MASS SPECTROMETRY OF DUBINIDINE AND DUBININE

Structure of Isodubinidine

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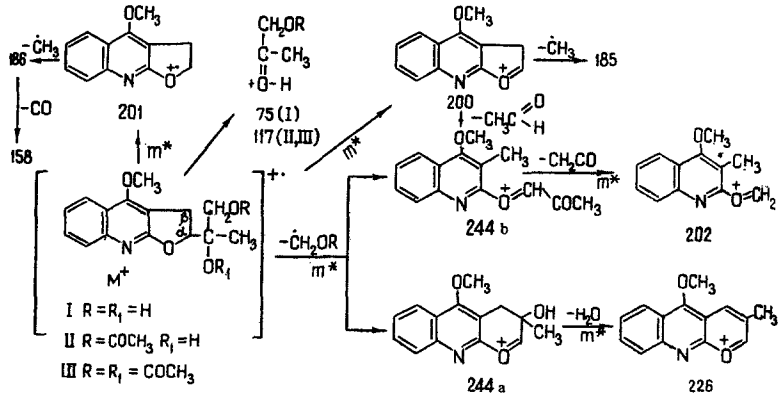
Studies of the mass spectra of the alkylquinolines [1], alkoxyquinolines [2], furano- and isofuranoquinolines [3, 4], carbostyryl derivatives [4], and pyranoquinolines [5] have been reported previously. We have studied the mass spectra of the dihydrofuranoquinoline alkaloids dubinidine (I) and dubinine (II) and of their derivatives acetyldubinidine (acetyldubinine) (III) and isodubinidine (IV).

Mass spectra of compounds I–V†

I *m/e*	276(5), 275(M) (33), 245(4), 244(21), 226(12), 202(23), 201(55), 200(100), 188(4), 186(12), 185(13), 173(12), 172(12), 170(3), 158(8), 156(4), 143(4), 142(4), 130(4), 115(4), 75,(5).
I–D_2 *m/e*	278(2), 277(15), 276(29), 275(21), 246(3,5), 245(17), 244(20), 227(3,5), 226(20), 204(3,5),203(18), 202(51), 201(95), 200(100), 187(8), 186(15), 185(18), 77(4), 76(5), 75(3,5).
II *m/e*	317(M) (17), 245(4), 244(21), 226(6), 202(18), 201(35), 200(100), 199(8), 186(8), 185(9), 173(8), 172(7), 158(4), 156(2), 143(3), 142(3), 130(4), 129(3), 117(5), 115(5).
III *m/e*	359(M) (17), 317(7), 300(5), 244(16), 227(7), 226(39), 214(6), 212(4), 202(15), 201(25), 200(100), 188(5), 186(8), 185(10), 173(6), 172(7), 158(5), 143(6), 142(10), 130(10), 129(11), 115(10).
IV*m/e*	276(11), 275(M) (58), 258(11), 245(4), 244(17), 240(4), 227(8), 226(100), 216(9), 214(15), 212(4), 202(4), 200(14), 190(4), 189(58), 188(64), 187(10), 186(11), 176(17), 175(6), 160(9), 146(6), 144(4), 134(16), 132(6), 130(4), 115(4), 77(9), 70(6).

In the mass spectra of substances I–III, the maximum peak is the ion with m/e 200 resulting from the expulsion of the side chain attached to the dihydrofuran ring (Scheme 1). An analysis of the mass spectrum of the deuterium analog I-D_2 shows that approximately 30–50% of the ions are formed in this way. The other ions with m/e 200 apparently result from the ion 244b through the elimination of a molecule of acetaldehyde and the closure of the five-membered ring. This hypothesis explains the partial shift of the peak with m/e 200 in the spectrum of the deuterium analog, since in the formulation of the ion 244b the deuterium atom migrates from the tertiary hydroxyl group to C_β, and in the closure of the five-membered ring hydrogen is split out preferentially (primary isotope effect [6]). The participation of rearrangements in the formation of the ion with m/e 200 is also confirmed by the fact that its intensity in relation to the total ionic current Σ% decreases in the spectrum of III in whose molecule there is no mobile hydrogen in a tertiary OH group (10% in the spectrum of I and 4.4% in the spectrum of III).



Scheme 1

†The percentage relative intensities are given in brackets.

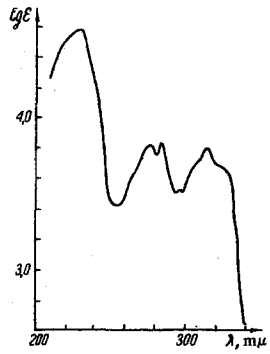
The elimination of the side chain from the dihydrofuran ring with the simultaneous migration of a proton from the tertiary hydroxyl group leads to an ion with m/e 201. This mechanism is confirmed by the isotopic shift by one unit in the spectrum of I-D_2 and also by a decrease in the intensity of this ion in the spectrum of III.

The splitting out of the side chain with the localization of the charge on it forms ions with m/e 75 (I) and 117 (II and III).

The cleavage of the dihydrofuran ring and the splitting out of a CH_2OR radical gives rise to ions with m/e 244. The latter may have a cyclic (a) or a linear (b) structure. In substance III, the ions with m/e 244 (a) and 117 are obtained after the ejection of a molecule of ketene. By eliminating a molecule of water, the ion with m/e 244 (a) becomes aromatized, being converted into an ion with m/e 226. The ion with m/e 244 (b), losing a molecule of ketene, gives an ion with m/e 202 which also undergoes an isotopic shift by one mass unit in the spectrum of I-D_2.

