SYNTHESIS AND PRODUCTS OF HYDROLYSIS OF 2-METHYL-5-(β-ARYLACRYLYL)-2-OXAZOLINES

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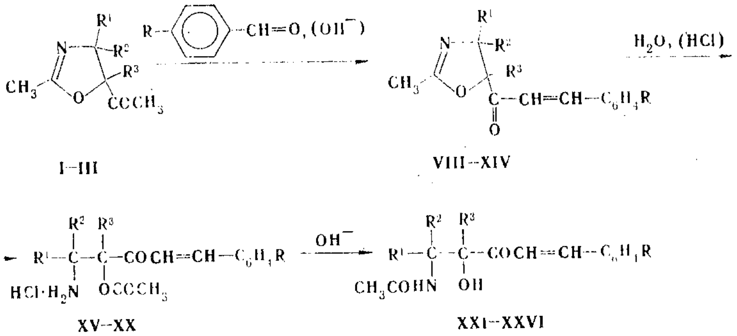
The condensation of 2-methyl-5-acetyl-2-oxazolines with p-R-substituted benzaldehydes in the presence of bases gave the corresponding 2-methyl-5-(β-arylacrylyl)-2-oxazolines, the hydrolysis of which with hydrochloric acid leads to hydrochlorides of alkyl-substituted 1-(p-R-styryl)-2-acetoxy-3-aminobutan-1-ones. Treatment of the latter with bases gives 1-(p-R-styryl)-2-hydroxy-3-N-acetyl-2,3-alkylbutan-1-ones.

2-Methyl-5-acetyl-2-oxazolines [1] have two methyl groups that are capable of undergoing a reaction of the aldol-crotonic type with aromatic aldehydes, viz., the methyl groups in the acetyl fragment and in the 2 position of the ring. In this connection we studied the regioselectivity of the reactions of 2,4,4-trimethyl- (I), 2,5-dimethyl- (II), and 2,4,5-trimethyl-5-acetyl-2-oxazolines (III) with aromatic aldehydes (IV-VII).

We established that in the presence of a methanol solution of alkali 2-oxazolines (I-III) react with aldehydes (IV-VII) to give the corresponding 2-methyl-5-(β-arylacrylyl)-2-oxazolines (VIII-XIV) in 80-85% yields (Table 1).



I, VIII, XV, XXI $R^1=R^2=CH_3$, $R^3=H$; II, IX–XII, XVI–XIX, XXII–XXV $R^1=R^2=H$, $R^3=CH_3$; III, XIII, XIV, XX, XXVI $R^1=R^3=CH_3$; $R^2=H$; VIII, IX, XIII, XVI, XX, XXII, XXVI $R=CH_3$; X, XVII, XXIII R=H; XI, XIV, XVIII, XXIV R=Br; XII, XIX, XXV R=Cl

According to the data from thin-layer chromatography (TLC) and the PMR spectra, the reaction mixtures do not contain admixed 2-styryl-5-acetyl-2-oxazolines and products of the addition of two molecules of the aldehyde to I-III.

The VIII-XIV structure were confirmed by spectral data and the results of elementary analysis (Table 1). Thus the IR spectra contain intense bands of C=N stretching vibrations (1650-1670 cm^{-1}) and a conjugated C=O group (1675-1690 cm^{-1}).

As compared with starting oxazolines I-III, the PMR spectra of VIII-XIV (Table 2) do not contain the signal of an acetyl group (2.12-2.15 ppm), but signals of aromatic protons (7.2-8.1 ppm) and two doublets of an AB system of olefin protons with a spin-spin coupling constant (SSCC) of 16 Hz, which constitutes evidence for their trans orientation, appear in the spectra.

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TABLE 1. 2-Methyl-5-(β-arylacrylyl)-2-oxazolines (VIII-XIV), 1-(p-R-Styryl)-2-acetoxy-3-aminobutan-1-ones (XV-XX), and 1-(p-R-Styryl)-2-hydroxy-3-N-acetylbutan-1-ones (XXI-XXVI)

