APPLICATION OF MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL INVESTIGATIONS

I. MASS SPECTRA OF β-QUINUCLIDONES AND β-BENZO(b)QUINUCLIDONES

A. I. Ermakov, Yu. N. Sheinker,
E. E. Mikhlina, L. I. Mastafanova,
V. Ya. Vorob'eva, A. D. Yanina,
L. N. Yakhontov, and R. G. Kostyanovskii

UDC 547.834.4 : 543.51 : 541.61.63

The mass spectra of 3-quinuclidone, methyl 5-ketoquinuclidine-2-carboxylate, ethyl 3- and 5-ketoquinuclidine-2-carboxylates, benzo(b)-3-quinuclidone, and ethyl 3-ketobenzo(b)quinuclidine-2-carboxylate were investigated. The fragmentation of the investigated compounds is realized through the open form of the molecular ion with cleavage of the bridge bond containing the carbonyl group and with subsequent elimination of carbon monoxide. The principal disintegration mechanisms were confirmed with isotope labels.

The mass spectra of some quinuclidines were investigated for the first time in [1] from the point of view of weakening of the amine stabilization in conformity with Bredt's rule. It was shown that, in contrast to the corresponding unbridged structures, the intensity of the peaks of the $[M-H]^{+\cdot}$ amine fragments is extremely insignificant in the mass spectra of quinuclidine, 2- and 4-azaquinuclidines, and other similar functional derivatives. In addition, this regularity is not observed in some cases, and the intensity of the peaks corresponding to α cleavage proves to be quite high [2, 3].

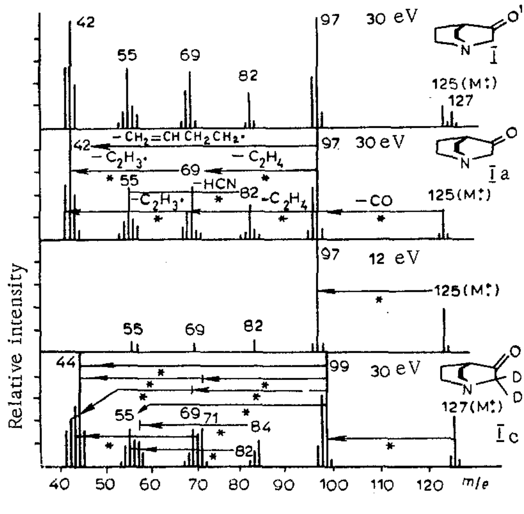


Fig. 1. Mass spectra of β-quinuclidones and β-benzoquinuclidones.

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1404-1410, October, 1972. Original article submitted February 22, 1971.

The assumption that these fragments are formed from the open form of the molecular ion was confirmed by an analysis of the low-voltage mass spectra, in which the intensity of the peaks corresponding to α cleavage was sharply reduced. At the same time, the corresponding fragments for the unbridged amines remain the maxima in the spectra, even when the ionizing voltage is lowered to 12 eV [4].

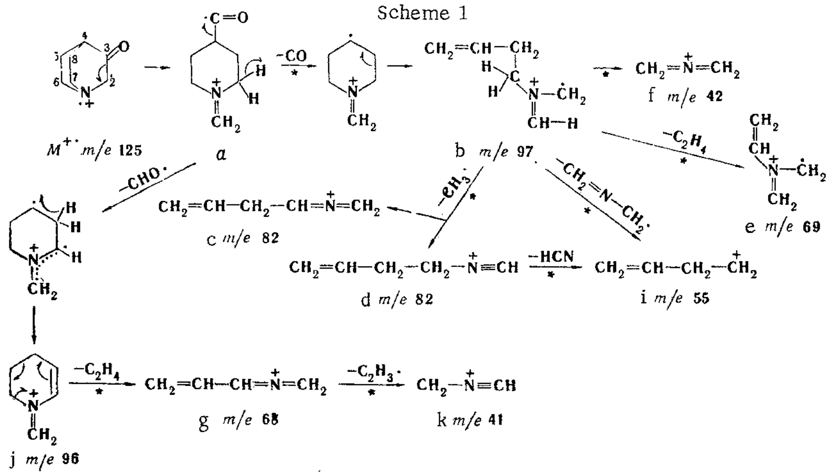
In the present investigation it is shown that for the investigated β-quinuclidones and β-benzo(b)quinuclidones the fragmentation actually proceeds through the open form of the molecular ion with cleavage of the bridge bond containing the carbonyl group. Subsequent elimination of carbon monoxide gives fragments characteristic for this class of compounds.

