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REACTION OF β-ARYLACRYLOYLOXIRANES WITH PHENYLHYDRAZINE

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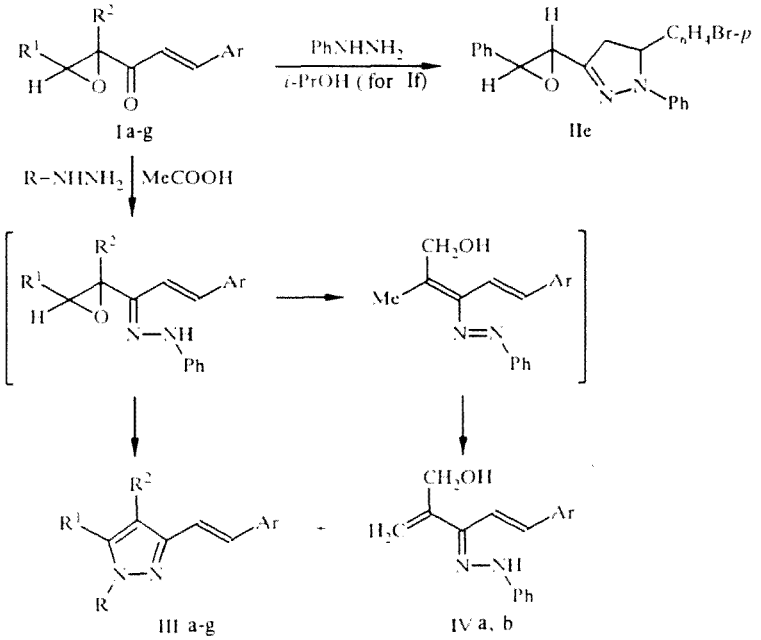
The reaction of β-arylacryloyloxiranes with phenylhydrazine under the conditions of acid catalysis leads to 3-arylvinyl-1-phenylpyrazoles and 2-hydroxymethyl-5-aryl-1,4-pentadien-3-one phenylhydrazones.

It is known that the reaction of epoxy ketones with phenylhydrazine leads to the corresponding phenylpyrazoles or phenylazoolefins [1-4]. In the opinion of the authors in [3, 4], the initial products of this reaction (the phenylhydrazones) are converted by an electron shift with opening of the oxirane ring into azoolefins, which undergo cyclization to the phenylpyrazoles through the hydrazoenol form.

Earlier we investigated the reaction of β-arylacryloyloxiranes with hydrazine hydrate [5]. Here it was established that the reaction takes place through the intermediate α,β-epoxyalkylpyrazolines, the subsequent transformation of which also includes an electron shift with opening of the epoxide ring and aromatization of the pyrazoline ring as a result of migration of the exocyclic double bond, leading to the β-hydroxyalkylpyrazoles. It seemed interesting to determine how general this process is for N-substituted epoxyalkylpyrazolines. For this purpose in the present work we studied the reaction of α,β-arylacryloyloxiranes with phenylhydrazine.



I, III, IV a Ar = Ph, R^1 = H, R^2 = Me; b Ar = p-BrC_6H_4, R^1 = H, R^2 = Me; c Ar = p-MeO, R^1 = H, R^2 = Me; d Ar = Ph, R^1 = R^2 = Me; e Ar = R^1 = Ph, R^2 = H; f Ar = p-BrC_6H_4, R^1 = Ph, R^2 = H; g Ar = p-$MeOC_6H_4$, R^1 = Ph, R^2 = H

It was found that the reaction of phenylhydrazine with β-arylacryloyloxiranes (Ia-g) in alcohols leads to a complex mixture of colored substances, which cannot be separated by chromatography. In the case of compound (If) 5-(p-bromophenyl)-

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	Found, %			Molecular formula	Calculated, %			mp	Yield, %
	C	H	N		C	H	N		
IIf	65.4	4.3	6.4	$C_{23}H_{19}BrN_2O$	65.9	4.65	6.7	185...188	25
IIIa	82.8	5.9	10.4	$C_{18}H_{16}N_2$	83.0	6.2	10.8	94...96	80
IIIb	63.4	4.2	8.0	$C_{18}H_{15}BrN_2$	63.7	4.5	8.3	101...102	65
IIIc	78.4	6.4	9.6	$C_{19}H_{18}N_2O$	78.6	6.3	9.7	119...120	79
IIId	83.0	6.5	10.1	$C_{19}H_{18}N_2$	83.2	6.6	10.2	oil	75
IIIe	85.3	5.5	8.7	$C_{23}H_{18}N_2$	85.7	5.6	8.7	140...141	73
IIIf	68.6	3.8	6.7	$C_{23}H_{17}BrN_2$	68.8	4.3	7.0	137...139	36
IIIg	81.6	5.5	7.9	$C_{24}H_{20}N_2O$	81.8	5.7	8.0	168...169	65
IVa	77.3	6.2	9.9	$C_{18}H_{18}N_2O$	77.7	6.5	10.1	144...145	8
IVb	60.3	4.6	7.5	$C_{18}H_{17}BrN_2O$	60.5	4.8	7.8	153...155	10

