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# Orthogonally Protected Dendronized Polymers: Synthesis, Characterization and Chemical Modification

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Presented by

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## List of Publications

**A Series of First- and Second-Generation Dendronized Polymers with Orthogonally Protected Amine Groups in the Periphery**
R. Al-Hellani, A. D. Schlüter.*
*Macromolecules* **2006**, *39*, 8943-8951.

**Covalent Connection of Individualized, Neutral, Dendronized Polymers on a Solid Substrate Using a Scanning Force Microscope**
R. Al-Hellani, J. Barner, J. Rabe,* A. D. Schlüter.*
*Chem. Eur. J.* **2006**, *12,* 6542-6551

**On the Synthesis and Selective Deprotection of Low-Generation Dendrons with Orthogonally Protected Peripheral Amine Groups and a Possible Impact of the Deprotection Conditions on the Stability of Dendronized Polymers Skeleton**
R. Al-Hellani, A. D. Schlüter.*
*Helvetica Chimica Acta* **2006**, *89*, 2745-2763

**Synthesis of Orthogonally Protected, Second Generation Dendronized Polymers**
R. Al-Hellani, A. D. Schlüter.*
*Polym. Mater. Sci. Eng. Prepr.* **2004**, *41*, 167.

## Oral and Poster Presentation

[1] *Minisymposium on Dendronized Polymers*, Vortrag, Humboldt Universität, Berlin, Deutschland **März 2006**

[2] *Makromolekulares Kolloquium*, Poster, Freiburg Universität, Freiburg, Deutschland, **Feb. 2006**

[3] *Fall Meeting of Polymer Group of Switzerland*, Poster, Universite de Neuchâtel, Neuchâtel, Schweiz, **Nov. 2005**

[4] *Material Science Days at ETH-Zürich*, Poster, Zürich, Schweiz, **März 2005,** und **März 2006**

[5] *American Chemical Society 228$^{th}$ National Meeting and Exposition*, Poster, Philadelphia, USA, **Aug. 2004**

[6] *20th Anniversary Meeting of Polymer Group of Switzerland*, Poster, ETH-Zürich, Zürich, Schweiz, **Nov. 2004**

[7] *SFB 448-Mesoskopisch strukturierte Verbundsysteme*, Poster, Technische Universität Berlin, Berlin, Deutschland, **März 2003**

[8] *3$^{rd}$ International Dendrimer Symposium*, Poster, Freie Universität Berlin, Berlin, Deutschland, **Sept. 2003**

## Summary

Dendronized polymers comprise hundreds even thousands of "surface" functional groups (peripheral end groups). These groups are known to play a key role in the property engineering of these intriguing macromolecules. By the proper choice of these groups, fundamental issues and sophisticated aspects can be addressed, for example, solubility, the attachment of cell-targeting units, azide moieties, drugs, compactization of DNA, etc. Almost all dendronized polymers known today carry only one kind of functional group (either amine or hydroxyl). This limits the options for surface engineering of these macromolecules and therefore, a strategy was required to overcome this limitation and to increase the options for surface decoration.

The present thesis describes a synthetic way toward dendronized polymers which carry defined and variable proportions of orthogonally protected peripheral amino groups at each repeat unit (Figure A). A set of first (G1) and second generation (G2)

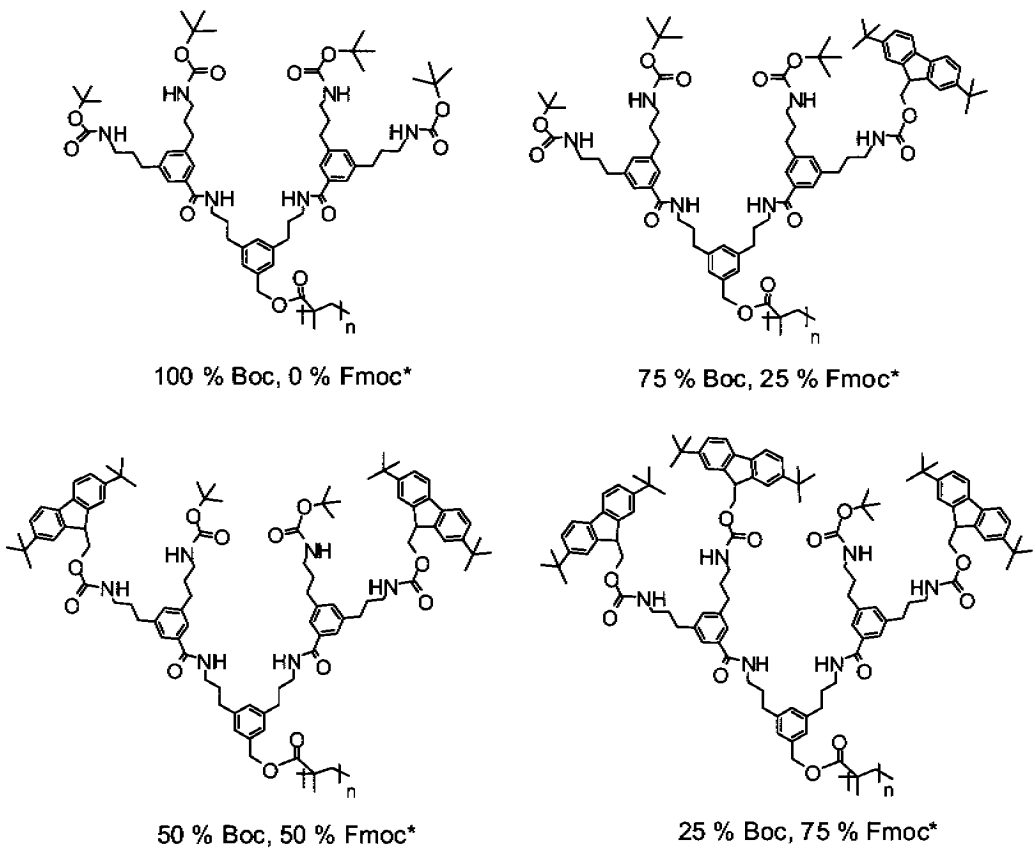
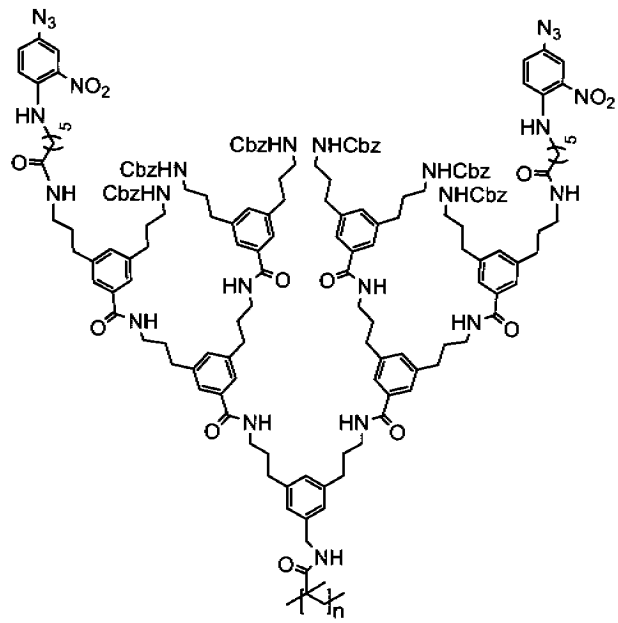



**Figure A**

orthogonally protected, methacrylate-based dendronized polymers was synthesized using the macromonomer route. The polymers carry a predetermined number of Boc

(*tert*-butyloxycarbonyl) and Fmoc* (2,7-di(*tert*-butyl)-9-fluorenyloxycarbonyl) protected peripheral amino groups at each repeat unit. On the G1 level, polymers carrying either 1Boc and 1Fmoc*, or 2Fmoc* were obtained. And on the G2 level, polymers carrying either, 2Boc and 2Fmoc*, or 3Boc and 1Fmoc*, or 1Boc and 3Fmoc* groups were obtained. The selective removal of these protecting groups on the polymer level was then proven so as to allow later introducing predetermined numbers of functional groups at each repeat unit.

This thesis reports also the synthesis of a neutral, high-molar-mass, acrylamide-based, third generation dendronized polymer, **71c**, which carry a defined number of azide groups at its periphery (Figure B). An attach-to-route was used in which a first generation (G1) dendronized polymer was reacted with a second generation (G2) dendron. The degree of structure perfection of the resulting dendronized polymer was quantified as 99.8 %. This value was obtained after the introduction of a fluorescence label (dansyl chloride) at the sites that remained unaffected by the dendronization.




71c

**Figure B**

In cooperation with the group of Prof. Rabe (Humboldt University, Berlin), the polymer, **71c**, was then spin-coated onto highly oriented graphite that was precoated with an ultrathin layer of $C_{12}H_{25}NH_2$, which was introduced to provide a well-defined substrate for dendronized polymer adsorption and manipulation. Scanning Force microscopy (SFM) revealed single dendronized polymers, which could be moved

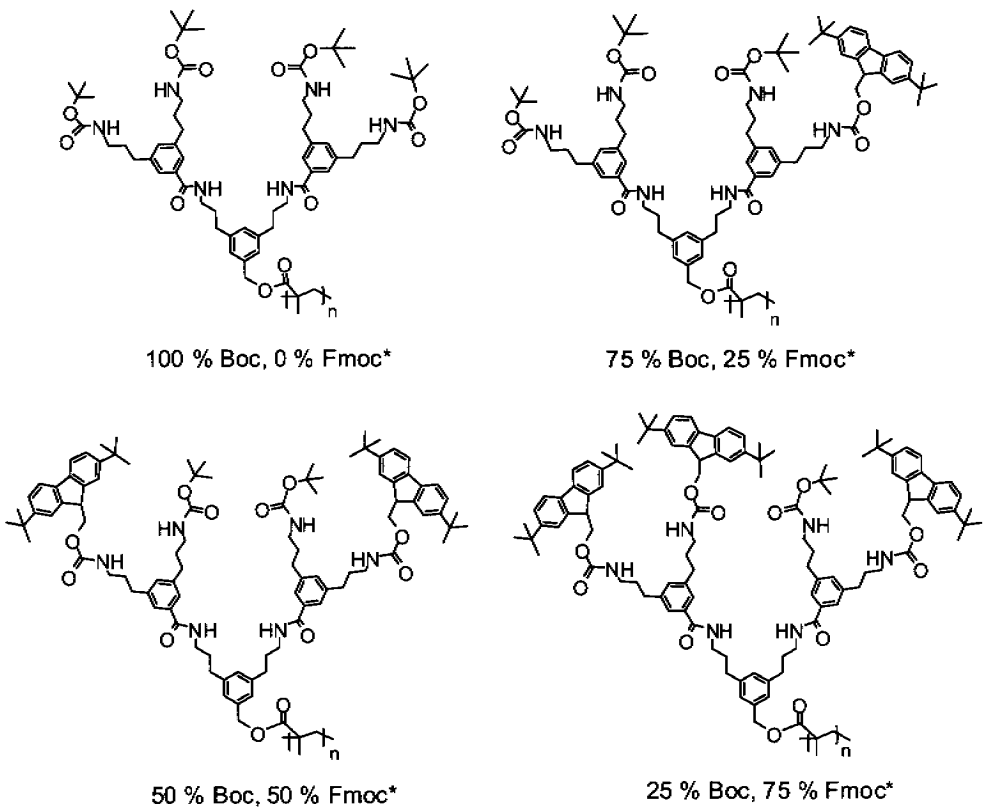
across the surface and welded by covalent cross-linking induced by photochemical decomposition of the azides into highly reactive nitrenes. The successful formation of covalent bonds between two dendronized polymers was confirmed mechanically challenging the link with scanning force microscopy. More SFM experiments were carried out with the polymer, **71c** to form heterojunction bonds. An experiment of this kind was carried out between dendronized polymer **71c** and DNA single strands after they have been co-adsorbed onto the same substrate. Another experiment was carried out also between dendronized polymer **71c** and the step-edge of HOPG to form a heterojunction linkage.

Finally, a method was developed for the quantification of structure perfection of dendronized polymers synthesized according to the attach-to-route. An acrylate-based G3 dendronized polymer, was first prepared by reacting a first generation acrylate based dendronized polymer carrying two free amino groups at each repeat unit with a second generation dendron carrying active ester groups. The resulted polymer was then submitted to hydrogenolysis which led to the cleavage of a G3 dendron right at the linkage point to the polymer backbone (de-dendronization). NMR investigation on the cleaved dendron showed that almost all the free amino groups of the G1 polymer have reacted with the G2 dendron.

## Zusammenfassung

Dendronisierte Polymere weisen Hunderte ja sogar Tausende von an der Oberfläche lokalisierte, funktionelle Gruppen auf (periphere Endgruppen). Diese Gruppen spielen für die Eigenschaften dieser faszinierenden Makromoleküle eine Schlüsselrolle. Durch eine passende und korrekte Wahl der funktionellen Gruppen können sowohl grundlegende, als auch spezielle Eigenschaften gezielt gesteuert werden, zum Beispiel: Löslichkeit, Wechselwirkung mit Zellen, chemische Reaktivität durch Anbringen von Aziden, kovalente Bindung von Arzneimitteln, Kondensierung von DNA, usw. Fast alle dendronisierten Polymere die heute bekannt sind, tragen nur eine Art von peripheren Endgruppen (entweder eine Aminogruppe oder eine Hydroxylgruppe). Die schränkt die Optionen für die Oberflächenmodifizierung dieser Makromoleküle stark ein. Um diese Einschränkung zu überwinden, wurde eine entsprechende Strategie entwickelt, um die Möglichkeiten der Oberflächenfunktionalisierung zu erweitern.

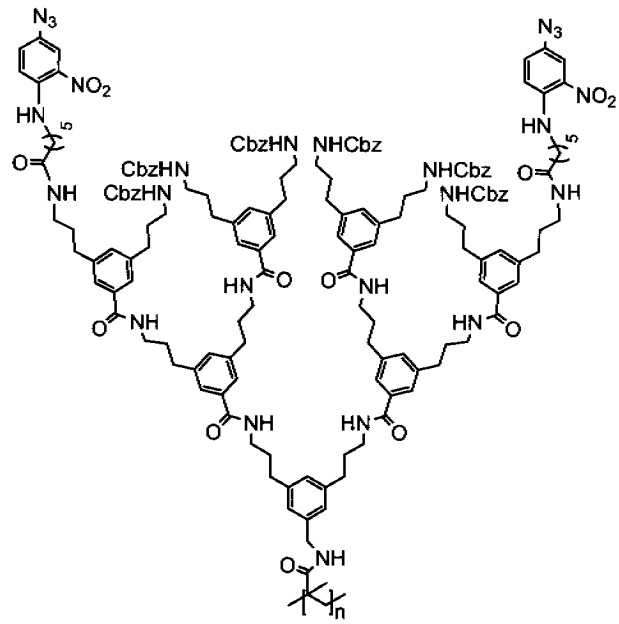
Die vorliegende Arbeit beschreibt ein synthetisches Verfahren zur Herstellung von dendronisierten Polymeren, die definierte und variable Anteile von orthogonal geschützten Aminogruppen in jeder konstitutiven Repetiereinheit tragen (Figur A).




**Figur A**

Ein Satz erster (G1) und zweiter (G2) Generation orthogonal geschützter, Methacrylat-basierter, dendronisierter Polymere wurde mit dem Makromonomer-Verfahren synthetisiert. Die Polymere tragen in jeder Repetiereinheit eine vorbestimmte Anzahl von Boc- (*tert*-Butyloxycarbonyl) und Fmoc*- (2,7-Di(*tert*-butyl)-9-fluorenyloxycarbonyl) geschützten Aminogruppen. G1-Polymere wurden hergestellt, die entweder 1 Boc-Gruppe und 1 Fmoc*-Gruppe enthielten, oder 2 Fmoc*-Gruppen. G2-Polymere wurden gebildet, die entweder 2 Boc- und 2 Fmoc*-Gruppen, oder 3 Boc-Gruppen und 1 Fmoc*-Gruppe, oder 1 Boc-Gruppe und 3-Fmoc*-Gruppen enthielten. Auf der Stufe der Polymeren wurde die selektive Entschützung dieser geschützten Gruppen nachgewiesen. Dies ermöglichte später, dass eine bestimmte Anzahl funktioneller Gruppen in jeder sich wiederholten Einheit eingeführt werden konnte.

Die Arbeit berichtet auch über die Synthese eines neutralen, hochmolekluaren, Acrylamid-basierten dendronisierten Polymeren der dritten Generation (G3), 71c. Dieses Polymere hat an der Peripherie eine definierte Anzahl von Azidgruppen (Figur B). Zur Herstellung wurde das sogenannte „attach-to-route"-Verfahren verwendet, bei welchem ein G1-Polymer mit einem G2-Dendron zur Reaktion gebracht wurde. Der Grad der Strukturvollkommenheit dieses dendronisierten Polymeren wurde auf 99,8% quantifiziert. Dieser Wert wurde bestimmt, in dem eine fluoreszierende Gruppe (Dansylchlorid) mit den freien Amino-Gruppen zur Reaktion gebracht wurde.




**Figur B**

In einer Zusammenarbeit mit der Gruppe von Prof. Rabe (Humboldt Universität, Berlin), wurde das Polymer 71c dann mittels „spin coating“ auf hoch orientierten Graphit (HOPG) aufgetragen, der vorgängig mit einer ultradünnen Schicht von Dodecylamin ($C_{12}H_{25}NH_2$) bedeckt wurde. Diese Dodecylamin-Schicht wurde eingeführt, um eine geeignete Unterlage für die Adsorption und Manipulation der dendronisierten Polymere zur Verfügung zu stellen. Mit der Kraft-Mikroskopie (SFM) konnten einzelne dendronisierte Polymere nachgewiesen und auf der Oberfläche bewegt werden. Einzelne Polymermoleküle konnten auch durch eine photochemische Reaktion (Zersetzung der Azide) kovalent miteinander verbunden werden. Die erfolgreiche Bildung von kovalenten Bindungen zwischen zwei benachbarten dendronisierten Polymeren wurde mittels SFM bestätigt. Weitere SFM-Experimente wurden mit dem Polymere 71c ausgeführt, um Heteroverknüpfungen zu bilden. Ein Experiment dieser Art wurde zwischen dem dendronisierten Polymeren 71c und einkettiger DNA durchgeführt, nachdem beide Moleküle vorgängig zusammen auf die Oberfläche aufgebracht wurden. Ein anderes Experiment wurde auch zwischen dem dendronisierte Polymeren 71c und einer vorhandenen HOPG-Schichtgrenze ausgeführt, um eine Heteroverknüpfung zu bilden.

Schließlich wurde eine Methode für die Quantifizierung der Strukturvollkommenheit von dendronisierte Polymeren entwickelt, die nach dem „attach-to route“-Verfahren synthetisiert wurden. Ein Acrylat-basiertes G3 dendronisiertes Polymeres wurde zuerst hergestellt. Dabei wurde ein Acrylate-basiertes G1 dendronisiertes Polymeres, welches zwei freie Amino-Gruppen an jeder Repetiereinheit aufwies, mit einem G2-Dendron, welches aktive Ester-Gruppen enthielt, umgesetzt Das resultierende Polymere wurde dann der Hydrogenolyse unterworfen, welche zur Abspaltung des G3-Dendrons führte, direkt am Verbindungspunkt zum Polymer-Rückgrat (De-dendronisierung). Die NMR-Untersuchung des abgespaltenen Dendrons zeigte, dass fast alle freien Amino-Gruppen des G1 Polymeren mit dem G2 Dendron reagierten.

# 1. Introduction

In recent years a new class of macromolecules, the so-called dendronized polymers has been explored. It is the subject of high interest in the field of covalent synthesis of nanometer-sized molecules. Dendronized polymers originate from the dendrimer and polymer concepts that have already been studied and well defined by many researchers. Dendrimers,[1-3] a novel class of structurally controlled, highly branched macromolecules, are comprised of a multifunctional core unit to which dendrons are attached. Dendrons are regularly branched segments consisting of repeating units with an $AB_n$ ($n \geq 2$) type functional group pattern as shown in Figure 1. Dendrimers are synthesized through stepwise, repetitive reaction sequences that guarantee completed generations (Gx). A high degree of control over molecular weight and shape is achieved depending on the synthetic strategy (convergent or divergent strategy) and on the number of the repeating units. Mostly the exterior layer of a dendrimer contains chemically active groups (e.g., $-NH_2$, -OH, $-CO_2H$) that can be modified covalently to provide various functionalities, leading to dendrimers with desired properties.

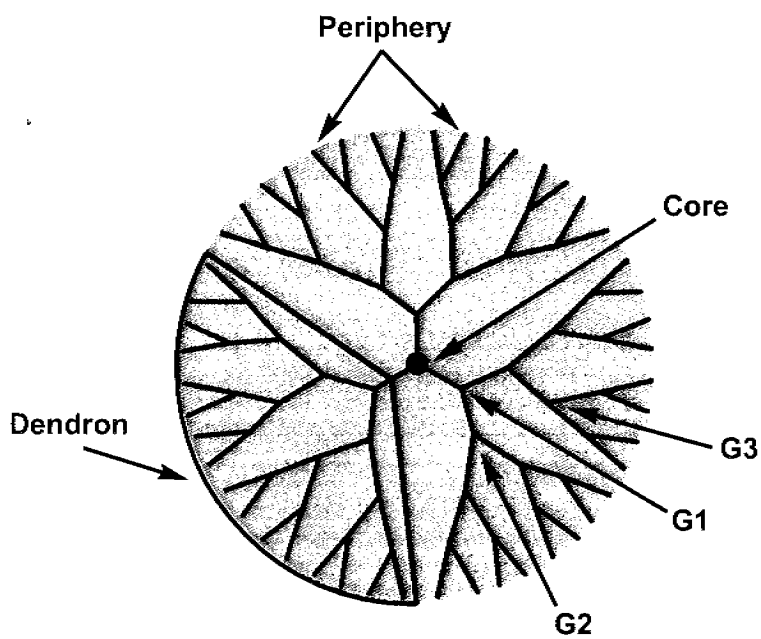



**Figure 1.** Schematic description of the main structural features of a dendrimer. Core: multifunctional center molecule; Dendron: branched segment attached to core; Generation: repeating unit, G1: first generation, G2: second generation, G3: third generation.

Dendronized polymers or dendrigraft polymers are a subclass of comb-like polymers with the comb's teeth being dendrons. They are prepared from linear polymers (e.g. polystyrene, polymethaacrylate) that possess functional groups along the backbone, ideally one at every repeat unit, to which dendrons are attached (Figure 2). These polymers are characterized by their highly branched three-dimensional structures that provide a nearly cylindrical shape with lengths and diameters of several hundred and 3-12 nanometers, respectively.[4,5] Additionally, as already mentioned for the dendrimers, many representatives carry "surface" groups (referred to as peripheral groups) which can be modified and further functionalized.[6]

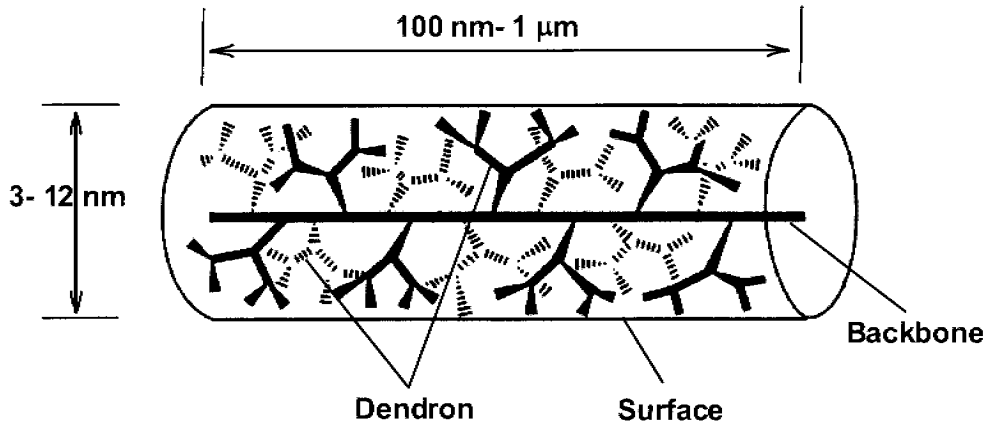



**Figure 2.** Schematic description of the main structural features of a dendronized polymer.

Dendronized polymers, as mentioned above, are hybrid structures that result from combining the polymer and the dendrimer concept. The dendrons are not attached to a central core of a dendrimer, but rather to a linear polymer instead. Connecting dendrons of increasing sizes and generations, leads to an increase in repulsive forces between consecutive dendrons. This causes the backbone of the polymer to stretch from a random coil, which is the case for a conventional polymer, to nearly all-trans zigzag for large dendrons which renders the polymer a cylindrically shaped object. Figure 3 illustrates this transition of a coiled polymer into a cylindrical molecular object by attachment of dendrons with increasingly higher generations.[7]

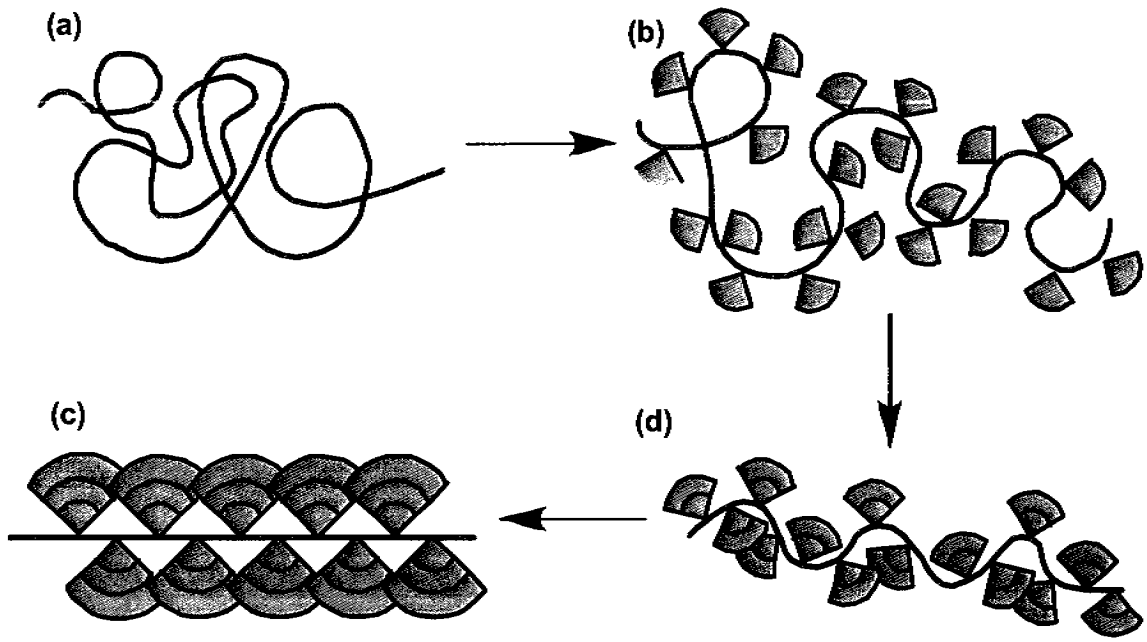



**Figure 3a-d**. Schematic representation of a coiled polymer backbone's stretching by attaching increasingly sterically demanding dendrons. (a) Conventional polymer without any dendrons; (b) first generation dendron; (c) second generation dendron; and (d) third generation dendron attached to the same chain.

## 1.1 Historical Overview

The first step toward preparation of dendronized polymers was reported in a scientific paper in 1991 as Comb-burst polymers by Tomalia.[8] A polyethylene imine prepared by living cationic polymerization of 2-ethyl-2-oxazoline and subsequent deprotection was used as the core for the synthesis of rod-shaped poly(amidoamine) such as **1** (Figure 4). This polymer at that time was called "dendrimer with polymeric core" and aimed at possible applications focused on molecular composites and crystallinity modifiers for polymeric materials.

