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AN EXAMPLE OF A NOVEL SYNTHETIC APPROACH TO ALKENYLPYRROLES

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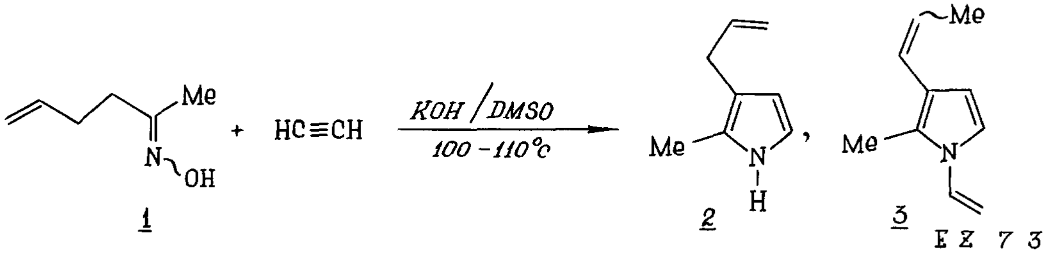
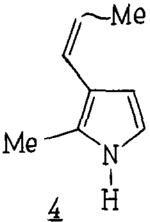
Summary: The synthesis of 2-methyl-3-(2-propenyl)pyrrole (2) and E- and Z-2-methyl-3-(1-propenyl)pyrroles (3) via the reaction of 3-butenyl methyl ketoxime (1) with acetylene in the KOH-DMSO system is reported.

Pyrroles with unsaturated substituents are known to be useful starting species for syntheses of a variety of functionalized pyrrole compounds which now attract an ever-growing attention[1,2], but synthetic procedures for their preparation are so far quite limited[1]. Recently, a new general method both for the pyrrole ring construction and the vinyl group introduction therein (to the nitrogen atom) by the reaction of ketoximes with acetylene in the KOH-DMSO superbasic system (Trofimov reaction[3,4]) has been discovered and systematically explored[5-9].However, no experimental details of this reaction with unsaturated ketoxime have been heretofore published.

In this letter we sketch for the first time our study of the Trofimov reaction in the ethylenic ketoxime series. The latter prove to undergo readily the above reaction to form the expected alkenylpyrroles in good or satisfactory yields. The example of the one-step transformation of 3-butenyl methyl ketoxime (1) into 2-methyl-3-(2-propenyl)pyrrole (2) and 2-methyl-3-(1-propenyl)pyrrole (3, E and Z), described here, is typical and displays well two important features, namely, that the reaction can be either stopped selectively on the stage of the pyrrole ring formation with no NH-vinylation and prototropic isomerization of the alkenyl radical or completed up to N-vinylpyrrole with the alkenyl radical double bond entirely shifted towards the pyrrole ring:



The non-N-vinylated pyrrole 2 having a non-isomerized alkenyl radical is obtainable when the reaction temperature does not exceed 100°C and the heating time is within 1 hr with no large exceed of acetylene in the closed reaction vessel under the pressure of 50-100 psig. The synthesis of pyrrole 2 can be also attained under the atmospheric pressure by passing acetylene through the stirring reaction mixture. In the latter case the reaction should be carried out until traces of other pyrroles (3-5) become detectable (TLC, GLC).



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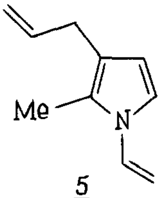

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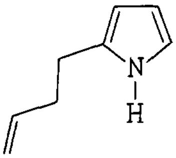
The pyrroles 4 and 5 are usually observed in the reaction solution together with pyrroles 2 and 3 but separation of such a mixture is laborous[10]. At a higher temperature (110°C) with about a 10-fold excess of acetylene under the pressure of 150-200 psig, both the isomerization and vinylation processes are completed after 3 hrs to result in the pyrrole 3 (E- and Z-isomers) as the only isolable reaction product.

The reaction proceeds as a regiospecific process up to 100°C: neither pyrroles 6-8 nor their N-vinylated derivatives have been found in the reaction mixture, i.e., only the CH_2 group adjacent to the oxime function of the 3-butenyl radical enters the pyrrole ring under these conditions.



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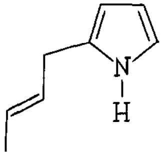

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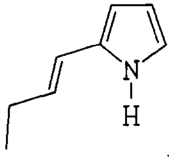

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This implies a stereospecific participation of the E-form of the ketoxime 1 in the pyrrole ring formation, since the latter represents a major configuration of this ketoxime. The fact that the yield of pyrroles 3 (80%) can exceed the E-form content (67%) is explained by an $E \rightleftharpoons Z$ interconversion[11,12]. However, according to earlier observations on the regiodirection of the Trofimov reaction[5-7,13], the CH_3 group of the ketoxime 1 can be also involved in the pyrrole ring and, therefore, pyrroles 6-8 can be formed if the synthesis is carried out at a higher temperature (140°C)[10] which shifts the configuration equilibrium towards the Z-form.