When the mass spectra of 3-quinuclidone and benzo(b)-3-quinuclidone (Ia and IIa) (Figs. 1 and 2) are compared, the analogy in their disintegration is primarily apparent. The fragments with m/e 97 and 145, the peaks of which are the maximum ones in the spectra, are formed as a result of the loss of 28 mass units by the molecular ions of Ia and IIa. It follows from the mass spectra of the O^{18}-labeled compounds (I and II in Figs. 1 and 2) that this detachment corresponds to the elimination of carbon monoxide (rather than C_2H_4, as assumed in [2]) from the open form of the molecular ion which can be represented as a and a' (schemes 1 and 2).

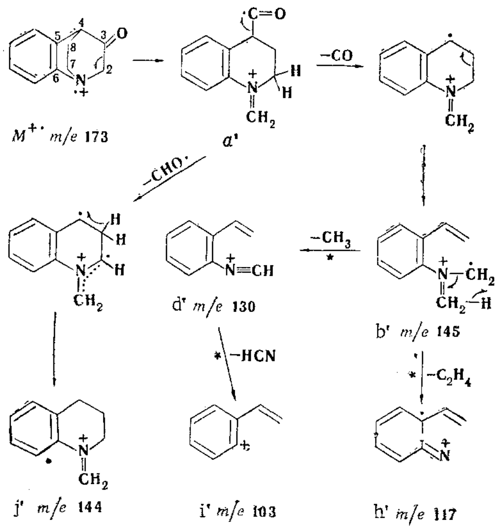
The structure of the resulting ions (b and b') explains the origin of fragments c and d with m/e 82, e with m/e 69 ($m^* = 49.5$), and f with m/e 42 ($m^* = 18.4$) in the spectra of the quinuclidone, and of d' with m/e 130 ($m^* = 116$) and h' with m/e 117 ($m^* = 94.5$) in the spectra of benzo(b)quinuclidone. The splitting out of hydrogen cyanide from fragments d and d' gives hydrocarbon ions i with m/e 55 and i' with m/e 103.

Fragments with m/e 96 and 144, the peaks of which have high intensities (~50% of the maximum peak) in the spectra of I and II, are formed during the elimination of formyl radicals from the open molecular ions. In this case, the most probable process is elimination of a hydrogen atom from the α position. Fragments j and j' with m/e 96 and 144, which have partially conjugated bonds, are formed as a result of simultaneous

Scheme 1



Scheme 2



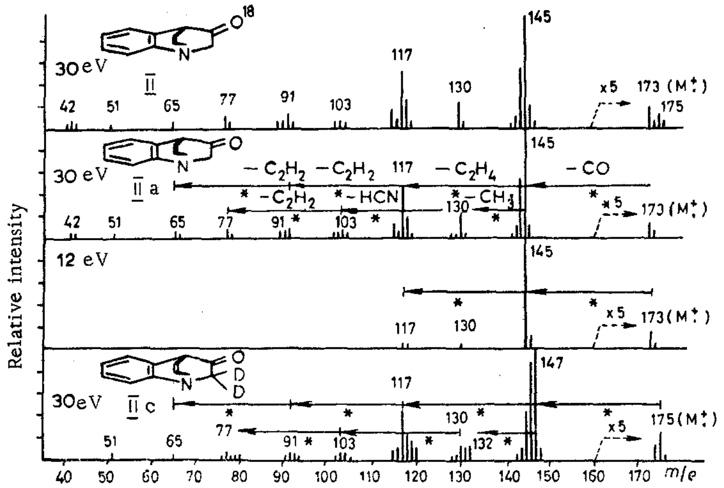


Fig. 2. Mass spectra of β-quinuclidones and β-benzoquinuclidones.

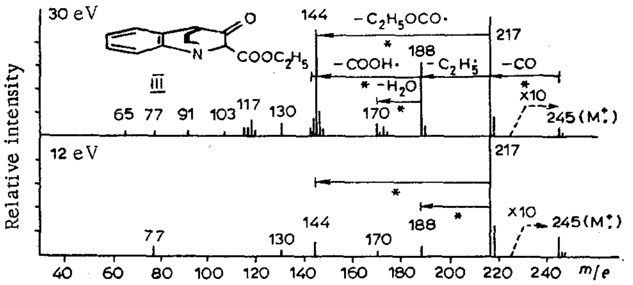


Fig. 3. Mass spectra of β-quinuclidones and β-benzoquinuclidones.

hydrogen rearrangement, for example, during the migration of a hydrogen atom from C_8 to the radical center attached to C_4.† This process is also in agreement with the subsequent disintegration of the fragment with m/e 96; this is confirmed by the presence of metastable ions corresponding to the formation of ions g with m/e 68 (m* =48) and k with m/e 41 (m* =24.5).

