SYNTHESIS AND PROPERTIES OF 1-(2-BROMOETHYL)-, 1-(2-ALKOXYETHYL)-AND 1-(2-DIALKYLAMINOETHYL)2-ALKYLPYRROLES

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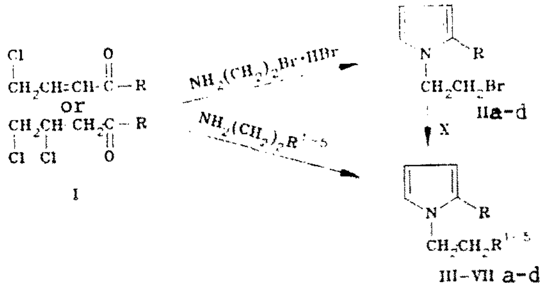
The reaction of 3-chloropropenyl alkyl ketones or 2,3-dichloropropyl alkyl ketones with 2-substituted ethylamine derivatives leads to the formation of the hitherto unknown 1-(2-R-ethyl)-2-alkylpyrroles.

It has previously been shown that the reaction of ammonia or primary amines with β,γ-dihalopropyl ketones leads to the formation of pyrrole derivatives [1].

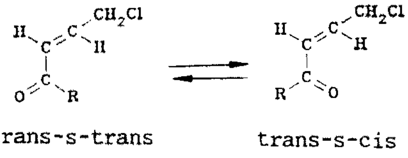
In the present work we found that in the reaction of 3-chloropropenyl alkyl ketones or 2,3-dichloropropyl alkyl ketones with β-bromo-, β-alkoxy-, or β-dialkylaminoethylamines, in the present of hydrogen halide acceptors, the corresponding 1-(2-bromo-, 2-alkoxy-, or 2-dialkylaminoethyl)-2-alkylpyrroles are formed:



I—VII a $R=CH_3$; b $R=C_2H_5$; c $R=C_3H_7$; d $R=C_4H_9$; III $R^1=OCH_3$; IV $R^2=OC_2H_5$; V $R^3=N(C_2H_5)$; VI R^4-piperidino; VII $R^5=NHC_2H_5$; $X=NaOCH_3$, $NaOC_2H_5$, $HN(C_2H_5)_2$, piperidine$NH_2C_2H_5$

It was found that with increase in the molecular weight of the starting 3-chloropropenyl alkyl ketones, beginning from 3-chloropropenyl propyl ketone, simultaneously with the corresponding 2-propylpyrroles, a secondary reaction product is formed – 2-propylfuran 11% – and from 3-chloropropenyl butyl ketone 17% of 2-butylfuran is obtained.

This is probably explained by the fact that the starting 3-chloropropenyl alkyl ketones exist in the form of two configuration isomers – trans-s-trans and trans-s-cis, whereby, in particular for the latter isomer, the most favorable steric conditions are created for an intramolecular cyclization into the corresponding 2-alkylfurans:



In fact, in the IR spectra of 3-chloropropenyl alkyl ketones two bands are observed of the stretching vibrations of carbonyl groups in the 1715-1702 and 1680-1676 cm^{-1} regions, corresponding to the trans-s-trans and trans-s-cis isomers. According to the obtained data on the intensity of these bands, the proportion of the trans-s-cis-isomer in the mixture increases with increase in the length and degree of branching of the alkyl radical of the ketone, which leads to the formation of significant amounts of furans in the case of high-molecular-weight ketones.

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TABLE 1. 1-(2-Bromoethyl)-, 1-(2-Alkoxyethyl)- and 1-(2-Dialkylaminoethyl)-2-alkylpyrroles

Compound	Empirical formula	bp, °C (mm Hg)	d_4^{20}	n_D^{20}	Yield, %
IIa	$C_7H_{10}BrN$	102 ... 103 (3)	1,2076	1,5247	65
IIb	$C_8H_{12}BrN$	117 ... 119 (4)	1,1939	1,5230	66
IIc	$C_9H_{14}BrN$	124 ... 126 (3)	1,1712	1,5214	64
IIIa	$C_8H_{13}NO$	51 ... 53 (3)	0,9917	1,4846	76
IIIb	$C_9H_{15}NO$	60 ... 61 (3)	0,9781	1,4810	73
IIIc	$C_{10}H_{17}NO$	70 ... 72 (4)	0,9562	1,4788	70
IIId	$C_{11}H_{19}NO$	80 ... 81 (4)	0,8823	1,4770	65
IVa	$C_9H_{15}NO$	65 ... 66 (2)	0,9519	1,4795	81
IVc	$C_{11}H_{19}NO$	88 ... 89 (3)	0,9376	1,4764	74
Vb	$C_{12}H_{22}N_2$	109 ... 110 (2)	0,9612	1,4942	75
Vc	$C_{13}H_{24}N_2$	119 ... 120 (2)	0,9213	1,4919	72
Vd	$C_{14}H_{26}N_2$	132 ... 134 (3)	0,9097	1,4900	63
VIb	$C_{13}H_{22}N_2$	114 ... 115 (3)	0,9797	1,5054	75
VIc	$C_{14}H_{24}N_2$	119 ... 120 (2)	0,9741	0,5026	71
VId	$C_{15}H_{26}N_2$	129 ... 130 (2)	0,9662	1,5007	67
VIIa	$C_9H_{16}N_2$	90 ... 92 (1)	0,9561	1,4990	76

