

A Combined ESI- and MALDI-MS(/MS) Study of Dendrimers Persulfonated at their Periphery: Falsely Negative Results by MALDI MS and Analysis of Defects

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I. Introduction

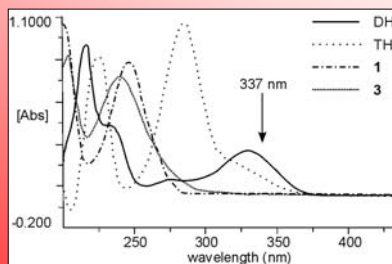
Mass spectrometry, in particular MALDI-MS, is often used as a method to characterize dendritic molecules with respect to their molecular masses and the determination of structural defects, which can come from incomplete functionalization during synthesis.

We have investigated TREN- and POPAM-based dendrimers persulfonated at their periphery by MALDI and ESI.

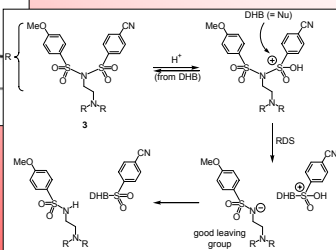
While ESI provides evidence for the purity of the samples, MALDI spectra appear to point to the existence of such defects which would originate from an incomplete substitution. In this case, MALDI leads to falsely negative results and the defects are generated during the ionisation process.

Furthermore, collision experiments were carried out in an FT-ICR mass spectrometer cell with mass-selected dendrimer ions from electrospray ionization. These experiments allowed detailed insight into the structure of the dendrimers. Different fragmentation patterns were observed depending of their exact structures. The nature of the charge is also important for the fragmentation process. The fragmentation pathways of the protonated species differ much from those binding a sodium or potassium ion.

III. Mechanism of the fragmentation

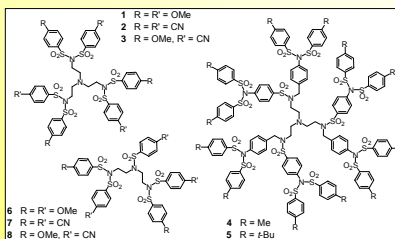


It is well known that arylsulfonyl groups can be used as photocleavable protective groups. At the wavelength of 337 nm of our MALDI laser, the dendrimers didn't show any absorption. Thus a photocleavage process can be safely excluded.



A more reasonable mechanism is an arylsulfonyl group cleavage during the thermal MALDI process by means of a nucleophilic attack of the acidic matrix (figure right). The arylsulfonyl group is replaced by a proton. The mechanism is in line with the preferential loss of cyano arylsulfonyl groups in **3**, since the electron withdrawing substituent increases the electrophilicity of the SO₂ unit.

II. Persulfonated TREN-Dendrimers



We observed very clean spectra for the TREN-dendrimers, if we use ESI as the ionization method. Dendrimer **1** (top spectrum) shows intensive peaks for the protonated molecule and the Na⁺ and K⁺ adducts. There are only some minor signals of defect structure **6** in the spectrum.

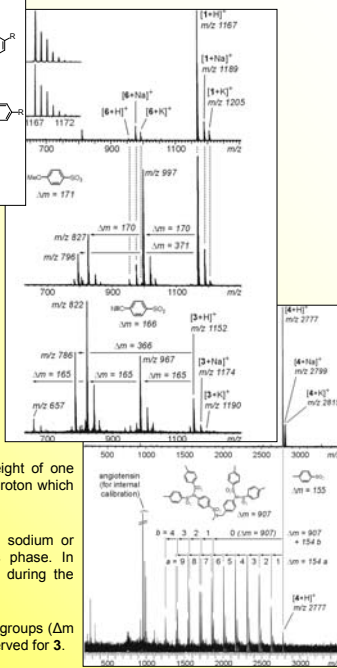
If we use MALDI (center trace) for the ionization of **1**, we observe several additional fragment signals, which are attributed to the loss of terminal arylsulfonyl groups ($\Delta m = 171$). From the MALDI spectra, one would arrive at the wrong conclusion that these signals belong to defect structures, which originate from an incomplete synthesis.

The mass difference of 1 Da between the molecular weight of one branch and the observed mass difference is caused by a proton which replaces the sulfonyl group.

