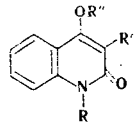
FRAGMENTATION OF SUBSTITUTED 4-HYDROXY-2-QUINOLONES UNDER THE INFLUENCE OF ELECTRON IMPACT

V. G. Zaikan, Z. S. Ziyavidinova,
and N. S. Vul'fson

UDC 547.831 : 543.51

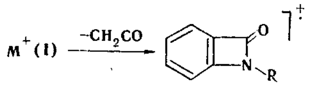
The general principles of the mass-spectral disintegration of 4-hydroxy-2-quinoline derivatives containing various substituents attached to the nitrogen in the 3 position were established. It was found that the disintegration of 4-hydroxy-2-quinolone and its N-substituted derivatives proceeds primarily through cleavage of the heterocyclic ring, while the principal pathways of the disintegration of 3-acyl derivatives are associated with fragmentation of the acyl group.

We have previously reported [1] a mass-spectrometric investigation of a number of substituted 6-methyl-4-hydroxy-2-pyridones. The fragmentation of substituted 4-hydroxy-2-quinolones and of other substituted 2-quinolones under the influence of electron impact has been extremely inadequately studied, though they are similar to the latter with respect to their structures and chemical properties. Only the mass spectra of 2-quinolone itself and its N-, 3-, and 4-methyl derivatives have been examined in detail [2]. However, a study of the pathways of the mass-spectral disintegration of substituted 4-hydroxy-2-quinolones, in addition to its independent interest, is also of importance in that a number of alkaloids are 4-hydroxy-2-quinolone derivatives (for example, see [3-5], in which data from the mass spectra are presented). The present paper is devoted to a mass-spectrometric investigation of 4-hydroxy-2-quinolone (I), its N-methyl (II) and N-phenyl (III) analogs, 4-acetoxy-2-quinolone (IV), its N-methyl analog (V), 3-acetyl-4-hydroxy-2-quinolone (VI), its N-methyl (VII) and N-phenyl (VIII) analogs, and 3-propionyl- (IX) and 3-n-hexanoyl-4-hydroxy-2-quinolone (X). The data from the mass spectra of these compounds are presented in Table 1.



I-X

I R=R′=R″=H; II R=CH_3, R′=R″=H; III R=C_6H_5, R′=R″=H; IV R=R′=H, R″=$COCH_3$; V R=CH_3, R′=H, R″=$COCH_3$; VI R=R″=H, R′=$COCH_3$; VII R=CH_3, R′=$COCH_3$, R″=H; VIII R=C_6H_5, R′=$COCH_3$, R″=H; IX R=R″=H, R′=COC_2H_5; X R=R″=H, R′=COC_5H_{11}-*n*



a *m/e* 119 (R=H)
m/e 133 (R=CH_3)
m/e 195 (R=C_6H_5)

The mass spectra of hydroxyquinolones I-III are characterized by intense molecular ion peaks that predominate in the spectra. As in the case of the corresponding 6-methyl-4-hydroxy-2-pyridone derivatives [1], a low-intensity doublet of M − 28 and M − 29 peaks (ejection of CO and CHO) is observed in the spectra of I and III, but in contrast to the former, another appreciable M − 17 peak appears in the spectra of I-III.

A. V. Topchiev Institute of Petrochemical Synthesis, Academy of Sciences of the USSR. M. M. Shemyakin Institute of the Chemistry of Natural Compounds, Academy of Sciences of the USSR, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1516-1521, November, 1974. Original article submitted February 22, 1974.

TABLE 1. Mass Spectra of I-X (intensities in percent of $\Sigma_{50}^{M^+}$)

