# MASS SPECTROMETRIC STUDY OF RING-CHAIN TAUTOMERS OF 3-AMINO(HYDROXY)PYRAZOLIDINES

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The mass spectrometric fragmentation of substituted 3-amino-, 3-hydrazino-, and 3-hydroxypyrazolidines has been studied. In the gas phase these compounds exist partly as the acyclic tautomers.

Ring-chain tautomeric conversions play an important role in organic chemistry [1, 2]. In the study of this kind of conversion it is of considerable interest to investigate the effect of structural factors and state of aggregation on the ease of formation and relative stability of the cyclic and linear tautomers.

Lately, mass spectrometry has been used widely; it enables the content of tautomeric forms to be estimated in the gas phase, where solvation effects and intermolecular interactions are absent. In the presence of individual fragmentation of each possible tautomeric structure, one can estimate even the quantitative proportions of tautomers of molecular ions ($M^+$) from the data on mass spectrometric decomposition [3-7]. A relation has been established between the proportion of tautomeric forms and the state of aggregation of such compounds as substituted azines [4], alkyl(aryl)benzazolylazoketoximes [5], 2-hydroxymorpholines that contain nitrogen and oxygen [6], and oxazolidines and β-diketoximes [7].

It has previously been shown [8, 9] that hydroxypyrazolidines in solution exist mainly in the cyclic form, but their hydrazino derivatives are predominantly linear, and the fraction of the latter form increases with increase of solvent polarity.

It was therefore of interest to study the possible identification of the cyclic and linear forms of such compounds in the gas phase. For this purpose, we obtained and analyzed the mass spectra (Table 1) of the 3-amino(hydrazino)pyrazolidines I-XIV and the hydroxypyrazolidines XV-XVII.

A I-XVII B

It is known that the loss of the radical located in α-position to nitrogen is typical for $M^+$ of pyrazolidines [10] and aminoisoindoles [11]. 2-Hydroxymorpholines in the gas phase show two tautomeric forms of $M^+$; the presence of the linear structure N-(β-hydroxyethyl)-N-(β-oxoethyl)amine is confirmed by the formation of the $[M - CHO]^+$ and $[M - CH_2OH]^+$ ions [6].

Starting from what has been said above and the general concepts of the mass spectrometric behavior of alicyclic and aliphatic compounds containing nitrogen [12], it might be presumed that in such compounds the charge would be localized predominantly on nitrogen. For $M^+$ of form A one might expect scission of the C–X bond to form $[M - R^1XH]^+$; and for $M^+$ of the linear structure B, dissociation of the hydrazine bond and the β-C–C bond to form $[M - HNCOR^2]^+$ and $[M - R^1X = CHCH_2]^+$, respectively.

The mass spectra of compounds I-XIX (Table 1) in all cases contain $M^+$ peaks the stability of which (Table 2) depends only slighly on the electronic properties of the aryl substituent

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TABLE 1. Mass Spectra of Compounds I-XIX*

