MASS-SPECTRAL BEHAVIOR OF NITROHYDROXY- AND NITROMETHOXYMETHYLINDOLES

P. B. Terent'ev, R. A. Khmel'nitskii,
O. A. Solov'ev, L. G. Yudin,
A. N. Kost, and E. Ya. Zinchenko

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The principal pathways in the fragmentation of isomeric nitrohydroxy- and nitromethoxymethylindoles containing functional groups in the benzene ring were established by means of high-resolution mass spectrometry and deuterium labeling. The fragmentation of these compounds proceeds via different pathways as a function of the orientation of the functional substituents and the pyrrole nitrogen atom and differs from the fragmentation of other nitroarenes. The data obtained make it possible to reliably identify isomeric substances.

We have previously shown [1] that under the influence of electron impact nitromethylindoles undergo nitro–nitrite rearrangement, the probability of which depends on the position of the nitro group in the indole ring. It has also been established that the position of the functional groups relative to the pyrrole ring also affects the character of the dissociative ionization of indoles containing other functional groups such as hydroxy [2], methoxy [1], and carboxy and carbalkoxy [2, 3].

In order to establish the character pathways in the fragmentation of functional derivatives of nitroindoles and ascertain the effect of the orientation of the functional groups and the pyrrole ring on the character of the fragmentation of these compounds we studied the mass spectra of 4-nitro-5-hydroxy-1,2- (I), 6-nitro-5-hydroxy-1,2- (II), 4-nitro-5-methoxy-1,2- (III), 6-nitro-5-methoxy-1,2- (IV), 6-nitro-5-methoxy-2,3- (V), 6-nitro-5-trideuteromethoxy-2,3- (VI), 5-nitro-6-methoxy-2,3- (VII), 7-nitro-6-methoxy-2,3- (VIII), 6-nitro-7-methoxy-2,3-dimethylindole (IX), and 6-nitro-7-methoxy-1,2,3-trimethylindole (X). The mass spectra obtained are presented in Table 1.

It is apparent from an examination of the data presented in Table 2 that the introduction of a hydroxy or methoxy group in the methylnitroindole molecules as a rule appreciably stabilized the molecular ion. The W_M values of the isomeric nitro-2,3-dimethylindoles range from 5.3 to 10.7 [1].

A comparison of the stabilities with respect to electron impact of nitromethylindoles and methoxymethylindoles shows that nitromethoxyindoles are more stable by a factor of $\sim$1.5-2 than nitroindoles and are less stable by the same factor than methoxyindoles.

As in the nitromethylindole series, "methylindole" fragmentation processes, i.e., the loss of a hydrogen atom or a methyl group with subsequent elimination of HCN [4], are not characteristic for the molecular ions of I-X. All of the major primary processes in the dissociative ionization of the investigated compounds proceed in a manner similar to the fragmentation of nitro- and methoxy(hydroxy)arenes. However, in addition to the fragmentation pathways typical for o-nitroanisole (o-nitrophenol), in some cases one also observes the formation of specific ions that characterize a strictly determined orientation of the substituents and the pyrrole ring. This is particularly noticeable in the case of compounds in which the functional groups are in the ortho position relative to the pyrrole nitrogen atom (VIII-X).

4- and 6-Nitro-5-hydroxy-1,2-dimethylindoles

An analysis of the data in Table 2 and Scheme 1 makes it possible to conclude that although most of the observed processes (A, B, and C) are also characteristic for o-nitrophenol [5], the fraction of rearranged nitrite ions in the mass spectra of I and II is

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TABLE 1. Mass Spectra of I-V and VII-X

