

SYNTHESIS OF ISOXAZOLYLIMIDAZOLIN-5-ONES

B. PRAMEELA, E. RAJANARENDAR and A. KRISHNA MURTHY

Department of Chemistry, Kakatiya University, Warangal 506009, India

Received May 31, 1988

Accepted July 6, 1988

1-(3-Methyl-5-styryl-4-isoxazolyl)-2-styryl-4-benzylideneimidazolin-5-ones (*III*) have been synthesized by the interaction of isoxazole Schiff bases (*I*) with 4-benzylidene-2-methyloxazol-5-one (*II*).

Methyl substituted five and six membered oxygen heterocycles have been converted into nitrogen analogues, bearing styryl group, on treatment with Schiff base^{1,2}. In this transformations we have utilized isoxazole Schiff bases in the synthesis of isoxazolyl quinazolin-4-ones³. In continuation of our studies in this direction we have studied the interaction of isoxazole anils with 4-benzylidene-2-methyl-5-oxazolones.

The required Schiff bases namely 4-benzylidenamino-3-methyl-5-styrylisoxazoles (*I*) were prepared starting from 3,5-dimethyl-4-nitroisoxazole⁴. Regioselective styrylation of 3,5-dimethyl-4-nitroisoxazole under Knoevenagel conditions followed by reduction of nitro group with stannous chloride-hydrochloric acid gave 4-amino-3-methyl-5-styrylisoxazole⁵, which on condensation with various benzaldehydes in refluxing ethanol afforded 4-benzylidenamino-3-methyl-5-styrylisoxazoles⁶.

The reaction of 4-benzylidene-2-methyl-5-oxazolone⁷ (*II*) with isoxazole anils (*I*) has been carried out by refluxing in glacial acetic acid for 3 h. Some of the products have separated from the clear reaction mixture on cooling whereas others precipitated on diluting the reaction mixture. Analytical and spectral data show the products to be 1-(3-methyl-5-styryl-4-isoxazolyl)-2-styryl-4-benzylideneimidazolin-5-ones (*III*).

The mechanism of the transformation involves the Michael addition of the oxazolone methyl group to the azomethine moiety, the ring opening of the oxazolone nucleus and recyclisation to the imidazolone ring¹.

The IR spectrum of *III* showed a peak at 1 680 cm⁻¹ due to imide carbonyl and another peak at 970 cm⁻¹ due to styryl group in *trans* configuration. The ¹H NMR spectrum showed singlet at δ 2.3 due to isoxazole methyl group. The two hydrogens of styryl ethylenic bond on isoxazole appear as multiplet between δ 6.4 and 6.8. The lone proton of the benzylidene moiety shows at δ 8.05 as a singlet. Another multiplet further in the lower field between δ 8.3 to 8.5 is assignable to the hydrogens of the ethylenic linkage of 2-styryl group. The aromatic protons appeared as complex

multiplet in the region from δ 7.3 to 7.6. The mass spectrum of *III*d shows molecular ion peak at m/z 491. The base peak of the spectrum appears at m/z 131 due to cinnamoyl cation.

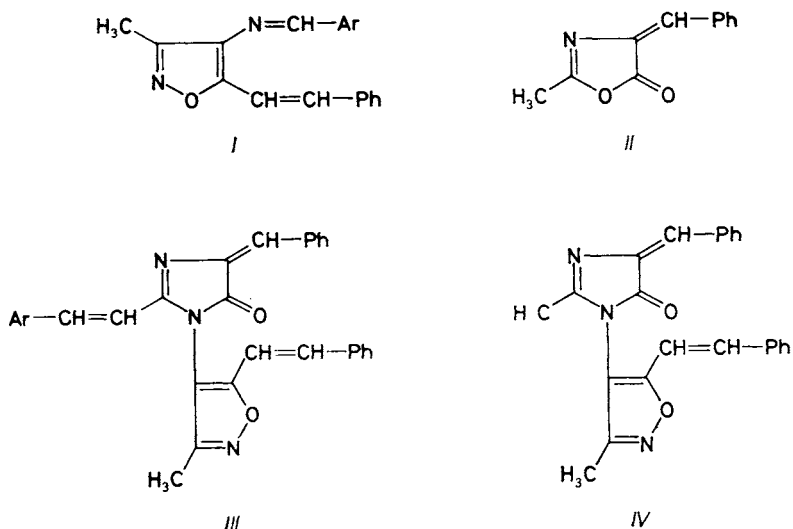
The structure of products *III* was further confirmed by unambiguous synthesis starting from 4-amino-3-methyl-5-styrylisoxazole. Reaction of this with oxazolone (*I*) in acetic acid gave 1-(3-methyl-5-styryl-4-isoxazolyl)-2-methyl-4-benzylideneimidazolin-5-one (*IV*a). Heating of *IV*a with benzaldehyde in 2-propanol for 4 hours gave a product identical with that of *III*a in all aspects, i.e. m.p., mixed m.p., TLC and superimposable IR spectra.

