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PROTON AFFINITY DETERMINATIONS AND PROTON - BOUND DIMER STRUCTURE INDICATIONS IN C_2 TO C_{15}, α,ω-ALKYLDIAMINES

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ABSTRACT

The "kinetic method" was used to determine the proton affinity (PA) of α,ω-alkyldiamines from collision induced dissociation (CID) studies of protonated heterodimers. These PA values were consistently lower than those reported in the proton affinity scale. The apparent discrepancy was rationalized in terms of differences in the conformation of the protonated diamine monomers. The minimum energy species, formed by equilibrium proton transfer processes, have a cyclic conformation and the ion charge is shared by both amino-groups which are bridged by the proton. On the other hand, the species formed through dissociation of protonated dimers have a linear structure and the charge is localized on one of the amino-groups. Thus, the difference in the PA values obtained by both methods is a measure of the additional stability acquired by the protonated diamines through cyclization and charge delocalization.

The major collision dissociation pathway of the protonated diamine monomers involved elimination of an ammonia moiety. Other reactions observed included loss of the second amino-group and several other bond cleavages. CID of the protonated dimers involved primarily formation of a protonated monomer through cleavage of the weaker hydrogen bond and subsequently loss of ammonia at higher collision energies. As observed from the CID studies, doubly charged ions were also formed from the diamines under conditions of the electrospray ionization.

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INTRODUCTION

The "kinetic method"

The "kinetic method" has been used to obtain thermodynamic data on ions, as described in detail elsewhere [1-11]. Originally it was used to study the dissociation of proton bound dimers in the field free region of a reverse geometry magnetic mass spectrometer, but subsequently collision induced dissociation (CID) methods were also successfully deployed [9-10]. The kinetic method was used to study the proton affinities (PAs) of aliphatic and aromatic amines [1-2], the acidity of carboxylate anions [3,10], alkoxide ions [4,11] and nitrates [5], to differentiate between stereo isomers and determine alkali ion affinities [6,7] and the PAs of amino acids [8,9].

The basis of the method is to compare the rates of competitive dissociation channels (1a) and (1b), as represented by reaction (1):

$$A\cdot\cdot H^{+}\cdot\cdot B \text{ -----} \begin{cases} \text{--->}\ A + BH^{+} & (1a) \\ \text{--->}\ AH^{+} + B & (1b) \end{cases}$$

It was demonstrated that a linear relationship existed between the logarithm of the product ion peak height ratios AH^{+}/BH^{+} and the proton affinities of the fragments, A and B. The underlying logic was that for similar species A and B the competitive fragmentation of the protonated dimer should have similar entropy changes and that the reverse activation energy would be small as the reaction involves a simple bond cleavage process. Therefore the rate of fragmentation in each channel should be controlled by the relative activation energies, i. e. it should be proportional to the proton affinity difference:

$$PA_{(A-B)} = \ln(AH^{+}/BH^{+}) * R\,T \qquad (2)$$

where, $PA_{(A-B)}$ is the difference between the proton affinities of compounds A and B, $\ln(AH^{+}/BH^{+})$ is the natural logarithm of the intensity ratio of the protonated free bases (monomers) formed by dissociation of the mixed protonated dimer, R is the gas constant and T is the effective temperature.

However, some caution must be practiced as the site through which hydrogen bonding occurs in the proton bound dimer may not necessarily be the same as site of protonation in the free base. Whenever this is the case, discrepancies between PA values obtained by kinetic methods and by "classic" thermodynamic equilibrium or bracketing methods may occur.

It was shown recently that there was good agreement between these methods and the results obtained from CID studies [11]. It was also noted that special care had to be taken when the effective ion temperature was calculated, as, for example, differences in the temperature were observed between primary and secondary alcohols [11].

Diamines

Diamines, particularly α,ω-diamines, are placed close to the top of the NIST proton affinity (PA) scale, which is the most comprehensive compilation of such data [12]. The evaluated PAs from this compilation are shown in Table 1. Proton affinities of these compounds were calculated by Aue *et. al.* [13] who invoked intramolecular hydrogen bonding (proton bridging) to rationalize the high gas-phase basicities of the diamines. Experimental results from equilibrium measurements of four diamines, relative to dimethylamine and trimethylamine, in a high pressure ion source of a mass spectrometer were reported by Yamadagni and Kebarle [14]. The PA values of 1,2-

diaminoethane, 1,3-diaminopropane, 1,5-diaminopentane and 1,7-diaminoheptane were given as 234.9, 243.3, 243.3 and 243.3 kcal/mol, respectively, in that work. These high values arose, in part, from the high PA values assigned to the reference compounds (for example, the PA of n-butylamine was taken as 222.8 vs 218.4 kcal/mol in the NIST database [12]. Later Lau *et. al.* [15] reported the gas-phase basicity of 1,5-diaminopentane as being 26.2 kcal/mol above that of ammonia, i.e. (195.6+26.2) 221.8, quite close to the previously reported values. Using similar experimental methods, Meot-Ner *et. al.* [16] gave the PA values for 1,2-diaminoethane, 1,3-diaminopropane and 1,4-diaminobutane as 227.8, 235.3 and 239.5 kcal/mol, respectively.

