ALKENYLATION BY 5-HEXEN-2-ONE OXIME: PROTOTROPIC ISOMERIZATION UNDER TROFIMOV REACTION CONDITIONS

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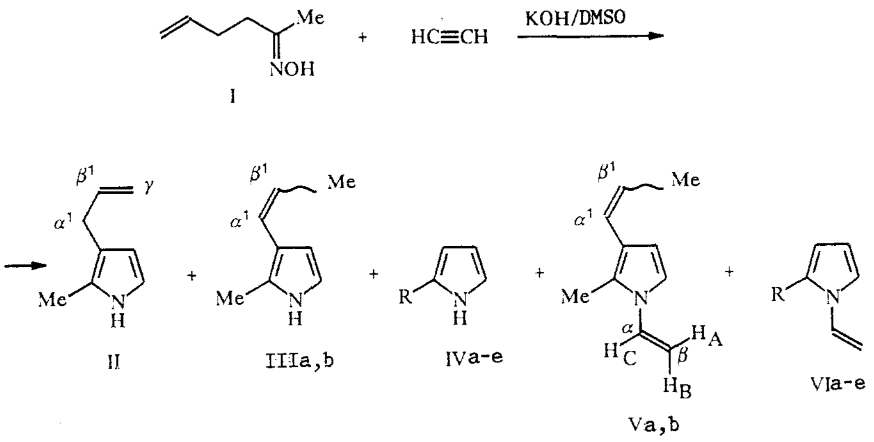
From 5-hexene-2-one oxime (I) and acetylene in KOH/DMSO, 2-methyl-3-(2-propenyl)pyrrole (II), E- and Z-2-methyl-3-(1-propenyl)pyrroles (III), and E- and Z-1-vinyl-2-methyl-3-(1-propenyl)pyrroles (V) were synthesized. The isomerization of the alkenyl radical of pyrroles II was studied.

It is known [1, 2] that pyrroles with unsaturated substituents receive attention as convenient starting materials for the synthesis of different functionalized pyrrole compounds. However, their restricted availability limits their usefulness. In our view, a convenient and promising method for the synthesis of pyrroles with unsaturated carbon—carbon bonds in a side chain might be the reaction of alkenone oximes with acetylene by the Trofimov reaction [3, 4]. The aim of our work was thus the study of the reaction of 5-hexene-2-one oxime with acetylene in the KOH/DMSO system.

From the mechanism of the reaction [4] and the results of the indicated study, the process may be represented by the following scheme:



I-VIa: R = 3-butenyl; b: R = E-2-butenyl; c: R = Z-2-butenyl; d: R = E-1-butenyl; e: R = Z-1-butenyl.
IIIa and Va — E-isomers; IIIb and Vb — Z-isomers.

The presence of the unsaturated substituent in the starting ketone I increases the preparative significance of the reaction because of the controllable formation of its prototropic isomerization products. In the given case the isomerization took place in 93% yield and the E:Z isomer ratio for pyrroles III and V was 7:3. The regiospecificity of the reaction in the temperature range of 90-110°C is shown by the absence of compounds IVa-e and VIa-e among the reaction products. The latter is explained by the large reaction rate of the methylene groups adjacent to the oxime function compared to the methyl group under these conditions. The implication of the latter in the formation of the pyrrole ring probably may occur under more vigorous temperature conditions [4], although even above 120°C strong tar formation is already observed.

Observations of the dynamic processes by GLC indicates the following succession for the formation of the reaction products: I → II → III → V. This introduced the possibility of obtaining pure pyrrole II, by arresting the process at the stage of formation of the pyrrole ring (before the appearance of compounds III and V). Pure N-vinylpyrrole V is obtained by exhaustive vinylation of 5-hexene-2-one oxime in an autoclave under acetylene pressure (after consumption of the preceding I-III). The isolation of pyrrole III directly from the reaction mixture is not advisable because of difficulty with its decomposition. It is possible to discontinue the addition of acetylene before the appearance of the N-vinylpyrrole V in the reaction mixture, leaving the opportunity only

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TABLE 1. Chemical Shifts (δ, ppm) of the Protons in 2-Methylpyrroles

Compound	H_A	H_B	$NH(H_C)$	H_4	H_5	α'—CH_2, (α'—H)	β'—H	2-Me	γ—CH_2, (β'—Me)
II			7,40	5,80	6,31	3,07	5,85	2,05	4,90
IIIa			7,80	6,20	6,52	6,25	5,77	2,19	1,81
IIIb			7,80	6,32	6,59	6,24	5,48	2,13	1,87
Va	4,89	4,47	6,69	6,61	6,77	6,20	5,77	2,09	1,81
Vb	4,51	4,51	6,69	6,29	6,81	6,18	5,47	2,09	1,85

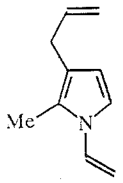
TABLE 2. Chemical Shifts for ^{13}C (ppm, compared to TMS) for 2-Methylpyrroles [3]

Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	C_α	C_β	$C_{\alpha'}$	$C_{\beta'}$	2-Me	C_γ (β'—Me)
II	122,5	116,1	109,0	114,6			30,5	138,0	10,7	113,6
Va	124,5	120,2	107,3	115,8	130,2	96,1	123,5	120,6	9,0	14,5
Vb	126,5	119,3	110,4	115,2	130,2	96,7	121,4	122,6	9,3	14,7

for the isomerization II ⇄ III. However, it is extremely convenient to isomerize pyrrole II in the KOH/DMSO system under nonaqueous conditions. At 110°C the equilibrium concentration of pyrroles II:III is established in 1.5 h.

