

CLAISEN REARRANGEMENT TAKING PLACE IN THE MASS SPECTROMETER

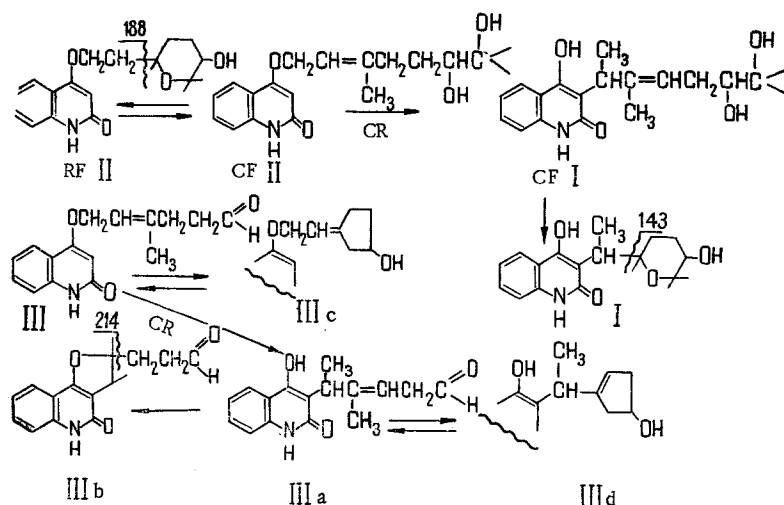
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UDC 543.51

It has been shown previously that bucharidine (I) is a product of the anomalous (β) Claisen rearrangement of bucharaine (II) [2] (Scheme 1). The great similarity of the mass spectra of I and II was noted (Fig. 1). The fundamental difference in the spectra of these substances is the presence of the peak of the ion of 4-hydroxyquinolin-2-one with m/e 161 in the spectrum of II, and its absence from the spectrum of I. This ion derives from the molecular ion of II by the cleavage of an O-C bond of the side chain with the migration of one hydrogen atom. In I, the splitting off of the substituent at C_3 , which is unlikely, would be necessary for the appearance of a similar ion.

The mass numbers of the majority of the other ions in the spectra of I and II, taken at $\sim 100^\circ\text{C}$ with an energy of 40 V for the ionizing electrons, are satisfactorily explained by the ring-chain tautomerism of the side chains. A study of the spectra of I and II shows [1] that under the conditions of mass spectrometry there are ions which derive from the chain form (CF) of the molecule I and, conversely, ions from the ring form (RF) II.

To study the tautomerism of the side chains of I and II, solutions of the substances in CD_3OD were heated in sealed tubes at 100°C for a day. As a result, the M^+ peak in the mass spectrum of the deuterio analog of I was shifted by three mass units and the peak with m/e 143 by one mass unit in accordance with the number of active hydrogens in the molecule under consideration. This shows that in bucharidine, under the usual conditions, the equilibrium is shifted completely in the RF direction.



In the spectrum of bucharaine II deuterated in the same way, the shift in the M^+ peak amounted to six units. The increase in the number of hydrogen atoms replaced by deuterium is due to a labile equilibrium between the CF and RF of II (Scheme 2). Thanks to the primary isotope effect [3], in the cleavage of the

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from *Khimiya Prirodnikh Soedinenii*, No. 5, pp. 577-583, September-October, 1970. Original article submitted May 11, 1970.

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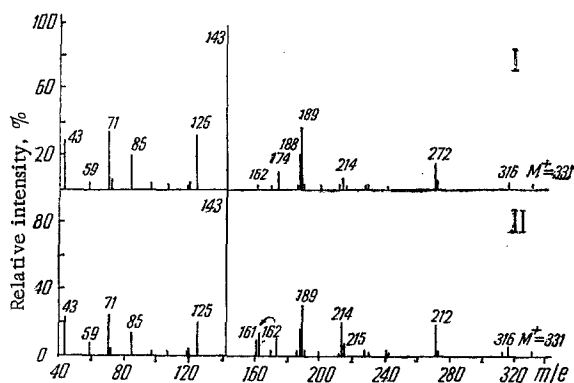


Fig. 1. Mass spectra of I) bucharidine and II) bucharaine.