EXPERIMENTAL

The work was carried out on an API-III triple quadrupole atmospheric pressure ionization mass spectrometer fitted with an Ionspray (pneumatically assisted electrospray ionization source) made by Sciex (Thornhill, Ontario, Canada) shown schematically in Figure 1. The triple quadrupole instrument and operating procedures were described in detail earlier [17]. The proton-bound monomers and dimers enter the vacuum system through a small orifice (OR) and are then introduced into the first mass spectrometer (Q1) via a quadrupole ion lens (Q0). The ion of interest was mass selected by appropriately tuning Q1 to allow only a single m/z ion to enter the collision region, the second quadrupole, Q2. This mass spectrometer is operated in the RF-only mode and acts as an ion-confining lens. By introducing controlled levels of argon into Q2 the mass-selected ions are forced to collide with the inert gas molecules and some of them undergo collision induced dissociation (CID). The third mass spectrometer, Q3, is used to measure the masses and intensities of the ions leaving Q2, i. e. the undissociated parent ion and the fragment (or product) ions formed through CID processes. The peak intensities are reported relative to the most abundant peak in the spectrum. It should be noted that the API-III has a unique pumping system, based on liquid helium cooled cryogenic surfaces.

All the compounds studied here, ranging from 1,2-diaminoethane to 1,10-diaminodecane, were commercially available from Aldrich and were used without purification. Protonated molecules and proton-bound clusters corresponding to heavier diamines, with 11 to 15 carbons, were also observed in the mass spectra of the longer chain diamines. Their presence made it possible to expand this study well beyond the range of the purchased chemicals. The compound, or compounds, of interest were dissolved in a 50:50 water-methanol mixture, and the solution was injected into the electrospray ionization source at a rate of 5 microliter/minute.

Procedure

The proton bound dimer was mass selected in the first mass spectrometer. The intensity ratio between the signals of the two protonated monomers into which it fragmented was measured. The natural logarithm of this ratio was multiplied by the effective temperature, T, and the gas constant, R (0.083 kJ/mole degree), and the result was taken as the difference in the proton affinity between the two monomers (in kJ/mole). Several such measurements were made between the same and different pairs of diamines. In some cases, the mass selected parent ion was a composite of several such pairs. For example, the CID spectrum of the parent ion at m/z 275 (nominally $C_{15}H_{39}N_4^+$) showed that it was made of three different pairs of protonated diamine monomers: 1,7-diaminoheptane and 1,8-diaminooctane (at m/z 131 and 145), 1,6-diaminohexane and 1,9-diaminononane (at m/z 117 and 159) and 1,5-diaminopentane and 1,10-diaminodecane (at m/z 103 and 173), as shown in Figure 2a. Another example is shown in Figure 2b for the parent ion at m/z 261 (nominally $C_{14}H_{37}N_4^+$). Note that the sum of each pair of product ions is always 1 dalton higher than that of the parent ion, which is an outcome of the fact that the proton from the parent ion may in some cases reside on the one monomer and in other cases on the second monomer. Care was taken to calculate the intensity ratios only of ion pairs that complement each other to make up the parent ion.

RESULTS AND DISCUSSION

1. The effective temperature and proton affinity scale

Reference compounds were used to calibrate the effective temperature and to anchor the proton affinity values to the NIST proton affinity scale [12]. The compounds used for this purpose were di-isopropylamine $(iC_3H_7)_2NH$, triethylamine $(C_2H_5)_3N$, and tributylamine $(C_4H_9)_3N$, which have proton affinities of 230.2, 232.0 and 235.4 kcal/mol, respectively [12]. The heterodimer formed by each pair of amines was mass selected and the intensity ratio of the fragments (the corresponding protonated free bases) was used to calculate the effective temperature, according to equation 3:

$$T = PA_{(A-B)}/[\ln(AH^+/BH^+) * R] \qquad (3)$$

The results showed that the effective temperature was 60 K.

2. The proton affinity of diamines

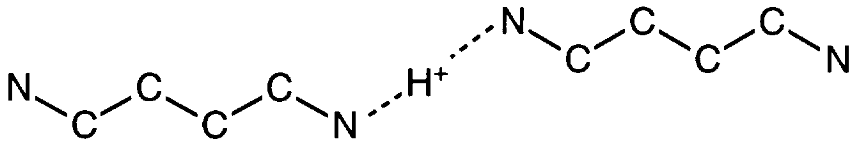
The results for the diamines are summarized in Table 1, as are the evaluated proton affinities and the PAs of the equivalent normal primary aliphatic amines, taken from the NIST compilation [12]. The trend, observed in many homologous series [12], of increasing PA with the hydrocarbon chain length does not hold for the diamines once the number of carbon atoms exceeds 4 or 5 (Table 1).

