PYRROLES FROM KETOXIMES AND ACETYLENE.

43.* 1,2-DIHALOALKANES AND VINYL CHLORIDE IN THE SYNTHESIS OF 2-(4-ALKYLTHIOPHENYL)PYRROLES

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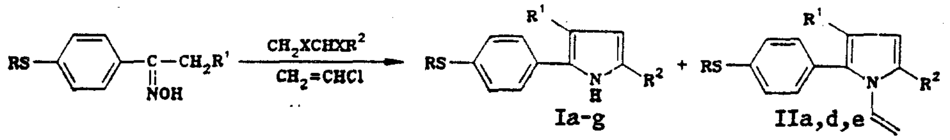
2-(4-Alkylthiophenyl)-3- and 2-(4-alkylthiophenyl)-5-methylpyrroles and their 1-vinyl derivatives were synthesized by the reaction of alkyl(4-alkylthiophenyl)ketoximes with dihaloalkanes or vinyl chloride in the KOH–DMSO system at 120-140°C and atmospheric pressure.

On the basis of "acetyleneless" variants of the Trofimov reaction [2] we have synthesized 2-(4-alkylthiophenyl-3- and 2-(4-alkylthiophenyl)pyrroles Ia-g, as well as their 1-vinyl derivatives IIa, d, e from 4-alkylthiophenylalkylketoximes and 1,2-dihaloalkanes or vinyl chloride using the KOH–DMSO superbase eliminating and catalytic system.



I, II a $R=CH_3$, $R^1=H$, $R^2=H$; b $R=C_2H_5$, $R^1=H$, $R^2=H$; c $R=i\text{-}C_3H_7$, $R^1=H$, $R^2=H$; d $R=CH_3$, $R^1=CH_3$, $R^2=H$; e $R=C_2H_5$, $R^1=CH_3$, $R^2=H$; f $R=CH_3$, $R^1=H$, $R^2=CH_3$; g $R=C_2H_5$, $R^1=H$, $R^2=CH_3$

Pyrroles Ia (in 48% yield) and IIa (in 10% yield) are formed when the reaction of 4-methylthioacetophenoxime with a fourfold excess of 1,2-dichloroethane is carried out in the KOH–DMSO superbase medium at 130°C.

The remaining syntheses were carried out similarly in the KOH–DMSO superbase medium.

Pyrrole Ib was obtained in 62% yield in the reaction of 4-ethylthioacetophenoxime with a threefold excess of 1,2-dibromoethane: only traces of 1-vinyl derivative IIb are detected in the reaction mixture by TLC.

Only pyrrole Ic is formed in 61% yield in the reaction of 4-isopropylthioacetophenoxime with a threefold excess of 1,2-dichloroethane at 120°C.

Pyrroles Id, e (54% overall yield) and 1-vinylpyrroles IId, e (54% overall yield) were obtained in the action of 4-methylthio- and 4-ethylthiopropiophenoxime with a five- to sixfold excess of vinyl chloride.

TABLE 1. UV Spectra of Pyrroles Ia-c, e-g

Compound	λ, nm	$\varepsilon \cdot 10^{-3}$
Ia	306	32,2
Ib	306	33,0
Ic	303	31,5
Ie	304	20,2
If	314	31,6
Ig	317	31,7

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*See [1] for Communication 42.

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TABLE 2. PMR Spectra of Pyrroles I and II

Compound	Chemical shifts, ppm								
	NH	3-H	4-H	5-H	H_α	H_β	$H_\beta{}^1$	C_6H_4	R
Id	8,02	—	6,03	6,63	—	—	—	7,03	2,47 (SCH_3); 2,23 (CH_3)
Ie	8,02	—	6,08	6,65	—	—	—	7,31	2,87 (CH_2S); 1,35 (CH_3); 2,23 (CH_3)
If	7,96	6,24	5,80	—	—	—	—	7,22	2,41 (SCH_3); 2,25 (CH_3)
Ig	7,95	6,34	5,91	—	—	—	—	7,30	2,89 (CH_2S); 1,27 (CH_3); 2,30 (CH_3)
IIh	—	—	5,98	6,85	6,59	4,42	4,94	7,23	2,43 (SCH_3); 1,97 (CH_3)
IIe	—	—	6,05	6,94	6,65	4,49	4,92	7,27	2,88 (CH_2S); 1,31 (CH_3); 1,98 (CH_3)

