ELSEVIER

Evidence for the formation of acyclic ions from the radical cations and cyclic ions from the protonated molecules of α,ω-diamines upon loss of ammonia

Ana M. Fernandes [a],[*],[1], A.J. Ferrer Correia [a], Roel H. Fokkens [b], Nico M.M. Nibbering [c]

[a] *Departamento de Química, Universidade de Aveiro, 3810-193 Aveiro, Portugal*
[b] *Laboratory of Supramolecular Chemistry and Technology, University of Twente, 7500 AE Enschede, The Netherlands*
[c] *Laser Centre and Chemistry Department, Vrije Universiteit, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands*

Dedicated to the late Professor Pierre Longevialle for his important contributions to gas-phase ion chemistry and mass spectrometry.

Abstract

The structural characterization of the ions generated by the electron ionization-induced loss of ammonia from the molecular ions of α,ω-diamines, using ion/molecule reactions in combination with collision-induced dissociation (CID) studies, is described. The results of the experiments of ion/molecule reactions using dimethyl disulfide exclude the distonic radical cation structure for those long-lived ions proposed earlier by other authors for ions generated within a few microseconds following ionization. The unimolecular and CID characteristics of the ions $[M–NH_3]^{\bullet+}$ of 1,4-diaminobutane and 1,5-diaminopentane and of their fragment ion $m/z = 56$, are discussed in terms of the structures $CH_3CH_2CH=CHNH_2^{\bullet+}$ and $CH_3CH_2CH_2CH=CHNH_2^{\bullet+}$ for the ions $[M–NH_3]^{\bullet+}$, respectively. The structure of the closed shell ions resulting from loss of ammonia from the protonated α,ω-diamines was also probed through the CID spectra of model ions prepared by chemical ionization with methane in the chemical ionization source of the mass spectrometer. (Int J Mass Spectrom 217 (2002) 55–63) © 2002 Elsevier Science B.V. All rights reserved.

Keywords: α,ω-Diamines; Ion structures; Collision-induced dissociation; Ion/molecule reactions; Ammonia loss

1. Introduction

In a paper published in 1976, Mayerl and Hesse [1] proposed distonic cyclic structures for the ions generated by the electron ionization-induced loss of NH_3 from the molecular ions of 1,4-diaminobutane and 1,5-diaminopentane. Distonic ions [2,3] only started to receive considerable attention in the early 1980s

when a few papers were published demonstrating the existence of stable isomers of the radical cations of methanol, methylamine and methyl chloride with the unusual structures, $CH_2OH_2^{\bullet+}$ [4,5], $CH_2NH_2^{\bullet+}$ [6,7] and $CH_2ClH^{\bullet+}$ [8], respectively. The term distonic ions, introduced in 1984 by Yates and co-workers [9], refers to ions that formally arise by removal of an electron from a zwitterion or a diradical. The interest in these species is explained by their stability, since theoretical and experimental results have shown that distonic radical ions can be more stable than their isomers with conventional structures, and also by the

---

* Corresponding author. E-mail: afernandes@dq.ua.pt
[1] Previous publications have appeared under the name Ana M. Cardoso.

fact that there are no stable neutral molecules from which they can be formed by ionization. However, they are quite common since radical cations can isomerize to distonic ions prior to fragmentation, the products of fragmentation reactions are often distonic ions [2,3] and their intermediacy in rearrangement processes has also been described [10]. The mass spectrometric methods used to identify distonic ions have been diverse and include: determination of heats of formation, ab initio calculations [11], unimolecular and collision-induced dissociation (CID) characteristics [12], analysis of neutralization reionization spectra [13] and ion/molecule reactions [14]. As far as we know, since Mayerl and Hesse's [1] paper, there were no further studies on the $[M–NH_3]^{\bullet+}$ ions of α,ω-diamines in order to confirm their possibly long-lived distonic cyclic structure. However, indirect evidence has been provided that from the molecular ion of N,N,N',N'-tetramethyl-1,4-diaminobutane the even-electron and cyclic N,N-dimethylpyrrolidinium ion is generated by the loss of a dimethylamino radical [15].

This paper describes several mass spectrometric experiments, such as unimolecular and CIDs and ion/molecule reactions performed on the $[M–NH_3]^{\bullet+}$ from 1,4-diaminobutane and 1,5-diaminopentane to probe their possibly distonic radical ion structure. In order to compare the behavior of radical cations and closed shell ions the structural characterization of the ions resulting from loss of NH_3 from the protonated 1,4-diaminobutane and 1,5-diaminopentane, in a chemical ionization source, is also described.

