EXPERIMENTAL

PMR spectra were taken on T-60 and Varian XL-100/12 instruments in DMSO-d_6 and acetone-d_6 with TMS as internal standard; and ^{13}C NMR spectra were taken at 50°C in DMSO-d_6 on a CFT-20 instrument; UV and IR spectra were recorded on Perkin-Elmer 402 and 577 instruments, respectively. The individuality of the 3-acyl-2-methylindole oximes was checked by TLC on Silufol in the benzene–ethyl acetate (5:1) and benzene–methyl ethyl ketone (20:1) systems, with development of the spots by iodine vapor.

The 3-acyl-2-methylindole oximes (Ia-k) were obtained by a standard procedure [1], and their constants and yields are given in Table 1.

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SYNTHESIS OF O-VINYL ETHERS OF 3-ACYLINDOLE OXIMES AND THEIR HETEROCYCLIZATION TO PYRROLYLINDOLES

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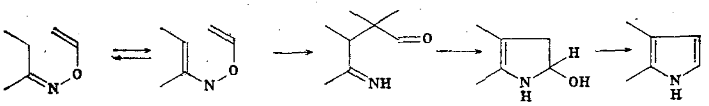
O-vinyl ether of 3-acylindole oximes have been synthesized and the possibility has been shown of their thermal conversion into pyrrolylindoles, which permits a heterocyclization mechanism including the stage of [3,3]-sigmatropic shift to be suggested.

In 1970, B. A. Trofimov et al. proposed a basically new method for constructing the pyrrole ring — the heterocyclization of ketoximes with acetylene in a superbasic medium [1]. We extended this heterocyclization to 3-acylindole oximes, which enabled the previously unknown 3-(pyrrol-2-yl)indoles to be obtained [2].

The question of the mechanism of the Trofimov reaction cannot be regarded as has been answered hitherto, although the discoverers of the reaction themselves have recently tended towards the opinion that the process takes place through the stage of a [3,3]-sigmatropic shift in O-vinyloximes formed as intermediates [3].



To answer the question of the possibility of such a mechanism in the case of ketoximes of the indole series, we set ourselves the aim of synthesizing O-vinyl ethers of 3-acylindole oximes and investigating the possibility of their conversion into the corresponding pyrrolylindoles. As a prerequisite for this was used the fact that 3-acylindole oximes exist predominantly in the syn configuration [4, 5] which may ensure the six-membered transition state that is necessary for a sigmatropic rearrangement.

The O-vinyl ether of 3-acetyl-1-methylindole oxime (Ia) was obtained from the corresponding oxime and acetylene in the superbasic medium KOH/DMSO at 65-70°C under an acetylene pres-

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TABLE 1. O-Vinyl Ethers of 3-Acylindole Oximes

Compound	Reaction temperature, °C	mp, °C	UV spectrum, λ_{max}, nm (log ε)	PMR spectrum		Found			Empirical formula	Calculated			Yield, %
				a-H	b-H	C, %	H, %	M^+		C, %	H, %	M	
Ia	65	65—67	—	4,85	4,22	73,6	6,6	214	$C_{13}H_{14}N_2O$	72,9	6,5	214	54*
Ib	60	37—39	223 (4,41), 280 (4,01)	4,63	4,13	73,2	7,2	228	$C_{14}H_{16}N_2O$	73,7	7,0	228	10
Ic	50	75—77	223 (4,42), 284 (4,04)	4,40	4,05	74,7	7,6	232	$C_{15}H_{18}N_2O$	74,4	7,4	232	21
Id	45	54—56	225 (4,45), 287 (4,05)	4,55	4,10	74,7	8,1	256	$C_{16}H_{20}N_2O$	75,0	7,8	256	25

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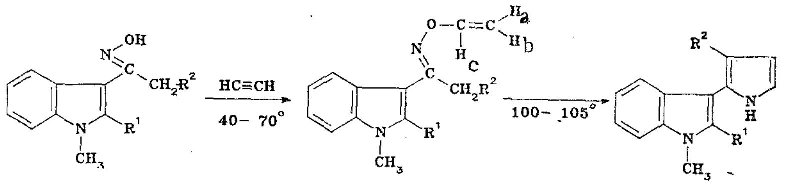
*Yield on the oxime that took part in the reaction.

sure of 10-12 atm. The special features of the structure of 3-acyl-1,2-dimethylindole oximes [5] permits their O-vinyl ethers to be obtained under substantially milder conditions: at a temperature of 40-70°C and atmospheric pressure.



