MASS-SPECTRAL INVESTIGATION OF INDOLIZINE DERIVATIVES

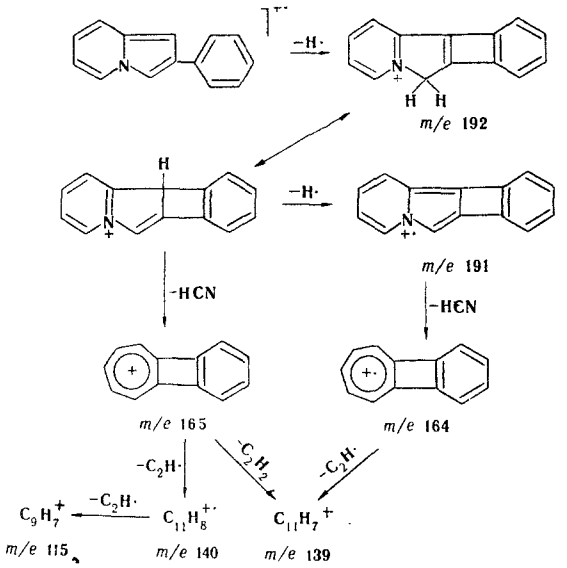
P. B. Terent'ev, S. M. Vinogradova, and A. N. Kost

UDC 547.759.4:543.51

The dissociative ionization of substituted 3-aroylindolizines proceeds with the successive loss of an aryl residue and CO. Detachment of OH and CHO groups proceeds simultaneously. The stabilities of the indolizines and the similarly constructed indole derivatives are compared.

Indolizines are indole isomers, but the difference in the structures of these compounds should be reflected in their behavior under the influence of electron impact. A relatively detailed investigation of the mass-spectral behavior of indole derivatives has been made [1], but the behavior of indolizines under the influence of electron impact has been described in only one paper [2].

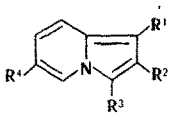
We have investigated the mass spectra of a number of acyl- and arylindolizines (Table 1). It was found that the mass spectrum of 2-phenylindolizine (I) is similar to the mass spectra of the isomeric phenylindoles [3], but the stability of I(W_M = 33.6) is higher that the stability of 2-phenylindole (W_M = 26.8) and lower than the stability of 3-phenylindole (W_M = 42.8). In addition, more intense signals of $(M-H)^+$ and $(M-2H)^+$ ions are observed in the mass spectrum of I, and their fraction in the total ion current exceeds 14%. Finally, the presence of very intense doubly charged ions, the sum of the intensities of which constitutes 18.9% of the total ion current, is characteristic for the mass spectrum of indolizine I.



When there is a pyridyl group in the 1 position of the indolizine ring, the stability of the molecule with respect to electron impact increases sharply, as a result of which II

M. V. Lomonosov Moscow State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 509-513, April, 1975. Original article submitted February 7, 1974.

TABLE 1. Mass Spectra of Indolizines



Compound	R¹	R²	R³	R⁴	Mass spectrum:* (m/e)/I, %
I	H	C_6H_5	H	H	193 192 191 190 165 115 100 28,4 21,6 9,1 10,8 10,8 96,5 96 95,5 83 17,0 3,7 12,5 18,7
II	4-C_5H_4N	H	H	H	194 193 192 167 166 141 100 3,8 1,6 1,5 1,8 1,8 140 139 97 83,5 1,3 1,3 1,8 2,4
III	4-C_5H_4N	H	COC_6H_5	H	298 297 296 270 269 221 100 14,3 2,5 4,5 18,2 22,1 193 192 166 105 20,8 10,7 3,0 4,4
IV	2-C_5H_4N	H	COC_6H_5	H	298 297 269 221 193 192 100 15,3 16,7 9,0 29,1 20,8 105 85 83 77 7,4 12,9 11,5 20,9
V	CN	H	COC_6H_5	H	246 245 218 169 141 114 100 15,7 17,6 41,0 22,6 23,6 105 81 77 192 35,2 17,7 64,8 1,6
VI	2-C_5H_4N	H	$COC_6H_4NO_2$-*p*	H	343 313 297 296 284 269 100 35,5 4,5 7,2 8,1 6,3 268 221 193 192 7,6 5,8 22,1 15,7
VII	4-C_5H_4N	H	$COC_6H_4NO_2$-*p*	H	343 313 297 296 284 269 100 20,9 6,8 13,2 3,7 2,8 268 221 193 192 3,7 7,2 11,6 6,5
VIII	2-C_5H_4N	H	COC_6H_5	Br	378 376 349 347 301 299 97,4 100 5,4 5,8 3,3 4,5 273 271 193 77 8,0 3,3 8,5 21,5
IX	4-C_5H_4N	H	COC_6H_5	Br	378 376 349 347 301 299 96,5 100 2,8 2,9 6,4 8,6 273 271 193 77 4,2 5,0 7,1 22,0
X	2-C_5H_4N	H	COC_6H_5	$COOC_2H_5$	370 341 340 314 313 297 100 12,4 8,8 3,1 10,9 3,4 265 237 192 77 7,5 3,6 7,4 14,6
XI	$COOCH_3$	C_6H_5	COC_6H_5	H	355 324 297 296 268 267 100 12,9 5,6 7,7 10,2 11,1 191 190 105 77 9,8 12,6 26,7 10,2
XII	$COOCH_3$	C_6H_6N†	COC_6H_5	H	370 369 340 339 311 293 100 14,0 4,1 17,5 5,3 9,1 283 282 105 77 4,1 4,7 12,8 12,2
XIII	$COOCH_3$	$COOCH_3$	COC_6H_5	H	337 306 278 274 260 219 100 19,0 5,9 23,0 11,0 5,8 190 189 105 77 4,5 5,8 11,5 19,0

