

Synthesis of Some New Substituted 3-(2-Hydroxy-5-Methyl-Phenyl)-4-Aroyl-5-Aryl Isoxazolines

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Seven different 3-aryylflavanones and 3-aryylchromanones were synthesised from 1,3-propanedione by literature method. The compounds **III(a)–III(g)** were reacted with hydroxylamine hydrochloride in pyridine medium to give **IV(a)–IV(g)**, 3-(2-hydroxy-5-methylphenyl)-4-aryyl-5-aryyl isoxazolines. The structures were confirmed on the basis of chemical and spectral analysis.

Key words: Synthesis, substituted 3-(2-hydroxy-5-methylphenyl)-4-aryyl-5-aryyl isoxazolines

INTRODUCTION

Isoxazolines can be effectively used as antibacterial¹, antitubercular, antiviral, antifungal, herbicidal and insecticidal agents^{2–5}.

Synthesis of isoxazolines has been reported by the action of $\text{NH}_2\text{OH}\cdot\text{HCl}$ on hydroxy chalcones and flavanones⁶. Borkhade *et al.*⁷ synthesised isoxazolines from *o*-hydroxychalcones and corresponding flavanones. Gimil Aziz *et al.*⁸ synthesised isoxazolines from fluorochalcones. Jamode⁹ reported the synthesis of 3,5-diaryl isoxazolines using ethylenediamine from 2'-hydroxy chalcones, flavanones and 3-arylidine flavanones. Rajput and Jamode¹⁰ have synthesised 3,5-diaryl isoxazolines from 2'-hydroxy-3-chlorochalcones in ethanol containing piperidine. Kedar¹¹ have reported the synthesis of 3,5-diarylisoxazolines in EtOH in presence of alkali. Kakade^{12(a)} synthesised 3,5-diaryl isoxazolines in DMSO using $\text{NH}_4\text{OH}\cdot\text{HCl}$. Chincholkar and Jamode^{12(b)} have synthesised some new 4-aryyl substituted isoxazolines using $\text{NH}_2\text{OH}\cdot\text{HCl}$ in methanol. Patil and Jamode¹³ have synthesised some new chloro-substituted 4-aryyl isoxazolines by condensation of $\text{NH}_2\text{OH}\cdot\text{HCl}$ with 3-aryylflavanones in dioxane containing little piperidine. Kedar¹¹ synthesised substituted 3,5-diaryl-4-aryyl isoxazolines in dioxane in presence of piperidine. Here we succeeded in synthesising substituted 3-(2-hydroxy-5-methylphenyl)-4-aryyl-5-aryyl isoxazolines using pyridine as a solvent.

EXPERIMENTAL

Melting points of all compounds were determined on Tempo melting point apparatus and are uncorrected. Compounds **I**, **II**, **III(a)–III(g)** and **IV(a)–IV(g)** were prepared in the laboratory by known method. m.p. and purity of compounds were checked by TLC on silica gel-G plates. The structures of compounds **III(a)** and **IV(e)** were confirmed by chemical analysis, IR and NMR spectra.

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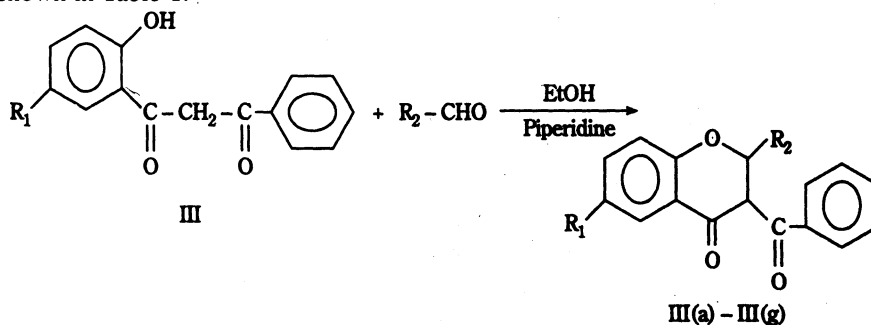
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Synthesis of Compounds I, II, III(a)–III(g)

Compounds I, II, III(a)–III(g) were synthesised by known literature method. 2-Benzoyl-oxy-5-methylacetophenone (II), m.p. 66°C was synthesised from 2-hydroxy-5-methylacetophenone (I), m.p. 54°C by benzylation. The compound (III), m.p. 90°C was synthesised from compound (II) by B.V.T. reaction.

Synthesis of 3-arylflavanones and 3-arylchromanones III(a)–III(g)

A mixture of 1-(2-hydroxy-5-methylphenyl)-3-phenyl-1,3-propanedione (III) (0.02 M) and an aromatic aldehyde (0.02 M) was refluxed in 30 mL ethanol containing 0.05 mL piperidine for 30 min and processing by literature method to give compounds III(a)–III(g). Physical data of compounds III(a)–III(g) are as shown in Table-1.



where $R_1 = \text{CH}_3$, $R_2 =$ as shown in Table-1.