Compound*	m/e values (intensities of the ion peaks in percent relative to the maximum peak)
I	207 (10,0), 206 (100), 176 (9,5), 148 (9,5), 145 (18,0), 133 (5,2), 132 (11,5), 131 (16,2), 130 (22,0), 129 (6,3), 117 (7,2), 116 (5,4), 103 (5,8), 95 (7,0), 91 (7,1), 89 (10,5), 77 (13,3), 73 (15,2), 65 (6,4), 63 (6,5), 45 (20,0).
II	207 (10,0), 206 (100), 176 (11,0), 173 (5,0), 161 (7,6), 148 (12,0), 145 (43,0), 132 (37,0), 131 (37,2), 130 (26,0), 117 (14,0), 116 (11,6), 103 (8,8), 95 (5,0), 91 (11,0), 90 (11,5), 89 (19,0), 78 (9,4), 77 (18,4), 66 (6,0), 65 (13,4), 63 (13,4), 51 (7,8), 45 (10,5).
III	221 (11,5), 220 (100), 173 (33,0), 162 (6,2), 147 (52,3), 146 (13,7), 145 (15,4), 144 (68,0), 143 (22,0), 142 (11,0), 132 (8,3), 131 (20,1), 130 (17,4), 129 (7,3), 119 (20,1), 117 (6,8), 116 (11,9), 115 (19,4), 103 (11,0), 91 (12,8), 89 (14,8), 78 (13,7), 77 (18,4), 63 (13,8).
IV	221 (11,5), 220 (100), 190 (7,3), 173 (27,0), 146 (8,2), 145 (9,0), 144 (68,0), 143 (21,2), 142 (11,0), 132 (11,9), 131 (25,0), 130 (12,6), 117 (6,2), 116 (11,2), 115 (19,5), 103 (8,2), 91 (12,3), 89 (11,2), 77 (12,5), 63 (95,0)
V	221 (11,3), 220 (100), 173 (18,0), 147 (17,5), 145 (5,6), 144 (50,0), 143 (19,2), 131 (12,5), 130 (7,1), 115 (5,0), 77 (8,4).
VII	221 (11,7), 220 (100), 205 (33,5), 159 (8,8), 147 (14,8), 146 (8,8), 144 (48,7), 143 (21,8), 131 (34,6), 130 (8,2), 115 (7,1), 103 (5,0), 77 (9,9).
VIII	221 (11,6), 220 (100), 219 (12,1), 205 (48,0), 174 (19,6), 159 (46,9), 144 (6,9), 131 (19,4), 130 (8,6), 103 (6,6), 89 (5,9), 77 (8,7), 63 (6,3).
IX	221 (6,2), 220 (62,0), 204 (7,5), 203 (72,0), 187 (6,6), 175 (11,5), 174 (14,7), 173 (100), 160 (7,1), 159 (14,7), 158 (7,9), 131 (9,2), 130 (7,8), 103 (6,5), 78 (11,0), 77 (11,0), 63 (5,5), 45 (17,5).
X	235 (10,6), 234 (86,4), 218 (12,0), 217 (97,0), 203 (6,2), 189 (10,5), 188 (20,0), 187 (100), 174 (10,5), 173 (11,8), 172 (7,8), 158 (5,0), 45 (16,0).

*Ions with peak intensities $\geqslant 5\%$ are presented.

higher by a factor of three than in the mass spectrum of o-nitrophenol. This is probably explained by the fact that the nitro group in both compounds is located in a quasi-meta position with respect to the nitrogen atom of the pyrrole ring, in which the electron density should be somewhat reduced [6]. We have previously shown that a decrease in the electron density on the carbon atom bonded to the nitro group increases the probability of the indicated rearrangements [1].

It should also be noted that the fragmentation of o-nitrophenol via pathway A is not very significant, whereas the ion peak with mass 145 has considerable intensity (2.3 and 5.5, respectively*) in the mass spectra of I and II; this is also associated with the presence of an annelated pyrrole ring, which evidently promoted stabilization of the rearranged intermediate states. Finally, owing to the effect of the pyrrole ring, profound rearrange-

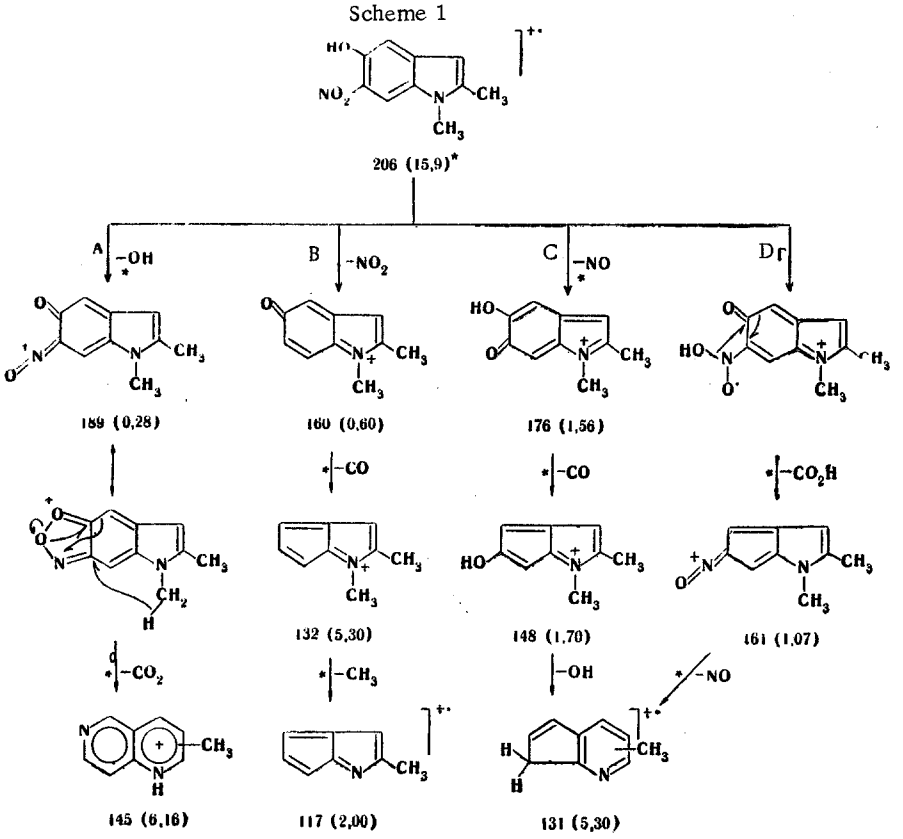
*Here and subsequently, the intensities of the ion peaks in percent relative to the total ion current are presented.