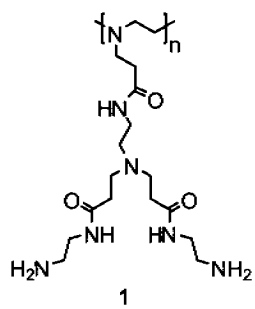



**Figure 4.** Chemical structure of comb-burst polymer reported by Tomalia.[8]

In 1992, Hawker and Fréchet et al.,[9] synthesized a styrene-based copolymer with roughly two mole percent of repeating units carrying Fréchet type dendrons. Afterwards, Schlüter et al.[10] reported the first synthesis of a dendronized polymer where nearly all repeating units carried dendrons. Rigid-rod poly([1.1.1.]propellane)s and poly(*p*-phenylene)s were prepared and then Fréchet-type dendrons attached. The degree of conversion was determined by $^{1}$H-NMR intergration and found to be virtually 100%. Since then, research on dendronized polymers developed into a whole new and growing field at the interface of organic chemistry, polymer chemistry, and material science. This can be judged from the high number of publications and from the number of groups that are working on dendronized polymers at the present time. Figure 5 illustrates a few examples of dendronized polymers: **2**, **3**, and **4**, synthesized lately by Fréchet et al.,[11] Percec et al.,[12,13] and Schlüter et al.,[14] respectively.

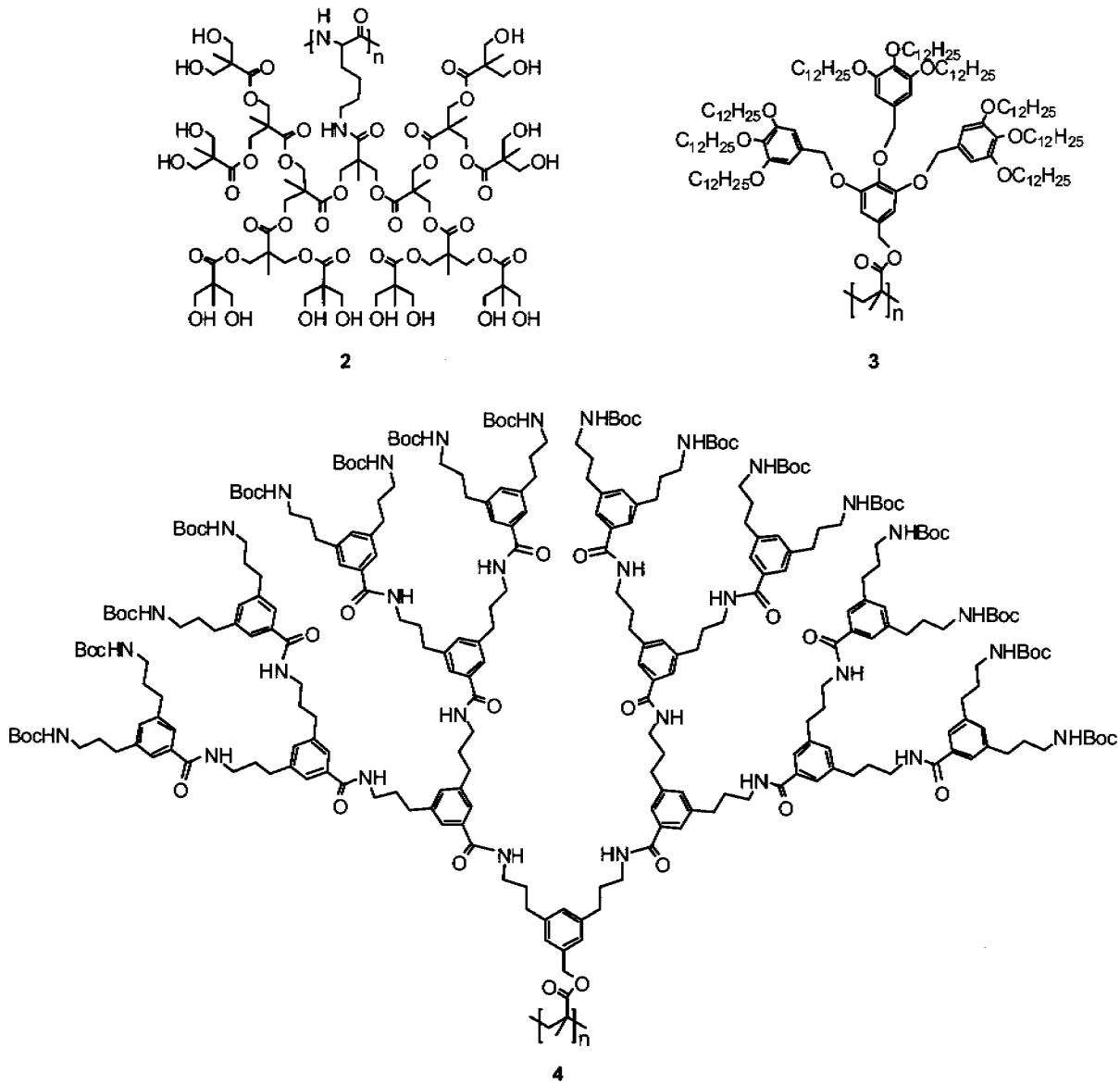



**Figure 5.** Chemical structures of dendronized polymers: **2**, G4-dendronized poly(L-lysine) prepared by Fréchet et al. in **2002**;[11] **3**, G2-dendronized siloxane polymer prepared by Percec et al. in **1997**;[12,13] and **4**, G4-dendronized polymethylmethacrylate prepared by Schlüter et al. in **2004**.[14]

## 1.2 Synthetic Strategies to Dendronized Polymers

Mainly two different synthetic methodologies have been reported for synthesis of dendronized polymers, named as routes I (attach-to route)[8] and II (macromonomer route).[15] Lately, route I was further subdivided into two subroutes Ia (graft-to) and Ib (graft-from).[5] The main differences between these routes are:

Both routes Ia and Ib start from a linear polymer e.g. polystyrene or polymethacrylates which carries reactive functional groups along its backbone. In Route Ia, the intended dendronized polymer is then obtained via attachment of preformed dendrons of the desired generation, typically between G1 and G4, through their focal points in one single step to the anchor groups along the starting polymer backbone (Figure 6a). In contrast, in route Ib, pre-formed G1-dendrons are attached in a series of subsequent reactions to the starting polymer. This results in homologous series of PG1, PG2, etc., until the dendronized polymer with the final generation is reached (Figure 6b).

On the other hand, in route II, dendronized polymers are obtained via connecting a polymerizable group to the focal points of preformed dendrons and subsequent polymerization of the thus obtained macromonomers by using either step- or chain-growth polymerization reactions (Figure 6c).[4,15] These routes will be discussed in more detail and some examples of dendronized polymers synthesized by these routes are shown in the next paragraphs.

It is worthwhile to mention here that combinations of these strategies may as well be successfully applied. The advantages of the different routes can be combined. Few examples have been reported using a combination of the macromonomer route and graft-to or graft-from routes.[16,17]

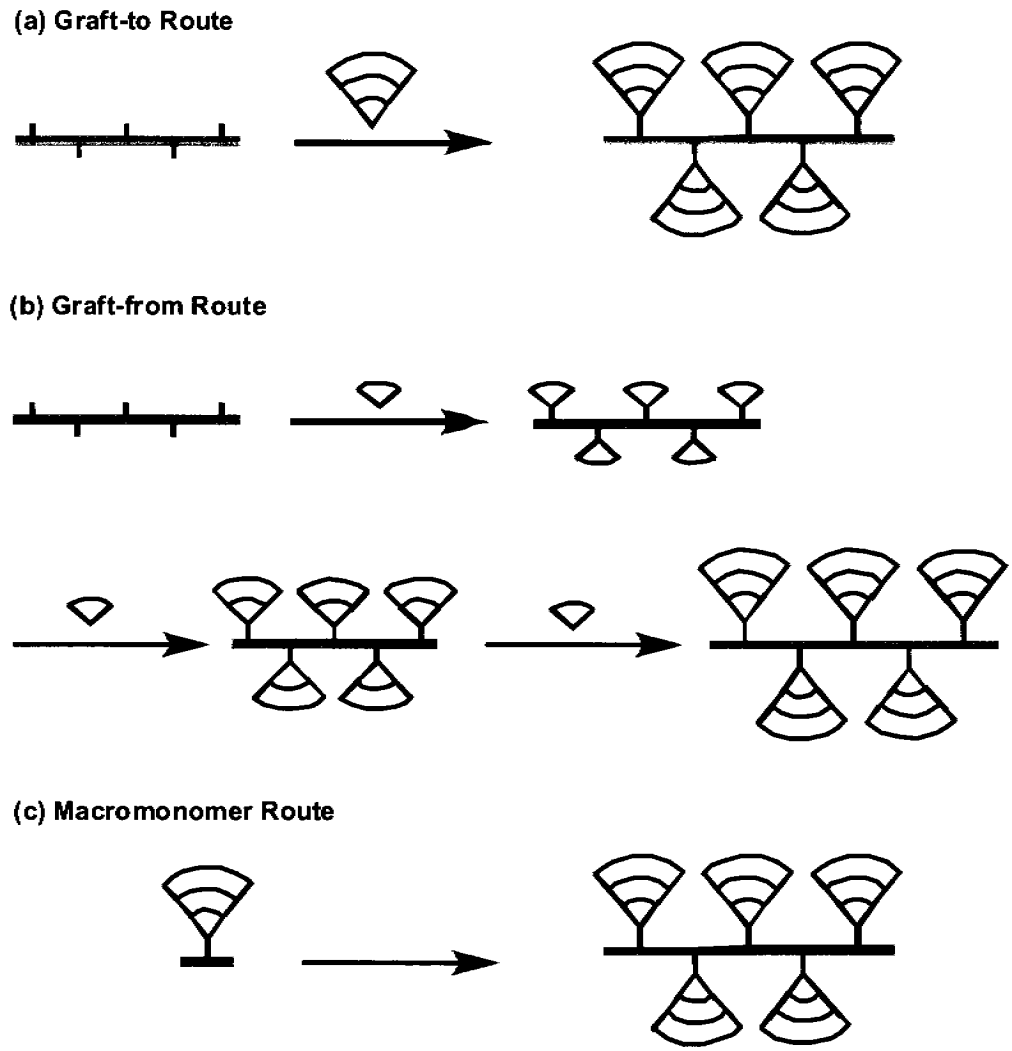
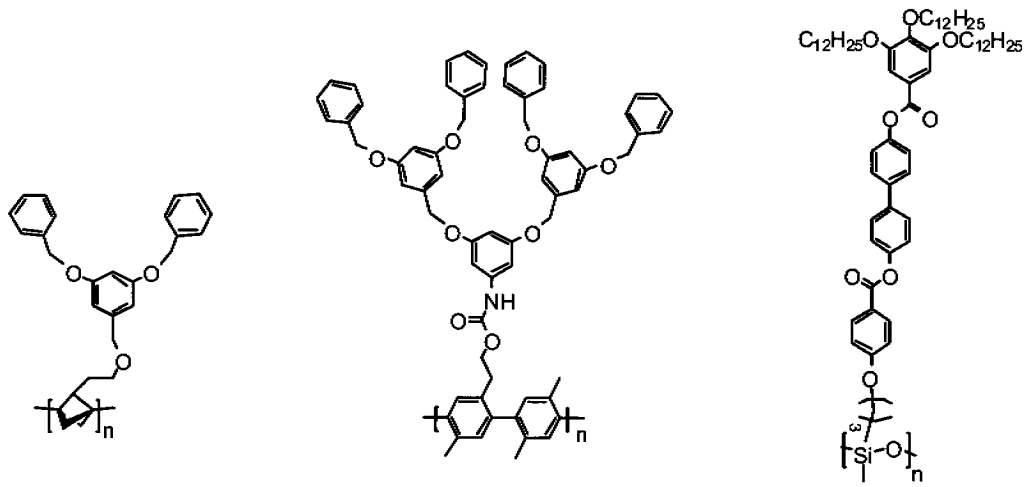



**Figure 6a-c.** Schematic illustration of the three different synthetic strategies toward dendronized polymers. (a) graft-to route (route Ia); (b) graft-from route (route Ib); and (c) macromonomer route (route II).

### *1.2.1 Graft-to route*

In route Ia (graft-to route), pre-formed dendrons of the desired generations, usually larger than G1, are connected through their focal points to the pre-fabricated linear polymer's functional groups. This is being done at each repeating unit and in a single step. The advantage of this route is its low synthetic effort. However, achieving a complete coverage is a major problem which is due to two reasons: (1) the low accessibility and the short distance between the anchor groups that may be buried along the random coiled polymer chain. (2) The steric hindrance at a not yet dendronized (reacted) functional groups along the polymer backbone imposed by the neighbouring dendrons' large size. Additionally, it will also be a serious problem to

separate defectious structures from the desired product. Because of these problems, only few dendronized polymers have been prepared via this route. Hawker et al. [18] reported an extended study on the impact of both dendron size and distance of functional groups along a backbone on the achievable degree of dendronization. Fréchet-type polyether dendrons of different generation numbers were prepared and then coupled to polystyrene backbones containing varying degrees of functionality. The results showed that at high degrees of functionality and high dendron generation couplings could not be driven to completion, which resulted in low degrees of dendronization. The highest degree of dendronization, the authors could achieve, was approximately 20 %. Schlüter et al.[10] reported the synthesis of dendronized poly([1.1.1.]propellane)s **5**, and poly(*p*-phenylene) **6** (Figure 7). From NMR investigations, they found that the degree of coverage is not affected by the degree of polymerization, but decreases with increasing dendron generation. Percec et al. [19] obtained dendronized polymer **7** (Figure 7) by grafting Percec-type dendrons to poly(hydrogenmethylsiloxane) in a hydrosilation reaction. By using characterization methods such as differential scanning calorimetry (DSC), wide and small-angle X-ray scattering (WAXS and SAXS), and thermal optical polarized microscopy, the authors found that polymer **7** exhibits an enantiotropic hexagonal columnar mesophase. The columns of the mesophases were generated by the elongated polymer backbone penetrating through the center of the column and tapered extended mesogens radiating out of it.



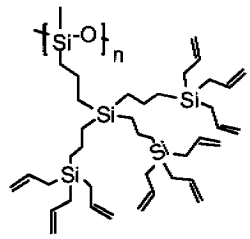

**5** **6** **7**

**Figure 7**. Examples of dendronized polymers obtained via graft-to route. **5** and **6**, obtained by Schlüter et al.[10] and **7**, obtained by Percec et al.[19]

### *1.2.2 Graft-from route*

In route Ib, the desired dendronized polymer is obtained in a stepwise synthetic procedure. Pre-formed G1 dendrons are attached to a linear polymer in a two-step deprotection-coupling reaction. These subsequent reactions result in a series of homologous polymers (PG1, PG2, etc.), until the dendronized polymer with the desired generation is reached. In this case, the obtained polymers have more controlled structures than that of the graft-to route (route Ia). The smaller G1 building blocks can diffuse into the polymer coil and react more easily even with the last remaining docking sites than higher generation dendrons. Nevertheless, one still has to apply highly efficient coupling chemistries. The disadvantages here are: (1) the required high number of simultaneous coupling steps could create defect structures, in particular for higher generations. Any eventual defects cannot be removed because the defectious polymers are too similar to the desired polymer, both structure- and size-wise. (2) The lack of characterization methods for the product with respect to the degree of dendron attachment. Although route Ib faces these problems, judging by the number of recent publications, it appears to be more attractive and feasible under certain circumstances than route Ia.

Many examples based on route Ib have been reported. The main goals were either to quantify coupling efficiencies and structure perfection or to further modify aiming at certain applications. Mery et al.[20] and Kim et al.[21,22] independently reported polysiloxane-based dendronized polymers on G1, and G2 level similar to **8** (Figure 8), however, they failed to obtain a third generation polymer. Recently, Fréchet et al.[23,24] and Schlüter et al.[25,26] reported interesting examples of dendronized polymers similar to **9** and **10**, respectively, using a graft-from strategy (Figure 8). The authors claimed in their examples that dendronization on G1 and G2 level is feasible and that a coverage of virtually 100 % can be achieved for low and high molar mass polymers. However, on the G3 and G4 level, the reaction conditions and types of solvents played an important role in achieving this non-trivial goal.



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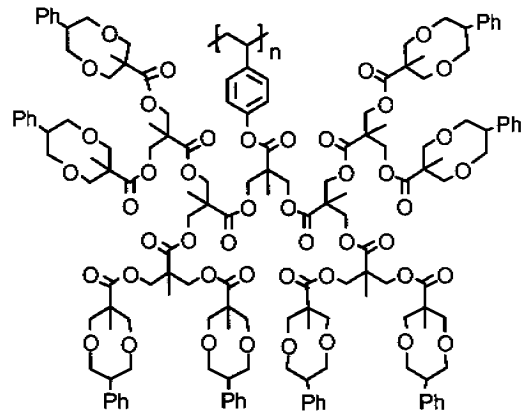

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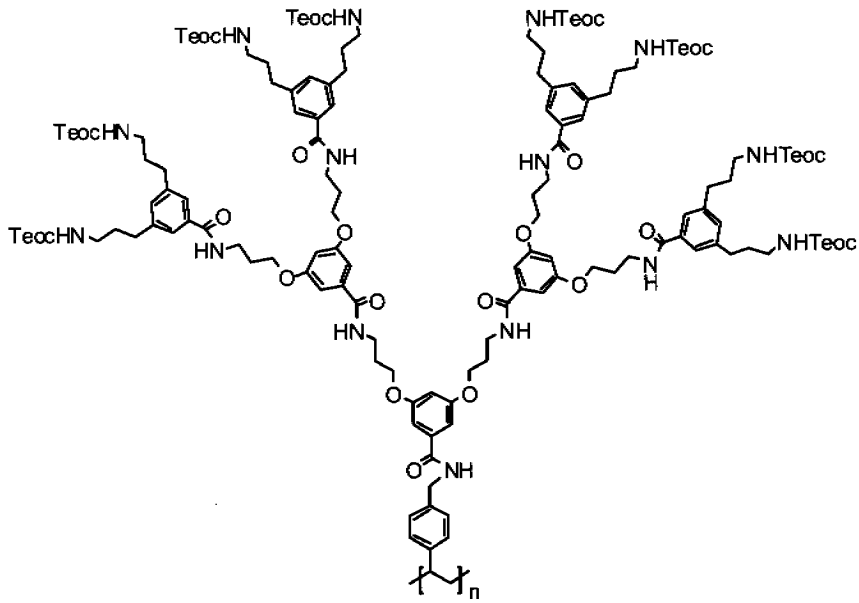

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**Figure 8**. Examples of dendronized polymers, **8**, **9**, and **10**, obtained via graft-from route by Mery,[20] Fréchet,[23] and Schlüter,[25] respectively.

### *1.2.3 Macromonomer route*

In route II, dendronized polymers are obtained via polymerization of macromonomers already carrying the final dendron. The advantage of this route is that the obtained dendronized polymers are basically structurally perfect regarding their dendron structures, which as pointed out is sometimes a critical aspect for routes Ia and Ib. On the other hand, the price to be paid for this advantage is the maximally achievable molar mass. Due to steric hindrance, the polymerization of macromonomers, especially those with high generations, furnishes only relatively

short chains, low molar mass products. Dendronized polymers synthesized by using the macromonomer route have been developed broadly in recent years. New techniques were introduced to improve the synthetic conditions and macromonomer compatibility with polymerization conditions to achieve high molar mass and narrowly distributed dendronized polymers. Different polymerization procedures have been applied including radically initiated, step-growth polymerization, transition metal catalyzed chain growth, etc. Figure 9 illustrates few examples of the macromonomers and dendronized polymers structures reported to date. Dendronized polymers, **11**, **12**, **13**, and **14** were obtained using ring opening metathesis polymerization,[27] free radical polymerization,[28] coordination polymerization,[29,30] and polycondensation,[31] respectively.

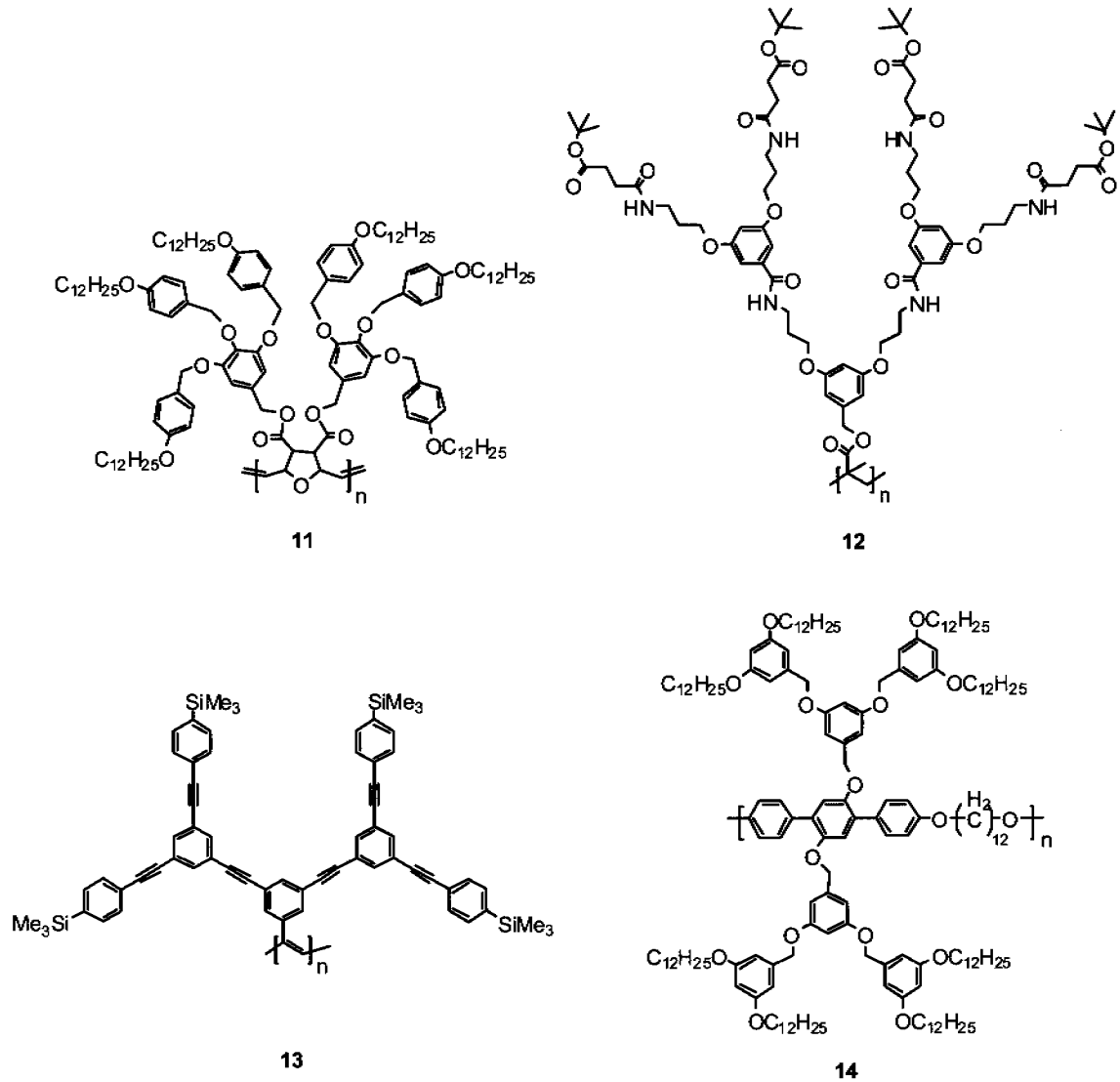



**Figure 9.** Examples of dendronized polymers, **11**,[27] **12**,[28] **13**,[30] and **14**[31] obtained via macromonomer route.

## 1.3 Characterization of Dendronized Polymers

The large size and unusual conformation of dendronized polymers make their characterization down to the molecular structure a challenge. This refers especially to (a) the quantification of structure perfection of those representatives which were prepared using the attach-to-route (b) determination of the degree of polymerization and its distribution, and, finally (c), the shape of these polymers in bulk and solution.
NMR spectroscopy, which is commonly used to characterize chemical compounds in solution, can often not reasonably be applied to dendronized polymers due to the considerable line width of the signals. Specifically for high molar and high generation samples, the signals can be so broad that they overlap with one another. Also they tend to be featureless as shown in Figure 10, which displays a $^1$H-NMR spectrum of a third generation dendronized polymer with a structure similar to **4.**

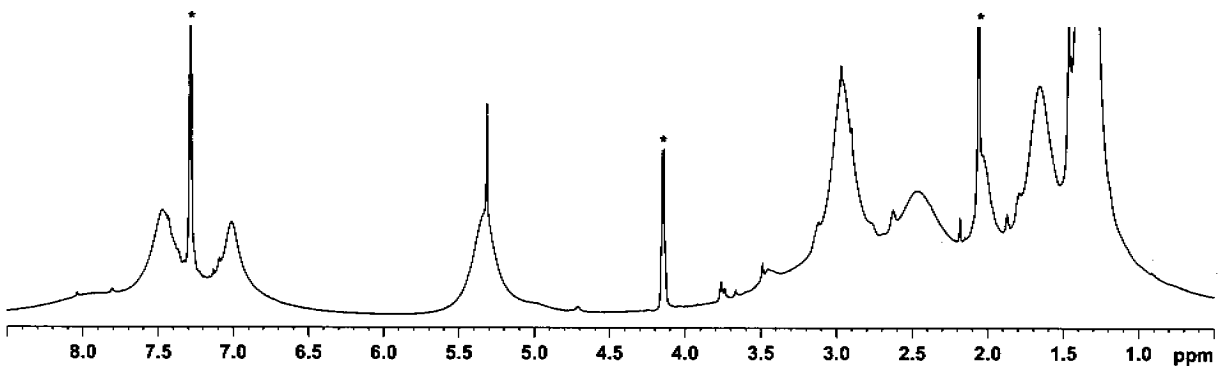



**Figure 10.** $^1$H-NMR spectrum of third generation dendronized polymer with a structure similar to **4**. Solvent signals are marked with (*).

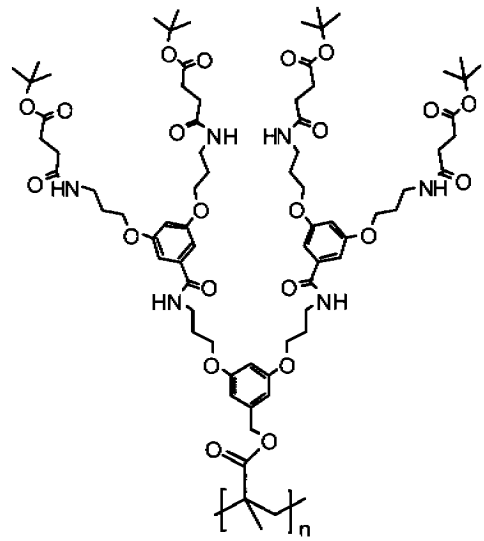
Attempts were made to use MALDI-TOF mass spectrometry as a tool for determination of molar mass of dendronized polymers, but sofar they basically failed. The key problem was that no way could be found how to get dendronized polymers into gas phase. Irrespective of the matrix used and how the sample was prepared only oligomeric structures could be made fly. Also elemental analysis sometimes turned out to be problematic due to entrapped solvent molecules and impurities.
As previously mentioned, dendronized polymers that are prepared using attach-to strategies suffer from the lack of tools for quantification of structure perfection. The determination of the degree of coverage by NMR spectroscopy is complicated by

broad and overlapping signals. Only in few cases, where the molecular weight did not exceed several hundred thousands, it could be successfully applied.[32] Another example was reported where the degree of coverage had been quantitatively determined with methods that are commonly used for large molecular objects in biochemistry and biology, such as proteins. UV and fluorescence spectroscopy were used for this purpose after appropriate labelling of dendronized polymers as demonstrated by Schlüter et al. in their synthesis of G1 to G4 dendronized poly(styrene)s.[16,25]

Gel permeation chromatography (GPC) is a commonly used method for molecular weight determination of polymers. Samples are fractionated according to their hydrodynamic volume and the molecular weights are calculated according to calibration curves generated from standard polymer samples with a known molecular weight, for example, narrowly distributed polystyrene or PMMA standards. The highly branched structures of dendronized polymers, however, make their hydrodynamic volume in solution to deviate strongly from that of conventional polymers. This causes the molecular weight determination of dendronized polymers by GPC to be somewhat unreliable. The two main factors which play a role here are: (1) the compactness of the dendritic side chains. (2) The overall shape in solution, which approaches a more rodlike shape especially for high generation polymers. The first factor leads to underestimation of the molecular weight due to the fact that the branched polymers display a lower hydrodynamic volume than the linear ones.[33] The later, on the other hand exerts the opposite effect. High generation dendronized polymers exhibit an extended, nearly cylindrical shape, which results in two independent radii in solution, the large one of which results in an overestimation of the molecular weight. To avoid the above mentioned opposing factors, scientists used GPC with multiple detection methods such as light scattering (LS) and small angle neutron scattering (SANS) to determine the molecular weight more accurately.[28,34-36]

Scanning force microscopy (SFM) has recently been introduced as a tool for determining molecular weight of dendronized polymers. Samples are spin-coated on solid substrates such as highly oriented pyrolitic graphite (HOPG) or mica, and then the contour lengths and length distributions are measured using a sufficiently broad statistical ensemble. With these values, minimum threshold molecular weights have been estimated.[37,38] One drawback of this tool is that it cannot be used in case of

strong aggregation. Lately, Schlüter and Rabe et al.[28] have determined the molecular weight of second generation dendronized polymers **15** (Figure 11) with high molar mass, using gel permeation chromatography (GPC), light scattering, analytical ultracentrifugation, and scanning force microscopy (SFM). The molecular weight values of **15** obtained by these different methods matched reasonably well, specifically considering the respective limits of the methods used.