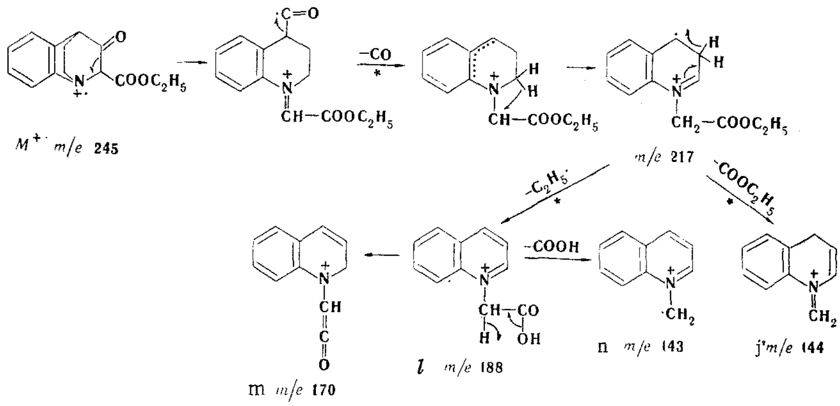
The schemes for the disintegration of I and II are in accordance with the mass spectra of these compounds with a deuterium label at C_2, in which one observes a shift of the peaks of fragments with m/e 82, 69, 68, and 42 for I and 130 for II to higher masses in conformity with the proposed structures. The presence of a peak with m/e 69 in the mass spectrum of Ic is explained by the elimination of CD_2CH_2 from the fragment with m/e 99 (m* =48). This process is apparently due to the isotope effect [6]. We note that the apparent increase in the overall relative intensities of peaks with m/e 67-71 in the mass spectrum of Ic as compared with that of Ia does not affect the $\Sigma_{67-71}/\Sigma_{40}$ value, which is identical in both cases (Σ_{67-71} is the ion current of the group of peaks with m/e from 67 to 71, while Σ_{40} is the total ion current).

The fragmentation processes characteristic for I and II also develop during the disintegration of ethyl 3-ketobenzo(b)quinuclidine-2-carboxylate (III). As in the preceding cases, the maximum peak in the spectrum (Fig. 3) is the peak of the $|M-CO|^{+\cdot}$ fragment with m/e 217 (m* =192), which is formed from the open form of the molecular ion. The presence of intense and unambiguously identifiable metastable ions in the mass spectrum of III makes it possible to represent the overall scheme of the disintegration of this compound (see scheme 3).

The detachment of a carbethoxy group from the $|M-CO|^{+\cdot}$ fragment (m* =95.5) gives an ion with m/e 144. The high intensity of the peak of this fragment (95% of the maximum) can be explained only by the stability of structure j'. Thus, as a result of the rearrangement depicted in the scheme, the resulting ion with m/e 144 can have the same structure as the fragment with the same mass number in the disintegration of II. A similar rearrangement apparently also occurs in the formation of ion *l* with m/e 188, which

---

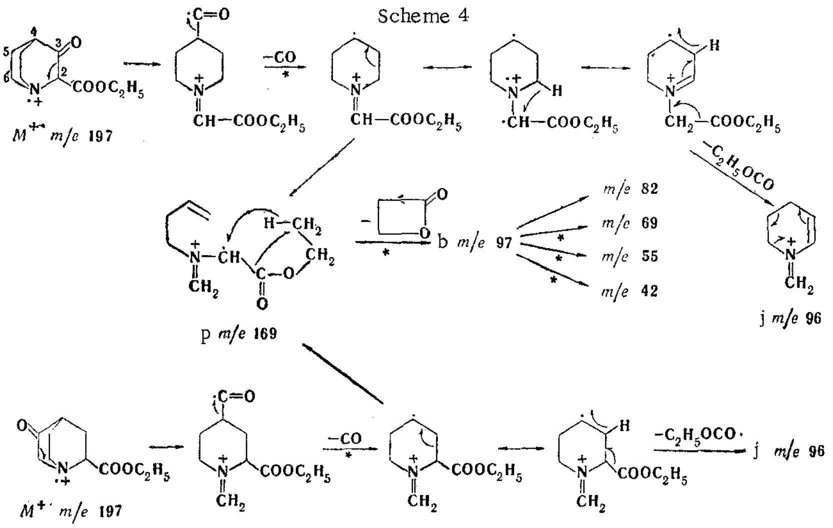
†The migration of a hydrogen atom to the adjacent radical center was discussed, for example, in [5].



then disintegrates to fragments m with m/e 170 (m* = 154) and n with m/e 143. The peak of the fragment with m/e 145 in the spectrum of III is due to the elimination of butyrolactone from the $|M=CO|^{+\cdot}$ ion. This process is particularly characteristic for V and VI (Fig. 4). The practically completely identical character of the spectra of ethyl 3- and 5-ketoquinuclidine-2-carboxylates (V and VI),† with the presence of identical metastable ions, is a direct confirmation of fragmentation from the open molecular ion.

