Ion Trap Tandem Mass Spectrometry of Poly(propylene imine) Dendrimers

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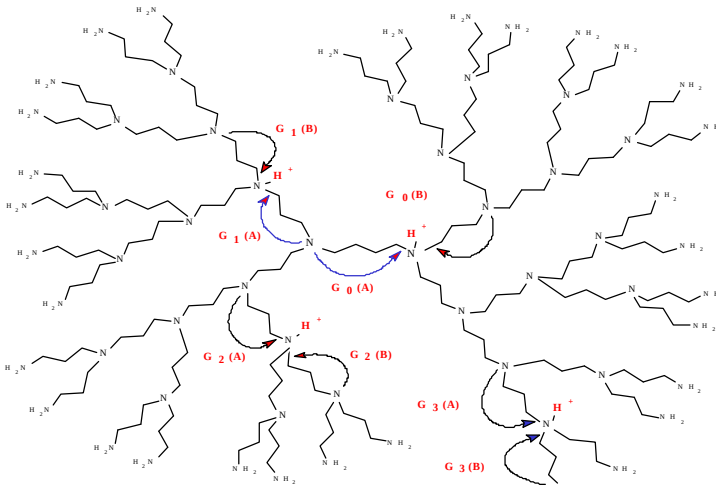
Ions derived from electrospray ionization of poly(propylene imine) dendrimers (generations 1-5, synthesized from a 1,4-diaminobutane core) were subjected to ion trap tandem mass spectrometry. In some cases, ion/ion proton transfer reactions were used to form low charge state parent ions from higher charge state ions generated by electrospray [1,2]. In addition, ion/ion proton transfer reactions performed on product ions formed by ion trap collisional activation of multiply charged parent ions facilitated interpretation of MS/MS spectra. Almost all of the products derived from dendrimer parent ions could be rationalized based on a set of dissociation processes involving a previously noted intramolecular nucleophilic attack by a nearest-neighbor nitrogen atom on a carbon alpha to a protonation site [3,4]. For a given protonation site, attack can occur either from the adjacent nitrogen closer to the interior or closer to the exterior of the dendrimer. The processes that lead to the dominant products are highly dependent upon parent ion charge state. Singly charged ions fragment primarily by processes directed by protonation at a diaminobutane nitrogen whereas highly charged parent ions fragment largely by processes directed by protonation closer to the periphery of the dendrimer. MS/MS data for singly charged ions of series of synthesis failure products in the fourth and fifth generation dendrimers were collected. The results show that ion trap tandem mass spectrometry can provide information about the composition of mixtures of isomeric products resulting from side reactions that occur during the course of the multi-step syntheses of the dendrimers.

All MS^2 spectra are dominated by products from competing S_Ni mechanisms. A generalized scheme for designating these products is shown in the scheme shown below. G_n represents the likely protonation site from which the dissociation takes place, where n is the generation number in which the nitrogen was added (e.g., n=0 represents a 1,4-diaminobutane nitrogen.) The letters A or B in parentheses represent the direction from which nucleophilic attack on a carbon alpha to the protonation site occurs. “A” represents attack from an interior nitrogen, “B” represents attack from an exterior nitrogen. The subscripts “a” and “q” in the spectra indicate if the product is a quaternary ammonium ion (q) or a protonated amine (a). Only multiply-charged parent ions yield protonated amine products.



MS/MS can provide information regarding the mixtures of isomeric ions produced as a result of incomplete syntheses. Incomplete synthesis products can arise from failures that occur on the final step and/or from the propagation of deficiencies from errors in previous generations. In fact, products comprised of more than one missing moiety (i.e., a C_3H_7N or NH_3 group) are comprised of isomers. It is clear from Figure 1, which shows the MS/MS spectrum of the $(M+H)^+$ ion of the complete generation 5

dendrimer, that MS/MS can provide at least limited information about the composition of isomeric mixtures. The $G_0(A)$ process provides information about the distribution of products with missing segments on one side of the dendrimer. The $G_0(B)$ and $G_1(A)$ processes provide information at the quarter dendrimer level. The $G_2(A)$ and $G_3(A)$ processes provide information at the one-eighth and one-sixteenth levels, respectively. For singly-charged ions, the G_0 processes provide the best ion statistics.

