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NOTE

A Novel Synthesis of Some Isomeric Isoxazoles

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β-(2′-Furyl)-acrylophenone dibromide (**Ia–c**) react with hydroxylamine hydrochloride in pyridine to give 3-(2″-hydroxy-3″-substituted-5″-chlorophenyl)-5-(2′-furyl)-isoxazoles (**IIa–c**) while in methanol the corresponding 3-(2′-furyl)-5-(2″-hydroxy-3″-substituted-5″-chlorophenyl) isoxazoles (**IIIa–c**) are obtained contrary to the isomerization of isoxazoles (**IIa–c**) in pyridine.

Isoxazoles are of vital importance as drugs. Okuda *et al.*[1] discovered their antibacterial properties. The antitubercular[2] and antifungal[3] activities of isoxazoles are also well known. Mittal and Singhal[4] synthesised antimicrobial isoxazoles from different substituted benzenediazonium chlorides. Basinski and Jerzmanowska[5] reported the formation of two isomeric isoxazoles from ω-formyl-*o*-hydroxyacetophenone and hydroxylamine. Thakar *et al.*[6] synthesised 3-(2′-furyl)-5-(2-hydroxyphenyl)-isoxazole from 1,3-propanediones by the action of hydroxylamine hydrochloride in methanol. Borkhade and Marathey[7] however have reported the formation of other isoxazoles by the reaction between *o*-hydroxydibenzoyl methane and hydroxylamine hydrochloride in pyridine. Recently Nair and Wadodkar[8] have reported the synthesis of isomeric isoxazoles from 1-(2′-furyl)-3-(2″-hydroxyphenyl)-1,3-propanedione in pyridine and methanol respectively. Isoxazoles also have been synthesised from chalconedibromides[9–13]. Literature survey reveals that isoxazoles and their isomers have not been prepared from 2-hydroxy-3-substituted-5-chloro-β-(2′-furyl)-acrylophenonedibromides (**Ia–c**). This prompted us to synthesise some isomeric isoxazoles from β-(2′-furyl)-acrylophenonedibromides.

The melting points were determined in an open capillary tube and are uncorrected. The IR spectra were scanned on Perkin-Elmer spectrophotometer using KBr pellets. The ^{1}H NMR spectra were recorded on "Varian CFT-20" in $CDCl_3$ using TMS as reference (chemical shifts in δ, ppm downfield from TMS). Purity of the compounds synthesised was tested by TLC on silica gel-G coated microscopic slides.

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β-(2′-Furyl)-acrylophenone dibromides **(Ia–c)** were prepared by literature method[14].

Synthesis of 3-(2″-hydroxy-5″-chlorophenyl)-5-(2′-furyl)-isoxazole (IIa)

Mixture of 2-hydroxy-5-chloro β-(2′-furyl)-acrylophenonedibromide **(Ia)** (0.01 mol) and hydroxylamine hydrochloride (0.012 mol) in pyridine (20 mL) was refluxed for 3 h. Contents were cooled, diluted with water and acidified with 1 : 1 HCl. The crude product thus obtained was crystallised from ethanol to get **(IIa)** (Scheme-1) in 78% yield, m.p. 147°C. % Analysis: Found C = 59.31; H = 2.76, N = 5.04%; $C_{13}H_8O_3NCl$ requires C = 59.65; H = 3.05; N = 5.35%.

IR (KBr): 3160–3130 cm^{-1} ν(—OH), 1610 cm^{-1} ν(C=C), 1575 cm^{-1} ν(>C=N—), 965–950 cm^{-1} ν(>C=N—O), 890, 830 cm^{-1} ν(2′-furyl), 740 cm^{-1} ν(C—Cl).

PMR ($CDCl_3$): 6.3–7.8 δ (m, 7H, Ar—H and heteroaromatic H), 12.1 δ (s, 1H, —OH).

Synthesis of 3-(2′-furyl)-5-(2″-hydroxy-5″-chlorophenyl)-isoxazole (IIIa)

Mixture of 2-hydroxy-5-chloro-β-(2′-furyl)-acrylophenone dibromide **(Ia)** (0.01 mol) and hydroxylamine hydrochloride (0.012 mol) in methanol (20 mL) refluxed for 5 h and cooled to obtain the product which was crystallized from ethanol to get the compound **(IIIa)** (Scheme-1) in 70% yield, m.p. 159°C. % Analysis: Found C = 59.20; H = 2.82; N = 4.97; $C_{13}H_8O_3NCl$ requires C = 59.65; H = 3.05; N = 5.35%).

IR (KBr): 3180 cm^{-1} ν(—OH), 1635 cm^{-1} ν(C—O), 1605, 1575 cm^{-1} ν(>C=N—), 880–850 cm^{-1} ν(2′-furyl), 735 cm^{-1} ν(C—Cl).

PMR ($CDCl_3$): 6.5–8.0 δ (m, 7H, Ar—H and heteroaromatic H), 11.8 δ (s, 1H, OH).

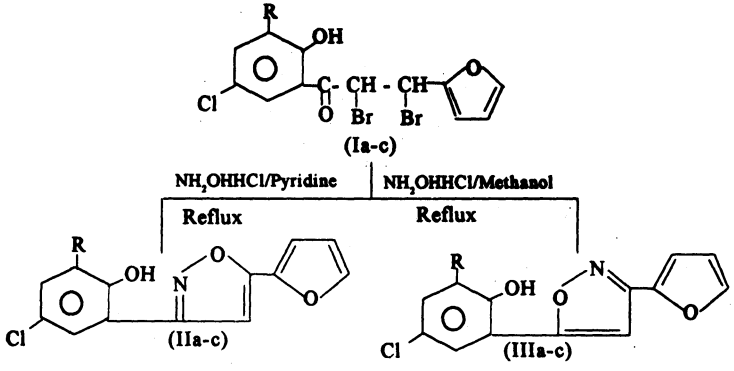
Other members of the series were synthesised in a similar manner and their characterisation data are given in Table-1.

TABLE-1
CHARACTERISATION DATA ISOXAZOLES (IIa–c) AND ISOMERIC ISOXAZOLES (IIIa–c)

Compd	R	m.p. (°C)	Yield (%)	m.f.	% Found (Calcd.)		
					C	H	N
IIb	NO_2	176	78	$C_{13}H_7O_5N_2Cl$	50.42 (50.89)	2.11 (2.28)	8.72 (9.13)
IIc	Br	136	75	$C_{13}H_7O_3NClBr$	45.52 (45.81)	1.66 (2.05)	3.80 (4.11)
IIIb	NO_2	172	82	$C_{13}H_7O_5N_2Cl$	50.50 (50.89)	1.98 (2.28)	8.68 (9.13)
IIIc	Br	164	70	$C_{13}H_7O_3NClBr$	45.37 (45.81)	1.85 (2.05)	3.67 (4.11)

The chemical properties and molecular formula of compound **(IIIa)** indicate that it is similar to compound **(IIa)**. However, the m.p. of **(IIa)** is 147°C and that

of **(IIIa)** is 159°C. The mixed melting point shows considerable depression. These facts clearly indicate that the compound **(IIIa)** is isomeric with compound **(IIa)**. Compound **(IIa)** might have been formed *via* 1,2-addition in pyridine while **(IIIa)** by 1,4-addition in methanol.



where (a) R = H, (b) R = NO_2 and (c) R = Br.

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