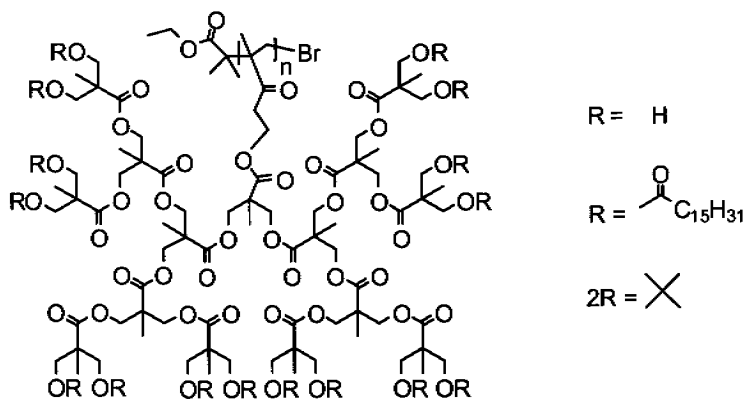


**15**

**Figure 11.** Structure of dendronized polymer **15** used for molar mass determination using different methods.

Several studies have also been carried out in order to investigate bulk and solution properties of dendronized polymers. Percec et al. investigated the supramolecular structures and self-assembly of poly(methacrylate)s and poly(styrene)s with bulky tapered side chains (structures not shown here) in the condensed state with differential scanning calorimetry (DSC), X-ray diffraction (XRD), and scanning force microscopy.[39,40] The authors found that the shape of dendronized polymers is determined by their degree of polymerization (DP). At low DP`s they have a spherical shape, whereas at high DP's, they form cylinders. Recently, the same family of dendronized polymers was investigated by magic-angle spinning (MAS) NMR spectroscopy.[40] The self-assembly process of the above mentioned polymers was found to be sensitively affected by the dendrons' size and flexibility of linking groups, whereas the polymer backbone was found to have virtually no effect on the process.[14,30,]

Recently, Hult et al.[41,42] reported their investigation on the bulk and solution properties of dendronized polymers with a methacrylate backbone bearing pendant aliphatic polyester G2-G4 dendrons based on 2,2-bis(methylol)propionic acid and with hydroxyl, acetonide, or hexadecyl end-group functionalities (Figure 12). The study was performed by using rheological measurements, DSC, dynamic light scattering, turbidimetry, and $^{1}$H-NMR spectroscopy self-diffusion techniques. The authors found from DSC measurements that the glass transition temperature of the amorphous polymers increased with increasing size of the dendrons. $^{1}$H-NMR spectroscopical self-diffusion and longitudinal relaxation data revealed that larger dendrons lead to a larger rod diameter that approximately doubled by increasing the generation of dendronized polymer from two to four. Rheological measurements demonstrated that the complex viscosity at low frequency increased with dendron size.




**16**

**Figure 12**. Structures of the fourth generation dendronized polymers with hyroxyl end-groups, aliphatic hexadecyl chains (C16), and acetonide end-groups investigated by Hult et al.[42]

Lezov et al.[43] found that dendronized polymers in solution show a coil-like conformation and the equilibrium rigidity increased with generation number. This study was based on dendronized polymers with polystyrene backbone and G1 to G4 Frechet-type dendrons (structure not shown here) by using light-scattering, viscometry, isothermal diffusion, and electric and flow birefringence methods.

## 1.4 Potential Applications of Dendronized Polymers

Dendronized polymers are amongst the largest molecules ever prepared. They have several unique and important features, such as their nearly cylindrical shape with nanometer dimensions, their surface which can be engineered and functionalized, and the rigidity of their backbones. These charateristics make them unique macromolecules and interesting candidates for a variety of applications. Figure 13 represents an overview of application fields in which dendronized polymers could be used. More details about the potential application areas of dendronized polymers will be explained in the following.

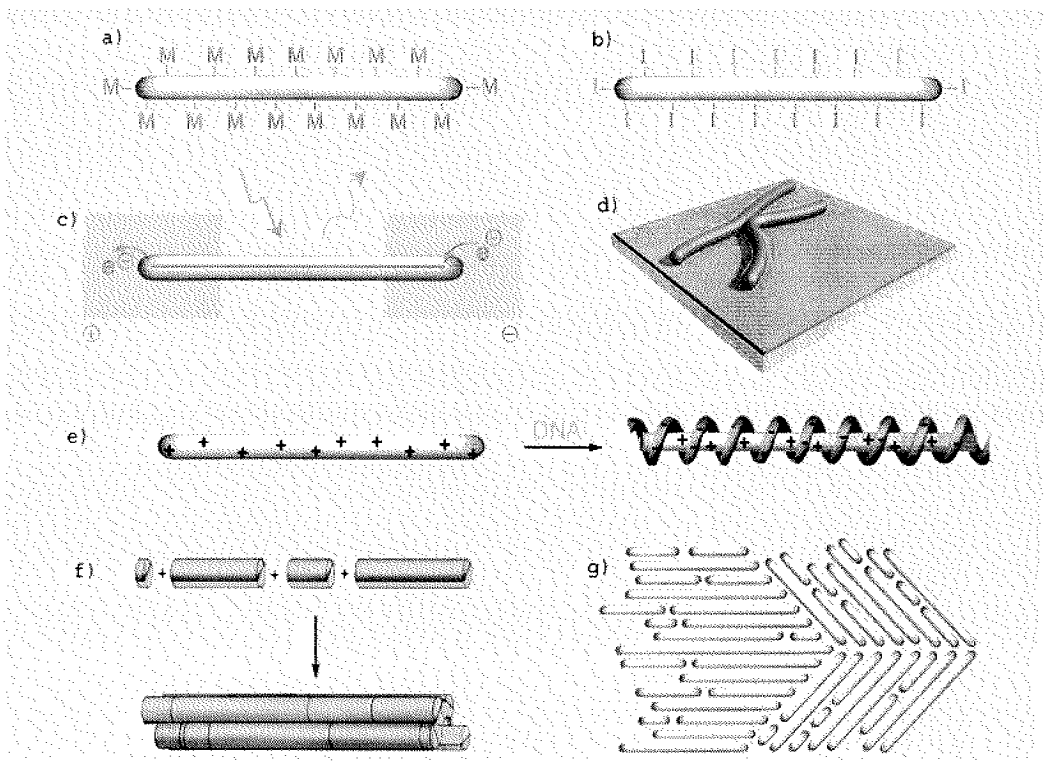



**Figure 13**. Dendronized polymers, represented as white/gray (or blue/red) cylinders, as a) catalyst (M) supports in nanodimensions; b) polyinitiator for the synthesis of "hairy" functional derivatives; c) energy transfer, light harvesting, and/or electrically conducting materials; d) objects for covalent attachment by the move-connect-prove strategy between individualized molecules on solid surfaces; e) novel, ultrahighly charged polyelectrolytes, for example, wrapping with DNA and subsequent gene transfection studies; f) lengthwise segregated polar/nonpolar constituents of novel "supercylinders"; g) nanoobjects for surface patterning and to induce periodicity changes from the Angstrom to nanometer scale.

So far, dendronized polymers have been investigated in several potential application fields such as catalysis,[44-46] electro-optical materials,[47-52] nanoobjects for single molecule experiments and surface patterning,[25,38,53] nanoscopic building blocks,[54-59] and in bioscience.[11,60-63]

First steps toward using dendronized polymers in a very interesting research area namely in drug delivery applications have been done. Grayson and Fréchet [23] and Lee et al.[11,60] have prepared such polymers bearing ester dendrons based on backbones ranging from nondegradable poly(4-hydroxy)styrene to biodegradable polymers such as substituted polycaprolactone and poly(*L*-lysine). In recent biodistribution studies, a positive correlation was observed between the size of these dendronized polymers and their blood circulating time. The long circulating nature of these high molar mass polymers is important because it had been found that enhanced tumor accumulation is observed for polymers with long circulation half-lives. More interesting about these polymers is their ability to be functionalized with many drugs, chromophores or ligands either at their peripheries or in the interiors. Another report appeared by Schlüter and Rabe et al.[63] where the complex formation of DNA molecules with polycationic dendronized polymers was investigated. Amine-terminated G2-G4 dendronized polystyrene was used which possessed almost the same chain length and polydispersity but with varying number of surface charges and the radii. The complexes obtained were adsorbed on mica coated with positively charged polymer (Figure 14). From the SFM images and contour length measurements it was found that DNA strands are tightly wrapped around the cylindrical dendronized polymer. This study could in principle be useful for nonviral gene delivery systems, and could also help to optimize the transfection efficiency based on the structure of the vector system.

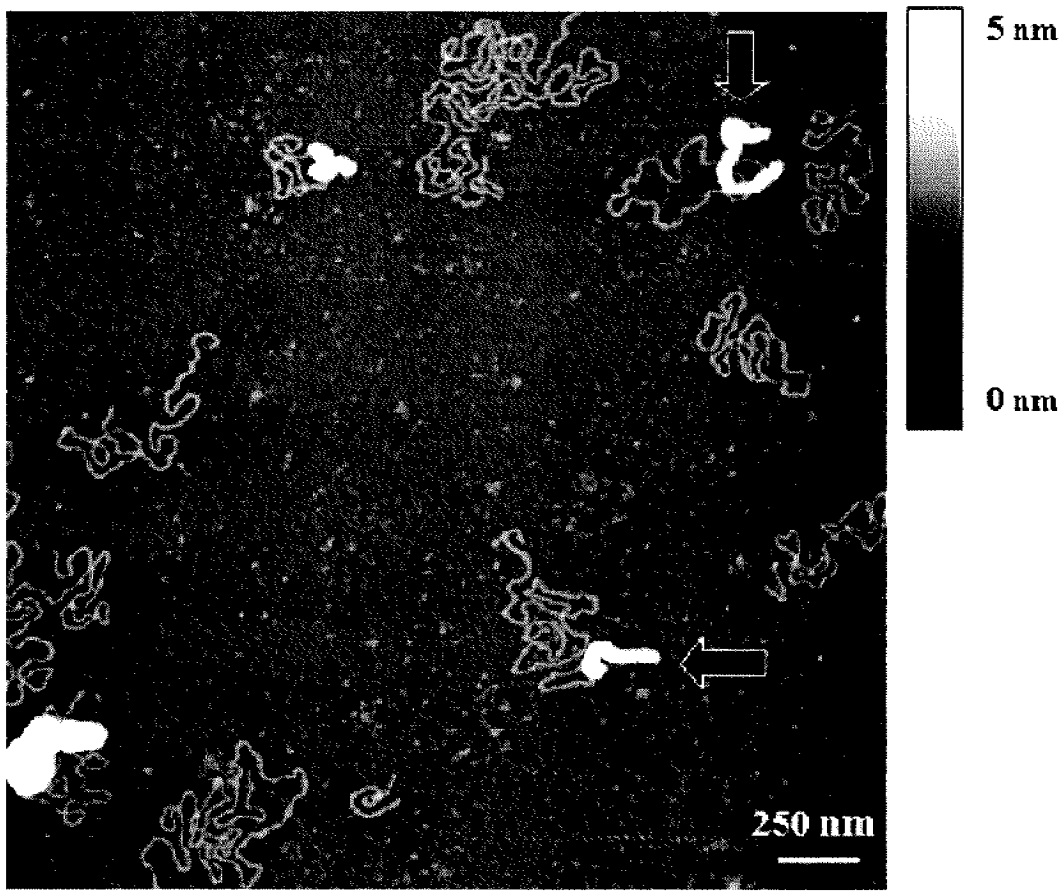



**Figure 14**. High resolution SFM image of DNA and G4-Dendronized polymer complex onto poly-L-ornithine coated mica.[63]

Dendronized polymers with conjugated backbones are of special interest because of their potential applications as optical and electronic materials.[51,64,65] Many examples have been reported where conjugated linear polymers were used as the backbones of dendronized polymers, including poly(p-phenylene)s,[66-68] poly(p-phenylene-vinylene)s,[47] poly(p-phenylene-ethynylene)s,[69] poly(triacetylene)s,[70] poly(acetylene)s,[29] poly(thiophene)s,[71,72] and poly(fluorene)s.[52,73] The advantages of using dendronized conjugated polymers as electrically conducting organic materials are: (1) The presence of dendritic side chains which act as solubilizers, improving processability without a loss in mechanical or thermal stability provided by the rigid polymer backbone structure. (2) The size of dendritic side groups can be well controlled in "generations" so that the morphology is varied systematically without affecting electronic structure. (3) Finally, the dense dendron decoration provides an efficient shielding, and thus prevents the aggregation of molecules.[48] However, from the reported examples it seems that more investigations are still needed in order to

make these materials available for commercial applications. Aida et al. reported the first blue light-luminescent dendronized polymers **17** (Figure 15) with poly(p-phenylene-ethynylene)s as conjugated backbone wrapped with flexible poly(benzylether) dendrons.[69] Fluorescence measurements on different generations of **17** showed that the luminescence activity was significantly enhanced due to the steric effect and antenna function of the dendron. Müllen et al.[74] reported novel dendronized poly(fluorene)s **18** which bear Müllen-type dendrons as shown in Figure 15. Polymer **18** showed a high glass transition temperature of 250 °C which is a prerequisite for high stability application in optoelectronic devices. The authors have also reported in this work that Müllen-type dendrons do not interfere with charge transport or the emission property of the material but rather help to improve the color stability of the devices. Dalton et al.,[75,76] however, reported dendronized polymers for organic non-linear optical applications. The purpose in using dendronized polymers was to increase the optimum loading density of chromophores, and hence, the electro-optic efficiency. The obtained electro-optic coefficient of dendronized polymers such as **19** showed greater electro-optic efficiency than even the best inorganic materials like lithium niobate.

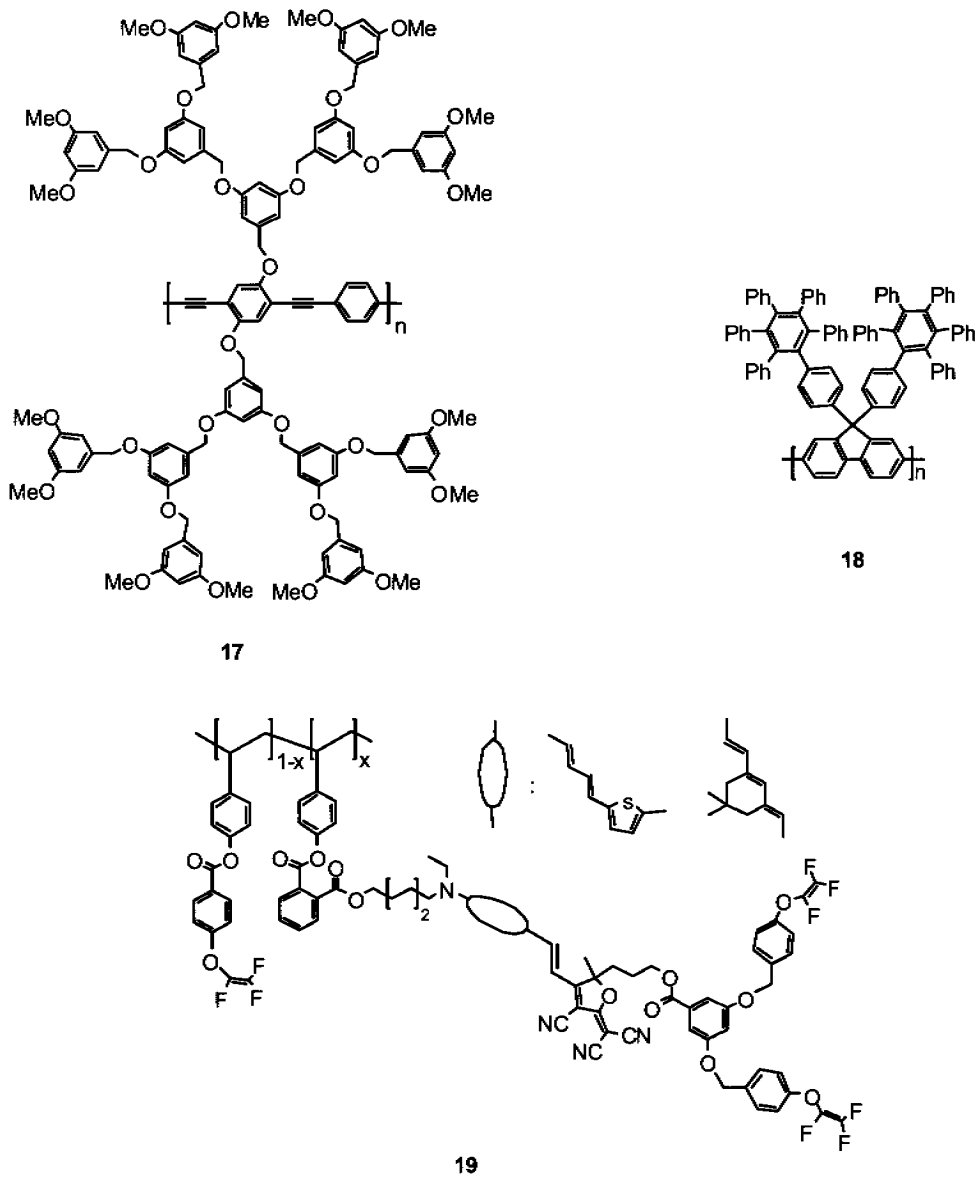
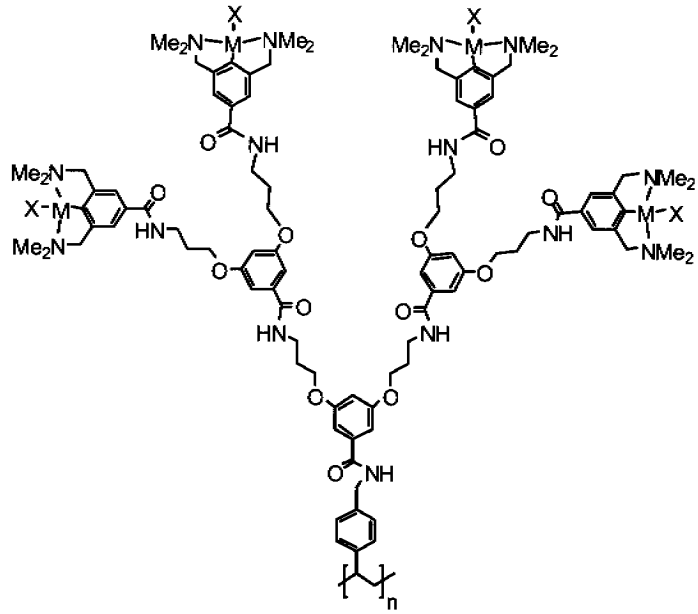


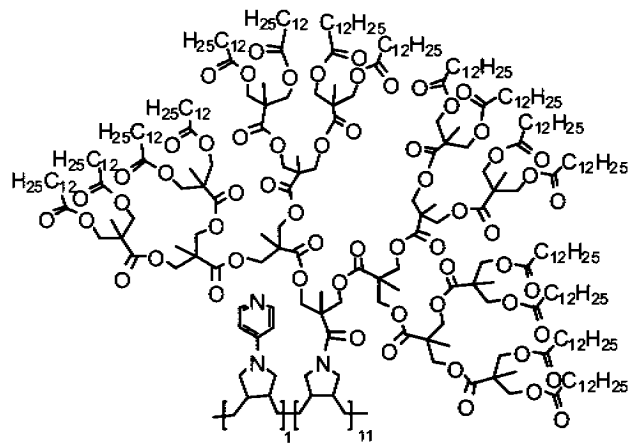

**Figure 15.** Structure of dendronized polymers **17**,[69] **18**,[74] and **19**[76] that have been investigated for opto-ectronic applications.

Recently, reports appeared which dealt with catalysis, where catalytically active sites were attached either on the "surface" or in the interior of dendronized polymers. Schlüter and van Koten et al. reported a series of G1-G3 dendronized polymers of structure **20** which were decorated with van Koten's famous NCN-palladium and platinum pincers (Figure 16).[45] The test reaction for the catalytic activity was the aldol condensation of benzaldehyde and methyl isocyanoacetate. It was found that the activity per metal center was slightly lower compared to a low molecular weight model catalyst. This was interpreted as evidence that all metal centers were well

accessible on the dense surface and not buried in the polymer. On the other hand, Fréchet et al. reported a catalyst carrier for the difficult esterfication of a tertiary alcohol with pivalic anhydride.[44] *para*-(Dimethylamino)pyridine was attached to approximately 10 % of non-dendronized pyrrolidino repeat units and the rest of these units was dendronized with G4-polyester-type dendrons. A pronounced catalytic effect was observed and ascribed to a microenviromental effect created by the dendronized polymer **21** (Figure 16). This was the first steps in this direction and more investigations are obviously needed to judge whether dendronized polymers can be used as catalysts. Nevertheless, a clear drawback of these polymers as catalyst support is the need for a considerable synthetic effort and high costs.



**20**



**21**

**Figure 16.** Chemical structure of dendronized polymers which have been used for catalysis **20**(G2)[45] and **21**(G4).[44] **20** carries the catalytically active site (the metallo pincers) in the periphery whereas **21** has them (the aminopyridine) located in the dendronized polymers interior at the backbone.

The scanning force microscopy (SFM) technique has recently been found to not only be an invaluable tool for manipulation and contour length determination of dendronized polymers, but also as a tool for the full exploitation of potential applications of dendronized polymers. Recently, Schlüter et al., Rabe et al.[38] have reported a significant step toward the construction of nanoscopic objects utilizing a true bottom-up approach by using SFM and high generation dendronized polymers. The idea was to perform a "move-connect-prove" sequence, as outlined in figure 17a. The real experiment, however, is described in figure 17b. Two strands of

dendronized polymers, decorated with thousands of photosensitive azide groups in their periphery, were brought into tight contact using the SFM tip. Upon irradiation with UV-light, the azides decomposed into highly reactive nitrene intermediates. These nitrenes then underwent an inter- and intra-molecular reaction with the surrounding. So, the site where dendronized polymers were in intimate contact led to formation of a covalent chemical bond. The linkage was then mechanically challenged by pulling the two strands apart from each other using the SFM tip. The stress caused the dendronized polymer strands to rupture at a position of impact and not on the new linkage.

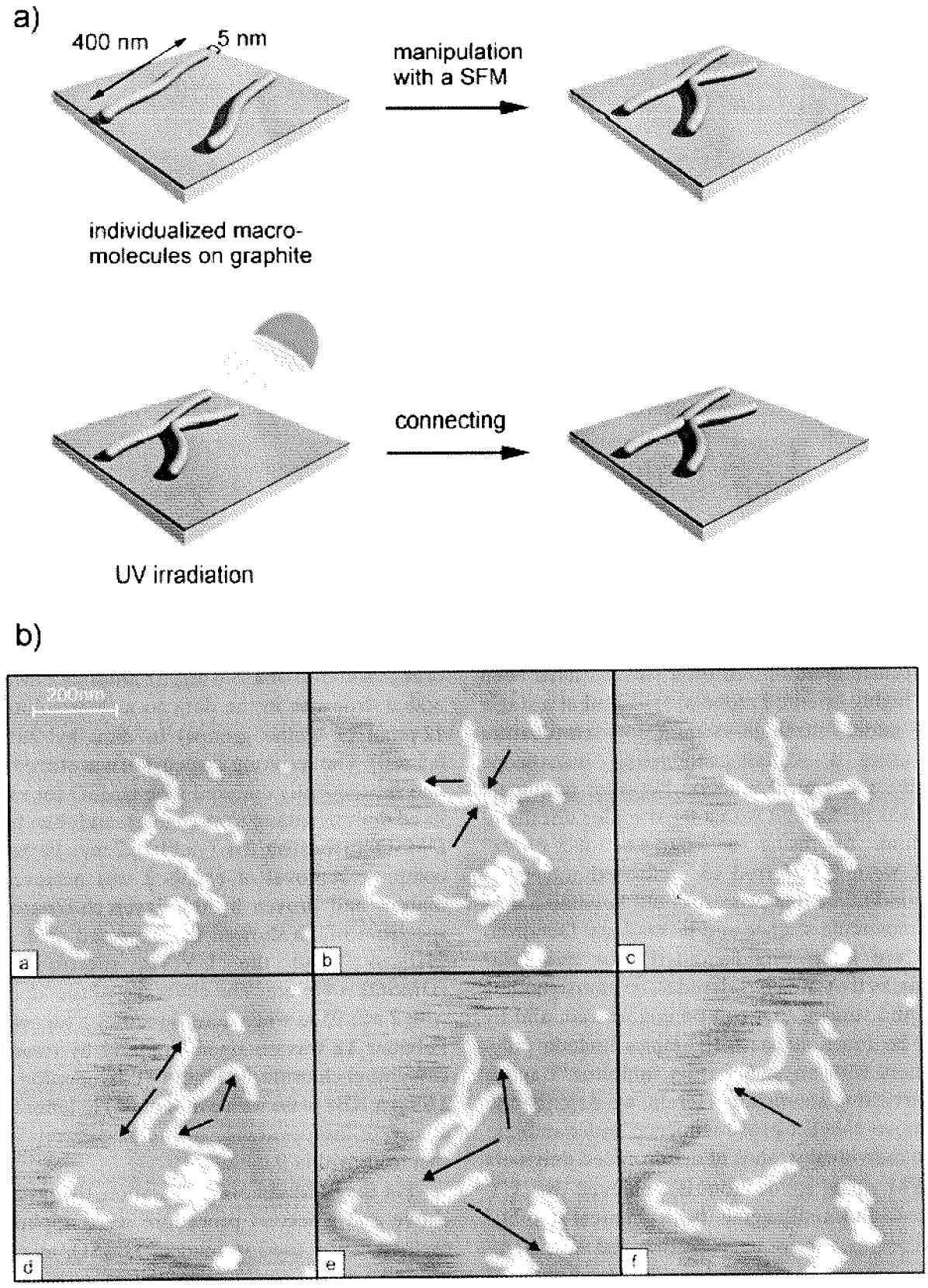



**Figure 17**. (**a**) represents a schematic illustration and (**b**) a real experiment of "move-connect-prove" sequence of SFM images in which two individual dendronized polymers are covalently connected by a photochemically induced cross-linking reaction. The *arrows* in (**b**) represents the SFM tip direction.

## 1.5 Orthogonally Protected Systems

Synthesis of polyfunctional molecules such as peptides, oligosaccharides, etc. requires selective introduction of functional groups into their structures. So, when a chemical reaction has to be carried out selectively at one reactive site, other reactive sites must be temporarily blocked. For this purpose, many protecting groups for different kinds of reactive sites (e.g. amine, alcohol, acid, etc.) have been developed and used. These groups can be removed by mild reagents such as acid, base, or enzymes. However, only few of them are orthogonal, which means a protecting group can be removed in the presence of other groups and vice versa. Figure 18 describes the principle of orthogonal groups on compound **1** (e.g. **1** can be a peptide chain, dendrimer, etc). This compound carries two amino groups that are orthogonal. As can be seen in the figure, one amino group is protected with protecting group **X** (e.g. *tert*-butyloxycarbonyl group (Boc)) while the other group is protected with **Y** (e.g. benzyloxycarbonyl group (Cbz)). The removal of protecting group **X** furnishes compound **2** which still carries protecting group **Y**. This allows selective introduction of a functional group **A** (e.g. fluorescence label, photosensitive label, enzyme, etc.). Consequently, protecting group **Y** could then be removed and selectively replaced by another functional group, **B**. This process results in a compound **8** that carries two different functional groups, **A** and **B**, at the same time. The same process can also be accomplished by first selectively removing protecting group **Y** from compound **1**. After introducing functional group **A** into compound **5**, **X** protecting group from compound **6** can then be selectively replaced by functional group **B** to furnish compound **8**. These processes are of great importance for building multifunctional materials and diverse molecular frameworks.

