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A MASS SPECTROMETRIC INVESTIGATION OF ALKALOIDS OF THE GALANTHAMINE TYPE

R. Razakov, V. N. Bochkarev, Kh. A. Abduazimov, N. S. Vul'fson, and S. Yu. Yunusov

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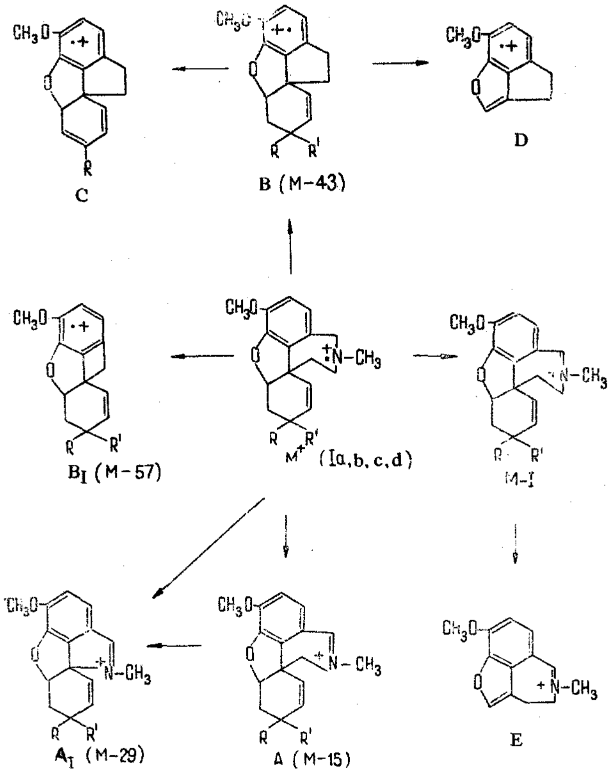
Continuing a mass spectrometric study of the alkaloids of the Amaryllidaceae [1–3], we have studied the mass spectra of galanthamine (**Ia**, R = H, R' = OH), its stereoisomer epigalanthamine (**Ib**, R = OH, R' = H), O-acetylgalanthamine (**Ic**, R = H, R' = $OCOCH_3$), and narwedine (**Id**, R + R' = 0).

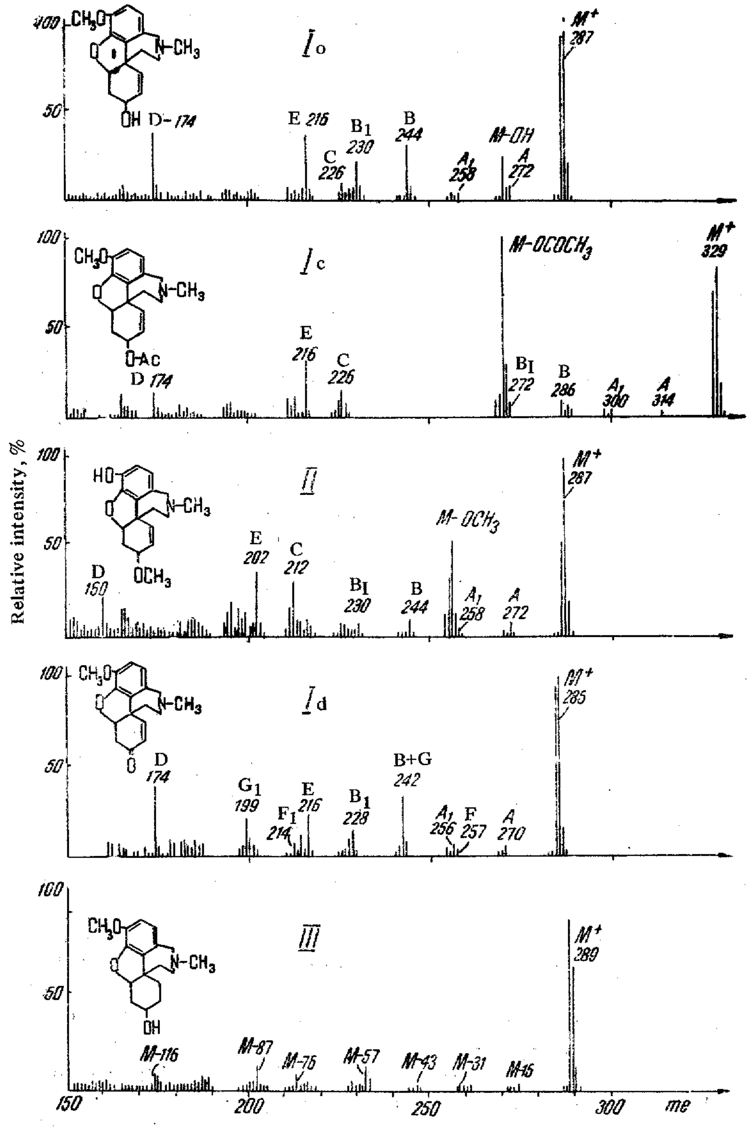
The mass spectra of epigalanthamine and galanthamine (differing in the stereochemistry of hydroxyl group) did not differ substantially. Characteristic for the spectra of all the substances studied was the presence of a strong (for **Ia**, **b**, and **d**, the maximum) peak of the molecular ion. The peak of the M − 1 ion, the formation of which leads to an extension of the system of conjugated double bonds (Scheme 1) is also of high intensity.



