Optical activity of chiral dendritic surfaces

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indicating metallic character. The hyperbolic PNS $I_{1}-Y^{**}$ bounds regions with very different degrees of valence electron localization, that is of different bonding character. One has the impression that the metallically conducting $3\times 10^{24}$ nets are separated by insulating hyperbolic layers.

The cubic phase RhBi$_4$ as a whole is isotropic. Nevertheless, the atomic distribution and electronic structure show intrinsically a strongly anisotropic, layerlike structure. However, due to the hyperbolic (non-Euclidean) form of these layers, all anisotropic components are compensated in the crystal.

The formation of regions with very different localization of the valence electrons and the resulting microscopic anisotropy should influence the electro-kinetical properties and may correlate to the superconductivity of the compound ($T_{c} = 2.9 - 3.4$ K$^{17,17}$).

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Optical Activity of Chiral Dendritic Surfaces**
Johan F. G. A. Jansen, H. W. I. Peerlings, Ellen M. M. de Brabander-Van den Berg, and E. W. Meijer*

Macroscopic, nanoscopic, and mesoscopic chirality are among the intriguing new key words in the studies of chiral clusters, associated complexes, homo- and heterogeneous catalysts, and of many polymers.$^{[11]}$ Major drawbacks for these studies are, generally, the complexity of the materials under investigation and their lack of long-range order. Therefore, comprehensive studies of macroscopic chirality are primarily performed on single crystals and synthetic bilayers.$^{[12]}$ However, for a better understanding of the chiroptical features of non-ordered structures, well-defined materials are required. Dendrimers are promising candidates for the preparation of well-defined chiral materials with nanoscopic dimensions.$^{[13]}$ To the best of our knowledge only chiral dendrimers of lower generations have been prepared and no irregularities in the chiroptical properties of these enantiomerically pure dendrimers are reported$^{[14]–[16]}$ Newkome et al.$^{[17]}$ modified an amine-terminated dendrimer with enantiomerically pure tryptophane, whereas Seebach et al.$^{[18]}$ prepared some dendrimers with a chiral core and Chow et al.$^{[19]}$ prepared dendrimers with a chiral spacer. Hudson and Daṁha$^{[20]}$ synthesized a nucleic acid based chiral dendrimer, Mitchell$^{[21]}$ a glutamic acid based dendrimer, while Denkewalter disclosed a number of dendrimeric structures based on amino acids.$^{[22]}$

Larger chiral dendrimers with a more dense packing of functional groups in the shell have not been studied so far. Recently, we successfully prepared chiral structural phases of nanometer dimensions based on poly(propylene imine) dendrimers (DAB-dendr-(NH$_2$)$_n$)$_{10}^{[23]}$ that are terminated with amino acid derivatives and we presented evidence that these compounds are useful as dendritic "boxes" (DAB-dendr-(NH$_2$-BOC-L-Phe)$_n$; Fig. 1)$^{[11]}$. Due to the dense packing of the shell and the presence of internal cavities, we are able to encapsulate a variety of guests into these dendritic boxes; guests that are physically locked. The synthesis of this and other amino acid modified dendrimers is summarized in Scheme 1. Here we report on the peculiar chiroptical properties of these dendritic boxes and discuss the structure of highly curved chiral dendritic surfaces.

The investigation presented here was triggered by the observation that the specific optical rotation of the DAB-dendr-(NH$_2$-BOC-L-Phe), decreases to almost zero on going from dendrimers of the first generation ($|\alpha|_{D} = -11$; $c = 1$, CHCl$_3$) with four end groups to dendrimers of the fifth generation ($|\alpha|_{D} = -0.1$; $c = 1$, CHCl$_3$) with 64 end groups. A more thorough investigation employing a variety of different amino acid derivatives reveals that this decrease of optical rotation with increasing generation is a general phenomenon for all the amino acids studied (Table 1). The most striking results are found for the DAB-dendr-(NH$_2$-BOC-$\alpha$-Z-L-Lys)$_n$, in which the $|\alpha|_{D}$ value decreases from $-28$ ($c = 1$, CHCl$_3$) for the first generation dendrimer ($x = 4$) to $0$ ($c = 1$, CHCl$_3$) for the fifth generation dendrimer ($x = 20$).

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Table 1. Selected specific rotations of modified poly(propylene imine) dendrimers.