Compound	mp, °C	R	R¹	R²	R³	Found, %			Empirical formula	Calculated, %		
						C	H	N		C	H	N
VIII	49—51	CH_3	CH_3	CH_3	H	74,6	7,5	5,2	$C_{16}H_{19}NO_2$	74,7	7,4	5,4
IX	57—59	CH_3	H	H	CH_3	74,2	6,4	5,4	$C_{15}H_{17}NO_2$	74,1	6,7	5,8
X	46—47	H	H	H	CH_3	73,2	6,3	5,9	$C_{14}H_{15}NO_2$	73,4	6,5	6,1
XI	56—57	Br	H	H	CH_3	54,3	4,4	4,2	$C_{14}H_{14}BrNO_2$	54,5	4,5	4,5
XII	49—50	Cl	H	H	CH_3	63,2	5,1	5,4	$C_{14}H_{14}ClNO_2$	63,7	5,3	5,3
XIII	72—73	CH_3	CH_3	H	CH_3	74,3	7,5	5,2	$C_{16}H_{19}NO_2$	74,7	7,4	5,4
XIV	86—87	Br	CH_3	H	CH_3	56,9	5,4	4,4	$C_{16}H_{18}BrNO_2$	57,1	5,3	4,2
XV	169—172	CH_3	CH_3	CH_3	H	61,4	6,4	4,6	$C_{16}H_{21}NO_3 \cdot HCl$	61,6	6,7	4,5
XVI	178—181	CH_3	H	H	CH_3	60,0	6,2	4,8	$C_{15}H_{19}NO_3 \cdot HCl$	60,5	6,4	4,7
XVII	162—165	H	H	H	CH_3	59,4	5,8	4,7	$C_{14}H_{17}NO_3 \cdot HCl$	59,2	6,0	4,9
XVIII	176—179	Br	H	H	CH_3	43,1	4,4	3,5	$C_{14}H_{16}BrNO_3 \cdot HCl$	46,3	4,4	3,7
XIX	168—171	Cl	H	H	CH_3	52,7	4,8	4,6	$C_{14}H_{16}ClNO_3 \cdot HCl$	52,8	5,0	4,4
XX	174—177	CH_3	CH_3	H	CH_3	61,8	6,5	4,4	$C_{16}H_{21}NO_3 \cdot HCl$	61,6	6,7	4,5
XXI	134—136	CH_3	CH_3	CH_3	H	69,9	7,4	5,0	$C_{16}H_{21}NO_3$	70,0	7,6	5,1
XXII	151—152	CH_3	H	H	CH_3	68,3	7,6	5,3	$C_{15}H_{19}NO_3$	69,0	7,3	5,4
XXIII	112—114	H	H	H	CH_3	68,1	6,7	5,4	$C_{14}H_{17}NO_3$	68,1	6,9	5,7
XXIV	148—149	Br	H	H	CH_3	51,5	4,9	4,2	$C_{14}H_{16}BrNO_3$	51,5	4,9	4,3
XXV	139—141	Cl	H	H	CH_3	59,5	5,1	4,8	$C_{14}H_{16}ClNO_3$	59,7	5,7	5,0
XXVI	162—164	CH_3	CH_3	H	CH_3	70,8	7,5	5,0	$C_{16}H_{21}NO_3$	70,0	7,6	5,1

TABLE 2. PMR Spectra of 2-Methyl-5-(β-arylacrylyl)-2-oxazolines (VIII-XIV), 1-(p-R-Styryl)-2-acetoxy-3-aminobutan-1-ones (XV-XX), and 1-(p-R-Styryl)-2-hydroxy-3-N-acetylbutan-1-ones (XXI-XXVI)

Compound	Chemical shifts, ppm (SSCC, Hz)						
	R	R¹	R²	R³	CH_3	CH=CH dd (16)	C_6H_4
VIII	2,3 s	0,93 s	1,3 s	4,3 s	1,95 s	6,8; 7,5	6,7—7,8 m
IX	2,26 s	3,66 dq (14,1; 2)	3,93 dq (14,1;2)	1,36 s	1,96 t (1,2)	6,9; 7,6	6.7—7,8 m
X	—	3,68 dq (14,1; 2)	3,94 dq (14,1;2)	1,32 s	1,95 t (1,2)	6,8; 7,5	6,7—7,8 m
XI	—	3,43 dq (14,1; 2)	3,90 dq (14,1;2)	1,40 s	1,90 t (1,2)	6,9; 7,5	7,4 s
XII	—	3,36 dq (15,1; 2)	3,93 dq (15,1; 2)	1,33 s	1,93 t (1,2)	6,9; 7,5	6,7—7,8 m
XIII	2,3 s	0,90 d (8)	3,76 qd (8,1;2)	1,33 s	1,96 d (1,2)	6,9; 7,5	6,7—7,8 m
XIV	—	0,90 d (3)	3,8 qd (8,1; 2)	1,33 s	1,96 d (1,2)	6,9; 7,5	7,4 s
XV	2,3 s	1,33 s	1,46 s	5,33 s	2,16 s	6,9; 7,7	6,9—7,8 m
XVI	2,3 s	3,46 s	3,46s	1,6 s	2,13 s	6,9; 7,6	6,9—7,8 m
XVII	—	3,44 s	3,44 s	1,53 s	2,13 s	6,9; 7,6	6,9—7,8 m
XVIII	—	3,43 s	3,43 s	1,53 s	2,13s	6,9; 7,7	7,5 s
XIX	—	3,46 s	3,46 s	1,53 s	2,13s	6,9; 7,6	6,9—7,8 m
XX	2,3	0,96 d (6)	3,6 q (6)	1,50 s	2,13s	6,9; 7,6	6,9—7,8 m
XXI	2.3 s	1,36 s	1,36 s	4,33 d (8)	1,8 s	7,0; 7,6	6,9—7,8 m
XXII	2,26 s	3,0—3,93 s	2,9—3,93 m	1,4 s	1,83 s	7,0; 7,6	6,9—7,8 m
XXIII	—	3,2—4 m	3,2—4 m	1,3 s	1,83 s	7,0; 7,6	6,9—7,8 m
XXIV	—	3,2—4 m	3,2—4 m	1,3 s	1,83 s	7,0; 7,6	7,4s
XXV	—	3,0—4 m	3,0—4 m	1,3 s	1,83 s	7,0; 7,6	6,9—7,8 m
XXVI	2,3 s	1,2 d (8)	3,6 q (8)	1,56 s	1,83 s	7,0; 7,6	6,9—7,8 m

