INVESTIGATION OF THE REACTION OF VINYLOXYPYRIDINES AND N-VINYLPYRIDINES WITH BROMINE

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The addition of bromine to vinyl derivatives of 2-hydroxypyridine, 2-hydroxylepidine, and 8-hydroxyquinoline was studied. The behavior of the compounds differs as a function of the structure and the position of the vinyl group attached to the oxygen or nitrogen of the pyridine ring. A complex involving the unshared electron pair of the nitrogen atom is obtained with 2-vinyloxypyridine and bromine. N-Vinyl-2-pyridone and 2-vinyloxylepidine add bromine primarily at the double bond of the vinyl group. This reaction proceeds in a more complex fashion with N-vinyl-2-lepidone and 8-vinyloxyquinoline. The structures of the synthesized compounds were investigated by means of IR and PMR spectra.

The bromination of nitrogen-containing heterocycles has been investigated by a number of researchers [1-4] who assume that the reaction forms perbromides which are either π-complexes or complexes with a donor-acceptor bond between nitrogen and bromine. There is no information in the literature regarding the halogenation of vinyl derivatives of the pyridine and quinoline series.

In this paper we have studied the effect of molecular bromine on 2-vinyloxypyridine (I), 2-vinyloxylepidine (II), 8-vinyloxyquinoline (III), N-vinyl-2-pyridone (IV), and N-vinyl-2-lepidone (V). The bromination was carried out in carbon tetrachloride, acetic acid, and diethyl ether at −20 to 75°C at various component ratios. In all cases, despite considerable changes in the reaction conditions, one observes the formation of primarily one bromination product with mp 103-105° (VI), the yield of which varied. It should be noted that the order of mixing of the components does not affect the product yields. The bromination proceeds most favorably at +20° in CCl_4 and at a starting component ratio of 1 : 1. A study of the composition and structure of VI indicates that it contains two bromine atoms and a free vinyl group. Molecular bromine apparently reacts with the unshared electron pair of the nitrogen atom. Complex VI markedly lowers the reactivity of the vinyloxy group with respect to electrophilic reagents, and subsequent addition of bromine to the C=C bond is not observed. The IR spectroscopic data confirm this direction for the process. The bands at 860, 930, 1640, and 3110 cm^{-1}, which characterize vibrations of the vinyl group, are retained in the spectrum of VI. Shifts in the ring bands ($1378 \rightarrow 1340$, $1470 \rightarrow 1500$, and $1585 \rightarrow 1570$ cm^{-1}) are observed along with a reduction in their intensities. The band at 1268 cm^{-1}, which is due to the vibrations of the C−O−C ether group in starting I, is shifted to 1225 cm^{-1} in VI. One can probably not exclude the participation of the unshared pair of oxygen in the formation of a complex with bromine. The liberation of a slight amount of a viscous mass which has great adhesion to glass is observed during the reaction. Compound VI is quite soluble in water and alcohol, partially soluble in acetone, and insoluble in deithyl ether.

The introduction into the I molecule of a benzene ring condensed with it and an electron-donating methyl substituent in the para position to the nitrogen (II) promotes a change in the direction of the bromination. The polarizability of the electron cloud of the molecule apparently increases markedly in this case to favor an increase in the reactivity of the double bond of the vinyl group. Additional feeding of electrons to the pyridine ring makes possible the addition of bromine to the C=C bond to form 2-(α,β-dibromoethoxy)-lepidine (VII). One cannot exclude the possible interaction of excess bromine with the nitrogen atom.

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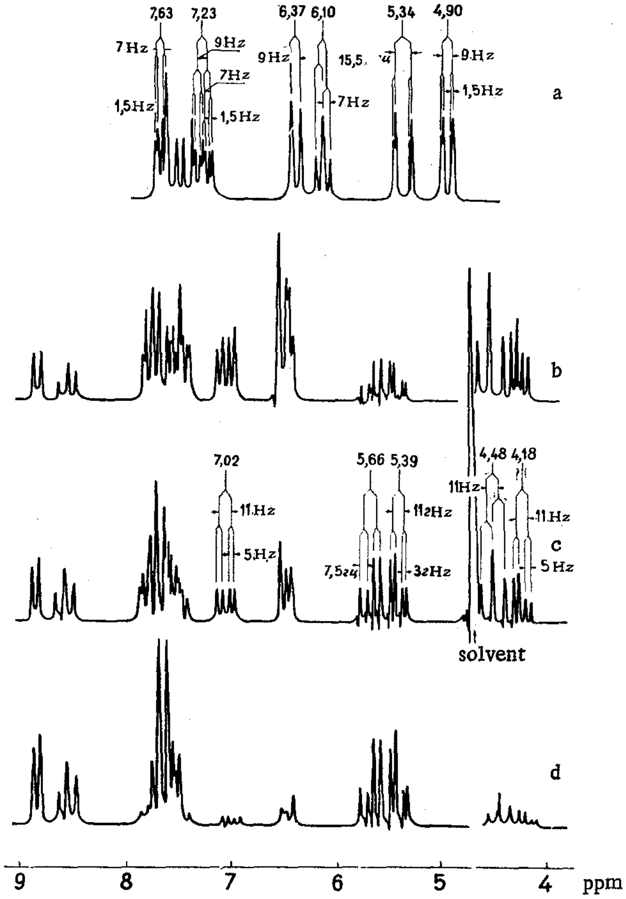
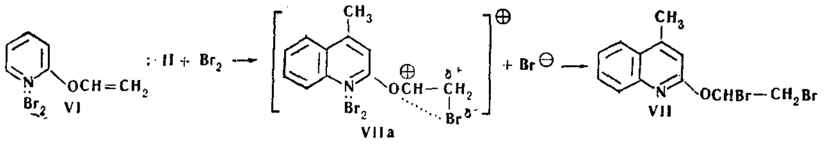
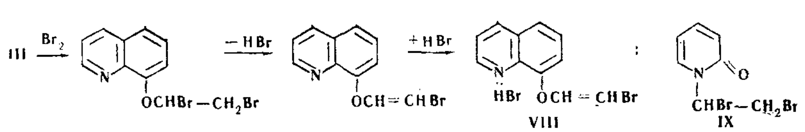


