COMPARATIVE STUDY OF MASS-SPECTROMETRIC BEHAVIOR OF 2,6-DIARYL-4-(OXO,OXIMINO,AMINO)PIPERIDINES

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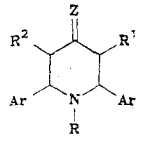
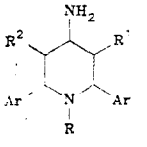
The fragmentation of the investigated piperidine derivatives, which was confirmed by data from the high-resolution spectra, by the DADI spectra, and by the fragmentation of the deutero analogs, proceeds with cleavage of the piperidine ring and is due to the competitive distribution of the charge on the ring nitrogen atom and on the structural elements that contain functional groups and an aryl radical. The dependence of the mass spectra of 4-(oxo,oximino,amino)piperidines on the nature and position of the substituents in the ring, as well as on the character of the functional group in the 4 position of the ring, was investigated.

It is known that the fragmentation of various piperidine derivatives is determined primarily by localization of the positive charge on the ring nitrogen atom and is accompanied by the formation of amine fragments [1-3]. At the same time, the development of ions that contain functional groups is characteristic for the fragmentation of 2- and 4-oxopiperidines and 4-N-substituted aminopiperidines and arylpiperidines [4-7].

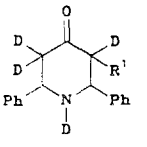
In this connection it seemed of interest to investigate and compare the character of the processes involved in the fragmentation of 3-alkyl(phenyl)2,6-diaryl-4-oxopiperidines I-XVI and their oximes XVII-XXIII, as well as 3-phenyl-2,6-diaryl-4-amino-piperidines XXIV-XXVI, to ascertain the effect of a functional group in the 4 position on the fragmentation, and to establish empirical principles that are due to the nature and position of the substituents in the piperidine ring.



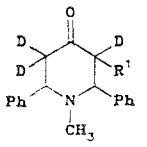
I-XXIII



XXIV-XXVI



I, III, IV



XI, XIV

I—XVI Z=O; XVII—XXIII Z=N—OH; I—IX, XVII—XXI, XXIV, XXV R=H; X—XVI, XXII, XXIII, XXVI R=CH_3; I, V, XI, XVIII R^1=CH_3; II, XII R^1=C_2H_5; III, XIII, XVII R^1=*n*-C_3H_7; IV, XIV, XXII R^1=*iso*-C_3H_7; VI—IX, XVI, XIX—XXI, XXIII—XXVI R^1=C_6H_5; X R^1=H; XV R^1=*n*-C_5H_{11}; I—IV, VI—XVII, XIX—XXVI R^2=H; V, XVIII R^2=CH_3; I—VI, X—XIX, XXII—XXIV, XXVI Ar=C_6H_5; VII, XX Ar=*p*-BrC_6H_4; VIII Ar=*p*-HOC_6H_4; IX, XXI, XXV Ar=*p*-$CH_3OC_6H_4$;

The mass spectra of I-XXVI, which were investigated for the first time, were analyzed using data from the high-resolution mass spectra (HRMS). The sequence of the fragmentation was established using the DADI method in the case of III, XIV, XVII, and XIX.

The dissociative ionization of 4-oxopiperidines I-XVI and their oximes XVII-XXIII is characterized by the formation of molecular ions (M^+) with high and medium intensities and by the low selectivity of their fragmentation ($S_{1/2}$ = 4-7, Table 1). The stabilities (W_M) of the M^+ ions of oximes XVII-XXIII are, on average, greater by a factor of 1.5 than the stabilities of the molecular ions of the corresponding ketones. The M^+ peaks in the mass spectra of 4-aminopiperidines XXIV-XXVI have low relative intensities (2-6%).

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TABLE 1. Data from the Mass Spectra of I-XXVI*