Evaluation of the enthalpy of activation of the isomerization process under these conditions (in the temperature interval of 90-120°C) gives $\Delta H = 58$ kJ/mole. The "reverse" isomerization of pyrrole III under these conditions gives exactly the same ratio of structural isomers II and III. As with the corresponding E- and Z-isomer ratio (7:3), this probably reflects the thermodynamic equilibrium and it occurs through a transition state [5] characteristic of alkenylarenes.

The presence of the vinyl group in pyrrole V probably increases its stability to a great extent compared to structure VII, which is not found among the reaction products, although it should be.

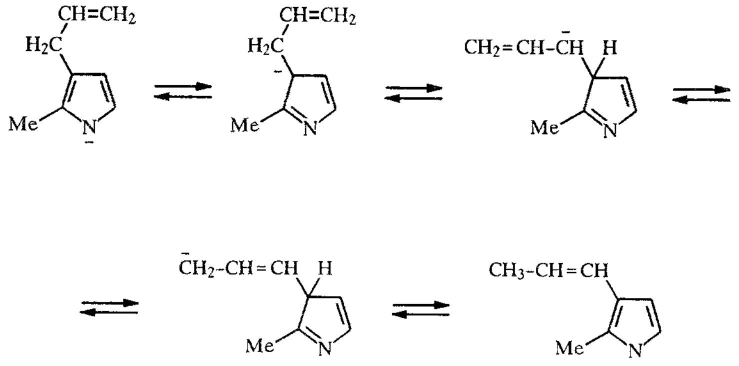


VII

It is also interesting that a direct vinylation according to the following scheme does not occur:

$$\mathrm{II} \xrightarrow{HC\equiv CH} \mathrm{VII}$$

The considerably easier ionization of the NH bond in the super-basic KOH/DMSO solution [6] compared to the CH bond of the allyl substituent probably promotes the prototropic rearrangement because of the delocalization and disproportionation of the negative charges.



If it were not for such an influence, then in evaluation of the rates of processes II → III and III → V the rate of the vinylation II → VII could exceed the rate of the isomerization of VII → V (starting from the temperature conditions of the synthesis) by almost a factor of ten. In a word, the rearrangement of the allyl radical into 1-propenyl takes place extremely rapidly at the point of the vinylation of the NH bond.

The structures of the synthesized pyrroles were confirmed by NMR spectroscopy (cf. Tables 1 and 2).

EXPERIMENTAL

The ^1H (200.13 MHz) and ^{13}C NMR (50.3 MHz) were obtained on a Bruker WP-200 SY instrument, the IR spectra on a Specord IR-75 spectrometer, and GLC analyses were carried out with an LKh-80 chromatograph, with a cathetometer detector, He carrier gas, column 2 m × 3 mm with a liquid phase of DC-550 on Chromatone NAW-HMDS.

2-Methyl-3-(2-propenyl)pyrrole (II). To a mixture of 5 g (0.044 mole) of oxime I, 1.5 g (0.027 mole) of ground KOH in 50 ml of DMSO at 90-95°C was added acetylene over 2.5 h. The reaction was turned off and the reaction mixture was cooled to 20°C, diluted with 2 volumes of water, and extracted with diethyl ether (2 × 20 ml). The organic layer was dried with potash and the ether was evaporated. The residue was separated by TLC on Al_2O_3, eluting with 1:1 hexane/ether to give 2.43 g (0.02 mole, 46%) of pyrrole II with bp 90°C (8 mm Hg), n_D^{20} 1.5158, d_4^{20} 0.8956. The IR spectrum (thin film): 720, 920, 1000, 1280, 1380, 1420, 1490, 1540, 1560, 1640, 3010, 3400 cm^{-1}. Based upon the recovery of 2.21 g of oxime I from the reaction mixture, the yield of pyrrole II was 81%.

3-Methyl-3-(1-propenyl)pyrrole (III) was obtained by the isomerization of pyrrole II $\rightleftarrows$ III. A mixture of 1 g (0.008 mole) of pyrrole II, 0.3 g (0.005 mole) of KOH previously calcined at 550°C, and 10 ml of anhydrous DMSO was boiled (120°C) for 1.5 h with stirring in an atmosphere of N_2. A sample was withdrawn every 15 min for TLC analysis. After workup as described above, a mixture of 0.93 g (0.008 mole) of pyrrole III (IIIa:IIIb = 7:3) and 0.03 g of pyrrole II were isolated, and an additional 0.04 g of the latter were recovered. The isomerization of an isolated mixture by the above conditions gave a ratio of pyrroles III and II of 93:7, and of the isomers IIIa and IIIb of 7:3. The enthalpy of activation [7] of the process II → III was calculated by graphing the dependence of log (k/T)—1/T, the rate constants for the forward reaction every 10°C in the 90-120°C temperature range from the kinetic curves for the disappearance of pyrrole II and the formation of pyrrole III, allowing for the reversibility of the process [8]. The actual concentrations of pyrroles II and III were evaluated by GLC analyses.

1-Vinyl-2-methyl-3-(1-propenyl)pyrrole (V). A mixture of 10 g (0.088 mole) of oxime I, 3 g (0.053 mole) of KOH, 100 ml of DMSO, and acetylene (10 atm) was heated (110°C) in a rotating autoclave for 3 h. Workup gave 10.4 g (0.07 mole, 80%) of pyrrole V, bp 98-99°C (5 mm Hg), n_D^{20} 1.5717, d_4^{20} 0.9254. IR spectrum: 575, 845, 855, 930, 955, 1642, 2865, 2888, 2920, 3120 cm^{-1}. Ratio of isomers Va:Vb = 7:3.

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