PYRROLES FROM KETOXIMES AND ACETYLENE.

35.* SYNTHESIS OF 2-(4-ALKYLTHIOPHENYL)PYRROLES AND THEIR 1-VINYL DERIVATIVES

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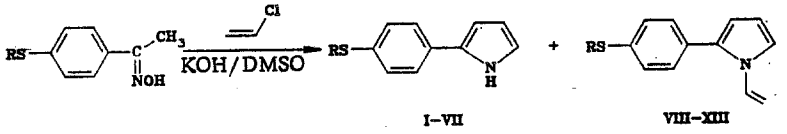
2-(4-Alkylthiophenyl)- and 2-(4-phenylthiophenyl)pyrroles and their 1-vinyl derivatives were synthesized by the reaction of 4-alkylthio- and 4-phenylthioacetophenone oximes with vinyl chloride in a KOH–DMSO system at 120 and 130°C and at atmospheric pressure.

As we know, several antibiotics belong to the class of arylpyrroles [2-5], and therefore these compounds are becoming more interesting. We therefore developed a method for the synthesis of sulfur-containing 2-(4-alkylthiophenyl)-, 2-(4-phenylthiophenyl)-pyrroles (I-VII) and their 1-vinyl derivatives (VIII-XIII), which may be suitable compounds in a search for biologically active compounds (Tables 1 and 2). The method is based on a new variant of the Trofimov reaction [6, 7], starting from 4-alkylthio- and 4-phenylthioacetophenone oximes and vinyl chloride, using the superbasic KOH-DMSO catalytic system, taking into account the experience of the preceding investigations described in [8-11].



I-VII VIII-XIII

I, VIII R=Et; II, IX R=Pr; III, X R=*iso*-Pr; IV, XI R=Bu; V, XII R=*iso*-Bu; VI, XIII R=*t*-Bu; VII R=Ph

The frequencies of the skeletal vibrations of the pyrrole ring in the IR spectra of compounds I-XIII are common to all of them: 1550, 1420, 1380, and 1110 cm^{-1}. The intense band at 710 cm^{-1} corresponds to the C–H deformational vibrations, the benzene ring is identified from the bands at 830 (nonplanar C–H deformational vibration), 1460, 1490-1500, 1575, 1590

TABLE 1. Physicochemical Constants of Pyrroles I-XIII

Compound	T_{bp}, °C (mm Hg), or mp, °C	d_4^{20}	n_D^{20}	Found, %				Emperical formula	Calculated, %			
				C	H	N	S		C	H	N	S
I	133—134	—	—	70,7	6,3	6,8	15,5	$C_{12}H_{13}NS$	70,9	6,4	6,9	15,8
VIII	165—167 (3)	1,0688	1,6340	73,2	6,4	6,3	13,7	$C_{14}H_{15}NS$	73,3	6,6	6,1	14,0
II	118—119	—	—	71,8	6,9	6,3	14,6	$C_{13}H_{15}NS$	71,8	7,0	6,4	14,8
IX	172—174 (1)	1,0520	1,6080	73,9	6,9	5,5	13,0	$C_{15}H_{17}NS$	74,0	7,0	5,8	13,2
III	77—78	—	—	71,7	6,8	6,3	14,6	$C_{13}H_{15}NS$	71,8	7,0	6,4	14,8
X	150 (1)	1,0609	1,6096	74,2	7,2	5,6	13,0	$C_{15}H_{17}NS$	74,0	7,0	5,8	13,2
IV	93—94	—	—	72,5	7,3	5,8	13,7	$C_{14}H_{17}NS$	72,7	7,4	6,1	13,9
XI	166—168 (1)	1,0910	1,5884	74,4	7,3	5,2	12,2	$C_{16}H_{19}NS$	74,7	7,4	5,4	12,5
V	104—105	—	—	72,5	7,3	5,9	13,6	$C_{14}H_{17}NS$	72,7	7,4	6,1	13,9
XII	168—170 (2)	0,9972	1,5788	74,5	7,3	5,3	12,3	$C_{16}H_{19}NS$	74,7	7,4	5,4	12,5
VI	112	—	—	72,5	7,2	5,9	13,7	$C_{14}H_{17}NS$	72,7	7,4	6,1	13,9
XIII	167—168 (1)	0,9960	1,5895	74,4	7,3	5,2	12,2	$C_{16}H_{19}NS$	74,7	7,4	5,4	12,5
VII	Tcarboniz 175—176	—	—	76,3	5,1	5,4	12,5	$C_{16}H_{13}NS$	76,5	5,2	5,6	12,8

*See [1] for Communication 34.