Compound	m/z values** (I_{rel}, %); $S_{1/2}$
I	77 (20), 78 (22), 91 (21), 104 (100), 106 (50), 117 (23), 118 (20), 132 (20), 133 (18), 194 (16), 265 (25); $S_{1/2}=5$
I-D_4	77 (16), 78 (20), 91 (14), 106 (100), 108 (40), 118 (25), 119 (18), 134 (26), 135 (18), 195 (11), 269 (20)
II	55 (52), 77 (26), 91 (45), 104 (100), 106 (66), 117 (34), 132 (27), 147 (25), 194 (64), 264 (41), 279 (99); $S_{1/2}=6$
III	55 (95), 91 (29), 104 (100), 106 (86), 117 (33), 131 (19), 132 (21), 194 (48), 208 (24), 264 (98), 293 (90); $S_{1/2}=5$
III-D_4	56 (100), 91 (18), 106 (76), 108 (73), 118 (22), 132 (30), 134 (14), 195 (19), 211 (19), 268 (52), 297 (51)
IV	69 (78), 77 (28), 91 (43), 104 (100), 106 (72), 131 (27), 146 (13), 194 (41), 208 (19), 278 (56), 293 (53); $S_{1/2}=6$
IV-D_4	70 (60), 78 (11), 91 (26), 106 (100), 108 (60), 132 (36), 147 (7), 195 (29), 211 (14), 282 (50), 297 (42)
V	77 (11), 78 (9), 91 (39), 106 (43), 117 (57), 118 (100), 133 (63) 146 (29), 194 (67), 222 (7), 279 (56); $S_{1/2}=5$
VI	77 (12), 90 (37), 91 (21), 104 (36), 106 (22), 118 (100), 131 (11), 194 (65), 195 (34), 208 (12), 327 (60); $S_{1/2}=5$
VII	77 (15), 78 (21), 90 (30), 91 (15), 118 (100), *182* (14), *209* (8), *273* (12), *350* (11), *364* (5), *483* (14); $S_{1/2}=7$
VIII	65 (18), 77 (14), 91 (100), 118 (13), 121 (65), 122 (45), 147 (31), 226 (22), 240 (26), 324 (5), 359 (77); $S_{1/2}=5$
IX	77 (21), 91 (89), 118 (26), 119 (30), 134 (100), 136 (37), 161 (41), 225 (8), 254 (38), 268 (21), 387 (49); $S_{1/2}=6$
X	65 (5), 77 (29), 78 (20), 91 (31), 104 (93), 118 (96), 120 (100), 131 (13), 146 (39), 160 (10), 202 (13), 279 (55); $S_{1/2}=4$
XI	77 (24), 78 (23), 91 (28), 104 (96), 118 (73), 120 (100), 131 (13), 146 (39), 160 (10), 202 (13), 279 (55); $S_{1/2}=4$
XI-D_3	77 (36), 91 (39), 106 (90), 118 (60), 119 (29), 121 (100), 132 (43), 148 (28), 163 (10), 205 (11), 282 (45)
XII	55 (37), 77 (20), 91 (32), 104 (73), 118 (78), 120 (90), 131 (20), 146 (29), 216 (12), 278 (24), 293 (100); $S_{1/2}=4$
XIII	55 (100), 77 (25), 91 (37), 104 (66), 118 (68), 120 (96), 131 (18), 146 (23), 230 (7), 278 (50), 307 (61); $S_{1/2}=5$
XIV	69 (98), 77 (26), 91 (39), 104 (75), 118 (76), 120 (100), 131 (36), 146 (15), 230 (9), 292 (46), 307 (70)
XIV-D_3	70 (84), 77 (34), 91 (16), 106 (70), 118 (40), 121 (100), 132 (30), 148 (11), 191 (10), 295 (25), 310 (55)
XV	55 (98), 77 (21), 91 (27), 104 (53), 118 (72), 120 (100), 131 (17), 146 (19), 222 (11), 278 (26), 335 (47); $S_{1/2}=4$
XVI	77 (12), 90 (17), 91 (18), 103 (11), 104 (18), 118 (100), 120 (44), 131 (8), 146 (6), 222 (4), 341 (27); $S_{1/2}=5$
XVII	91 (27), 96 (15), 104 (35), 106 (100), 117 (14), 186 (11), 194 (69), 208 (15), 265 (16), 291 (30), 308 (87); $S_{1/2}=6$
XVIII	77 (18), 82 (25), 91 (32), 104 (22), 106 (86), 118 (32), 172 (20), 189 (10), 194 (65), 277 (55), 294 (100); $S_{1/2}=6$
XIX	77 (16), 91 (29), 104 (42), 106 (90), 116 (18), 130 (33), 194 (90), 195 (44), 208 (16), 325 (50), 342 (100); $S_{1/2}=5$
XX	77 (30), 91 (21), 103 (97), 116 (53), 130 (100), *182* (30), *184* (75) *273* (15), *350* (28), *481* (30), *498* (30); $S_{1/2}=8$
XXI	91 (18), 116 (20), 130 (30), 134 (40), 136 (100), 225 (12), 254 (13), 267 (11), 268 (14), 385 (33), 402 (64); $S_{1/2}=7$
XXII	77 (16), 91 (22), 96 (17), 104 (10), 118 (27), 120 (100), 146 (12), 222 (9), 305 (63), 307 (13), 322 (83); $S_{1/2}=6$
XXIII	77 (16), 91 (23), 103 (28), 104 (15), 116 (21), 118 (22), 120 (100), 130 (43), 265 (13), 339 (39), 356 (58); $S_{1/2}=5$
XXIV	65 (5), 77 (6), 91 (15), 104 (17), 106 (15), 119 (8), 148 (17), 180 (13), 194 (100), 311 (3), 328 (2); $S_{1/2}=4$
XXV	91 (13), 119 (32), 121 (14), 134 (25), 136 (17), 210 (8), 225 (9), 240 (69), 254 (100), 268 (4), 388 (6); $S_{1/2}=4$
XXVI	77 (14), 91 (27), 104 (25), 118 (42), 119 (48), 120 (100), 132 (7), 180 (15), 222 (7), 325 (9), 342 (6); $S_{1/2}=4$

