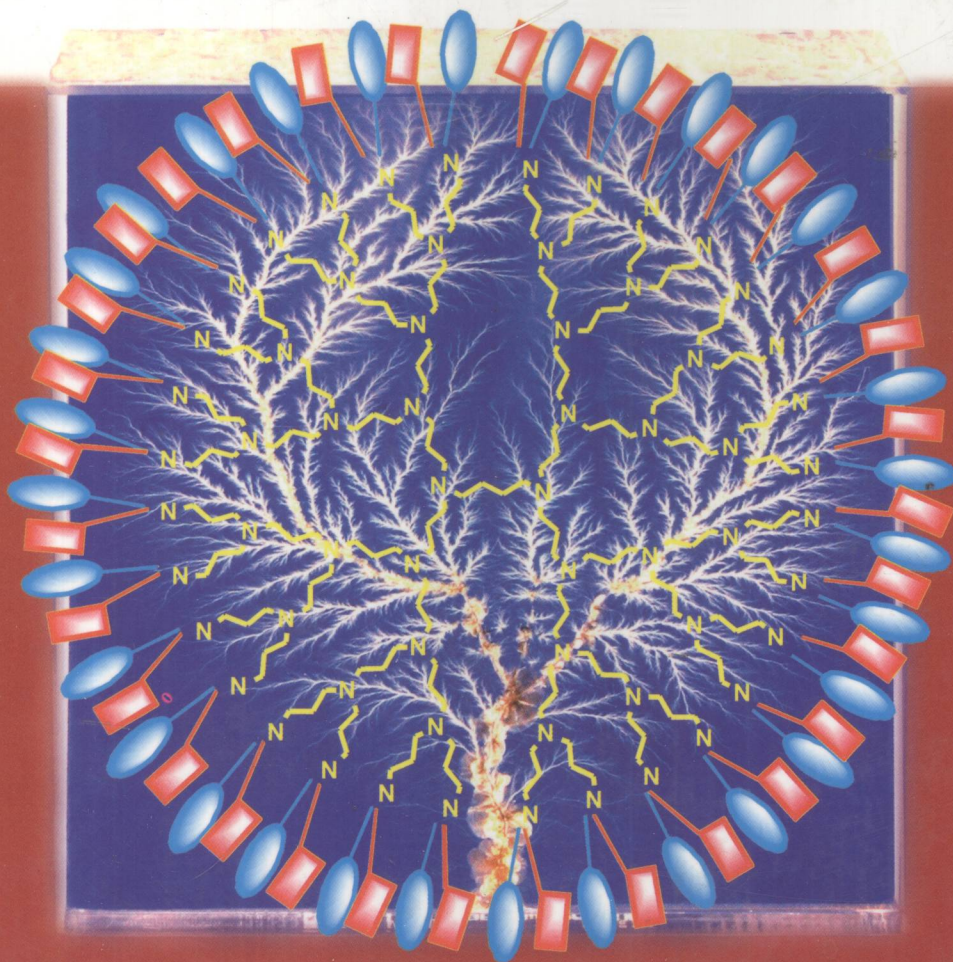


Fritz Vögtle, Gabriele Richardt and  
Nicole Werner

 WILEY-VCH

# Dendrimer Chemistry

Concepts, Syntheses, Properties, Applications



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Fritz Vögtle, Gabriele Richardt and Nicole Werner

## Dendrimer Chemistry



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## Cover

The branched treelike "*Lichtenberg Figure*" has been generated by bombarding a plexiglass block with electrons which in one of the electron generators at the Max-Planck-Institut für Strahlenchemie had been boosted to reach the impact energy necessary to enter the highly isolating material. The electrons are slowed down and immobilized in the plexiglass which then is being negatively charged. When after the electron bombardement the plexiglass block is contacted by an earthed electrode, the negative charges are removed through this contact. The discharge process is accompanied by tiny lightnings which melt the plexiglass and thus generate the finely branched figure. Since the discharge cannot be controlled accurately, a unique figure is formed each time. These figures have been named "*Lichtenberg Figures*", after the physicist and philosopher Georg Christoph Lichtenberg (1742–1799) of the University of Göttingen. In his treatise "*Über eine neue Methode, die Natur und die Bewegung der elektrischen Materie zu erforschen*", Lichtenberg has described the novel phenomenon using the notion "positive and negative electricity" for the first time. – The photo of the "*Lichtenberg Figure*" in a plexiglass block has been superimposed by a schematic drawing of a poly-bifunctionalized dendritic molecule.