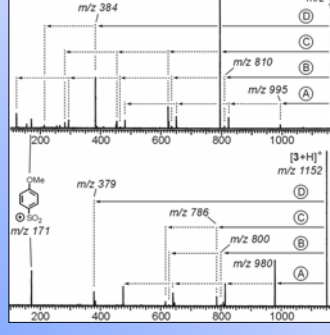
The fragment ion at m/z 796 without the corresponding sodium or potassium adducts is formed in the highly diluted gas phase. In contrast, the cleavage of the arylsulfonyl groups occurs during the ionisation in the MALDI matrix.

The preferential cleavage of cyano-substituted arylsulfonyl groups ($\Delta m = 165$) as compared to the methoxy-sulfonyl groups is observed for **3**.

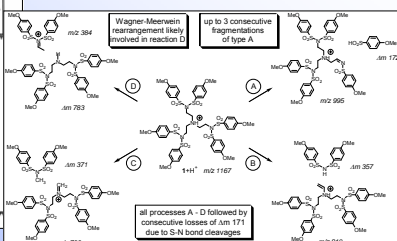
The ESI spectrum of **4** shows the G2 dendrimer to be structurally perfect. In contrast, the MALDI spectrum reveals two series of branch fragmentation.



IV. MS/MS Experiments

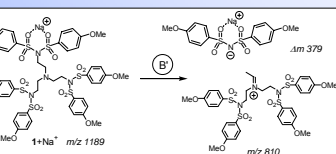
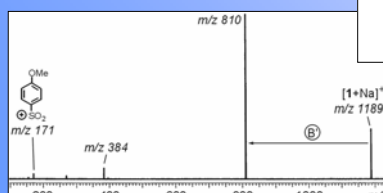


The protonated intact dendrimers were mass-selected in form of their monoisotopic parent ions in a FT-ICR cell. Through collisions with argon atoms fragmentation is induced. We could observe different fragmentation pathways (A - D).



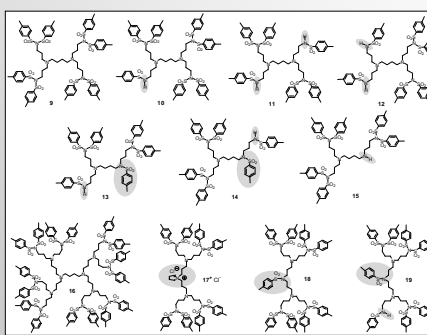
In comparison, there is no peak in the CID spectra which is also observable in the MALDI. This is in agreement with the formation of the MALDI fragment in the matrix rather than the gas phase.

In addition, we have carried out the CID of the sodium adducts. The main product at m/z 810 belongs to the reaction pathway B', which is analogous to B of the protonated ions.



While the spectrum of [1+H]⁺ shows a signal with high abundance at m/z 796 (channel C), the sodium adduct does not induce the same fragmentation reaction. This becomes clear, if we assume different locations for the charge. From this we conclude, that the Na⁺-ions to be attached to the periphery of the dendrimers.

V. Persulfonated POPAM-Dendrimers



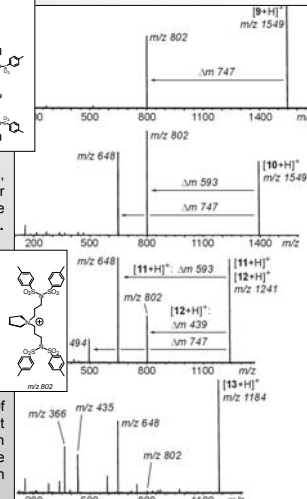
The synthesis of the structurally perfect G1 POPAM dendrimer was feasible, whereas any attempt to synthesize the generation G2 failed. Only the defect structure 17-CI with half of the POPAM scaffold could be isolated.

MS/MS experiments of the structures **9** - **15** permit to determine the defects and to gather structural informations for each of them.

Dendrimer **9** undergoes only one fragmentation reaction, according to a mechanism which was described earlier by Meijer et al. (top spectrum). The energetically favored ring closure reaction could also be observed for the defect structures **10** - **12**.

If one sulfonyl group is missing, the molecule is not any more symmetrical. Therefore, we observe two fragments in the spectrum of **10** (second trace).

The situation becomes more complex for an isomeric mixture of **13** - **15** (bottom trace) where the defects are directly located at the POPAM scaffold. Other reaction pathways can compete with the Meijer reaction. Compound **13** is the major part of the mixture indicated through a signal at m/z 648 that can also be found in the spectrum of dendrimer **10**.



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