# SYNTHESIS OF ISOMERIC O-(PHENYLVINYL)-ACETOPHENONE OXIMES AND THEIR REARRANGEMENT TO PYRROLES

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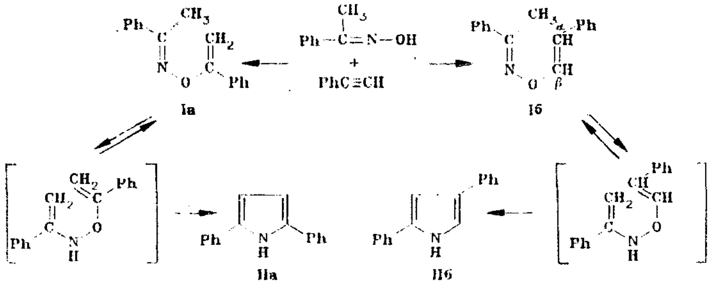
Methods were developed for the radioselective synthesis of α- and β-O-(phenylvinyl)-acetophenone oximes. Their conversion to 2,5- and 2,4-diphenylpyrroles, respectively, confirms the mechanism of this process, including a step of [3,3]-sigmatropic displacement.

In recent years, in the discussion of the mechanism of the conversion of ketoximes to pyrroles in the interaction with acetylene in a superbasic medium, weighty evidence has appeared in support of an O-vinyl oxime pathway for the process, including a step of [3,3]-sigmatropic displacement. Thus, O-vinyl ethers of ketoximes have been isolated and converted to pyrroles [1, 2], and in certain cases it has been possible to isolate the previously suggested [3] intermediates of this process — 2-hydroxy-$\Delta^1$-pyrrolines [4].

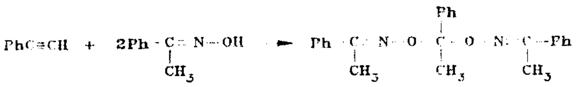
Up to the present time the reaction of heterocyclization has been investigated chiefly on the example of unsubstituted acetylene. When a monosubstituted alkyne, incapable of prototropic isomerization, for example, phenylacetylene, is used, two isomeric phenylpyrroles, IIa, b, can be formed, which is due to different directions of addition of oximes at the triple bond.



However, on the only example of participation of phenylacetylene in this reaction [5], the authors isolated only α-phenylpyrrole, which was interpreted as an argument against the sigmatropic nature of the process [3]. It seemed strange that β-phenylpyrrole was not detected under the selected conditions, since a careful selection of the conditions is necessary for high regioselectivity of nucleophilic addition to phenylacetylene [6].

The purpose of this investigation was to develop a regioselective synthesis of α- (Ia) and β-O-(phenylvinyl)acetophenone oximes (Ib) and to study their conversion to pyrroles.

By analogy with the well-known Kucherov reaction, we used specific catalysis by mercury salts to obtain the α-ester Ia. When mercury trifluoroacetate and tosylate were used, addition at the α-carbon atom was observed, but the yield of the α-ether Ia was very low, since the process of addition of two molecules of the oxime to phenylacetylene with the formation of 1,1-bis(acetophenonoximino)-1-phenylethane (III) predominated:



$$PhC\equiv CH + 2Ph-\underset{CH_3}{C}=N-OH \rightarrow Ph-\underset{CH_3}{C}=N-O-\overset{Ph}{\underset{CH_3}{C}}-O-N=\underset{CH_3}{C}-Ph$$

III

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We were able to select conditions for the production of the α-ether Ia (~20°C, mercuric acetate, excess of phenylacetylene) without the formation of a bis-adduct III, but this required a substantial increase in the duration of the process (to two months).

In the IR spectrum of the ether Ia the band of the nonplanar deformational vibrations of the terminal $CH_2$ group (915 $cm^{-1}$) is observed. In the case of PMR in the region of the vinyl protons (4.71 and 5.03 ppm), two doublets of the nonequivalent protons with $J_{gem}$ = 2 Hz, appeared.

Nucleophilic addition of the oximate anion to phenylacetylene was used for the synthesis of the β-ether Ib. The optimum reaction conditions proved to be the use of the potassium salt of acetophenone oxime in DMSO and a twofold excess of phenylacetylene at room temperature. Raising the reaction temperature to 50°C leads to the pyrrole IIa (formed from the ether Ia) in addition to the ether Ib, which is evidence of a decrease in the regioselectivity of the addition. In the PMR spectrum of the ether Ib in the region of the vinyl protons (5.26 ppm) a signal of α-H appears in the form of a doublet with $J_{cis}$ = 10 Hz. The signal of the β-H proton, however, falls in the region of the aromatic protons on account of the unshielding by the oxygen atom.

Isomeric vinyl ethers Ia, b were converted to the corresponding pyrroles IIa,b in a superbasic medium. Thus, heating of the α-ether Ia in the system KOH/DMSO at 45°C for 8 h gave 25% 2,5-diphenylpyrrole (IIa). Under the same conditions the β-ether Ib does not form 2,4-diphenylpyrrole (IIb), only raising the temperature to 100°C leads to the expected pyrrole. Evidently the more rigorous conditions of conversion of the β-ether Ib to the pyrrole IIb are due to the necessity for an initial cis-trans isomerization, since only the trans-configuration of the ether provides for the necessary steric conditions for a sigmatropic rearrangement.

The necessity of conducting the heterocyclization in superbasic medium is due to the fact that the [3,3]-sigmatropic rearrangement should be preceded by a base-catalyzed isomerization of O-vinyl oximes to N,O-divinylhydroxylamines. Actually, an attempt at thermal conversion of the ethers Ia,b (150°C, 10 min) in the absence of a strong base leads only to trace amounts of the corresponding pyrroles (according to the data of thin-layer chromatography), and substantial resinification is observed.