2. Experimental

1,4-Diaminobutane dihydrochloride was purchased from Merck and used without further purification. The dihydrochloride salt of 1,5-diaminopentane (Merck) was prepared by shaking 1,5-diaminopentane with a 1:1 mixture of hydrochloric acid and ethanol. To this solution petroleum ether was added until precipitation occurred, the volume was reduced, the solution cooled and the crystals filtered.
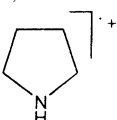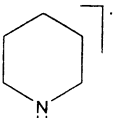
All mass spectrometric measurements were performed with use of instruments at the former Institute of Mass Spectrometry of the University of Amsterdam, The Netherlands.

Accurate mass measurements were performed on a VARIAN MAT 711 conventional geometry double focusing mass spectrometer. The operating parameters were: electron energy 70 eV, ion source temperature 150–200 °C and a resolution of 15,000 (10% valley definition).

Electron ionization mass spectra, mass analyzed ion kinetic energy (MIKE) and CID spectra were obtained with use of a Micromass ZAB-2HF coupled to a Micromass 11/250 data system under the following operating conditions: accelerating potential 8000 V, electron energy 70 eV and ion source temperature of 200 °C. The MIKE spectra were obtained by varying the electrostatic analyzer voltage, the main beam energy being 8000 eV. The CID spectra were obtained using helium as a collision gas at a pressure such that the intensity of the main beam was reduced by 50%. The chemical ionization mass spectra were obtained with use of the same instrument using methane as a reagent gas at a source housing ion gauge indicated pressure of 5×10^{-6} Torr. In all measurements the samples were introduced via a heated inlet system at temperatures 150–200 °C.

All Fourier transform ion cyclotron resonance (FTICR) experiments were performed by using a Bruker Apex 47e FTICR mass spectrometer (Bruker Daltonics, Billerica, USA) equipped with a 4.7 T superconducting magnet and an external ion source. Instrument details have been reported previously [16]. 1,4-Diaminobutane, 1,5-diaminopentane and the other compounds listed in Table 1 were generated in the external ion source by 70 eV electron ionization. Subsequently, the generated ions were gated for 70 ms to the FTICR cell where they were trapped and thermalized 80 ms by a pulsed valve addition of nitrogen gas to a pressure of about 10^{-4} mbar followed by a pump-down time of about 100 ms. Next, only $m/z = 71$ or 85 was isolated from the mixture of ions. This was accomplished by ejecting all other ions from the FTICR cell using the correlated RF irradiation

Table 1
Reactions of ions given in the first column with dimethyl disulfide

| Ion	m/z	Product ion m/z	Reaction[a]
[M–NH$_3$]$^{\bullet+}$	71	94, 96	Electron transfer
1,4-Diaminobutane		95, 97	Formal H$^+$ transfer
	71	94, 96	Electron transfer
		95, 97	Formal H$^+$ transfer
[M–NH$_3$]$^{\bullet+}$	85	94, 96	Electron transfer
1,5-Diaminopentane		95, 97	Formal H$^+$ transfer
	85	94, 96	Electron transfer
		95, 97	Formal H$^+$ transfer

[a]The formal H$^+$ transfer most probably corresponds with a successive electron transfer and hydrogen abstraction, see text.

[16], avoiding unwanted off-resonance excitation of the selected ions [17]. The selected ions were allowed to react with dimethyl disulfide molecules, admitted to the FTICR cell through a leak-valve, up to partial pressures of about 1.5×10^{-8} mbar (ion gauge manometer reading) with a background pressure of about 10^{-9} mbar.

3. Results and discussion

3.1. Structural elucidation of the ions [M–NH$_3$]$^{\bullet+}$ of 1,4-diaminobutane and 1,5-diaminopentane

The mechanism proposed by Mayerl and Hesse [1] for the elimination of NH$_3$ from the molecular ion of 1,4-diaminobutane is shown in Scheme 1. They
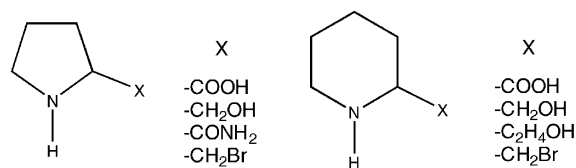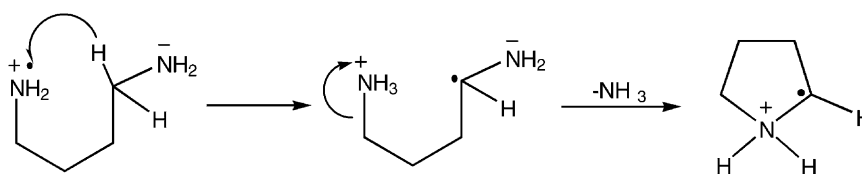
Scheme 2.