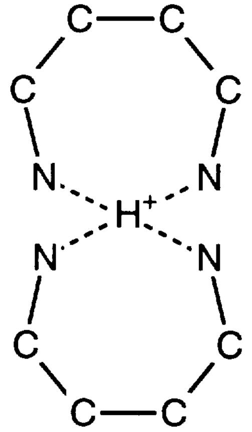
Table 1: The proton affinities of diamines and aliphatic normal alkylamines.

Compound		**Proton Affinity**			
$H_2N(CH_2)_nNH_2$	n	This work	Other[a]	$CH_3(CH_2)_nNH_2$[a]	D[b]
1,2-diaminoethane	2	223.6	225.9	217.9	2.3
1,2-diaminopropane	3	225.3			
1,3-diaminopropane	3	226.6	234.1	218.4	7.5
1,4-diaminobutane	4	230.6	237.6	218.9	7.0
1,5-diaminopentane	5	227.7	238.1	218.9	10.4
1,6-diaminohexane	6	227.0	237.7	219.0	10.7
1,7-diaminoheptane	7	225.7	238.0	220.4	12.3
1,8-diaminooctane	8	225.5			
1,9-diaminononane	9	226.6			
1,10-diaminodecane	10	228.1		220.7	
1,11-diaminoundecane	11	231.3			
1,12-diaminododecane	12	232.0			
1,13-diaminotridecane	13	232.4			
1,14-diaminotetradecane	14	233.0			
1,15-diaminopentadecane	15	231.9			

a) Reference 12.
b) - The stabilization energy of cyclization, i.e. the difference between NIST value and this work (cyclic and unbridged conformation).

There is a systematic difference, increasing with the chain length, between the proton affinity values obtained in this work and the NIST values, as shown in Table 1. The structure of protonated diamines, formed under equilibrium conditions [13-16] has been assumed to be that of an intramolecular proton bridged ring. A similar configuration, of proton induced cyclization, was proposed for diamines [18], amino-alcohols [19] and other polyamines [20] from ion mobility spectrometry (IMS) measurements at atmospheric pressure. The systematic difference in PAs indicates that the protonated diamines formed by fragmentation of the dimer species do not have the same structure, i.e. are not cyclic. It therefore appears that when the protonated dimer disintegrates the proton remains attached to one of the amino groups of the product ions and that rearrangement to the more stable, and thermodynamically favored conformation, does not take place in the time scale of the CID experiment. The fact that the site of protonation in the product ions is on a single amino group, indicates that the protonated dimer is formed by a proton bridge between the two monomer units that make up the dimer (schematic 1a). A more complex structure involving all four nitrogen atoms (amino groups) may also be visualized (schematic 1b). However, it would be sterically crowded with four amino-groups surrounding the proton, and the CID should yield the "normal" protonated diamines with the intramolecular ring, which evidently is not the case.





1a **1b**

Schematic conformation of protonated diamine dimers

When the hydrogen bond that bridges the two monomer units is cleaved, as the outcome of a collision of the dimer with the inert gas, the proton may go either to one monomer unit or to the other. The ratio between these two fragments depends on the relative basicity at the binding site, i.e. the relative strength of the hydrogen bond to the local amino group. As Table 1 shows, the PA values obtained in this work for the diamines are higher than those of the corresponding normal aliphatic mono-amines, as expected for two compounds of this type [12].

These results indicate that CID may offer a novel method of producing ions, protonated molecules in this case, which have conformations which are not normally accessible by conventional methods.

The proton affinities of larger diamines, 1,11-undecanediamine through 1,15-pentadecanediamine, are also presented in Table 1. These compounds existed as trace impurities in the smaller diamines, but due to their higher proton affinities were preferentially protonated, and demonstrated a high tendency to participate in mixed dimer formation with the more abundant, but lower PA, diamines. Thus, it was possible to carry out CID studies on such mixed dimers and estimate the PA values of these large diamines.

3. Dissociation pathways of protonated diamine monomers and dimers

The active dissociation channels of the protonated monomers and dimers were also studied. The major dissociation channel, observed in all of the protonated diamine monomers, was loss of 17 mass units, corresponding to the elimination of ammonia:

$$H_2N(CH_2)_nNH_3^+ \text{--->} (CH_2)_nNH_2^+ + NH_3 \qquad (4)$$

This could be followed by elimination of the second ammonia unit, leaving an ionized hydrocarbon skeleton. Other common dissociation channels in all of these diamines involved cleavage of C-C or C-N bonds, such as the formation of an ion at m/z 30 formed by cleavage of the C-C bond in the position alpha to the amino group:

$$H_2N(CH_2)_nNH_3^+ \text{--->} CH_2NH_2^+ + CH_3(CH_2)_{n-2}NH_2 \qquad (5)$$

Other dissociation channels observed in these CID studies led to the formation of product ions by single bond cleavages in different parts of the hydrocarbon chain. A typical CID spectrum, in this case of protonated 1,5-diaminopentane is shown in Figure 3. Ammonia is eliminated from the parent ion at m/z 105, giving the product ion at m/z 86 and loss of both ammonia groups gives the product ion at m/z 69. Cleavage of an alpha C-C bond gives the product ion at m/z 30 (reaction 5), while other single C-C cleavages give the product ions at m/z 44 and 74, and the ion at m/z 41 which is probably $C_3H_5^+$ formed by additional cleavage of a C-C bond after elimination of one or two ammonia moieties.

