# PYRROLES FROM KETOXIMES AND ACETYLENE.

## 44.* METHYL ARYL KETOXIMES WITH REACTIVE SUBSTITUENTS

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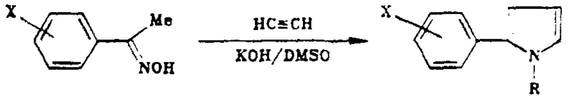
*The Trofimov reaction was extended to methyl aryl ketoximes with substituents in the benzene ring that are unstable with respect to the action of a strongly basic medium. The corresponding pyrroles and their 1-vinyl derivatives were obtained. 4-Nitroacetophenone oxime, from which only 2-phenyl- and 1-vinyl-2-phenylpyrrole were obtained, and 4-bromoacetophenone oxime, the reaction of which leads to the formation of 1-vinyl-2-(4-vinyloxyphenyl)pyrrole in addition to the principal 2-(4-bromophenyl)pyrrole, constituted exceptions.*

Alkyl aryl ketoximes with substituents in the benzene ring that are unstable with respect to strongly alkaline media condense with acetylene under the conditions of the Trofimov reaction to give pyrroles and their 1-vinyl derivatives in low yields [2, 3]. For example, 4-bromoacetophenone oxime (Ia) reacts with acetylene to give either 2-(4-bromophenyl)pyrrole (IIa) (36%) [2] or 1-vinyl-2-(4-bromophenyl) pyrrole (IIIa) (22%) [3].

In order to ascertain the behavior of methyl aryl ketoximes with other reactive substituents in the Trofimov reaction and obtain new pyrroles and 1-vinylpyrroles we continued our investigation of this reaction with ketoximes: $XC_6H_4C(=NOH)Me$ (X = 4-Br, 4-OH, 4-F, 3-$NH_2$, 4-$NH_2$, 4-$NO_2$) (Table 1).



Ia-f IIa-f, IIIa-g

X = 4-Br: Ia, IIa R = H, IIIa R = $CH_2{=}CH$; Ib X = 4-OH; X = 4-$CH_2{=}CHO$; IIb R = H, IIIb R = $CH_2{=}CH$, IIIg R = CH = CHSMe; X = F: Ic, IIc R = H, IIIc R = $CH_2{=}CH$; X = 3-$NH_2$: Id IId R = H, IIId R = $CH_2{=}CH$; X = 4-$NH_2$: Ie IIe R = H, IIIe R = $CH_2{=}CH$; If X = 4-$NO_2$, X = H: IIf R = H, IIIf R = $CH_2{=}CH$; M = Li, Na, K

As a result of our investigations, we observed that the yield of vinylpyrrole IIIa in the condensation of ketoxime Ia with acetylene increases to 35% with a decrease in the reaction temperature to 90°C (instead of 100°C) (expt. No. 3) with retention of all the other conditions [3]. At 60°C (expt. No. 4), in addition to pyrrole IIa, we were able to isolate a compound (2%) that, with respect to its IR and PMR characteristics, corresponds to 1-vinyl-2-(4-vinyloxyphenyl)pyrrole (IIIb) [4]. This fact confirms the previous assumption of saponification of the bromine atom by a strong base [3] and explains the significantly better yields of pyrrole and 1-vinylpyrrole obtained in the condensation with acetylene of 4-chloroacetophenone oxime, in which replacement of the chlorine atom bonded to the aromatic ring by a hydroxy group occurs under more severe conditions than the analogous replacement of the bromine atom.

Vinylpyrrole IIIb is obtained in higher (27%, expt. No. 5) yield and with a higher degree of purity from 4-hydroxyacetophenone oxime (Ib); in this case, its unvinylated precursor IIb is detected (by TLC) in the reaction mass

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*For communication 43, see [1].

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TABLE 1. Reaction Conditions and Yields of Pyrroles and 1-Vinylpyrroles