| Compound | m/z (relative intensity, %) |
|---|---|
| I | 281 (14.0), 238 (7,0), 223 (17,0), 163 (10,0), 150 (17,0), 146 (71,0), 132 (100,0), 120 (28,0), 119 (17,0), 91 (17,0), 77 (43,0) |
| II | 295 (4,0), 237 (4,0), 163 (4,0), 150 (6,0), 146 (100,0), 132 (6,0), 120 (7,0), 118 (10,0), 104 (9,0), 91 (15,0), 77 (15,0) |
| III | 359 (8,0), 301 (9,0), 212 (83,0), 189 (9,0), 163 (22,0), 150 (67,0), 146 (100,0), 130 (67,0), 120 (24,0), 104 (33,0), 77 (58,0) |
| IV | 311 (20,0), 253 (7,0), 162 (100,0), 150 (18,0), 146 (46,0), 135 (14,0), 112 (10,0), 108 (23,0), 104 (10,0), 91 (8,0), 77 (15,0) |
| V | 326 (25,0), 283 (14,0), 268 (13,0), 177 (64,0), 163 (14,0), 150 (100,0), 146 (69,0), 130 (22,0), 108 (30,0), 104 (22,0), 77 (36,0) |
| VI | 295 (0,3), 163 (2,0), 150 (10,0), 146 (100,0), 132 (7,0), 120 (7,0), 118 (5,0), 108 (15,0), 104 (11,0), 91 (15,0), 77 (26,0) |
| VII | 287 (37,0), 243 (17,0), 228 (33,0), 189 (12,0), 163 (33,0), 150 (75,0), 146 (100,0), 139 (100,0), 120 (62,0), 108 (87,0), 104 (33,0) |
| VIII | 292 (9,0), 249 (14,0), 234 (10,0), 177 (60,0), 164 (16,0), 149 (28,0), 129 (8,0), 116 (28,0), 112 (20,0), 92 (23,0), 77 (42,0) |
| IX | 341 (3,0), 191 (17,0), 189 (30,0), 163 (90,0), 150 (28,0), 147 (10,0), 121 (40,0), 119 (12,0), 108 (44,0), 104 (80,0), 77 (60,0) |
| X | 324 (20,0), 266 (10,0), 189 (17,0), 175 (32,0), 163 (60,0), 146 (100,0), 121 (20,0), 108 (16,0), 105 (77,0), 91 (7,0), 77 (50,0) |
| XI | 290 (4,0), 231 (8,0), 155 (4,0), 129 (15,0), 121 (20,0), 113 (14,0), 105 (100,0), 87 (25,0), 77 (50,0), 43 (30,0) |
| XII | 248 (10,0), 189 (17,0), 163 (100,0), 150 (14,0), 146 (22,0), 121 (50,0), 108 (17,0), 104 (67,0), 99 (40,0), 91 (22,0), 77 (39,0) |
| XIII | 214 (3,0), 156 (6,7), 129 (100,0), 105 (17,0), 98 (58,0), 87 (83,0), 85 (21,0), 71 (16,0), 69 (21,0), 59 (29,0), 43 (66,0) |
| XIV | 262 (36,0), 189 (24,0), 163 (100,0), 150 (32,0), 146 (80,0), 121 (32,0), 113 (32,0), 108 (32,0), 104 (31,0), 91 (28,0), 77 (60,0) |
| XV | 206 (29,0), 189 (7,0), 163 (100,0), 150 (37,0), 146 (37,0), 121 (15,0), 108 (64,0), 104 (37,0), 95 (28,0), 91 (37,0), 77 (71,0) |
| XVI | 296 (7,0), 205 (4,7), 191 (45,0), 175 (10,1), 173 (6,5), 148 (12,0), 122 (7,0), 105 (45,0), 104 (8,9), 91 (100,0), 77 (21,0) |
| XVII | 220 (34,0), 178 (47,0), 177 (100,0), 163 (19,0), 160 (15,7), 145 (15,7), 135 (37,5), 118 (28,0), 107 (50,0), 91 (14,0), 77 (56,0) |
| XVIII | 220 (26,0), 177 (100,0), 146 (87,0), 121 (4,0), 119 (6,8), 104 (42,0), 91 (15,0), 77 (75,0), 71 (18,7), 65 (7,7), 43 (31,0) |
| XIX | 234 (18,0), 191 (78,0), 162 (4,6), 146 (100,0), 120 (17,0), 118 (19,0), 107 (16,0), 104 (85,0), 91 (27,0), 77 (90,0), 43 (66,0) |
| $I_D$ | 282 (17,0), 281 (6,7), 223 (16,0), 162 (31,0), 146 (60,0), 133 (76,0), 132 (81,0), 119 (50,0), 104 (78,0), 91 (50,0), 77 (100,0) |
| $XV_D$ | 207 (19,0), 206 (10,0), 163 (60,0), 146 (60,0), 121 (11,0), 119 (10,0), 108 (15,0), 104 (45,0), 91 (27,0), 77 (100,0), 65 (10,0) |

*The molecular ion peak and the 10 most intense peaks are given.