In fact, the identical character of the spectra can be explained only by the formation of ions p and ions j during the fragmentation of both compounds via the following scheme:

Scheme 4



The elimination of carbon monoxide from the open forms of the molecular ions with cleavage of the C_7-C_8 bonds leads to the formation of identical (for V and VI) fragment p with m/e 169. The one-step ejection of butyrolactone from ion p (m* = 56) occurs through a six-membered transition state with the formation of fragment b with m/e 97, similar to the corresponding fragment in the disintegration of I. A graphical illustration of this process is the fragmentation of deuterated (at the ethyl group) compound VI (Fig. 4), in the mass spectrum of which the peak with m/e 97 is shifted by one unit toward the high-mass side. This shows up particularly distinctly at 12 eV. In addition, the increase in the intensity of the peak with m/e 97 as compared with the peak with m/e 96 at a low ionizing voltage is a confirmation of the occurrence of this rearrangement through the energetically favorable six-membered transition state. In the disintegration of V and VI, fragment b explains the formation of ions with m/e 82, 69, 55, and with m/e 42 (see the first scheme given above). As in the disintegration of I, these processes are confirmed by metastable ions. In the mass spectrum of deutero analog VI (with respect to C_6), the peaks of fragments with m/e 82, 69, and 42 were shifted, respectively, to higher masses, while the peak of the fragment with m/e 55 retained its intensity and mass number, as was already observed in the disintegration of I.

α-Detachment of a carbethoxy group from $|M-CO|^{+\cdot}$ ions leads to the formation of the most intense fragment with m/e 96. It follows from a joint examination of the mass spectra of Ia, Ic, IV, V, VI, VIa,

---

† In [2] the spectrum of this compound was distorted, apparently because of the position of the sample in the metal inlet system.

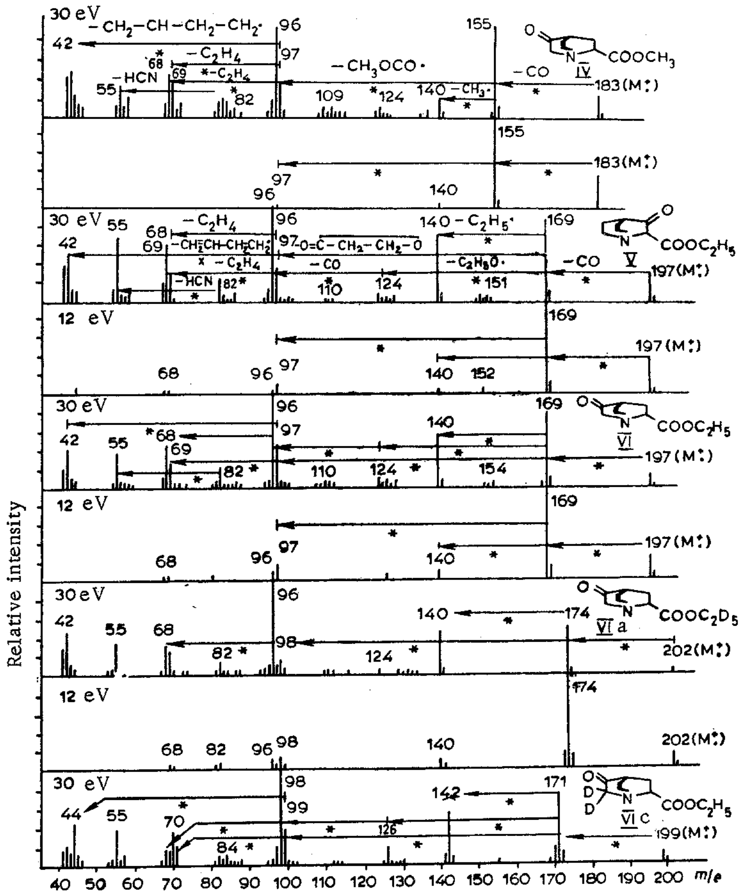


Fig. 4. Mass spectra of β-quinuclidones and β-benzoquinuclidones.

and VIc that ions with m/e 96 for V and VI and fragment j in the disintegration of I should be identical in structure. Consequently, in this case also the formation of a fragment with m/e 96 for V and VI can also be represented as being the result of the rearrangement depicted in the scheme. We note that a metastable ion ($m^* = 59.5$) corresponding to direct detachment of $CH_3OCO^{\bullet}$ is observed in the mass spectrum of I; while subsequent splitting out of $C_2H_5O^{\bullet}$ ($m^* = 90$) and CO ($m^* = 74$) is also characteristic for V and VI.