The protonated dimers dissociated mainly by cleavage of the hydrogen bond at the protonation site, into either of the two protonated monomers, as shown in Figure 2. At higher collision gas thickness (CGT) values, ions corresponding to the elimination of ammonia from the protonated monomer were observed, accompanied by additional product ions as shown in reaction 4. In no case was cleavage of a covalent bond (C-C or C-N) observed without concomitant monomer formation, i. e. the hydrogen bond was always the first bond to be cleaved in the CID spectra of these protonated dimers and mixed dimers.

4. Collision dissociation cross sections of protonated dimers

The cross section for collision induced dissociation was determined by plotting the logarithm of the fraction of undissociated protonated dimers (the parent ion) as a function of the collision gas thickness. The slope of the line corresponds to the collision cross section. Figure 4 depicts such typical plots of this sort for pure protonated dimers of 1,7-diaminoheptane, 1,8-diaminooctane and 1,9-diaminononane. The general trend is that the slope of these plots, i.e. the cross sections, increase simply with the size (or mass) of the parent ion in the diamine homologous series.

5. Doubly charged ions

Under the conditions of electrospray ionization, multiply charged ions are frequently observed when polyamine bases are studied. In the present study doubly protonated, and doubly charged, diamines were observed, as shown in Figure 5 for diprotonated 1,9-diaminononane at m/z 79.9 (nominally 80). The identity of these ions was established from their mass (half of a diprotonated molecular ion), and by their CID spectrum which led to formation of ions with higher masses than the parent ion.

CONCLUSION

The results presented above demonstrate one of the pitfalls of using the "kinetic method" for deriving thermochemical data from the ratio of product ions in collision induced dissociation studies. The observed difference between proton affinity values of diamines obtained from equilibrium measurements (NIST data) and these CID studies was attributed to the fact that the conformation of the product ions in the latter method was with the proton attached to a single amino group and not to both groups in a cyclic structure as in the former experiments. Therefore, in this case the kinetic method may be used to estimate the proton affinities of unbridged protonated diamines. The stabilization energy resulting from cyclization may be derived from the difference between the PAs of the cyclic and unbridged diamines. Thus, the last column of Table 1 gives this stabilization energy, where data for the cyclic structures was available. The fact that this value increases with length of the hydrocarbon chain is indicative of the strain in the smaller cyclic structures, where part of the gain in stabilization energy is offset by the extra strain. This strain is also the reason that the difference between the PA of 1,2-ethanediamine and n-propylamine is smaller than between the corresponding larger homologues (see Table 1).

The CID results also give insights into the structure of the mixed and pure dimers, which may be elucidated as having a single hydrogen bond bridging the two monomer units. The CID studies of protonated diamine monomers showed that elimination of ammonia was the favored dissociation channel for these species. At higher CGT values other dissociation channels observed were loss of a second ammonia unit and cleavage of different C-C bonds in the hydrocarbon skeleton. The CID studies of all the protonated dimers, mixed or pure, showed that cleavage of the hydrogen bond was favored over breaking covalent bonds, which is expected from bond energy considerations.

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ELECTROSPRAY IONIZATION
Sciex API-III "Ionspray" MS/MS