**Source:** Max-Planck-Institut für Strahlenchemie, Mülheim an der Ruhr. We thank Dr. W.E. Klotzbücher for providing the photograph and related information.

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## ***Further Reading***

Sliwa, W., Kozlowski, C.

### **Calixarenes and Resorcinarenes Synthesis, Properties and Applications**

2009  
Hardcover  
ISBN: 978-3-527-32263-3

Diederich, F., Stang, P.J., Tykwinski, R.R. (eds.)

### **Modern Supramolecular Chemistry Strategies for Macrocycle Synthesis**

2008  
Hardcover  
ISBN: 978-3-527-31826-1

Schalley, C.A. (ed.)

### **Analytical Methods in Supramolecular Chemistry**

2007  
Hardcover  
ISBN: 978-3-527-31505-5

J. Dodziuk, H. (ed.)

### **Cyclodextrins and Their Complexes Chemistry, Analytical Methods, Applications**

2006  
Hardcover  
ISBN: 978-3-527-31280-1

## Preface

The positive feedback we have received regarding of our book “Dendritische Moleküle” in German gave us good reason to prepare a corresponding international edition in English. Since this fast developing research area of dendritic molecules has gained international recognition and promises to generate more applications in the “high chem” field as well as in technology, we chose the new title “Dendrimer Chemistry”. Nevertheless, this three-author book goes far beyond chemistry, touching on important topics in material and life sciences.

We have aimed to provide short introductory explanations for non-experts, e.g. in areas such as spectroscopic methods and new methodologies in adjacent disciplines, in order to make this interdisciplinary book easier to read for students and not only for chemists.

Apart from the modified title and the new cover illustration and legend, many corrections, additions, hints and remarks have been added to the text and the illustrations. Dozens of recent literature references from 2007 and 2008, especially to new books and overviews, have been included in all chapters to keep the book up to date.

It is especially pleasing that the publisher could maintain the style of the illustrations, in particular the red and green colors symbolising host and guest molecules, respectively, throughout the book.

We hope that this most recent overview on dendritic molecules in chemistry (and beyond) will be useful not only as an introduction and source of general information, but also as a basis for future teaching and research in all disciplines of chemistry as well as material and life sciences.

We would like to thank Dr. Heike Nöthe, STM-books, Wiley-VCH-Verlag, for her valuable advice in the course of production of this book and Mr. Anthony Rackstraw for his excellent translation of the German manuscript into English.

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Bonn, September 2008

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## 1

## Introduction

## 1.1

## Historical – Cascade molecules and dendrimers

In 1978 Vögtle *et al.* [1] described a series of synthetic “cascade molecules” [2–4] as the first tangible representatives of compounds exhibiting potentially perpetual branching. Starting from diverse primary monoamines and diamines, “cascade synthesis” was performed to attach spacer units of propylenamine structure whose N atoms served as a 1 → 2 branching point (formal branching of a bond into two new ones) during each subsequent repetitive step [5].

In the simplest case, reaction of a primary *monoamine* via a two-fold Michael reaction with acrylonitrile (bis-cyanoethylation) led to the *dinitrile* (Fig. 1.1). Subsequent reduction of the two nitrile functions – by hydrogenation with sodium borohydride in the presence of cobalt(II) ions – afforded the corresponding terminal *diamine*. Repetition (iteration) of this synthetic sequence, consisting in Michael addition followed by reduction, provided the first – structurally variable – access to regularly branched, many-armed molecules.

