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# Dendrimers as building blocks for nanoscale synthesis

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**Abstract**: The study of dendritic molecules, such as dendrimers, hyperbranched and dendronized polymers, and molecular "bottle brushes" has received increasing interests in recent years. They are essential building blocks for both covalent and supramolecular assemblies and have promising technological and biomedical applications. In this report several aspects of dendrimers are collected, including definition of dendrimers and dendrons, synthesis, characterization, and their properties and applications.

**Keywords:** *Dendrimers; Dendrons; Nanotechnology; Mass spectrometry; Biomedicine; Supramolecular chemistry*

## Introduction

Dendrimers [1, 2] represent a unique class of macromolecules that play an important role in the emerging field of nanotechnology. The rapidly accelerating research and development activities in dendrimers and dendritic materials provide critically needed nanoscale building blocks suitable for the development of high performance materials. Dendrimers are widely recognized as the most versatile, compositionally and structurally controlled nanoscale building blocks available. They combine considerable molecular weights with monodispersity and well-defined size, shape, and multivalent functionalities.

## Dendrimers and Dendrons

Dendritic molecules [2] are defined as repeatedly multibranched compounds with a certain degree of perfection that is related to the symmetry and dispersity of the species. The area of dendritic molecules can be divided into the low-molecular weight and the high-molecular weight species. The first category encompasses multifunctional compounds that can be used as central branching points (cores) and dendrimers that are composed of a core unit and dendrons radiating out of it whereas the second includes hyperbranched [3] polymers, dendronized [4] polymers, and brush-polymers [5]. A typical dendrimer molecule has an initiator core, several interior layers composed of repeating units, and multiple active terminal groups (Fig. 1).

The interest in studying dendritic molecules is based on the fact that they are inherently different from their linear (polymer) analogues. Compared to polymers dendrimers reveal varied physical properties [1e,2,6] due to their monodispersity, such as viscosity, flexibility, and density distribution. This can lead to new materials.

Commercially available polypropylene amine dendrimers (POPAM) [7] and polyamidoamine dendrimers (PAMAM) [8] belong to the most frequently studied branched species and numerous reports on POPAM and

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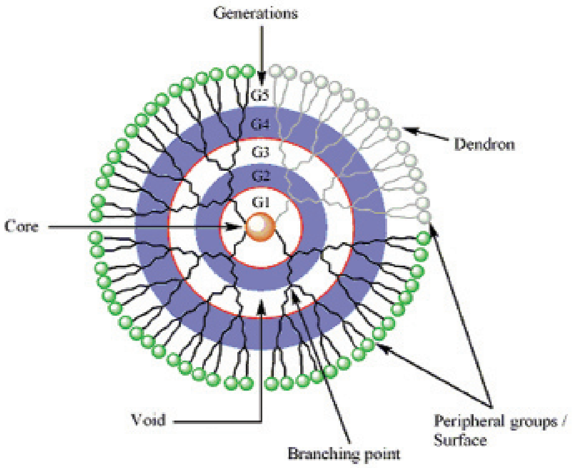

Figure 1 Schematic representation of a dendrimer

PAMAM dendrimers decorated with various functional groups can be found in the literature.

## Dendrimer Synthesis

In synthetic organic chemistry the creation and design of dendritic compounds is a relatively new field. The first successful attempt to create and design simple fractal-like structures by organic synthesis was carried out divergently by Vögtle and coworkers [9] in 1978. These molecules were initially defined as cascade molecules or arborols[10]. Dendrimer is an internationally accepted term. The name dendrimer is derived from two Greek words dendron meaning "tree" or "branch" and meros meaning "part" in Greek.

The synthesis of the first and many other dendrimers even in industry is based on the idea of iterative reaction steps. As shown in Figure 2, the core building unit ethylene diamine reacts with the monomeric branching unit acrylonitril in a Michael-type addition. Reduction of the nitril leads to a polypropylene amine dendrimer of generation 1, in which we already have four amino groups. One reaction cycle is finished therewith. With further preparative reaction cycles, dendrimers with more peripheric primary amine units are obtained.

Traditionally, two different synthetic concepts are available for the preparation of dendrimers, either the divergent [11] or convergent [12] growth approach:

a) In the divergent method branching unit by branching unit is attached to the core molecule, thus multiplying the number of peripheral groups dependent on the branching multiplicity.