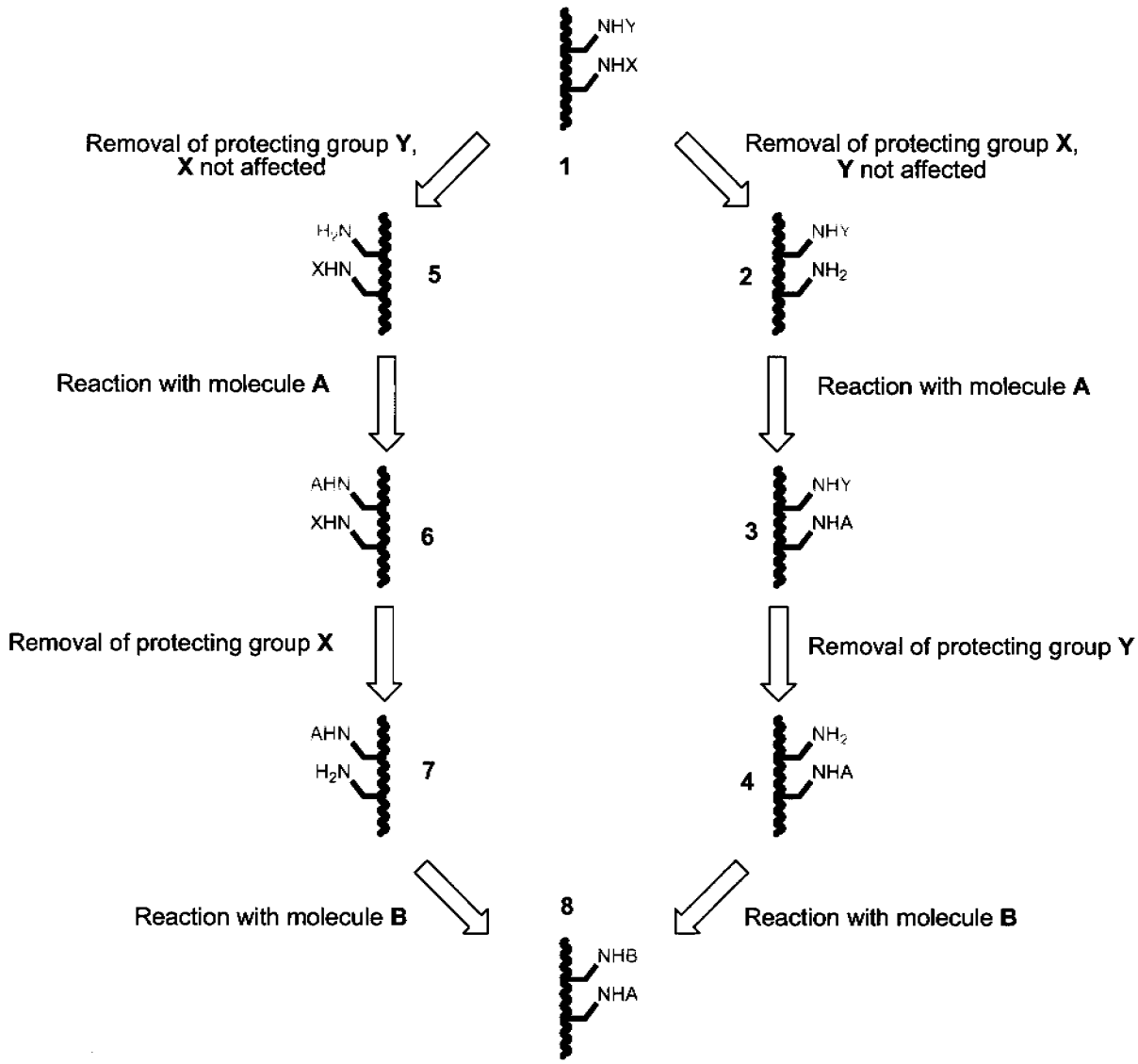



**Figure 18**. Schematic diagram of selective introduction of different functional groups into compound **1**.

## 2. Aims of the thesis

The present thesis is part of a long-term project supported by the German Science foundation (DFG) and ETH start-up funds. It focuses on the preparation of dendronized polymers with individually addressable functional groups and quantification of structure perfection of dendronized polymers prepared by using the attach-to-route. It is divided into three main aims which are:

1. Controlled surface modification of dendronized polymers is a challenging goal for both synthesis and many application-related issues. So far, almost all dendronized polymers carry only one kind of functional group at the periphery (mostly either amine or hydroxyl) which are typically uniformly protected with only one kind of protecting group. Typical examples are those which carry exclusively *tert*-butyloxycarbonyl (Boc) protected amine groups as the peripheral functional units.[14] This limits the options for "surface" engineering by having to modify either all amines at once or a certain amount of them randomly distributed over the entire macromolecule. A site selective attachment of, e.g., two different sites is therefore not possible.
In order to overcome this limitation of surface modification, **the first aim** of the present thesis (part 3.2) was **to synthesize a series of orthogonally protected dendronized polymers carrying amines with two different protecting groups in various proportions and generations.** Selective deprotection should then allow for introducing predetermined numbers of entities to each repeat unit.

2. As described in paragraph 1.4, the author's research group in collaboration with the group of Prof. Rabe, Humboldt University, Berlin, reported a very interesting experiment using SFM.[38] Two strands of dendronized polymers were covalently "welded" together while co-adsorbed on a solid surface under ambient conditions with the SFM using a "move-connect-prove" sequence. During the progression of the experiment, the authors however faced two critical issues which are: (1) the preparation of the individual chains on the substrate under conditions in which the adsorption energy has exactly the right magnitude. It should not be too high, so that the molecules can be moved with the SFM tip without tearing them apart, and it should not be too low either, because otherwise the molecules will diffuse on the

surface and form aggregates. (2) The presence of impurities due to the method used for the synthesis of these dendronized polymers. To avoid these issues and to widen the applicability of such experiments, **the second aim** of this thesis (part 3.3) was therefore to employ chemistry which avoids the above critical issues by using the approach of orthogonal protection. In other words, the aim was **to synthesize dendronized polymers carrying pre-determined, specific amounts of photocrosslinkable groups,** with the remaining peripheral functional groups providing the option to be either charged or non-charged, right as the preparations on the solid substrates required.

3. As mentioned in sections 1.2.1 and 1.2.2, dendronized polymers prepared either by graft-to route or graft-from route have the intrinsic disadvantage that their structure will have defects due to an incomplete coverage of the starting dendronized polymers with dendrons. Although this coverage can be driven to values above 99 %, it still has to be quantified in each case, which is a rather tedious procedure. To date, UV and fluorescence spectroscopy have been used for this purpose after appropriate labeling.[25] Each of these methods has its intrinsic limitations and uncertainties and involves a considerable effort. It was, therefore, the **third important aim** of this thesis (part 3.4) **to develop an independent and perhaps simpler method for quantification of structure perfection of dendronized polymers which were synthesized according to the attach-to route**. Specifically it should be clarified whether NMR spectroscopy could at all be used as a tool to solve such a problem.

# 3. General Part

## 3.1 Synthetic Strategy

The synthesis of the orthogonally protected dendrons and their corresponding dendronized polymers was accomplished by a series of subsequent reactions. This has required large amounts of building blocks and also very efficient chemistry. Therefore, the synthetic methods had to be chosen carefully. In particular, methods with high yields and simple purification procedures were needed.

Dendrons **22** and **23** (Figure 19) were often used as building blocks for the synthesis of macromonomers and thus, dendronized polymers by Schlüter et al.[77,78] These dendrons consist of an aromatic branching unit which carries one ester group at the focal point and two amino groups that are often protected with the Boc group. The idea was to modify the synthesis of these building blocks such that another protecting group could be introduced. This would then allow the desymmetrization, which is needed for the orthogonally protected dendrons, to take place at a very early stage of the sequence. Figure 19 further shows the structure of dendron **24** which is an example of the obtained orthogonally protected dendrons. This dendron carries Boc and Cbz amino protecting groups at the same time.

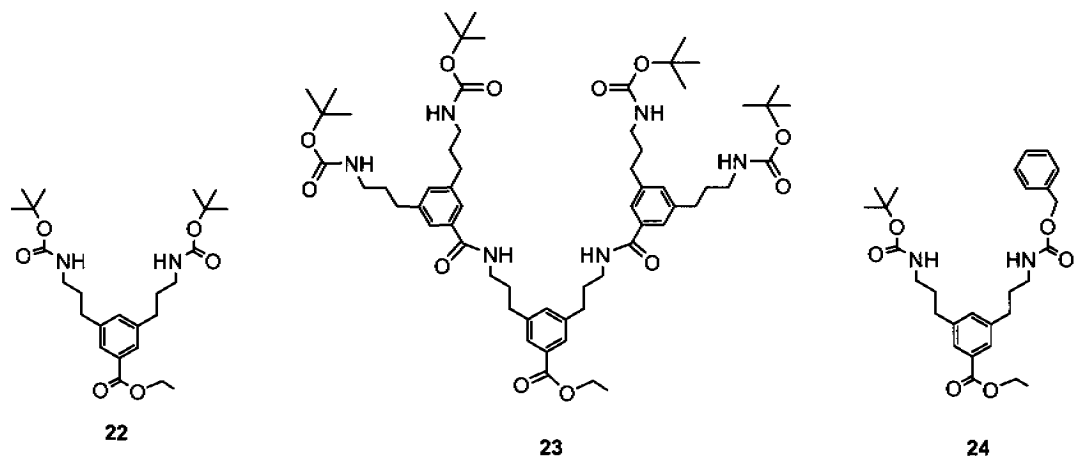



**Figure 19**. Chemical structures of the building blocks **22**,[77] **23**,[77] and **24**, used for the synthesis of dendronized polymers.

The formation of the above mentioned alkyl-aryl branching units required connection of an $sp^3$-carbon to an $sp^2$-carbon. One of the most often used procedures for such connections was found to be the $Pd^0$-catalyzd Suzuki-Miyaura cross-coupling reaction (SMCC). This procedure tolerates a large number of functional groups such as ester, alcohol, ether, protected amino groups, etc. It also proceeds under mild conditions and with high yields. Due to these advantages, SMCC was applied in order to obtain the required orthogonally protected branching units.

In order to synthesize the second and higher generation dendrons from the obtained branching units of the SMCC reaction, an amide coupling procedure was suggested. This procedure is often used in peptide and dendrimer chemistry and exhibits a high tolerance towards other synthetic protocols and purification methods. High generation dendrons can be obtained from the reaction of the carboxyl groups of one branching unit with the amino functional groups of another branching unit. The coupling can be carried out under very mild conditions and also with high yields by using coupling agents.

Different orthogonal amino protecting groups were needed to obtain the various dendrons and their corresponding dendronized polymers. Only two combinations of amino protecting groups were convincingly shown to be orthogonal. The first combination was found to be the *tert*-butyloxycarbonyl group (Boc) with the benzyloxycarbonyl group (Cbz), and the second combination was Boc with 2,7-di(*tert*-butyl)-9-fluorenyloxycarbonyl group (Fmoc*). Therefore, these combinations were chosen as amino protecting groups in this thesis.

In the following, the mechanisms of SMCC, amide-coupling and the deprotection reactions will be discussed in detail. Other reactions that have been used during the synthesis will be briefly discussed where further explanation is necessary.

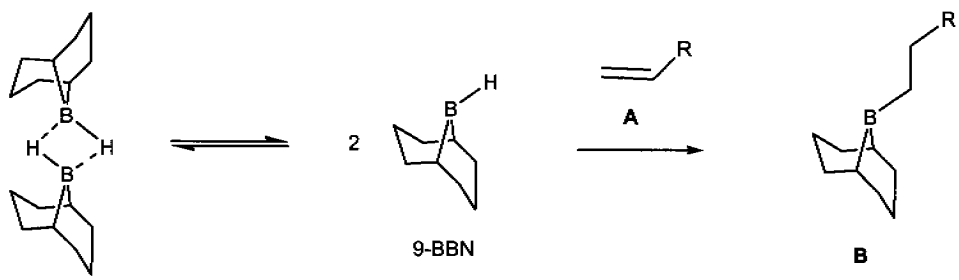
### *3.1.1 Reaction Mechanisms*

#### 3.1.1.1 Suzuki-Miyaura Cross-Coupling (SMCC)

The palladium-catalyzed cross-coupling of organic halides or triflates with organoboranes under basic conditions is known as Suzuki-Miyaura cross-coupling. This coupling has achieved prominence as one of the most important methods for the

formation of new carbon-carbon bonds which proceeds in the presence of many functional groups.

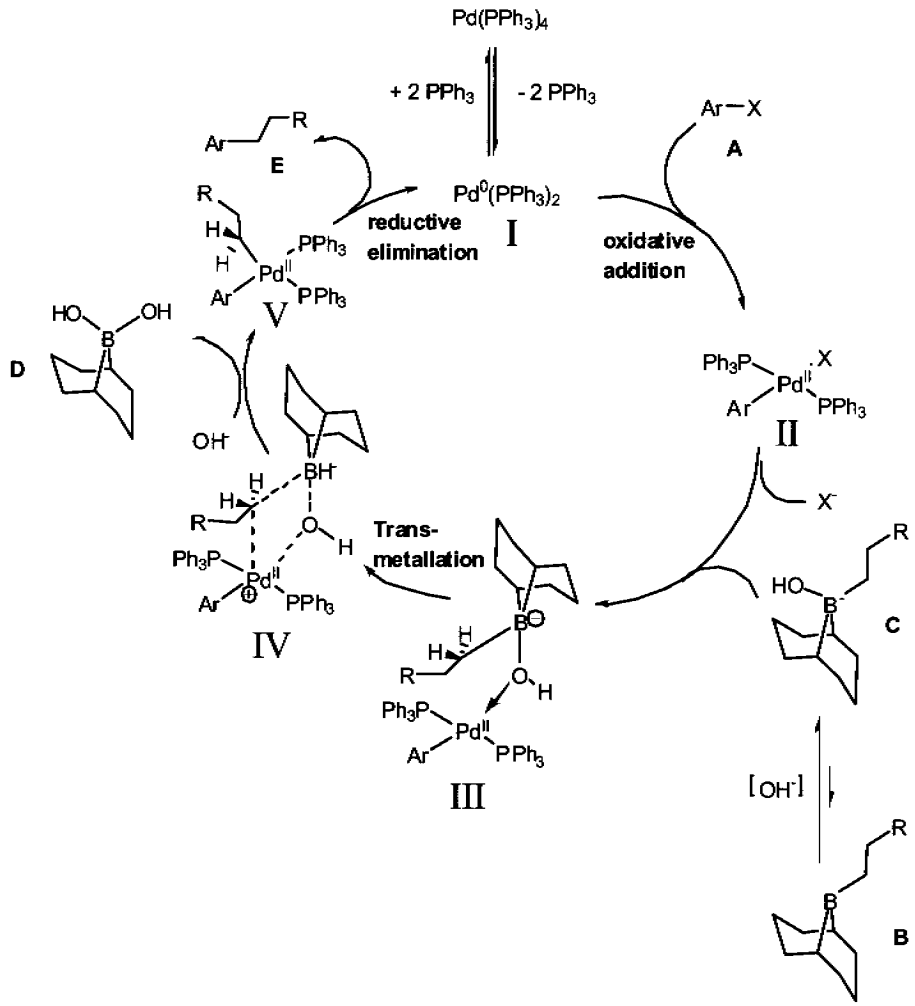
SMCC was discovered in 1979 by Suzuki and Miyaura[79] who reported the direct cross-coupling reaction of 1-alkenylboronic esters and 1-iodo-1-alkenes in the presence of a base as well as a palladium catalyst. A detailed mechanism for the cross-coupling was reported later by Soderquist et al.[80] and was understood as a catalytic cycle of organoborane compounds. The catalytic cycle involves three sequences which are oxidative addition, trans-metallation, and reductive elimination. The organo boranes are first prepared by *in situ* hydroboration of an olefin with primary or secondary boranes. Usually 9-borabicyclo[3.3.1.]nonan (9-BBN) is used for regioselectivity reasons. The reaction mechanism begins with the dissociation of the 9-BBN dimer which then reacts with the less hindered carbon of alkene **A** to furnish an *anti*-Markovnikov product **B** as shown in Scheme 1.




**Scheme 1**. Hydroboration of olefin **A** with 9-BBN yielded product **B**.

Scheme 2 illustrates the catalytic cycle of carbon-carbon bond formation. A catalytically active intermediate $Pd^0(PPh_3)_2$ **I** is first formed in solution by the dissociation of two ligands from the precursor $Pd[PPh_3]_4$. Addition of an organic electrophile **A** to the zerovalent and coordinationally unsaturated **I** gave complex **II** in *trans*-configuration. On the other hand, the boron atom of compound **B** was quaternized by addition of a base to give compound **C**. The base was added in order to enhance the nucleophilicity of the organic group on the boron atom. The complexation of compound **C** with **II** gave a pseudo-square-pyramidal hydroxo-$\mu_2$-bridged intermediate **III**. The alkylboran-Pd-trans-metallation then proceeded through a distorted square intermediate **IV** with the retention of configuration at the $\alpha$–CH2 of the alkylsubstituent to *cis*-$Pd^{II}$-complex **V**.[81] During this process, a second equivalent

of base attacks the boron to form **D**. The final step in the catalytic cycle, the reductive elimination, proceeds quickly to form the coupling product **E**, and also to regenerate the catalytically active intermediate **I**.



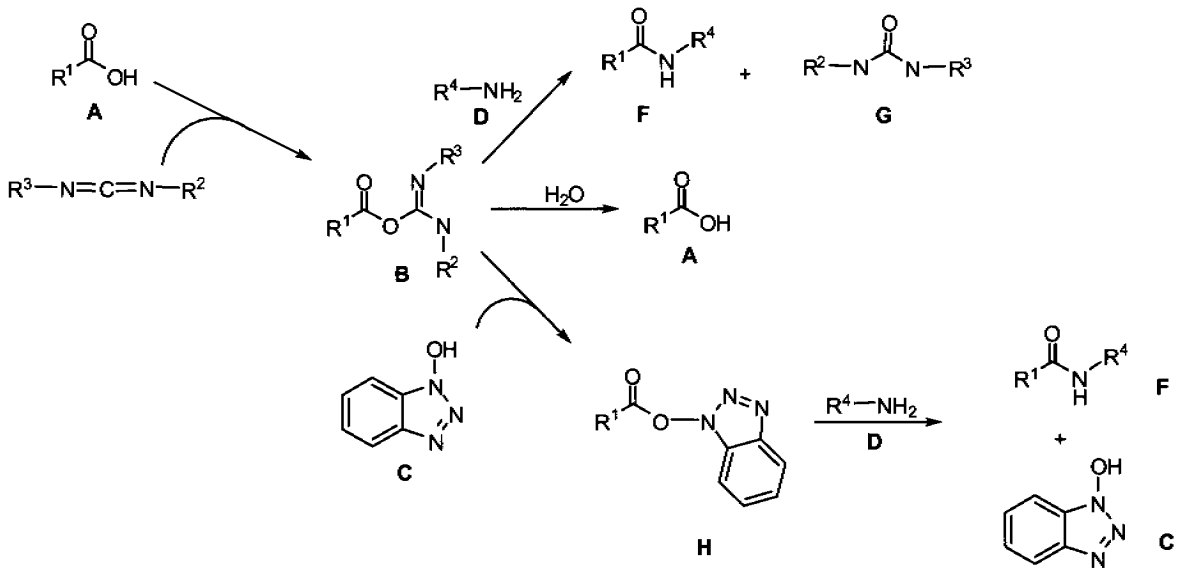

**Scheme 2**. Mechanism of the Suzuki-Miyaura cross-coupling reaction.[79,80]

### 3.1.1.2 Amide Coupling

When carboxylic acids are treated with primary or secondary amines, salts are obtained. The salts can be pyrolyzed to give the corresponding amides at high temperature (200- 300 °C).[82] This method is not convenient and is seldom of preparative value due to the side reactions that can happen at high temperature. Due to the importance of amide coupling in the synthesis of solution and solid-phase peptides, many methods have been developed in the last twenty years. The reaction

between amines and carboxylic acids can now be made to proceed in high yields and under mild conditions by the use of coupling agents.[83]

The main role of the coupling agents is to activate the carboxylic acid group by increasing the electrophilicity of its carbonyl carbon. The reaction between the carboxylic acid group and the coupling agent forms as reactive intermediates either an anhydride or an active ester. The most important and most often used coupling agents are the carbodiimides, especially *N, N'*-dicyclohexylcarbodiimide (DCC),[84] and *N, N'*-(3-dimethylaminopropyl)-ethylcarbodiimide hydrogen chloride (EDC).[85] The mechanism is described in scheme 3.




**Scheme 3**. Amide coupling mechanism.[85,86]

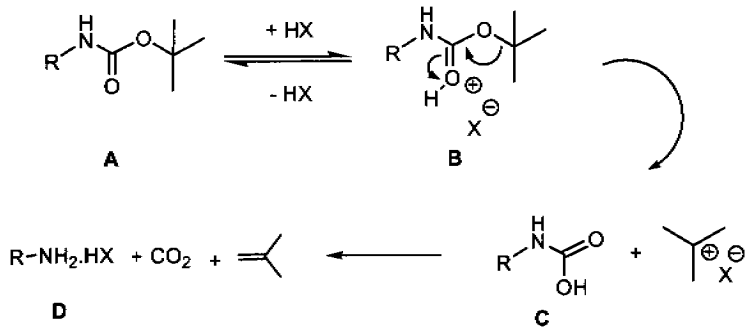
The carbodimide reacts first with the carboxyl group of **A** to form an amine-reactive *O*-acylisourea intermediate **B**. This intermediate **B** may then either react with the amine group of molecule **D** to yield the product **F** and urea **G**, or it will hydrolyse in the presence of water to reform the starting compound **A**. To avoid hydrolysis, another coupling agent **C** which is a good nucleophile e.g. hydroxyl-benzotriazole (HOBt),[86] or hydroxyl-succinimide (HOSu)[87] is usually added to the mixture to give intermediate **H** which is a stable reactive intermediate. The addition of these new agents also avoids the formation of N-acetylated urethane in later stages. Intermediate **H** then reacts with the amino group of molecule **D** to form the desired product **F** and to regenerate the coupling agent **C**.

Usually the amide coupling is done in presence of a non-nucleophilic base such as triethylamine ($Et_3N$), or *N*-ethyldiisopropylamine in order to deprotonate the acid and to avoid the protonation of the amine.
Recently, new coupling agents, such as *o*-(benzotriazol-1-yl)-N,N,N`,N`-tetramethyluroniumtetrafluoroborate (TBTU)[88] and *o*-7-azabenzotriazol-1-yl)-*N,N,N`,N`*-tetramethyluroniumhexafluorophosphate (HATU),[89] have been developed. These coupling agents can quickly generate intermediates with a very high reactivity towards nucleophiles. One drawback of these reagents is their price. They are much more expensive than the coupling agents described above, and are therefore not considered in this thesis. Only the systems EDC/HOBt and DCC/HOSu were used.

### 3.1.1.3 Deprotection Reactions

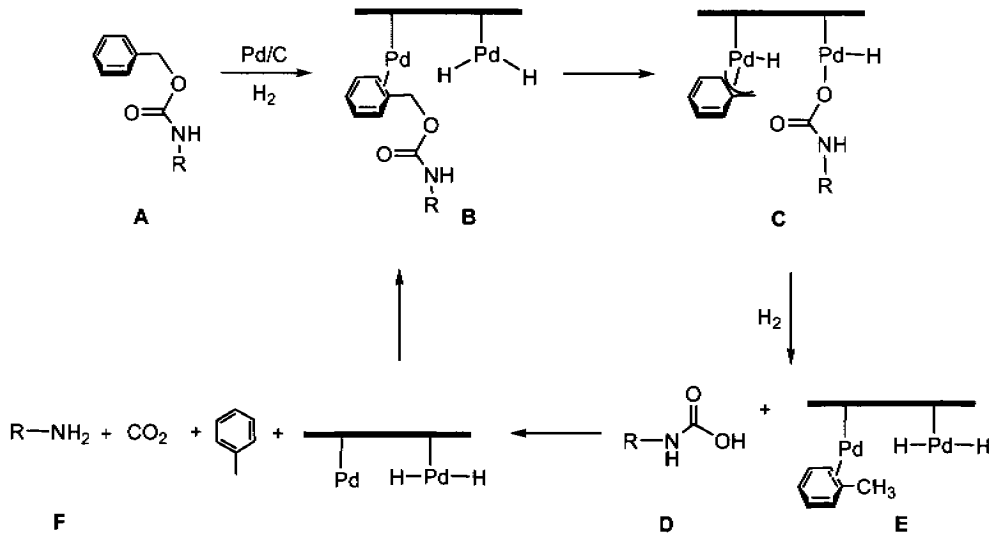
Selective temporary protection or inactivation of a chemically reactive functionality is an important tool in the field of organic and bioorganic chemistry, especially for controlled synthetic work, e.g. the synthesis of peptides, oligosaccharides, etc. For that reason, numerous sophisticated protecting groups have been developed for almost all kinds of functional groups (amines, alcohols, carbonyl groups, etc). These protecting groups can be removed under mild deprotection conditions, for instance the use of acid, base, enzymes, etc.[90,91] However, only a few of them can be used as an orthogonal set, i.e. a protecting group can be removed in any order by applying reagents and/or conditions without affecting the other protecting group.
The best orthogonal set of amine protecting groups found for this work was the combination of Boc and Cbz which can be deblocked by acid and hydrogenolysis, respectively. Another orthogonal combination that was also used was Boc and Fmoc* which are labile in acidic and basic medium, respectively. The mechanisms of the removal of Boc, Cbz, and Fmoc* will be discussed in detail in the following.
The Boc group is one of the most frequently used protecting group for the amine functionality due to its chemical stability towards basic and mild acidic conditions. The removal of this group can be accomplished by using several different conditions. The milder of them is 25 % aqueous HCl or trifluoroacetic acid ($CF_3COOH$) in dichloromethane at room temperature. The detailed mechanism of the removal of Boc is shown in scheme 4. The carbonyl group of compound **A** is first protonated in the presence of acid to yield intermediate **B** that decomposes further into the

carbamic acid intermediate **C** and *tert*-butyl cation. Intermediate **C** then slowly decomposes to furnish product **D** and carbon dioxide whereas the anion assists the acid regeneration from the *tert*-butyl cation to produce isobutylene.



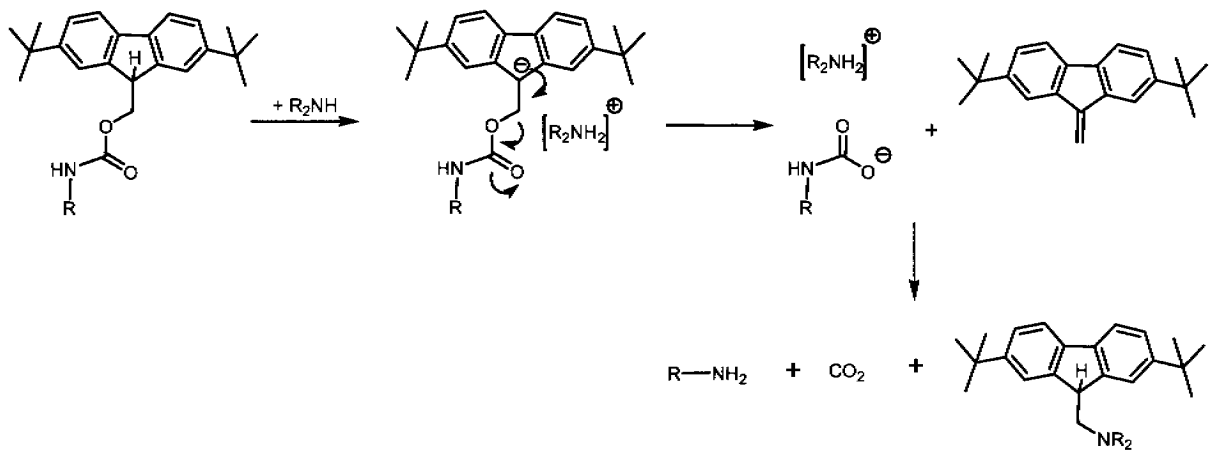

**Scheme 4.** Mechanism of removal of the Boc group in acidic medium.[92]

The Cbz group on the other side is usually removed by hydrogenolysis which involves the use of hydrogen gas in the presence of a transition metal catalyst such as palladium (Pd). Hydrogen donors such as 1,4-cyclohexadiene, formic acid, or ammonium formate can also be employed to facilitate the deprotection process.[93] Other methods like harsh acidic conditions (e.g. $HBr/CF_3COOH$) may also be applied to remove the Cbz group.The detailed mechanism of removal of Cbz is shown in scheme 5. It involves several reaction sequences. First, the metal suface (usually palladium dispersed on charcoal) binds to both the $H_2$ gas and the reactant **A** to give the complex **B**. The conversion of complex **B** into complex **C** is followed by a transfer of one hydrogen atom from the metal surface to an oxygen to form the carbamic acid **D** and complex **E**. Finally, **D** decomposes slowly into the product **F** and carbon dioxide, whereas complex **E** decomposes into toluene and the activated metal surface.