Oxazolines VIII-XIV are hydrolyzed to give the hydrochlorides of alkyl-substituted 1-(β-R-styryl)-2-acetoxy-3-aminobutan-1-ones in 95% yields when they are treated with concentrated hydrochloric acid (Table 1).

The structure of salts XV-XX are confirmed by spectral data and the results of elementary analysis (Table 1).

The IR spectra of XV-XX contain intense bands of stretching vibrations of C=C bonds (1600-1610 cm^{-1}), ester and conjugated carbonyl groups (1735 and 1690 cm^{-1}), and an ammonium group N–H bond at 2900-3400 cm^{-1}.

Doublets of an AB system of olefin protons at 6.8-8.3 ppm with SSCC = 16 Hz and a multiplet of aromatic protons at 7.2-8.1 ppm are observed in the PMR spectra (Table 2) of hydrochlorides XV-XX. As compared with the starting VIII-XIV, the signal of the CH_3 group attached to the C_2 atom of the 2-oxazoline ring is shifted 0.3-0.5 ppm to weaker field. The character of the multiplicity and the geminal constant of the protons attached to the ring

C_4 atom change, and the additional splitting of the protons attached to C_4 and the CH_3 group in the 2 position that is characteristic for IX-XIV (1.5 Hz) vanishes in the case of XVI-XX.

Treatment of salts XV-XX with base does not lead to the formation of free amines but gives the corresponding 1-(p-R-styryl)-2-hydroxy-3-N-acetyl-2,3-dialkylbutan-1-ones (XXI-XXVI) in close to quantitative yields (Table 1). This rearrangement is stereospecific and hypothetically has a mechanism similar to that previously proposed in [2].

Bands of a conjugated C=O group at 1670-1675 cm^{-1}, amide I and II bands at 1642 and 1536 cm^{-1}, respectively, and amide NH bands at 3210 and 3345 cm^{-1} are observed in the IR spectra of XXI-XXVI.

A doublet of an AB system of olefin protons at 6.8-8.3 ppm with SSCC = 16 Hz and a multiplet of aromatic protons at 7.2-8.1 ppm are observed in the PMR spectra of amides XXI-XXVI (Table 2) and in the spectra of XV-XX. In addition, a signal of an OH group at 4.0-5.0 ppm and a broad signal of an amide NH group at 6.0-7.5 ppm appear in the spectra.

EXPERIMENTAL

The PMR spectra of 10% solutions of VIII-XIV in CCl_4 and 10% solutions of XV-XXVI in d_6-acetone were recorded with a Tesla BS-467 spectrometer with hexamethyldisiloxane as the internal standard. Thin-layer chromatography was carried out on Silufol plates by elution with ether—hexane (3:1 for VIII-XIV and 9:2 for XXI-XXVI).

2-Methyl-5-(β-arylacrylyl)-2-oxazolines (VIII-XIV). A 0.5-ml sample of a 15% solution of KOH in methanol was added at 20°C to a solution of 0.05 mole of oxazolines I-III and 0.05 mole of benzaldehydes IV-VII in 50 ml of methanol. After 4 h, the reaction mixture was poured into 300 ml of cold water, and the precipitated crystals were removed by filtration and recrystallized from hexane.

1-(p-R-Styryl)-2-acetoxy-3-amino-2,3-alkylbutan-1-one Hydrochlorides (XV-XX). A 0.025-mole sample of concentrated HCl was added to a solution of 0.02 mole of VIII-XIV in 50 ml of acetone, and the reaction mixture was allowed to stand at 20°C for 24 h, after which it was diluted with 100 ml of ether. The precipitated crystals were recrystallized from 2-propanol—methyl ethyl ketones (2:1).

1-(p-R-Styryl)-2-hydroxy-3-N-acetyl-2,3-dialkylbutan-1-ones (XXI-XXVI). A 0.01-mole sample of XV-XX was added to a suspension of 20 ml of a saturated solution of Na_2CO_3 in 50 ml of CH_2Cl_2, and the mixture was stirred until salts XV-XX dissolved completely (0.5-1.5 h). The solvent was then removed by distillation on a water bath, and the residue was recrystallized from CCl_4.

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