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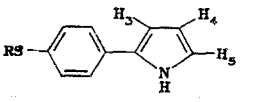
TABLE 2. Reaction Conditions and Yields of Pyrroles I-XIII

Pyrrole	T_{mp} of oxime, °C	Reagents, mole				Temperature of reaction, °C	Duration of reaction, h	Yield, %
		ketoxime	vinyl chloride	KOH	DMSO			
I VIII	87	0,1	0,5	0,6	2,11	130	3	45 7
II	72	0,005	0,05	0,055	1,41	130	1,5	38
II* IX	64	0,028	0,14	0,168	1,41	130	3	40 8
III X	64	0,05	0,25	0,3	1,41	130	3	42 6
IV XI	78	0,02	0,1	0,12	1,41	130	3	43 6
V	76	0,025	0,25	0,275	2,11	120	3	43
V* XII	76	0,02	0,3	0,32	2,11	120	5	24 22
VI XIII	80	0,015	0,15	0,165	1,41	130	3	36 8
VII	178	0,005	0,025	0,03	1,41	130	3	19

*The experiment was carried out with vinyl bromide.

TABLE 3. Data on PMR Spectra of Pyrroles 

R	Chemical shift of ring protons, δ, ppm*					Chemical shifts of protons of substituents at the S atom, δ, ppm (J, Hz)
	NH	3-H	4-H	5-H	Ar—H	
Et	8,21	6,34	6,14	6,63	7,23	CH_2 — 2,83 q (6); CH_3 — 1,24 t (6)
Pr	8,21	6,42	6,17	6,72	7,36	CH_2S — 2,90 m (6); CH_2 — 1,65 m (6); CH_3 — 1,09 m (6)
iso-Pr	8,39	6,42	6,21	6,70	7,31	CH — 3,27 m (6); CH_3 — 1,27 d (6,5)
Bu	8,28	6,42	6,21	6,72	7,30	CH_2S — 2,88 br.t (6); $(CH_2)_2$ — 1,56 unresolved br.s CH_3 — 95 t (6,5)
iso-Bu	8,28	6,45	6,24	6,70	7,31	CH_2S — 2,80 d (7); CH — 1,81 m (6); CH_3 — 1,09 d (6)
t-Bu	8,47	6,41	6,19	6,72	7,38	$(CH_3)_3$ — 1,26 s
Ph	8,1	6,49	6,18	6,79	7,51†	

*The SSCC of pyrrole ring protons $J_{3\text{-H}-4\text{-H}}$, $J_{4\text{-H}-5\text{-H}}$, $J_{5\text{-H}-NH}$ are approximately equal for all the compounds and are equal to ~3 Hz.
†The proton signals of two phenyl rings overlap and a broadened multiplet is observed.

cm^{-1} (skeletal vibrations of the ring). In these compounds the frequencies and intensities of the latter three bands are lower than those in alkylphenylpyrroles. The stretching vibration band of the C=C vinyl group is characterized by a 1642 cm^{-1} frequency, a band with a maximum at 3380 cm^{-1} (in mineral oil) corresponds to the NH group, and a weak band in the 530-550 cm^{-1} region belongs to the stretching of the C—S group.

The PMR spectra of some of the pyrroles synthesized are given in Table 3 and correspond completely to the proposed structure.

EXPERIMENTAL

The PMR spectra of 10% solutions of the compounds were run on a Varian T-60 spectrometer in CCl_4, using HMDS as internal standard. The IR spectra were run on a Specord IR-75 spectrophotometer in a thin layer and in KBr tablets. The individual state of the compounds was verified by the TLC method on Silufol UV-254 plates.

2-(4-Ethylthiophenyl)pyrrole (I) and 1-Vinyl-2-(4-ethylthiophenyl)pyrrole (VIII). A mixture of 19.5 g (0.1 mole) of methyl-4-ethylthiophenylketoxime (mp 87°C) and 33.6 g (0.6 mole) of KOH is added in portions every 30 min, in the course of 2 h 30 min to 150 ml of DMSO, while 31.2 g (0.5 mole) of vinyl chloride are passed gradually through a bubbler. Stirring and heating are continued for another 30 min, the mixture is cooled to 20°C, diluted with cold water, and the reaction product is extracted by benzene (5 × 100 ml). The benzene extracts are washed with water and dried over K_2CO_3. Benzene is distilled off, and the residue is distilled in vacuo. A mixture of pyrrole I and 1-vinylpyrrole VIII is obtained, from which the main part of pyrrole I is isolated by crystallization from isooctane. Pyrrole I and 1-vinylpyrrole VIII remaining in the mother liquor are separated chromatographically in a thin layer of Al_2O_3 for TLC (ether–hexane, 1:2). Yield, 9.2 g (45%) of pyrrole I and 1.5 g (7%) of pyrrole VIII.

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