*The molecular-ion peak M^+ and the 10 most intense peaks are presented.

**The m/z values based on ^{79}Br are given in italics.

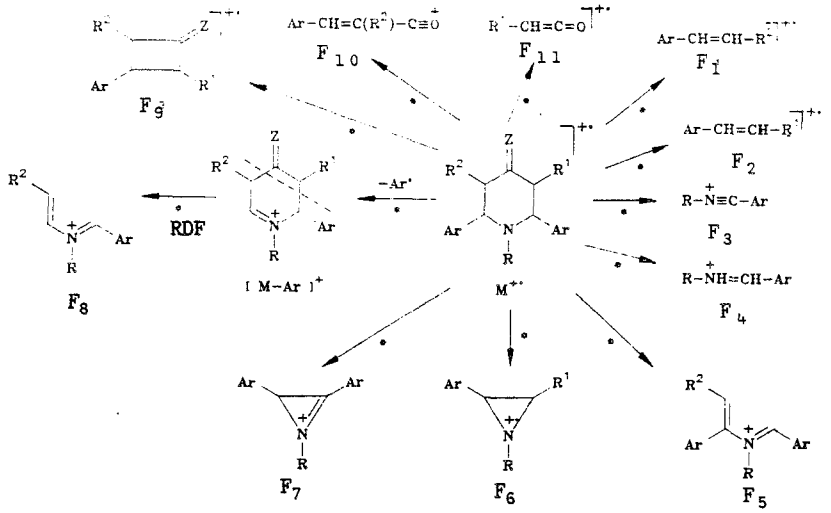
TABLE 2. Elementary Compositions of the Isobaric Ions from Data on I-XXV