Fig. 1. PMR spectra: a) N-vinyl-2-pyridone (IV); b) N-(α,β-dibromoethyl)-2-pyridone (IX) 20 min after dissolving in CD_3OD; c) IX, 1 h after dissolving in CD_3OD; d) IX after 4 h.



We propose that bromine adds according to the usual scheme of a two-step reaction with participation of an intermediate carbonium ion which has "bromonium" character (VIIa) [5]. The coordination forces in the complex are destroyed under the influence of polar solvents such as ethanol. A confirmation of this is the fact that the product of the bromination of II isolated from the reaction mixture initially has an elevated percentage of bromine (which amounts to 54% or higher); the composition changes after washing of the precipitate with alcohol, and the percentage of bromine becomes 47%, which corresponds to two bromine atoms per mole of II (VII). The bands at 3120, 1648, and 947 cm^{-1}, which are due to the vibrations of a terminal C=C bond, have completely disappeared in the IR spectrum of VII; this also attests to the participation of the vinyl group in the reaction with bromine.

The bromination of III, in which the vinyl group is situated in the ring which does not contain nitrogen, proceeds in a more complex fashion. Regardless of the reaction temperature (which ranges from −10 to 20°) and the component ratio, a mixture of products which contains from 45 to 66% bromine is formed. The IR spectra of brominated III constantly contain a band of medium intensity at 1630 cm^{-1}. On the basis of an investigation of the properties of the compounds and their IR spectra, we propose that the bromination of III proceeds at two reaction centers through β-elimination of ethoxyquinoline dibromide.

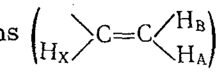


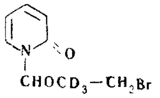
VIII

IX

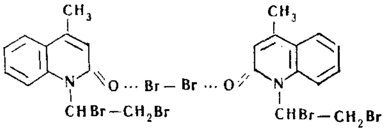
The presence of a complex of III with Br_2, formed due to the unshared electron pair of nitrogen, is also possible in the reaction mixture of products. It is difficult to isolate individual compounds from this complex multicomponent mixture.

In contrast to I, N-vinyl-2-pyridone (IV) adds bromine at the double bond at 20° and a component ratio of 1 : 1 to form N-(α,β-dibromoethyl)-2-pyridone (IX).

PMR spectroscopy was used to establish the structure of IX. The spectrum of IV consists of seven groups of lines (Fig. 1a). The β protons  of the vinyl group (δ_A 4.90 ppm, δ_B 5.34 ppm) resonate at strongest field, while the $H_{(5)}$ (6.10 ppm),* $H_{(3)}$ (6.37 ppm), $H_{(4)}$ (7.23 ppm), H_X (7.45 ppm), and $H_{(6)}$ (7.63 ppm) signals are more on the weak-field side. Moreover, the two extreme lines of the H_X signal are superimposed on the $H_{(6)}$ and $H_{(4)}$ signals, thereby distorting them. The multiplicity of the signals is due to the spin−spin interaction of the corresponding protons and is characterized by the following interaction constants: $J_{AX} = 9$, $J_{BX} = 15$, $J_{AB} = 1.5$, $J_{34} = 9$, $J_{45} = J_{56} = 7$, $J_{46} = 1.5$ Hz. The investigation of the PMR spectrum of IX confirms the formation of N-(α,β-dibromoethyl)pyridone. However, its spectrum contains considerably more resonance lines and, in addition, the intensities of some signals decrease with time, while those of others increase (Fig. 1b and c). Under the conditions used to measure the spectrum in CD_3OD, the formation of a side product − the deuterated methoxybromide of 2-pyridone (X) − was possible.