TABLE 3. ^{13}C NMR Spectra of Pyrroles I and II

Compound	Chemical shifts, ppm										
	2-C	3-C	4-C	5-C	C_α	C_β	C_i	C_o	C_m	C_p	C_R
Ia	131,48	105,91	110,25	118,43	—	—	130,07	124,11	127,53	137,06	16,20
Ic	132,99	106,82	110,29	120,12	—	—	132,99	124,72	133,40	131,93	38,83 (CH); 23,38 (CH_3)
Ie	128,01	116,52	112,59	118,40	—	—	134,05	127,24	130,31	133,05	13,14 (CH_3)
If	129,92	106,62	108,38	130,82	—	—	131,87	124,40	128,26	135,38	13,04 (CH_3); 16,20 (SCH_3)
Ig	130,05	106,85	108,44	130,72	—	—	132,60	124,37	130,88	133,24	13,04 (CH_3)
IIh	133,43	109,97	110,14	117,88	131,91	98,16	129,26	129,42	126,44	137,49	15,65
IId	128,40	118,38	111,96	116,36	131,95	96,05	129,97	126,19	131,51	137,66	11,76 (CH_3); 15,64 (SCH_3)
IIe	126,66	118,48	111,96	116,42	131,98	97,08	Midden	128,26	131,93	135,98	11,76 (CH_3); 14,42 (CH_2CH_3); 27,38 (CH_2S)

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*The data for Ia and IIa were previously published in [3].

The reaction of 4-methylthio- and 4-ethylthioacetophenoxime with 1,2-dibromopropane leads to the formation of pyrroles If and Ig in 48 and 45% yields, respectively. Excess alkali as compared with 1,2-dibromopropane makes it possible to increase the yields of pyrroles If, g, but traces of pyrroles If, g are detected when an equimolar ratio of alkali and 1,2-dibromopropane is used.

To obtain pyrroles in high yields it is necessary to add the 1,2-dihaloalkane to a suspension consisting of excess KOH, the ketoxime, and DMSO. The presence of a methyl group in the pyrrole ring facilitates vinylation of the pyrroles (the yields of pyrroles IId, e are higher than the yields of the unmethylated analogs) [3, 4].

Side products in the reaction of oximes Ia, b with dihaloethanes are 1,2-bis(arylideniminoxy)ethanes [5], which are formed in very small amounts in the reaction and were not investigated by us.

Pyrroles Ia-c and IIa are identical with respect to their physicochemical characteristics to those previously obtained [3, 4].

In the UV absorption spectra of the synthesized 2-(4-alkylthiophenyl)pyrroles Ia-c, e-g the long-wave absorption band corresponding to a $\pi-\pi^*$ transition of the A_{1g}–B_{2u} type is shifted bathochromically relative to phenylpyrrole [6] by 15-19 nm, while its intensity increases by a factor of more than 1.5 (Table 1). This effect is due to the inclusion of the sulfur atom in p–π conjugation.

The inclusion of an alkyl substituent in the 5 position of the pyrrole ring of If, g leads to a bathochromic shift of the long-wave absorption band.

The decrease in the extinction of the band in the spectrum of pyrrole Ie is explained by disruption of the conjugation of the π systems of the benzene and pyrrole rings as a result of the introduction of an alkyl substituent into the 3 position of the pyrrole ring [7].

The ^{1}H and ^{13}C NMR chemical shifts of the synthesized pyrroles (Tables 2 and 3) are in good agreement with the chemical shifts of other arylpyrroles and their N-vinyl derivatives [2, 8].

EXPERIMENTAL

The PMR spectra of 10% solutions of the investigated compounds in CCl_4 were recorded with a Varian T-60 spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The ^{13}C NMR spectra of 50% solutions of the pyrroles in CCl_4 were recorded with a Varian XL-100/12 spectrometer (25.2 MHz) under conditions of complete noise decoupling of the protons at a sample temperature of 25°C [with tetramethylsilane (TMS) as the internal standard]. The individuality of the pyrroles was monitored by TLC [Silufol UV-254, hexane–ether (2:1)]. The UV spectra of solutions of the compounds in anhydrous ethanol were obtained with a Puus Unicam SP-8000 spectrophotometer. The concentrations of the solutions were $(3\text{-}5)\cdot10^{-3}$ mole/liter.

The results of elementary analysis were in agreement with the calculated values.

2-(4-Methylthiophenyl)pyrrole (Ia, $C_{11}H_{11}NS$) and 1-Vinyl-2-(4-methylthiophenyl)pyrrole (IIa, $C_{13}H_{13}NS$). A mixture of 10.4 g (58 mmoles) of 4-methylthioacetophenoxime, 45.5 g (812 mmoles) of finely ground KOH, and 120 ml of DMSO was heated to 130°C, after which 23 g (232 mmoles) of 1,2-dichloroethane in 30 ml of DMSO was added dropwise with vigorous stirring in the course of 3 h. The reaction mixture was then stirred for another hour at the same temperature. It was then cooled to room temperature and poured into ice water (800 ml). The aqueous mixture was extracted with benzene (five 80-ml portions), and the extract was washed three times with 30% KOH solution and dried with potassium carbonate. The benzene was removed by distillation to give a mixture of pyrrole Ia and 1-vinylpyrrole IIa, from which the bulk of pyrrole Ia was isolated by crystallization from isooctane. The pyrrole Ia and 1-vinylpyrrole IIa in the mother liquor were separated by chromatography [Al_2O_3, ether–hexane (2:1)] to give 5.3 g (48.3%) of pyrrole Ia and 1.2 g (9.6%) of pyrrole IIa.