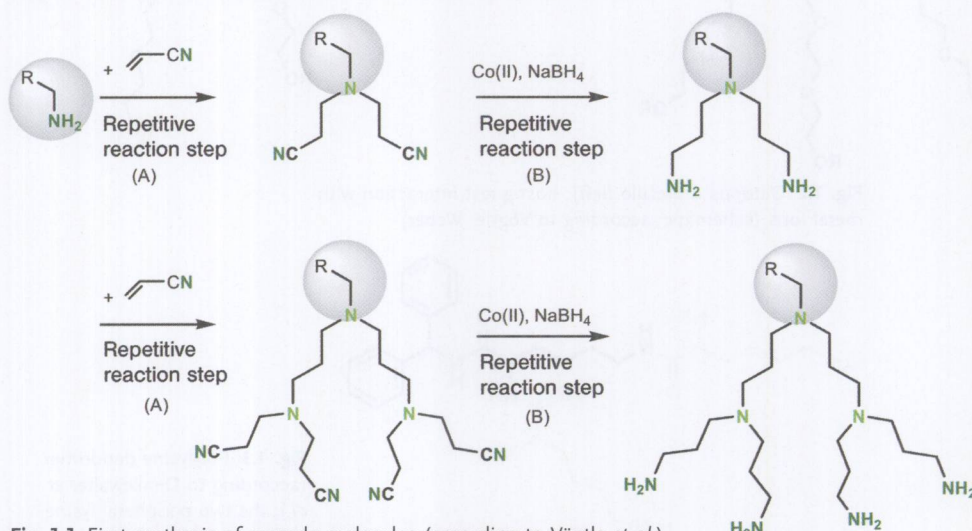


Fig. 1.1 First synthesis of cascade molecules (according to Vögtle *et al.*)

Several years earlier (1974), the same group had already described many-armed, albeit non-branched, molecules as *octopus molecules* [6], whose numerous arms were used for complexation with metal ions (Fig. 1.2). These octopus molecules can be regarded as forerunners of nitrogen-containing propylenamine cascade molecules since they already demonstrated the utility of many adjacent functional arms – all the more readily attainable by branching – for example for host-guest interactions [6].

Initially, further development of highly branched (cascade-type, dendritic) molecules proceeded slowly for many years, probably due to the synthetic and analytical obstacles to be overcome at the time with these species, which occupy an intermediate position at the boundary between low-molecular weight and high-molecular weight compounds.

Denkewalter *et al.* described a pathway to polylysine dendrimers (Fig. 1.3) via divergent synthesis in 1981 patents (see Section 2.1) [7].