based their assumption that hydrogen radical abstraction occurs from the methylene groups in positions 1 or 4, on the shifts observed in the electron ionization spectra of 1,1,4,4-tetradeuterodiaminobutane and 2,2,3,3-tetradeuterodiaminobutane.

The studies on the structural elucidation of the [M–NH$_3$]$^{\bullet+}$ ions ($m/z = 71$ for 1,4-diaminobutane and $m/z = 85$ for 1,5-diaminopentane) described in the present paper, began by extending the labeling with deuterium to the amino groups. The MIKE spectrum of the ion $m/z = 92$ (D$_2$N(CH$_2$)$_4$ND$_2$$^{\bullet+}$) shows a cluster of peaks at $m/z = 72$, 73, 74 and 75 where the loss of 20 Da (ND$_3$ or eventually ND$_2$H + H$^{\bullet}$) represents only 7% of the sum of the intensities of the peaks that compose this cluster. From this observation it can be concluded that the participation of hydrogen atoms from the amino group, in the elimination of NH$_3$ is non-significant.

Assuming that the [M–NH$_3$]$^{\bullet+}$ ions are distonic, the strategy used was the comparison of their CID spectra with the CID spectra of reference distonic ions prepared inside the ion source of a mass spectrometer by a simple and clear one step fragmentation of the molecular ions of the model compounds indicated in Scheme 2.

From the analysis of the electron ionization mass spectra of these compounds the dominant fragmentation is α-cleavage with loss of the substituent and
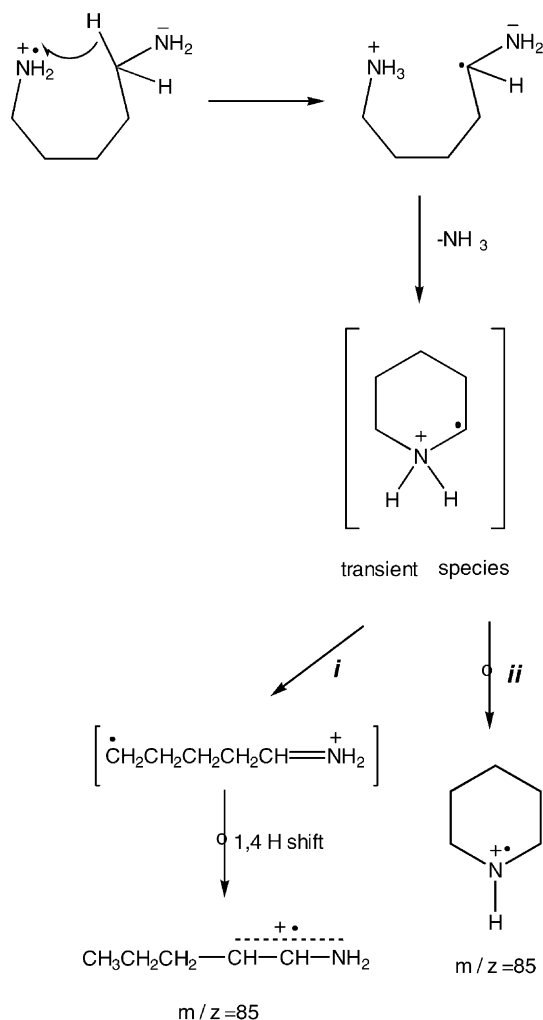
Scheme 1.

formation of a protonated imine. Ions $m/z = 71$ and 85 have, in most cases, an abundance close to the expected ^{13}C contribution from the adjacent peak. When $X = CH_2Br$, ion $m/z = 71$ is observed with a relative peak intensity of 11%. However, the origin of this ion could not be ascertained, so there was no suggestion for its structure on mechanistic grounds. Chemical ionization or fast atom bombardment were also used as ionization methods, expecting that protonation would occur on the nitrogen atom followed by possible loss of the substituent. However, no $m/z = 71$ and 85 ions were observed.