Figure 1 – MS^2 of $(M+H)^+$ of DAB-*dendr*-$(NH_2)_{64}$

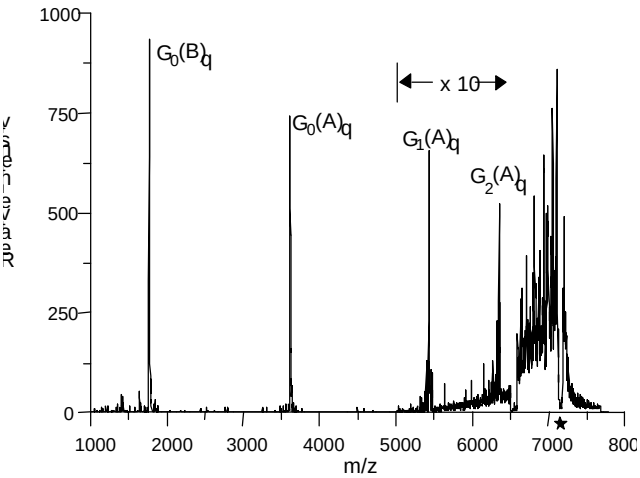


Figure 2 - MS^2 spectra of DAB-*dendr*-$(NH_2)_{64}$ $(M-6X+H)^+$ ions

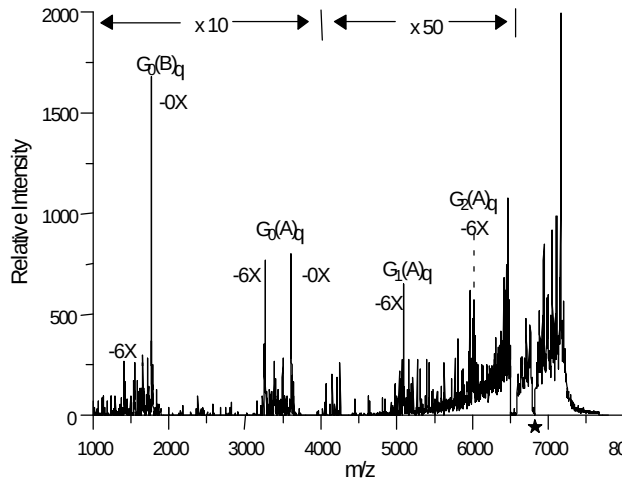


Figure 2 shows the MS/MS spectrum of the $(M-6X+H)^+$ ion population from the fifth generation dendrimer sample where X = 57.1 Da (C_3H_7N). This ion population reflects an isomeric mixture of structures with six missing C_3H_7N sub-units. A variety of structures can be drawn with six missing sub-units but the mixture is constrained by the history of synthesis failures in the evolution of the fifth generation species from generations one to five. Clearly, Figure 2 shows that the mixture is not dominated by the statistically most probable set of components. Such a set would show an equal distribution of three missing sub-units on a side. The data show, via the $G_0(A)_q$ products, that the most probable situation is one in which all six missing sub-units are on one side of the dendrimer. Furthermore, the $G_0(B)_q$ and $G_1(A)_q$ products indicate that mixture components with six missing sub-units on the same quarter of the dendrimer are abundant.

In summary, the poly(propylene imine) dendrimers show simple decomposition chemistry under ion trap collisional activation conditions. The primary decomposition reactions are consistent with the general S_Ni mechanisms described previously [3,4]. The extent to which each of the possible channels contributes to the MS/MS spectrum is highly dependent upon charge state. This charge state effect is most easily rationalized on the basis of changes in favored sites of protonation as a result of Coulomb repulsion associated with multiple protonation. Ion trap MS/MS of $(M+H)^+$ ions promises to be useful for drawing conclusions about the composition of isomeric mixtures arising from side reactions associated with dendrimer synthesis. Further work is necessary to determine the extent of structural information that can be obtained from multiply charged ions.

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