X



XI

The fact of the substitution of bromine on introduction into the reaction of foreign nucleophiles was well established in studies of the bromination in methanol of other α,β-unsaturated compounds [5]. The replacement of bromine by an OCD_3 group leads to a change in the chemical shifts and spin−spin interaction constants. The redistribution of the signal intensities, however, is evidence that substitution of bromine proceeds gradually with time. Considering what has been stated above, we will interpret the spectrum of IX dissolved in CD_3OD_3(Fig. 1c) in the following way. The methylene protons of IX, which form an AB system, resonate at the strongest field. The signal of one of them is represented by a quartet (δ 4.18 ppm), while that of the other is a triplet (δ 4.48 ppm). The multiplicity of these signals is due to spin−spin interaction of these protons with each other and with the proton of the CHBr group, the signal of which (δ 7.02 ppm) is a quartet [$J_{AB} = J_{A(B)X} = 11$ Hz, $J_{B(A)X} = 5$ Hz] for the same reason. The methylene protons of X, however, resonate at weaker field (δ 5.39 and 5.66 ppm). Moreover, the signals of both protons are quartets, which indicates a change in the character of the rotation about the $CH-CH_2Br$ bond in X as compared with IX and, consequently, a preferred relative positioning of the AB and X protons ($J_{AB} = 11$ Hz, $J_{A(B)X} = 7.5$ Hz, and $J_{B(A)X} = 3$ Hz). The signals of the ring protons [$H_{(3)}$ and $H_{(5)}$] of IX through superimposition give a multiplet

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*The shifts (σ) are indicated in parentheses.

TABLE 1. Products of the Bromination of Vinyl Derivatives of the Pyridine and Quinoline Series at 20°

Comp.	mp	Empirical formula	Br, % found	Br, % calc.	Yield, %
VI	103—105	$C_7H_7Br_2NO$	56,6	56,9	88
VII	143—145	$C_{12}H_{11}Br_2NO$	47,2	46,3	65
VIII	160—165	$C_{11}H_8BrNO \cdot HBr$	46,1	48,3	63
IX	85—88	$C_7H_7Br_2NO$	57,2	56,9	71
XI	115—120	$C_{24}H_{22}Br_6N_2O_2$	55,6	56,4	62

at 6.36-6.52 ppm. The multiplicity of the signal at 7.31-7.87 ppm is due to superimposition of the signals of the $H_{(4)}$ and $H_{(6)}$ protons of IX as well as the H_X signal and the $H_{(3)}$ and $H_{(5)}$ protons of X. Finally, the doublet and triplet at weak field (δ 7.90 and 8.51 ppm, J_{56} = 7 Hz, $J_{34} = J_{45}$ = 9 Hz) belong to the $H_{(6)}$ and $H_{(4)}$ protons of X.

The IR spectrum of IX does not contain absorption bands characteristic for the vinyl group, while the band peculiar to the carbonyl group becomes narrow and intense at 1680 cm^{-1}.

According to the results of elementary analysis, brominated V contains three bromine atoms per molecule. It is possible that the second bromine molecule is coordinately bonded to the carbonyl groups of two molecules of V. The IR spectrum of XI does not contain free vinyl group peaks, while the frequency of the C=O vibrations is shifted to 1610 cm^{-1}.

EXPERIMENTAL

Bromination of 2-Vinyloxyprydine (I). A solution of 1.7 ml (0.01 mole) of I in 40 ml of CCl_4 was added dropwise at −20° in the course of 45 min to 0.73 ml (0.01 mole) of bromine in 50 ml of CCl_4 with constant stirring. The bromine color vanished at the end of the reaction. The carbon tetrachloride was removed in vacuo at room temperature to give 3.49 g (86%) of VI, which was dissolved in ethanol and precipitated with diethyl ether to give a product with mp 102-105°. Found %: C 29.1; H 2.8; Br 57.2. $C_7H_7NO \cdot Br_2$. Calculated %: C 29.9; H 2.51; Br 56.9.

Reaction of 8-Vinyloxyquinoline (III) with Bromine. A solution of 2.3 g (0.01 mole) of III in 40 ml of CCl_4 was added dropwise at −10° to a solution of 2.1 g (0.01 mole) of bromine in 60 ml of CCl_4. An orange precipitate formed and was repeatedly washed with CCl_4 and diethyl ether to give 1.5 g of brominated III with mp 89-90°. Found %: C 25.9; H 1.8; Br 66.1. $C_{11}H_9NOBr_4$. Calculated %: C 26.9; H 1.9; Br 65.1.

N-(α,β-Dibromoethyl)-2-pyridone (IX). This was obtained by dropwise addition of 0.87 ml (0.016 mole) of bromine in 40 ml of CCl_4 to 2 g (0.016 mole) of IV in 20 ml of CCl_4 in the course of 1 h at 20°. Colorless crystals precipitated from the solution and were washed with CCl_4 and absolute diethyl ether and vacuum dried to constant weight to give 3.3 g of IX (Table 1).

The bromides of vinyl derivatives of 2-hydroxylepidine and 8-hydroxyquinoline (VII, VIII, and XI, Table 1) were similarly obtained at 20°.

The PMR spectra were recorded with a JNM-4H-100 spectrometer at room temperature. Hexamethyldisiloxane was used as the internal standard. The integral intensities of the signals were taken into account in interpreting the spectra. Since we did not discuss the absolute chemical shifts, the AB part of the ABX system was analyzed using the AX approximation [6].

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