2-(4-Ethylthiophenyl)pyrrole (Ib, $C_{12}H_{13}NS$). This compound was similarly obtained from 9.75 g (50 mmoles) of 4-ethylthioacetophenonoxime and 28.2 g (150 mmoles) of 1,2-dibromoethane in the presence of 28.2 g (510 mmoles) of powdered KOH and 100 ml of DMSO (4 h, 130°C). The yield was 6.3 g (62.1%).

2-(4-Isopropylthiophenyl)pyrrole (Ic, $C_{13}H_{15}NS$). This compound was similarly obtained from 5.22 g (25 mmoles) of 4-isopropylthioacetophenoxime and 7.5 g (75 mmoles) of 1,2-dichloroethane in the presence of 14 g (250 mmoles) of powdered KOH and 60 ml of DMSO (4 h, 120°C). The yield was 3.3 g (60.8%).

3-Methyl-2-(4-methylthiophenyl)pyrrole (Id, $C_{12}H_{13}NS$) and 1-Vinyl-3-methyl-2-(4-methylthiophenyl)pyrrole (IId, $C_{14}H_{15}NS$). By a procedure similar to that used to obtain pyrrole IIa, 1.9 g (35.8%) of pyrrole Id, with mp 132°C, was obtained from 5 g (26 mmoles) of 4-methylthiopropiophenonoxime (mp 88°C) and 9.8 g (156 mmoles) of vinyl chloride in the presence of 14.6 g (260 mmoles) of KOH and 100 ml of DMSO (3.5 h, 130°C). Simultaneously isolated was 1.1 g (18.5%) of 1-vinylpyrrole IId with bp 142°C (1 mm), n_D^{20} 1.6305, and d_4^{20} 1.1020.

3-Methyl-2-(4-ethylthiophenyl)pyrrole (Ie, $C_{13}H_{15}NS$) and 1-Vinyl-3-methyl-2-(4-ethylthiophenyl)pyrrole (IIe, $C_{15}H_{17}NS$). A 12.5-g (200 mmoles) sample of vinyl chloride was bubbled into a heated (130°C) suspension consisting of 100 ml of DMSO, 16.8 g (300 mmoles) of powdered KOH, and 6.27 g (30 mmoles) of 4-ethylthiopropiophenonoxime (mp 71°C) with vigorous stirring in the course of 3 h, and the mixture was heated for another 30 min. Standard workup gave 2.9 g (44.6%) of pyrrole Ie with mp 50°C. Simultaneously isolated was 0.7 g (9.6%) of pyrrole IIe with bp 155°C (1 mm), n_D^{20} 1.6118, and d_4^{20} 1.1243.

The reaction of 6.27 g (30 mmoles) of 4-ethylthiopropiophenoxime and 28.2 g (150 mmoles) of 1,2-dibromoethane in the presence of 35.3 g (630 mmoles) of KOH, 120 ml of DMSO (5 h, 140°C) gave 3.5 g (53.8%) of pyrrole Ie and 0.8 g (11%) of pyrrole IIe, the constants of which coincided with the constants of Ie and IIe, obtained from vinyl chloride as described above.

5-Methyl-2-(4-methylthiophenyl)pyrrole (If, $C_{12}H_{13}NS$). This compound was similarly obtained from 6.03 g (33 mmoles) of 4-methylthioacetophenonoxime and 20 g (99 mmoles) of 1,2-dibromopropane in the presence of 27.72 g (495 mmoles) of finely ground KOH and 120 ml of DMSO (5 h, 130°C); the yield of product, with mp 143°C, was 3.2 g (47.8%).

5-Methyl-2-(4-ethylthiophenyl)pyrrole (Ig, $C_{13}H_{15}NS$). This compound was similarly obtained from 5.85 g (30 mmoles) of 4-ethylthioacetophenonoxime and 30.3 g (150 mmoles) of 1,2-dibromopropane in the presence of 35.3 g (630 mmoles) of KOH and 100 ml of DMSO (4.5 h, 140°C). The yield of the product, with mp 115°C, was 2.96 g (45.1%).

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