TABLE 2. Intensity of Characteristic Ion Peaks in Mass Spectra of 3-Aminopyrazolidines I-IX, 3-Hydrazinopyrazolidines, and 3-Hydroxy(alkoxy)pyrazolidines X-XIX (% $\Sigma_{39}$)

| Compound* | $R^1$ | $R^3$ | $W_M$ | $\Phi_1$ | $\Phi_2$ | $\Phi_3$ | $\Phi_4$ | $\Phi_5$ | $\Phi_6$ | $\Phi_7$ | $\Phi_8$ | $\Phi_9$ | $\Phi_{10}$ | [A]/[B] | A, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I | $C_6H_5$ | $C_6H_5$ | 2,6 | 0,4 | 11,0 | 2,6 | 1,5 | 0,9 | 15,5 | 0,3 | 4,8 | 2,6 | 9,6 | 2,6 | 72,1 |
| II | 4-$CH_3C_6H_4$ | $C_6H_5$ | 1,9 | 0,2 | 15,6 | 1,0 | 1,0 | 0,2 | 15,6 | 0,4 | 2,7 | 1,0 | 4,7 | 6,6 | 85,7 |
| III | 4-$BrC_6H_4$ | $C_6H_5$ | 1,7 | 0,8 | 8,5 | 1,3 | 1,8 | 0,2 | 14,0 | 0,2 | 2,5 | 0,6 | 4,8 | 2,8 | 73,8 |
| IV | 4-$CH_3OC_6H_4$ | $C_6H_5$ | 1,9 | 0,4 | 9,6 | 1,4 | 3,0 | 0,2 | 19,6 | 19,6 | 1,9 | 0,3 | 3,0 | 2,2 | 69,3 |
| V | 4-$NO_2C_6H_4$ | $C_6H_5$ | 4,3 | 0,3 | 9,4 | 1,7 | 2,0 | 1,9 | 8,7 | 0,3 | 3,0 | 1,4 | 5,0 | 2,4 | 70,0 |
| VI | $CH_2$—$C_6H_5$ | $C_6H_5$ | 0,1 | 0,03 | 14,0 | 0,3 | 0,6 | 0,1 | 14,0 | 0,2 | 3,0 | 0,6 | 7,0 | 12,7 | 92,6 |
| VII | $C_6H_{11}$ (cyclo) | $C_6H_5$ | 1,7 | 0,5 | 3,4 | 0,9 | 1,1 | 0,7 | 2,0 | 0,7 | 1,1 | 1,1 | 1,0 | 1,4 | 59,0 |
| VIII | 4-$NO_2C_6H_4$ | $CH(CH_3)_2$ | 0,9 | 0,2 | 1,1 | 0,6 | 4,8 | 0,8 | 3,4 | 2,1 | 0,9 | 1,2 | 5,8 | 0,2 | 14,7 |
| IX | $HNC_6H_4NO_2$ | $C_6H_5$ | 0,4 | 3,3 | 2,4 | — | 9,0 | 0,1 | 0,5 | 0,5 | 7,3 | 3,0 | 5,0 | 0,6 | 37,5 |
| X | $NHCOC_6H_5$ | $C_6H_5$ | 4,7 | 2,5 | 14,2 | 1,4 | 8,5 | 0,3 | 4,5 | 1,4 | 2,5 | 0,7 | 7,1 | 1,5 | 59,6 |
| XI | $NHCOC_6H_5$ | $CH(CH_3)_2$ | 0,9 | 0,7 | 1,6 | 0,5 | 2,8 | — | 1,1 | 0,2 | 0,5 | 0,5 | 5,6 | 0,7 | 39,6 |
| XII | $N(CH_3)_2$ | $CH(CH_3)_2$ | 0,5 | 2,2 | — | 0,8 | 12,0 | — | 2,5 | 0,5 | 2,0 | 2,5 | 8,0 | 0,2 | 14,2 |
| XIII | $CH(CH_3)_2$ | $C_6H_5$ | 1,5 | 2,0 | 2,6 | 1,6 | 12,0 | — | 4,8 | 0,8 | 8,0 | 0,8 | 3,0 | 0,3 | 23,1 |
| XIV | $NHCOCH_3$ | $C_6H_5$ | 3,5 | 2,0 | 6,8 | 1,2 | 8,5 | 0,2 | 2,7 | 0,7 | 2,7 | 0,7 | 5,1 | 0,8 | 45,8 |
| XV | H | $C_6H_5$ | 2,2 | 0,5 | 2,3 | 0,2 | 3,2** | 3,2 | 5,3 | 0,3 | 2,3 | 1,0 | 4,2 | — | 21,0 |
| XVI | H | $CH_2$—$C_6H_5$ | 2,8 | 0,4 | 1,3 | 1,3 | 0,4 | 11,1 | 0,7 | 0,7 | 2,2 | 3,0 | 25,0 | 0,7 | 41,4 |
| XVII | H | $C_6H_5$ | 6,5 | — | 2,4 | — | 15,5** | 15,5 | 0,4 | — | — | — | 8,7 | — | 100 |
| XVIII | $CH_3$ | $C_6H_5$ | 4,9 | — | 13,4 | — | 0,2 | 15,0 | 3,0 | 0,1 | 6,4 | 1,0 | 11,6 | — | 100 |
| XIX | $C_2H_5$ | $C_6H_5$ | 2,0 | — | 10,0 | — | 0,3 | 7,8 | 3,6 | 0,4 | 8,6 | 0,8 | 9,3 | — | 100 |

