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STRUCTURE OF ANABASAMINE

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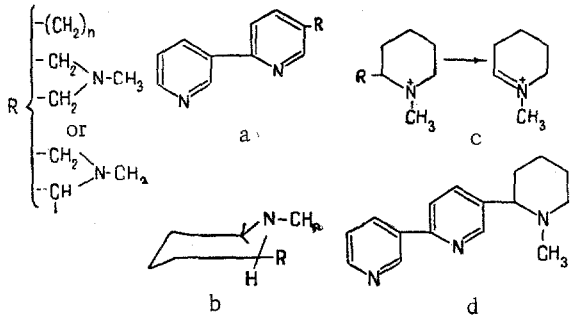
The alkaloid anabasamine, which we isolated some time ago from A. aphylla L. [1, 2], has the composition $C_{16}H_{19}N_3$. The three nitrogen atoms in it are tertiary and it contains one $\rangle N-CH_3$ group.

A comparison of the UV spectra of anabasamine (Fig. 1), 2,3'-bipyridyl, and some of its derivatives [3] permitted the assumption that the unsaturated part of the molecule of anabasamine is 2,3'-bipyridyl.

In the IR spectrum of anabasamine (Fig. 2), bands appear at 3090-3030 cm^{-1} (aromatic C-H), 2550-2780 (C-H bond in the α position to a tertiary aliphatic nitrogen atom), 1560-1593, 1470 (C=C and C=N bonds in substituted pyridines), and 1330 cm^{-1} (deformation vibrations of the C-H bonds in $\rangle N-CH_3$).

In the region of the nonplanar vibrations of the C-H bonds, there are bands at 805 cm^{-1} (1,3-substitution in the β nucleus and 1,2,4-substitution in the α nucleus of the bipyridyl). Thus, on the basis of these results we can propose the following structural fragments for the molecule of anabasamine (a).



The proton spectrum of the substance (Fig. 3, A) consists of nine signals with different degrees of splitting and a ratio of the intensities of 1 : 2, 1 : 2, 2 : 2, and 1 : 3 : 6. In the weak-field region the spectrum shows the presence of seven aromatic protons and in the region of stronger fields twelve aliphatic protons.

From a consideration of the signals in the weaker-field region it can be seen that they correspond primarily to the protons of the 2,3'-bipyridyl system.

In the NMR spectrum of anabasamine, a triplet (2.8 ppm) corresponds to the β proton of the β nucleus, and a doublet (0.9 ppm) to the α proton of the β nucleus with slight splitting from the meta protons, the latter being shifted by about 0.6 ppm in the direction of lower fields as compared with the signal of the α proton of pyridine (1.5 ppm). We consider that the shift in the signal of this proton is caused by the interaction of the unshared pair of the neighboring nitrogen with this proton of the nucleus, i.e., the 2,3'-bipyridyl is present in the cis conformation [4].

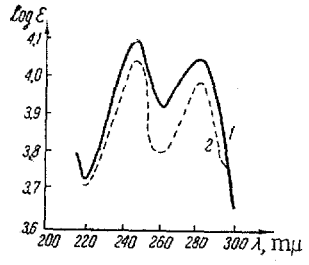


Fig. 1. UV spectra of anabasamine (in ethanol) (1) and of 2,3'-bipyridyl (in water) (2).

The triplet (1.5 ppm) corresponds to the two α' protons of the different nuclei. The presence in the spectra of an incompletely resolved structure shows that the over-all signal is the sum of a singlet and a doublet.

The doublet (1.8 ppm) corresponds to the γ proton of the β nucleus (the slight decrease in the chemical shift of this proton is due to the influence of the ring current of the neighboring α nucleus), and the doublet (2.4 ppm) to the β' and γ protons of the α nucleus.

In the region of stronger fields in the NMR spectrum of anabasamine there is a narrow signal at 8.15 ppm ($\rangle N-CH_3$ group) and a broad poorly resolved signal (6 protons) at 8.4-8.8 ppm (3 ordinary CH_2 groups).

The signal at 7.2 ppm corresponds to the 2 α protons in the $\rangle N-CH_2$ fragment of a piperidine. The multiplet at 8.0-8.1 ppm must be assigned to the tertiary hydrogen atom in the $\rangle CH-N-CH_3$ group.

In this case, the increased value for the tertiary proton can be explained by the fact that the substituent on it must be present in the equatorial position. Increased shielding is caused by the interaction of the axial unshared pair of

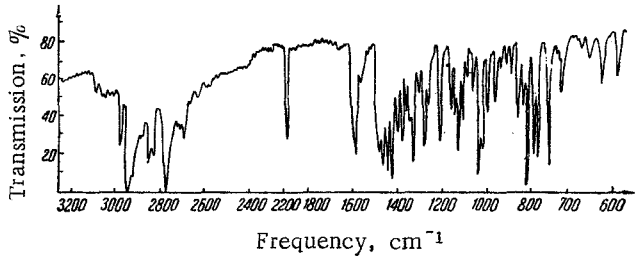


Fig. 2. IR spectrum of anabasamine in KBr tablets.

the nitrogen with the α axial proton of piperidine. Thus, the combination of data given above permits the deduction of the most probable structure for the aliphatic moiety of the anabasamine molecule as (b). An additional indication of the correctness of this assumption can be obtained by considering the NMR spectrum of N-methylanabasine (Fig. 3, B). The individual peaks in the high-field region are identical.