Compound	m/z	Precise mass of the ion		Elementary composition of the ion	Intensity ratio
		determined	calc.		
I	104	104,0500	104,0499	C_7H_6N (F_3)	1
		104,0623	104,0624	C_8H_8 (F_1)	4
II	104	104,0498	104,0499	C_7H_6N (F_3)	1
		104,0603	104,0624	C_8H_8 (F_1)	4
	131	131,0856	131,0858	$C_{10}H_{11}$ (F_2 – H)	3
		131,0492	131,0495	C_9H_7 (F_{10})	4
	132	132,0921	132,0936	$C_{10}H_{12}$ (F_2)	2
		132,0816	132,0811	$C_9H_{10}N$ [$F_6 - CH_3$]$^+$	1
III	104	104,0495	104,0499	C_7H_6N (F_3)	1
		104,0623	104,0624	C_8H_8 (F_1)	4
IV	104	104,0489	104,0499	C_7H_6N (F_3)	1
		104,0599	104,0624	C_8H_8 (F_1)	2
	117	117,0700	117,0702	C_9H_9 [$F_2 - C_2H_5$]$^+$	1
		117,0586	117,0577	C_8H_7N [$F_6 - C_3H_7 - H$]$^+$	1
VI	104	104,0483	104,0499	C_7H_6N (F_3)	1
		104,0614	104,0624	C_8H_8 (F_1)	2
VIII	120	120,0450	120,0448	C_7H_6NO (F_3)	1
		120,0586	120,0573	C_8H_8O (F_1)	1
IX	134	134,0593	134,0604	C_8H_8NO (F_3)	1
		134,0728	134,0729	$C_9H_{10}O$ (F_1)	4
X	146	146,0725	146,0729	$C_{10}H_{10}O$ (F_9)	1
		146,0965	146,0967	$C_{10}H_{12}N$ (F_8)	2
XI	118	118,0658	118,0655	C_8H_8N (F_3)	2
		118,0782	118,0780	C_9H_{10} (F_2)	1
XII	131	131,0496	131,0495	C_9H_7O (F_{10})	3
		131,0854	131,0858	$C_{10}H_{11}$ [$F_2 - H$]$^+$	2
	174	174,1019	174,1041	$C_{12}H_{14}O$ (F_9)	3
		174,1272	174,1279	$C_{12}H_{16}N$	2
XIII	146	146,0971	146,0967	$C_{10}H_{12}N$ (F_8)	5
		146,1082	146,1092	$C_{11}H_{14}$ (F_2)	1
XIV	131	131,0495	131,0495	C_9H_7O (F_{10})	1
		131,0856	131,0856	$C_{10}H_{11}$ ($F_2 - CH_3$)	1
	146	146,0962	146,0967	$C_{10}H_{12}N$ (F_8)	4
		146,1072	146,1092	$C_{11}H_{14}$ (F_2)	1
XVI	118	118,0417	118,0417	C_8H_6O (F_{11})	2
		118,0662	118,0655	C_8H_8N (F_3)	1
	222	222,1039	222,1041	$C_{16}H_{14}O$ (F_9)	1
		222,1281	222,1279	$C_{16}H_{16}N$ (F_5)	3
XVII	104	104,0496	104,0499	C_7H_6N (F_3)	2
		104,0625	104,0624	C_8H_8 (F_1)	3
XIX	104	104,0489	104,0499	C_7H_6N (F_3)	1
		104,0614	104,0624	C_8H_8 (F_1)	2
XX	182*	181,9620	181,9604	C_7H_5NBr (F_3)	1
		181,9731	181,9729	C_8H_7Br (F_1)	2
XXI	134	134,0604	134,0604	C_8H_8NO (F_3)	2
		134,0730	134,0729	$C_9H_{10}O$ (F_1)	3
XXII	146	146,0965	146,0967	$C_{10}H_{12}N$ (F_8)	2
		146,1099	146,1092	$C_{11}H_{14}$ (F_2)	1
XXIV	104	104,0497	104,0499	C_7H_6N (F_3)	1
		104,0623	104,0624	C_8H_8 (F_1)	4
XXV	134	134,0608	134,0604	C_8H_8NO (F_3)	1
		134,0728	134,0729	$C_9H_{10}O$ (F_1)	3

*The ion peak containing the ^{79}Br isotope is presented.

The fragmentation of 2,6-diaryl-4-(oxo,oximino, amino)-piperidines I-XXVI is due to the formation of common ions and can be represented by Scheme I.

Scheme 1



The presence of aryl substituents in the 2 and 6 positions gives rise to the development of hydrocarbon ions F_1 and F_2. Their compositions and the one-step character of their formation from the M^+ ions are confirmed by data from the mass spectra of the deutero analogs, the HRMS (Table 2), and the DADI spectra. In conformity with the Stevenson–Audier rule [8], the high intensities of the peaks of the F_1 fragments in the mass spectra of 3-alkyl-2,6-diphenyl-4-piperidinones I-IV and X-XV are associated with the lower ionization energy (IE) of styrene (8.86 eV) as compared with the IE of piperidine (9.2 eV) and cyclohexanone (9.14 eV) [9].

Fragmentation that is due to localization of the positive charge on the ring nitrogen atom and proceeds with opening of the ring is also characteristic for I-XXVI. The formation of fragments F_3 and F_4 with medium and high intensities is caused by cleavage of the $C_{(2)}$–$C_{(3)}$ and $C_{(6)}$–$N_{(1)}$ bonds and is accompanied by processes involving the migration of hydrogen atoms. In the development of the F_4 ion a hydrogen atom migrates to the piperidine nitrogen atom from the 5 or 3 position of the ring; this is confirmed by data from the mass spectra of the deutero analogs of I, III, and IV and XI and XIV, in which fragment F_4 contains two deuterium atoms and one deuterium atom, respectively.