* I—XIV XH=NH, XV—XIX XH=O; I—XV, XVII—XIX $R^2=CH_3$, XVI $R^2=C_6H_5$; I—XV, XVIII, XIX $R^4=H$, XVI XVII $R^4=CH_3$.

**Ions $\Phi_4$ and $\Phi_5$ identical in elemental composition.

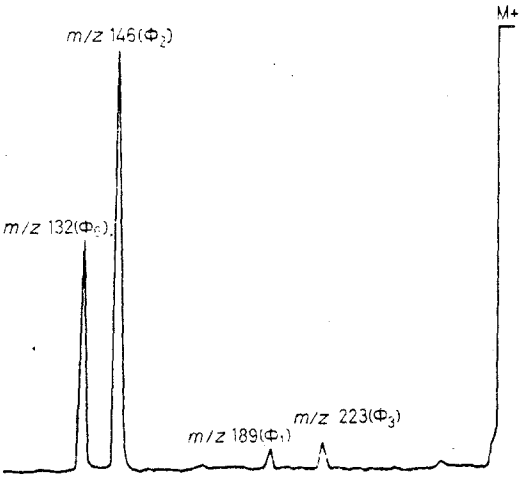
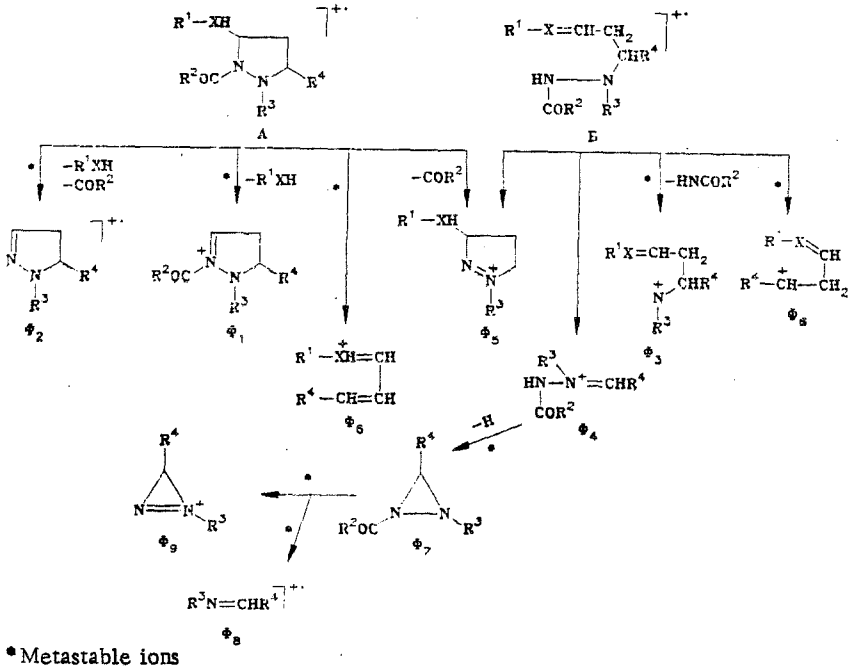



Fig. 1. DADI spectrum of the molecular ion of compound I.

