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Reactions of *trans*-1-(β-Aroylvinyl)pyridinium Bromides with Hydroxylamine Hydrochloride

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Abstract—Reactions of *trans*-1-(β-aroylvinyl)pyridinium bromides with hydroxylamine hydrochloride lead to a mixture of substituted isoxazoles regardless of the substituent nature in the aromatic core and the solvent.

Keywords: *trans*-1-(β-aroylvinyl)pyridinium bromide, hydroxylamine hydrochloride, oxazole, oxime, nucleophilic addition

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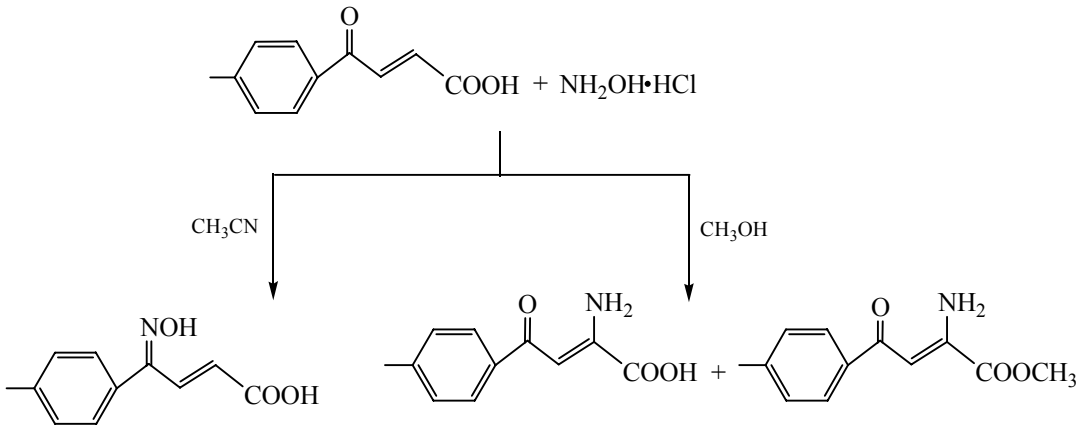
We have recently proposed a convenient method to prepare *trans*-1-(β-aroylvinyl)pyridinium bromides from *trans*-β-aroylacrylic acids [1]. In this work we attempted to introduce the electron-withdrawing group other than carboxyl into the molecule of β-aroylacrylic acids and compared the behavior of the starting and final compounds in the reaction with hydroxylamine hydrochloride.

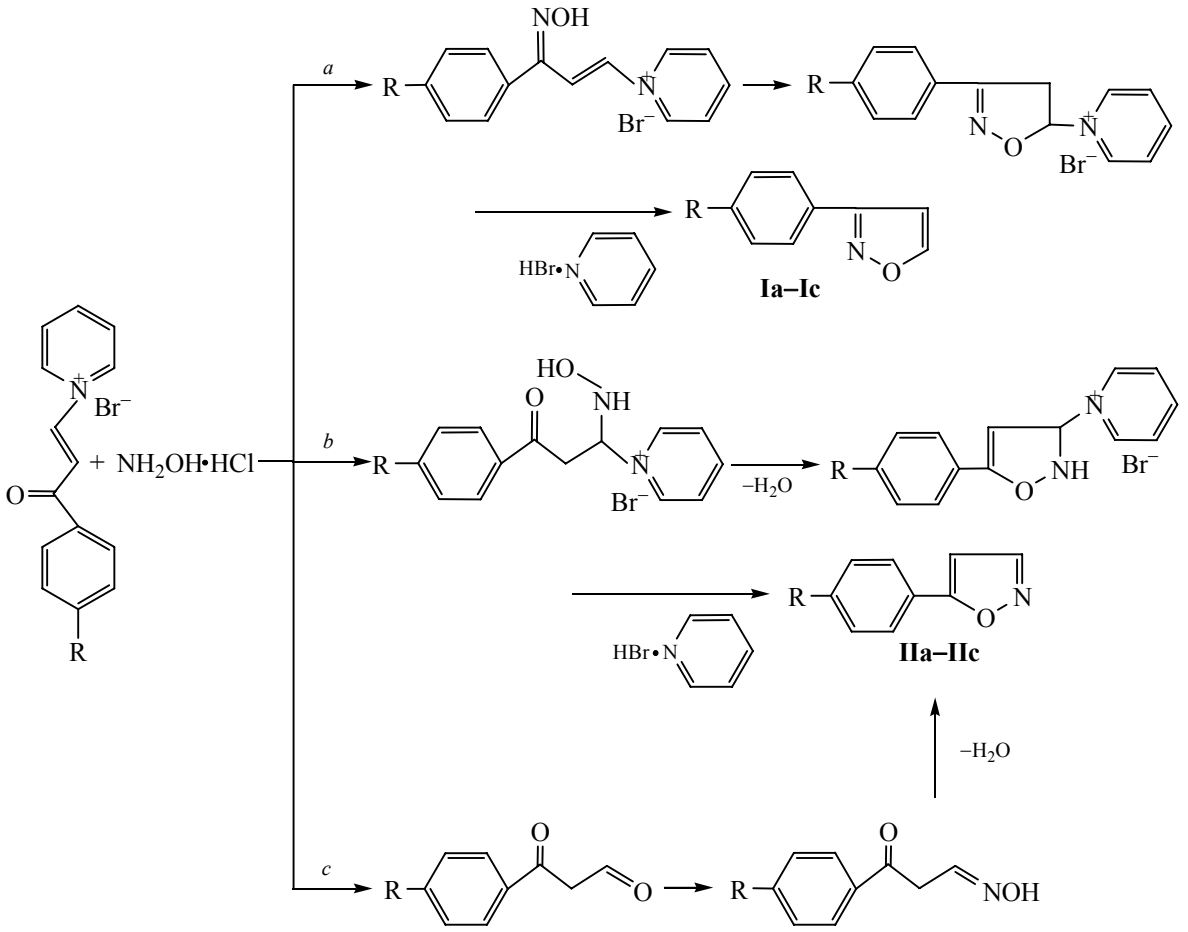
It has been earlier found that the reaction of hydroxylamine hydrochloride with *trans*-β-aroylacrilic acids occurs via nucleophile attack at the carbonyl group or C=C double bond. The reaction direction depends on the nature of the substituent in the aromatic ring (donor methyl group reduces the electrophilicity of the carbonyl group and directs the nucleophilic attack to the C=C double bond) and on the solvent nature [2] (Scheme 1).