<table>
<thead>
<tr>
<th>Number of end groups</th>
<th>(generation)</th>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
<th>(4)</th>
<th>(5)</th>
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<tr>
<td>BOC amino acid</td>
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<tr>
<td>l-alanine (L-Ala)</td>
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<td>-26</td>
<td>-33</td>
<td>-14</td>
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<td>(CHCl₃)</td>
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<td>-27</td>
<td>-28</td>
<td>-22</td>
<td></td>
</tr>
<tr>
<td>(CHCl₃)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>l-leucine (L-Leu)</td>
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<td>-23</td>
<td>-21</td>
<td>-13</td>
<td>-10</td>
<td></td>
</tr>
<tr>
<td>(CHCl₃)</td>
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</tr>
<tr>
<td>l-methionine (L-Met)</td>
<td>-16</td>
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<td>-11</td>
<td>-10</td>
<td>-2</td>
<td></td>
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<tr>
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<td></td>
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<tr>
<td>t-(S)-benzylcysteine</td>
<td>+56</td>
<td>+42</td>
<td>+26</td>
<td>+13</td>
<td>+5</td>
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</tr>
<tr>
<td>e-(Z)-L-lysine</td>
<td>-28</td>
<td>-8</td>
<td>-3</td>
<td>-1</td>
<td>0.0</td>
<td>[a]</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L-phenylalanine (L-Phe)</td>
<td>-11</td>
<td>-7</td>
<td>-2</td>
<td>-1</td>
<td>-0.1</td>
<td>[a]</td>
</tr>
<tr>
<td>(CHCl₃)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D-phenylalanine (D-Phe)</td>
<td>+10</td>
<td>+7</td>
<td>+2</td>
<td>+1</td>
<td>+0.1</td>
<td>[a]</td>
</tr>
<tr>
<td>(CHCl₃)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>l-tyrosine (L-Tyr)</td>
<td>+19</td>
<td>+9</td>
<td>+1</td>
<td>-0.2</td>
<td>-0.1</td>
<td>[a]</td>
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<tr>
<td>(DMSO)</td>
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</table>

[a] Error approximately ± 0.2. [b] In DMSO [α] = -13. [c] In CHCl₃, [α] = +15.

Fig. 1. Space-filling model of DAB-dend-(NH-t-BOC-L-Phe)ₙₙₙ, the t-BOC-L-Phe end groups are given in red, while the core atoms are given in green, white, and blue.

Drinal (x = 64). Dramatic changes are also observed for L-(S)-benzylcysteine and the L-tyrosine derivatives. For the smaller amino acids (Ala, Val and Leu) the decrease in optical rotation is less pronounced. As the number of chiral end groups per weight unit is roughly independent of the generation (in each new generation both the number of end groups and the molecular weight double), the decrease in the [α]D values with increasing generation is not due to the reduction of chiral chromophores. Furthermore neither concentration nor temperature effects are responsible for this decrease in optical activity, as nearly identical rotations are observed for c = 0.1, 1, and 4 in chloroform at temperatures of 20 and 55 °C in the L-Phe dendrimer series. However, a significant solvent dependency of the specific rotations was noticed for the lower generations and was investigated in detail for the model compound N-t-BOC-L-Phe-propylamide. Specific optical rotations were dependent on the dielectric constant of the solvent, varying from [α]D = 7.3 (c = 1, toluene) to [α]D = -6.4 (c = 1, acetonitrile) for the model compound. The behavior of the corresponding dimeric model compound from diaminobutane and two L-Phe residues deviated remarkably from all other ones. The dimer is only slightly soluble, indicative of intermolecular hydrogen bonding, and the optical rotation is large ([α]D = 22, c = 1, CHCl₃; see Fig. 4). The peculiar behavior of symmetric dipeptides is the subject of many recent studies. Finally, we have demonstrated that the protected amino acids do not undergo racemization in the coupling method employed; analysis of the amino acids after acid-catalyzed hydrolysis by HPLC using chiral stationary phases revealed an enantiomeric excess of greater than 96%.

Circular dichroism (CD) and optical rotatory dispersion (ORD) studies in conjunction with UV/Vis absorption spectroscopy have been performed to gain a better insight into the peculiar chiroptical effects observed. The restricted solubility of the dendritic boxes hampers the use of the entire spectral range. Most of the Cotton effects (CEs) present in the CD spectra of the lower generations decrease with generation; the results of the L- and D-Phe series are given in Figure 2. Both the CE of the car-
The optical behavior of the amino acid modified dendrimers is in sharp contrast with the optical rotations found for chiral dendrimers with more rigid end groups. The rigid dendritic camphor sulfonamides (Fig. 4) and camphanic amides have almost identical rotations \([\alpha]_D \approx 23; \ c = 1, \ \text{CHCl}_3\) and \([\alpha]_D \approx -18; \ c = 1, \ \text{CHCl}_3\), respectively) for all generations. Furthermore, the corresponding N-propyl camphor sulfonamide model compound showed a specific rotation independent of solvent \([\alpha]_D \approx 25; \ c = 1, \ \text{CHCl}_3\).