| Expt. No. | Exptl. conditions | | | | | | Pyrrole | Yield, % | Vinylpyrrole | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|
| | oxime | $T_r$, °C*1 | t, h | M | oxime: MOH molar ratio | acetylene pressure, atm | | | | |
| 1 | Ia | 80 | 2 | K | 2:1 | 13 | IIa | 36 [2] | IIIa | — |
| 2 | Ia | 100 | 3 | K | 1:1 | 12 | IIa | Traces | IIIa | 22 [3] |
| 3 | Ia | 90 | 3 | K | 1:1 | 12 | IIa | Traces | IIIa | 35 |
| 4 | Ia | 60 | 3 | K | 1:1 | 14 | IIa | 20 | IIIb | 2 |
| 5 | Ib | 100 | 3 | K | 1:1,4 | 10 | IIb | Traces | IIIb | 27*2,<br>0,05*3 [4] |
| 6 | Ib | 100 | 5 | K | 1:3 | — | IIb | 2 | IIIb | — |
| 7 | Ic | 90 | 2 | K | 1:1 | 12 | IIc | 11 | IIIc | Traces |
| 8 | Id | 90 | 3 | K | 1:1 | 12 | IId | 2 | IIId | 19 |
| 9 | Ie | 96 | 5 | K | 1:1 | — | IId | 14 | IIId | Traces |
| 10 | Ie | 70 | 3 | K | 1:1 | 12 | IIe | Traces | IIIe | 30 |
| 11 | Ie | 70 | 3 | K | 2:1 | 12 | IIe | Traces | IIIe | 14 |
| 12 | Ie | 90 | 3 | K | 1:1 | 12 | IIe | Traces | IIIe | 22 |
| 13 | Ie | 80 | 3 | Li | 1:1 | 12 | IIe | 25 | IIIe | Traces |
| 14 | Ie | 96 | 4,5 | K | 1:1 | — | IIe | 20 | IIIe | Traces |
| 15 | Ie | 90 | 5 | Na | 1:1 | — | IIe | 2 | IVe | 3*4 |
| 16 | If | 100 | 3 | K | 1:2 | 14 | II*5 | 7 | III*5 | 1 |

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*1 $T_r$ is the reaction temperature.

*2 The yield was not optimized.

*3 Yield of IIIg.

*4 Yield of O-vinyl ketoxime IVe.

*5 2-Phenylpyrrole (II) and its N-vinyl derivative III are formed.

TABLE 2. Constants of Pyrroles and 1-Vinylpyrroles

| Compound | mp, °C | Lit. | Compound | bp, °C (hPa) | $d_4^{20}$ | $n_D^{20}$ | Lit. |
|---|---|---|---|---|---|---|---|
| IIa | 158...160 | [2] | IIIa | 123...124 (1,33) | 1,3860 | 1,6469 | [3] |
| IIb | 106...107 | | IIIb | 122...128 (2,66) | 1,0722 | 1,6118 | [4] |
| IIc | 129 | | IIId | 150...154 (1,33) | 1,1171 | 1,6548 | |
| IId | 84...86 | | IIIe | 153...156 (1,33...2,66) | 1,1138 | 1,6628 | |
| IIe | 151...153 | | | | | | |

in trace amounts. In the reaction at atmospheric pressure (expt. No. 6) we were able to obtain pyrrole IIb in only 2% yield, and vinylpyrrole IIIb was not detected in the reaction mass (by GLC), which, however, contained a number of unidentified compounds. The presence of $CH_2$=CHO and $CH_2$=CHN groups in the IIIb molecule makes it a promising monomer and intermediate for fine organic synthesis. As has already been noted [4], in addition to pyrroles IIb and IIIb, Z-1-(2-methylthiovinyl)pyrrole (IIIg) is formed in low yield in this reaction.

In the condensation of 4-fluoroacetophenone oxime (Ic) with acetylene, in addition to possible saponification of the fluorine atom, regeneration of 4-fluoroacetophenone (IVc) (24%) becomes most appreciable as compared with other methyl aryl ketoximes, particularly when calcined KOH and dry DMSO are used. Ketone IVc is evidently formed due to nucleophilic addition of a hydroxide ion to the C=N bond of ketoxime Ic. 2-(4-Fluorophenyl)pyrrole (IIc) (11%, expt. No. 7) was obtained in the case of reaction in an autoclave. 1-Vinyl-2-(4-fluorophenyl)pyrrole (IIIc) is formed as an impurity under these conditions.

The expected pyrrole could not be isolated in the condensation of methyl perfluorophenyl ketone oxime with acetylene.