Scheme 1

The further decomposition of the molecular ion takes place in several directions. One of them is connected with the contraction of ring C with the retention of the nitrogen atom in a similar manner to what is found in the mass spectrum of hexamethylenimine [4, 5]. The ions A (M − 15) and A_1 (M − 29) so formed are of low intensity (see Scheme 1 and the figure). Another direction of decomposition consists in the contraction of ring C with the expulsion of the nitrogen atom. The ions so formed, B (M − 43) and B_1 (M − 57), have a high intensity (see Scheme 1 and the figure). The transitions $M^+ \rightarrow B$ and $M^+ \rightarrow B_1$ are confirmed by the presence in the mass spectrum of **Ia** of metastable peaks with m/e 207.5 (calculated: 207.44) and m/e 184.5 (calculated: 184.44), respectively. The third direction of decomposition leads to the formation of the fragments E and D through the elimination of ring C from the ion M − 1 and B, respectively. The transition (M − 1) → E is confirmed by the presence in the mass spectrum of **Ia** of a metastable peak with m/e 163 (calculated: 163.11).

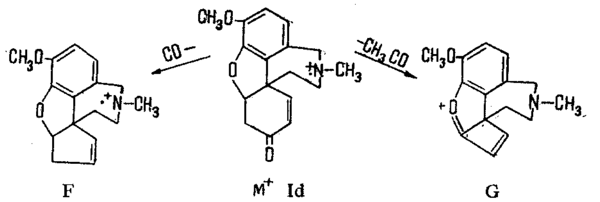
Also characteristic for compounds **Ia** and **Ic** is the elimination of the substituent R' in the form of a radical or a neutral molecule from the molecular ion and from the ion B. In the first case R' is eliminated mainly in the form of a radical and in the second case in the form of a neutral molecule HR'.



Mass spectra of galanthamine (Ia), O-acetylgalanthamine (Ic), chlidanthine (II), narwedine (Id), and lycoramine (III).

A study of the features of the fragmentation of the alkaloids of the galanthamine type has enabled us to obtain additional information on the structure of chlidanthine, isolated by Boit from the plant Chlidanthus fragrans [6]. On the basis of chemical characteristics, a partial formula was proposed for this alkaloid, in which, however, the positions of the double bond and of the methoxyl substituent were not determined.

The presence in the spectrum of chlidanthine of peaks typical for alkaloids of the galanthamine type (see figure, **I**) permits the conclusion that chlidanthine has a similar structure [8], expressed by formula **II**. The presence of a carbonyl group in the molecule of narwedine (**Id**) has no fundamental influence on the three routes of the fragmentation of the molecular ions of the alkaloids of the galanthamine type considered above. In this case the spectrum also has strong peaks of M^+, $M - 1$, and fragment formed by the cleavage of ring C with the retention and with the expulsion of the nitrogen atom, as well as fragments due to the elimination of ring B from the ions $M - 1$ and B (see figure, **I**). In addition to this, a series of specific features of fragmentation is recorded; for example, the expulsion of a CO group (28 m.u.) from the molecular ion and ion B, which is characteristic for cyclic ketones (ions F and F_1, respectively). In addition, the peak $M - 43$ in the spectrum of narwedine has a greater intensity than in the spectra of the other alkaloids of the galanthamine type. This is probably due to the fact that in addition to the formation of the ion B the elimination from the molecular ion of **Id** of the group of atoms CH_3CO is possible, leading to the formation of the ion G with a system of conjugated double bonds, as is shown in Scheme 2. A similar expulsion of a CH_3CO group takes place from ion B, which leads to the appearance of the ion G_1 with m/e $M^+ - 86$.



F M⁺ Id G

Scheme 2

In the spectrum of lycoramine (**III**), which is a dihydro derivative of galanthamine (**Ia**), the molecular and the $M - 1$ ions have a very high intensity. The intensity of the peaks of the fragmentary ions is low.

We have observed a similar pattern in the spectra of dihydro derivatives of alkaloids of the lycorine type [3]. In the spectrum of lycoramine, all the fragments formed as a result of the same types of decomposition as are characteristic for galanthamine appear: contraction of ring C both with the retention and with the loss of the nitrogen atom, elimination of ring B from the $M - 1$ ion, expulsion of an OH group from the molecular ion and of water from fragments containing ring B (see figure, II). The sample of chlidanthine was kindly provided by Dr. Doepke (Humboldt University, Berlin, GDR).

Experimental

The mass spectra were recorded on a standard MKh-1303 instrument fitted with a system for introducing the sample directly into the ion source at 110–130° C with an energy of the ionizing electrons of 30–70 eV.

Conclusions

1. Features of the mass spectrometric behavior of alkaloids of the galanthamine type have been established: the presence of strong M^+ and $M - 1$ peaks, the contraction of ring C with the retention or with the expulsion of the nitrogen atom, and the elimination of the elements of ring B.

2. Additional information on the structure of the alkaloid chlidanthine has been obtained.

3. The similarity of the mass spectrometric behavior of a dihydro derivative of galanthamine (lycoramine) and of dihydro derivatives of alkaloids of the lycorine type have been shown.

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Institute of the Chemistry of Natural Compounds AS USSR

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