However, interaction of *trans*-1-(β-aroylvinyl)pyridinium bromides with hydroxylamine hydrochloride under the same conditions led to unexpected results. Regardless of the nature of the substituent in the aromatic core, the reaction performed in methanol or acetonitrile medium afforded a mixture of the corresponding 3-aryl-1,2-oxazole **Ia**–**Ic** and 5-aryl-1,2-oxazole **IIa**–**IIc** in the ratio of 1 : 1, 3 : 2, and 3 : 2, respectively (Table 1).

Scheme 1.



Scheme 2.



R = CH_3 (**a**), Cl (**b**), Br (**c**).

The reaction could occur via the three independent pathways *a*–*c* (Scheme 2).

Formation of 3-aryl-1,2-oxazoles **Ia**–**Ic** (*a*) included nucleophilic addition to the carbonyl group to form the oxime, followed by intramolecular nucleophilic addition at the double bond with elimination of pyridine.

The reaction pathway *b* included nucleophilic addition at the double bond to give the enol undergoing further cyclization into the hemiketal followed by dehydration and pyridine elimination to yield compounds **IIa**–**IIc**. Formation of compounds **IIa**–**IIc** (*c*) could occur via initial hydrolysis of the starting vinylpyridinium salt to form the corresponding aldehyde, followed by isomerization and cyclization of its oxime into the hemiketal and dehydration of the latter.

The structures of the compounds obtained were confirmed by ^{1}H NMR spectroscopy (Table 2) and X-ray diffraction analysis (Table 3).

Table 1. Yield and elemental analysis data for 3(5)-aryl-1,2-oxazoles **I** and **II**

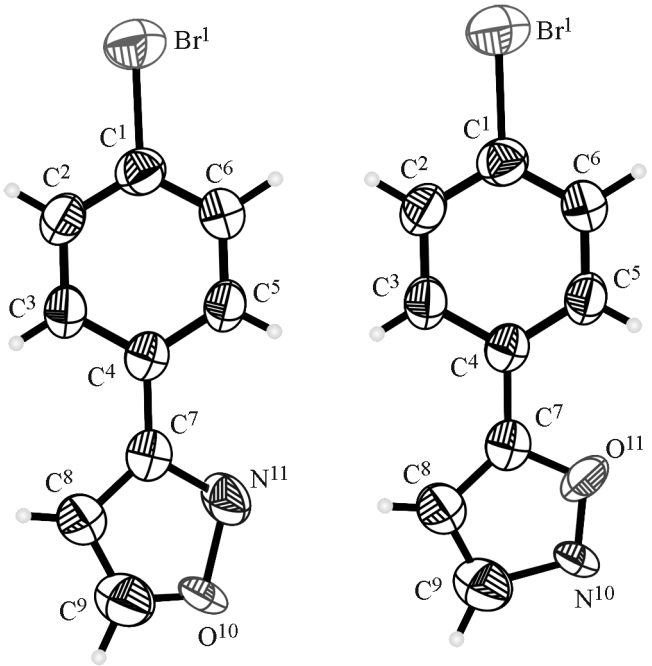
Compound	Yield, %		Found, %			Formula	Calculated, %		
	I	**II**	C	H	N		C	H	N
a	35.4	35.4	75.43	5.68	8.76	$C_{10}H_9NO$	75.47	5.66	8.80
b	40.7	26	65.30	3.58	8.44	C_9H_6ClNO	65.25	3.62	8.45
c	41.2	26.4	48.27	2.63	6.23	C_9H_6BrNO	48.21	2.67	6.25