**Scheme 5**. Detailed mechanism of Cbz-deprotection by hydrogenolysis.[92]

Finally Fmoc*, which is a derivative of Fmoc, is usually removed under mild basic conditions, to result in the liberation of the free amine product (Scheme 6). The rapid deprotonation of the fluorene group ($pK_a$ = 23), which is greatly facilitated by the aromatic nature of the resultant dibenzocyclopentadienide anion, is accomplished with piperidine or morpholine in DMF. In a subsequent slower step, elimination generates dibenzofulvene (itself an unstable species that rapidly adds nucleophiles) and a carbamate residue, which then decomposes with loss of carbondioxide to release the free amine.




**Scheme 6**. Mechanism of Fmoc*-deprotection in basic medium.[94]

## 3.2 Synthesis of Orthogonally Protected Dendronized Polymers

This part of the thesis is subdivided into two sections:
(1) Synthesis of first and second generation dendrons with defined ratios of orthogonally protected amino groups in the periphery (Boc and Cbz) and the subsequent selective removal of these groups (section 3.2.1).
(2) Synthesis of high molar mass first and second generation dendronized polymers which carry a predetermined number of Fmoc* and Boc protected peripheral amines at each repeat unit and the subsequent selective removal of these groups (section 3.2.2).

Parts of this work have been published in: Macromolecules **2006**, *39*, 8943-8951; and Helvetica Chimica Acta **2006**, *89*, 2745-2763

As previously mentioned, the thesis was begun with the aim of overcoming the limitation of surface engineering of dendronized polymers, and increasing the options for surface decoration of these polymers. The idea was to develop a synthetic way for the preparation of dendronized macromonomers and polymers which carry defined and variable proportions of orthogonally protected peripheral amines at each repeat unit. Selective removal of the protecting groups should then allow for introducing predetermined numbers of functional groups at each repeat unit.
So far, in the laboratory of Schlüter et al.,[14,56,95,96] a several-gram-scale route to first (G1) through fourth generation (G4) dendrons with *tert*-butyloxycarbonyl-(Boc) protected amine groups has been developed. The synthesis of these dendrons was proven to be reliable and effective and has, therefore, been applied to the synthesis of a wide variety of dendronized polymers.[56,95,96] An extension to this strategy was to introduce another amine protecting group to the surface of these dendronized polymers on G1 and G2 levels. By referring to books on protecting groups for amines,[92] only the combination of Cbz and Boc, or 9-fluorenylmethyleneoxycarbonyl (Fmoc) and Boc, was most convincingly shown to be orthogonal. Fmoc/Boc was not considered as ideal because of serious concerns regarding the solubility of dendronized polymers carrying a high load of these relatively flat and conformationally rigid units at the macromolecule's "surface".[97] On the other hand,

Boc/Cbz groups are known to be orthogonal from low molar mass chemistry, and were therefore the natural next choice.

For this purpose, G1 and G2 dendrons were first synthesized with two and four peripheral amino groups, respectively. These dendrons carry the orthogonal Boc and Cbz protecting groups in all possible combinations. Thus, on the G2 level the dendrons carry 4 Bocs, 3 Bocs and 1 Cbz, 2 Bocs and 2 Cbzs, 1 Boc and 3 Cbzs, and, finally, 4 Cbzs. It was then of utmost importance to check the degree of orthogonality of the chosen protecting groups first on the dendron level because: (1) any incomplete deprotection on the dendron level cannot be improved later on the polymer level; and (2) to ensure that there will be no problems for high molar mass dendronized polymers which can carry easily hundreds if not thousands of protected amino groups per macromolecule. These groups were found from $^1$H-NMR spectroscopy to be virtually orthogonal to each other. Therefore, as next step, one of the perspective G2-dendrons was connected to a polymerizable unit and the resulting macromonomer was then polymerized using free radical polymerization to furnish a high molar mass dendronized polymer on a G2 level. Selective removal of Boc in 25 % aqueous HCl gave the corresponding deprotected polymer. $^1$H-NMR investigations showed no defects in the polymer structure and from the integration of the signals, Cbz was found virtually not to be affected. However, removal of Cbz using Pd/C and 3.5 bar $H_2$ gas led to defects in the polymer skeleton. The dendrons which were attached to the backbone through benzylic ester linkages were found to be sensitive to the deprotection conditions. This was not expected for two reasons: (1) the contact surface required for hydrogenolysis between the used heterogenous catalyst (Pd/C) and the polymer backbone was expected to be unavailable; and (2) the polymer backbone is wrapped by densely packed dendritic side chains which were expected to prevent the catalyst from penetrating through it. The fact that the benzylic esters were cleaved off upon treatment with $H_2$ (Pd/C) was a disappointing finding as it suggests that Cbz is not a good protecting group for dendronized polymers that are based on acrylat polymerizable groups. However, this was easily avoided by replacing the acrylate polymerizable group by acrylamide using the Mitsunobu reaction. Nevertheless, the unwanted and unexpected cleavage (de-dendronization) provided interesting new options which will be discussed in detail in part 3.4.

The removal of Cbz was then tried with a dendronized acrylamide-based polymer. At this stage there were no problems with the polymer skeleton but it was almost impossible to quantitatively and reproducibly remove Cbz irrespective of the numerous conditions that were tried. It was therefore decided to try the combination 2,7-di(*tert*-butyl)-9-fluorenyloxycarbonyl (Fmoc*) and Boc instead. Recently, Fmoc*, with two *tert*-butyl groups in its structure, was reported as a more soluble analogue of the Fmoc group.[94] Additionally, an easy procedure was reported for the synthesis of an attractive Fmoc* precursor, the Fmoc* succinimidyl active ester which allows its 20 gram scale preparation via three steps and at very low cost.[94]

The same strategy was then followed for the synthesis of a set of first (G1) and second generation (G2) dendronized methacrylate-based macromonomers with varying ratios of Fmoc* and Boc protected amino groups. These macromonomers were polymerized into high molar mass G1 and G2 dendronized polymers. Figure 20 illustrates the structure of the obtained orthogonally protected G2-dendronized polymers.

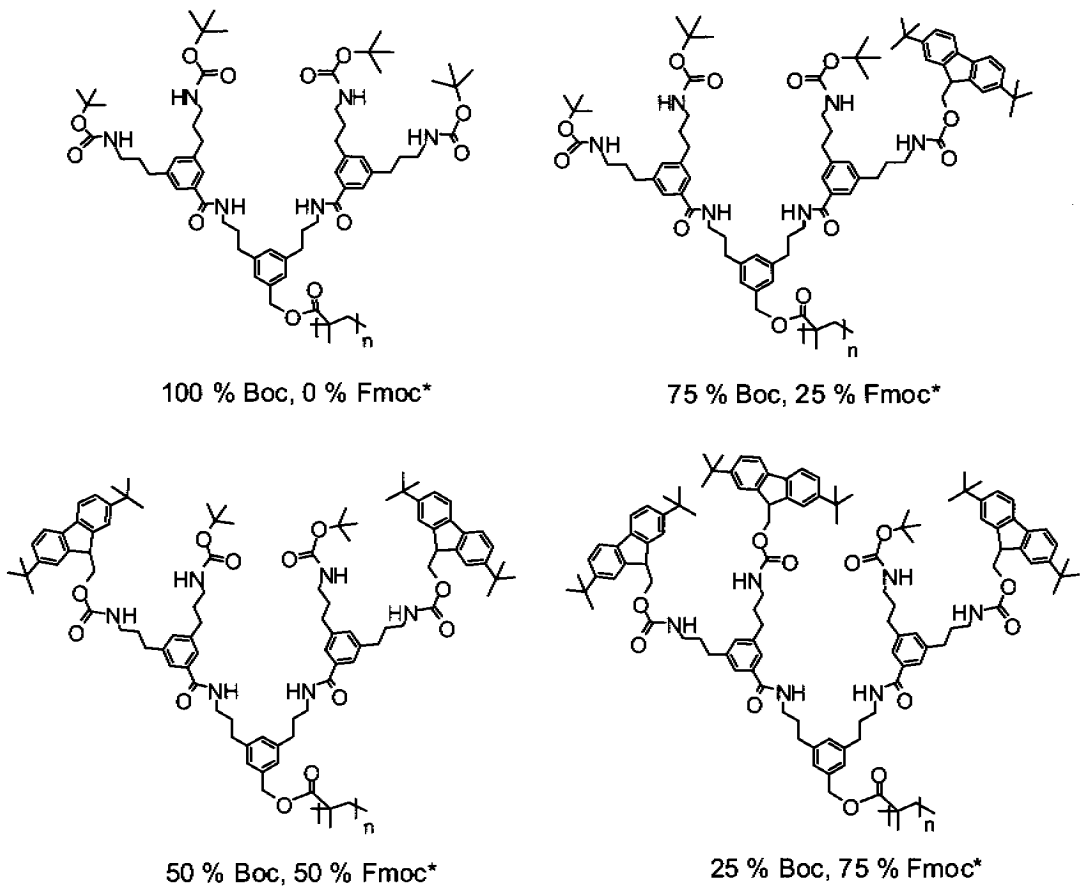



**Figure 20.** Chemical structures of the obtained orthogonally protected, second generation polymethaacrylates.

The selective removal of both protecting groups on the polymer level was accomplished by using 25 % aqueous HCl for removing of Boc and 25 % aqueous piperidine for removing of Fmoc*. However, a rigorous quantification of the respective degrees of removal of protecting groups was difficult to achieve. In the $^{1}$H-NMR spectra, an unfavourable signal overlap at 1.4 ppm was observed between the (only) signal of Boc and the *tert*-butyl signal of Fmoc*. Whereas the removal of Fmoc* could be demonstrated by the complete disappearance of several signals (4.1 and 4.3 ppm), the removal of Boc could only be confirmed in the decreased intensity of a signal superimposed by Fmoc*. These results together with the considerable line widths and some contamination with water rendered $^{1}$H-NMR integration too unreliable to be used for quantification of the removal of the protecting groups. Therefore, the deprotection degree was then assessed by high-field $^{13}$C-NMR spectroscopy.

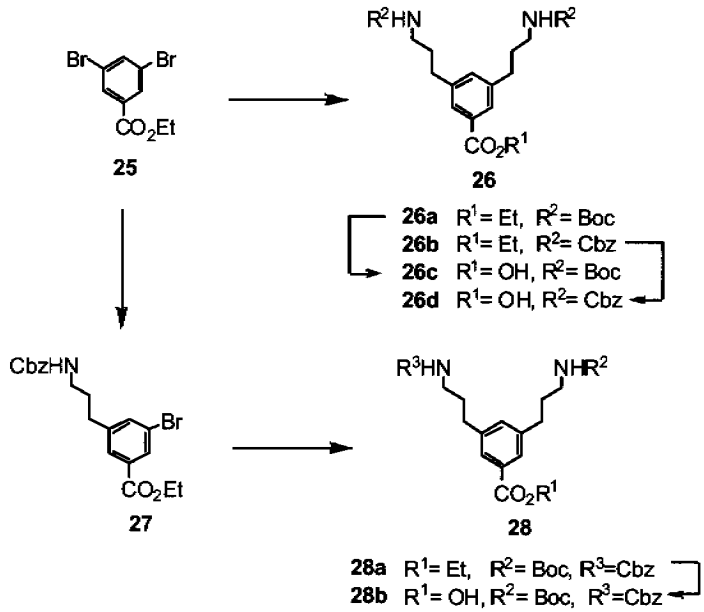
### 3.2.1 Synthesis of G1- and G2-dendrons carrying Boc and Cbz peripheral amino protecting groups

#### *3.2.1.1 Synthesis of the building blocks*

Three different building blocks were synthesized as starting precursors for the preparation of the orthogonally protected dendrons. Scheme 7 outlines the synthetic sequences of these precursors. Some of them have already been described previously but they were improved in the present work to provide pure products on a larger scale.

The synthesis was begun with the dibromo ester **25** which was converted into both the symmetric G1-dendrons **26a**[14] and **26b**[78] and the non-symmetric analog **28a** using the Suzuki-Miyaura cross-coupling reaction. In order to achieve the important desymmetrization, starting material **25** was first converted into the "mono-armed" compound **27** and then transformed into dendron **28a**. The synthesis of dendron **28a** was based on the work done by Müller.[98] However, the scale on which these steps were performed was significantly increased, such that the key compound **28a** was prepared and is now available on the 20 g scale with an overall yield of analytically pure material of 56% with respect to **25**. The ester function of the obtained dendrons **26a**, **26b**, and **28a** was saponified to give the corresponding carboxylic acids **26c**,

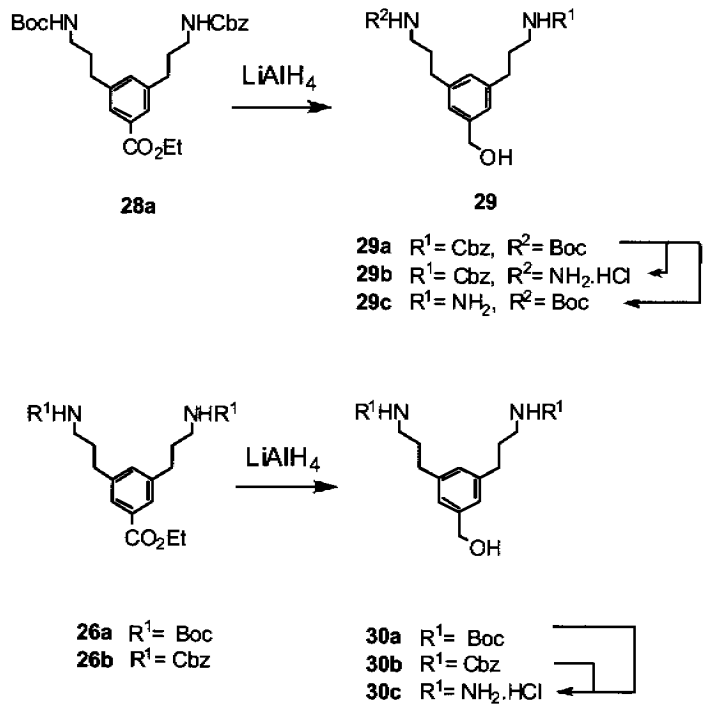
**26d**, and **28b** in 80-95 % yields. The acid dendrons will be needed later on to build high generation dendrons via amide coupling (see schemes 9 and 10).




**Scheme 7**. Synthesis of the building blocks.

### *3.2.1.2 Synthesis of G1-dendrons carrying either 2Boc, or 1Boc and 1Cbz, or 2Cbz, peripheral amino protecting groups*

The ester groups of the dendrons **26a**, **26b**, and **28a** were reduced to give the corresponding alcohols **29a**, **30a**, and **30b** using $LiAlH_4$ as reducing agent (Scheme 8). These hydroxy groups will be later used for attaching polymerizable units. The reactions were done at a temperature below 10 °C in order to avoid attack at the Cbz-protecting group. When the same reaction was carried out at 20 °C, the yield of **29a** for example was dropped from 81 % (at 5 °C) to ca. 25 %.




**Scheme 8.** Synthesis of G1-dendrons, **29a** carrying 1Boc and 1Cbz, **30a** carrying 2Bocs, **30b** carrying 2Cbzs, and their selectively deprotected counter parts **29b**, **29c**, and **30c**.

The removal of Boc of dendrons **29a** and **30a** was done with 25 % aqueous HCl solution, whereas the removal of Cbz of **29a** and **30b** was carried out by catalytic transfer hydrogenation using Pd/C and $H_2$ gas. The yields were above 95 % and the degree of deprotection was checked by high-field NMR spectroscopy. The spectrum of **30a** has already been reported.[96] Emphasis was of course focused on the orthogonally protected dendron **29a** to assess the selectivity of deprotection. Figure 21 shows the $^1$H-NMR spectra of dendron **29a** and its deprotected counter parts **29b** and **29c**. Spectrum (**a**) represents the starting dendron **29a**, whereas (**b**) and (**c**) are the spectra of the dendrons **29b** and **29c** in which Boc and Cbz were removed, respectively. The signals of the protecting groups appeared as expected at the following chemicals shifts: Boc at $\delta$ 1.42 ppm (signal i in spectrum (**a**)) and Cbz at $\delta$ 5.01 and 7.30 (signals g and h in spectrum (**a**)). Spectra (**b**) and (**c**) show that removal of the protecting groups were complete. The relevant shift range of the protecting groups was also amplified considerably (not shown here) in order to confirm their removal. Furthermore, from the intensity of the NMR signals of the

remaining protecting group and the dendritic fragments, it was found that the remaining protecting group had stayed untouched.

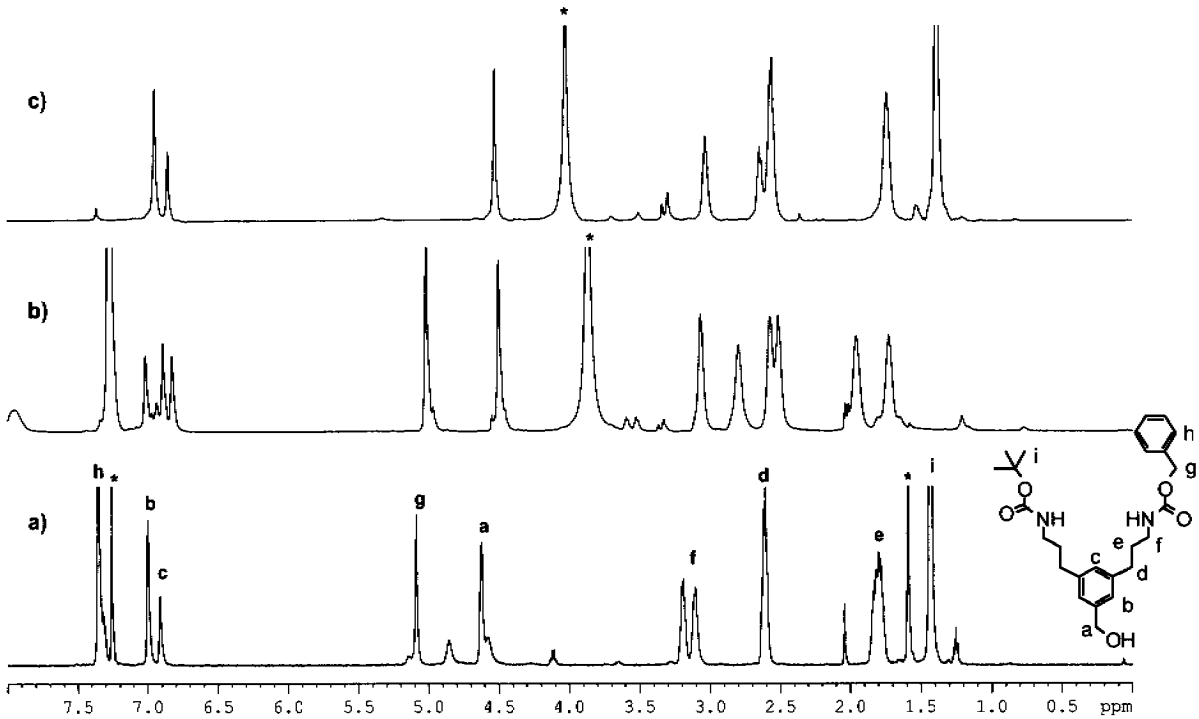
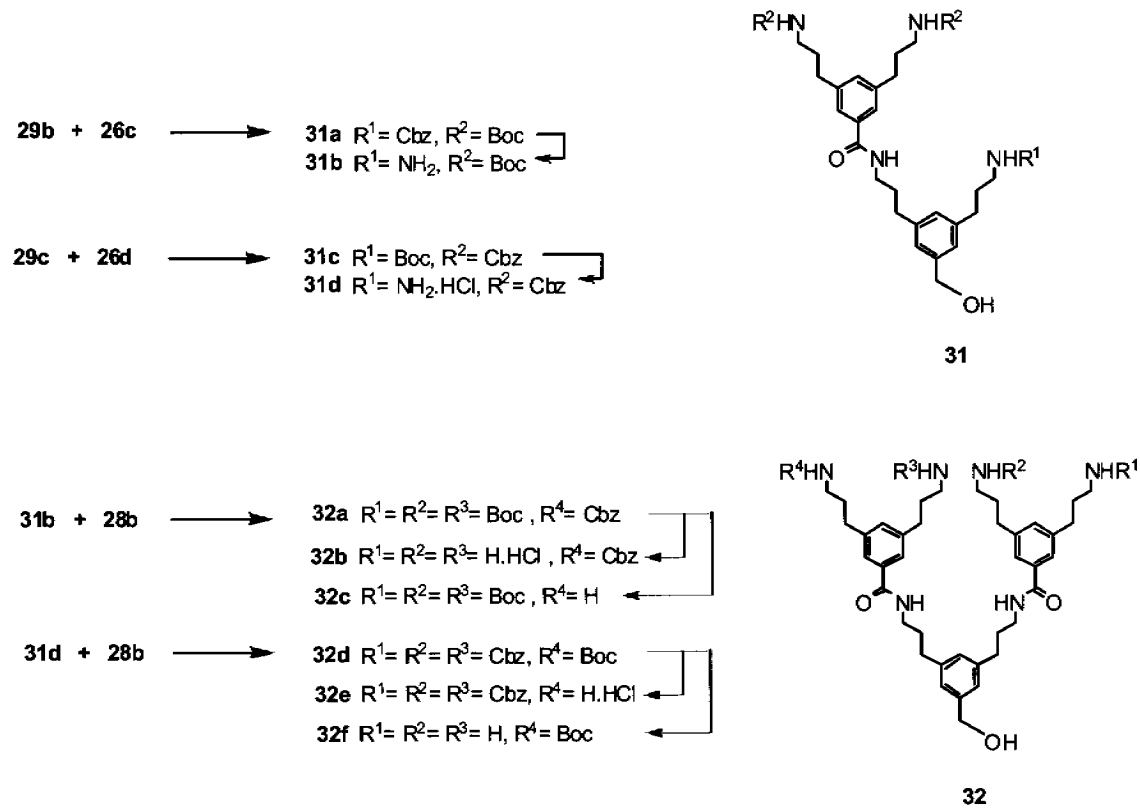



**Figure 21.** $^1$H-NMR spectra of dendron **29a** (**a**), and its selectively deprotected counter parts **29b** (**b**) and **29c** (**c**). Solvent signals of $CDCl_3$, $CD_3OD$, and $D_2O$ are marked with (*).

### *3.2.1.3 Synthesis of G2 dendrons carrying either 3Boc and 1Cbz, or 1Boc and 3Cbz peripheral amino protecting groups.*

Coupling of the amino groups of the G1-dendrons **29b** and **29c** with the carboxylic acid groups of **26c** and **26d** using the HOBt/EDC system gave the mono-coupled G2-dendrons **31a** and **31c**, respectively, in a yield of 65-80%. In order to obtain the orthogonally protected G2-dendrons carrying 3Bocs and 1Cbz or 1Boc and 3Cbzs, the Cbz group of **31a**, and the Boc group of **31c** were removed, and the resulting dendrons **31b** and **31d** were further reacted with **28b** to yield dendrons **32a** and **32b**, respectively, as shown in scheme 9.




**Scheme 9**. Synthesis of G2-dendrons, **32a** carrying 3Bocs and 1Cbz, **32d** carrying 1Boc and 3Cbzs, and their respective selectively deprotected counter parts **32b**, **32c**, **32e**, and **32f**.

The same procedure as described above (see section 3.2.3.2) was used for removal of Boc and Cbz groups. **32b** and **32e** were obtained by treating dendrons **32a** and **32d** with 25 % aqueous HCl respectively. Whereas the catalytic transfer hydrogenation of Cbz of dendrons **32a** and **32d** was done with a longer reaction time (14 h instead of 3 h) to give dendrons **32c** and **32f**, respectively. The deprotection reactions of **32a** and **32d** were investigated by high-field $^1$H-NMR. Figure 22 shows the $^1$H-NMR spectra of dendrons **32a** (spectrum **a**), **32d** (spectrum **d**) and their corresponding deprotected counter parts **32b** (spectrum **b**), **32c** (spectrum **c**), **32e** (spectrum **e**), and **32f** (spectrum **f**). The spectra of the deprotected dendrons did not show any indication of the presence of the removed protecting groups, even if the relevant shift ranges were amplified considerably. Furthermore, the intensity of the signals of the remaining protecting group in dendrons **32b**, **32c**, **32e**, and **32f**, were compared with the signals of the dendritic skeletons. This was done by using NMR spectra recorded with pulse sequences so as to allow for reliable integrations. The resulted integrations did not show any indication for any eventual loss of some of the

remaining protecting group during the deprotection reactions. The spectra of the starting dendrons were recorded in $CDCl_3$, and those of the deprotected dendrons were recorded in $CDCl_3/CD_3OD$ mixtures.