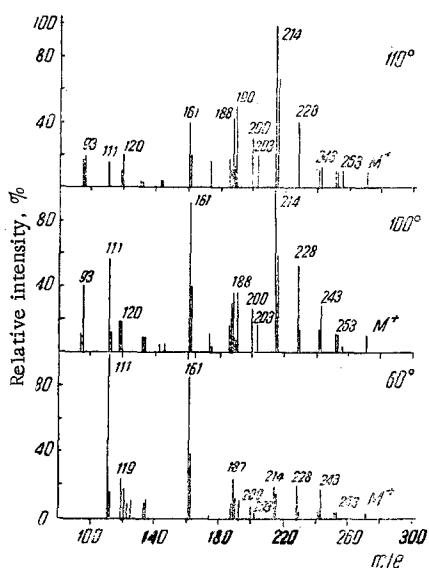
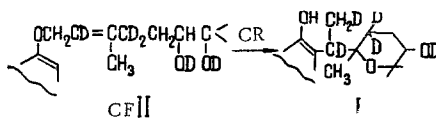


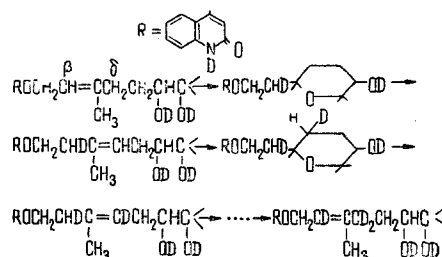
Fig. 2. Mass spectra of bucharinal (III) at 60, 100, and 110°C.

the spectrum gives an intermediate picture: approximately 50% of the ions with m/e 189 and 188 contain two deuterium atoms each and about 50% of the ions with m/e 143 contain two deuterium atoms. Let us also consider the ion with m/e 174 resulting from the detachment of a methyl radical from the ion with m/e 189, which is confirmed by a metastable peak at 160.2 amu. If this process began with the RF of II, the peak with m/e 174 should have been shifted by one unit (only through N-D) in the spectrum of the product of the prolonged treatment of II with deuteromethanol. In actual fact, the peak with 174 amu is shifted completely by two and partially by three mass units. These facts, and also the great similarity of the mass spectra of bucharaine and bucharidine taken under similar conditions permit the assumption that during mass spectrometry II is converted into I in the manner of a Claisen rearrangement.



We may note, in the first place, that there is not one peak in the spectrum of I which could not be present in the spectrum of II, while the reverse does not hold. Now let us consider the cause of the "anomalous" shift of the peaks in the spectra of the deuterio analogs. If the Claisen rearrangement (CR)

ring it is mainly a hydrogen atom that splits off from the β - or δ -carbon atom and passes into the hydroxy group. Then the latter undergoes exchange with the deuterium of the solvent and on renewed ring closure adds to the corresponding carbon atom.



The brief deuteration of II in the lock system of the mass spectrometer led to the displacement of M^+ by only three mass units, as in I.

Let us consider more strictly the probable causes of the similarity of the spectra of I and II. All the most common ions in the region of low masses (< 150 amu) originate from the ion with m/e 143, whose structure is similar in both cases. A series of comparatively weak peaks is formed at the expense of a phenyl nucleus with an amide group which is also present in both molecules. Considerably more unexpected is the coincidence of the intensities of the peaks with m/e 189, 188, and 174 in the spectra of I and II. While in I the ions with m/e 189 and 188 appear as the result of the α cleavage that is characteristic for aromatic systems, in II these ions must be due to γ cleavage, and only from the RF. If this is true, the displacement of the peaks with m/e 189 and 188 in the spectrum of the product of the rapid deuterium exchange of II must amount to two units (a D atom attached to N and one in the tertiary hydroxy group, passing to the β -carbon atom on ring closure), and the displacement of the peak with m/e 143 must amount to one unit. An analysis of

TABLE 1.

m/e t°C	271 (M ⁺)	228	214 215	187 188 190	161	119 120	111
60	0,6	4,5	4,5	11	18	9	23
100	1,6	8	23	14	13	5	8
110	1.7	8	31	19	8	5	3

TABLE 2.