Isodubinidine (IV) was obtained previously [7] by the action of alcoholic alkali on dubinidine methiodide. Substance IV has a composition similar to I, which is explained by the usual isomerization of a 4-methoxyquinoline derivative into the corresponding N-methylquinolin-4-one [7].

However, unlike dubinidine, isodubinidine is not oxidized by periodic acid, and its UV spectrum is typical for quinolin-2-one derivatives (figure). Consequently, we consider that the action of alcoholic alkali on dubinidine methiodide leads to the saponification of the dihydrofuran ring. This is characteristic for this group of alkaloids [8]. Then the formation of a dihydropyran ring takes place by condensation between the phenolic hydroxyl group in position 4 and the tertiary hydroxyl group in the side chain.



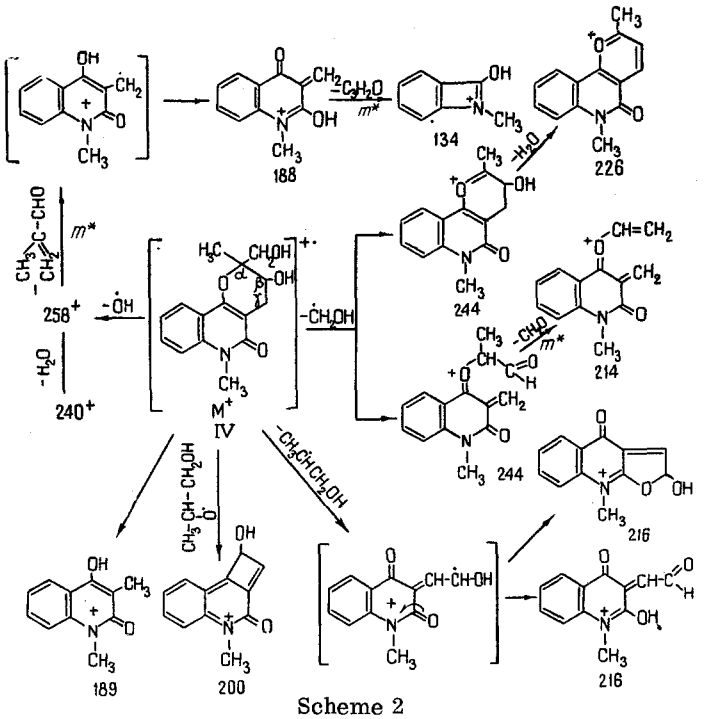
UV spectrum of isodubinidine.

A study of the mass spectrum of isodubinidine has shown that it differs from the mass spectra of compounds I–III and has a definite analogy with the mass spectra of dihydroflindersine and flindersine [9]. In the spectrum of IV, the maximum peak is that with m/e 226, corresponding to the peak with m/e 212 in the spectrum of flindersine; the next most intense peak with m/e 188 corresponds to the peak with m/e 174 in the spectrum of dihydroflindersine.

On the basis of what has been said above, the structure of 1-methyl-(α-methyl-β-hydroxy-α-hydroxymethyl-α,β-dihydropyrano)quinolin-2-one may be proposed for isodubinidine.

Fragmentation of the molecular ion of isodubinidine is shown in Scheme 2. The maximum peak with m/e 226 is formed as a result of the expulsion of a hydroxymethyl radical and a molecule of water. The successive ejection of these neutral fragments is not revealed by means of metastable peaks. At the same time, an m* peak with a maximum at about 185.5 m/e corresponding to the 275 → 226 + 49 transition is observed. Cases in which the elimination of two fragments of a molecule takes place in the form of a metastable one-stage process have been described in the literature [10]. The ion with m/e 258 is most probably formed by the cleavage of an O—C bond and the elimination of a primary hydroxyl. This ion then decomposes with the liberation of water or with the expulsion of a molecule of methacrylaldehyde, being converted into the strong ion with m/e 188. The detachment of a hydroxymethyl group from the molecular ion may also take place as a consequence of the primary cleavage of the C_β—C_γ bond; after isomerization a noncyclic ion of different form with m/e 244 appears, which eliminates formaldehyde and forms an ion with m/e 214.

The ion with m/e 188 decomposes with the liberation of a molecule of propargylaldehyde and is converted into an ion with m/e 134, the further decomposition of which we have described previously [5]. In addition to the ion with m/e 188, the mass spectrum of isodubinidine has the strong peak of an ion with m/e 189 apparently formed directly from M^+ by the cleavage of the $C_\beta—C_\gamma$ and $O—C_\alpha$ bonds. In the spectrum of the deuterium analogue, both peaks are shifted by one mass unit, which confirms the transfer of deuterium from the secondary OD group to the charged fragment on fragmentation. The molecular ion IV may also decompose with the cleavage of the $O—C_\alpha$ bond, the migration of H to the tertiary carbon atom, the cleavage of the $C_\alpha—C_\beta$ bond, and the elimination of a secondary propanol radical. This gives rise to a radical ion with m/e 216, rearranging into an ammonium ion with a formylmethylene side chain or with a dihydrofuran ring (see Scheme 2). The ion with m/e 200 is analogous to the ion isobaric with it in the mass spectrum of folifine [5]. The experimental conditions have been given in the previous paper [5].



Scheme 2

CONCLUSIONS

1. Features of the fragmentation of dubinidine and dubinine are explained by the presence of a branched side chain in the dihydrofuran ring.

2. The structure of isodubinidine has been elucidated on the basis of its chemical characteristics and UV and mass spectra.

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