Ions F_5-F_7 are typical amine fragments, and their development is characteristic for the dissociative ionization of various piperidine derivatives [2, 3, 6, 7]. The contribution of fragment F_5 to the total ion current in the fragmentation of I-XXVI does not exceed 5% (Table 2), and its formation is due to opening of the ring and the migration of a hydrogen atom from the 6 position to the fragment being eliminated. This is confirmed by the 3 to 2 amu shift of the peak of the F_5 ion to the large m/z region in the mass spectra of the deutero analogs of I, III, and IV and XI and XIV, respectively.

The formation of an F_6 fragment is observed only in the fragmentation of the unsubstituted (at the nitrogen atom of the piperidine ring) I-IX, XVII-XXI, XXIV, and XXV; this may serve as a mass-spectral criterion for distinguishing the latter from their N-methyl-substituted analogs X-XVI, XXII, XXIII, and XXVI. The peak of the F_6 ion in the mass spectra of the deutero analogs of I, III, and IV is shifted 2 amu to the high-mass region, while its elementary composition is confirmed by data from the high-resolution mass spectra (HRMS) for γ-piperidones I-V (Table 2).

Rearrangement amine fragment F_7 has high and medium intensities in the fragmentation of 4-(oxo,oximino)piperidines I-IX and XVII-XXI and the maximum intensity in the mass spectra of 4-(aminopiperidines XXIV and XXV, whereas in the case of their N-methyl analogs X-XVI, XXII, XXIII, and XXVI the percentage of the indicated ions in the mass spectra decreases markedly (Table 3). The introduction of a chemical label of the groups (Br, OH, CH_3O) into the phenyl substituents in the 2 and 6 positions of the piperidine ring of VII-IX, XX, XXI, and XXV makes it possible to establish unambiguously the nature and mechanism of formation

TABLE 3. Intensities of the Peaks of the Characteristic Ions (% Relative to Σ_{50}) in the Mass Spectra of I-XXVI

Compound	M^+	$[M-OH]^+$	$[M-R']^+$	$[M-Ar]^+$	F_1	F_2	F_3	F^4	F_5	F_6	F_7	F_8	F_9	F_{10}	F^*_{11}	F_{12}	77	91
I	6,9	—	—	—	18,5	4,6	4,6	11,6	1,2	4,2	3,7	—	—	0,7	—	—	4,6	4,9
II	13,8	—	4,7	—	9,2	2,1	2,3	7,6	2,2	2,9	7,3	—	—	1,7	5,9	—	3,0	5,2
III	11,9	—	10,6	—	8,7	1,3	2,2	9,3	2,6	1,5	5,2	—	—	2,1	10,3	—	1,5	3,1
IV	8,8	—	7,6	—	9,1	1,7	4,5	9,7	2,6	0,8	5,5	—	—	3,7	10,6	—	3,8	5,8
V	11,7	—	—	—	16,1	—	2,3	6,9	1,1	10,2	10,8	—	—	0,5	—	—	1,8	6,3
VI	12,5	—	—	—	4,0	1,6	2,0	3,7	1,9	3,7	10,8	—	—	1,8	16,7	—	2,0	3,5
VII	5,9	—	—	—	4,7	—	—	—	1,7	4,1	3,7	—	—	2,7	16,9	—	2,5	2,5
VIII	15,6	0,3	—	—	1,2	0,5	1,2	7,3	4,2	1,3	3,4	—	—	5,0	2,1	—	2,3	16,2
IX	8,8	—	—	—	11,2	1,3	2,8	5,2	2,9	1,1	5,3	—	—	5,8	3,7	—	2,9	12,5
X	3,5	—	—	2,3	16,1	—	16,7	17,4	0,9	—	0,9	2,8	1,4	5,2	—	—	5,0	5,4
XI	11,0	—	—	2,2	15,9	3,9	8,1	16,6	1,0	—	1,0	6,5	1,7	2,2	—	—	4,0	4,7
XII	17,7	—	3,5	1,7	10,6	1,4	11,3	13,0	1,4	—	0,9	4,2	0,4	1,7	5,4	—	2,9	4,6
XIII	10,1	—	6,7	0,9	8,9	0,5	9,2	12,9	0,9	—	0,7	2,7	0,7	2,4	13,5	—	3,4	4,9
XIV	10,9	—	5,8	1,1	9,5	0,4	9,6	12,6	1,1	—	0,8	1,6	0,6	2,4	12,4	—	3,4	4,9
XV	9,3	—	4,1	0,8	8,3	0,3	11,3	15,7	1,7	—	0,6	2,9	0,5	2,7	15,4	—	3,3	4,2
XVI	8,7	—	—	0,8	4,6	1,3	8,4	11,2	0,8	—	0,8	1,5	0,3	2,0	17,1	—	3,1	4,5
XVII	15,6	4,4	1,5	—	3,1	0,9	2,1	14,7	2,2	1,5	10,1	—	1,1	—	0,7	2,2	1,3	4,0
XVIII	16,1	7,3	—	—	4,3	—	2,9	11,5	2,0	2,4	8,7	—	1,3	—	1,2	3,3	2,4	4,3
XIX	17,9	7,1	—	—	4,0	1,0	2,0	12,9	2,3	4,3	12,9	—	1,7	—	2,6	4,7	2,3	4,1
XX	6,1	4,9	—	—	3,3	0,3	1,6	7,3	0,5	2,4	4,6	—	1,5	—	4,3	8,1	2,4	1,7
XXI	13,4	5,4	—	—	4,0	0,7	2,6	16,5	1,6	1,9	2,1	—	1,8	—	3,3	4,9	2,1	3,0
XXII	17,3	10,5	2,2	0,7	1,7	0,7	4,5	16,7	1,5	—	1,0	1,3	1,3	—	1,2	2,8	2,7	3,7
XXIII	13,8	7,5	—	0,6	2,8	0,9	4,2	18,9	0,9	—	0,9	0,6	2,5	—	4,0	8,1	3,0	4,3
XXIV	0,7	—	—	—	4,6	4,6	1,4	5,3	1,1	2,1	35,2	—	0,7	0,5	2,8	—	1,8	5,3
XXV	1,5	—	—	—	4,8	4,4	1,6	4,4	1,0	2,3	25,7	—	0,5	1,0	8,2	—	1,0	3,3
XXVI	1,5	—	—	1,4	6,3	3,8	10,5	25,0	0,8	—	1,5	1,5	—	1,0	12,0	—	3,5	6,8