m/e t°C	331 (M ⁺)	313	272	242 243	228	214 215	188 189	161 162	143	125
100	1,5	2,5	7	2	2	7	16	7	36	7
65	1,0	3,5	8	4	3	25	10	13	11	2,5

does actually take place, then in the ring closure of the CF of I the deuterium atom appears in the methylene group of the tetrahydropyran ring and the peak of the ion with m/e 143 is shifted by one additional unit, while the ions with m/e 189 and 188 will contain only one D atom attached to the nitrogen. If the CR does take place, the deuterium atoms in the side chain of the molecule of II subjected to prolonged deuteration, are distributed in such a way that the ion with m/e 174 can contain one additional deuterium atom (in the α -methine group). The partial shift by three units is explained by the fact that in the formation of the ion with m/e 189 either H or D may migrate to the ion of the aromatic radical.

To prove the occurrence of a CR in the mass spectrometer, we studied the spectra of the product of the periodate oxidation of bucharaine, the aldehyde bucharinal (III), in whose molecule the formation of the RF of the side chain with the participation of the ethylene bond is unlikely. The spectra were taken at different temperatures in the inlet tube (Fig. 2). Table 1 gives the intensities of the main peaks of the mass spectra of III relative to the total ion current, $\Sigma\%$.

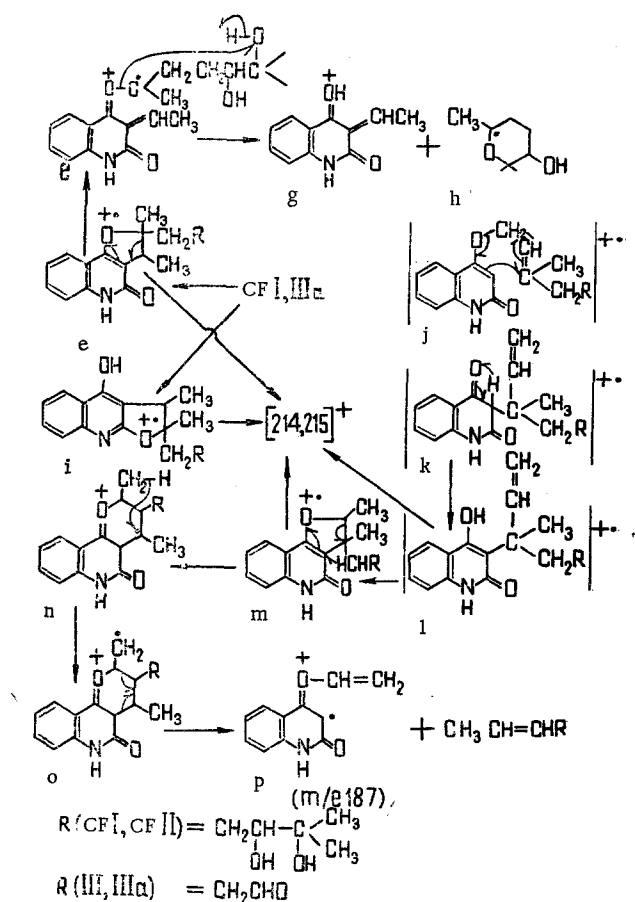
The relatively greater instability of the molecular ion at a low temperature can be explained by the ease of the α rupture of the side chain of III which results in peaks with m/e 161 (charge in the nucleus) and 111 (charge in the side chain) appearing as the strongest in this spectrum. When the temperature is raised, the proportion of these ions decreases sharply, the stability of M⁺ increases and so does the occurrence of the ions with 186-190, 214, and 215 amu. The formation of the two latter ions, and especially the group of ions with m/e 186-190, from the molecular ion of III appears difficult. However, if the occurrence of a CR is assumed, the appearance of these ions can be explained. As a result of the CR, the ion of the aldehyde IIIa (see Scheme 1) is obtained, from which the dihydrofuranoquinolin-2-one IIIb is easily formed [4]. The ions with m/e 214 and 215 result from the splitting out of a primary propanol radical or a molecule of acrolein from IIIb. The formation of these ions takes place by a similar mechanism in the fragmentation of bucharaine, but the formation of a ring via the double bond, even with the phenolic hydroxyl, is obviously less likely than the formation of a tetrahydropyran ring by molecule I. In addition to this, the peak with m/e 214 is also present in the spectrum of I, although it is less strong. Its appearance is due to the ring closure of the CF of I at the phenolic hydroxyl under the conditions of mass spectrometry.

