DISSOCIATIVE IONIZATION OF METHYL-SUBSTITUTED HYDROXYQUINOLINES

N. A. Klyuev, R. A. Khmel'nitskii, G. A. Mal'tseva, L. N. Zhukauskaite, and A. N. Kost

UDC 543.51:547.831.6.7

The mass spectra of the following methyl-substituted hydroxyquinolines have been studied in the range of energies of the ionizing electrons of 15-50 eV: 2-hydroxy-4-methylquinoline, 6-hydroxy-2-methylquinoline, 6-hydroxy-4-methylquinoline, 8-hydroxy-2-methylquinoline, 8-hydroxy-4-methylquinoline, 2,6-dihydroxy-4-methylquinoline, and 4,6-dihydroxy-2-methylquinoline. It has been shown that the processes of dissociative ionization for the series of compounds investigated take place exclusively from the keto forms of the molecular ions. The stability to electron impact is determined largely by the degree of enolization of the structures considered. The values of the selective decomposition are given and a scheme is proposed for the identification of the isomeric methyl-substituted hydroxyquinolines.

In the condensation of aromatic amines with β-dicarbonyl compounds, the problem generally arises of establishing the structure of the hydroxyquinoline formed, since the direction of cyclization depends strongly on the structure of the reagents, the solvent, the pH of the medium, and the temperature of the process. Thus, it is known that with aromatic amines β-oxo esters form either 2-hydroxy- or 4-hydroxy compounds depending on the acidity of the medium and the temperature [1, 2]. Fairly frequently, 2- and, particularly, 4-hydroxyquinolines are found among natural compounds (for example, see [3, 4]). Difficulties are always encountered in the determination of their structure, and therefore the drawing up of a correlation between the mass spectra of model samples and their structure appears to be of considerable interest.

We have considered the mass spectra of the following methyl-substituted hydroxyquinolines: 2-hydroxy-4-methylquinoline (I), 6-hydroxy-2-methylquinoline (II), 6-hydroxy-4-methylquinoline (III), 8-hydroxy-2-methylquinoline (IV), 8-hydroxy-4-methylquinoline (V), 2,6-dihydroxy-4-methylquinoline (VI), and 4,6-dihydroxy-2-methylquinoline (VII). This is the first time that the mass spectra of compounds (I-III, VI, and VII) have been obtained and interpreted; the mass spectra of compounds (IV) and (V) have been given partially by other authors [5]. The mass spectra were taken on an MKh-1303 instrument (compounds II-V) with a modified recording device at a temperature of the inlet system and of the ion source of 250°C at accelerating voltages of 50, 30, 20, and 15 eV and cathodic emission currents of 1.5 and 1.0 mA. In view of the low volatility of the hydroxyquinolines substituted in the pyridine ring, the mass spectra of compounds (I, VI, and VII) were taken on an LKB-9000 mass spectrometer with the direct introduction of the samples under similar recording conditions. The purity of the compounds was checked by GLC.

Table 1 gives the mass spectra of compounds (I-VII) taken at an energy of the ionizing electrons of 50 eV. The intensities of the peaks of the ions are given as percentages of the maximum peak in the spectrum of the sample, taken as 100%, only peaks with an intensity ≥1% being considered. The same table gives the stabilities of the molecules to electron impact (W_M), these being the ratios of the intensi-

K. A. Timiryazev Moscow Agricultural Academy. Kaunass Medical Institute. M. V. Lomonosov Moscow State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 972-978, July, 1973. Original article submitted July 12, 1972.

TABLE 1. Mass Spectra of Methyl-Substituted Hydroxyquinolines (intensities of the peaks in % of the maximum peak)