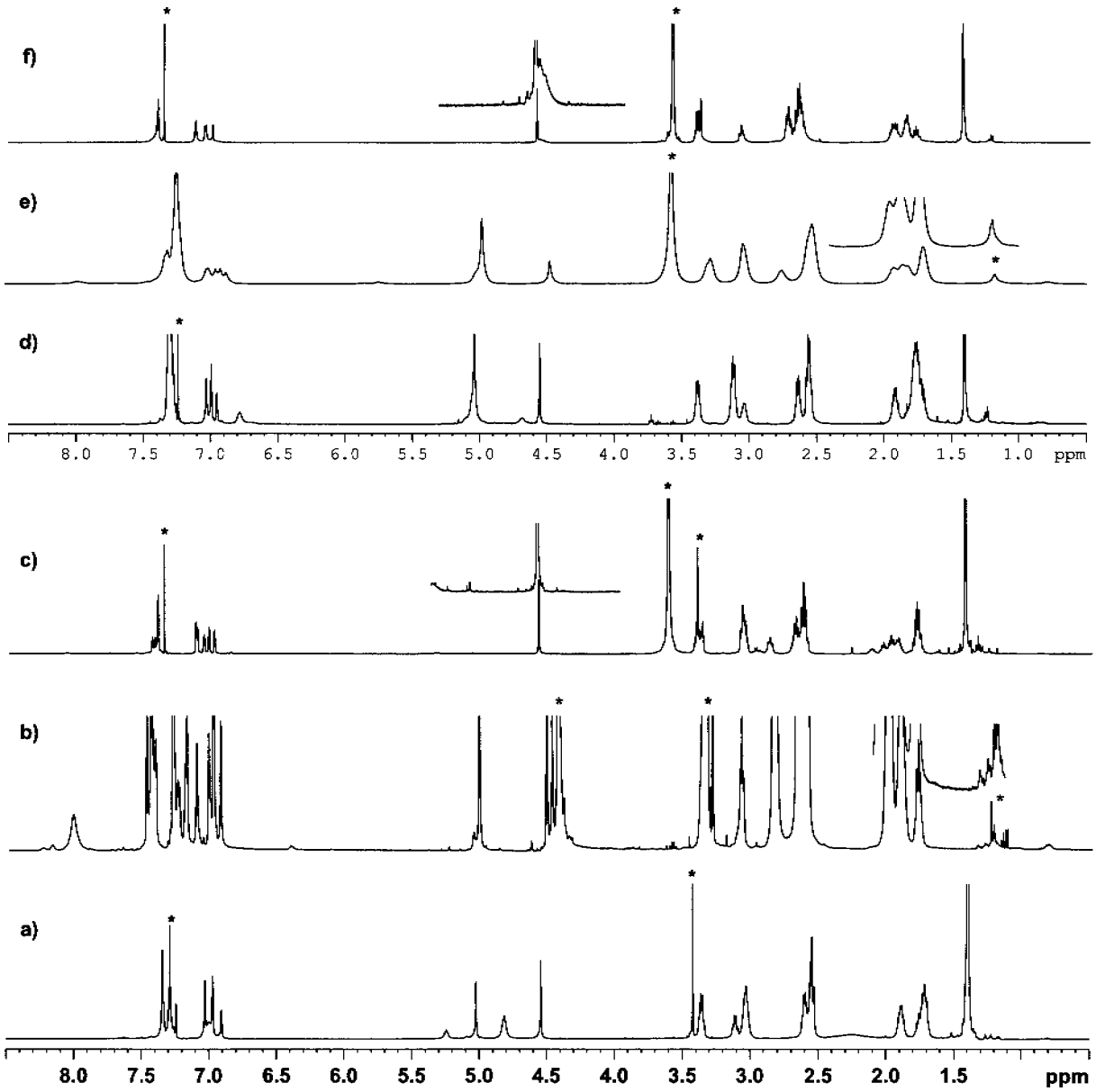
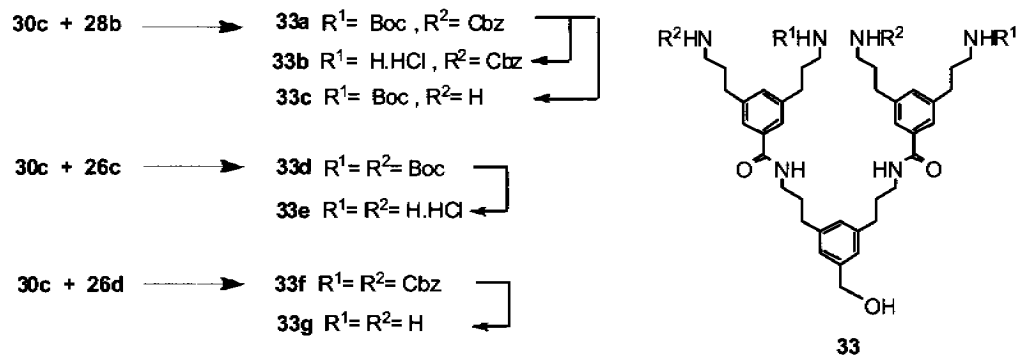



**Figure 22.** $^1$H-NMR spectra of dendrons, **32a** (**a**), **32d** (**d**), and their selectively deprotected counter parts **32b** (**b**), **32c** (**c**), **32e** (**e**), and **32f** (**f**). Solvent signals of $CD_3OD$, $CDCl_3$, $D_2O$ and grease are marked with (*).

### *3.2.1.4 Synthesis of G2 dendrons carrying either 2Boc and 2Cbz, or 4Boc, or 4Cbz peripheral amino protecting groups*

To complete the set of the orthogonally protected G2 dendrons, **33a**, **33d**, and **33f** were synthesized (scheme 10). These three dendrons were obtained by reacting dendron **30c** with **28b**, **26c**, and **26d**, respectively, using the same HOBt/EDC amide coupling conditions as described before (see section 3.2.3.3). The dendrons were obtained on a larger scale than **32a** and **32d** because of the lower number of steps involved in the synthesis as compared to **32a** or **32d**. The yields were 70-85 %.




**Scheme 10**. Synthesis of G2-dendrons, **33a** carrying 2Bocs and 2Cbzs, **33d** carrying 4Bocs, **33f** carrying 4Cbzs, and their respective selectively deprotected counter parts **33b**, **33c**, **33e**, and **33g**.

The removal of the Boc group of dendrons **33a** and **33b** went smoothly by using a 25 % aqueous HCl solution to give dendrons **33b** and **33e**, respectively. However, the removal of the Cbz groups especially in case of dendron **33f**, required harsher catalytic transfer hydrogenation conditions. 5 % aqueous formic acid was used as hydrogen donor instead of hexa-1,4-diene and the reaction was carried out for two cycles (each cycle 14 h) in order to completely remove the Cbz groups (NMR spectrum is not shown here). Figure 23 shows the $^1$H-NMR spectra of dendron **33a** (spectrum **a**) and its deprotected counter parts **33b** (spectrum **b**) and **33c** (spectrum **c**). The same investigation as described above (see section 3.2.3.3) was carried out to proof the removal of the protecting groups.

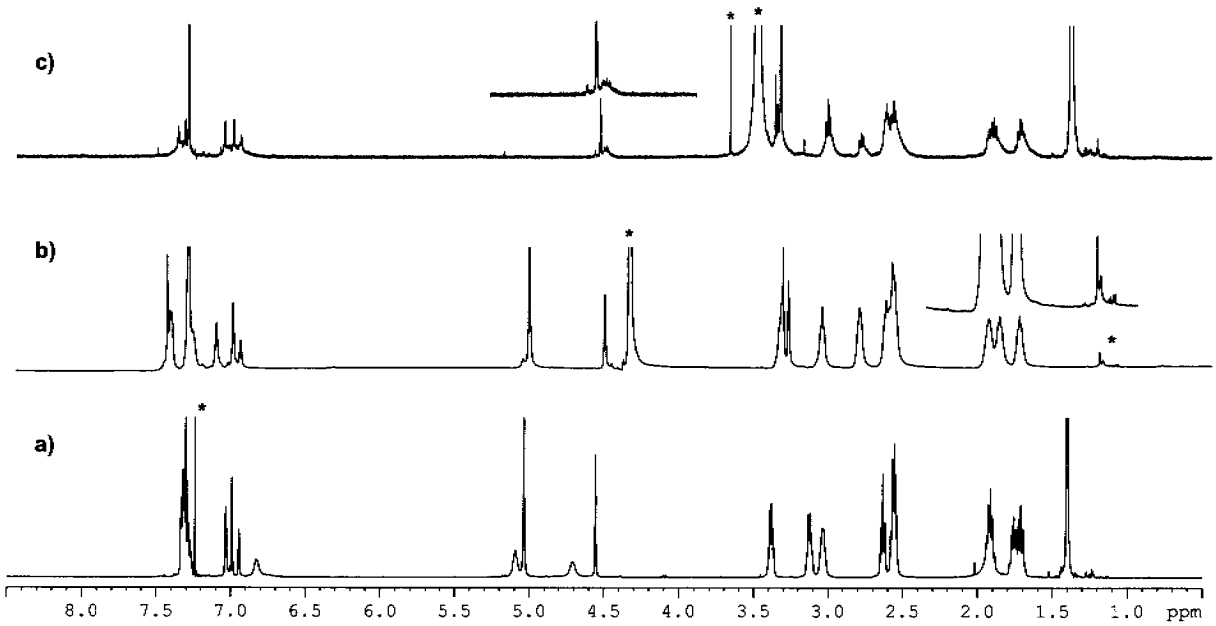
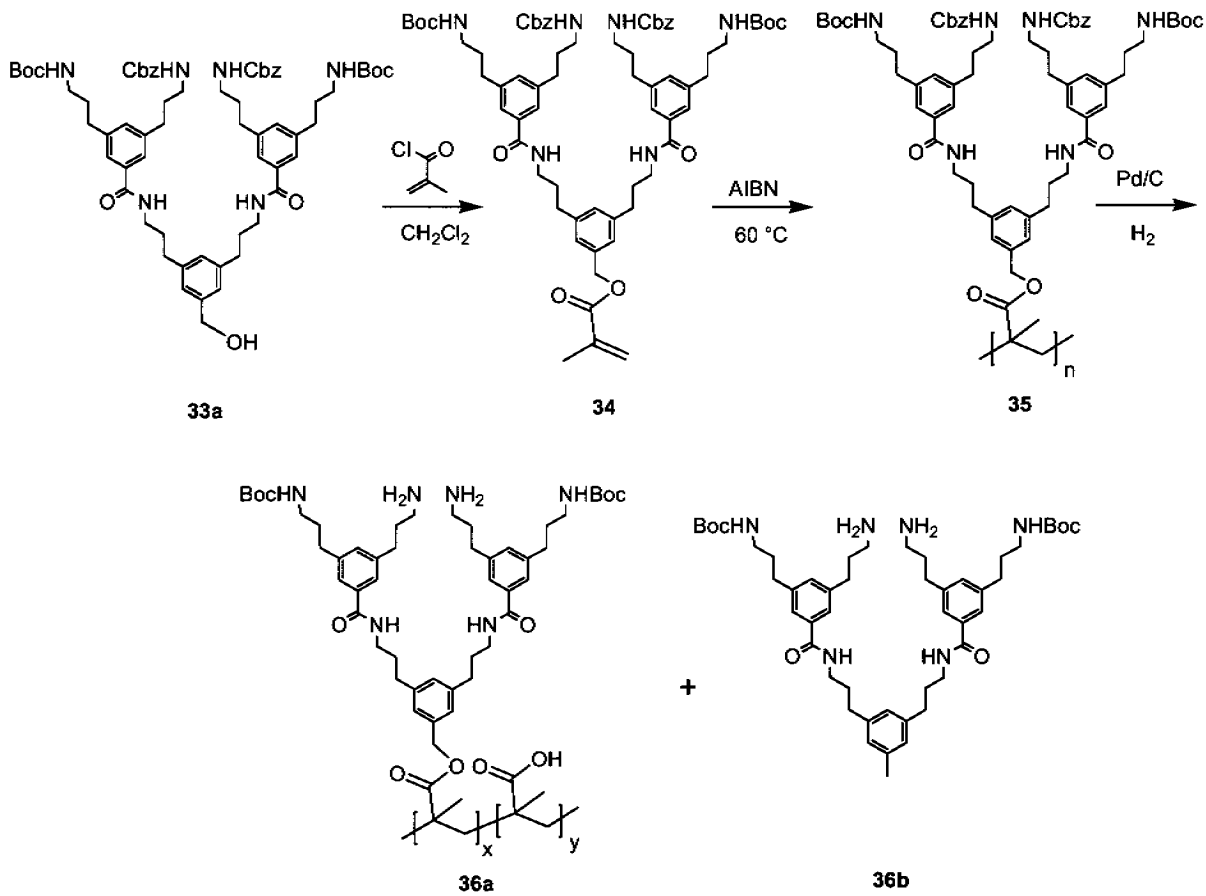



**Figure 23.** $^1$H-NMR spectra of dendron **33a** (**a**), and its selectively deprotected counter parts **33b** (**b**) and **33c** (**c**). Solvent signals of $CD_3OD$, $D_2O$ and grease are marked with (*).

### *3.2.1.5 Synthesis of G2 dendronized polymethacrylate carrying 2Boc and 2Cbz peripheral amino protecting groups*

The first attempt toward achieving orthogonally protected dendronized polymethacrylate carrying Boc and Cbz protecting groups was done by using G2-dendron **33a**. The hydroxyl group of **33a** was reacted with methacrylol chloride (polymerizable unit) to give the corresponding macromonomer **34**, which is then polymerized (scheme 11). The polymerization gave polymer **35** with high molar mass (Mw = 8 x $10^5$, PDI = 2.3). The selective removal of the Boc group of polymer **35** gave the corresponding deprotected counter part without any defect in the structure of the polymer and Cbz had stayed untouched. However, the selective removal of the Cbz group of polymer **35** by catalytic transfer hydrogenation gave the two products **36a** and **36b**. The deprotection conditions of Cbz led to the cleavage of the dendron from the polymeric backbone. Figure 24 shows $^1$H-NMR spectroscopy of the starting polymer, **30** (spectrum (**a**)) and the resulted products **36a** and **36b** (spectrum (**b**)). As can be seen in spectrum (**b**), many sharp signals appeared which refer to the cleaved dendron (product **36b**).




**Scheme 11**. Synthesis of G2-dendronized polymethacrylate **35** carrying 2Bocs and 2Cbzs and the corresponding products **36a** and **36b** that were obtained by catalytic transfer hydrogenation.

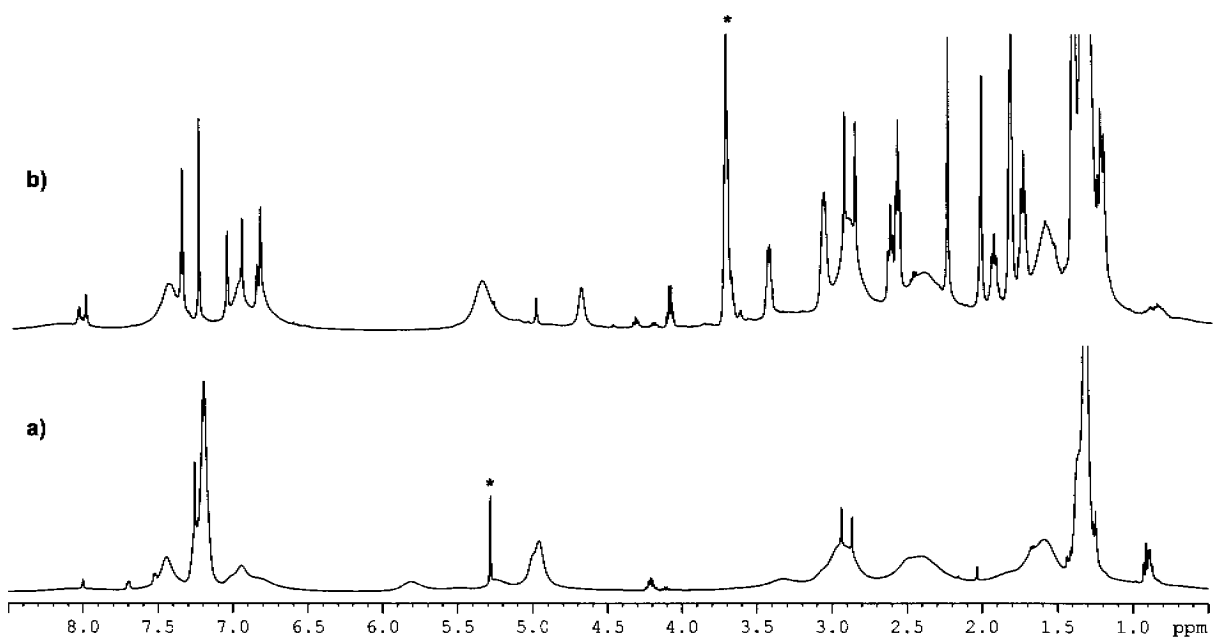
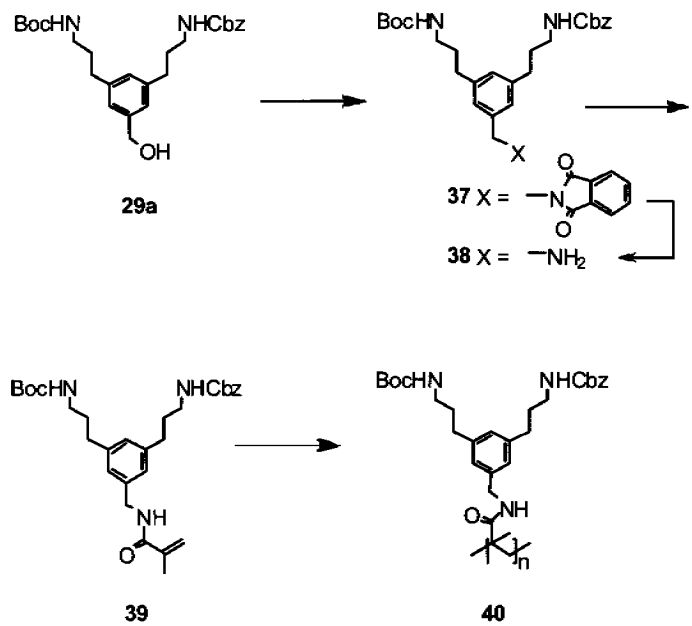



**Figure 24**. $^1$H-NMR spectra of polymer **34** (spectrum **a**), and the corresponding products **35** and **36** (spectrum **b**). Solvent signals of $CD_2Cl_2$ and $D_2O$ are marked with (*).

### *3.2.1.6 Synthesis of G1dendronized polymethacrylamide carrying 1Boc and 1Cbz peripheral amino protecting groups*

The cleavage of dendron **36** from the polymer backbone of **34** (scheme 11) was avoided by exchanging the polymethacrylate backbone by polymethacrylamide. This was carried out by using the Mitsunobu reaction procedure (scheme 12). The hydroxyl group of the dendron **29a** was reacted with mesylchloride and the isolated product was then reacted with potassium phthalimide to give the product **37** in a yield of 85 %. The reaction of dendron **37** with hydrazine hydrate gave the dendron **38**. The monomer **39** is then obtained by the reaction of dendron **38** with methacrylol chloride. Polymerization of the macromonomer **39** using dibenzoylperoxide as initiator at 70 °C, furnished polymer **40** (Mn = 5 x $10^5$, PDI = 2.7). The removal of Cbz, however, using different catalytic transfer hydrogenation procedures and conditions led only to partially deprotected polymers. A procedure to completely removing Cbz could not be established and therefore, the project was stopped at this point.

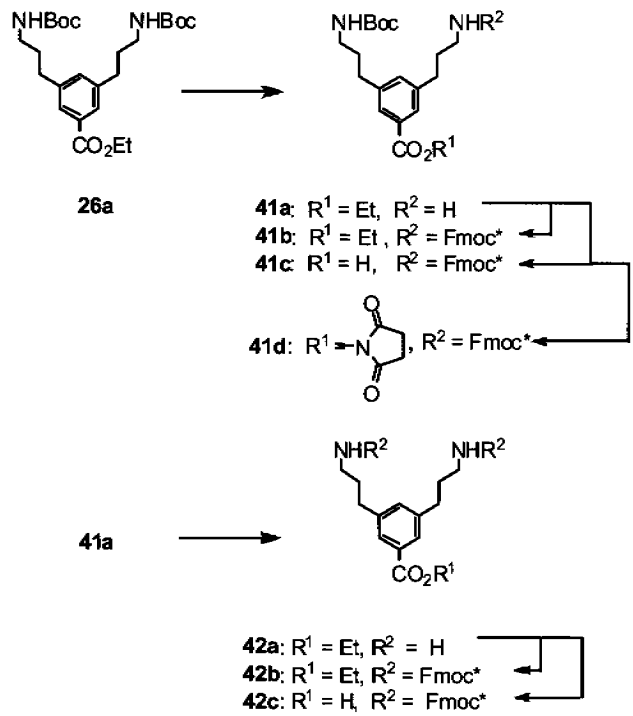



**Scheme 12**. Synthesis of orthogonally protected G1-dendronized polymethacrylamide **40** carrying 1Boc and 1Cbz.

### 3.2.2 Synthesis of a set of orthogonally protected G1 and G2 dendronized polymers carrying Boc and Fmoc* peripheral amino protecting groups

#### *3.2.2.1 Synthesis of precursors*

Scheme 13 describes the synthesis of the building blocks **41d** and **42c**. Compound **26a**, which was prepared on the 150 g scale according to literature procedures,[96] was subjected to a desymmetrization step at this stage of the entire sequence. It was treated with three equivalents of trifluoro acetic acid for 2 days to furnish compound **41a**, which still carries one Boc protected amine. Compound **41a** was isolated on the 20 g scale and in a yield of 65%. Most of the other product was unchanged starting material **26a** which was recovered and reused. The introduction of Fmoc* to the compound **41a** was carried out according to conventional procedures whereby the Fmoc* succinimidyl active ester derivative[99] proved to be superior in terms of less byproducts as compared to the originally reported Fmoc* chloroformate.[94] The Fmoc* succinimidyl active ester was therefore used to give **41b** in a yield above 90 %. Compound **41c** which is an important building block for the synthesis of various G2-dendrons could not be directly synthesized from **41b** because focal point saponification led to partial removal of Fmoc*. Therefore, the ester group of dendron **41a** was first saponified and the resulting product was subjected to Fmoc* succinimidyl active ester to give **41d** on the 2 g scale and in a yield of 90-95% over the two steps. The dendron **42b** with its two Fmoc* protected amines was easily obtained from **26a** by exchanging Boc by Fmoc* on the 2 g scale. However, in order to obtain compound **42c** which is important for building higher generation dendrons and thus, polymers, compound **42a** was saponified and then reacted with the Fmoc* succinimidyl active ester to give **42c** in a yield above 85 %.

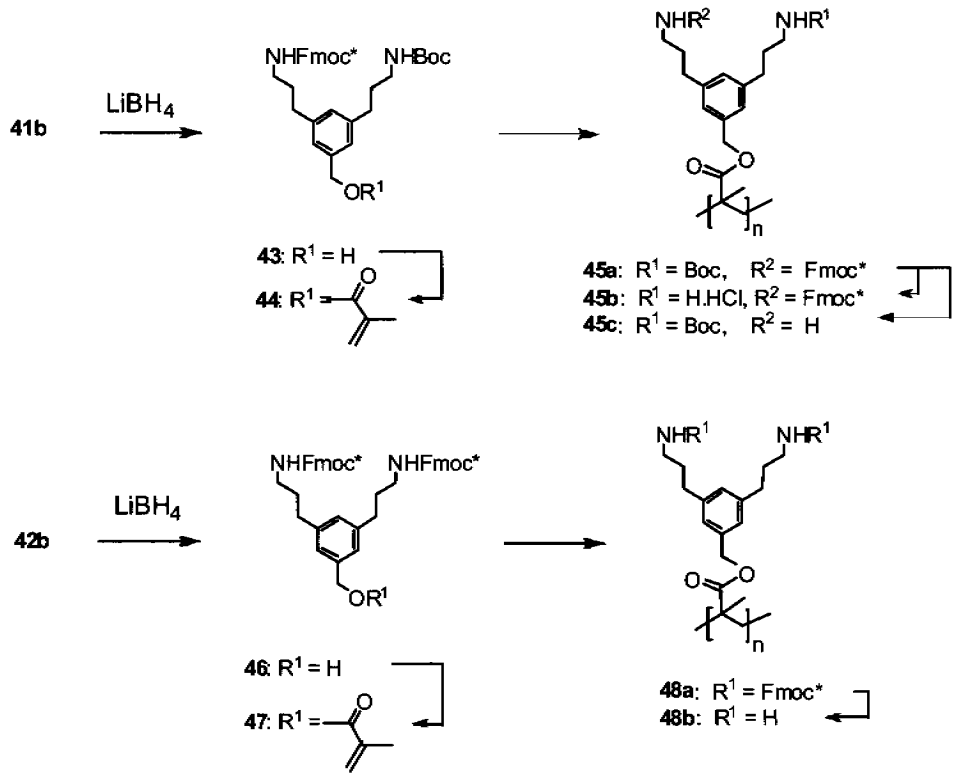



**Scheme 13.** Synthesis of the building blocks **41d** and **42c**.

### *3.2.2.2 Synthesis of G1 dendronized polymethacrylate carrying either 1Boc and 1Fmoc* or 2Fmoc* peripheral amino protecting groups*

Scheme 14 describes how the G1-methacrylate macromonomers and their corresponding dendronized polymer with the protecting group patterns Fmoc*/Boc (**44**) and Fmoc*/Fmoc* (**47**) were accessed. The reduction of focal points of dendrons **41b** and **42b** were done with lithium borohydride instead of lithium aluminium hydride in order to avoid attack on Fmoc*. The obtained dendrons **43** and **46** were reacted with freshly distilled methacrylic acid chloride, which is an important point whenever high molar masses of the corresponding polymers are concerned, to furnish G1 macromonomer **44** and **47** respectively. The polymerizations of **44** and **47** occurred without addition of initiator precursors by placing the flasks containing the highly concentrated solutions of monomers in DMF into preheated oil baths (70 °C) for 14 h. The yields and molar masses are summarized in table 1. The removal of Boc groups of polymer **45a** was done by using 25 % aqueous HCl to give **45b** in a yield of 90 %. However, Fmoc* groups of **45a** and **48a** were removed with 25 % piperidine in DMF solution for 48 h to furnish polymers **45c** and **48b**, respectively. The 2,7-di-*tert*-

butyldibenzofulvene derivative that formed during the latter deprotection was removed by extracting it into hexane. For recovery by precipitation the deprotected polymers **45c** and **48b**, the free amino groups of these polymers were protonated by the application of 0.1 N HCl. Otherwise, redissolving of a once-dried polymer was difficult. The quantification of the respective degrees of deprotection was investigated by NMR spectroscopy and will be described in details for the respective G2-dendronized polymers.

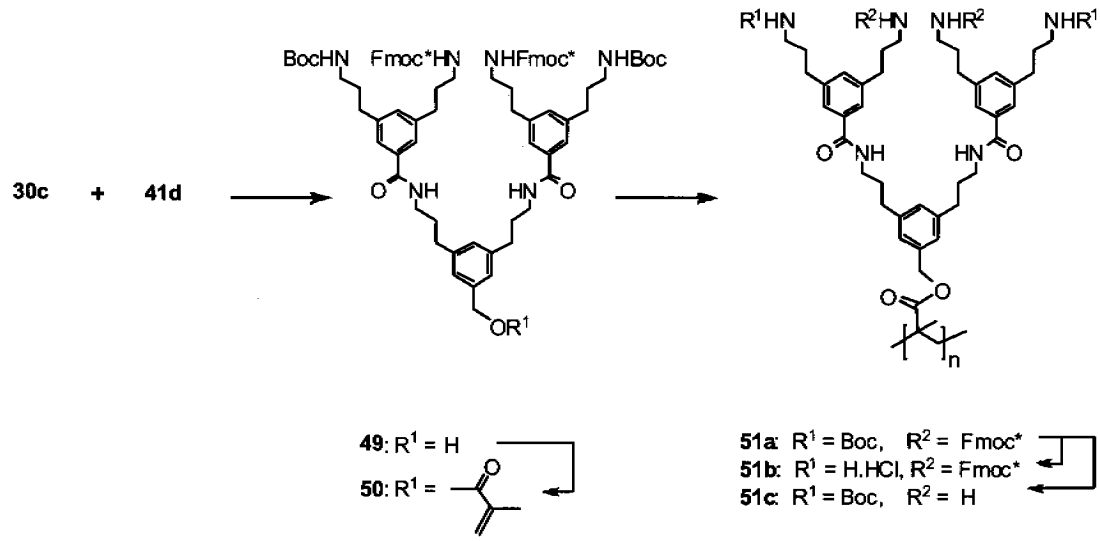



**Scheme 14**. Synthesis of G1-dendronized polymethacrylate, **45a** carrying 1Boc and 1Fmoc*, **48a** carrying 2Fmoc* groups, and their respective selectively deprotected counter parts **45b**, **45c**, and **48b**.

### *3.2.2.3 Synthesis of G2 dendronized polymethacrylate carrying 2Boc and 2Fmoc* peripheral amino protecting groups*

Scheme 15 describes the synthesis of G2 polymer **51a** which carries two Bocs and two Fmoc*s. The sequence was started from the known branching unit **30c**[96] which was reacted with 2.4 equivalents of **41d** to give the G2 dendron **49**. This dendron was converted into macromonomer **50** which was then polymerized as described

above (see section 3.2.2.2) but for longer time (22 h instead of 14 h) to give polymer **51a**.The molar mass and yield are summarized in table 1.




**Scheme 15.** Synthesis of G2-dendronized polymethacrylate **51a** carrying 2Bocs and 2Fmoc*s and its selectively deprotected counter parts **51b** and **51c**.

Selective removal of Boc and Fmoc* groups of **51a** was done using the same procedures for deprotection as described previously (see section 3.2.2.2) to furnish **51b** and **51c**. In order to explore whether these groups are truly orthogonal to one another even when hundreds or thousands of them are on the same molecule as in this case, A rigorous quantification of the respective degrees of removal was carried out on **51a** and its deprotected counter parts **51b** and **51c**. Figure 25 shows the $^{1}$H-NMR spectra of **51a**, **51b**, and **51c**, whereas figure 26 shows the $^{13}$C-NMR spectra of the same polymers. $^{1}$H-NMR spectroscopy was not enough to completely proof the orthogonallity of these groups. An unfavourable signal overlap was observed between the (only) signal of Boc and the *tert*-butyl signal of Fmoc*. However, the disappearance of Fmoc* showed in the decreased intensity of several signals (1.35 ppm, and 7.45 ppm) and the complete disappearance of the signal at $\delta$= 4.1 ppm even after the relevant shift range was considerably amplified (Figure 25c). The disappearance of Boc showed only in the decreased intensity of a signal superimposed by Fmoc* at $\delta$ = 1.35 ppm (Figure 25b). This was not considered as

evidence that Boc is completely removed due to the considerable line widths and also some contamination with water.