TABLE 2. Intensities* of the Peaks of Some Characteristic Ions in the Mass Spectra of I-X

Compound	W_M	$[M-30]^+$ (NO or CH_2O)	$[M-NO_2]^+$	$[M-OH]^+$	$[M-CH_3]$	$[M-H]^+$	$[M-CH_2O-NO_2]^+$	$[M-CH_2O-OH]^+$	$[M-NO-CO]^+$	$[M-NO-CO-CH_3]$	$[M-CH_2O-OH-NO]^+$
I	15,4	1,20	0,61	0,35	—	0,20	—	—	1,20	0,65	—
II	15,9	1,56	0,60	0,28	—	0,40	—	—	1,70	0,93	—
III	15,7	0,67	—	—	0,23	0,26	9,80	4,70	0,89	7,50	3,10
IV	18,9	1,26	—	—	0,82	—	11,70	4,65	0,63	0,74	3,65
V	35,4	0,87	—	—	0,80	0,93	16,20	5,80	0,33	5,60	6,20
VII	26,2	—	0,47	—	7,80	0,58	11,30	0,49	—	3,44	5,05
VIII	31,1	0,28	5,46	—	13,3	3,67	1,93	—	—	0,28	0,33
IX	13,2	0,31	0,52	14,80	0,24	0,39	0,45	19,50	—	0,49	0,55
X	17,6	0,49	3,62	17,70	0,24	—	0,91	18,20	—	0,36	0,29

*In percent relative to the total ion current (Σ_{39}).

Scheme 1



ment of the molecule via pathway D, which is accompanied by elimination of a COOH group and subsequent loss by the ion with mass 161 of an HCNH fragment, becomes possible. A change in the position of the nitro group relative to the hydroxy group does not have a substantial effect on the overall character of the fragmentation.

Isomeric Methoxynitromethylindoles

An analysis of the mass spectra of III-V and VII leads to the conclusion that "methylindole" fragmentation also is not characteristic for them and that processes with the participation of the nitro and methoxy groups primarily take place. An examination of the metastable ions, the high-resolution mass spectra, and the mass spectrum of deutero analog VI provides evidence that the elimination of a methyl group is realized exclusively from the methoxy group.

The pathway of dissociative ionization of III-VII depends to a considerable extent on the orientation of the functional groups and the pyrrole ring. Large W_M values (from 19 to 35) are characteristic for the entire group of these compounds, which contain methoxy and nitro groups in the 4, 5, or 6 position. The successive processes involving the loss of CH_2O and NO_2 (ion with mass 144), CH_2O and OH (173), or CH_2O, OH, and NO (143, Table 2) particles proceed intensively. These three fragmentation pathways are also typical for the mass-spectral fragmentation of o-nitroanisole [7, 8].

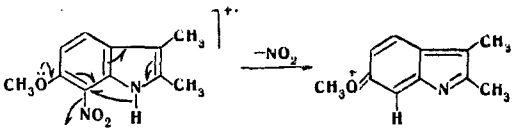
However, appreciable differences in the intensities of the peaks of the characteristic ions are observed in this series (Scheme 2, Table 2). Thus the relative intensity of the $[M - CH_3]^+$ ion peak increases sharply for the mass spectrum of VII, which contains a methoxy group in the quasi-meta position relative to the pyrrole nitrogen atom. On the other hand, the ion peak with mass 173, which is formed by elimination of CH_2O and OH groups from the molecular ion, has a relative intensity that is lower by a factor of 10 than the relative intensities of the molecular ions of III-V.

*Here and subsequently, the m/e values are given (the peak intensities in percent relative to the total ion current are given in parentheses).

In the case of isomers III and IV, which are formed by the nitration of 5-methoxy-1,2-dimethylindole, the successive loss of NO, CO, and CH_3 by the 4-nitro compound is a more energetic process (by a factor of 10) than in the fragmentation of the 6-nitro isomer.