TABLE-1
PHYSICAL DATA OF COMPOUNDS *III(a)–III(g)

Sr. No.	Compd. No.	R_2	m.f.	m.p. (°C)	Yield (%)
1.	III(a)		$\text{C}_{23}\text{H}_{18}\text{O}_3$	148	75
2.	III(b)		$\text{C}_{24}\text{H}_{20}\text{O}_4$	155	80
3.	III(c)		$\text{C}_{21}\text{H}_{16}\text{O}_4$	125	69
4.	III(d)		$\text{C}_{25}\text{H}_{20}\text{O}_3$	116	64
5.	III(d)		$\text{C}_{23}\text{H}_{15}\text{NO}_5$	120	68
6.	III(f)		$\text{C}_{23}\text{H}_{18}\text{O}_4$	146	60
7.	III(g)		$\text{C}_{24}\text{H}_{18}\text{O}_5$	136	56

*All compounds III(a)–III(g) gave satisfactory elemental analysis.

IR for III(a) (cm^{-1}): 1596–1568 (C=O) stretching of aroyl group), 1348 (pyrone), 1290–1173 (A—O), 1492 cm^{-1} (stretching vibration in aryl (C=C) bond).

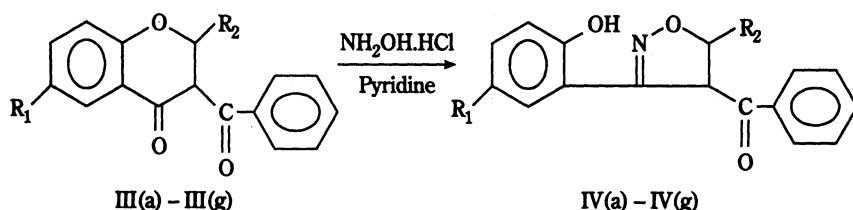
NMR for III(a): 2.35 δ (s, 3H, Ar—CH₃), 5.05 δ (d, 1H, C₃H, $J_{AB} = 12$ Hz), 6.05–6.13 δ (d, 1H, C₂H, $J_{AB} = 12$ Hz), 6.7–7.85 δ (m, 13H, Ar—H).

Synthesis of 3,5-diaryl-4-aryloxyisoxazolines

3-Benzoylflavanones and 3-benzoylchromanones (0.01 M) **III(a)–III(g)** and $\text{NH}_2\text{OH}\cdot\text{HCl}$ (0.02 M) were refluxed in 20 mL pyridine for 3–4 h. Then the reaction mixture was cooled, poured in water and acidified with 1 : 1 HCl. The obtained product was triturated with and crystallized from ethanol to give compounds **IV(a)–IV(g)** from the corresponding **III(a)–III(g)**.

Physical data for compounds **IV(a)–IV(g)** are given in Table-2.

Reaction:



where $R_1 = \text{CH}_3$, $R_2 =$ as shown in Table-2.

TABLE-2
PHYSICAL DATA OF COMPOUNDS **IV(a)–IV(g)***

Sr. No.	Compd. No.	R ₂	m.f.	m.p. (°C)	Yield (%)
1.	IV(a)		C ₂₃ H ₁₉ NO ₃	178	61
2.	IV(b)		C ₂₄ H ₂₀ NO ₄	170	69
3.	IV(c)		C ₂₁ H ₁₇ NO ₄	148	67
4.	IV(d)		C ₂₅ H ₂₁ NO ₃	60 (decomposes) 155 polymerises	62
5.	IV(d)		C ₂₃ H ₁₈ N ₂ O ₅	103	68
6.	IV(f)		C ₂₃ H ₁₉ NO ₄	168	58
7.	IV(g)		C ₂₄ H ₁₉ NO ₅	152	64

*All compounds **IV(a)–IV(g)** gave satisfactory elemental analysis.

IR for Compound IV(e) (cm^{-1}): 3652–3292 (—OH) stretching, 3069–3005 (C—H) stretching aromatic, 2965–2920 (C—H) stretching, 1792–1737 ((C=O) of aroyl group), 1536–1350 due to NO_2 group, 1216–1101 (CH_3 group), 979–938 cm^{-1} (C=N—O) stretching.

NMR for Compound IV(e): 2.30–2.37 δ (s, 3H, Ar— CH_3) 3.77 δ (d, 1H, H_B), 5.58 δ (d, 1H, H_A), 7.41–8.25 δ (m, 12H, Ar—H), 8.45 δ (s, 1H, Ar—OH).

Mechanism

Formation of isoxazoline involves 1,2 addition of NH_2OH to carbonyl group giving an adduct. The adduct then loses water molecule to give mono-oxime which on cyclisation and rearrangement gives 4-royl isoxazoline. The steps of mechanism are suggested by Barnes and Spriggs¹⁴

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