*Ions F_{11} of II-IV and XII-XV correspond to fragments F'_{11}, while ions F_{11} of XVII-XXIII correspond to fragments F''_{11}, presented in Schemes 2 and 3, respectively.

of the F_6 and F_7 ions, since in the case of the fragmentation of 2,3,6-triphenyl-substituted 4-(oxo,oximino,amino)piperidines VI, XIX, and XXIV fragment F_7 can be represented as the product of fragmentation of ion F_6 caused by the elimination of a hydrogen atom from it.

One of the principal pathways in the fragmentation of piperidine derivatives that contain a substituent in the α position is the splitting out of this substituent [2, 6, 7]. However, the formation of an $[M - Ar]^+$ ion is not observed in the fragmentation of 2.6-diaryl-4-(oxo,oximino,amino)piperidines I-IX, XVII-XXI, and XXIV-XXV. At the same time, its development is characteristic for the N-methyl analogs and is accompanied by the ejection of an aryl radical only from the 6 position, since the subsequent fragmentation of the $[M - Ar]^+$ ion is due to retrodiene fragmentation (RDF) of the ring [2, 7, 10; p. 76] with the formation of common fragment F_8 with m/z 146. Its nature is confirmed by data on the fragmentation of deutero analogs and the HRMS of X, XII-XIV, and XXII (Table 2).

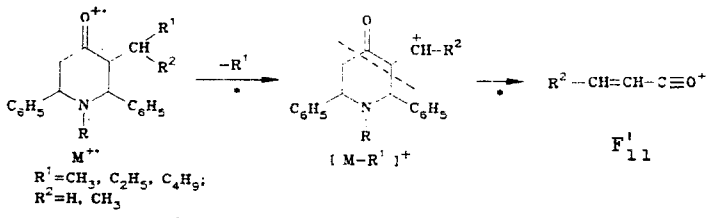
The existence of a keto group in γ-piperidones I-XVI causes the occurrence of competitive fragmentation processes associated with the possibility of localization of the positve charge on it. One observes F_9 ions, which have low intensities, only in the fragmentation of N-methyl-substituted γ-piperidones X-XVI (Table 3). Their formation is confirmed by the fragmentation of the deutero analogs of XI and XIV and by the elementary compositions established from the HRMS for X-XII and XIV.