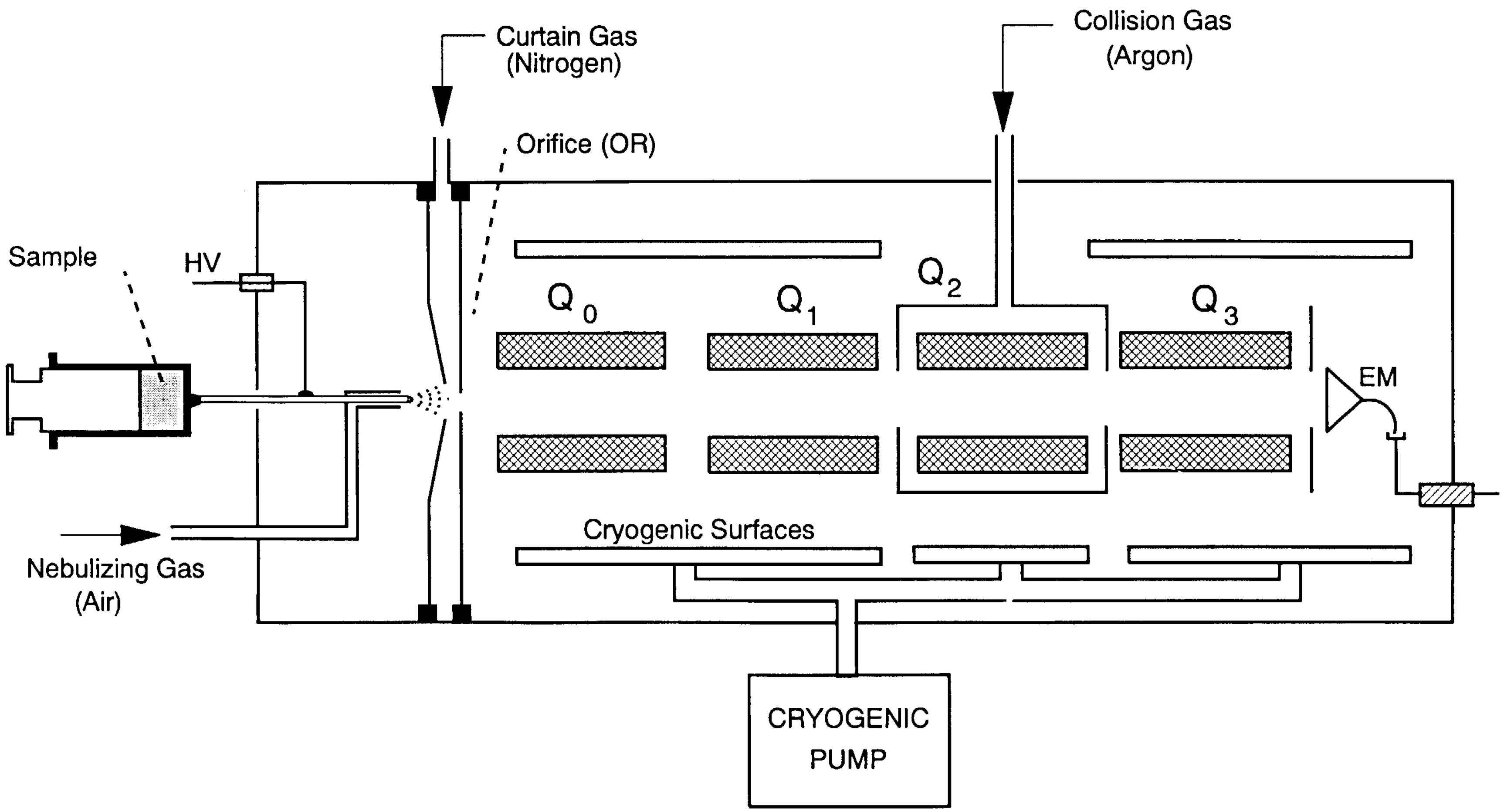

Figure 1. Schematic diagram of the API-III triple quadrupole mass spectrometer with the Ionspray (pneumatically assisted electrospray) atmospheric pressure ionization source.