Ion/molecule reactions represent another strategy that can be used in the positive identification of distonic radical ions. One of the most interesting bimolecular reactions used to positively identify distonic ion structures is the reaction with dimethyl disulfide [18,19]. A variety of ions with conventional and distonic ion structures has been investigated and the observations are that conventional radical cations react by charge exchange with dimethyl disulfide, while distonic ions abstract $CH_3S^\bullet$. Assuming a ring-closed distonic radical cation structure for the long-lived $[M–NH_3]^{\bullet+}$ ions of 1,4-diaminobutane and 1,5-diaminopentane, the isomers with a conventional radical cation structure would be the molecular ions of pyrrolidine and piperidine, respectively, as generated upon electron ionization. The reactions of these four ions with dimethyl disulfide have been performed in a FTICR mass spectrometer under conditions described in Section 2. The results presented in Table 1 show that no $CH_3S^\bullet$ abstraction occurs in any case. On the contrary, both ions react in a very similar way with CH_3SSCH_3 by charge exchange generating the ions $m/z = 94$ and 96 which in part may react further by hydrogen atom abstraction from either the neutral species in the collision complex or the neutral compounds present in the FTICR cell to give ions $m/z = 95$ and 97. The latter is supported by the observation that the peaks at $m/z = 94$, 95, 96 and 97 are already present at short reaction times and that the peaks at 95 and 97 only slowly increase at longer reaction times. Anyhow, the absence of $CH_3S^\bullet$ abstraction in the reaction with dimethyl

disulfide rules out a distonic radical ion structure (cyclic or acyclic) for the long-lived ions $[M–NH_3]^{\bullet+}$ of 1,4-diaminobutane and 1,5-diaminopentane.

This observation suggests that after the initial hydrogen atom abstraction which is followed by NH_3 loss (see first step in Scheme 1), the fragment ion isomerizes to a radical cation with a conventional structure. Two possible pathways are proposed and exemplified for 1,5-diaminopentane in Scheme 3.

In pathway (i), the supposed initially generated cyclic distonic ion as transient species undergoes ring opening to give an acyclic radical cation, having the

Scheme 3.

Table 2
MIKE spectra[a] of the ions [M–NH₃]$^{\bullet+}$ of 1,4-diaminobutane and 1,5-diaminopentane

Amine	m/z of fragment ions				
	30	43	44	56	70
H₂N〜〜〜NH₂	–	70%	13%	17%	–
H₂N〜〜〜〜NH₂	4%	19%	<1%	75%	<1%

[a]The relative abundances are expressed as the percentage of the sum of the intensities of all fragment ions.

Table 3
Accurate mass measurements on the ions $m/z = 43$ and 56 of 1,4-diaminobutane and 1,5-diaminopentane

| Ion	Amine	El. composition	Calc. mass	Exp. mass	Error (ppm)
56	$H_2N(CH_2)_4NH_2$	C_3H_6N	56.050024	56.04997	−1
	$H_2N(CH_2)_5NH_2$	C_3H_6N	56.050024	56.04997	−1
43	$H_2N(CH_2)_4NH_2$	C_3H_7 (8%)	43.054775	43.05529	12
		C_2H_5N (72%)	43.042199	43.04304	20
	$H_2N(CH_2)_5NH_2$	C_2H_5N	43.042199	43.04312	21

structure of an α-cleaved aminocyclopentane, which then through a 1,4-hydrogen shift rearranges to a stable radical cation with an enamine structure. Pathway (ii) assumes isomerization of the cyclic distonic ion as transient species to the radical cation of piperidine. To probe the piperidine (and pyrrolidine) structures, the collision-induced dissociation spectra of the molecular ions of piperidine (and pyrrolidine) have been compared with the collision induced dissociation spectra of the ions $m/z = 85$ and 71 of 1,5-diaminopentane and 1,4-diaminobutane, respectively. The spectra are shown in Fig. 1 and their differences are so marked that the pyrrolidine and piperidine structures can be ruled out for the ions m/z 71 and 85, respectively.

The unimolecular dissociation characteristics of ions $m/z = 71$ and 85, shown in Table 2, might give some insight into the structure of these metastable ions. Accurate mass measurements have been performed on the ions of $m/z = 43$ and 56 formed inside

the ion source, for both diamines, and the results are presented in Table 3.