m/e	I	II	III	IV	V	VI	VII	VIII	IX	X
75		1,0	0,7	0,6	1,2	0,7		1,3		
76	1,1	2,0	1,1	1,3	2,0	1,5	1,8	2,7		0,8
77	2,7	5,9	4,3	3,1	6,3	4,0	5,2	10,0	3,5	3,2
78	1,1	3,3	0,7	0,6	3,2	0,7	2,0	1,3		0,4
89		1,0	0,9	0,6	0,9	0,7	1,3	1,1	0,7	0,6
90	1,1	1,5	0,4	0,4	0,9	0,9	1,0	0,6	1,1	0,8
91	1,9	2,0	0,4	0,6	2,2	0,9	1,8	0,6	0,6	0,6
92	8,0	1,5	1,9	3,2	1,1	4,0		2,7	3,8	2,4
93	1,1		0,3	0,4	0,2	0,5		0,6	0,6	0,4
95	0,7		0,3							
97	0,7		0,3							
102			0,4			0,4	0,6	0,9		
103		1,0		0,4	0,7	0,5	1,2	0,8		0,4
104	1,9	6,5	0,4	1,8	5,3	1,1	2,4	0,8	1,4	1,0
105	2,7	7,4	0,3	2,3	6,0	0,5	2,0	0,8	0,8	0,6
106					1,0		1,1			
115			0,6				0,3	0,8	0,6	0,4
116			0,4	0,4					0,6	0,4
117					0,8					
118		1,0			1,2		0,6			
119	15,8	1,0		10,5	1,0	2,0	0,5		1,7	1,2
120	8,0			4,8	0,2	6,2	0,1	0,5	7,0	3,9
121	0,7			0,4		0,5			0,6	0,4
130		1,0						0,6		0,4
131								0,9		
132	1,5	6,9		2,3	5,1	0,7	2,0	0,3	0,7	0,6
133	1,9	3,4		2,9	2,1	0,6	1,3		0,8	0,4
134		1,9		0,3	1,2		5,8			
135							0,4			
138			1,3							
139			1,0							
143				0,4						
144						0,5			0,8	0,8
145									0,3	
146		17,8			8,0	0,9	2,0		1,1	1,0
147		2,0			1,9					
151			0,4					0,6		
152			0,9					1,4		
153			0,4					0,6		
154								0,2		
158		3,0								
159					0,3					
160				0,6		0,4			0,6	0,2
161	23,0			34,4		1,5			9,3	6,2
162	2,7			3,4					1,1	1,0
163				0,3					0,2	
164								0,4		
165			0,6					0,6		
166			2,9					2,7		0,4
167			5,2					4,1		
168			1,2					1,5		
169								0,4		
170							0,4		1,1	0,8
171							0,3			
172							0,2			
174							0,7			0,4
175		22,8			7,3		0,9			0,7
176		3,0			1,6		0,2			
177								0,3		
178			0,5					0,6		
179			0,5					0,6		
180			1,9					0,8		
181			0,6					0,6		
187							0,2			
188						25,6	0,4	0,6	26,1	13,8
189						3,2	0,3		3,5	2,2
190						0,4			0,6	0.4
194			0,6					0,4		
195			15,5					3,6		
196			3,1					2,0		
197			0,4					0,2		
202							21,0			0,6
203				11,2		24,5	3,1			9,0
204				1,6		2,8	0,4			1,2
208			0,7							
209			0,4							
215										0,8
216							0,6		0,8	19,6
217					2,5		16,2		18,9	3,1
218					0,4		2,6		2,9	0,4
219							0,3		0,5	
220			0,3							
230										1,6

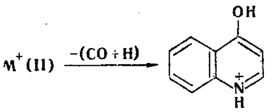
TABLE 1 (continued)

m/e	I	II	III	IV	V	VI	VII	VIII	IX	X
231										0,6
235			1,0					0,5		
236			14,7					0,4		
237			18,0							
238			3,2							
239			0,4							
258										0,4
259										6,4
260										1,1
261										0,3
264								4,7		
265								1,0		
266								0,1		
278								1,8		
279								6,2		
280								1,2		

The peak of the M—42 ion (a), the formation of which is evidently associated with the elimination of ketene from the molecular ion, is the second most intense peak in the mass spectra of I and III and is appreciable in the spectrum of II.

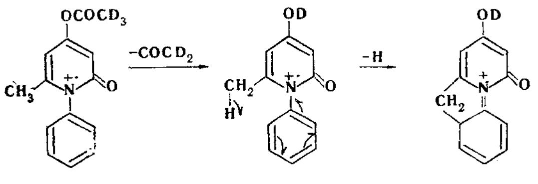
Disintegration of the molecular ions with ejection of a ketene radical ($\dot{C}H{=}C{=}O$) proceeds only in the case of hydroxyquinolone I (the peak with m/e 120). In principle, this type of fragmentation, together with the formation of ion *a*, can also be observed in the spectrum of II. However, both of these peaks are of lower intensity than the peak of the M—43 ion (m/e 132).