TABLE 2. PMR Spectra of the Synthesized Compounds

Compound	Chemical shifts, ppm, SSCC (J), Hz
IIf	2.78 (1H, dd, J = 8.0, J = 17.5, 4-H), 3.38 (1H, dd, J = 11.8, J = 17.5, 4-H), 3.90 (1H, d, J = 1.0, CH—CH), 4.00 (1H, d, J = 1.0, CH—CH), 5.12 (1H, dd, J = 11.8, J = 8.0, 5-H), 6.70...7.60 (14H,m, Harom)
IIIa	2.12 (3H, s, CH_3), 6.90 (1H, d, J = 16.0, =CH), 7.10 (1H, d, J = 16.0, =CH), 7.45 (1H, s, 5-H), 7.25 (10H,m, Harom)
IIIb	2.15 (3H, s, CH_3), 6.90 (1H, d, J = 16.0, =CH), 7.08 (1H, d, J = 16.0, =CH), 7.50 (1H, s, 5-H), 7.30 (9H,m, Harom)
IIIc	2.17 (3H, s, CH_3), 3.70 (3H, s, OCH_3), 6.80 (1H, d, J = 16.0, =CH), 7.40 (1H, d, J = 16.0, =CH), 7.50 (1H, s, 5-H), 6.70 (2H, d, J = 9.0, Harom), 7.04 (2H, d, J = 9.0, Harom), 7.24 (5H,m, Harom)
IIId	2.05 (3H, s, CH_3), 2.15 (3H, s, CH_3), 6.98 (1H, d, J = 16.0, =CH), 7.15 (1H, d, J = 16.0, =CH), 7.28 (10H,m, Harom)
IIIe	6.76 (1H, s, 4-H), 7.23 (1H, d, J = 16.0, =CH), 7.40 (1H, d, J = 16.0, =CH), 7.30...7.54 (15H,m, Harom)
IIIf	6.75 (1H, s, 4-H), 7.15 (2H, s, HC=CH), 7.22...7.35 (10H,m, Harom), 7.38 (2H, d, J = 9.0, Harom), 7.46 (2H, d, J = 9.0, Harom)
IIIg	3.84 (3H, s, CH_3O), 6.70 (1H, s, 4-H), 6.90 (2H, d, J = 9.0, Harom), 7.43 (2H, d, J = 9.0, Harom), 7.08 (1H, d, J = 16.0, =CH), 7.15 (1H, d, J = 16.0, =CH), 7.30 (10H,m, Harom)
IVa	4.12 (3H, bs, CH_2OH), 5.12 (1H, d, J = 1.0, =CH_2), 5.76 (1H, d, J = 1.0, =CH_2), 6.60 (1H, d, J = 16.0, HC=CH), 6.90 (1H, d, J = 16.0, HC=CH), 7.30 (10H, m, Harom), 8.62 (1H, bs, NH)
IVb	4.10 (2H, d, J = 4.5, CH_2O), 4.30 (1H, t, J = 4.5, OH), 5.14 (1H, d, J = 1.0, =CH_2), 5.76 (1H, d, J = 1.0, =CH_2), 6.50 (1H, d, J = 16.0, HC=CH), 6.90 (1H, d, J = 16.0, HC=CH), 7.10 (4H,m, Harom), 7.34 (5H, s, Harom), 8.68 (1H, bs, NH)

1-phenyl-3-(1,2-epoxystyryl)-2-pyrazoline (IIf), analogous with the intermediate in the reaction with hydrazine hydrate [5], was isolated. The IR spectrum of the product did not contain the characteristic absorption of the conjugated enone system in the region of 1620-1680 cm^{-1}. The PMR spectrum contained an AMX system of signals for the protons of the pyrazoline ring, an AB system for the protons of the oxirane ring, and a strong multiplet for the protons of the aromatic rings.

In the reaction of the β-arylacryloyloxiranes (Ia-g) with phenylhydrazine under the conditions of acid catalysis, which activates the nucleophilic addition of substituted hydrazines and increases the reactivity of the epoxide ring, the direction of attack by the reagent changes, and 3-β-arylvinyl-1-phenylpyrazoles (IIIa-g) are isolated with yields of 36-80% as the main product (Table 1). In the PMR spectra of compounds (IIIa-d) the signal of the protons of the 4-Me group of the pyrazole ring appears 2.05-2.17 ppm. In the downfield region the AB system of the vinyl protons in the region of 6.80-7.40 ppm with a spin—spin coupling constant of 16.0 Hz, the singlet of the proton at $C_{(5)}$ in the pyrazole ring (7.45-7.50 ppm) in compounds (IIIa-c), and the multiplet of the protons of the two aromatic rings are observed. In the case of compounds (IIIe-g), the signal for the proton at position 4 of the pyrazole ring appears at 6.70-6.76 ppm (Table 2).