MIKE and CID spectra, as well as ab initio calculations have been used in the characterization of five ion structures for the $C_3H_6N^+$ cations ($m/z = 56$) [20]. The elucidation of the structure of the $C_3H_6N^+$ ion generated by loss of an ethyl group from the [M–NH₃]$^{\bullet+}$ ion ($m/z = 85$) of 1,5-diaminopentane might support the proposed enamine structure for ion $m/z = 85$ (Scheme 4).

The model compound chosen to probe the structure of the ion $m/z = 56$ of 1,5-diaminopentane has been allylamine since the [M-H]$^+$ ions will have the structure $CH_2=CH–CH=NH_2^+$. The CID spectra of the ions $m/z = 56$ from allylamine and 1,5-diaminopentane are presented in Table 4. Excluding the contributions of the unimolecular decompositions observed for both ions to the CID spectra, the similarity of the relative abundances of the fragment
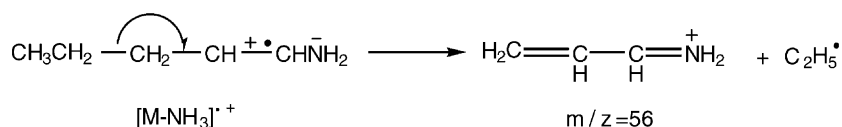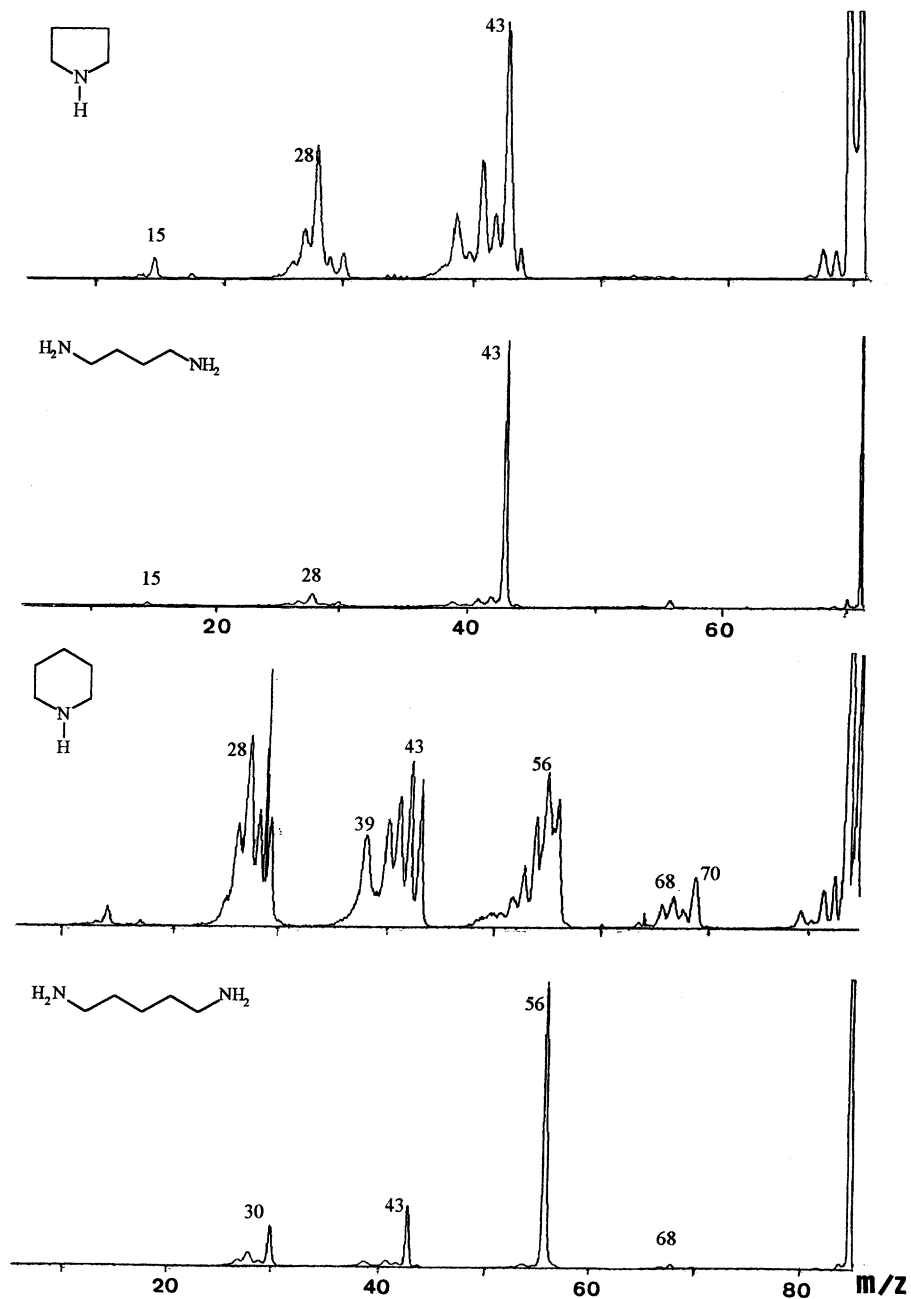

