MASS-SPECTROMETRIC INVESTIGATION OF 3-ACYLINDOLE OXIMES

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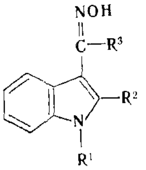
Fragmentation pathways that are due to fragmentation of the oximine grouping and are typical for all of the oximes, and lead to $[M-OH]^+$, $[M-NHOH]^+$, and $[M-C(R^3)-NOH]^+$ ions are characteristic for the mass spectra of 3-acylindole oximes. In addition, the presence of a nucleophilic indole ring leads to a number of specific rearrangement processes, particularly to the Beckmann rearrangement.

We have previously synthesized 3-acylindole oximes and have established the fine peculiarities of their structures by means of various physicochemical methods [1].

It is known that processes involving the dissociative ionization of organic compounds that take place in the gas phase frequently model and mimic the chemical transformations of these compounds in solutions. In this connection, we became interested in a study of the possibility of the occurrence in the gas phase of the Beckmann rearrangement of the molecular ions of oximes. The literature data on this question are rather contradictory [2-4]. The existence of the Beckmann rearrangement has been proven in a number of cases [5], whereas in other cases it does not take place or occurs prior to ionization as a thermal process [6, 7]. Since the 3 position in the indole ring has increased nucleophilicity, in the case of 3-acylindole oximes one might have expected the occurrence of the Beckmann rearrangement in the gas phase under the influence of electron impact.

In a study of the mass-spectrometric behavior of a large series of 3-acylindole oximes (Ia-n) we established that the stabilities of their molecular ions range from 1.5 to 11.7% (Table 1) and that an increase in the size of R^3 leads to a decrease in the W_M values, as in the case of alkylarenes and alkylhetarenes [8]. An increase in the number of methyl groups in the pyrrole ring increases the stability of the molecule with respect to electron impact only slightly. This makes it possible to assume that the positive charge in the molecular ion

TABLE 1. Intensities of the Peaks of the Characteristic Ions ($\%\Sigma_{40}$) in the Mass Spectra of Ia-n



Compound	R^1	R^2	R^3	W_M	F_1	F_2	F_5	F_6	F_7	F_{11}
Ia	H	H	CH_3	10,0	3,3	4,4	12,2	1,8	—	5,8
Ib	CH_3	H	CH_3	6,4	3,7	2,3	4,7	1,0	—	2,7
Ic	H	CH_3	CH_3	11,0	8,1	2,9	2,7	1,2	—	4,1
Id	CH_3	CH_3	CH_3	11,7	11,7	3,1	4,4	2,9	0,4	7,6
Ie	H	H	C_2H_5	6,3	3,7	3,6	2,0	3,5	1,6	4,5
If	CH_3	H	C_2H_5	7,4	4,7	2,5	14,7	4,1	2,0	5,0
Ig	H	CH_3	C_2H_5	8,6	6,5	3,1	5,0	2,7	1,6	5,7
Ih	CH_3	CH_3	C_2H_5	10,8	9,4	2,7	7,5	2,9	2,0	6,6
Ii	H	CH_3	C_3H_7	2,9	3,0	3,0	5,0	4,1	1,1	3,3
Ij	H	H	C_4H_9	3,5	5,7	3,3	4,7	4,0	1,1	5,7
Ik	H	CH_3	C_4H_9	4,7	2,7	3,6	5,8	4,0	1,1	4,3
Il	H	H	*iso*-C_4H_9	1,5	2,0	4,0	4,0	5,7	5,7	4,1
Im	CH_3	H	*iso*-C_4H_9	6,5	5,9	1,4	4,2	10,4	2,2	4,5
In	H	CH_3	*iso*-C_4H_9	5,3	2,2	3,5	5,7	6,1	7,0	3,9