The mass spectrum of II differs sharply from the spectra of I and III with respect to a considerable increase in the intensity of the M—29 ion peak. In our opinion, this may be associated with the fact that the ejection of Co+H from the molecular ion of II involves the inclusion of a $-CH_3$ group in the ring and the formation of a stable hydroxyquinolinium ion (b):



b m/e 146

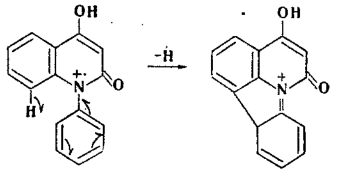
A peculiarity of the mass spectrum of hydroxyquinoline III as compared with the spectra of I and II is the high intensity of the M—1 peak (65% of the magnitude of the M^+ peak). A similar effect of an N-phenyl group was also observed in the case of 6-methyl-4-hydroxy-2-pyridones [1]. Unfortunately, the low percentage of deuterium incorporation in the 4-OH group during deuterium exchange with C_2H_5OD directly in the mass spectrometer for both III and for its analog in the α-pyridone series does not answer the question of the nature of the eliminated hydrogen atom. It has been assumed for 6-methyl-4-hydroxy-2-pyridones [1] that in the formation of the $(M+1)^+$ ion the hydrogen atom may depart both from the 4-OH group and from the $6\text{-}CH_3$ group as a consequence of the ortho effect. In a mass-spectrometric study of XI synthesized by acetylation of 1-phenyl-4-hydroxy-2-pyridone with trideuteroacetic anhydride in pyridine it was found that one of the principal peaks, M − 43, in the spectrum of its unlabeled analog is due to two-step elimination of a $COCH_3$ group. This conclusion was drawn on the basis of the fact that the peak of a metastable ion for the $M^+ \rightarrow M{-}42$ transition ($M^* = 166.2$) is observed in the spectrum of 1-phenyl-4-acetoxy-6-methyl-2-pyridone, whereas on passing to 4-trideuteroacetoxy analog XI the most intense peaks with m/e 200 (M—43) and 201 (M—42) of the spectrum of the unlabeled analog are shifted by 1 amu to m/e 201 and 202, respectively. This can mean only that the ion formed after the ejection of CD_2CO from the molecular ion of XI subsequently loses a hydrogen atom rather than a D atom, most likely from the $6\text{-}CH_3$ group:



M+ (XI)

c

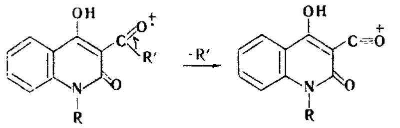
Ion c, the structure of which most likely corresponds to the molecular ion of 1-phenyl-4-hydroxy-6-methyl-2-pyridone, is formed as a result of elimination of ketene from the 4-acetoxy group, and it can therefore be assumed that the hydrogen atom from the M^+ ion of the latter also departs from the 6-CH_3 group. Unfortunately, we were unable to synthesize the 1-phenyl-4-acetoxy and 1-phenyl-4-trideuteroacetoxy analogs in the 2-quinolone series. However, in analogy with 2-pyridones, the following mechanism for the formation of the $(M-1)^+$ ion (b) can be assumed in the case of III (although one also cannot deny the possibility of ejection of a hydrogen atom from the 4-OH group):



M^+ (III)   d $(M-1)^+$

The first act in the disintegration of the molecular ions of 4-acetoxy-2-quinolones IV and V entails the elimination of ketene from the 4-$COCH_3$ group. The structures of the ions formed in this case are evidently analogous to those of the molecular ions of I and II, respectively (inasmuch as a ketene molecule is most likely eliminated from acetates of aromatic and vinyl alcohols through a four-membered transition state), and the mass spectra of IV and V below the M—42 peaks (from m/e 161 and 175, respectively) are completely identical to the spectra of I and II.

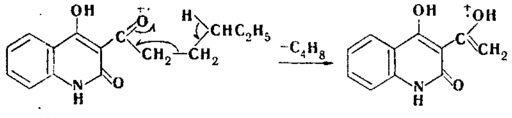
The molecular ion peaks in the spectra of hydroxyquinolones VI-X are among the most intense peaks. The most characteristic disintegration of the M^+ ion entails the ejection of an alkyl radical from the 3-acyl group and the formation of ions e. The peaks of these ions predominate in the spectra of VI, VII, and IX.