Scheme 4.

Fig. 1. CID spectra of the molecular ions of pyrrolidine, piperidine and of the $[M–NH_3]^{\bullet+}$ of 1,4-diaminobutane and 1,5-diaminopentane.

Table 4
CID spectra[a] of the $[M–H]^+$ ion of allylamine (A) ($m/z = 56$) and of the fragment ion $m/z = 56$ from 1,5-diaminopentane (B)

Amine	m/z of fragment ions											
	15	25	26	27	30	37	38	39	40	51	52	54
A	1%	2%	9%	16%	8%	3%	5%	10%	3%	3%	8%	25%
B	1%	1%	9%	19%	8%	3%	5%	12%	2%	2%	8%	28%

[a]The peaks corresponding to the unimolecular decompositions observed in the MIKE spectra have been excluded from the calculations of the relative abundances. The relative abundances are expressed as the percentage of the sum of the abundances of all fragment ions in which the abundances <1% are not included.

ions of $m/z = 56$, points strongly to an identical structure.

In conclusion, direct evidence is presented that the long-lived $[M–NH_3]^{\bullet+}$ ions of both diamines do not have a distonic radical cation structure. The hypothesis of isomerization to a conventional cyclic structure is also eliminated on the basis of the results of the CID spectra of pyrrolidine and piperidine. Although direct evidence for the enamine structure is not presented due to the difficulty of obtaining a suitable model compound (several attempts have been made to synthesise 2-*n*-propylcyclobutylamine to generate by electron ionization the enamine ion structure m/z 85 as reference ion, but unfortunately they have failed), the elucidation of the structure of ion $m/z = 56$ strongly supports that the $[M–NH_3]^{\bullet+}$ ions of both diamines have the proposed enamine structure.

3.2. Structural elucidation of the ions $[M + H–NH_3]^+$ of 1,4-diaminobutane and 1,5-diaminopentane

In the chemical ionization mass spectra of the α,ω-diamines described in the literature, the most abundant fragment ion corresponds to loss of NH_3 [21]. Audier et al. [22] and Weinkam [23] proposed a cyclic structure for these ions based on the comparison of estimated heats of formation of several hypothetical cyclic and acyclic structures for the $[M + H–NH_3]^+$ ions.

The studies, described in the previous section for the radical cations generated by loss of ammonia from the EI generated molecular ions of 1,4-diaminobutane and 1,5-diaminopentane, have been extended to the closed shell ions produced by ammonia loss from the
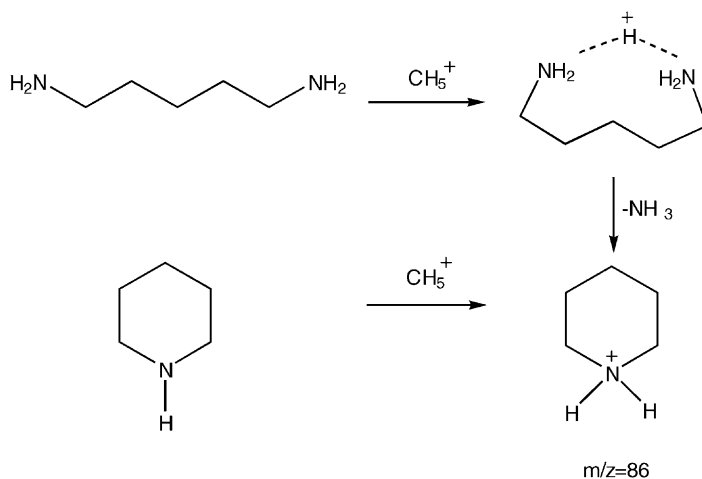
Scheme 5.

protonated α,ω-diamines. The compounds have been protonated with CH_5^+ in a chemical ionization source and the only fragment ion observed in the MIKE spectra of the $[M + H]^+$ corresponds to loss of ammonia. To probe experimentally the cyclic structure proposed previously by other authors [22,23], the CID spectra of protonated pyrrolidine and piperidine were compared

with the CID spectra of the ions $[M + H–NH_3]^+$ of 1,4-diaminobutane and 1,5-diaminopentane, respectively (Scheme 5).