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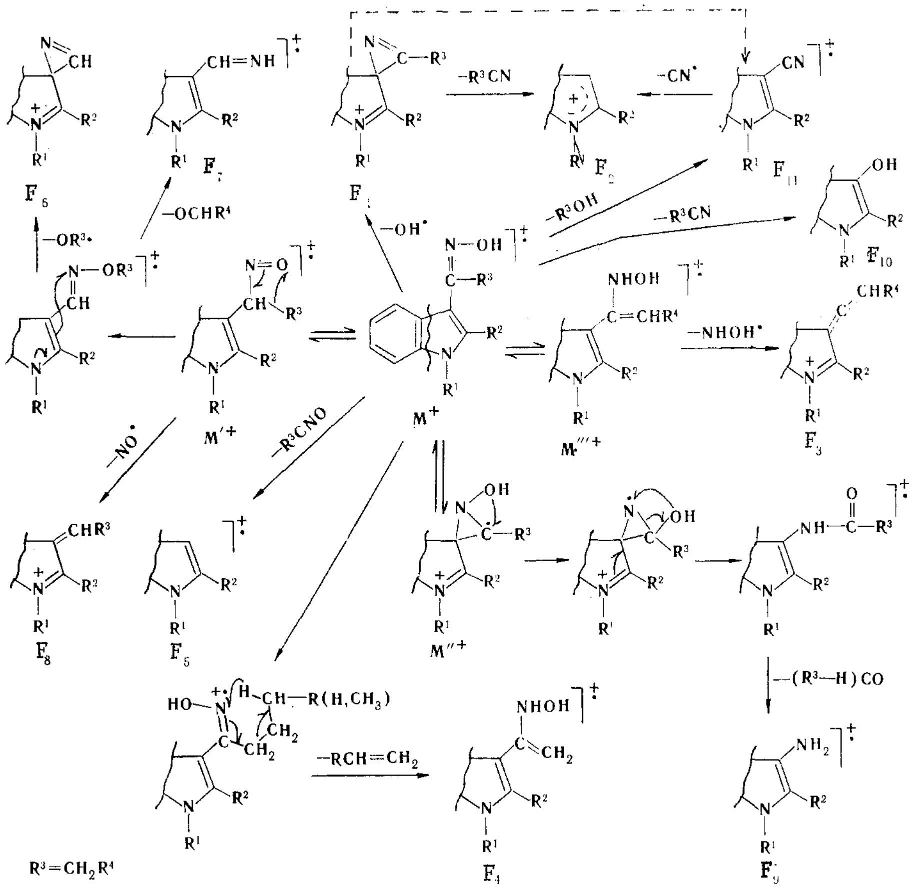
is concentrated to an appreciable extent in the region of the oximine grouping.

The character of the fragmentation of the 3-acylindole oximes that we investigated is determined by the presence of an oximine grouping and is typical for this class of compounds. Moreover, specific fragmentation pathways that are due to the presence of a heterocyclic ring are observed. Thus the presence of $[M - OH]^+$ (F_1), $[M - C(R^3)NOH]^+$ (F_2), and $[M - NHOH]^+$ (F_3) ion peaks is typical for all of the oximes (see the scheme presented below). The intensities of the peaks of the first two ions (see Table 1) range from 1.4 to 11.7%,* and they decrease as the length or degree of branched character of R^3 increases but increase when a methyl group is introduced in the 2 position of the indole ring; the intensities of the F_3 ion peaks are low and do not exceed 1.2%. A process associated with the McLafferty rearrangement [8], which leads to F_4 ions, the intensities of the peaks of which increase from 0.1 to 2.4% as R^3 becomes larger, is also a traditional fragmentation pathway of oximes Ii-n.



In addition to the F_2 ions, more intense peaks of F_5 ions, the mass numbers of which increase by one unit in the mass spectra of deuterated oximes Ib, e, are observed in the mass spectra of all of the oximes; this confirms their formation as a result of the elimination of a molecule of a nitrile oxide from the molecular ion.