*The 10 most intense ions [the $(M+1)^+$ ion peaks are not presented].

†2-Methyl-5-pyridyl.

has doubled stability (W_M = 63.4), but the character of its disintegration on the whole is retained and consists in the successive loss of two HCN molecules by the molecular ion and $(M-H)^+$ ion with subsequent analogous fragmentation of the resulting hydrocarbon ions.

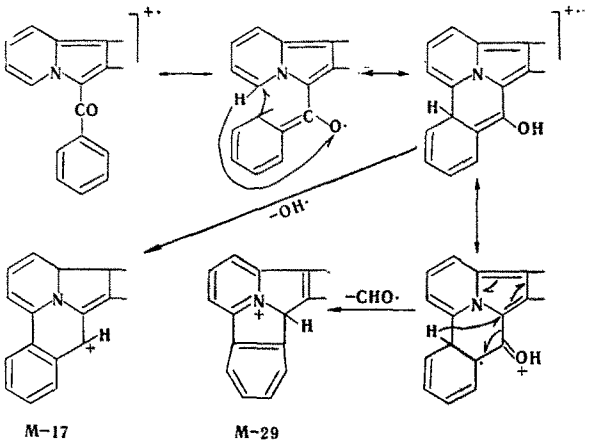
As expected, the introduction of a benzoyl group into the 3 position of the indolizine ring increases the number of channels of disintegration of the molecular ion, and this leads to a decrease in the stability (W_M = 47.3 for III). Let us note that this shows up particularly clearly when there is an α-pyridyl residue in the 1 position (IV, VI, VIII, and X). The intensity of the $(M-H)^+$ ions decreases simultaneously, and the $(M-2H)^+$ ions practically disappear. This compels us to assume the existence of a process with participation of both the acyl and the pyridyl groups; this process will be examined below. The pathway of fragmentation of most of the 3-aroylindolizines (III-X) is similar in character to that of the

TABLE 2. Metastable Transitions in the Mass Spectra of Indolizines V-XIII

Compound	M—Ar	M—CHO	M—OH	M—Ar—CO	M—CH_3COO
III	164,0	243,0	—	168,5	—
IV	—	—	—	168,5	—
V	116,0	—	213,0	117,5	—
VI	142,0	257,5*	—	—	—
VII	142,0	257,5*	—	—	—
VIII	—	320,0	—	—	—
IX	238,0	320,0	—	246,0	—
X	—	314,0	—	—	—
XI	—	—	322,0	—	—
XII	232,0	—	—	—	262,0
XIII	—	—	—	—	229,0

*The metastable transitions for M—NO are presented.

aroylindoles [4] and consists in successive loss of an aryl and carbonyl group by the molecular ion [which is confirmed by the corresponding metastable ions (Table 2)] with subsequent elimination of HCN molecules, as is observed for acylindoles [4]. The presence of M-17 and M-29 ions is characteristic in this case. The presence of M—OH (M-17) ions, the formation of which was explained by detachment of the hydroxyl group from the enol form of benzoylindole with hydrogen transfer from the nitrogen atom to the oxygen atom of the carbonyl group, was also recently noted during an analysis of the mass spectra of 3-benzoylindoles. In the case of indolizines, it is impossible to imagine any kind of enolization of the benzoyl group, and the formation of such ions requires a different explanation. Consequently, it might be assumed that the molecular ion rearranges with subsequent loss of an OH or CHO group.



It should be noted that the $(M-17)^+$ and $(M-29)^+$ ions are also present in the mass spectra of VIII-X, which contain substituents in the 6 position of the indolizine ring, whereas in VI and VII, the spectra of which are practically identical to one another, the loss of 17 and 29 amu occurs after prior loss of a nitrogen oxide molecule by the molecular ion. The one-step character of these processes was confirmed in most cases by means of the corresponding metastable ions (Table 2).

Fragmentation characteristic for the functional group in the pyridine ring of the indolizine occurs primarily after the formation of the $(M-29)^+$ ion and, for example, in X, is characterized by the M-29-C_2H_4 ion (m/e 313; metastable ion with an apparent mass of 287.3), which then loses a CO_2 molecule to give an ion with m/e 269. Similarly, in the case of VIII and IX the $(M-29)^+$ ions loses Br to give an ion with m/e 268.