m/e	I	II	III	IV	V	VI	VII
26	3,2	2,1	2,8	1,1	1,0	1,1	6,2
27	4,8	3,7	4,3	3,3	2,7	2,3	13,6
28	7,5	14,3	16,1	7,6	6,1	3,1	23,0
29	4,8	13,1	14,7	3,2	3,3	1,0	7,0
30	1,3	4,2	1,2	1,0	—	—	—
38	1,6	2,1	2,1	1,8	1,0	—	—
39	14,3	12,5	7,8	12,5	14,5	6,6	37,0
40	3,9	13,6	19,2	8,8	2,6	1,2	8,6
41	4,8	10,0	11,5	5,0	4,3	1,6	6,2
42	4,7	8,8	3,6	5,0	4,1	2,2	9,0
43	4,6	16,3	14,6	4,2	3,4	1,5	4,1
44	8,4	12,1	11,8	8,2	6,3	1,0	2,5
45	1,2	4,3	3,3	2,1	1,0	—	1,2
50	6,3	7,5	5,0	4,3	2,1	1,8	12,3
51	7,6	11,3	14,5	8,3	9,8	5,4	24,6
52	2,1	7,5	6,1	5,0	5,7	4,3	27,6
53	1,0	2,2	3,6	1,2	1,1	3,1	18,6
54	—	—	—	—	—	—	4,9
55	—	—	1,2	6,7	—	1,5	6,1
61	—	—	1,0	—	—	—	3,7
62	3,9	1,6	3,6	—	—	—	9,9
63	9,5	11,3	9,2	8,3	6,8	3,9	18,6
64	8,7	6,8	2,8	5,0	4,1	2,2	7,4
65	7,9	—	4,4	7,5	6,8	8,1	14,8
66	6,3	—	1,4	2,1	—	1,6	4,5
75	1,2	1,0	3,9	—	4,2	1,2	4,5
76	7,9	2,3	4,7	3,0	3,7	1,8	6,2
77	12,7	15,0	20,9	20,8	10,6	3,9	9,9
78	4,8	2,1	5,0	1,6	8,7	2,4	8,6
79	—	—	1,4	—	1,4	1,2	4,5
89	7,9	11,3	4,8	13,3	4,3	3,3	5,8
90	3,2	—	1,5	5,0	2,7	3,1	5,3
91	4,8	—	1,0	—	2,3	9,3	13,9
101	—	7,3	3,3	—	2,7	1,0	2,0
102	4,8	8,8	6,2	6,7	6,4	1,8	2,5
103	9,5	12,5	15,0	12,5	7,5	1,5	2,0
104	4,8	1,6	5,1	5,0	2,3	1,2	2,5
105	—	—	2,1	—	—	—	—
116	—	—	2,1	—	—	1,6	2,9
117	—	—	1,0	—	—	6,6	11,1
118	—	—	—	—	—	7,5	16,0
128	—	—	3,3	—	2,7	1,6	2,5
129	—	—	2,2	5,0	3,7	—	3,3
130	79,4	25,0	34,5	36,7	29,7	5,9	3,2
131	31,7	16,3	27,8	42,3	42,4	1,5	1,2
132	4,8	—	5,8	6,7	4,0	—	2,6
145	—	—	—	—	—	4,2	5,3
146	—	—	—	—	—	8,2	50,0
147	—	—	—	—	—	17,9	36,7
148	—	—	—	—	—	1,6	5,3
158	3,9	15,0	21,2	—	2,4	—	—
159	100,0	100,0	100,0	100,0	100,0	—	2,5
160	12,1	12,3	13,0	12,6	12,2	—	3,3
161	1,0	1,0	1,4	1,2	1,4	—	—
174						2,8	11,1
175						100,0	100,0
176						15,8	16,5
177						1,6	2,0
W_M	24,2	21,3	23,2	26,4	28,6	36,0	15,8
$S_{1/2}$	3,0	8,0	5,0	4,0	3,5	7,3	13,0

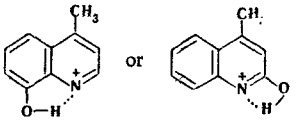
ties of the polyisotopic peak of the molecular ion to the total ion current (ΣI), and the selectivity values ($S_{1/2}$), which correspond to the minimum numbers of peaks the sum of the intensities of which amounts to half ΣI.

A comparison of the values of W_M for compounds (I-VII) shows that in the general case the introduction of a hydroxy group into the quinoline nucleus leads to a considerable reduction of the stability W_M as compared with quinoline (34.5) and with 2-, 4-, and 8-methyl-substituted quinolines, the values of W_M of which are 37.2, 47.1, and 30.3, respectively [6].

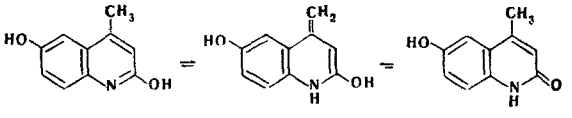
This fact is explained not only by an increase in the possible channels of decomposition as a result of the introduction of the hydroxy group into the quinoline nucleus, but also by a substantial disturbance of the aromaticity of the system because of the presence of the keto form in the excited molecular ion [7]. It may be considered that the observed differences in the values of W_M (Table 1) in the series of com-

pounds (I-VII) depends primarily on the ratio of the keto and enolic forms in the excited molecular ion which, in its turn, is determined by the position of the methyl substituent in the initial molecule [6, 8]. An increase in the proportion of the enolic form [9], i.e., a rise in the tendency to the formation of a "rigid" aromatic structure in compounds (I, IV, and V) leads to large values of W_M. And, conversely, the predominance of a nonconjugated system (the ketonic form) in compounds (II) and (III) naturally causes a fall in the value of W_M (Table 1).