The presence of intense (up to 10%) peaks of F_6 and F_7 ions, the compositions of which were confirmed by the high-resolution mass spectra, proved to be unusual in the mass spectra of the investigated oximes. The formation of these ions can be explained proceeding from the assumption of a hydroximino–nitroso tautomeric transformation in the molecular ion ($M \rightleftarrows M'$) with subsequent migration of R^3 to the oxygen atom and subsequent elimination of alkoxy groups (the formation of the F_6 ion) or an aldehyde (the F_7 ion). The presence in the mass spectra of Ia-d, l, n of peaks of $[M - NO]^+$ ions (F_8) of low intensities (0.1-0.5%), the compositions of which were also confirmed by the high-resolution mass spectra, is indirect evidence for the presence in the gas phase of a molecular ion in the nitroso form.

Another specific fragmentation process is the Beckmann rearrangement of the molecular ions of oximes Ia-n to give acylaminoindoles; this probably takes place with the participation

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*Here and subsequently, the intensities of the ion peaks in percent relative to Σ_{40} are presented.

TABLE 2. Mass Spectra of 3-Acylindole Oximes Ia-n

Compound	m/z values (relative intensities of the ion peaks in percent of the maximum peak)*
Ia	174 (76), 157 (27), 142 (48), 117 (100), 116 (36), 115 (34), 89 (39), 63 (35), 62 (21), 51 (23)
Ib	188 (100), 171 (65), 156 (48), 143 (38), 131 (84), 130 (41), 117 (74), 115 (52), 77 (55), 63 (49)
Ic	188 (100), 171 (85), 156 (43), 155 (34), 154 (66), 131 (28), 130 (30), 77 (45), 63 (26), 51 (30)
Id	202 (88), 185 (100), 171 (25), 170 (65), 169 (39), 159 (20), 158 (20), 145 (38), 144 (26), 115 (27)
Ie	188 (62), 171 (32), 143 (30), 142 (38), 130 (25), 117 (100), 116 (31), 115 (41), 89 (29), 63 (32)
If	202 (42), 185 (32), 157 (28), 156 (34), 155 (19), 146 (18), 144 (26), 131 (100), 130 (17), 69 (47)
Ig	202 (100), 185 (87), 168 (48), 157 (34), 156 (67), 155 (60), 131 (67), 130 (42), 69 (33), 57 (49)
Ih	216 (95), 199 (100), 184 (20), 183 (26), 172 (21), 171 (31), 170 (70), 169 (50), 145 (80), 144 (29)
Ii	216 (50), 199 (59), 170 (30), 157 (80), 156 (64), 155 (66), 131 (98), 130 (59), 77 (100), 51 (58)
Ij	216 (50), 199 (99), 158 (44), 157 (43), 143 (70), 142 (100), 130 (49), 117 (82), 116 (58), 115 (69)
Ik	230 (65), 213 (47), 171 (65), 157 (68), 156 (74), 155 (60), 131 (100), 130 (62), 77 (58), 41 (65)
Il	216 (16), 199 (28), 159 (24), 144 (78), 143 (78), 142 (56), 130 (41), 117 (56), 116 (55), 41 (100)
Im	230 (51), 213 (57), 172 (27), 158 (22), 157 (100), 156 (43), 132 (35), 131 (40), 77 (40), 41 (54)
In	230 (61), 213 (32), 171 (39), 158 (100), 157 (87), 156 (55), 155 (40), 131 (81), 130 (51), 77 (50)

*The 10 most intense ion peaks are presented; the peaks of the isotope ions were excluded.

of the 3 position of the indole ring with the subsequent splitting out of ketene and the formation of F_9 ions. The elementary compositions of these ions were confirmed by the high-resolution mass spectra, while the participation of the hydroxy hydrogen atom in their formation follows from a comparison of the mass spectra of the deuterated and undeuterated samples.

Finally, from an analysis of the mass spectra it follows that the molecular ions of the oximes that we investigated undergo a secondary Beckmann rearrangement, also not once noted in the literature [9], to give pseudomolecular ions of 3-oxindoles (F_{10}) or 3-cyanoindoles (F_{11}). The formation of ions of the F_{11} type is unknown for acetophenone oximes and is dominant and specific in the secondary Beckmann rearrangement for oximes of the indole series.