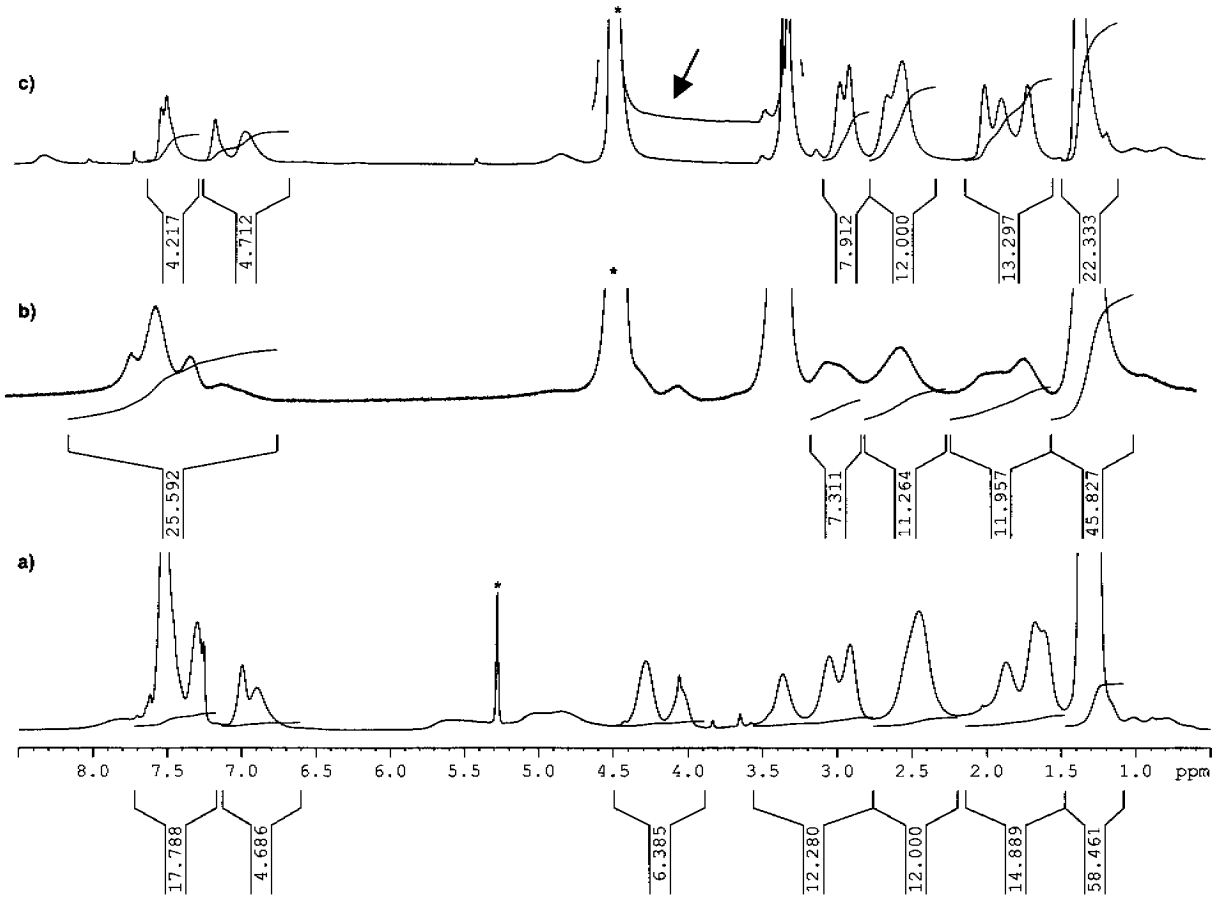



**Figure 22.** $^1$H-NMR spectra of polymer **51a** (spectrum **a**) and its selectively deprotected counter parts **51b** (spectrum **b**), and **51c** (spectrum **c**). Solvent signals of $CD_2Cl_2$ and $D_2O$ are marked with (*).

For that reason, the removal degree of the protecting group was then assessed by $^{13}$C NMR spectroscopy. Highly concentrated solutions of the protected polymer **51a** and partially deprotected counter parts **51b** and **51c** were measured until at least 30,000 pulses had been accumulated. A representative series of spectra is shown for polymers **51a-51c** (Figure 26). In the spectrum of the fully protected G2 polymer **51a** (Figure 26a), the signals of both protecting groups can be seen clearly. For the assessment special attention was given to the pair of *tert*-butyl signals of each protecting group which absorbed at rather different chemical shifts (Fmoc*: $\delta$ = 31.7 ($CH_3$) and 34.9 ($C_{quat}$); Boc: $\delta$ = 28.6 ($CH_3$) and 79.8 ($C_{quat}$). Figures 26b and 26c show the spectra of the Boc-deprotected polymer **51b** and the Fmoc* deprotected polymer **51c**, respectively. The corresponding signals disappeared quantitatively as far as this can be said for the given signal-to-noise ratio. There are a few further

important observations to be mentioned. In the experiments aiming at removal of Boc only deprotected products of Boc were observed and none of a possible removal of Fmoc*.[100] Obviously, the Fmoc* groups remained unaffected. On the other hand, the Fmoc*-deprotected polymer **51c** did not show any remaining fluorescence, which indicates that all Fmoc* groups had, in fact, been removed completely. Together with the substantial and rigorous evidence that Boc can be quantitatively removed in closely related polymers carrying exclusively Boc protected amines,[96] it is concluded that also in the cases described here both protecting groups can be selectively removed without mutual interference. It should be mentioned that the deprotections cause some shift changes which makes interpretation of the spectra in Figures 26 more complicated. This refers specifically to the $\alpha$-$CH_2$-shifts which absorb between $\delta$ = 29.00 and 35.00 ppm depending upon whether they carry a protecting group or not. The spectrum in Figure 26b has much broader signals than the other two which is attributed to its reduced solubility and increased aggregation tendency in the NMR solvent ($CDCl_3/CD_3OD$).

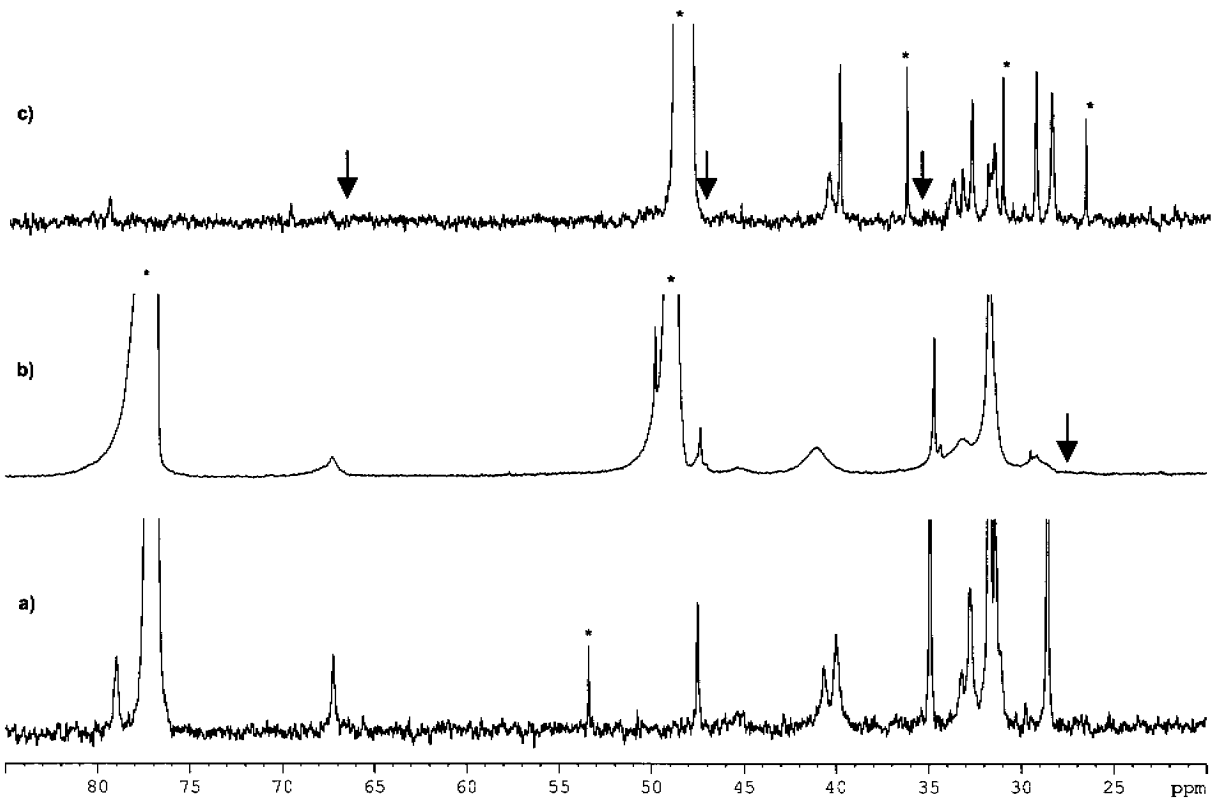
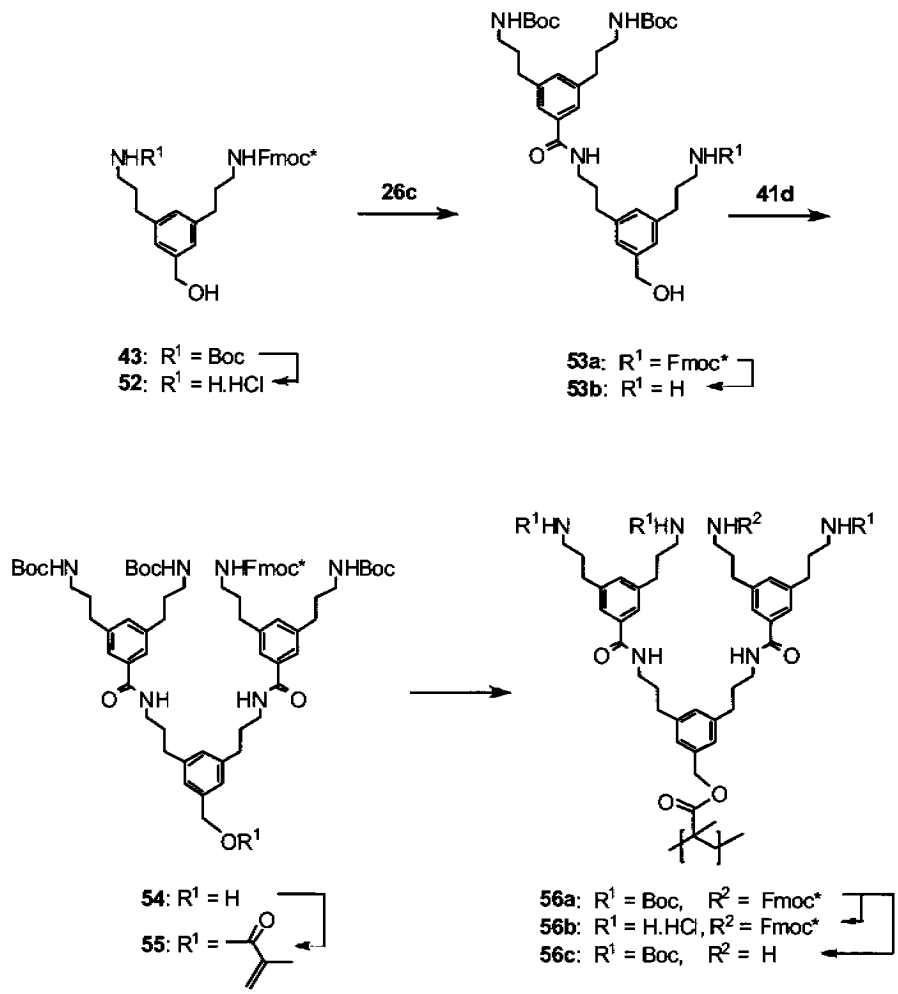



**Figure 26**. High field parts of the $^{13}C$ NMR spectra of polymer **51a** which carries 2Fmoc*s and 2Bocs (spectrum **a**), and its selectively deprotected counterparts **51b** carrying 2Fmoc*s and 2 unprotected amines (spectrum **b**) and **51c** carrying 2Bocs and 2 unprotected amine (spectrum **c**). The solvent signals of d-DMF, $CD_3OD$, and $CDCl_3$ are marked with (*).

### *3.2.2.4 Synthesis of G2 dendronized polymethacrylate carrying 3Boc and 1Fmoc* peripheral amino protecting groups*

Scheme 16 describes the synthesis of G2 polymer **56a** which carries 3Bocs and 1Fmoc*s. The sequence starts from the branching unit **43** which after removal of its Boc protecting group, was reacted with 1.2 equivalents of **26c** to give the homo-coupled G2 dendron **53a** in 85% yield. The removal of Fmoc* group of dendron **53a** yielded **53b** which was reacted with **41d** to give G2 dendron **54**. The reaction between the hydroxyl group of **54** and freshly distilled methacrylic acid chloride went smoothly to give the macromonomer **55**. Same polymerization procedure as used above (see section 3.2.2.2) was applied here to give polymer **56a**. The molar mass and yield are summarized in table 1.




**Scheme 16**. Synthesis of G2-dendronized polymethacrylate **56a** carrying 3Bocs and 1Fmoc*, and its selectively deprotected counter parts **56b** and **56c**.

The selective removal of both Boc and Fmoc* went smoothly using same procedures (see section 3.2.2.2). The quantification of the respective degrees of deprotection was achieved in the same way as described above (see section 3.2.2.3). Figure 27 shows the $^{13}$C-NMR spectra of starting polymer **56a** (spectrum **a**) and its deprotected counter parts **56b** where Boc is removed (spectrum **b**), and **56c** where Cbz is deprotected (spectrum **c**). As can be seen clearly from Figure 27, the selective deprotection is quantitatively achieved.

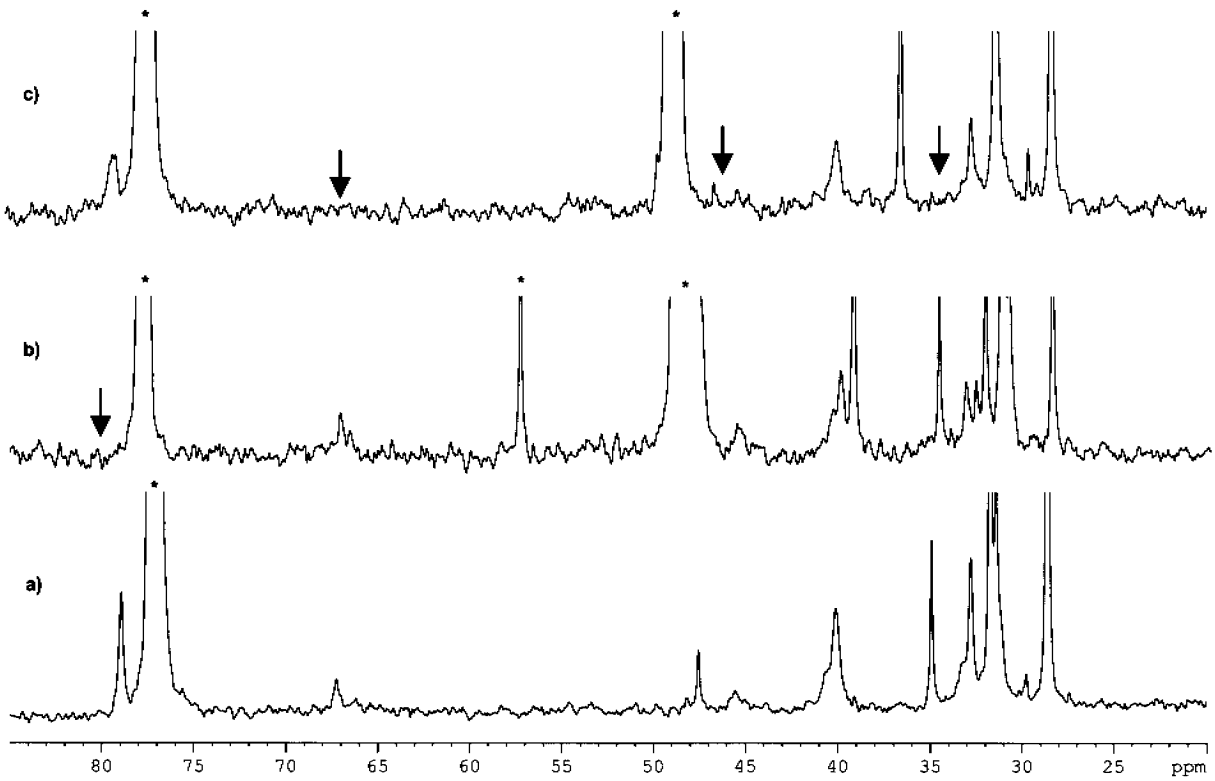
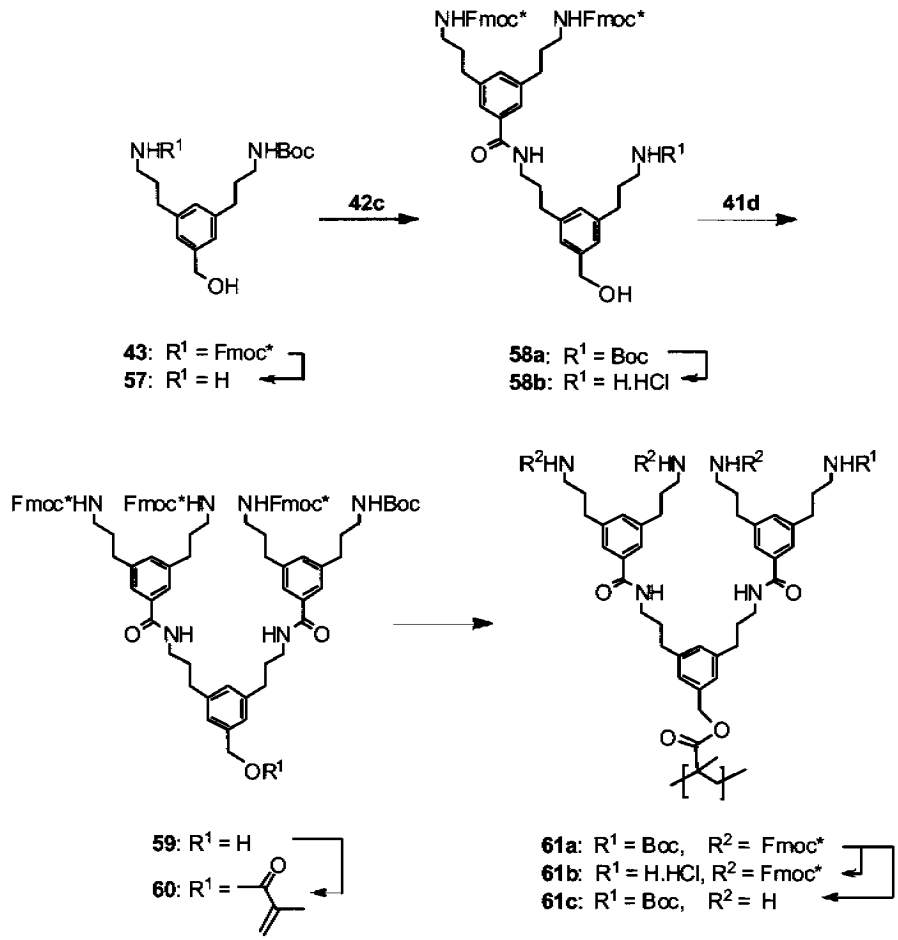



**Figure 27**. High Field parts of the $^{13}$C-NMR spectra of polymer **56a** which carries 1Fmoc* and 3Bocs (spectrum **a**), and its selectively deprotected counterparts, **56b** carrying 1Fmoc* and 3 unprotected amines (spectrum **b**), and **56c** carrying 3Bocs and 1 unprotected amine (spectrum **c**). The solvent signals of $CD_3OD$ and $CDCl_3$ are marked with (*).

### *3.2.2.5 Synthesis of G2 dendronized polymethacrylate carrying 1Boc and 3Fmoc* peripheral amino protecting groups*

In order to complete the set of orthogonally protected G2 dendronized polymethacrylate with Boc and Fmoc* groups, the synthetic sequence to obtain the last G2 polymer **61a** with 1Boc and 3Fmoc*s is described in scheme 17. Only a few

comments will be added. The polymerization of macromonomer **59** was done only for short time (10 h) otherwise, the polymer could not be dissolved anymore due to the low solubility of the polymer which now carries 3Fmoc* groups at every repeating unit. This made polymer **61a** to have lower molar mass than polymers **51a** and **56a**. The molar mass and the yield is summarized in table 1.




**Scheme 17**. Synthesis of G2-dendronized polymethacrylate **61a** which carries 1Boc and 3Fmoc*s, and its selectively deprotected counter parts **61b** and **61c**.

The molar masses and the polymerization conditions of polymers **45a**, **48a**, **51a**, **56a**, and **61a** are summarized in table 1. Together with the known G1 and G2 polymers **66** and **63** (Figure 28) which have exclusively Boc peripheral amino protecting groups, the polymers **45a**, **48a**, **51a**, **56a**, and **61a** described above form a complete set of dendronized polymers in which the Boc and Fmoc* protecting groups are systemtically varied.

| monomer | [M] mol/L | time h | yield % | $M_n$ x $10^5$ g/mol | PDI |
|---|---|---|---|---|---|
| **44** | 4.6 | 16 | 75 | 9.5 | 3.3 |
| **47** | 3.7 | 16 | 59 | 2.4 | 2.1 |
| **50** | 2.3 | 22 | 83 | 5.4 | 2.1 |
| **55** | 3.9 | 20 | 75 | 7.2 | 2.5 |
| **60** | 2.2 | 10 | 83 | 1.9 | 2.0 |

**Table 1**. Monomer concentrations, polymerization times, polymer yields, and polymer molar masses for the polymerizations of macromonomers **44**, **47**, **50**, **55**, and **61** into the corresponding. The reactions out in DMF at 70 °C without initiator precursors added.

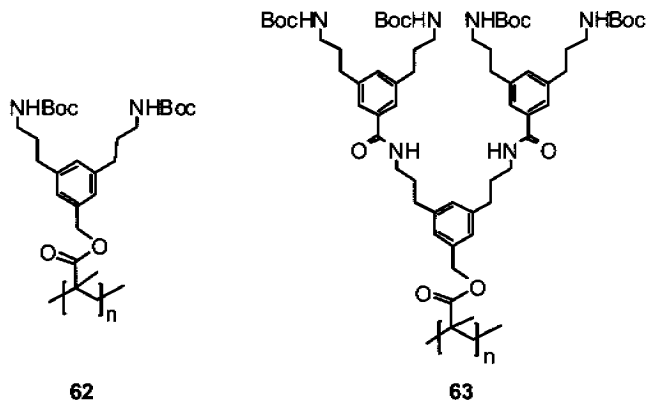



**Figure 28**. Structure of polymers **62** and **63** carrying exclusively Boc peripheral amino protecting groups.[96]

## 3.3 Covalent Connection of Individualized Neutral Dendronized Polymers on a Solid Substrate Using a Scanning Force Microscope

This part of the thesis was done in collaboration with the group of Prof. Rabe (Humboldt University, Berlin).

Parts of this work have been published in: *Chem. Eur. J.* **2006**, *12,* 6542-6551.

As previously mentioned (paragraph 1.4), two strands of positively charged dendronized polymers were covalently "welded" together on a highly oriented pyrolitic graphite (HOPG) surface under ambient conditions with SFM using "move-connect-prove" sequences.[38] The welding was achieved by randomly distributed azide groups on the periphery of the dendronized polymer which upon UV irradiation decomposed to nitrenes and thus, underwent non-selective bond forming reactions which led to the covalent cross-linking between the strands. The intrinsic problem of that experiment was the presence of impurities, which was due to the fact that the experiments were carried out with dendronized polymers prepared on the solid substrate directly from the reaction mixture. According to the author`s view, these impurities played an important role in immobilizing the dendronized polymers on HOPG since they can form a soft adsorbate layer, which may slow down the diffusion of the adsorbed dendronized polymers. In order to avoid this problem and to create a broader basis for move-connect-prove sequences, procedures were developed to reduce the sensitivity of the experiment towards this problem (i) by employing a chemistry which avoids the simultaneous presence of side products like in the previous case,[38] and (ii) by pre-coating the solid substrate with a soft organic monolayer that guaranteed the immobilization of single adsorbed dendronized polymers and still allowed their manipulation.[101]

This was accomplished by synthesis of a non-charged third generation dendronized polymer of high molar mass. 25% of the peripheral amino groups of this polymer carried azide functions for cross-linking and the remaining 75% were benzyloxycarbonyl (Cbz) protected. The synthesis was carried out by the attach-to procedure. Functionalized G2 dendrons were bound to the two amine anchor groups presented per repeat unit of a high molar mass G1 dendronized polymers. Since the synthesis involved hundreds of such coupling steps per macromolecule, the degree

to which the entire conversion could be achieved was determined quantitatively. For that purpose residual amine groups in the former G1 dendronized polymer which had not reacted with a G2 dendron were amplified by reacting them with 5-dimethylaminonaphthalene-1-sulfonyl (dansyl) chloride, a potent fluorescence label commonly used in biochemistry.[102] The degree to which dansyl was covalently incorporated into the polymer structure was determined by fluorescence intensity measurements. The results of which were confirmed in an independent, structurally somewhat different system which will be discussed in part 3.4.

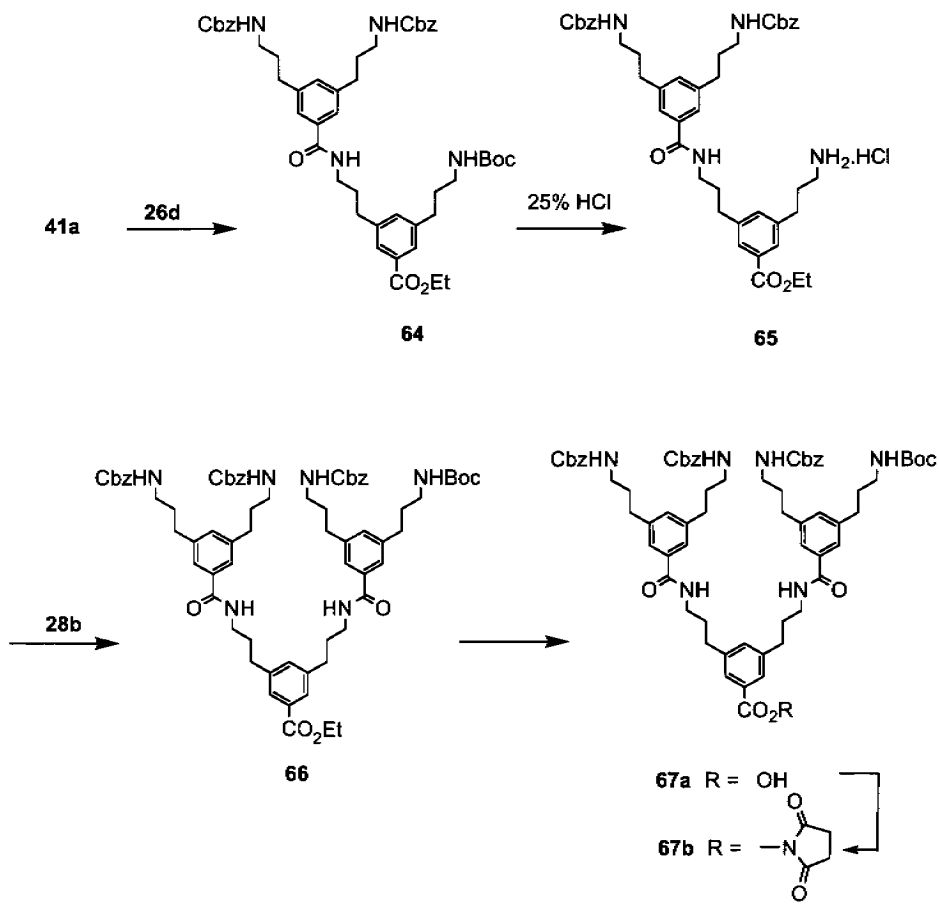
The characterized G3-dendronized polymer was then prepared by spin-coating from chloroform onto a quasi-2D network on HOPG. This gave a sub-monolayer of mostly individual dendronized polymers on HOPG pre-coated with a layer of $C_{23}H_{47}COOH$. Single dendronized polymers were manipulated with the SFM tip in contact-mode for a new move-connect-prove sequence. Several experiments were then carried out to prove that the irradiation led to a covalent connection in the positions where the individual dendronized polymer chains were in tight contact. The synthesis and results are discussed in detail in the following.