Additional stabilization of the molecular ion can also take place through the possible formation of an intramolecular hydrogen bond in the isomeric compounds (I), (IV), and (V) containing the hydroxy group in positions 2 and 8 of the quinoline nucleus (W_M 24.2, 26.4, and 28.6, respectively). When the hydroxy group is in position 8, this bond is stronger, since an energetically more favorable five-membered ring is formed [10].



The marked difference in the values of W_M observed for the isomeric compounds (VI) and (VII) on the introduction of a second hydroxy group into the quinoline nucleus is difficult to explain. Obviously, the initial molecule in the excited state can exist in the form of the following structures [using compound (VI) as an example]:



A B C

It may be assumed that the considerable increase in W_M for compound (VI) in the series of compounds (I-VII) is connected with the predominant existence of the molecular ion in the form of the structure A or, rather, B, which is confirmed by the absence of the fragmentary ion $(M-H)^+$ in its mass spectrum [6]. Conversely, in compound (VII) the molecular ion exists exclusively in the keto form (structure C), which leads to a fall in the aromaticity of the system as a whole and, consequently, to a decrease in W_M.

The value of $S_{1/2}$ also depends on the mutual positions of the methyl substituent and the hydroxy group (Table 1). Thus, compounds (I, III, V, and VI), containing the methyl group in position 4 of the quinoline ring decompose with higher selectivities (lower values of $S_{1/2}$) than the corresponding 2-substituted analogs. The value of the selectivity depends mainly on the probability of the formation of the ion $(M-CO)^+$ or, in other words, on the ease of passage of the molecular ion into the corresponding keto form in the hydroxyquinolines studied [11]. Compounds having the hydroxy group in position 2 or 8 of the quinoline nucleus are distinguished by a greater intensity of the peak of the $(M-CO)^+$ ion and, consequently, have a lower selectivity (Table 1).

Since, according to quantum-chemical calculations [12], the greatest electron density in the hydroxyquinoline nucleus is concentrated on the oxygen atom, it must be expected that the initial stages of the decomposition of the molecular ions of the hydroxyquinolines will lead to the localization of the positive charge on the oxygen atom. The nature of the decomposition of compounds (I-VII) confirms this hypothesis. The loss of the neutral particle CO from the molecular ion under the action of electron impact permits the statement that in the excited state the decomposition of the systems studied takes place predominantly from the keto form of the molecular ion of the corresponding hydroxyquinoline.

The mobility of the hydrogen atom of the hydroxy group, which is connected with the ease of the tautomeric transitions in positions 2 and 4 of the quinoline nucleus, and also the possibility of the formation of an intramolecular hydrogen bond in position 8 of the ring facilitate the splitting off of the neutral particle CO from the molecular ion, and therefore the intensity of the peak of the ion $(M-CO)^+$ for compounds (I, IV, and V) is about 1.5-2 times higher than for the compounds (II and III) isomeric with them.

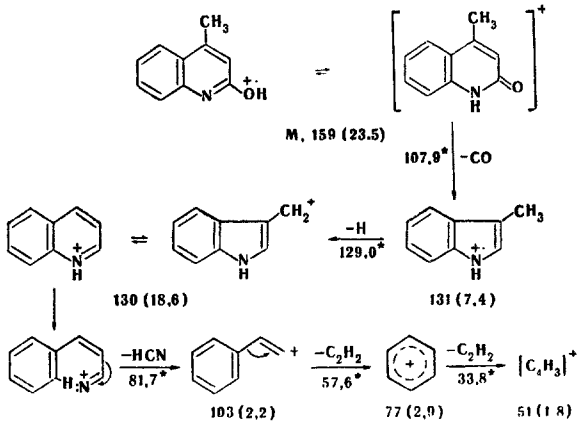
With a lowering of the energy of the ionizing electrons to 20 eV, the probability of low-energy processes connected with the splitting out of a CO particle from the molecular ion in compounds (I-VII) rises monotonically, as a rule.