TABLE 2. PMR Spectra of 1-(2-Bromoethyl)-, 1-(2-Alkoxyethyl)-, and 1-(2-Dialkylaminoethyl)-2-alkylpyrroles

Compound	δ ppm (in CH_3OH)					
	3-H, m	4-H, m	5-H, m	CH_2—CH_2, t; t	R	R^{1-5}
IIa	5,64	5,82	6,43	3,48; 3,84	2,15 s	—
IIIa	5,65	5,80	6,35	3,41; 3,70	2,19 s	3,50 s
IVa	5,64	5,84	6,40	3,48; 3,82	2,14 s	1,10 t; 3,32 q
Vb	5,62	5,80	6,32	2,65; 3,72	1,51 t; 2,70 q	0,90 t; 2,20 q
VIb	5,60	5,73	6,30	2,40; 3,70	1,56 t; 2,74 q	1,39 m; 2,35 m
VIIa	5,63	5,78	6,34	2,42; 3,67	2,16 s	1,23 t; 3,14 q

The furans are formed according to the following scheme:

To prevent the side formation of 2-alkylfuran and to increase the yield of 1-(2-bromoethyl)-2-alkylpyrroles, we utilized the reaction of 2,3-dichloropropyl alkyl ketones with β-bromoethylamine hydrobromide.

It was found that 2-alkylfurans are not formed in this reaction and the yield of 1-(2-bromoethyl)-2-propylpyrrole increases from 49 to 64%.

In the IR spectra of all the synthesized pyrrols IIa-VIIa, besides the characteristic absorption bands for the pyrrole ring at 3100-3140 (ν_{C-H}), 1467-1570 ($\nu_{C=C}$), in the ring), 710-784 cm^{-1} (δ_{C-H} in the ring), characteristic absorption bands of the functional groups are observed at 3340 (ν_{N-H}), 2800 (ν_{C-H}), 1200 (ν_{C-O-C}), and 725 cm^{-1} (ν_{C-Br}).

In the PMR spectra of all the synthesized pyrroles IIa-VIIa there are characteristic multiplet signals of 3-, 4-, and 5-H protons of the pyrrole ring (~5.60-5.82 and 6.43 ppm), triplets of the methylene groups of the 1-$CH_2CH_2R^{1-5}$ residue (or Br), proton signals of the alkyl radicals $R^{1,2}$ and functional groups in the ethyl chain.

1-(2-Alkoxyethyl)- and 1-(2-dialkylaminoethyl)-2-alkylpyrroles obtained by the reaction of 1-(2-bromoethyl)-2-alkylpyrroles with sodium alcoholates, secondary or primary amines in the presence of triethylamine.

EXPERIMENTAL

The purity of the synthesized compounds was monitored by GLC on a Chrom-3-IKZ chromatograph (mobile phase – PMS-100, carrier – Chromosorb W) and TLC on Silufol UV-254 plates. The IR spectra were run on a UR-20 spectrophotometer (without a solvent); the PMR spectra – on a Tesla BS-487B spectrometer (80 MHz), using HMDS as internal standard. The starting 2,3-dichloropropyl alkyl ketones were obtained by the method described in [2].

The characteristics of the synthesized compounds are given in Tables 1 and 2. The data of the elemental analyses of compounds II-VII for C, H, Br, N correspond to the calculated values.

1-(2-Bromoethyl)-2-R-pyrroles. A solution of 8 g of sodium carbonate in 100 ml of water and 14 ml (0.1 mole) of triethylamine was added dropwise to a mixture of 10.3 g (0.05 mole) of β-bromoethylamine hydrobromide and 50 ml of benzene, and then a solution of 0.05 mole of 2,3-dichloropropyl alkyl ketone in 50 ml of benzene was added, while maintaining the temperature within 60-65°C. The reaction mixture was stirred for 6 h at this temperature. After cooling, the benzene layer was separated, washed with water, the aqueous layer was extracted with benzene, and the combined benzene extracts were dried over $MgSO_4$. After the evaporation of the solvent, the residue was distilled under vacuum in a nitrogen current.

1-(2-Alkoxy- or Aminoethyl)-2-R-pyrroles. A. A solution of 0.05 mole of 1-(2-bromoethyl)-2-R-pyrrole in 50 ml of absolute ether and 7 ml (0.05 mole) of triethylamine was added dropwise at 10-15°C, with stirring, to 0.05 mole of the corresponding sodium alcoholate, secondary or primary amine in 50 ml of absolute ether. The reaction mixture was stirred at room temperature for 1 h, and then was boiled for 5 h. After cooling, it was washed with water, the aqueous layer was extracted with ether, and the combined extracts were dried over $MgSO_4$. After the evaporation of the solvent, the residue was distilled under vacuum in a nitrogen current.

B. A solution of 0.05 mole of 2,3-dichloropropyl alkyl ketone in 50 ml of ether was added at 20-25°C, with stirring, to a solution of 0.05 mole of β-alkoxy- or β-dialkylaminoethylamine and 14 ml (0.05 mole) of triethylamine in 50 ml of ether, and the reaction mixture was boiled for 5 h. The separation and purification was carried out as described in the preceding procedure. According to the IR and PMR spectra, boiling points and refraction indices, the samples of pyrrole derivatives were identical with the pyrroles obtained by method A.

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