When the reaction of acetophenone oxime with phenylacetylene was conducted without a solvent, using potassium oximate as the base under rigorous conditions (140°C, 6 h), approximately equal amounts (5-6%) of the isomeric pyrroles IIa,b were isolated.

Thus, the conversion of isomeric O-vinyl oximes to the corresponding pyrroles confirms the sigmatropic nature of the heterocyclization process.

## EXPERIMENTAL

The IR spectra were recorded on a UR-20 instrument in $CCl_4$ and liquid petrolatum. The PMR spectra were recorded on a Tesla BS-497 instrument (100 MHz). The course of the reactions and the purity of the compounds were monitored on Silufol UV-254 in the system benzene—hexane, 1:1.

1,1-Bis(acetophenoneoximino)-1-phenylethane (III). A mixture of 1.35 g (10 mmoles) acetophenone oxime and 1 ml (10 mmoles) phenylacetylene in 10 ml acetonitrile and 0.2 g (0.45 mmole) mercury(II) trifluoroacetate was mixed for 6 h at 60°C. The solvent was distilled off under vacuum, the residue recrystallized twice from hexane. Yield 1.1 g (60%) of white crystals with mp 118-119°C (from hexane). PMR spectrum ($CCl_4$): 2.10 (3H, s, $\mathbf{CH_3}C{-}O{-}$); 2.35 (6H, s, $\mathbf{CH_3}C{=}N$); 6.90-7.50 ppm (15H, m, arom. protons). Found: C 77.7; H 6.3%. $C_{24}H_{24}N_2O_2$. Calculated: C 77.4; H 6.4%.

O-(α-Phenylvinyl)acetophenone Oxime (Ia). A mixture of 0.675 g (5 mmoles) acetophenone oxime, 0.75 ml (7.5 mmoles) phenylacetylene, and 0.1 g (0.3 mmole) mercury(II) acetate was left for two months at 20°C then chromatographed on silica gel 40/100 μm with a 1:3 benzene—hexane mixture; 0.04 g of the ether Ia was eluted, and 0.554 g of unreacted acetophenone oxime was eluted with benzene. Yield of the ether Ia 85% on the basis of the reacted oxime. White crystals with mp 95-96°K (from hexane). IR spectrum (liquid petrolatum): 915 $cm^{-1}$ (δ $CH_2$, nonplanar). PMR spectrum ($CCl_4$): 2.40 (3H, s, $\mathbf{CH_3}C{=}N$); 4.71 (1H, d, β-H, $J_{gem}$ = 2 Hz); 5.03 (1H, d, β'-H, $J_{gem}$ = 2 Hz); 7.00-7.90 ppm (10H, m, arom. protons). Found: C 81.1; H 6.0%. $C_{16}H_{15}NO$. Calculated: C 81.0; H 6.3%.

cis-O-(β-Phenylvinyl)acetophenone Oxime (Ib). A mixture of 0.875 g (5 mmoles) of potassium acetophenone oximate, 1 ml (10 mmoles) phenylacetylene, and 10 ml DMSO was left for 50 h at 20°C. To the solution we added 50 ml of benzene, 50 ml of water, and it was shaken, the benzene layer washed with 3 × 50 ml of water, and dried with $Na_2SO_4$. Benzene was distilled off under vacuum, the residue chromatographed on silica gel 40/100 μm with a 1:4 benzene—hexane mixture, 0.118 g of the ether Ib was eluted, yield 70% on the basis of the reacted oxime, white crystals, mp 75-77°C (from hexane). Benzene washed out 0.5 g of unreacted oxime. The PMR spectrum of the ether Ib ($CCl_4$): 2.38 (3H, s, $\mathbf{CH_3}C{=}N$); 5.25 (1H, d, α-H, $J_{\alpha\beta}$ = 10 Hz); 6.95-7.85 ppm (11H, m, β-H and arom. protons). Found: C 81.5; H 6.6%. $C_{16}H_{15}NO$. Calculated: C 81.0; H 6.3%.

2,5-Diphenylpyrrole (IIa). A mixture of 0.118 g (0.5 mmole) of the ether Ia, 0.028 g (0.5 mmole) KOH, and 3 ml DMSO was mixed for 8 h at 45°C. The reaction mixture was poured out into 20 ml of water, extracted with benzene (5 × 10 ml), dried with $Na_2SO_4$, and benzene distilled off under vacuum. The residue was chromatographed on silica gel 40/100 μm in the system benzene—hexane, 1:1. Yield 0.026 g (25%) 2,5-diphenylpyrrole, mp 143-144°C. According to the data of [5], mp 143.5-144°C. IR spectrum ($CCl_4$): 3480 $cm^{-1}$ (NH). PMR spectrum ($CCl_4$): 6.49 (2H, d, 3-H, 4-H, $J_{13} = J_{14}$ = 2 Hz); 7.00-7.80 ppm (11H, m, NH and arom. protons).

2,4-Diphenylpyrrole (IIb). A mixture of 0.237 g (1 mmole) of the ether Ib, 0.056 g (1 mmole) KOH, and 6 ml DMSO was heated with mixing to 105°C in 30 min and exposed at this temperature for another 30 min. Analogously to the preceding, 0.035 g (17%) 2,4-diphenylpyrrole, mp 176-177°C, was isolated. According to the data [7], mp 177-178°C. IR spectrum ($CCl_4$): 3465 $cm^{-1}$ (NH). PMR spectrum (acetone-$d_6$): 6.68 (1H, m, 5-H); 6.92-7.60 ppm (12H, m, 3-H, NH, arom. protons).

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