A number of phenomena other than trivial ones, like racemization or concentration effects, can explain the remarkable observations presented above for the amino acid modified dendrimers. A decreasing/vanishing optical activity of dendrimers is observed for dendrimers with chiral end groups; whose optical activity is susceptible to changes in the local environment. We are prompted to propose an explanation based on the fact that the outer surface (shell) of these dendrimers exhibit a highly dense solid-like packing in solution, as has been demonstrated by \(^{13}\text{C}\) NMR relaxation measurements. The rigidity of the shell is probably enhanced by multiple hydrogen bonding of the amide and carbamate groups in the shell. This rigid, close packing will lead to a number of conformations that are frozen. Due to the sensitivity of the chiroptical properties of the amino acid derivatives to the molecular environment and, hence, to conformational disorder, it is hypothesized that an internal compensation effect of different chiral conformers in the dendritic surface causes the vanishing or decreasing optical activity of the dendrimers. Chiral conformers with a non-equilibrium conformation are formed, forced by the dense packing in the shell. This explanation is related to the discussions by Green and Garetz on how the configurational stereochemistry of polymers can lead to vanishing optical activities by compensation among diastereomeric states.

As these dendritic structures are highly organized, it is tempting to suggest that the conformational disorder in the shell is limited to the presence of only two frozen conformations with a kind of pseudo-enantiomeric relationship and almost opposite CD and ORD for both pseudo-enantiomers. It is well documented that the density of racemic crystals is higher than that of conglomerates and the most dramatic differences are found for amino acid derivatives. A pseudo mirror-image relation of conformers of enantiomerically pure compounds has been observed in X-ray studies of a number of crystals. We have performed a variety of preliminary studies using scalemic mixtures to evaluate this pseudo-enantiomer hypothesis, but a detailed interpretation is lacking. However, it is apparent from our results that the highly curved surface does not allow the packing of all amino acid derivatives into their preferred lowest energy conformations. This effect is probably strengthened by multiple hydrogen bonding.

The constant optical rotation of the camphor sulfonamide and camphamic amide dendrimers of different generations is in
full agreement with the insensitivity of its rotation with respect to changes in the molecular environment. The constant $[\alpha]_D$ value does not imply that the camphor sulfonamide and camphamic amide shells are not densely packed nor that they do not possess frozen-in conformations. However, in these densely packed surfaces the frozen-in conformations all have the same optical activity and no internal compensation effects are operative here. Also the number and strength of the hydrogen bonds in these cases will be lower than in the case of the amino acid derived dendrimers. Further research to elucidate the reasons for the observations presented here is in progress. It is foreseen that research on chiral dendrimers with highly packed shells will yield important information for this type of curved structures; structures that are so prominently present in nature.

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[12] The $[\alpha]_D$ values of the dendrimers of all generations are comparable to the specific optical rotation per chiral group. In the class of chiral dendrimers with a chiral core and achiral branches it is obvious that the optical rotation decreases with generation 5.


[14] A similar decrease in optical activity, although not as pronounced, is found for the amide absorption in trifluoroethanol. In this solvent, however, neither the aromatic nor the carbamate absorption could be detected with CD.


[19] In order to discriminate between disorder and pseudo-centrosymmetry, we performed experiments using secular mixtures of $\text{t}$-Phe and $\text{l}$-Tyr in the formation of the fifth-generation box. In sharp contrast to the $[\alpha]_D$ values of 0 for the pure $\text{t}$-Phe or $\text{l}$-Tyr, we found $[\alpha]_D = +16 (\pm 1, \text{DMSO})$ for the 50:50 amide-like mixture of $\text{t}$-Phe and $\text{l}$-Tyr, and optical rotations between +16 and 0 for the other mixtures studied. The trend observed is indicative for some kind of pseudo-centrosymmetric ordering in the shell, in which the case of the 50:50 amide-like mixture both units adopt their preferred conformation and still the most dense packing is formed.

[20] This conclusion seems at first glance to be in contrast with "la coupe du roi" in which both chiral halves are of the same handedness, however a chiral dendrimer surface possesses molecular chirality while "la coupe du roi" has only macroscopic chirality, see K. Mislow, Bull. Soc. Chim. Fr. 1994, 131, 534-538.