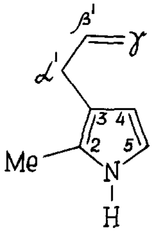
A mixture of 1 (88 mmol), KOH (53 mmol), H_2O (10 mmol), and DMSO (100 ml) was autoclaved with acetylene at 100°C for 1 hr (1 l rotating vessel, initial acetylene pressure at room temperature was about 50 psig). After an aqueous work-up followed by extraction (Et_2O), drying (K_2CO_3) and vacuum distillation the pyrrole 2 in a 30% yield was isolated, bp 90°C/8 mmHg,

n_D^{20} 1.5158, d_4^{20} 0.8956[14]. IR (neat, cm^{-1}): 720 vs, 1380 m, 1490 m, 1540 m, 1560 m, 3085 m (pyrrole ring)[15], 920 vs, 1000 s, 1280 m, 1420 m, 1640 s, 3010 v ($CH_2{=}CHCH_2$), 3400 vs, broad (NH).

Similarly, treatment of 1 (88 mmol) and KOH (53 mmol) with acetylene (1 l rotating autoclave, initial pressure at room temperature was about 200 psig, net input of C_2H_2 was 28 l) in DMSO (100 ml) at 110°C for 3 hrs afforded in a 80% yield the pyrrole 3 (E:Z 7:3), bp 98-99°C/5 mmHg, n_D^{20} 1.5717, d_4^{20} 0.9254. IR (neat, cm^{-1}): 575 m, 855 s, 955 vs, 1642 vs, 3120 w ($NCH{=}CH_2$)[15], 845 m, 930 m, 3030 m, (-CH=CH-), 2865 s, 2880 s, 2920 s (CH_3), no absorption in the 3200-3600 cm^{-1} region was observed.

Conclusive evidences for the structure of pyrroles 2 and 3 were furnished by the NMR spectra (Table).

Table. NMR spectra of pyrroles 2 and 3



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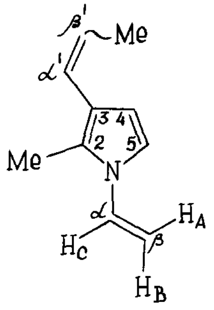

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^1H Chemical Shifts[16]

Pyrrole	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)
2			7.4	5.80	6.31	3.07	5.85	2.05	4.90
3-E	4.89	4.47	6.69	6.21	6.77	6.20	5.77	2.09	1.81
3-Z	4.94	4.51	6.69	6.29	6.81	6.18	5.47	2.09	1.85

^{13}C Chemical Shifts[16]

Pyrrole	C_2	C_3	C_4	C_5	C_α	C_β	$C_{\alpha'}$	$C_{\beta'}$	2-Me	C_γ (β'-Me)
2	122.5	116.1	109.0	114.6			30.5	138.0	10.7	113.6
3-E	124.5	120.2	107.3	115.8	130.2	96.1	123.5	120.6	9.0	14.5
3-Z	126.5	119.3	110.4	115.2	130.2	96.7	121.4	122.6	9.3	14.7

Thus, in the ^{1}H NMR spectrum of pyrrole 2, a multiplet of γ-CH$_2$ group (δH 4.90 ppm), quartet of triplets of β'-CH= (δH 5.85 ppm, ^3J(=CH-CH$_2$) 6.2 Hz) and doublet of triplets of α-CH$_2$ (δH 3.07 ppm, ^4J(CH$_2$-CH=CH$_2$) 1.6 Hz) are observed. The 1-propenyl group of pyrroles 3 gives signals of γ-CH$_3$ (δH 1.81 ppm, doubled doublet of doublets, ^3J(CH$_3$-CH) 6.8 Hz, ^4J(CH$_3$-CH=CH) 1.8 Hz, ^6J(CH$_3$-H$_4$) 0.4 Hz - for E-isomer; δH 1.85 ppm, doublet of doublets, ^6J(CH$_3$-H$_4$) 0 - for Z-isomer), -CH= (δH 5.77 ppm, doublet of quartets, ^3J(CH=CH) 15.5 Hz - for E-isomer, δH 5.47 ppm, doublet of quartets, ^3J(CH=CH) 11.4 Hz - for Z-isomer), -CH= (δH 6.20 ppm - for E-isomer, δH 6.18 ppm - for Z-isomer).

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14. Correct analytical data for both pyrroles 2 and 3 were obtained.
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16. NMR Spectra were recorded in CDCl$_3$ on a Bruker WP-200 NMR Spectrometer (200 and 50.3 Mhz for ^{1}H and ^{13}C, respectively).

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