Spectra

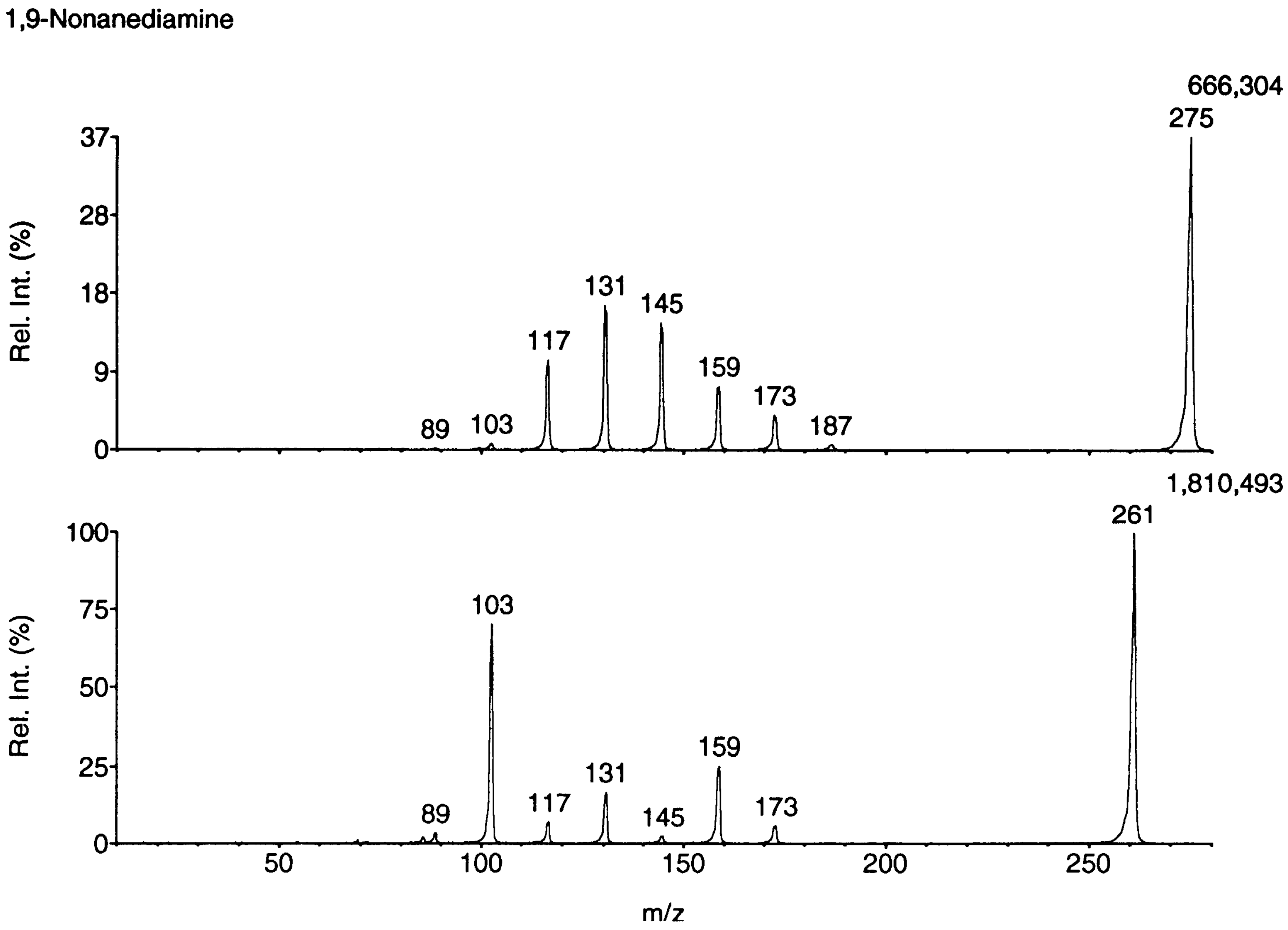

Figure 2a. The collision induced dissociation product ion mass spectrum of the parent ion at m/z 275 (nominally $C_{15}H_{39}N_4^+$). Note that pairs of protonated diamine monomers are produced through its dissociation: 1,7-diaminoheptane and 1,8-diaminooctane (at m/z 131 and 145), 1,6-diaminohexane and 1,9 diaminononane (at m/z 117 and 159) and 1,5-diaminopentane and 1,10-diaminodecane (at m/z 103 and 173)

