MASS SPECTROMETRY OF HAPLOFOLINE AND FOLIFINE

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Recently, in connection with a proof of the structure and the identification of the alkaloids of Haplophyllum tuberculatum [1], the mass spectrum of the dihydropyran alkaloid haplofoline (I) was briefly characterized [2].

This paper gives the results of a more detailed investigation of the mass spectra of I and also of N-methylhaplofoline (II), folifine (III) [3], and acetylfolifine (IV). These spectra are interesting because the main influence on the fragmentation of the molecular ion is exerted by the dihydropyran ring with a gem-dimethyl group position 13. The molecular ions of I and II and, in particular, III and IV, are less stable than M^+ of, for example, the quinolines and furanoquinolines [4, 5], where this ion is the maximum ion in the spectrum. The main routes of the degradation of I–IV can be discussed on the basis of the localization of the positive charge on the nitrogen atom (Scheme 1). The first act of the degradation of M^+ is the cleavage of the C_{13}—O bond. The further degradation of the ion formed takes place by various mechanisms. Most frequently a hydrogen atom migrates from C_{16} (or C_{15}) to the oxygen atom, after which the C_{11}—C_{12} bond breaks and the radical $C_4H_6R_1$ is expelled. The intensity of the ammonium ion is the greatest in the spectra of I–III and is very great in the spectrum of IV.

Deuteration of folifine (III) at the OH group has shown that, in addition to the migration of hydrogen from C_{15} or C_{16}, deuterium migrates to O_{14} (~60% of the ions) with the simultaneous cleavage of the C_{11}—C_{12} bond. The ions with masses one unit greater (189 and 175 amu) apparently have the structure of 2-hydroxy-3-methylquinolin-4-ones.

Less favorable is the cleavage of the C_3—C_{11} bond with the simultaneous migration of hydrogen from C_{12} to C_3. However, the corresponding low-intensity peaks are present in the spectra of all four substances (m/e 161 for I and 175 for II–IV).

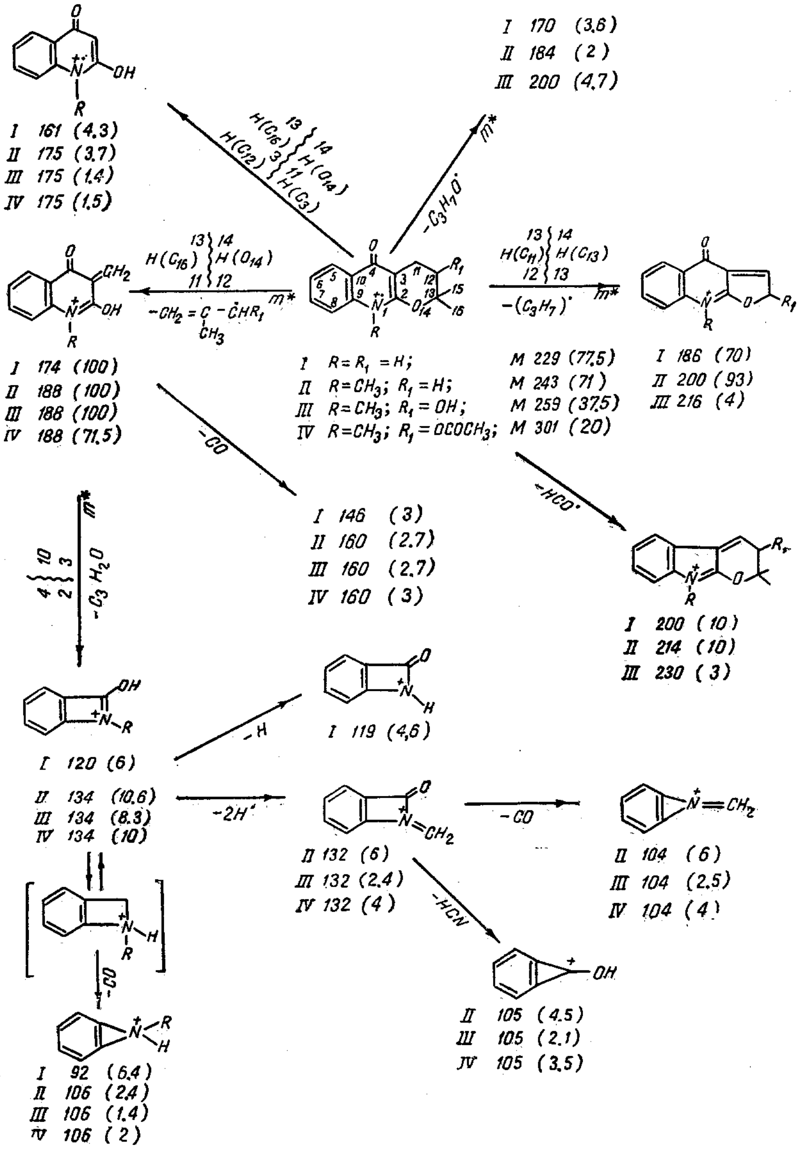
The other main process accompanying the cleavage of the C_{13}—O bond is the migration of H' from C_{11} to C_{13} and the cleavage of the C_{12}—C_{13} bond, as a result of which an isopropyl radical is lost and a cyclic ion with m/e 186 for I and 200 for II is obtained. The presence of an OH group in the molecule of III makes this process less significant, and in the corresponding spectrum the ion with m/e 216 has a lower intensity.