The factors that determine the yields of aminophenylpyrroles IId, e and IIId, e from aminoacetophenone oximes Id, e and acetylene are, as usual, the nature of the hydroxide cation, its concentration in DMSO, the reaction temperature, the reaction time, and the acetylene pressure (Table 1). The best yield (30%, expt. No. 10) of 1-vinyl-2-(4-aminophenyl)pyrrole (IIIe) can be obtained by condensation of ketoxime Ie with acetylene at 70°C in an autoclave using an equimolar ketoxime Ie:KOH ratio. In the case of a twofold decrease in KOH with retention of all the other conditions (expt. No. 11) the yield of vinylpyrrole IIIe decreases to 14%. A 20°C increase in the reaction temperature also leads to a decrease in the yield of this vinylpyrrole (expt. No. 12) and intensifies resinification. Unvinylated pyrrole IIe is formed in small amounts (~0.5%) under these conditions. Its yield can be increased to 25% (expt. No. 13) when KOH is replaced by LiOH and the reaction temperature is simultaneously decreased to 80°C (instead of 90°C). Pyrrole IIe was obtained in virtually the same yield with acetylene at atmospheric pressure at 96°C with an equimolar ketoxime Ie:KOH ratio (expt. No. 14). However, when KOH is

TABLE 3. IR and PMR Spectra of Pyrroles

| Compound | IR spectrum, ν, cm$^{-1}$ | PMR spectrum, δ, ppm |  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  | NH | X | 3-H | 4-H | 5-H | A—H* | B—H* | C—H* | $C_6H_4$ |
| IIb | 3390, 3430 (NH); 1490, 1600 (C= in the pyrrole and benzene rings ); 3050, 3100 (C—H arom.); 700, 710 (δ C—H); 1625 (C=C $OCH{=}CH_2$); 1015 (=C—O—C) | 8,40 | 4,44; 4,74; 6,64 | 6,28 | 6,43 | 6,82 |  |  |  | 6,98 . . . 7,41 |
| IIc | 3365, 3410 (NH); 1490, 1590 (C=C in the pyrrole and benzene rings ); 710 (δ C—H) | 8,34 |  | 6,27 | 6,34 | 6,81 |  |  |  | 7,38 . . . 7,02 |
| IId | 3200, 3320, 3390 (NH, $NH_2$); 1490, 1590, 1600 (C=C in the pyrrole and benzene rings); 700, 710 (δ C—H) | 11,05 | 5,03 | 6,06 | 6,34 | 6,80 |  |  |  | 6,70 . . . 7,10 |
| IIe | 3220, 3330, 3420 (NH, $NH_2$); 1500, 1590, 1605 (C=C in the pyrrole and benzene rings); 702 (δ C—H) | 10,86 | 4,50 | 6,02 | 6,17 | 6,65 |  |  |  | 6,54 . . . 7,26 |
| IIIb | 1640 (C=C , $NCH{=}CH_2$ $OCH{=}CH_2$); 1495, 1587 (C=C in the pyrrole and benzene rings); 705 (δ C—H) |  | 4,75; 4,40; 6,59 | 6,15 | 6,25 | 7,96 | 5,06 | 4,59 | 6,89 | 6,97 . . . 7,24 |
| IIId | 1640 (C=C , $NCH{=}CH_2$); 1500, 1600 (C=C in the pyrrole and benzene rings); 3030, 3100 (C—H arom ); 3206, 3365, 3450 ($NH_2$) |  | 3,62 | 6,19 | 6,24 | 7,04 | 5,09 | 4,60 | 6,90 | 6,55; 6,61; 6,71; 7,14 |
| IIIe | 1640 (C=C in $NCH{=}CH_2$); 1505, 1600 (C=C in the pyrrole and benzene rings) ; 3020, 3100 (C—H arom.); 710 (δ C—H); 3206, 3365, 3450 ($NH_2$) |  | 3,67 | 6,13 | 6,25 | 7,05 | 5,09 | 4,61 | 6,86 | 6,67 . . . 7,14 |

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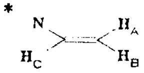
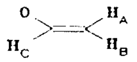
* 

$^2J_{AB}=1,0$; $^3J_{BC}=8,9$; $^3J_{AC}=15,8$ , 

$^2J_{AB}=2,0$; $^3J_{AC}=6,0$; $^3J_{AC}=15,0$ .

replaced by NaOH under the same conditions, pyrrole IIe is formed in only 2% yield (expt. No. 15), along with O-vinyl-4-aminoacetophenone oxime (IVe) (3%), the structure of which was confirmed by spectral data. The location of the amino group in the benzene ring of ketoximes Id, e does not have a substantial effect on the yields of the corresponding pyrroles IId, e (expts. Nos. 9 and 14) and vinylpyrroles IIId, e (expts. Nos. 8 and 12). Condensations of ketoximes Id, e with acetylene, even at a sufficiently low temperature, are accompanied by resinification due to polymerization of acetylene under the influence of the amine—DMSO system [5].