The development of another oxygen-containing F_{10} ion, which is characteristic for the fragmentation of cyclohexanone derivatives [11, p. 92], is due to a ketone type of fragmentation associated with cleavage of the $C_{(3)}$–$C_{(4)}$ and $C_{(6)}$–$N_{(1)}$ bonds in the M^+ ions of I-XVI and with migration of a hydrogen atom from the 5 position to the amine fragment split out. The fragmentation of the deutero analogs of I, III, IV, XI, and XIV, in the mass spectra of which the peak of the F_{10} ion is shifted 1 amu to the higher-mass region, serves as evidence for this pathway for the formation of the F_{10} ion. It is interesting to note that the dissociative ionization of γ-piperidones I-XVI is not accompanied bv the development of ions caused by the alternative cleavage of the $C_{(4)}$–$C_{(5)}$ and $C_{(2)}$–$N_{(1)}$ bonds; this is explained by the easier cleavage of the bond at the $C_{(3)}$ atom that is bonded to an alkyl or aryl radical. It should be noted that peaks of ions that are similar to F_{10} and contain a hydroxime group, are absent in the mass spectra of 4-oximinopiperidines XVII-XXIII.

The fragmentation of 3-phenyl-2,6-diaryl-4-oxopiperidines VI-IX and XVI leads to the formation of F_{11} fragments with m/z 118 (Scheme 1), which have the maximum intensity in the mass spectra of VI and VII, and are diagnostic in the case of the dissociative ionization of 4-oxopiperidines that contain a phenyl radical in the α position relative to the keto group.

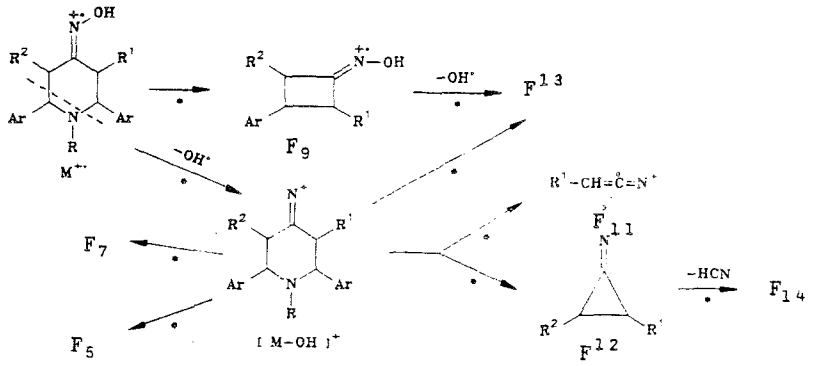
The fragmentation of 3-alkyl-substituted 4-oxopiperidines II-IV and XII-XV is accompanied by intensive splitting out of the alkyl substituent (Scheme 2). The fragmentation of 3-ethyl- and 3-isopropyl-4-oxopiperidines II and XII and IV and XIV is characterized by the formation of $[M - CH_3]^+$ ions of medium and high intensities, while peaks of $[M - C_2H_5]^+$ and $[M - C_4H_9]^+$ fragments, respectively, are observed in the mass spectra of 3-propyl- and 3-pentyl-4-oxopiperidines III, XIII, and XV. The subsequent fragmentation of the $[M - R^1]^+$ ions leads to the development of oxygen-containing F'_{11} fragments (55-100%). The mechanism of their formation is in agreement with data on the fragmentation of the deutero analogs of III, IV, and XIV and the HRMS (II-IV, XIV, XV) and the DADI spectra of III and XIV. The $[M - R^1]^+$ and F_{11} ions (Scheme 2) convey important information regarding the character of the substituents in the 3 position of the ring and make it possible to easily distinguish isomers III and IV and XIII and XIV, as well as III, IV, and XII, by mass spectrometry. One should particularly note the absence of a McLafferty rearrangement in the fragmentation of 3-alkyl-4-oxo-piperidines II-IV and XII-XV, whereas a McLafferty rearrangement is characteristic for the fragmentation of 2-alkyl-substituted cyclohexanones [12].

Scheme 2



The hydroxy radical of the oximino group substantially decreases the IE of the nitrogen atom bonded to it, which is responsible for the intensive occurrence of processes involving the fragmentation of oximes XVII-XXIII that are associated with localization of the positive charge on the exocyclic nitrogen atom. The $[M - OH]^+$ ion, the development of which is characteristic for the mass-spectral behavior of oximes [13, p. 221], dissociates via several pathways with the formation of F''_{11}, F_{12}, and F_{13} fragments, which convey information regarding the nature of the substituents in the 3 and 5 positions of the ring. Analysis of the DADI spectra of XVII and XIX showed tht the F_5 and F_7 fragments (Schemes 1 and 3) are products of the fragmentation of two ions – M^+ and $[M - OH]^+$ – and are caused by the competitive distribution of the charge between the nitrogen atoms in the M^+ ions of 4-oximinopiperidines XVII-XXIII.