TABLE 2. Scheme of the Identification of Methyl-Substituted Hydroxyquinoline Derivatives at an Energy of the Ionizing Electrons of 50 eV (intensities of the peaks of the characteristic ions in % of the total current)

Compound	Characteristic ions			
	M^+	$(M-1)^+$	$(M-28)^+$	$(M-29)^+$
I	23,5	—	7,4	18,6
II	19,4	2,9	3,2	4,8
III	23,9	5,0	6,6	8,2
IV	32,9	—	11,8	8,9
V	28,2	—	12,1	8,5
VI	32,5	—	5,8	2,7
VII	12,6	1,4	4,6	6,3

The decomposition of the isomeric compounds (I-V) is characterized in the general case by a sequence of successive processes: $M^+ \rightarrow (M-CO)^+ \rightarrow (M-CO-H)^+ \rightarrow [(M-CO-H)-HCN]^+$, the course of which is confirmed by a whole series of well-defined corresponding metastable peaks.

The splitting off of a CO particle from the molecular ion of compound (I) leads to the formation of a pseudomolecular ion with a mass of 131 having the structure of 3-methylindole. The decomposition of this structure takes place in accordance with a generally accepted hypothesis and is accompanied by the expansion of the pyrrole ring of the methylindole with the formation of a resonance-stabilized quinolinium ion [13]. The appearance in the spectrum of compound (I) of peaks of ions with masses 103, 77, and 51 confirms the hypothesis put forward. The decomposition of compound (I) is illustrated by the following scheme.†

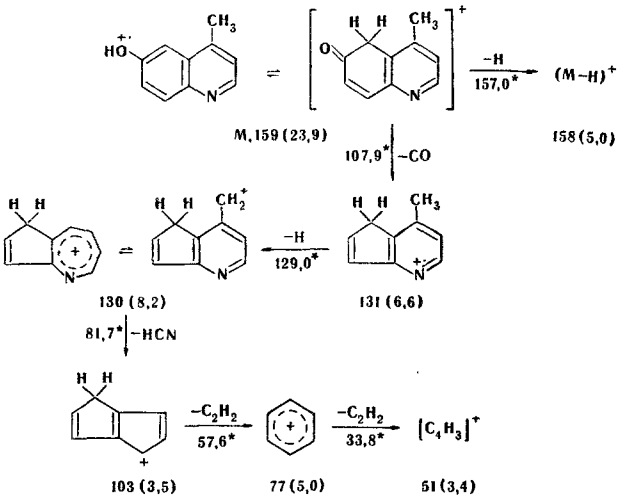


The marked increase in the intensity of the peak of the ion with mass 130 in compound (I) with a reduction in the energy of the ionizing electrons is caused by the formation in the decomposition process of an extremely stable structure – the quinolinium cation, which arises as the result of a low-energy rearrangement process.

In the decomposition of methyl and hydroxy substituents in different rings of the quinoline nucleus, the formation of such a cation is less likely (compounds II-V). The formation of a rearrangement ion with a mass of 130 in the case of compounds (I-V) and of a similar ion with mass 146 for compounds (VI and VII) is easily detected in a consideration and comparison of the values of the ratios of the intensities of the processes of $[(M-CO)-H]^+/(M-CO)^+$. For the series of compounds (II-V), this value of the ratio is close to unity over a wide range of energies. For compounds (I), (VI), and (VII) the ratio of the processes mentioned $[(M-CO)-H]^+/(M-CO)^+ \approx 3$ (at an energy of the ionizing electrons of 20 eV).

The dissociative ionization of compounds (II-V), each of which contains a hydroxy group in the benzene ring, takes place according to the following general scheme:

†Here and below, the figures under the formulas represent the mass numbers, and the figures in parentheses the intensities of the peaks of the corresponding ions in percentages of the total ionic current. Figures with an asterisk denote the apparent masses of the corresponding metastable transitions.



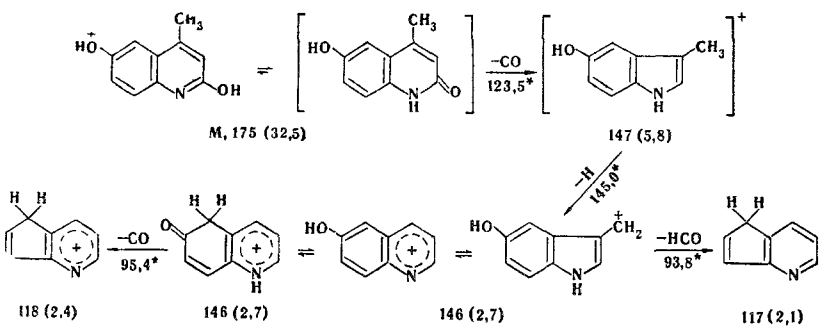
The presence or absence in the spectrum of one of compounds (I-VII) of the peak of the ion $(M-H)^+$ easily enables the position of the hydroxy group in the quinoline nucleus to be determined. Thus, for compounds (II, III, and VII) the intensity of the peak of the $(M-H)^+$ ion at an energy of the ionizing electrons of 50 eV is 2.9, 5.0, and 1.4% of the total ion current, respectively (with a lowering of the energy of the electrons to 20 eV, the intensity of this peak rises). In the case of compounds (I, IV, V, and VI), which have the hydroxy substituent in position 2 or 8 of the quinoline ring, the peak of the $(M-H)^+$ ion is absent.