Utilization of the three ethylenic double bonds of *III* in variety of 1,3-dipolar cyclo-additions is under progress.

TABLE I
Analytical data of isoxazolylimidazolin-5-ones *III*

Compound	Ar ^a	Formula (M.w.)	M.p. °C	Calculated/Found		
				% C	% H	% N
<i>III</i> a	phenyl	C ₃₀ H ₂₃ N ₃ O ₂ (457.5)	205	78.77	5.03	9.19
				78.75	5.01	9.17
<i>III</i> b	4-tolyl	C ₃₁ H ₂₅ N ₃ O ₂ (471.5)	227	78.98	5.30	8.91
				78.99	5.32	8.90
<i>III</i> c	4-methoxyphenyl	C ₃₁ H ₂₅ N ₃ O ₃ (487.5)	210	76.38	5.13	8.62
				76.35	5.09	8.63
<i>III</i> d	4-chlorophenyl	C ₃₀ H ₂₂ N ₃ O ₂ Cl (491.9)	242	73.31	4.48	8.55
				73.30	4.47	8.56
<i>III</i> e	2-chlorophenyl	C ₃₀ H ₂₂ N ₃ O ₂ Cl (491.9)	226	73.31	4.48	8.55
				73.33	4.46	8.58
<i>III</i> f	4-nitrophenyl	C ₃₀ H ₂₂ N ₄ O ₄ (502.5)	273	71.71	4.38	11.15
				71.73	4.35	11.14
<i>III</i> g	3-nitrophenyl	C ₃₀ H ₂₂ N ₄ O ₄ (502.5)	265	71.71	4.38	11.15
				71.72	4.37	11.16
<i>III</i> h	4-dimethylaminophenyl	C ₃₂ H ₂₈ N ₄ O ₂ (500.5)	258	76.80	5.60	11.20
				76.78	5.61	11.19
<i>III</i> i	3,4-methylenedioxyphenyl	C ₃₁ H ₂₃ N ₃ O ₄ (469.5)	258	74.25	4.59	8.38
				74.28	4.60	8.37
<i>III</i> j	2,4-dichlorophenyl	C ₃₀ H ₂₁ N ₃ O ₂ Cl ₂ (527.4)	268	68.57	4.00	8.00
				68.56	4.01	8.02

^a All the compounds were recrystallized from petroleum ether and benzene.



EXPERIMENTAL

The melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 282 instrument. ^1H NMR spectra were scanned on a Varian EM-390 spectrometer using tetramethylsilane as an internal standard. Mass spectrum was scanned on a Varian MAT CH-7 instrument at 70 eV.

1-(3-Methyl-5-styryl-4-isoxazolyl)-2-styryl-4-benzylideneimidazolin-5-ones (III)

A mixture of oxazolone (1 mmol) and isoxazole Schiff base (1 mmol) was refluxed in glacial acetic acid for 3 h. The crystalline solid that separated from the clear solution on cooling was filtered and recrystallized from petroleum ether and benzene. In some cases, where the solid has not separated, the reaction mixture was diluted and processed to give solid. The analytical data of *III* are included in Table I.

1-(3-Methyl-5-styryl-4-isoxazolyl)-2-methyl-4-benzylideneimidazolin-5-one (IV)

A mixture of oxazolone (1 mmol) and 4-amino-3-methyl-5-styrylisoxazole (1 mmol) was refluxed in acetic acid for 3 h. The product separated on cooling was recrystallized from alcohol. m.p. 198°. For $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}_2$ (369.4) calculated: 74.79% C, 5.14% H, 11.38% N; found: 74.77% C, 5.15% H, 11.35% N.

Styrylation of IV

A mixture of *IV* (1 mmol) and benzaldehyde (1 mmol) was refluxed in 2-propanol for 4 h. The solid separated on cooling was filtered and recrystallized from petroleum ether and benzene.

The authors are thankful to Prof. P. S. Rao, Head, Department of Chemistry, Kakatiya University, Warangal, for providing the facilities. One of us (B.P.) is grateful to CSIR, New Delhi, for the Senior research fellowship.

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