In the mass spectrum of anabasamine, the position of the peak of the molecular ion shows that the molecular weight of the base is 253. The same molecular weight has been obtained from the results of the NMR spectrum.

The strongest peak corresponds to m/e 98. The presence of this peak shows that part of the molecule of anabasamine is an α-substituted $\rangle N—CH_3$ piperidine system, since this ion appears only as the result of the elimination of an α substituent with the formation of the corresponding ammonium ion (c).

The most characteristic fragmentation for β- and γ-substituted aliphatic heterocyclic amines is that with cleavage of the bond between the α and β carbon atoms with the subsequent formation of ions of lower molecular weight because of the elimination of the substituent together with the carbon atom of the ring.

In the mass spectrum of anabasamine there are also the peaks $(M - 1)^+$, 224 (M − 29), and 210 (M − 43), and others formed in the usual way [5]. Consequently, in view of the information given above, we can put forward the most probable structural formula for anabasamine (d).

It is quite possible that the aromatic substituent—bipyridyl—occupies the equatorial position in the piperidine molecule. The oxidation of anabasamine with potassium permanganate under the conditions for the oxidation of anabasine [6] gave an acid with the composition $C_{11}H_8O_2N_2$, which, by decarboxylation, gave 2,3'-bipyridyl. By a direct comparison of the acid obtained with the synthetic product it was established that it is 2,3'-bipyridyl-5-carboxylic acid. The latter was synthesized by a known method [7].

Thus, the results of the experimental material completely agree with the structure proposed for anabasamine.

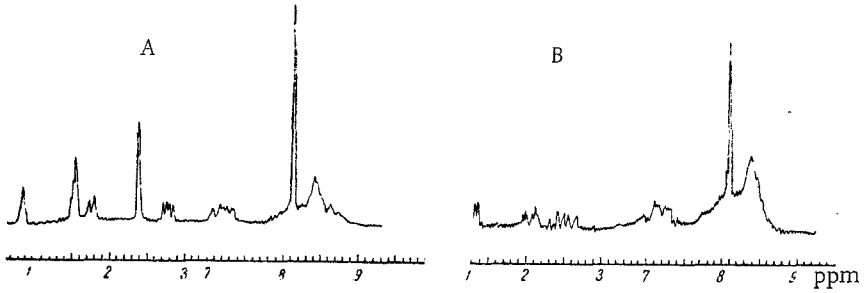


Fig. 3. NMR spectra of anabasamine in CCl_4 (A) and of N-methylanabasine in $CDCl_3$ (B).

Experimental

Anabasamine has mp 65–66° C, $[\alpha]_D$ +107° (c 3.65; ethanol), R_f 0.16 [1-butanol—water—hydrochloric acid (100 : 27 : 15)].

Found, %: C 76.28, 75.83; H 7.60, 7.47; N 16.52, 16.80; mol. wt. 253 (mass spectroscopy). Calculated for $C_{16}H_{19}N_3$, %: C 75.90; H 7.51; N 16.60; mol. wt. 253.

The NMR spectrum was recorded on a JNM-100 instrument, the IR spectrum (in tablets of potassium bromide) on a UR-10 spectrometer, and the mass spectrum on an MKh-1301 instrument.

Oxidation of anabasamine. A mixture of 2 g of anabasamine, 500 ml of water, and 10 g of potassium permanganate was heated for 12 hr. The residual potassium permanganate was decolorized by the addition of a few drops of methanol. The precipitate (manganese dioxide) was separated off and washed; the filtrate was evaporated to 1/4 bulk, cooled, washed with ether, and acidified with 10% hydrochloric acid to pH 6. The white flocculent precipitate which separated was filtered off and recrystallized from water, mp 280–281° C. Yield 1.3 g.

Found, %: C 66.55, 66.08; H 4.15, 3.99; N 14.39, 14.28. Calculated for $C_{11}H_8O_2N_2$, %: C 66.00; H 4.0; N 14.00.

A mixture with synthetic 2,3'-bipyridyl-5-carboxylic acid gave no depression of the melting point.

Decarboxylation of the oxidation product. A mixture of 0.2 g of the acid, 0.5 g of copper powder, and 5 ml of benzene was heated within a sealed tube in an autoclave at 210–230° C for 6 hr. After filtration and the distillation of the solvent, the residue—a viscous oil—was dissolved in ethanol, and the 2,3'-bipyridyl was precipitated in the form of a picrate, mp 162–163° C (ethanol).

Conclusions

1. A spectroscopic study of anabasamine, isolated from the seeds of the plant Anabasis aphylla L. has been carried out.

On the basis of UV, IR, NMR, and mass spectroscopic data, the structure 5-(N-methyl-2'-piperidyl)-2,3'-bipyridyl has been proposed as the most probable.

2. The structural formula of anabasamine has been confirmed experimentally through the production of 2,3'-bipyridyl-5-carboxylic acid by the oxidation of the base.

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