In the reaction of methyl-substituted β-arylacryloyloxiranes (Ia, b) with phenylhydrazine acyclic products, which were the phenylhydrazones of 5-aryl-2-hydroxymethyl-1,4-pentadien-3-ones (IVa, b), were isolated together with the main products [3-styrylpyrazoles (IIIa, b)] with yields of 8-10%. The PMR spectra of compounds (IVa, b) contained the signals for the protons

of the primary alcohol group at 4.10-4.30 ppm, the AX system of the protons of the methylene group at 5.14 and 5.76 ppm with a spin—spin coupling constant of 1.0 Hz, the AB system of the vicinal protons at 6.50-6.90 ppm with a spin—spin coupling constant of 16.0 Hz, and the signals of the protons of the aryl rings and hydrazone fragment.

Analysis of the structure of the phenylhydrazones (IVa, b) indicated oxidation—reduction disproportionation of the oxirane ring to the derivatives of allyl alcohol. Compounds (IVa, b) are clearly formed through the intermediate hydrazones of the epoxyenones (Ia, b), which are transformed into the hydrazones (IVa, b) by electron shifts with the migration of a proton. The motivating force of such a rearrangement can be assumed to be the formation of a conjugated polyene system with a mobile proton at the more basic nitrogen atom.

Thus, the reaction of β-arylacryloyloxiranes with phenylhydrazine takes place under the conditions of acid catalysis with opening of the oxirane ring and the isolation of β-arylvinylpyrazoles. The presence of a methyl group in the oxirane stimulates the occurrence of a concurrent process, involving oxidative—reductive rearrangement of the hydrazone of the unsaturated epoxy ketone.

EXPERIMENTAL

The PMR spectra of solutions of the substances in deuterochloroform or acetone-d_6 [in the case of compounds (IIf, IIIb, IIIf)] were obtained on Bruker WM-360 (360 MHz) and Tesla BS-56A (100 MHz) instruments with HMDS as internal standard. The IR spectra were measured on a Specord IR-75 spectrophotometer in carbon tetrachloride solutions. The reaction mixtures were analyzed by thin-layer chromatography on Silufol plates with a mixture of ether and hexane as eluant.

5-(p-Bromophenyl)-1-phenyl-3-(1,2-epoxystyryl)-2-pyrazoline (IIf). To 1.98 g (6 mmole) of 5-(p-bromophenyl)-1-phenyl-1,2-epoxy-4-penten-3-one (If) in 40 ml of isopropyl alcohol we added 0.7 ml (6 mmole) of phenylhydrazine in 10 ml of the same alcohol. The reaction mixture was boiled for 1 h, the solvent was evaporated on a film-type evaporator, and the product (IIf) was isolated from the oily residue by purification on aluminum oxide with a 1:1 mixture of methylene chloride and hexane as eluant. It crystallized after part of the methylene chloride had evaporated.

3-(β-Arylvinyl)-1-phenyl-5-R^1-4-R^2-pyrazoles (IIIa-g) and 5-Aryl-2-hydroxymethyl-1,4-pentadien-3-one Phenylhydrazones (IVa, b). To 0.01 mole of compounds (Ia-g) we added 1.4 g of phenylhydrazine in 20 ml of isopropyl alcohol and 0.5 ml of acetic acid. The obtained mixture was boiled for 1-2 h. The alcohol was evaporated on a film-type evaporator. The residue was diluted with 30 ml of water, neutralized with sodium carbonate solution, and extracted with ether (3 × 25 ml). The extract was dried over sodium sulfate. Compounds (IIIa-c) crystallized after part of the ether had evaporated. The mother solution after separation of the crystals was evaporated, and compounds (IVa, b) and an additional amount of the pyrazoles (IIIa-b) were isolated by chromatography on silica gel. The products were crystallized from alcohols. Compound (IIId) was isolated in the form of an oil after the reaction mixture was passed through a column of silica gel with a 3:1 mixture of ether and hexane as eluant. Compounds (IIIe, f) were isolated by chromatography on aluminum oxide with a 1:2 mixture of methylene chloride and hexane as eluant. Compound (IIIg) crystallized from the reaction mixture on cooling.

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REFERENCES

1. J. Elguero and C. Mazzin, Bull. Soc. Chim. France, No. 12, 3401 (1973).
2. D. L. Coffen and D. G. Korzan, J. Org. Chem., **36**, 390 (1971).
3. A. A. Akhrem, A. V. Kamernitskii, A. V. Skorova, and N. S. Pavlova-Grishina, Izv. Akad. Nauk. SSSR. Ser. Khim., No. 4, 901 (1973).
4. A. A. Akhrem and A. V. Skorova, Izv. Akad. Nauk. SSSR. Ser. Khim., No. 1, 190 (1974).
5. A. M. Zvonok, N. M. Kuz'menok, and L. S. Stanishevskii, Khim. Geterotsikl. Soedin., No. 5, 633 (1990).