We also recorded the mass spectra of I and II with a low temperature at the inlet system, under which conditions the spectrum of I scarcely changed. The values of $\Sigma\%$ obtained for II are given in Table 2.

Thus, when the temperature is lowered, the contribution of the ions arising from simple cleavage of the bonds of the side chain of II increases and the intensity of the peaks of the ions formed as a result of CR (143, 188, and 189 amu) decreases. A most interesting fact is the marked increase in the intensity of the ions with m/e 214 and 215, the first of which becomes the maximum ion. A satisfactory explanation of this can be found if it is assumed that, in addition to the "anomalous" (β) CR, the "normal" CR (γ inversion) takes place in the mass spectrometer and predominates over the β rearrangement at low temperatures. The usual treatment of the mechanism of γ inversion [4] can easily be described using the symbolism of mass spectrometric systems (Scheme 3). The molecular ions II and III (j) are converted via an intermediate six-membered state into the ions k and l, and then undergo ring closure to form the ion m. The ions e and i obtained through CR, and also the ions l and m, by splitting off a CH₂R radical, are converted into an ion with m/e 214. The ions of type e are converted by the scheme proposed by Corral [5] into ions with

m/e 188. Scheme 3 gives a variant for the molecule II (f) and shows that, in addition to the ion with m/e 188 (g), the neutral radical h, coinciding in structure with the ion having m/e 143, is formed. Under certain conditions, this fragment may be charged. Consequently, this process may be an additional source of the ions mentioned above. The ion with m/e 187 (p) readily arises from the ion m, although it is produced with far greater difficulty than from the ion e. The proposed scheme is in agreement with the following experimental facts: in the spectrum of III taken at 60°C , in the group of peaks with 186–190 amu the peak p predominates, and in the spectrum taken at 110°C it is the peak with m/e 188. The ion with m/e 190, whose peak is present in the spectra of III, apparently consists of a protonated form of the ion of 3-ethyl-4-hydroxy-quinolin-2-one.

Together with the interconversion forms of the molecular ions of the molecule (III) described above, some other conversions take place in the mass spectrometer. Thus, for example, the comparatively strong peaks of the ions $M-\text{H}_2\text{O}$ can be explained by the ring closure of the aldehyde group with a methyl group (see Scheme 1, IIIc and IIId). The interconversion $\text{III} \rightleftharpoons \text{IIIc}$ takes place even in the cold and, therefore, in the spectrum of the product of the rapid deuteration of III the peak of the molecular ion is shifted by two mass units and the peak of the ion with m/e 111 by one mass unit. In the spectrum of III there are also other peaks corresponding to the degradation of the forms IIIc and IIId ($M-19$, $M-33$, $111-\text{H}_2\text{O}$).



The ease with which the rearrangements of molecules II and III occur is obviously related to their thermal instability. We have recorded the spectra of the substances in which the energy of the ionizing electrons (14–18 V) is reduced at a temperature of about 100°C . Under these conditions, the peaks of the ion fragments must be practically absent or be of low intensity. In actual fact, the spectra contain a fairly large number of strong peaks predominating over the M^+ peaks, ions with odd masses (189, 215, and 243 amu) apparently representing the molecular ions of the products of thermal decomposition, whose occurrence is the most widespread. Of the ion fragments, peaks appear with m/e 143 (I and II) and 161 and 214 (II and III), and 272 (I–III), which characterizes the low stability of the corresponding bonds. There is no doubt that in the rearrangements discussed a considerable role is played by the temperature conditions of

the mass spectrometer, and the molecules undergoing change are particularly subject to electron impact. Also, the contribution of the ionizing energy is certainly large. Under laboratory conditions the CR of II into I takes place at a considerably higher temperature. It has also been found that the prolonged heating of II at 110°C (in deuteration) preserved the differences in the spectra of I and II.

The investigation of the mass spectra of substances similar to those studied is of interest for understanding the mechanism of chemical reactions and for finding relationships between the chemical and mass spectrometric behavior of compounds.

CONCLUSIONS

The Claisen rearrangement of bucharaine and of the aldehyde bucharinal takes place under the conditions of mass spectrometry. At low temperatures γ inversion predominates and at high temperatures the anomalous β rearrangement.

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