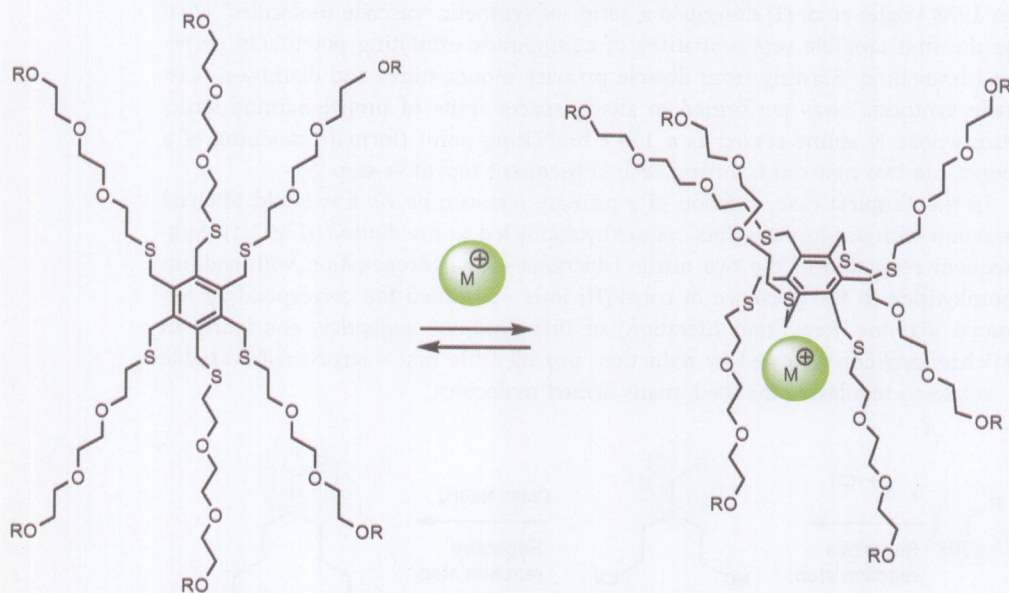


Fig. 1.2 Octopus molecule (left): host-guest interaction with metal ions (schematic; according to Vögtle, Weber)

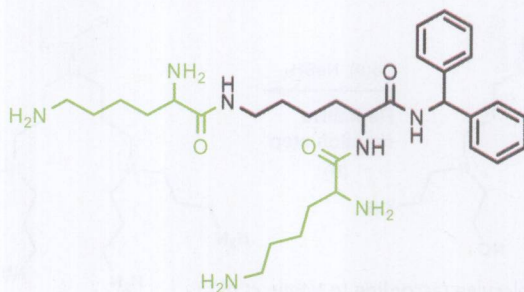


Fig. 1.3 Polylysine dendrimer (according to Denkewalter *et al.*); the two peripheral lysine units are shown in green



In 1982 Maciejewski developed a densest packing concept for polymers having a cascade-like structure [8]. On the basis of statistical considerations, in 1983 de Gennes (1991 Nobel laureate for physics) and Hervet presented limits to the growth of branched molecules (*starburst-limited generation*), paying due attention to the influence of steric hindrance [9]. Further statistical model calculations were combined with the “cascade theory” [10]. According to de Gennes, highly branched molecules are considered as “soft material” [11].

In 1985 Tomalia developed branched *poly(amidoamines)* (PAMAM), which he also designated as “starburst dendrimers” (Fig. 1.4) and generally propagated the name “dendrimer” (from the Greek *dendron* = tree and *meros* = part) [12]. Like the first cascade synthesis, the synthetic route again involved Michael addition (of methyl acrylate to ammonia). The resulting ester was converted into the primary triamine by reaction with an excess of ethylenediamine. Repetition of the reaction sequence (iteration) by analogy with the cascade synthesis led to dendrimers of up to the tenth generation – with decreasing purity and perfec-