The results are exemplified for piperidine and 1,5-diaminopentane in Fig. 2. Excluding the peaks due to the contributions of unimolecular decompositions, the spectra are almost superimposable which confirms
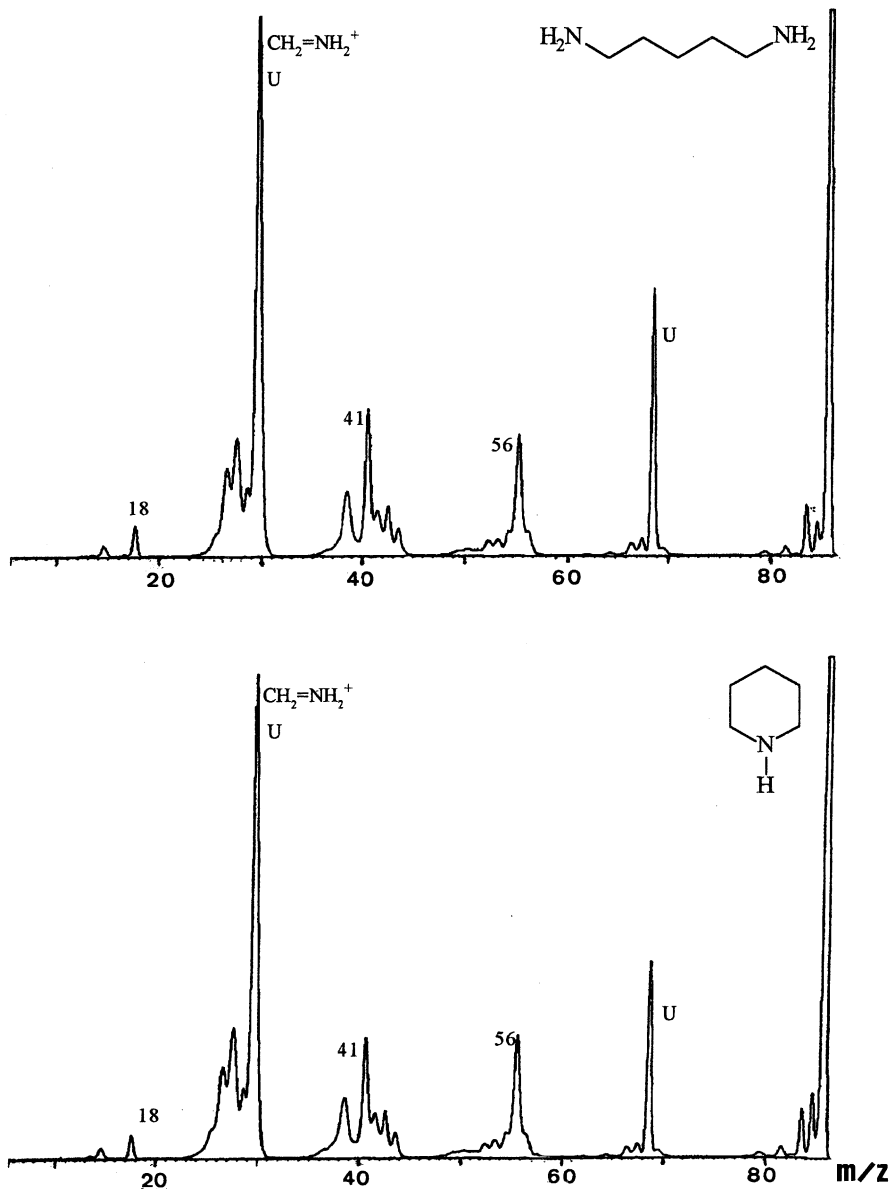

Fig. 2. CID spectra of ions $[M + H–NH_3]^+$ of 1,5-diaminopentane ($m/z = 86$) and $[M + H]^+$ of piperidine ($m/z = 86$).

experimentally the assumptions made earlier that the $[M + H–NH_3]^+$ ions of 1,5-diaminopentane have a cyclic structure [22,23]. This conclusion is also valid for the $[M + H–NH_3]^+$ ions of 1,4-diaminobutane.

