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STRUCTURE OF THE ALKALOIDS OF THE GENTIAN

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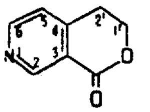
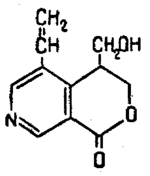
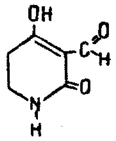
It has been reported previously that we have isolated from plants of the genus Gentiana three new alkaloids (gentianadine, gentianamine [1], and gentianaine [2]) and have established their structures as (I), (II), and (III), respectively. To check the correctness of structures (I), (II), and (III), we have studied the NMR spectra of these substances.



I



II



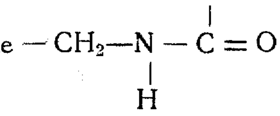
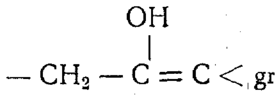
III

The NMR spectrum of gentianadine (I) (figure, a) clearly shows two two-proton triplets at 5.48 and 6.96 ppm (J = = 6.0 Hz) which, by their position and spin-spin coupling constants, relate to adjacent methylene groups of a lactone ring, i.e., to the protons of $-CH_2-CH_2-O-$. The strong-field signal at 6.96 ppm must obviously be ascribed to the $-CH_2-$ group conjugated with the pyridine ring and the signal at 5.48 ppm to the $-CH_2-O-$ group of the lactone ring.

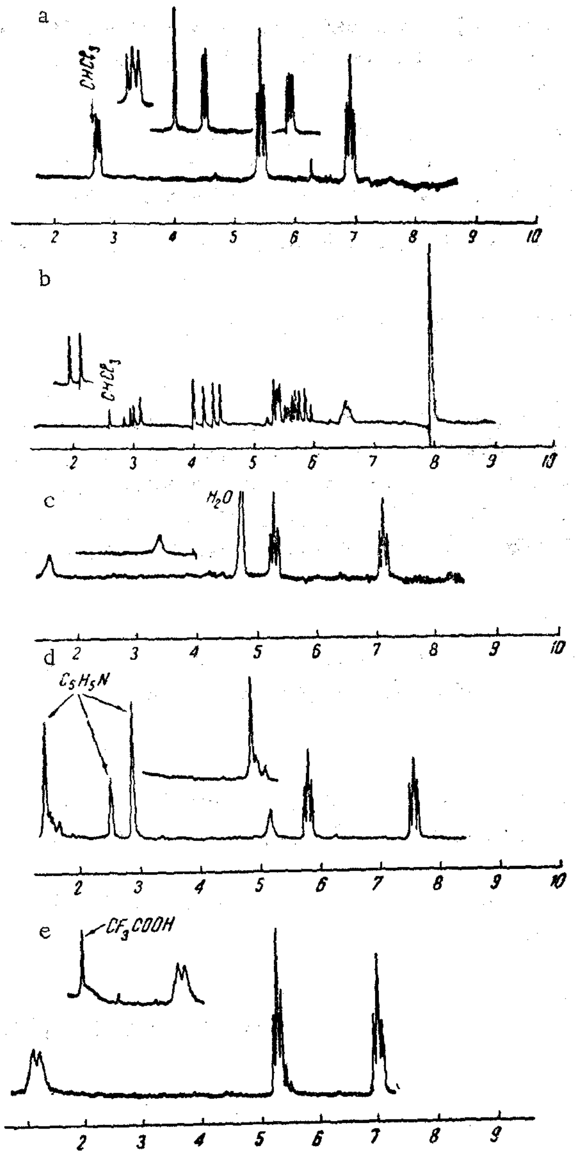
In the weak-field region in the spectrum of (I), a one-proton singlet at 0.88 ppm corresponds to an α-proton of a pyridine ring, and a one-proton doublet at 1.36 ppm (J = 6.0 Hz) and a one-proton quadruplet at 2.81 ppm (J = 6.0 Hz and J = 1.0 Hz) correspond to protons 6 and 5, respectively. Apart from the spin-spin coupling of protons 5 and 6, forming a system of the AB type (J_{AB} = 6.0 Hz), the spectrum of (I) also shows the interaction of protons 5 and 2 with a small constant (J = 1.0 Hz). The chemical shifts of protons 2 and 6 located in the α-position with respect to the nitrogen of the pyridine ring differ considerably, which can apparently be explained by the influence of the descreening action of the lactone carbonyl on proton 2, as a result of which its signal is shifted into a weaker field than the signal of proton 6.

Gentianamine (II) differs from gentianadine by the fact that it has a vinyl group in position 5 of the pyridine ring and a CH_2OH group in position 2' of the lactone ring. In view of the limited solubility of gentianamine (II) in $CDCl_3$, we recorded and interpreted the spectrum of its O-acetyl derivative. In the NMR spectrum of the latter (figure, b) in the strong-field region, a three-proton singlet appears at 7.96 ppm from the protons of the methyl group of $OCOCH_3$. The broad and poorly resolved one-proton signal at 6.57 ppm possibly relates to the methine proton 2'. Because of their nonequivalence, the protons of the methylene groups of the lactone ring and of the side chain, together with the methine proton 2', lead to the appearance in the 5–6-ppm region of a multiplet of 13 lines with an intensity of four proton units.