A pronounced difference is also observed in the processes involving the fragmentation of the isomeric nitro derivatives of 6-methoxy-2,3-dimethylindole (VII and VIII), since the molecular ion of VIII eliminates a nitro group energetically; this is uncharacteristic for the mass spectrum of VII. The subsequent fragmentation of this ion proceeds to only a slight extent, and the relative intensity of the $[M - NO_2 - CH_2O]^+$ ion peak with mass 144 is low. It may be assumed that the nitro group in VIII is removed from the plane of conjugation with the benzene ring under the influence of two ortho substituents ($-OCH_3$ and NH); this leads, on the one hand, to overall stabilization of the molecular ion and, on the other, to easy removal of the nitro group, possibly with simultaneous "push–pull" transfer of hydrogen and stabilization of the positive charge on the oxygen atom:

Scheme 2

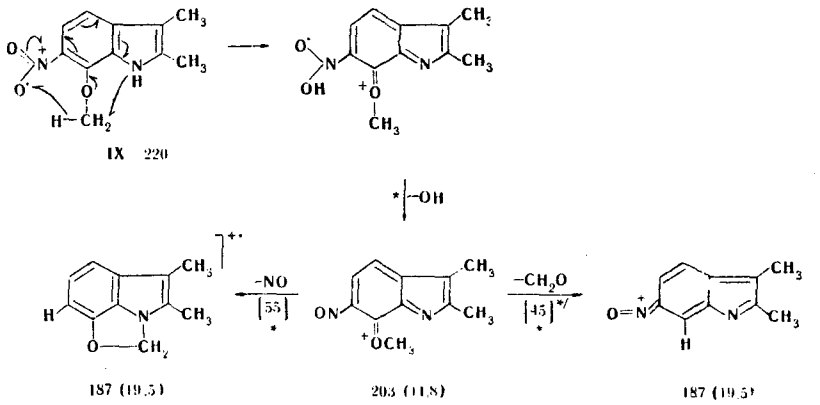


VIII 220 174

The increased probability of the loss of the nitro group in VIII leads to a sharp decrease in the intensity of all of the remaining fragmentation processes with the participation of the nitrogen atom of the nitro group (ions with masses 147, 144, and 143). Because of the same steric hindrance, the probability of processes involving the loss of a methyl group with subsequent elimination of the nitro group (ions with mass 205 and 159) increases markedly.

Compound IX, which has the opposite (as compared with VIII) orientation of substituents, has a molecular ion with low stability; this molecular ion, on the one hand, loses a methoxy group (this was not observed at all for the other isomers) and, on the other, forms an $[M - OH]^+$ ion with mass 203 with high probability. The peak of this ion is the maximum peak in the mass spectrum of IX. The loss of a hydroxyl group has not been previously observed in the mass spectra of o-nitroanisole [7, 8], and we therefore assume that the processes indicated above also proceed via "push–pull" transfer of a hydrogen atom in accordance with Scheme 3. The $[M - OH]^+$ ions subsequently eliminate NO and CH_2O particles with almost equal probabilities:

Scheme 3



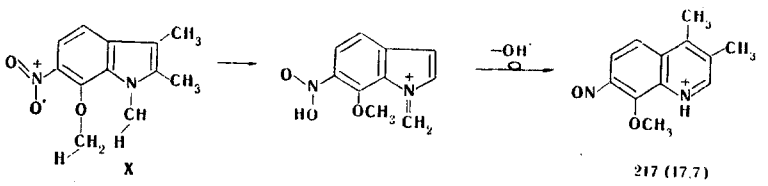
IX 220

187 (19.5) 203 (11.8) 187 (19.5)

The N-methyl homolog of IX (X) behaves similarly under electron impact, and this makes it possible to assume a similar mechanism for the formation of $[M - OH]^+$ ions with the participation of the hydrogen atom of the N-methyl group:

*The fraction of ions (in percent) of a given elementary composition in the component ion is presented in brackets.

Scheme 4



Thus an examination of the mass-spectral behavior of nitromethoxyindoles shows that, in contrast to o-substituted nitroarenes, the fragmentation of o-substituted nitroindoles is realized via specific pathways. The fragmentation pathways depend on the orientation of the nitro group and the other functional group with respect to the pyrrole nitrogen atom.

The positional nonidentical character of the substituting groups in the excited molecular ion makes it possible to reliably use the mass spectrometric method both for the identification of all of the examined isomeric pairs and, in a number of cases, for the determination of the structures of the compounds obtained in the nitration of indole derivatives [9].

EXPERIMENTAL

The mass spectra of I-X were obtained with a modified MKh-1303 spectrometer with introduction of the samples directly into the ion source at an ionization energy of 50 V. The high-resolution mass spectra were recorded with a JEOL JMS-01-SG-2 spectrometer at an ionization energy of 75 V. The synthesis of I-V and VII-X was described in [10].

6-Nitro-5-trideuteromethoxy-2,3-dimethylindole (VI). This compound was obtained by treatment of a solution of II in ethanol with trideuteromethyl iodide in the presence of sodium ethoxide.

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