Ia-d IIa-d

I, IIa R^1=H, R^2=H; b R^1=CH_3, R^2=H; c R^1=R^2=CH_3; d R^1=CH_3, R^2=$CH(CH_3)_2$

The relative ease of vinylation of the 3-acyl-1,2-dimethylindole oximes is apparently due to the greater accessibility of the hydroxy group for attack by acetylene due to the departure of the oxime grouping from the plane of the indole nucleus [5].

In the PMR spectra of the O-vinyl ethers (I), the signal of the a-H proton of the vinyl grouping at 4.40-4.85 ppm consists of a doublet of doublets with a vicinal constant J_{ac} = 14 Hz and geminal constant J_{ab} = 1 Hz. The signal of the b-H proton is also a doublet of doublets with a vicinal constant J_{bc} = 7 Hz and geminal constant J_{ba} = 1 Hz, and appears at 4.05-4.22 ppm. The signal of the c-H proton falls into the region of aromatic protons and increases the total integral intensity of the signals in this region by one proton unit.

The mass spectra of the O-vinyl ethers of the oximes (Ia-d) show the peaks of the molecular ions, the peaks of ions due to the splitting out of the O-vinyl group (M – 43) (100%), and those of ions connected with the complete elimination of the oxime grouping.

In a superbasic medium in the absence of acetylene, the O-vinyl oximes (Ia-d) are smoothly converted into the corresponding 3-(pyrrol-2-yl)indoles (IIa-d). This fact indicates that in the case of the 3-acylindole oximes heterocyclization takes place by the O-vinyl oxime route, including the stage of a [3,3]-sigmatropic shift. The use of a superbasic medium in the thermal transformation of the O-vinyl ethers into pyrroles is due to the necessity for the isomerization of these ethers into enehydroxylamines, in which the sigmatropic shift actually takes place.

It is known that a side reaction in the heterocyclization of ketoximes with acetylene is the N-vinylation of the pyrrole nucleus formed. As we have shown previously [2], in the case of 2-unsubstituted 3-acylindole oximes, it is possible to suppress this side reaction by changing the reaction conditions. In the case of the 3-acyl-2-methylindole oximes, however, it was impossible by any variations whatever in the reaction conditions to suppress the process of N-vinylation in the direct heterocyclization of such oximes with acetylene in a superbasic medium. This is due to some disturbance of the coplanarity of the system of the 2-methyl-3-(pyrrol-2-yl)indoles (IIb-d) caused by steric hindrance between the methyl group in position 2 of the indole nucleus and the pyrrole ring, as a result of which the pyrrole nitrogen atom, which has departed from the plane, becomes more accessible for attack by acetylene. In actual fact, in the UV spectra of the pyrroles (IIb-d), a hypsochromic shift of the long-wave absorption band (Table 2) by approximately 20-25 nm as compared with the 3-(pyrrol-2-yl)indoles is observed, the maxima of their long-wave absorption bands lying in the 315-320 nm region.

TABLE 2. 1-Methyl-3-(pyrrol-2-yl)indoles (II)

Compound	mp, °C	UV spectrum, λ_{max}, nm (log ε)	PMR spectrum, protons of the pyrrole nucleus		IR spectrum, NH, cm^{-1}	Found, %		Empirical formula	Calculated, %		Yield, %
			α-H	β-H		C	H		C	H	
IIa	108—110	212 (4,19), 245 (4,30), 320 (3,72)	6,26	6,80 6,46	3380	79,7	6,3	$C_{13}H_{12}N_2$	79,6	6,1	35
IIb	165—166	211 (4,24), 240 (4,31), 298 (3,80)	6,23	6,93	3360	79,8	6,8	$C_{14}H_{14}N_2$	80,0	6,7	36
IIc	158—160	212 (4,31), 237 (4,39), 296 (3,82)	6,13	6,86	3380	80,8	7,5	$C_{15}H_{16}N_2$	80,4	7,1	31
IId	170—172	210 (4,36), 242 (4,41), 295 (3,84)	6,23	6,85	3380	80,5	7,7	$C_{17}H_{20}N_2$	80,9	7,9	29