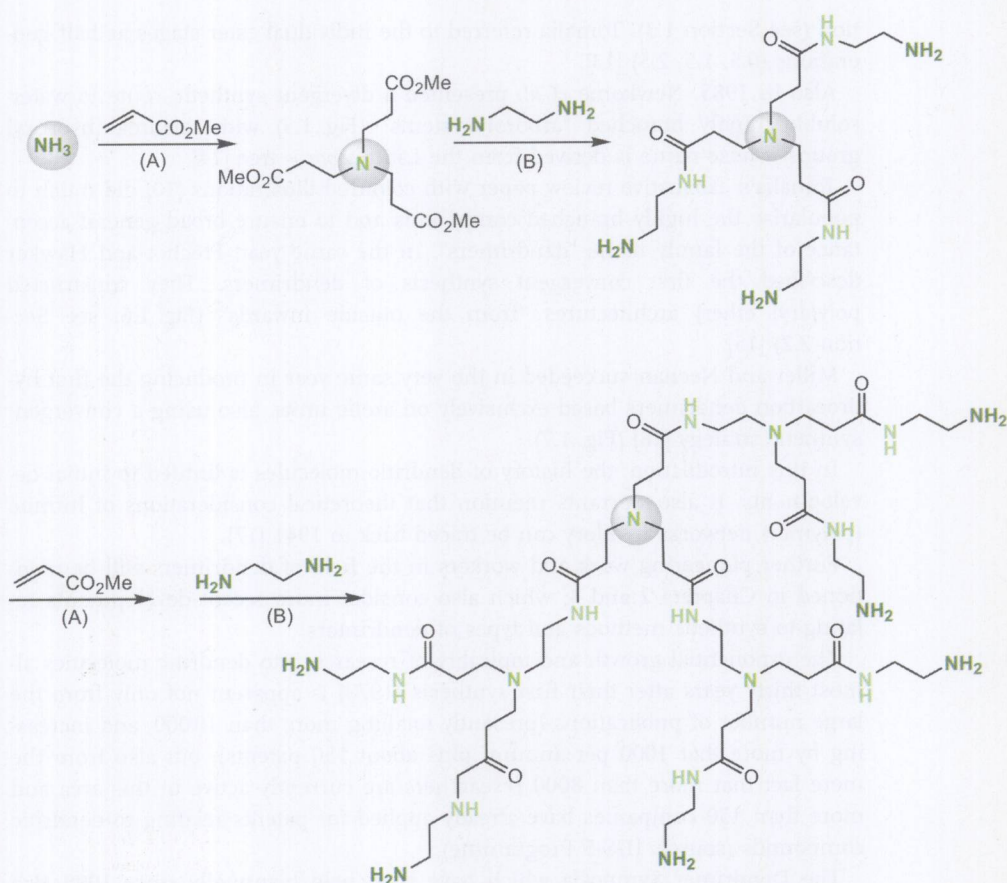


Fig. 1.4 Synthesis of poly(amidoamine) dendrimers (PAMAM; according to Tomalia *et al.*)

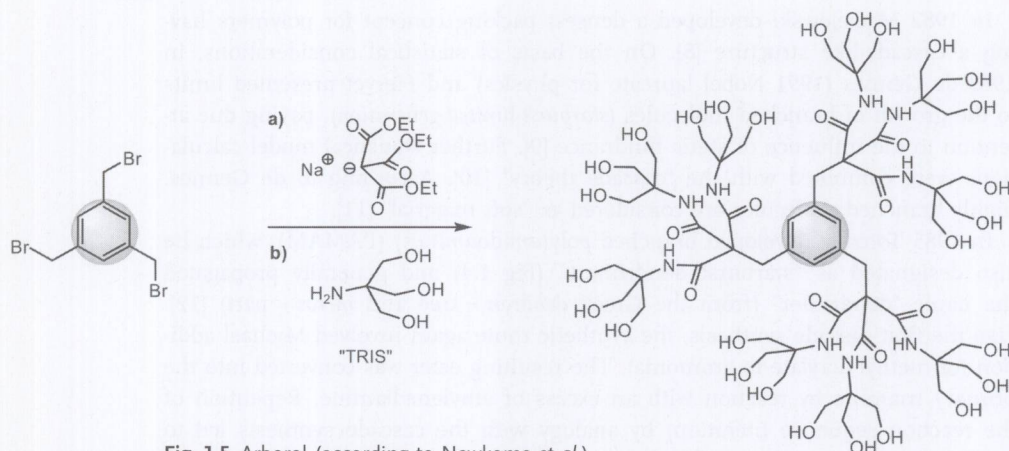


Fig. 1.5 Arborol (according to Newkome *et al.*)

tion (see Section 1.3). Tomalia referred to the individual ester stages as half generations (0.5, 1.5, 2.5) [13].

Also in 1985, Newkome *et al.* presented a divergent synthetic route to water-soluble, highly branched “arborol systems” (Fig. 1.5) with terminal hydroxyl groups, whose name is derived from the Latin *arbor* = tree [14].

Tomalia’s exhaustive review paper with coloured illustrations [10] did much to popularise the highly branched compounds and to ensure broad general acceptance of the family name “dendrimers”. In the same year, Fréchet and Hawker described the first convergent synthesis of dendrimers. They constructed poly(aryl ether) architectures “from the outside inwards” (Fig. 1.6; see Section 2.2) [15].

Miller and Neenan succeeded in the very same year in producing the first hydrocarbon dendrimers based exclusively on arene units, also using a convergent synthetic strategy [16] (Fig. 1.7).