M^+ (VI-X)   e m/e 188 (R=H)
m/e 202 ($R=CH_3$)
m/e 264 ($R=C_6H_5$)

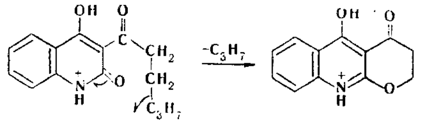
The acyl residue in the 3 position can be eliminated from the molecular ion in its entirety or in the form of ketene, but these processes are usually of low energic advantage, and only low-intensity $(M-43)^+$ and $(M-42)^+$ ion peaks are therefore observed in the spectra of VI-VIII. The acyl substituents are ejected primarily in the form of substituted ketenes ($CH_3CH=C=O$ or n-$C_4H_9CH=C=O$) only in the case of IX and X, and the corresponding peaks are quite intense.

Two special pathways of disintegration due to the presence of a long acyl chain are characteristic for 3-hexanoyl derivative X. One pathway is related to the McLafferty rearrangement through the carbonyl group of the acyl residue (ion f):



M^+ (X)   f m/e 203

The other pathway is due to the ejection of a propyl radical from the molecular ion, possibly as a result of the following process:



M^+ (X)   g m/e 216

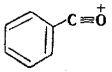
Ion peak g is the most intense peak in the mass spectrum of X. In addition, the (M—29) ion peak is of low intensity, apparently due to loss of a C_2H_5 radical from the 3-hexanoyl chain.

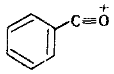
In the case of VI-X, the disintegration of the heterocyclic ring occurs to a lesser extent. A peak of medium intensity with m/e 120 in the spectra of hydroxyquinolones VI, IX, and X, which is shifted to m/e 134 and 195 on passing from VII and VIII, is apparently due to ejection of $C_{(3)}$ and $C_{(4)}$ atoms together with the substituents in the form of substituted ketene radicals. The presence of metastable ion peak $m^* = 76.5$ (calculated value 76.5) in the mass spectrum of VI shows that the ion with m/e 120 in this case is formed directly from ion e. However, in the disintegration of VII the ion with m/e 134 can be formed both from ion e ($m^* = 89$, calculated value 88.9) and from the molecular ion ($m^* = 82.4$, calculated value 82.3).

The low-molecular-weight regions of the mass spectra of I-X are characterized by a number of peaks common to all the spectra. Appreciable peaks with m/e 77 ($C_6H_5^+$) are present in all of the spectra. Peaks with m/e 92, which are evidently due to ions of the h type, are peculiar to the spectra of nitrogen-unsubstituted 2-quinolones I, IV, VI, IX, and X and N-phenyl-substituted III and VIII. A rather intense doublet of peaks with m/e 104 and 105 is present in all of the spectra, regardless of the nature of the substituent attached to the nitrogen atom. It may be assumed that, in the general case, they correspond to ions of the i and j composition. It should be noted that the spectrum of IV contains metastable ion peaks $m^* = 127.9$ (calculated value 127.7), 110 (calculated value 109.9), and 93 (calculated value 82.9), which correspond to successive ejection from the molecular ion of 42 amu and (twice) 28 amu [M^+ (m/e 203) → m/e 161 → m/e 133 → m/e 105].

The spectra of N-phenyl derivatives III and VIII contain appreciable peaks with m/e 167. The corresponding ions most likely include both benzene rings and the nitrogen atom, although their structures were not established.


h m/e 92


i m/e 104


j m/e 105

EXPERIMENTAL

The mass spectra were recorded with an MKh-1303 spectrometer with a system for direct introduction of the samples into the ion source at an ionization energy of 70 eV and sample-evaporation temperatures of 130-170°.

LITERATURE CITED

1. N. S. Vul'fson (Wulfson), V. G. Zaikin, Z. S. Ziyavidinova, V. M. Burikov, and S. K. Mukerjee, Org. Mass Spectrom., 5, 743 (1971).
2. J. Moller and O. Buchardt, Acta Chem. Scand., 21, 1668 (1969).
3. S. M. Sharafutdinova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 394 (1969).
4. Z. Sh. Faizutdinova, I. A. Bessonova, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 239 (1970).
5. Ya. V. Rashkes, Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 577 (1970).