In contrast to the esters of quinuclidine-2-carboxylic acids, for which α-detachment of the carbalkoxy group occurs directly from the molecular ion [2], the $|M-COOR|^{+\cdot}$ fragment is practically absent in the mass spectra of IV, V, and VI because of strong competition with CO elimination.

It is interesting that the intensities of the $|M-CO|^{+\cdot}$ peaks in the mass spectra of the investigated compounds remain the maximum ones when the ionizing voltage is lowered to 12 eV or below. The observed peculiarity in the behavior of the $|M-CO|^{+\cdot}$ fragments is apparently determined not so much by the low energy of activation of the elimination of CO as by the stability of the neutral and charged fragments formed.

Thus an examination of the results makes it possible to assume that the fragmentation of β-quinuclidones and β-benzoquinuclidones proceeds through the open form of the molecular ion with cleavage of the bridge bond containing the carbonyl group and with subsequent elimination of carbon monoxide. Subsequent cleavage of the bonds in the $|M-CO|^{+\cdot}$ ion proceeds with the formation of intermediate structures with m/e 97 and 96 for quinuclidones and with m/e 145 and 144 for benzoquinuclidones, which determine the subsequent steps in the fragmentation.

EXPERIMENTAL

The mass spectra were measured with an MKh-1303 mass spectrometer with "direct" introduction of the sample into the ion source at ionizing voltages of 50, 30, and 12 eV. The substances were purified prior to recording of the spectra by distillation or sublimation in vacuo. The isotopic labels in I and II were introduced by refluxing the compounds with H_2O^{18} + 5% KOH. The C_2-deuterated I and II were obtained by refluxing for 1 h with $D_2O + 5\%$ KOH, while C_6-deuterated VI was obtained by refluxing with C_2H_5OD. The following method was used to obtain ethyl group-deuterated VI: 0.23 g of 5-ketoquinuclidine-2-carboxylic acid hydrochloride (mp 297°), which was related to the quinine series with respect to the configuration of the substituents, was refluxed for 2.5 h with 2 ml of C_2D_5OH with continuous bubbling of a stream of hydrogen chloride through the mixture. The reaction mass was evaporated to dryness and treated with two 2-ml portions of anhydrous benzene. The solvent was removed by vacuum distillation, after which the esterification with C_2D_5OH was repeated. The base of the deuterated keto ester was isolated as in the description in [7].

The synthesis of the substances has been previously described: I [8], II [9], IV [10], V [2], and VI [7]. Compound III was obtained from 1-ethoxycarbonyl-4-ethoxycarbonyl-1,2,3,4-tetrahydrocholine and had bp 155-157° (0.8 mm).

LITERATURE CITED

1. R. G. Kostyanovskii, Doctoral Dissertation [in Russian], Moscow (1968).
2. R. G. Kostyanovskii (Kostyanovsky), E. E. Mikhlina, E. I. Levkoeva, and L. N. Yakhontov, Org. Mass Spectrometry, 3, 1023 (1970).
3. E. E. Mikhlina, F. K. Turchin, V. Ya. Vorob'eva, A. I. Ermakov, R. G. Kostyanovskii, Yu. N. Sheinker, and L. N. Yakhontov, Dokl. Akad. Nauk SSSR, 195, 1337 (1970).
4. R. G. Kostyanovskii and Kh. Khafizov, Dokl. Akad. Nauk SSSR, 198, 363 (1971).
5. C. Djerassi, Advances in Mass Spectrometry, 4, 199 (1969).
6. J. H. Beynon, Mass Spectrometry and Its Application to Organic Chemistry, Elsevier (1960).
7. L. N. Yakhontov, L. I. Mastafanova, and M. V. Rubtsov, Zh. Obshch. Khim., 30, 519 (1960).
8. E. E. Mikhlina and M. V. Rubtsov, Zh. Obshch. Khim., 29, 118 (1969).
9. A. D. Yanina, E. E. Mikhlina, K. A. Zaitseva, M. D. Mashkovskii, and L. N. Yakhontov, Khim.-Farmats. Zh., 7 (1969).
10. L. N. Yakhontov and M. V. Rubtsov, Zh. Obshch. Khim., 29, 2343 (1959).