The spectra of I–III have considerable peaks for the M — 29 ion. We consider the participation of the ethereal oxygen atom in the appearance of a fragment with 29 amu to be unlikely and assume that it is formed from the carbonyl group at C_4 with the migration of one H atom, apparently from C_{11}.

The presence of a number of significant peaks in the region of low mass numbers is connected mainly with the fragmentation of the ion having m/e 174 (188). The main process here is the expulsion of a C_3H_2O fragment (possibly in the form of propargyl aldehyde), which is confirmed by a metastable peak. This leads to the formation of an ion with m/e 120 (I) or 134 (II–IV). Subsequently, the ion with m/e 120, by expelling a hydrogen atom, is converted into an ion with m/e 119, and the ion with m/e 134, losing two hydrogen atoms, into an ion with m/e 132 which, in its turn, by eliminating CO or HCN, gives rise to ions with m/e 104 and 105. At the same time, both ions (120 and 134 amu) can exist in the amide form and, by losing a molecule of CO, be converted into ions with m/e 92 and 106, respectively. None of these transitions contradicts the features of the spectrum of the deutero analog of folifine.

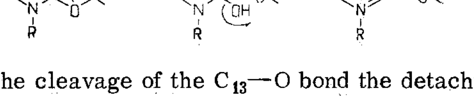
The formation of the fragment M – 59 (I–III) can be explained by the cleavage of the C_{12}—C_{13} bond, the subsequent migration of H· from C_{11} to C_{13}, and the cleavage of the C_2—O bond, the ion M — 59 being capable of existence both in the open and in the cyclic form (Scheme 2). In the case of IV, the appearance of an ion with m/e 200 can be explained by the successive splitting out of an acetyl radical from position 12 and of a molecule of acetone.

The elimination of the acetoxyl group in IV takes place in two ways: by the direct splitting out of CH_3COOH or by the detachment of $CH_3COO^{\cdot}$ after the cleavage of the C_{13}—O bond. The first of the ions loses $\dot{C}H_3$, which leads to the formation of the maximum peak with m/e 226. The stability of this ion can be explained by its stabilization in the oxonium form. Besides this, the participation of this form in the other processes of fragmentation is apparently slight, since, otherwise, the M — 15 ion should have a high intensity. In actual fact, its intensity does not exceed 15% rel. in the mass spectrum of I.



Scheme 1

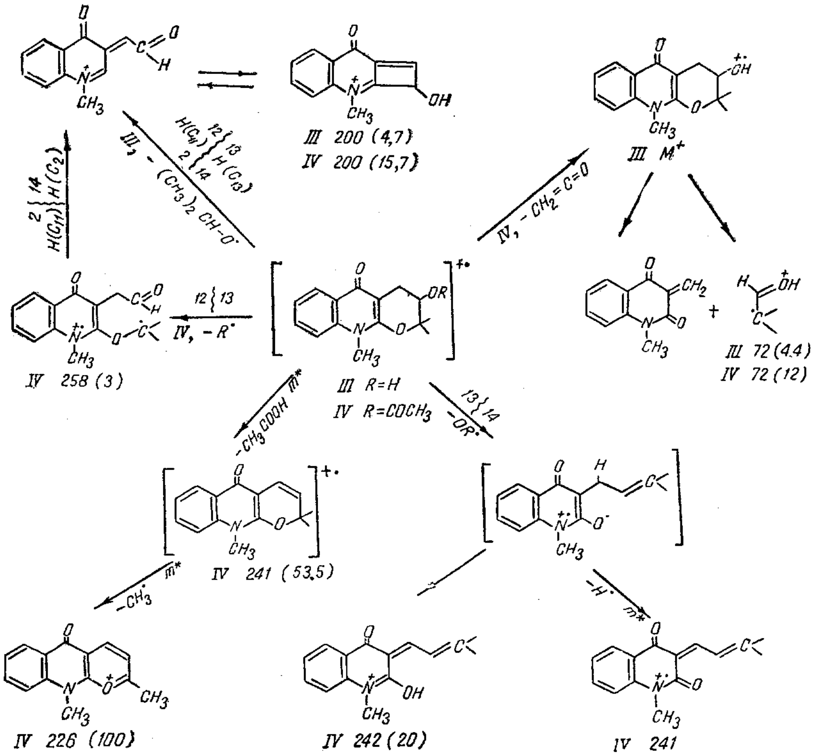
The mass spectra of I–III also have peaks of the M — 17 ions (IV: M − CH_3COOH − 17), which can be formed as a result of a rearrangement process:



For the folifine molecule, after the cleavage of the C_{13}—O bond the detachment of $OH^{\cdot}$ from C_{12} is more favorable, and, therefore, in the spectrum of the deutero analog the peak of the M — 17 ion has scarcely changed.

In the region of low mass numbers, the ion with m/e 72 has a considerable intensity in the spectra of III and IV. Since it is completely absent from the spectra of I and II it may be considered that its origin is connected with the localization of the charge on the oxygen atom at C_{12}.

This assumption is confirmed by the fact that in the spectrum of the deutero analog of folifine a peak of an ion with m/e 73 appears.



Scheme 2

The formation of the ion with m/e 72 in the case of IV takes place initially through a stage of the expulsion of ketene and then by the scheme shown above.

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