It has been found that the isolation of the intermediate O-vinyl ethers of 3-acyl-2-methylindole oximes and their subsequent thermal conversion into pyrrolylindoles is the only possible way of obtaining nonvinylated compounds. The reaction can be performed in stages: first at a temperature of 40-70°C in a superbasic medium with a feed of acetylene to yield the O-vinyloximes and then, when according to TLC a considerable amount of vinyl ethers has been formed in the reaction mixture, the feed of acetylene is stopped and the temperature is raised to 100-105°C to complete heterocyclization into 2-methyl-3-(pyrrol-2-yl)indoles (IIb-d).

The IR spectra of the pyrrolylindoles (II) each shows the absorption band of the stretching vibrations of the NH bond at 3360-3380 cm^{-1} (Table 2). The formation of a pyrrole ring is also shown by the appearance of characteristic multiplet signals in the 6.2-7.0 ppm region of the PMR spectra.

EXPERIMENTAL

UV spectra were taken on a Perkin-Elmer 402 instrument in ethanol, IR spectra on UR-20 and Perkin-Elmer 77 instruments in paraffin oil, and PMR spectra on T-60 and Tesla BS-498 instruments with a working frequency of 100 MHz in acetone-d_6 and DMSO-d_6 with TMS as internal standard. Mass spectra were taken on an MKh-1303 instrument with direct introduction of the sample into the ionization space at an inlet temperature 15-20°C below the melting point of the sample and with an energy of the ionizing electrons of 70 eV. The individuality of the compounds synthesized was checked by TLC on Silufol in the benzene—ethyl acetate (5:1) and benzene—methyl ethyl ketone (20:1) systems.

O-Vinyl Ether of 3-Acetyl-1-methylindole Oxime (Ia). A mixture of 3 g (0.016 mole) of 3-acetyl-1-methylindole oxime, 0.9 g (0.016 mole) of powdered caustic potash, and 40 ml of DMSO was charged into an autoclave, and, after it had been heated to 65°C, acetylene was fed in under a pressure of 10-12 atm. The reaction mixture was kept at this temperature for 3 h, with acetylene being fed three times, and then the autoclave was cooled and the contents were poured into water and extracted with ether. The ethereal extract was washed with water and dried with sodium sulfate, and the solvent was distilled off in vacuum. The residue was chromatographed on a column of neutral Al_2O_3 with heptane as the eluent. The yields of compound (Ia) and its constants are given in Table 1.

O-Vinyl Ethers of 3-Acyl-1,2-dimethylindole Oximes (Ib-d). With stirring and heating at 40-70°C, an equimolar amount of caustic potash was added to a solution of 1 g of a 3-acyl-1,2-dimethylindole oxime in 20 ml of DMSO, and the mixture was heated for another 30 min, after which a current of acetylene was passed into it for 12-18 h. The reaction mixture was cooled, poured into water, and extracted with ether, and the extract was dried with anhydrous sodium sulfate. The O-vinyl oximes (I) were isolated on a column of silica gel (40 × 100 μ) in the benzene—heptane (10:1) system in an atmosphere of argon (Table 1).

1-Methyl-3-(pyrrol-2-yl)indoles (IIa-d). A. A solution of 1 g of the O-vinyl ether of an oxime and a 1.2-fold excess of caustic potash in 20 ml of DMSO was stirred at 100-105°C until the ether had completely disappeared (according to TLC). The reaction mixture was then poured into water and extracted with benzene or ether, and the extract was dried with anhydrous sodium sulfate. The solvent was evaporated off and the residue was chromatographed on neutral Al_2O_3 in the benzene—heptane (10:1) system in an atmosphere of argon.

B. A solution of 1 g of a 3-acylindole and an equimolar amount of caustic potash in 20 ml of DMSO was stirred at 45-70°C for 30 min, and then a current of acetylene was passed in at the same temperature for 12-18 h. Then the feed of acetylene was stopped and the reaction mixture was heated at 100-105°C for 8-10 h. It was worked up by method A. The characteristics of the pyrrolylindoles (II) are given in Table 2.

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