Table 2. ^{1}H NMR spectral data for compounds **Ia**–**Ic**, **IIa**–**IIc**

Comp. no.	δ (DMSO-d_6–CCl_4, 1 : 3), ppm
Ia + **IIa**	2.2.41 br. s (3H, CH_3), 6.65 d (0.5H, =CH, *J* 1.9 Hz), 6.80 d (0.5H, =CH, *J* 1.7 Hz), 7.22–7.29 m (2H, C_6H_4), 7.67–7.73 m (2H, C_6H_4), 8.31 d (0.5H, =CHO, *J* 1.9 Hz), 8.66 d (0.5H, =CHO, *J* 1.7 Hz)
Ib + **IIb**	6.81 d (0.6H, =CH, *J* 1.9 Hz), 6.91 d (0.4H, =CH, *J* 1.7 Hz), 7.43–7.50 m (2H, C_6H_4), 7.81–7.88 m (2H, C_6H_4), 8.36 d (0.6H, =CHO, *J* 1.9 Hz), 8.72 d (0.4H, =CHO, *J* 1.7 Hz)
Ic + **IIc**	6.81 d (0.6H, =CH, *J* 1.9 Hz), 6.91 d (0.4H, =CH, *J* 1.7 Hz), 7.58–7.65 m (2H, C_6H_4), 7.74–7.81 m (2H, C_6H_4), 8.36 d (0.6H, =CHO, *J* 1.9 Hz), 8.71 d (0.4H, =CHO, *J* 1.7 Hz)

According to the XRD data, the ratio of isomers **Ib** and **IIb** molecules in the crystal was of 60 : 40 (see figure). Main crystallographic and structure refinement data are listed in Table 3.

In summary, reactions of *trans*-1-(β-aroylvinyl)-pyridinium bromides with hydroxylamine hydrochloride yielded a mixture of 3(5)-aryl-1,2-oxazoles regardless of the nature of the substituent in the aromatic ring and the solvent nature.



General view of the isomeric molecules **Ib** and **IIb**. Thermal ellipsoids are shown with 50% probability.

Table 3. Crystal structure data for [3(5)-*p*-bromophenyl]oxazoles **Ic** and **IIc**

Parameter	Value
Formula	C_9H_6BrNO
M	224.05
Crystal system	Monoclinic
Space group	*P*21/*c*
a, Å	10.453(2)
b, Å	13.985(3)
c, Å	5.8387(12)
β, deg	96.23(3)
V, Å^3	848.5(3)
Z	4
d_{calc}, g cm^{-3}	1.754
μ(MoK_α), mm^{-1}	4.789
F(000)	440
Crystal size, mm	0.25 × 0.32 × 0.40
T, K	293
λ, Å	0.71073
θ_{min}, θ_{max}, deg	2.0, 30.0
Scan ranges	$-14 \le h \le 14$; $-19 \le k \le 0$; $0 \le l \le 8$
Reflections collected	2698
Reflections observed [$I > 2.0\ \sigma(I)$]	1186
R, wR_2	0.0548, 0.1569

EXPERIMENTAL

^{1}H NMR spectra were recorded with a Varian Mercury-300 instrument at 303 K operating at 300.08 MHz relative to internal TMS reference.

Single-crystal X-ray diffraction analysis was carried out at room temperature using an Enraf-Nonius CAD-4 automatic diffractometer [graphitic monochromator, λ(MoK_α) = 0.71073 Å, ω/2θ-scanning]. The unit cell parameters were determined and refined accounting for 24 diffraction peaks (13.5 ≤ θ 15.0). The absorption was accounted for using the experimental azimuthal scanning curves (T_{min} = 0.38205, T_{max} = 0.71448) [3]. The structure was solved by direct method. Hydrogen atoms were placed in the geometrically determined positions and refined via a *rider* model [bond length C–H 0.93 Å, U_{iso}(H) = 1.2U_{eq}(C)]. The structure was refined by full-matrix anisotropic approximation for non-hydrogen atoms, and the hydrogen atoms were

refined isotropically. The computations were performed using SHELXTL software [4].

Crystallographic CIF data were deposited at the Cambridge Crystallographic Data Centre (CCDC 1027243).

3(5)-Aryl-1,2-oxazoles (I, II). A solution of 0.62 g (0.009 mol) of hydroxylamine hydrochloride in a minimum amount of water was added to a saturated solution of 0.0015 mol of *trans*-1-(β-aroylvinyl)pyridinium bromide in acetonitrile or methanol. The reaction mixture was refluxed during 27–30 h, cooled, and poured into 200 mL of water. The reaction products were extracted with chloroform and re-precipitated with diethyl ether. The resulting precipitate was filtered off, washed with ether, and dried in vacuum.

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