Observing individual generations in poly(propyleneimine) dendrimers with natural abundance $^{15}$N-NMR spectroscopy

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Abstract. Natural abundance $^{15}$N-NMR spectra of poly(propyleneimine) dendrimers are presented to show the usefulness of the technique in characterizing these highly branched and well-defined macromolecules. Inverse-gated decoupled measurements show the number and intensities of signals that reflect the generations in the dendrimers.

Dendrimers are a new class of well-defined, highly branched macromolecules with a branch point in each monomer unit, emanating from a central core. Due to the repetitive reaction sequence in the synthetic procedure, dendrimers can be obtained with a chosen number of generations and end groups. For one type of dendrimer, poly(propyleneimine), an efficient large-scale synthesis has been described. Starting from diaminobutane (DAB), double Michael addition of acrylonitrile yields a species with four cyano groups (DAB-dendr-(CN)$_4$). Catalytic hydrogenation with H$_2$/Raney-Co results in a molecule with four primary amine groups (DAB-dendr-(NH$_2$)$_4$). Repeating this sequence yields dendrimers with 8, 16, 32, 64, and 128 cyano or amine end groups.

Characterization of these molecules with various techniques ($^1$H- and $^{13}$C-NMR, IR, GPC, DSC) becomes more difficult at higher generations due to complications, such as overlap of signals in NMR. Recently, new NMR techniques like DOSY are used by Newkome et al. to determine the overall size of dendrimers. A new technique which may be useful to characterize the poly(propyleneimine) dendrimers is $^{15}$N-NMR spectroscopy, since nitrogen is a substantial component and is present in a unique chemical environment in each new generation. We have therefore measured the natural abundance $^{15}$N-NMR spectra of DAB-dendr-(CN)$_n$ ($n = 4, 8, 16, 32, 64$). The spectra have been obtained with $^1$H-decoupling in inverse-gated mode (decoupling on during acquisition and off during relaxation) to remove the NOE and thus obtain quantitative spectra. Hereby, we also avoid problems related to the negative gyromagnetic ratio of $^{15}$N: this causes a maximum NOE of $-4.93$ and allows for NOEs of ca. $-1$, which completely remove the signal in a normal decoupled spectrum.

The results of our measurements are shown in Figure 1 and Table 1. Characteristic signals are observed around 240 ppm (nitrite) and 40 ppm (tertiary amine). Up to $n = 32$ all generations are observed separately, indicating a stratified structure for the dendrimers. The integral ratios indeed confirm the exponential increase of the number of nitrogens in each generation. Since for $n = 32$ even the smallest signal of the central DAB nitrogens is visible, it can be concluded that defects are less than ca. 6%. For $n = 64$, it is no longer possible to observe all peaks within a reasonable acquisition period (60 h), but the observed chemical shifts are in good agreement with the results.
Table I Chemical shifts and integral ratios in the $^{15}$N NMR spectra.

<table>
<thead>
<tr>
<th>Product</th>
<th>Chemical shifts $^a$ (ppm)</th>
<th>Integral ratios $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAB-dendr-(CN)$_4$</td>
<td>34.9 243.2</td>
<td>1.9 : 4 (2 : 4)</td>
</tr>
<tr>
<td>DAB-dendr-(CN)$_8$</td>
<td>36.9 34.7 242.9</td>
<td>1.8 : 3.8 : 8 (2 : 4 : 8)</td>
</tr>
<tr>
<td>DAB-dendr-(CN)$_{16}$</td>
<td>39.3 36.6 34.7 243.0</td>
<td>2.5 : 3.8 : 8.2 : 16 (2 : 4 : 8 : 16)</td>
</tr>
<tr>
<td>DAB-dendr-(CN)$_{32}$</td>
<td>40.5 39.2 37.1 35.0 243.3</td>
<td>1.3 : 2.9 : 9.4 : 17.2 : 32 (2 : 4 : 8 : 16 : 32)</td>
</tr>
<tr>
<td>DAB-dendr-(CN)$_{64}$</td>
<td>- - 39.8 37.7 35.0 243.0</td>
<td>- - 6.5 : 13.6 : 28.2 : 64 (2 : 4 : 8 : 16 : 32 : 64)</td>
</tr>
</tbody>
</table>

$^a$ Shifts from right to left go from the cyano endgroup to the core to show similar environments. $^b$ Ratios are calculated with the cyano peak at the expected value. Ideal ratios are in parentheses. $^c$ Shifts can change because CHCl$_3$, instead of CDCl$_3$, was used as solvent and the spectrometer was locked on an internal (capillary) tube containing CDCl$_3$. Compared to the use of pure CDCl$_3$ as solvent this lock method affords $^{15}$N shifts that are ca. 0.3 ppm to lower field (higher frequency).

Figure 1. Tertiary amine region of inverse-gated $^{15}$N NMR spectra of DAB-dendr-(CN)$_n$ in CDCl$_3$ at 40.55 MHz on a Bruker AM 400 spectrometer. A 20 kHz spectral width was used with 64K data points. A 30° pulse (2.3 μs) and a delay of 30 s were used for $n$ = 4-16. For $n$ = 32: 90° (7 μs) and 60 s, for $n$ = 64: 90° and 120 s. Chemical shifts are related to liquid NH$_3$ at 25°C ($\delta$ = 0 ppm), and determined with an external reference of CD$_3$NO$_2$ ($\delta$ = 380.23 ppm). obtained for the lower generations. The integrals for $n$ = 64 show systematically lower values for interior nitrogen atoms. This aspect is being investigated further and may be related to changes in relaxation of the CN nitrogen atoms caused by denser packing in the outer layer. The chemical shift of the tertiary nitrogens is a good indicator of their position relative to the exterior of the dendrimer: stronger deshielding occurs in the interior, and apparently the distance from the nitrile group determines the chemical shift. The differences in chemical shifts observed (ca. 5 ppm) are larger than expected for solvent effects (e.g. triethylamine in different solvents shows only a 2 ppm range$^5$). This $^{15}$N-indicator of the internal medium in dendrimers can perhaps be correlated with the remarkable basicity observed for dendritic amines.$^6$ Preliminary work on DAB-dendr-(NH$_2$)$_n$ shows a smaller range for the chemical shifts of the interior amines. We conclude that the $^{15}$N-NMR technique is useful for characterizing these dendrimers and quantifying their structure. Future work will be aimed at enhancing the sensitivity of the technique by using INEPT and using relaxation studies for studying the DAB-dendr-(NH$_2$)$_n$ series and their derivatives.$^6$

References