In the condensation of ketoxime Ie with acetylene (expt. No. 14) nitriles (intense absorption in the IR spectrum at 2240 $cm^{-1}$) and an acetylenic alcohol [bands at 2120 $cm^{-1}$ (C≡C), 3280 $cm^{-1}$ (≡CH), and 3430 $cm^{-1}$ (OH)] with an unestablished structure were detected in the reaction mass [these products were isolated in small amounts by chromatography on thin loose layers of $Al_2O_3$ (elution with ether)]. The presence of an amino group in the benzene ring of pyrroles IId, e makes them unstable during storage. After a number of unsuccessful attempts, we were unable to obtain a pyrrole from 4-nitroacetophenone oxime (If): as a rule, it is recovered from the reaction [3]. We observed (expt. No. 16) partial splitting out of the $NO_2$ group and the formation of 2-phenylpyrrole and its 1-vinyl derivative, which were identical, with respect to GLC, IR, and $^1H$ and $^{13}C$ NMR spectral data [6, 7], to samples obtained in the condensation of acetophenone oxime with acetylene.

In the condensation of ketoxime If with acetylene at 12 atm (100°C, 3 h, ketoxime If:KOH molar ratio 1.3:1) we noted the formation of 4-phenylacetonitrile [IR spectrum: 2220 $cm^{-1}$ (C≡N)], which, as in the case noted above, is formed as a result of dehydration and rearrangement of starting ketoxime If [8].

The constants and IR and PMR spectra of the synthesized compounds are presented in Tables 2 and 3, respectively.

## EXPERIMENTAL

Chromatographic analysis was carried out with an LKhM-8 MD chromatograph with a catharometer as the detector; the column dimensions were 1 m × 3 mm, the support was chromaton N-AW HMDS, the stationary phase was 5% silicone DS-550, the temperature of the thermostat was 210°C, the temperature of the vaporizer was 300°C, the temperature of the catharometer was 220°C, and the carrier gas was helium. Thin-layer chromatography was carried out on Silufol UV-254 plates and fine loose layers of $Al_2O_3$. The IR spectra of microlayers of KBr pellets of the compounds were recorded with a Specord-75 spectrometer. The PMR spectra were obtained with a Tesla BS-567A spectrometer (100 MHz).

**1-Vinyl-2-(4-vinyloxyphenyl)pyrrole (IIIb).** A mixture of 8 g (53 mmoles) of ketoxime Ib, 4.2 g (75 mmoles) of KOH, and 100 ml of DMSO was heated for 3 h at 100°C in a rotating autoclave (1 liter) with acetylene at an initial pressure of 10 atm. The mixture was then cooled to room temperature and poured into 400 ml of cold water. The aqueous mixture was extracted with ether, and the ether extracts were washed with water and dried with potassium carbonate. The ether was removed, and the residue was distilled in vacuo to give 3 g (27%) of vinylpyrrole IIIb. The purity of the compound after additional purification by column chromatography [$Al_2O_3$, benzene—hexane (1:6)] was 98%.

**2-(4-Vinyloxyphenyl)pyrrole (IIb).** A 7.6-g (50 mmoles) sample of ketoxime Ib, 8.4 g (150 mmoles) of KOH, and 100 ml of DMSO were placed in a flask equipped with a stirrer, a reflux condenser, and a bubbling tube for admitting acetylene, and the mixture was heated for 45 min at 100°C. Acetylene was then bubbled into the mixture for 5 h without interrupting the vigorous stirring. After workup as described above, fractionation on plates with a fine loose layer of $Al_2O_3$ [hexane—ether (3:1)] gave 0.15 g (2%) of pyrrole IIb.