This fact shows that the elimination of a hydrogen atom from a methyl substituent that is characteristic for aromatic compounds does not take place in the case under consideration. Thus, our hypothesis of the possibility of the existence of an intramolecular hydrogen bond in the excited molecule (Table 2) is indirectly proved.

The presence of two hydroxy groups in the quinoline nucleus (compounds VI and VII) complicates the unambiguous determination of the decomposition mechanism, although each process taking place under the action of electron impact is fixed by the corresponding metastable peak. Probably, the process of the detachment of a CO particle from the molecular ion is due to a hydroxy group present in position 2 or 4 of the quinoline nucleus, since in this case the production of the oxo form becomes preferential. The elimination of CO takes place with the formation of a pseudomolecular ion having the structure of the corresponding hydroxyskatole. The elimination of hydrogen from this ion (mass 147) is responsible for the appearance in the spectrum of the peak of a rearranged ion with the 6-hydroxyquinolinium structure, the stability of which, as mentioned above, rises considerably with a fall in the energy of the ionizing electrons.

The dissociative ionization of various hydroxyskatoles has been studied in detail by high-resolution mass spectrometry [14], and therefore the interpretation of the peaks of the ions with masses 146, 118, 117, and 91 (Table 2) causes no difficulty. The decomposition of the ion with mass 146 takes place in two directions. The first is the elimination of a CHO group from this ion, leading to the appearance in the spectrum of a pseudomolecular ion with the structure of pyridine fused with cyclopentadiene, the decomposition of which is responsible for a group of peaks with masses 90, 89, 63, and 50. With a reduction in the energy of the ionizing electrons, this process ceases completely.

The other direction of the decomposition of the ion with mass 146 is the loss of a CO particle, which causes the appearance in the spectrum of an ion with a mass of 118; the intensity of the peak of this ion also rises with a fall in the energy of the ionizing electrons. The general scheme of the decomposition of compounds (VI and VII) is as follows:



The correlation that we have performed between the molecular structures and the main directions of decomposition of the methyl-substituted hydroxyquinolines (I-VII) permits the isolation of the characteristic peaks of the fragmentary ions, through which it is possible with a considerable degree of probability to identify samples obtained under various reaction conditions (Table 2).

LITERATURE CITED

1. A. K. Mallams and S. S. Israelstam, J. Org. Chem., 29, 3548 (1964).
2. K. Desai and C. M. Desai, Indian J. Chem., 5, 170 (1967).
3. O. Červinka and O. Bělovsky, Coll., 26, 3181 (1961).
4. M. Zuckner and C. Ritter, Tetrah. Lett., 741 (1965).
5. R. L. Stevenson, M. E. Wacks, and W. M. Scott, Org. Mass. Spectrum, 2, 261 (1969).
6. R. A. Khmel'nitskii and N. A. Klyuev, Dokl. TSKhA, 162, 393 (1971).
7. G. Schwarzenbach and E. Felder, Helv. Chim. Acta, 27, 1705 (1944).
8. S. F. Mason, J. Chem. Soc., 674 (1958).
9. M. I. Kabachnik, Zh. Vses. Khim. Obshchestva im. D. I. Mendeleeva, 7, No. 3, 263 (1962).
10. A. Albert and J. N. Phillips, J. Chem. Soc., 1294 (1956).
11. D. M. Clugston and D. B. Maclean, Can. J. Chem., 44, 781 (1966).
12. R. E. Burton and W. J. Davis, J. Chem. Soc., 1766 (1964).
13. J. Beynon, Mass Spectrometry and Its Application to Organic Chemistry, Elsevier, Amsterdam (1970).
14. R. Marchelli, W. D. Jamieson, S. H. Safe, O. Hutzinger, and R. A. Heacock, Can. J. Chem., 49, 1296 (1971).