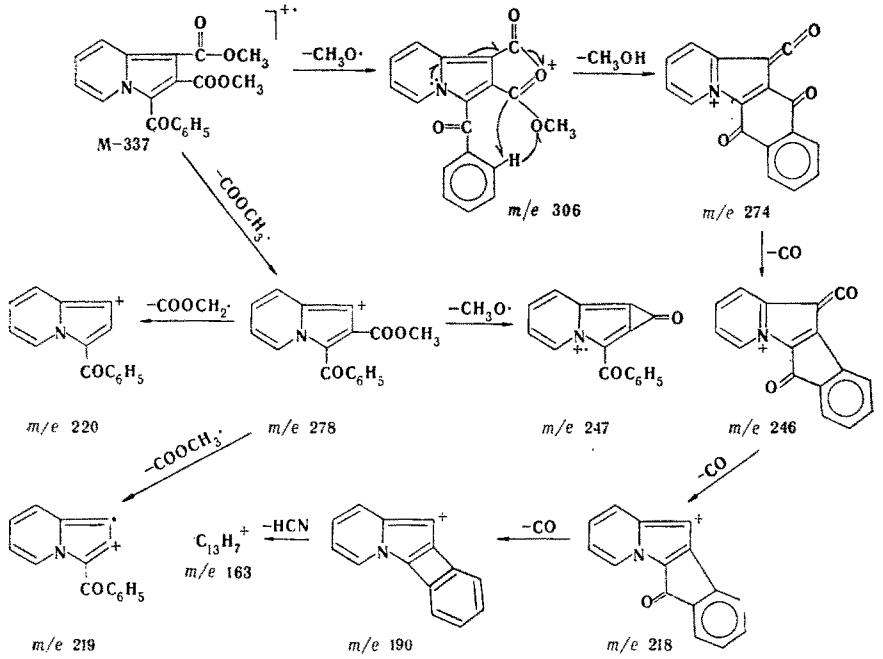
The introduction of a carbomethoxy grouping into the indolizine ring does not lead to substantial destabilization of the molecular ion, and XI, for example, has a stability

(W_M = 31.7) close to the stability of indolizine IV. Compound XII, which, as compared with indolizine XI, contains a 6-methyl-3-pyridyl residue, is even more stable with respect to electron impact, and its W_M value (49.8) is close to the value observed for III. Replacement of the phenyl group by a second carbomethoxy grouping (XIII) also leads to a rather stable molecule (W_M = 44.1).

In contrast to III-X, the molecular ions of indolizines containing a carbomethoxy group in the pyrrole ring give low-intensity $(M-C_6H_5)^+$ ions and practically do not give $M-C_6H_5CO$ ions. The primary fragment ions in the mass spectra of indolizines XI-XIII are formed, on the one hand, with the loss of a CH_3O radical from the carbomethoxy group in the 1 position of the indolizine ring* or, on the other, by complete detachment of the carbomethoxy grouping. In a number of cases this process is confirmed by the corresponding metastable ions (Table 2).

In the case of XIII, which contains two carbomethoxy groupings in the 1 and 2 positions of the indolizine ring, the $(M-CH_3O)^+$ ion then loses a molecule of methanol to give a cyclic anion, after which this ion successively loses three carbon monoxide molecules. In addition, the mass spectrum of XIII also contains a less-intense peak of an ion with mass 248, which corresponds to ejection of a $COOCH_2$ group from the $(M-CH_3O)^+$ ion. The loss of this grouping by the molecular ion was described in [2].

Thus 3-aroylindolizines display extreme stability with respect to electron impact as compared with the corresponding indole compounds, and when there are functional substituents in the pyrrole ring, fragmentation is determined primarily by these substituents.



EXPERIMENTAL METHOD

The individuality of the investigated substances was monitored by means of the PMR spectra and thin-layer chromatography (TLC) (on aluminum oxide). The mass spectra were recorded with an MKh-1303 spectrometer at an ionizing-electron energy of 50 eV and an emission current of 1.5 mA with introduction of the substances directly into the ionization region at 110-180°.

The authors thank A. B. Belikov for participating in the recording of the mass spectra.

LITERATURE CITED

1. A. A. Polyakova and R. A. Khmel'nitskii, Mass Spectrometry in Organic Chemistry [in

In the mass spectrum of XI, m = 296.0 was found for the process $355^+ \rightarrow 324^+ + 31$.

Russian], Khimiya, Moscow (1972).
2. G. Jones and I. Stanyer, Org. Mass Spectrometry, 3, 1489 (1970).
3. R. A. Khmel'nitskii, V. I. Vysotskii, I. I. Grandberg, A. N. Kost, and V. A. Budylin, Zh. Organ. Khim., 7, 1514 (1971).
4. J. C. Powers, J. Org. Chem., 33, 2044 (1968).
5. R. A. Khmel'nitskii, N. A. Klyuev, T. A. Kozik, V. N. Rusinova, and N. N. Suvorov, Khim. Geterotsikl. Soedin., 1240 (1974).