Scheme



*Metastable ions

and of $R^1$, and decreases when the aromatic radical at the nitrogen at position 1 is replaced by an aliphatic substituent (isopropyl, Table 2). In the spectra of these compounds one might expect to find $[M - HNC(OH)R^2]^+$ (the MacLafferty rearrangement), but such fragments do not appear. Consequently, in $M^+$ conformational rearrangement must be slower than dissociation of the corresponding bonds. The mass spectra of I-XVI contain the fragment ions $\Phi_1$-$\Phi_4$ and $\Phi_6$, that are typical for $M^+$ of both cyclic and linear tautomers (see diagram). Study of the mass spectra of the metastable ions by the DADI technique [13, 14] enabled us to establish that ions $\Phi_1$-$\Phi_3$ and $\Phi_6$ form in one step directly from $M^+$ (Fig. 1).

Analysis of the mass spectra of deutero derivatives I and XV showed that ions $\Phi_1$, $\Phi_2$, $\Phi_3$, and $\Phi_7$ contain no deuterium, and the peaks corresponding to ions $\Phi_4$ and $\Phi_5$ are shifted by one unit toward larger masses. In $\Phi_6$ deuterium is only partially retained; this confirms that $\Phi_6$ can form from either form A or form B.

To confirm the proposed scheme of ion fragmentation, mass spectra were obtained of known fixed cyclic forms, viz., the 1-phenyl-2-acetyl-3-methoxy(ethoxy)pyrazolidines XVIII and XIX Their mass spectra are characterized by intense peaks of ions $\Phi_1$, $\Phi_2$, $\Phi_5$, and $\Phi_6$, but $\Phi_3$ and $\Phi_4$ do not appear; the fragmentation sequence of $M^+$ and the fragment ions was established by a study of the mass spectra of the metastable ions by the DADI method.

Thus, it can be concluded that $M^+$ of compounds I-XVI in the gas phase exists in two tautomeric forms, cyclic A and linear B (Scheme).

For a quantitative estimate of the proportions of forms A and B in the gas phase we used ions $\Phi_1$ and $\Phi_2$ (cyclic form A) and $\Phi_3$, $\Phi_4$ and $\Phi_7$ (form B), and the fraction of cyclic A was determined from the ratio: A, % = $(\Phi_1 + \Phi_2/\Phi_1 + \Phi_2 + \Phi_3 + \Phi_4 + \Phi_7) \cdot 100$. In the case of compound XV, ion $\Phi_4$ was not included in the quantitative estimate of tautomer ratio because its elemental composition is the same as that of $\Phi_5$.

From Table 2 it follows that the introduction of either electron donor or electron acceptor substitutents into the phenyl group (radical $R^1$) does not affect the tautomer ratio in the gas phase (compounds I-V). Replacement of the aryl residue by benzyl (compound VI) increases the content of cyclic $M^+$, whereas in the case of alicyclic $R^1$ there is an appreciable increase in the fraction of linear $M^+$. The quantitative tautomer ratio changes sharply when the phenyl radical and the nitrogen at position 1 are replaced by isopropyl. This confirms the assumption given above that the positive charge is localized predominantly on the pyrazolidine ring nitrogens.

In contrast to aminopyrazolidines, in hydrazinopyrazolidines IX-XIV in the gas phase the fration of $M^+$ in form B increases, and it becomes preponderant in the spectrum of XII (Table 2).

According to our data the 3-hydroxypyrazolidines XV and XVI are present in the gas phase predominantly as noncyclic form B, in contrast to solutions [8].

The appearance of the $M^+$ tautomers in the gas phase may result from the different volatilities of the forms, which may cause the gas mixture to be enriched in the less polar form. Furthermore, we should not exclude the possibility of rearrangements taking place in $M^+$ itself; these can also cause the ions that are typical of the second tautomer to appear in the spectrum. In this connection, we obtained and analyzed the mass spectrum of hydroxypyrazolidine XVII, the crystal structure of which has been established by x-ray diffraction analysis to be cyclic only. As follows from the data of Table 3, in the gas phase this compound is exclusively in the cyclic form. Thus, the factors given above, at least for the compounds that we have studied, do not play a significant role, and the ratio of $M^+$ tautomeri forms observed in the gas phase in all probability quite accurately reflects the true ratio of tautomers of neutral molecules in the absence of solvating and intermolecular interactions

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