTIVITY OF SYNTHESIZED COMPOUNDS

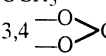
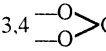
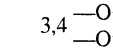
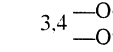
Compound No.	R	MIC (μg/mL)				
		S. aureus	*E. coli*	*Pr. mirabilis*	*E. aerogenes*	*Ps. aeruginosa*
3a	H	100	200	400	50	100
3b	OCH_3	25	200	400	50	50
3c	3,4 	25	200	200	50	50
6a	H	—	100	100	100	100
6b	OCH_3	—	50	100	100	100
6c	3,4 	—	100	100	100	50
Standard drug Chloramphenicol		12.5	6	12.5	12.5	12.5

TABLE-3
FUNGAL SPORE GERMINATION INHIBITION BY TITLE COMPOUNDS

Compound No.	R	% Spore germination inhibition	
		Colletotrichum	*Curvularia*
3a	H	62.00	57.90
3b	OCH_3	93.34	57.30
3c	3,4 	100.00	75.70
6a	H	97.78	62.00
6b	OCH_3	100.00	60.00
6c	3,4 	100.00	66.85

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