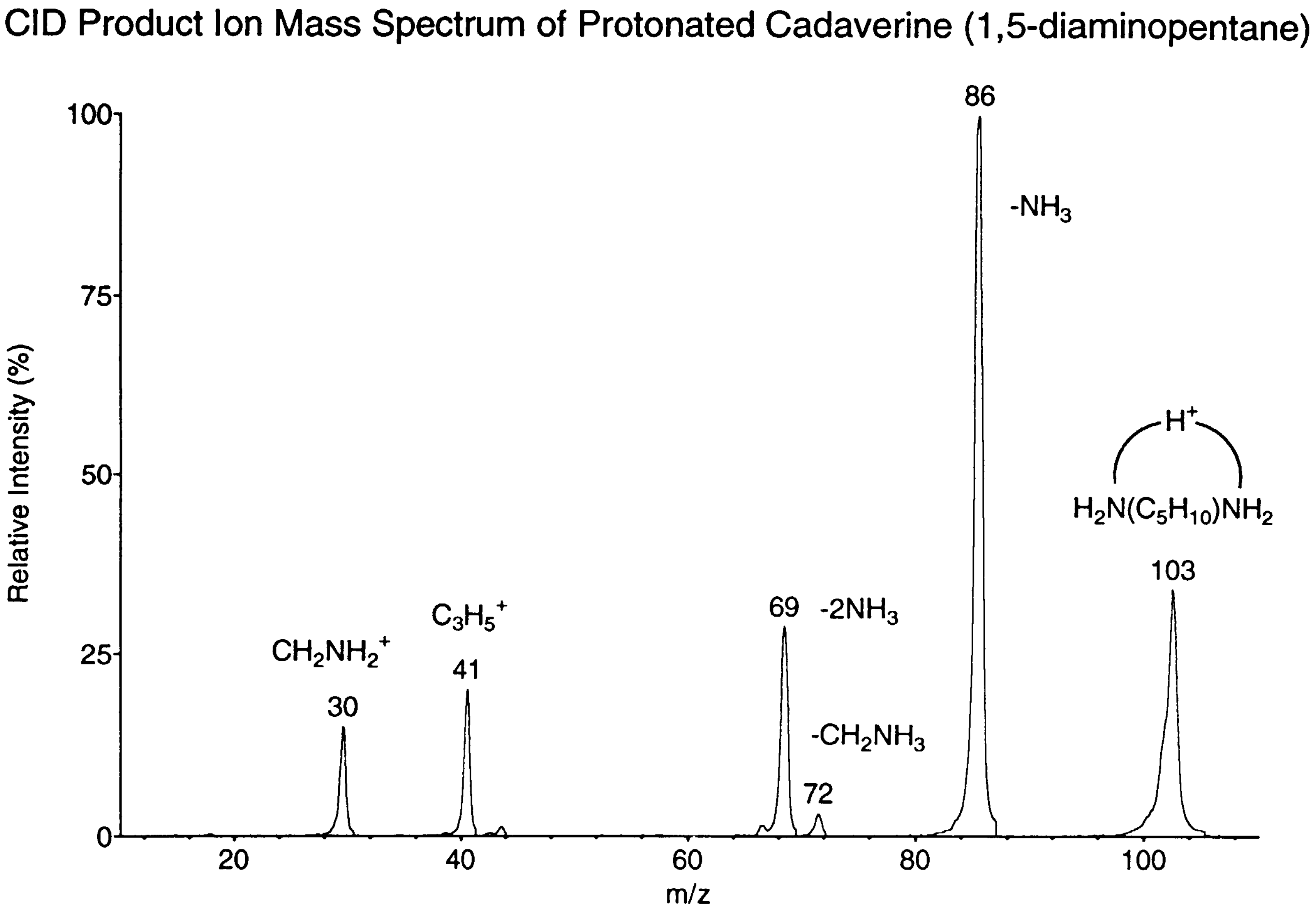

Figure 2b. The collision induced dissociation product ion mass spectrum of the parent ion at m/z mass 261 (nominally $C_{14}H_{37}N_4^+$).

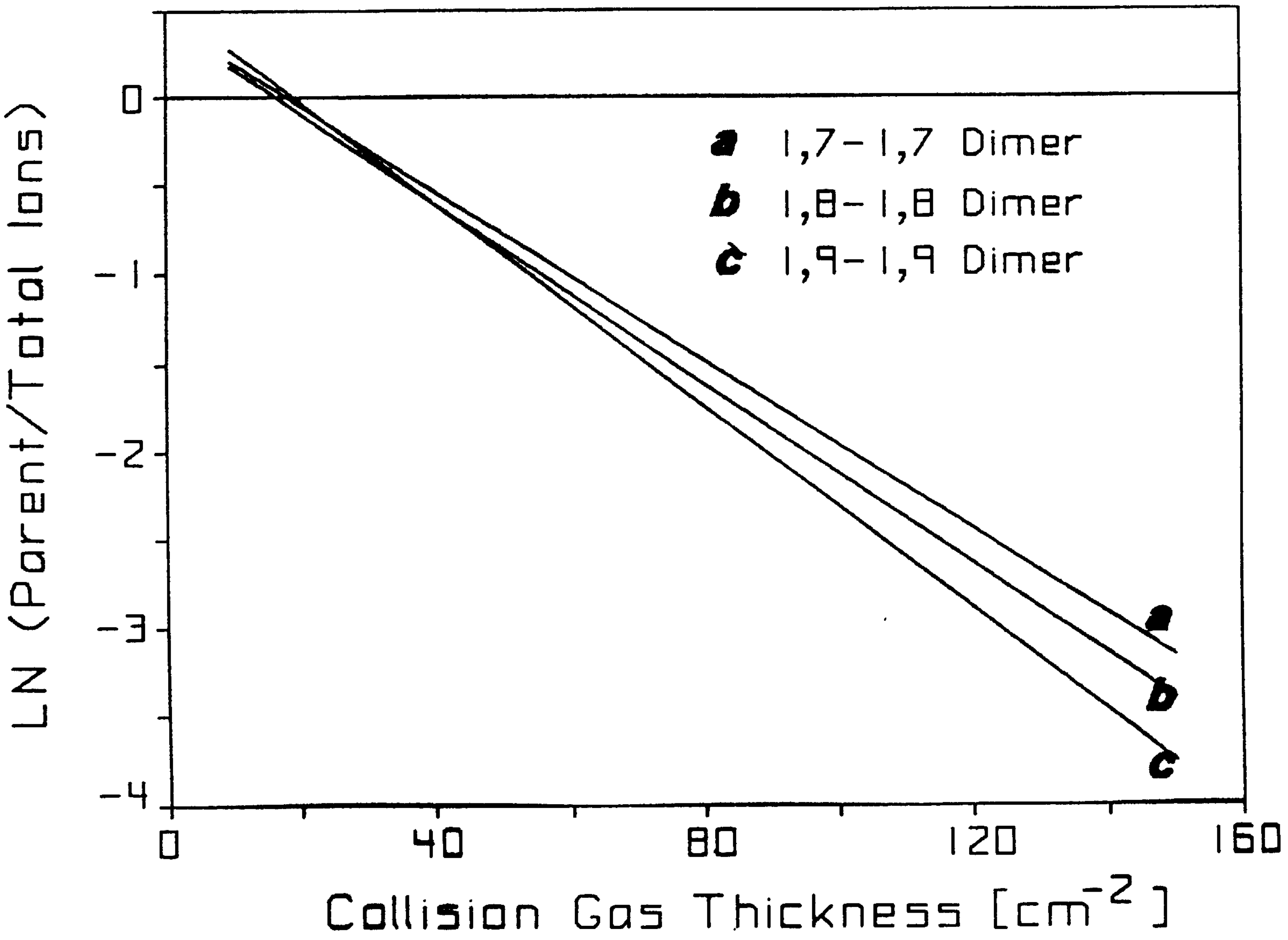

Figure 3. The CID product ion mass spectrum of the protonated monomer of 1,5-diaminopentane at m/z 105. The product ions at m/z 86 and 69 are produced by loss of one and two ammonia groups, respectively. The product ions at m/z 30, 44 and 74 are formed through single C-C cleavages.