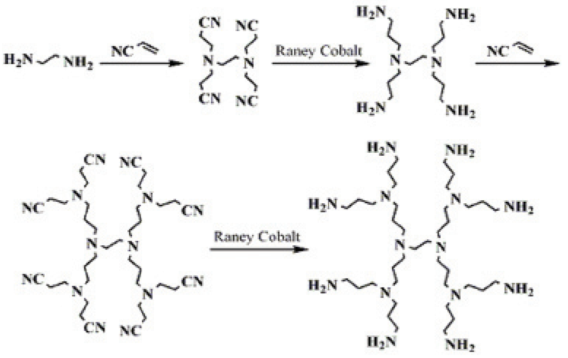

Figure 2 Repetitive synthesis of the first dendrimer

b) The convergent method follows the opposite path, the skeleton is built up step-by-step starting from the end groups towards the inside and finally reacted with a core molecule to give the complete dendrimer.

The large-scale production of dendrimers is usually performed by the divergent approach in which an accumulation of statistical defects is observed at higher generations. In contrast, the convergent method is a better way to prepare a defect-free dendrimer,

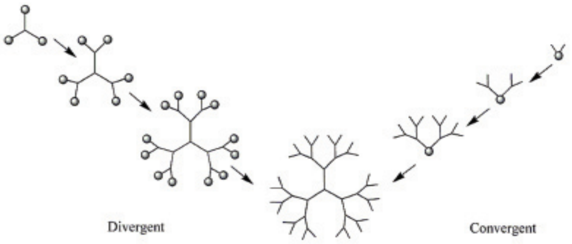

Figure 3 Strategies for dendrimer synthesis, The gray dots mark the functional groups.

but the purification process associated with this method is sometimes time consuming. Appropriately purified, convergently produced dendrimers are probably the most precise synthetic macromolecules that exist today.

## Characterization of Dendrimers

In principle, NMR experiments can help to identify the presence of structural defects, for example, through odd integrations, but the precision is not very high, especially for higher generations of dendrimers. Also, the exact nature of the defects is difficult to identify by NMR methods, because peaks are often broadened due to the large number of very similar building blocks located in different microenvironments. Mass spectrometry would have been the method of choice, but in 1978 none of the nowadays routinely used soft ionization techniques existed, with the exception of fast atom bombardment (FAB)[13]. However, FAB is quite limited in the availability of a sufficiently large mass range and applicability to substances of low polarity. Consequently, it took almost a decade for dendrimer chemistry to develop into a field of intense research.

Nowadays, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry is considered to be a highly valuable tool for the characterization of dendrimers[14] due to the large mass range of the mass analyzers usually coupled to the MALDI ion source [15].

## Properties and Applications of Dendrimers

Due to their precise architecture and construction, dendrimers possess inherently valuable physical, chemical and biological properties. These properties include:

- Efficient membrane transport: Dendrimers have demonstrated rapid transport capabilities across biological membranes.
- Low toxicity: Most dendrimer systems display very low cytotoxicity levels.
- Low immunogenicity: Dendrimers commonly manifest a very low or negligible immunogenic response when injected or used topically.
- High uniformity and purity: The synthetic process used produces dendrimers with uniform sizes, precisely defined surface functionality, and very low impurity levels.
- High loading capacity: Dendrimer structures can be used to store and carry a wide range of metals, organic or inorganic molecules by encapsulation and absorption.

Dendrimer research is currently associated with numerous technological [16] and biomedical [17] applications such as coatings and films, [18] in vivo contrast agents in X-ray and magnetic resonance imaging, [19] gene transfection agents, [20] materials for antibodies and inhibitors of nonspecific protein adsorption [21]. Several dendrimer-based products have been developed by different companies worldwide, for example: Starpharma´s VivaGel™ is designed as a topical microbicide to prevent the transmission of HIV and other sexually transmitted diseases. Stratus® CS, for cardiac marker diagnostic, commercialized by Dade Behring, is also based on dendrimers. The US Army Research Laboratory has developed Alert Ticket™ for anthrax detection.

## Conclusions

Dendrimers and dendrons are the most intensely investigated subset of dendritic polymers. In the past decade, over 5000 literature references have appeared dealing with this unique class of structure-controlled polymers. The controlled shape, size, and differentiated functionality of dendrimers; their ability to combine both organic and inorganic components; their compatibility with many other nanoscale building blocks such as DNA, metal nanocrystals, and nanotubes; their ability to provide both isotropic and anisotropic assemblies; their potential for ordered self-assembly; and their propensity to either encapsulate or be engineered into unimolecular functional devices make dendrimers uniquely versatile amongst existing nanoscale building blocks and materials. Additionally, selectively derivatized dendrimers and dendrons [22] are important subunits for the preparation of more elaborate macromolecular assemblies – "dendritic networks".

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