STUDY OF DERIVATIVES OF 3-HYDROXYPYRIDINE-1-OXIDE
BY THE METHOD OF NMR-\textsuperscript{1}H AND \textsuperscript{13}C SPECTROSCOPY

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In our previous work [1] we investigated the patterns manifested in the spectra of \textsuperscript{13}C of derivatives of 3-hydroxypyridine and compared the results obtained with the data of PMR spectroscopy. The influence of the NO group on the nature of the spectrum of 3-hydroxypyridine-1-oxide (I) on \textsuperscript{1}H and \textsuperscript{13}C nuclei is also of substantial interest. For this purpose, we investigated the spectra of a number of derivatives of (I). The values of the chemical shifts are cited in Table 1.

The NMR-\textsuperscript{13}C spectrum of (I), obtained under conditions of heteronuclear resonance with complete suppression of all the protons, contains five lines from the five nonequivalent carbon atoms of the ring. The largest shift corresponds to the C\textsubscript{3} carbon atom. The remaining lines of the spectrum were identified considering the influence of the N--O and OH groups, as well as the PMR spectrum of this compound.

As is well known, the presence of a N-oxide group in the ring increases the reactivity of the pyridine ring in the case of aromatic substitution [2]. An analogous influence has been noted after the introduction of a N-oxide group into the 3-hydroxypyridine molecule. The rate of acid isotopic exchange of hydrogen of the 2-position in (I) is substantially higher than for the unoxidized base [3].

The transition from 3-hydroxypyridine [1] to its N-oxide (I) is accompanied by a shift of the signals from the C\textsubscript{2}, C\textsubscript{4}, C\textsubscript{5}, and C\textsubscript{6} carbons into the region of the stronger magnetic field. The greatest shift is experienced by the signals from C\textsubscript{2} and C\textsubscript{6} (8.4 and 8.2 ppm); the signal of C\textsubscript{4} is shifted by 1.7 ppm, and that of C\textsubscript{5} by 1.3 ppm. The indicated change in the chemical shift is in full agreement with the electronic influence of the N--O group on the α- and β-positions of the ring.

In contrast to the spectrum of the unoxidized base, the PMR spectrum of (I) is easily interpreted. The signals were assigned on the basis of the spin–spin interaction constants between the protons of the ring (J\textsubscript{25} = 0.6, J\textsubscript{26} = 1.0, J\textsubscript{42} = 1.1, J\textsubscript{46} = 2.2, J\textsubscript{56} = 5.5, J\textsubscript{15} = 9.0 Hz). The redistribution of π-electron density in the ring after the introduction of a N--O group in the β-pyridol ring leads to a shift of the proton signals in the strong-field direction relative to 3-hydroxypyridine [1]; moreover, the amount of this shift varies in the sequence C\textsubscript{2}H > C\textsubscript{6}H > C\textsubscript{4}H (0.47, 0.32, 0.28 ppm, respectively). The N--O group has no significant influence on the shift of the signal from C\textsubscript{3}H.

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In the case of (II), the signal from the C\textsubscript{5} carbon experiences the greatest shift, then follows C\textsubscript{4}. The signal from the C\textsubscript{6} carbon is shifted in the opposite direction. For (III), a shift of all the signals into the region of a stronger field relative to the unoxidized base is observed, especially for C\textsubscript{2} and C\textsubscript{4} (9.6 and 1.9 ppm). The introduction of a methyl group into the 6-position has a greater influence on the chemical shift of the C\textsubscript{3} carbon than in the case of (II).

The interpretation of the PMR spectra of (II) and (III) showed that the chemical shifts of the α-protons lie in a weaker field region than those of the β- and γ-protons (see Table 1). The characteristic spin–spin
interaction constants for each series of compounds permit an unambiguous assignment of the signals. Together with methyl derivatives (II) and (III) we also studied aryl-substituted N-oxides (IV) and (V). The lines were assigned on the basis of the PMR spectra.