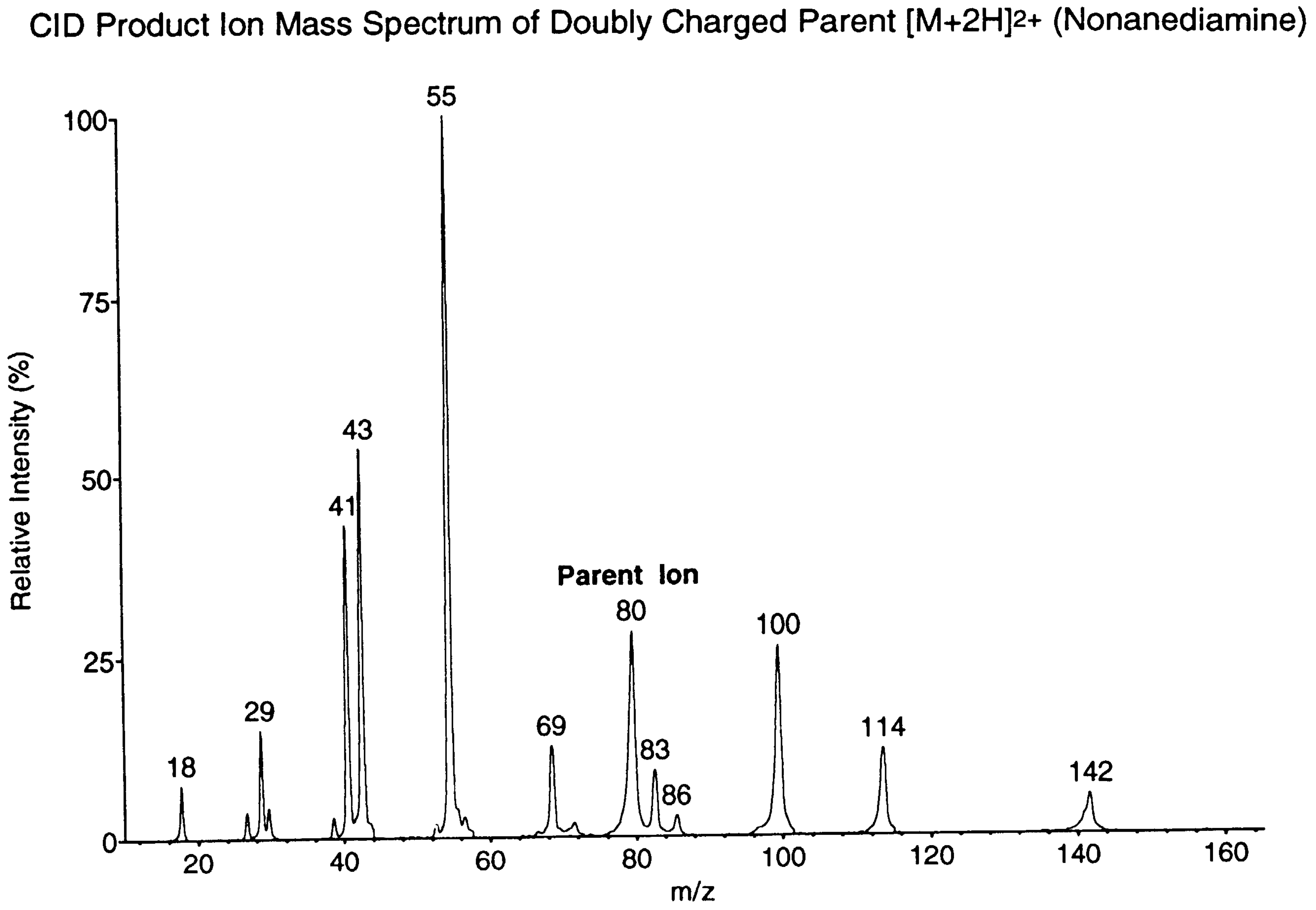

Figure 5. The CID product ion mass spectrum of the doubly charged parent ion at m/z 80 from 1,9-diaminononame $[M+2H]^{2+}$. Product ions at higher m/z values than the parent ion arise from both mass and charge elimination. For instance, the product ion at m/z 142 represents loss of NH_4^+ from the doubly charged dimer, or alternatively elimination of neutral ammonia from the singly charged monomer.