In this introduction, the history of dendritic molecules is limited to initial developments. It also warrants mention that theoretical considerations of infinite (polymer) networks by Flory can be traced back to 1941 [17].

Further pioneering work and workers in the field of dendrimers will be mentioned in Chapters 2 and 4, which also consider more recent developments relating to synthetic methods and types of dendrimers.

The exponential growth and topicality of research into dendritic molecules almost thirty years after their first synthesis (1978) is apparent not only from the large number of publications (presently totalling more than 10 000, and increasing by more than 1000 per annum, plus about 150 patents), but also from the mere fact that more than 8000 researchers are currently active in this area and more than 150 companies have already applied for patents relating to dendritic compounds (source: IDS-5 Programme).

The Dendrimer Symposia which have been held biannually since 1999 also reflect this development: The first International Dendrimer Symposium (IDS-



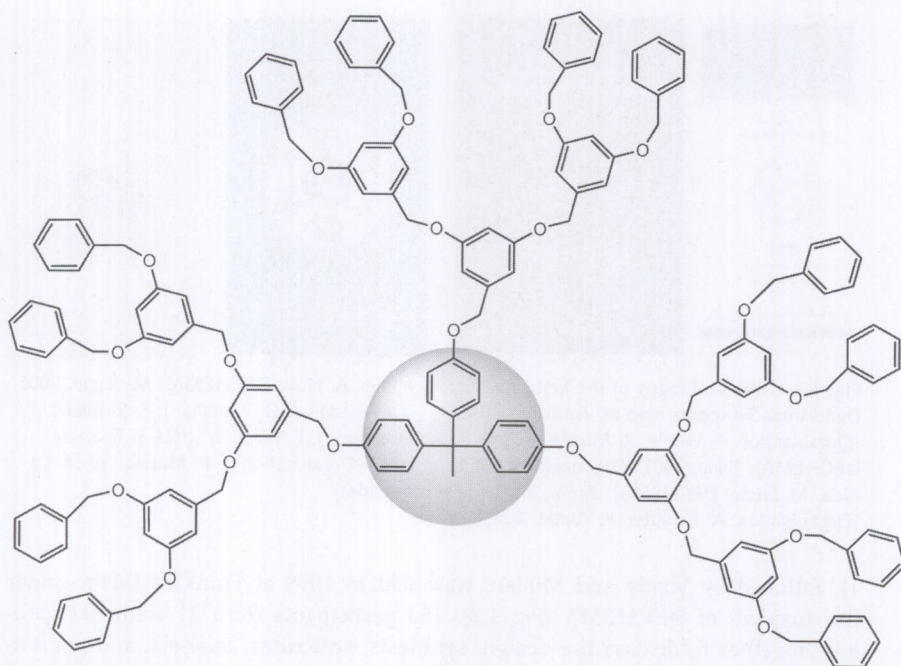


Fig. 1.6 Fréchet dendrimer

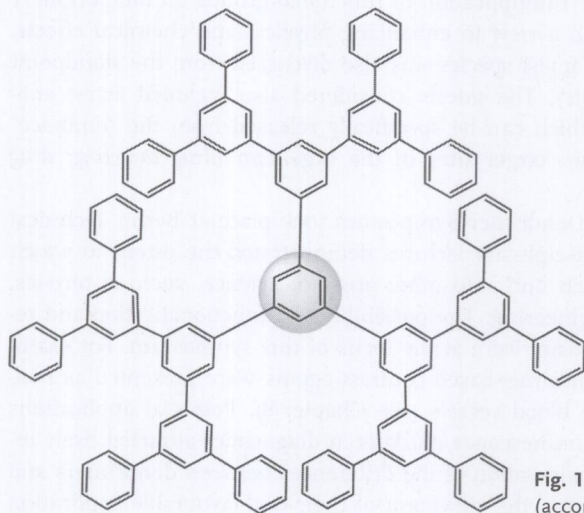


Fig. 1.7 Hydrocarbon dendrimers  
(according to Miller and Neenan)