The spectrum of $^{13}$C of (IV) with complete suppression of all the protons contains seven lines from 11 carbon atoms. The sequence of the signals of the pyridine ring in the direction of increasing field takes the form $C_3$, $C_2$, $C_6$, $C_5$, and $C_4$. The six carbon atoms of the phenyl ring give four lines. The line at 132.9 ppm was assigned to the $C_1'$ carbon, the two lines at 130.9 and 129.7 ppm to $C_2'$, $C_3'$, $C_5'$, and $C_6'$, and the line at 123.8 ppm to $C_4'$. A comparison of the chemical shifts of (IV) with the unoxidized base shows that the introduction of a N-oxide group causes a shift of the signals of the carbons in the strong-field direction both in the $\beta$-pyridol and in the phenyl ring. An especially strong shift is experienced by the signal from the $C_4$ carbon (4.8 ppm).

The PMR spectrum of (IV) in the region of a weak magnetic field contains a group of overlapping multiplets from the $C_3H$ proton of the $\beta$-pyridol ring and five protons of the phenyl ring. The presence of an N-oxide group in the ring causes a decrease in the chemical shifts of the signals from $C_3H$, $C_4H$, and the protons of the phenyl ring; the signals from $C_6H$ do not experience any appreciable shift in comparison with the shift of the corresponding proton of 2-phenyl-3-hydroxypyridine.

Like (IV), the sequence of the signals of $^{13}$C of the pyridine ring in (V) takes the form: $C_3$, $C_2$, $C_6$, $C_5$, and $C_4$ in the direction of increasing magnetic field. The six carbons of the phenyl ring give four lines in the spectrum, of which the signal of the $C_1'$ is situated at 139.5 ppm, $C_4'$ at 126.0 ppm; the remaining four carbon atoms give two lines of double intensity in the region of 129.6 and 129.2 ppm. The presence of a N–O group in the ring leads to a shift of all the carbon signals of the pyridine ring in the strong-field direction in the sequence $C_6 > C_5 > C_4$ relative to the arrangement of the signals in 2-benzyl-3-hydroxyprpyridine. An analogous strong-field shift is observed for the carbons of the benzyl ring and the $CH_2$ group.

A comparison of the chemical shifts of the carbons of the $\beta$-pyridol ring of (I) with the chemical shifts for (II), (IV), and (V) shows that in the series under consideration, only for (V) is there a tendency for a shift of all the signals of the atoms into the strong-field region, and the greatest shift is experienced by the signals from $C_4$ and $C_5$. In the case of (IV) there is a shift of the signal from $C_6$ 2.5 ppm in the weak-field direction. For (II) the signal from $C_6$ experiences the greatest weak-field shift (6.4 ppm) in comparison with (I). For (II), (IV), and (V) good correspondence of the chemical shifts of $^{13}$C and $^1$H to the $\pi$-electron density on the carbon atoms was obtained. For (I) the sequence of the charges
(C₄ > C₂ > C₅) takes a somewhat different form from the sequence for the chemical shifts (C₄ < C₅ < C₂). It should be noted that for derivatives of (I), just as for unoxidized bases, no correlation is observed between the chemical shift, π-electron density on the carbon atoms, and their reactivity in electrophilic substitution.

**EXPERIMENTAL METHOD**

The NMR-¹³C spectra were taken at the natural content of ¹³C on a JNM-PS-100 spectrometer with a Fourier transform system under conditions of heteronuclear resonance with complete suppression of all the protons. Untuned double heteronuclear resonance was used for the assignment of the spectra lines.

The PMR spectra were measured on a HA-100 Varian spectrometer at 29°. The investigated compounds were saturated 20% solutions in 1 N NaOD.

Dioxane (δ_TMS 67.6 ppm for ¹³C and 3.70 ppm for ¹H) was used as the internal standard for the spectra of ¹³C and ¹H. The accuracy of the measurement of the chemical shifts was ±0.1 ppm for ¹³C and ±0.02 ppm for ¹H. The values of the chemical shifts are expressed in the δ scale relative to tetramethylsilane.

**CONCLUSIONS**

1. An analysis of the parameters of the NMR-¹³C and ¹H spectra of derivatives of 3-hydroxypyridine and their N-oxides showed that transition from the unoxidized base to the N-oxide is accompanied by a shift of practically all the signals into a higher-field region.

2. The NMR data were compared with a calculation of the π-charges of derivatives of 3-hydroxypyridine-1-oxide in the anionic form. For 2-substituted 3-hydroxypyridine-1-oxides, a satisfactory correlation exists between the chemical shift and the π-electron density.

**LITERATURE CITED**