Scheme 3



As we have already noted, a peculiarity of the fragmentation of 4-aminopiperidines XXIV-XXVI is the appearance in the mass spectra of low-intensity M^+ peaks and characteristic $[M - NH_3]^+$ fragments (3-9%). The dissociative ionization of the indicated amines proceeds primarily with the formation of ions that is caused by localization of the positive charge on the piperidine nitrogen atom, as in the fragmentation of 4-(oxo,oximino)piperidines I-XXIII (Scheme 1). In the fragmentation of XXIV-XXVI the contribution of the characteristic $Ph-CH=CH-CH=\overset{+}{N}H_2$ (F_{10}) and $Ph-\overset{+}{C}H-CH=NH_2$ (F_{11}) ions, which are due to localization of the charge on the amino group in the 4 position of the ring, to the total ion current does not exceed 13%. The nature of the formation of the indicated fragments is confirmed by the mass spectrum of the deutero analog of amine XXVI, obtained under conditions of deuterium exchange of the substance with CD_3OD vapors directly in the ionization chamber of the apparatus, in which the peaks of the F_{10} and F_{11} ions are shifted 2 amu to the higher-mass region.

Taking into account the fact that the data on the fragmentation of piperidine derivatives under chemical-ionization (CI) conditions re limited [7, 14], we studied the CI spectra of the positive and negative ions of 4-oxopiperidines III, XII, XIV, and XV, as well as 4-oximinopiperidines XVII and XXII. As expected, the maximally intense peak in the CI spectra of the positive ions corresponds to the protonated molecular ion MH^+. In the CI spectra of the negative ions the principal signal is the signal of the $[M - H]^-$ ions, and the intensity of the peaks of the fragment ions does not exceed 15%. One should note the formation of $[M - H, - C_6H_5]^-$ ions (7-10%) in the case of the fragmentation of ketones III, XII, XIV, and XV and the characteristic $[M - H, - O]^-$ fragments (15%) for 4-oximino-piperidines XVII and XXII.

Thus a study of the dissociative ionization of 2,6-diaryl-4-(oxo,oximino,amino)piperidines I-XXVI has shown that the bulk of the ion current is due to the formation of F_3–F_8 fragments, which bear a positive charge on the piperidine nitrogen atom. Their contribution to the total ion current increases on passing from ketones I-XVI to oximes and aminopiperidines XVII-XXVI. An increase in the volume of the substituent in the 3 position of the ring in the fragmentation of 3-alkyl(phenyl)-2,6-diaryl-4-oxopiperidines I-VI and X-XVI leads to a certain decrease in the percentage of the hydrocarbon fragments (F_1, F_2, $C_6H_5^+$, $C_7H_7^+$) to the total ion current vis-à-vis a simultaneous increase in it of the specific mass of the oxygen-containing F_{10} and F_{11} ions.

The principles of the fragmentation of I-XXVI obtained in this research make it possible to establish the character and mutual orientation of the substituents in the piperidine ring,

as well as the nature of the functional group in the 4 position of the ring, and can be used for analytical purposes.

EXPERIMENTAL

Compounds I-XXVI were synthesized by the method in [15-17]. The mass spectra were obtained with an LKB-2091 spectrometer using a system for the direct introduction of the samples into the ion source; the electron energy was 70 eV, the emission current was 50 μA, and the temperature of the ion source was 250°C under conditions of temperature programming from 50°C to 200°C (v = 10°C/min). The precise values of the masses of the ions were determined relative to PPA with a Varian MAT-311 spectrometer at a resolution of 10,000. The DADI spectra were obtained with a Varian MAT-112 spectrometer with direct introduction of the samples into the source; the electron energy was 70 eV, and the temperature of the ionization chamber was 180°C. The CI mass spectra of the positive and negative ions were obtained by simultaneous recording with a Finnigan-4615 quadrupole mass spectrometer; the ionizing-electron energy was 70 eV, the pressure in the ionization chamber was 93.3 Pa, the input temperature was 100°C, and the reactive gas was ammonia. The deuterium analogs of I, III, IV, XI, and XIV were obtained by refluxing the corresponding ketones in CD_3OD in the presence of KOD for 12 h.

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