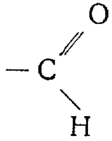
The three protons of the vinyl group, forming a system of the ABX type, are expressed by two systems of bands in the NMR spectrum: a two-proton quartet in the 4–4.5-ppm region—the AB part—and a one-proton quartet at 3.06 ppm—the X part. Protons 2 and 6 of the pyridine ring give rise to two one-proton singlets at 0.94 and 1.15 ppm.

The figure (c, d, and e) gives the NMR spectra of the alkaloid gentianaine (III) in three solvents. In spite of the apparent simplicity of the structure of (III) (the gentianaine molecule contains only seven hydrogen atoms), the analysis of its NMR spectrum proved not to be an easy task. In a consideration of the NMR spectrum of (III) (figure, c), the first thing noticed is the presence of two two-proton triplets at 5.30 and 7.09 ppm (J = 6.5 Hz) corresponding to the $-CH_2-CH_2-$ grouping. But the values of the chemical shifts of the methylene groups of (III), in particular at τ = 5.30 ppm, are strongly shifted in the weak-field direction. The weak-field signal (5.30 ppm) we ascribed to the  $-CH_2-\underset{\displaystyle H}{\underset{|}{N}}-\overset{|}{C}=O$ group, and the signal at 7.09 ppm to the  $-CH_2-\overset{\displaystyle OH}{\overset{|}{C}}=C<$ group. From this we can assume that the gentianaine molecule is nonplanar and, therefore, the amide carbonyl has a considerable influence on the methylene groups.

The presence of an aldehyde group in (III) was established chemically ("silver mirror" reaction) and by IR-spectroscopic methods [2]. However, the signal of the aldehyde proton in the NMR spectrum of (III) has an anomalous value of the chemical shift. Thus, for example, in D_2O it is 1.50 ppm. It is known that the signals of aldehyde protons are found



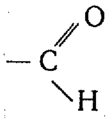
NMR spectra: gentianadine (a); O-acetylgentianamine (b); gentianaine in D_2O (c); gentianaine in deuteropyridine (d); gentianine in CF_3COOH (e).

in the −0.5 to +0.9-ppm region [3]. In gentianaine, the double bond apparently decreases the influence of the carbonyl group in  $-\mathrm{C}{\overset{\displaystyle O}{\underset{\displaystyle H}{\lessgtr}}}$ and gives a considerable diamagnetic shift in the strong-field direction.

The other two active hydrogens do not appear in the spectrum of (III) (figure, c) because of the change of −OH and >NH into −OD and >ND.

The spectrum of (III) (figure, d), taken in deuteropyridine, shows two one-proton signals: at 5.12 ppm which we ascribed to −OH and at 1.75 ppm, to >NH. When (III) was heated to 60° C, the −OH signal shifted in the strong-field direction more than the >NH signal.

In trifluoroacetic acid (figure, e), the −OH signal shifted in the weak-field direction to −0.80 ppm, obviously through the exchange of the −OH protons of the gentianaine and the acid; at the same time the >NH signal at 1.75 ppm did not take part in exchange. On heating, the −OH and the >NH signals shifted into the strong-field region.

In conclusion, we may mention that it is difficult from an analysis of the NMR spectrum of gentianaine to determine the mutual location of the  $-\mathrm{C}{\overset{\displaystyle O}{\underset{\displaystyle H}{\lessgtr}}}$ and −OH groups unambiguously.

The NMR spectra of gentianadine, O-acetylgentianamine, and gentianaine were recorded on a JNM-4H-100/100 MHz spectrometer. Tetramethylsilane was used as an internal standard, the signal from its protons being taken as 10 (τ scale). The spectra of gentianadine and O-acetylgentianamine were taken in $CDCl_3$ and those of gentianaine in D_2O, CF_3COOH, and deuterochloroform. For the recording of the spectrum of gentianaine in D_2O, an external standard was used—a capillary containing hexamethyldisiloxane. The concentrations of the substances varied between 4 and 7%.

Conclusions

An analysis of the NMR spectra of three new alkaloids of Gentiana (gentianadine, gentianamine, and gentianaine) has confirmed the correctness of the structures previously established for these compounds.

REFERENCES

1. A. S. Samatov, S. T. Akramov, and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 3, 182, 1967.
2. T. U. Rakhmatullaev, S. T. Akramov, and S. Yu. Yunsov, KhPS [Chemistry of Natural Compounds], 5, 32, 1969.
3. Elucidation of Structures, ed. K. W. Bentley (Technique of Organic Chemistry, ed. A. Weissberger, Vol. 11) [Russian translation], Moscow, 1967.

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