4. Conclusions

The results described in this paper present strong evidence for an enamine type structure for the long-lived ions generated by loss of NH_3 from the radical cations of 1,4-diaminobutane and 1,5-diaminopentane, while the loss of ammonia from the protonated diamines generates ions with the structure of protonated pyrrolidine and piperidine, respectively. For the $[M–NH_3]^{\bullet+}$ radical cations the enamine formation is probably due to a very fast ring opening of the supposed initially generated cyclic distonic ions as transient species followed by a 1,3-hydrogen shift in the case of 1,4-diaminobutane and a 1,4-hydrogen shift in the case of 1,5-diaminopentane, leading to a resonance stabilized enamine structure for these ions. In the protonated molecules the existence of a hydrogen bond between the two amino groups upon protonation might bring the protonated molecule to a conformation appropriate for cyclization during the ammonia loss probably occurring via an intramolecular S_N (i) type substitution reaction.

References

[1] F. Mayerl, M. Hesse, Helv. Chim. Acta 59 (1976) 127.

[2] S. Hammerum, Mass Spectrom. Rev. 7 (1988) 123.

[3] H.L. Kenttamaa, Org. Mass Spectrom. 29 (1994) 1.

[4] W.J. Bouma, R.H. Nobes, L. Radom, J. Am. Chem. Soc. 104 (1982) 2929.

[5] W.J. Bouma, J.K. MacLeod, L. Radom, J. Am. Chem. Soc. 104 (1982) 2930.

[6] J.L. Holmes, F.P. Lossing, J.K. Terlouw, P.C. Burgers, J. Am. Chem. Soc. 104 (1982) 2931.

[7] W.J. Bouma, J.M. Dawes, L. Radom, Org. Mass Spectrom. 18 (1983) 12.

[8] J.L. Holmes, F.P. Lossing, J.K. Terlouw, P.C. Burgers, Can. J. Chem. 61 (1983) 2305.

[9] L. Radom, W.J. Bouma, R.H. Nobes, B.F. Yates, Pure Appl. Chem. 56 (1984) 1831.

[10] A.M. Cardoso, A.J. Ferrer Correia, R.H. Fokkens, N.M.M. Nibbering, J. Am. Soc. Mass Spectrom. 1 (1990) 104.

[11] B.F. Yates, W.J. Bouma, L. Radom, Tetrahedron 42 (1986) 6225.

[12] T. Bjornholm, S. Hammerum, D. Kuck, J. Am. Chem. Soc. 110 (1988) 3862.

[13] C. Wesdemiotis, P.O. Danis, R. Feng, J. Tso, F.W. McLafferty, J. Am. Chem. Soc. 107 (1985) 8059.

[14] K.M. Stirk, L.K.M. Kiminkinen, H.I. Kenttamaa, Chem. Rev. 92 (1992) 1649.

[15] L. Frøsig, F. Turecek, J. Am. Soc. Mass Spectrom. 9 (1998) 242.

[16] L.J. de Koning, N.M.M. Nibbering, S.L. van Orden, F.H. Laukien, Int. J. Mass Spectrom. Ion Proc. 165/166 (1997) 209.

[17] A.J.R. Heck, L.J. de Koning, F.A. Pinkse, N.M.M. Nibbering, Rapid Commun. Mass Spectrom. 9 (1991) 406.

[18] K.M. Stirk, J.C. Orlowski, D.T. Leeck, H.I. Kenttamaa, J. Am. Chem. Soc. 114 (1992) 8604.

[19] J. Kauw, M. Born, S. Ingemann, N.M.M. Nibbering, Rapid Commun. Mass Spectrom. 10 (1996) 1400.

[20] G. Bouchoux, J.P. Flament, Y. Hopilliard, J. Tortajada, R. Flammang, A. Maquestiau, J. Am. Chem. Soc. 111 (1989) 5560.

[21] R.J. Weinkam, J. Org. Chem. 43 (1978) 2581.

[22] H.E. Audier, A. Milliet, C. Perret, J.C. Tabet, P. Varenne, Org. Mass Spectrom. 13 (1978) 315.

[23] R.J. Weinkam, Biomed. Mass Spectrom. 5 (1978) 334.