Thus the processes involved in the dissociative ionization of 3-acylindole oximes are characterized both as common (to all of the oximes) fragmentation pathways and as specific pathways of isomerization of the molecular ion that are associated with the presence of a nucleophilic indole ring.

EXPERIMENTAL

The mass spectra (Table 2) were obtained with a MAT-44S spectrometer with direct introduction of the samples into the ionization region at an ionizing voltage of 70 V and an input temperature 15-20°C below the melting points of the samples. The elementary compositions of the principal ions in the mass spectra of Ia,c were determined with an MAT-311A high-resolution spectrometer.

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PREPARATION OF OPTICALY ACTIVE 3-(1-METHYL-1-PHENYLPROPYL)INDOLE AND INVESTIGATION OF ITS CHIRAL-OPTICAL PROPERTIES

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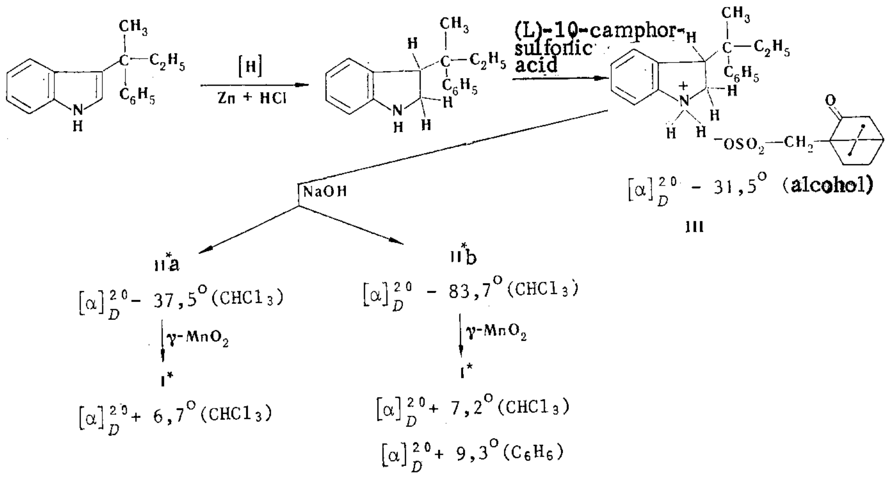
Optically active 3-(1-methyl-1-phenylpropyl)indole was obtained by dehydrogenation of the resolved [by means of (L)-10-camphorsulfonic acid] 3-(1-methyl-1-phenylpropyl)indoline. The chiral-optical properties of this product were investigated, and the possibility of the use of circular dichroism data for the identification of the chiral indole chromophore was demonstrated.

We have previously investigated the prototropic isomerization of 3-alkyl(aryl)indoles [1] and expressed the assumption that the process is intramolecular in character. To confirm this, it was necessary to synthesize 3-(1-methyl-1-phenylpropyl)indole (I), which contains a chiral substituent in the 3 position of the indole molecule. The investigation of the chiral-optical properties of this 3-alkylindole is of independent interest for the study of the stereochemistry of complex natural indole compounds.

Racemic indole I was obtained by alkylation with methylethylphenylchloromethane in the presence of dipyridinezinc chloride in metromethane [2]. We proposed to obtain optically active indole I* by the following sequence of transformations: reduction of indole to indoline, separation of the latter into its antipodes by means of (L)-10-camphorsulfonic acid, and, finally, production of the chiral 3-alkylindole by dehydrogenation of the optically active indoline.



Indoline II was isolated in 17% yield in the reduction of racemic indole I with zinc in hydrochloric acid. A new asymmetric center develops in the case of reduction in the 3 position of the indole molecule, and one therefore should have expected the formation of two pairs of diastereomeric salts.

The less soluble indoline salt III with specific rotation $[\alpha]_D^{20}$ −24.6° (alcohol) was isolated when equimolar amounts of racemic indoline II and (L)-10-camphorsulfonic acid were

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†Deceased.

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