**Pyrroles IIa, c-e and Vinylpyrroles IIIa, d, e (Table 1).** These compounds were similarly obtained.

**O-Vinyl-4-aminoacetophenone Oxime (IVe).** Acetylene was bubbled into a mixture of 7.5 g (50 mmoles) of ketoxime Ie, 2 g (50 mmoles) of NaOH, and 100 ml of DMSO heated to 90°C with continuous stirring for 5 h. Standard workup and chromatography on $Al_2O_3$ [pentane—ether (1:5)] gave 0.23 g (3%) of O-vinyl oxime IVe. IR spectrum (microlayer): 1615 ($\nu_{C=C}$ OCH—$CH_2$); 3080 ($\nu_{as}$ =C—O); 1085 ($\nu_s$ = C—O); 1500, 1600 ($\nu_{C=C}$ arom.); 3030, 3060 ($\nu_{CH}$ arom.); 3210, 3340, 3470 ($\nu_{NH_2}$); 2840, 2910, 2945 $cm^{-1}$ ($\nu_{H-C}$ $sp^3$). PMR spectrum ($d_6$-DMSO): 3.78 (2H, br, $NH_2$), 2.20 (s, =C—$CH_3$), 4.11 (1H, q, $H_{\beta\text{-cis}}$, $^2J = 1.5$ Hz, $^3J = 6.0$ Hz), 4.64 (1H, q, $H_{\beta\text{-trans}}$, $^3J = 14.0$ Hz), 6.89 (1H, q, α-H), 7.46 ppm (4H, m, $C_6H_4$).

## LITERATURE CITED

1. A. M. Vasil'tsov, E. A. Polubentsev, A. I. Mikhaleva, and B. A. Trofimov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 4, 864 (1990).

2. S. E. Korostova, L. N. Sobenina, R. N. Nesterenko, I. A. Aliev, and A. I. Mikhaleva, *Zh. Org. Khim.*, **20**, 1960 (1984).
3. B. A. Trofimov, S. E. Korostova, L. N. Balabanova, and A. I. Mikhaleva, *Khim. Geterotsikl. Soedin.*, No. 4, 489 (1978).
4. S. E. Korostova, A. I. Mikhaleva, S. G. Shevchenko, M. V. Sigalov, and V. Yu. Vitkovskii (Vitkovsky), *Sulfur Lett.*, **5**, 39 (1986).
5. B. A. Trofimov, A. I. Mikhaleva, S. E. Korostova, T. I. Vakul'skaya, I. S. Poguda, and M. G. Voronkov, *Zh. Prikl. Khim.*, **51**, 117 (1978).
6. B. A. Trofimov, S. E. Korostova, L. N. Balabanova, and A. I. Mikhaleva, *Zh. Org. Khim.*, **14**, 2182 (1978).
7. B. A. Trofimov, M. V. Sigalov, V. M. Bzhezovskii, G. A. Kalabin, S. E. Korostova, A. I. Mikhaleva, and L. N. Balabanova, *Khim. Geterotsikl. Soedin.*, No. 6, 768 (1978).
8. B. A. Trofimov and A. I. Mikhaleva, *N-Vinylpyrroles* [in Russian], Nauka, Novosibirsk (1984).

# NMR SPECTRA OF CYCLIC NITRONES.

## 6.* TAUTOMERIC EQUILIBRIUM OF β-OXO-NITRONES – 3-IMIDAZOLINE 3-OXIDE DERIVATIVES

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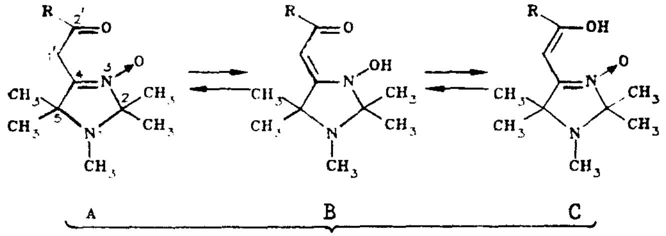
*It is demonstrated by $^{13}C$ NMR spectroscopy that β-oxo nitrones (3-imidazoline-3-oxide derivatives) exist in the form of an equilibrium mixture of three tautomeric forms with preponderance of the enolo nitrone and enehydroxylamino ketone forms.*

We have previously shown that cyclic β-oxo nitrones (pyrroline derivatives) exist in the form of a mixture of two tautomeric forms — oxo nitrone and enehydroxylamino ketone forms [2]. Enolo nitrone structures were assigned to the acyclic β-oxo nitrones (pyrroline 1-oxide derivatives) on the basis of an analysis of the UV spectra [3]. At the same time, the incorrectness of this assignment only on the basis of UV spectral data has been noted [4]. It was pointed out that acyclic β-oxo nitrones of the 3-imidazoline 3-oxide series exist in solutions in the enolized tautomeric form, but the question of the pathway of enolization has remained open [4].

We have investigated the tautomeric equilibrium of β-oxo nitrones Ia-f of the 3-imidazoline 3-oxide series using $^{13}C$ NMR spectroscopy.



I a-f

I a R=H; b R=$CH_3$; c R=$C_6H_5$; d R=$(CH_3)_3C$; e R=α-naphthyl; f R=$CF_3$

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*For communication 5, see [1].

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