### *3.3.1 Synthesis of G3 dendronized polymethacrylamide carrying Cbz and Azide groups in the periphery*

An orthogonal synthesis strategy was devised here according to which a G3-dendronized polymer would become available with a predetermined number of orthogonally protected amines of two different kinds per repeat unit. The protecting group combinations chosen for this were also either Cbz/Boc or Fmoc*/Boc. It was important to have a high molar mass G3-dendronized polymer with 25% of all amines protected with Boc and 75% with Cbz. The main thoughts behind this selection were as follows: With both the third generation and the high molar mass the dendronized polymer's mobility on HOPG was expected to be in a reasonable range. Additionally, as described before, large numbers of Boc groups can be easily cleaved off in the presence of also large numbers of Cbzs. Therefore, this opened the way for the attachment of an aromatic azide through active ester chemistry to the dendronized polymer.

### *3.3.1.1 Synthesis of an orthogonally protected G2 dendron carrying 1Boc and 3Cbz peripheral amino protecting groups.*

The synthesis of dendron **67b** which is an important precursor to reach the target dendronized polymer carrying 25% azide groups and 75% Cbz-protected peripheral amines is shown in scheme 18. The starting material was the dendron **41a** with one Boc and one free amine and the symmetrical dendron **26d** which had already been synthesized before (Scheme 13 and Scheme 7, respectively). The amide coupling of **41a** and **26d** was achieved using the HOBt/EDC system and gave **64** in a yield of 63%. Subsequent deprotection and addition of dendron **28b** furnished dendron **66** which carries three Cbz protected amines and one Boc in a yield of 85 %. To allow dendron **66** to be attached to a polymer, its focal point was converted into the active ester **67b**. This dendron was prepared on the 1 g scale.

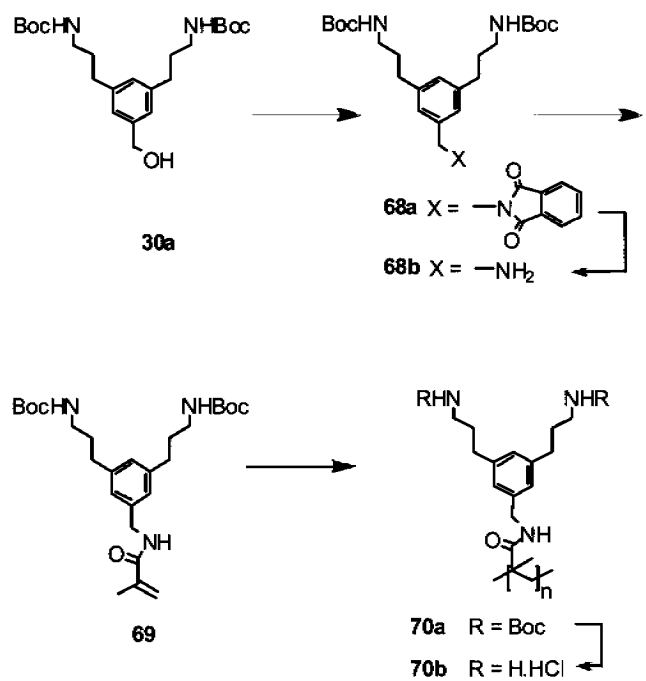



**Scheme 18**. Synthesis of orthogonally protected G2-active ester dendron **67b** carrying 1Boc and 3Cbz groups.

### *3.3.1.2 Synthesis of a G1-dendronized polymethacrylamide carrying two free peripheral amino groups.*

To arrive at the G1 dendronized polymethacrylamide **70a**, the benzylic alcohol group of dendron **30a** was mesylated and then reacted with potassium phthalimide to give **68a** which was then converted into the free amine **68b** with hydrazine (scheme 19). Dendron **68b** was connected to a polymerizable unit by reacting it with freshly distilled methacrylic acid chloride. The resulting G1 macromonomer **69** was prepared on the 5 g scale.

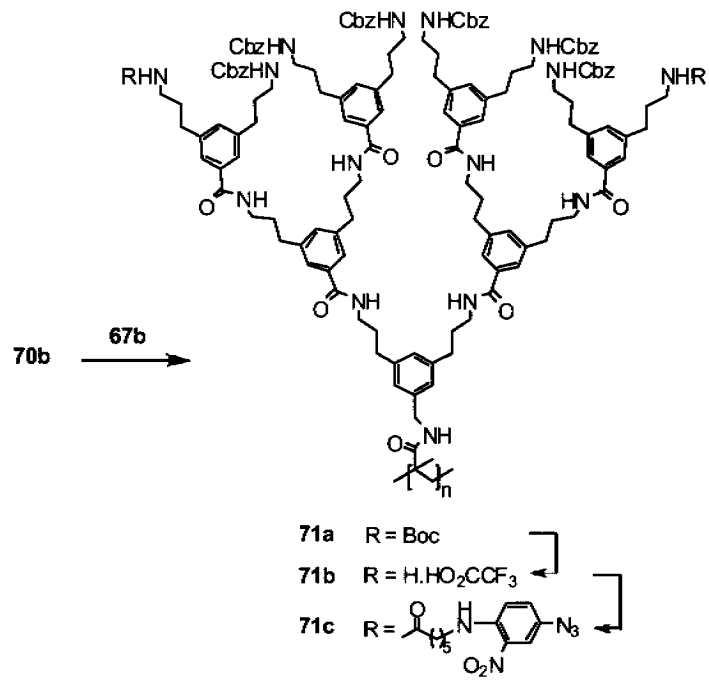
Polymerization were carried out with DBPO (0.15 mol-%) as radical initiator precursor at 70 °C in a highly concentrated solution in DMF (30% w/w). It was shown earlier that extremely high concentrations are a prerequisite for such polymerizations to give satisfying results regarding the molar masses. After considerable optimization work on the small scale, one gram of monomer **69** was finally polymerized to give the desired polymer **70a** in 70% yield and molar masses of $M_w$ = 1.4 x $10^6$ g/mol, PDI = 2.6 (GPC universal calibration). Dendronized polymer **70a** was then deprotected with aqueous 25% hydrochloric acid to give **70b** which was isolated by precipitation prior to its dendronization with G2 dendron **67b**.




**Scheme 19**. Synthesis of G1-dendronized polymethacrylamide **70b** carrying two free peripheral amino groups.

### *3.3.1.3 Synthesis of a G3 dendronized polymethacrylamide carrying 25 % azide groups and 75 % Cbz-protected peripheral amines.*

The synthesis method of the target dendronized polymer was of the "attach-to" kind. The G2 dendrons **67b** were attached to the G1 dendronized polymer **70b** using well established active ester coupling as shown in scheme 20. In our laboratory such coupling in several cases had proven to proceed virtually quantitative if the conditions were chosen carefully.[16] Polymer **70b** was dissolved in MeOH which contained 4-5 equivalents of triethylamine per ammonium group of **70b** and a solution of 1.5 equivalents of dendron **67b** per amine in MeOH and methylene chloride (1:2) was added dropwise. After stirring for two days, the solvent of the still homogenous solution was removed in vacuo, whereupon the polymeric residue was taken up in methylene chloride with some triethylamine and a solution of another 0.25 equivalents of dendron **67b** in the same solvent added. Stirring was continued for 12 hours, and after conventional work-up furnished polymer **71a**. For a quantitative determination of the dendronization efficiency see section 3.3.2.2. In order to introduce the azide function required for the cross-linking experiments, dendronized polymer **71a** was treated with excess trifluoro acetic acid until all Boc-signals in the 700 MHz $^1$H NMR spectrum had disappeared. The resulting 25% deprotected dendronized polymer was dissolved in chloroform and precipitated into ethylacetate/hexane (1:1) to give **71b**. This product was finally converted into **71c** by reacting it with the commercially available *N*-succinimidyl-6-(4-azido-2-nitroanilino)hexanoate in an excess of 1.5 equivalents per amine of **71b**. The conversion of this step was not determined. There is substantial evidence that succidinyl active esters react virtually quantitative with amine groups of dendronized polymers.[16]



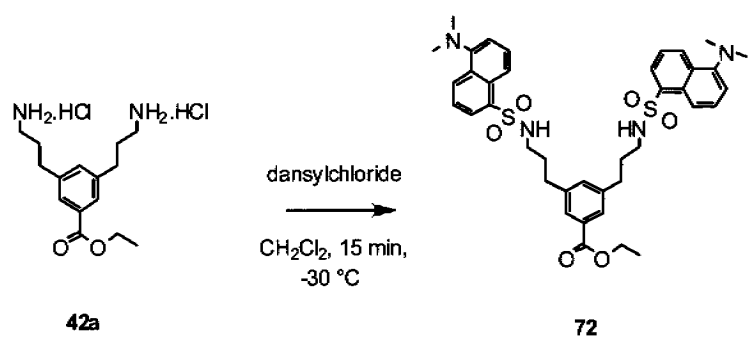

**Scheme 20**. Synthesis of G3-dendronized polymethacrylamide carrying 25 % azide groups and 75 % Cbz-protected peripheral amines.

### *3.3.2 Quantification of dendronization*

The efficiency of successive dendronizations of dendronized polymers with G1 dendrons has been quantitatively determined all the way up from G2 to G4 dendronized polymers.[16] The attachment chemistry was based on the reaction between amines and succinimidyl active esters which is known to proceed virtually quantitative, specifically if the active ester can be employed in large excess. Amine groups which happened to remain unaffected by the dendronization process were artificially amplified by attaching the Sanger reagent to them, which is a potent UV label for primary amines. The resulting UV absorptions were measured at $\lambda = 330$ nm to determine the degree to which the amines had been labelled. Assuming that all free amines had reacted with the reagent, this allowed deriving the dendronization efficiency. Under carefully chosen conditions efficiencies beyond 99% were determined per growth step indicating that the attach-to procedure can lead to near-perfect, high generation dendronized polymers. The present case differs somewhat from the previous one in that the G3 dendronized polymer **71a** was synthesized by reaction of the starting polymer **70b** not with G1 dendrons but rather with the G2

dendron active ester **67b**. Intuitively one would expect that in this case any remaining, not dendronized amine group of **70b** to be more effectively shielded than in the previous case, because it will be surrounded by sterically more demanding G2 rather than just G1 dendrons. This will hinder the diffusion of the dansyl label and its reaction with the remaining amines and thus could result in a too low fluorescence intensity and, therefore, falsely indicate a too high dendronization efficiency. It was therefore of some concern to collect evidence that the amines were still accessible by the dansylating reagent.

For this purpose, the model compound **72** which carries two dansyl groups was first prepared (Scheme 21). It served as a reference point for the fluorescence measurements and was prepared by reaction of the two unprotected amine groups of the corresponding G1 dendron **42a** (scheme 13) with 1.2 equivalents of dansyl chloride per amine group at -30 °C for 15 min. Despite these rather mild reaction conditions, product **72** was isolated in a yield of virtually 100%. Its fluorescence intensity, obtained from the peak areas, was measured in the concentration range 0.0274 – 219 μ*M* in chloroform (Figure 29). Up to a concentration of 27 μ*M* a linear relationship was observed indicating that there was no quenching. All subsequent measurements were therefore done in this concentration range although, once incorporated into the dendronized polymer structure, the dansyl units should not easily be able to undergo both intra- and intermolecular collisional self-quenching. The latter argument holds true only for those cases where a few amines scattered along the backbone carry dansyl labels. Otherwise the covalent fixation of labels to the same polymer chain results in concentrating them up which may go as far to render the above concentration dependence not applicable anymore.




**Scheme 21**. Synthesis of model compound **72** carrying two dansyl groups.

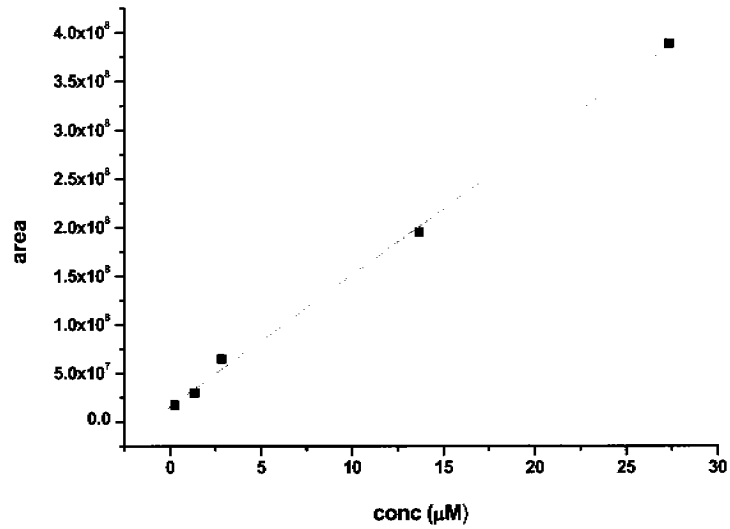
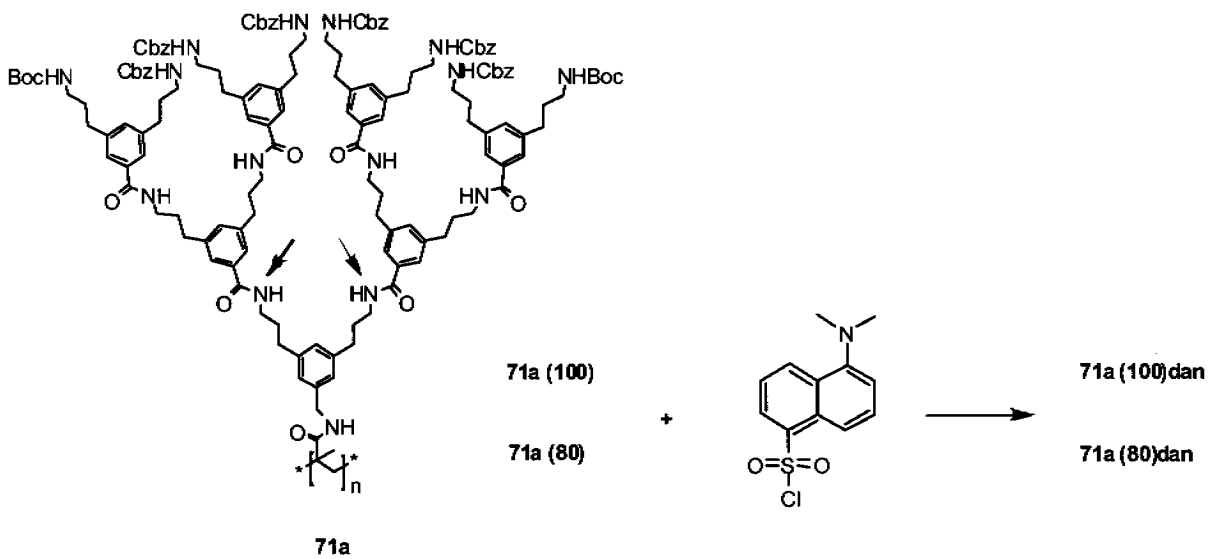



**Figure 29**. Concentration of the dansylated model compound **72** in chloroform (μM) against fluorescence intensity as obtained from signal areas at room temperature.

The dendronization efficiency was analyzed by dansylation of two different samples **71a** both of which were prepared from the identical batch of G1 dendronized polymer **70a** with $P_n$ = 1,100 and $P_w$ = 2,800. In the first sample, the starting dendronized polymer **70a** was deprotected and reacted with 2 equivalents of G2 dendron **67b** per amine group aiming at a complete coverage. With the second sample, coverage of 80% of the amines was attempted by reacting dendronized polymer **70b** with 0.8 equivalents of dendron **67b** per amine group. In the following, these samples will be referred to as **71a(100)** and **71a(80)**, respectively. Both samples were dansylated at somewhat more forceful conditions than those used for model compound **72** by employing -10 °C[103] and 2 h reaction time. For **71a(100)** one equivalent of dansyl chloride per amine of dendronized polymer **70b** was used to give **71a(100)dan** and for **71a(80)** 1.5 equivalents per expected free amine group were used to give **71a(80)dan** (scheme 22). If one assumes 1% of not dendronized amines in **71a(100)**, this would then correspond to a 100-fold excess of dansyl chloride whereas the excess employed in the case of **71a(80)** was much smaller. The intention behind the more forcing reaction conditions and the huge excess for the treatment of **71a(100)** was of course to drive the dansylation of any free amine to completion. The excess of dansyl chloride and any eventually formed low molar mass product between it and an inadvertently present nucleophile of some sort were removed by repeated

precipitation/dissolution cycles. After each such cycle the fluorescence intensity of the polymers was measured and the process continued until the intensity remained constant. This was typically the case after three cycles for **71a(100)dan** and one cycle for **71a(80)dan**. Additionally the polymers were checked by TLC. If the fluorescence intensity had reached the final value not even a trace of a bluely fluorescing component moved away from the polymer irrespective of the solvents used. Figure 30 compares typical fluorescence curves of **71a(100)dan** and **71a(80)dan** with model compound **72**. From a comparison of signal intensities, which is described in detail in the experimental part, dansylation degrees of 0.15 % and 18% were obtained for **71a(100)** and **71a(80)**, respectively. These values, in turn, reflect dendron coverages of 99.8% and 82%.




**Scheme 21**. Synthesis of dansylated G3 polymer **71a**.

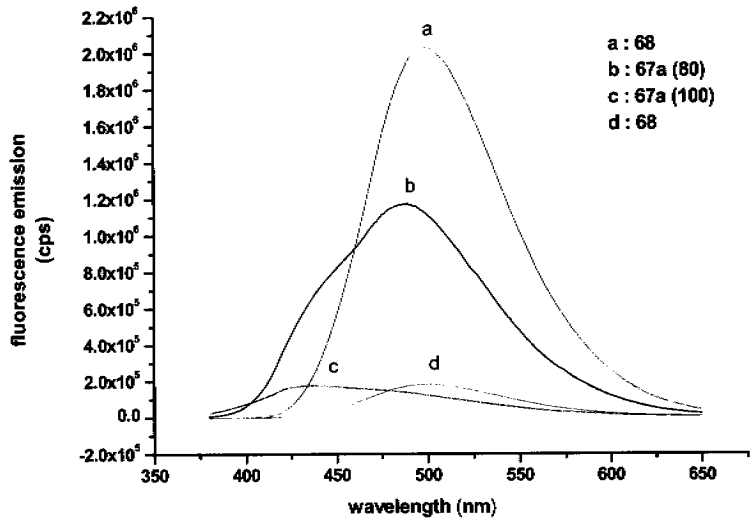
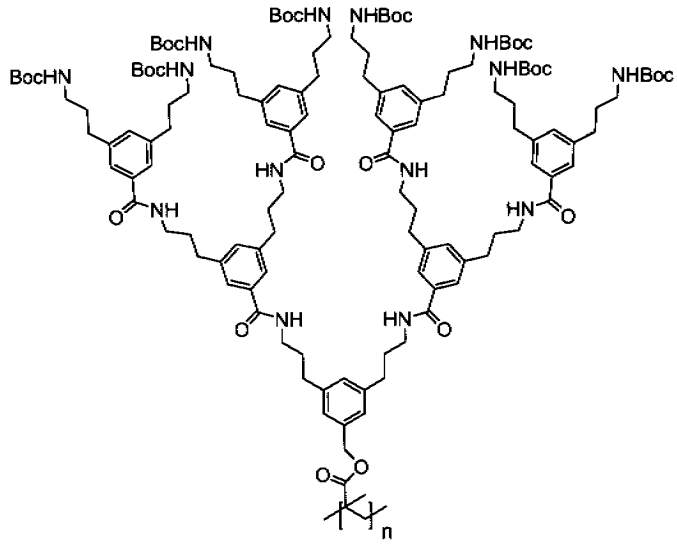



**Figure 30**. Fluorescence emission spectra of model compound **72** as well as polymers **71a(100)dan** and **71a(80)dan**.

The very high value for **71a(100)** was confirmed twice in independent experiments. It was even further substantiated by a closely related dendronization reaction leading to dendronized polymer **73** (Figure 31) which will be explained in detail in section 3.4 for which coverage of 99.7 % was found using exactly the same procedure as described above.




**73**

**Firgue 31**. Chemical structure of G3-dendronized polymer **73**.

Assuming that the quenching of fluorescence intensity is not occurring in **71a(100)dan** and **71a(80)dan** cases, this kind of analysis still has the intrinsic disadvantage of not providing any clue as to whether all non-dendronized amines have actually reacted with the label. This is why, as mentioned before, more forcing reaction conditions were applied[111] and a huge excess of the labelling agent (dansyl chloride) was employed. There are two other arguments which should be considered in this context. Firstly, dendronized polymer **71a(80)**, which was obtained from the reaction between the starting dendronized polymer **70b** with 0.8 equivalents of G2 dendron **67b**, gave a dansylation degree of 18%. This confirms not only that the dendronization goes almost to completion, even if the dendron, like in this case, is not in excess, but also that the dansylation obviously reaches completion, at least in this sterically less hindered case. Secondly, dendronized polymer **73** was obtained as a pure material in a yield of 91% after several precipitation/dissolution cycles which were implemented in order to remove the last traces of the G2 dendron. The dendron had been used in an excess of two per amine group. Because these cycles were associated with some losses of polymer, a yield in this percent range indicates a near-complete reaction course which does not leave much free space for another interpretation. The experiment was carried out with dendronized polymer **73** rather than **71a(100)** because the former was more abundantly available and the dendronization's yield could therefore be determined with higher accuracy (For more detail see section 3.4).

### *3.3.3 SFM move-connect-prove sequences*

Stable SFM imaging of **71c** was not possible if solutions with relatively low concentrations (c ≈ 0.05 mg/mL) was used. This observation indicated that single dendronized polymers were not immobilized on the basal plane of graphite, and possible impurities did not stablize them. However, at higher concentrations (c ≈ 0.5 mg/mL, depending on the polymer batch), a stable quasi 2D-network of dendronized polymers was formed (Figure 32a). This might be due to the inherent stability of the 2D-network. Alternatively, an increased concentration of impurities at the surface might form an organic monolayer, which caused a larger friction coefficient for the adsorbed dendronized polymers than did the bare basal plane of graphite, since the potential energy landscape across the surface exhibited increased amplitudes. To

differentiate between these cases, two strands in the network were cut in contact mode SFM. Figure 32b shows the resulting loose ends, with a length of about 80 nm each, immobilized on the surface. This observation, in the context of individualized dendronized polymers in the low-concentration experiment, was attributed to the increased concentration of impurities causing the immobilization. Moving two loose ends with the SFM together (Figure 32b,c) and apart again (Figure 32d) proved the reversibility of this kind of manipulation. After UV-illumination of two dendronized polymer strands previously moved together (Figure 32e), the same manipulation did not allow separation of the dendronized polymers any more (Figure 32f, g). Figure 32h-j shows that the junction point can be moved while the dendronized polymer breaks at a different position, thus, proving the strength of the new linkage. Note that the thickness of one of the newly formed loose ends was decreased at one position; this result indicated that it might consist of a duplex.[104] Note also the twisted, higher-order supramolecular structures.

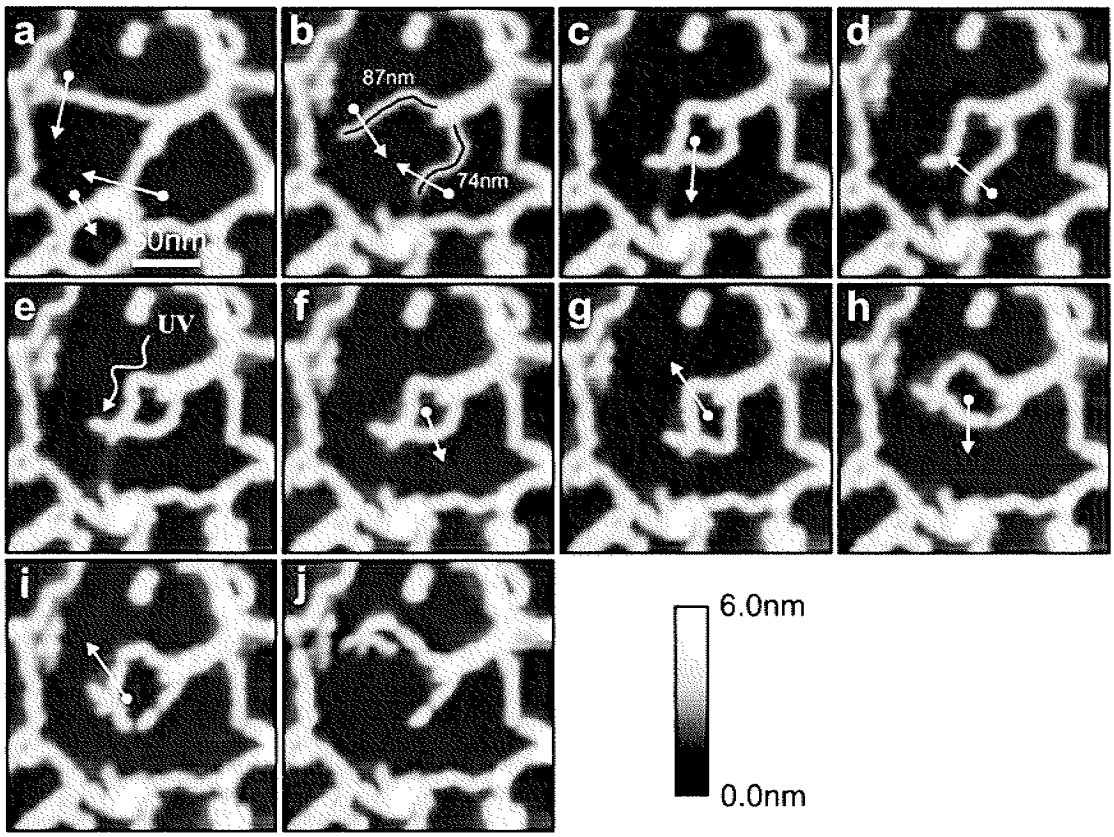



**Figure 32**: Move-connect-prove sequence of **71c** adsorbed to HOPG, probably with an immobilizing impurity layer. a) Initial conformation of the network; b) two loose ends (87 nm, 74 nm) were cut out of the network; c) forming and d) opening the junction; e) dendronized polymers were moved in tight contact again and illuminated *in-situ* with UV light (254 nm) for 5 min; f)-j) challenging the link mechanically until chain rupture.

In the case described above, the dendronized polymer immobilization was attributed to an ultrathin layer of organic impurities, and thus it was decided to render the experiment more clear-cut by pre-coating HOPG with a well defined organic layer, namely, a spin-coated monolayer of $C_{12}H_{25}NH_2$ or $C_{23}H_{47}COOH$.[101] In these cases dendronized polymers also adsorbed and immobilized from low concentrations, which allowed the observation of dendronized polymer aggregates and also single dendronized polymer strands. Figure 33a shows **71c** adsorbed onto a monolayer of $C_{12}H_{25}NH_2$ on HOPG, in which two probable aggregates 1 and 2 were visible. SFM manipulation was used to prove the aggregation and to dissect the aggregates into their components as a starting point for a move-connect-prove sequence. Figure 33b displays two individual strands 1 and 2 with lengths of 310 nm and 225 nm, respectively, extracted from these aggregates by eight manipulation steps. Interestingly, intramolecular clew-shaped arrangements could also be opened by lateral manipulation (Figures 33c,d). The initial conformation shown in Figure 33c exhibited a clew (in dashed circle) with the internal structure not being evident. A probable conformation of the polymer strand was sketched as a black line. Moreover, to the left and right of the clew two small dendronized polymer fragments (white arrows 1 and 2) were adsorbed onto the strand, thus acted as an absolute position marker along the chain at a separation of 25 nm. After two steps of manipulation the clew was opened, as revealed by an increase in the separation of the two markers along the contour to 63 nm. These facts proved clearly that individual dendronized polymers could be immobilized on the pre-coated HOPG, imaged in tapping mode SFM, and moved across the surface with high lateral accuracy in the contact mode. The process included individualizing of dendronized polymers by dissection of dendronized polymer aggregates, which will greatly simplify manipulation experiments at the single-molecular level.

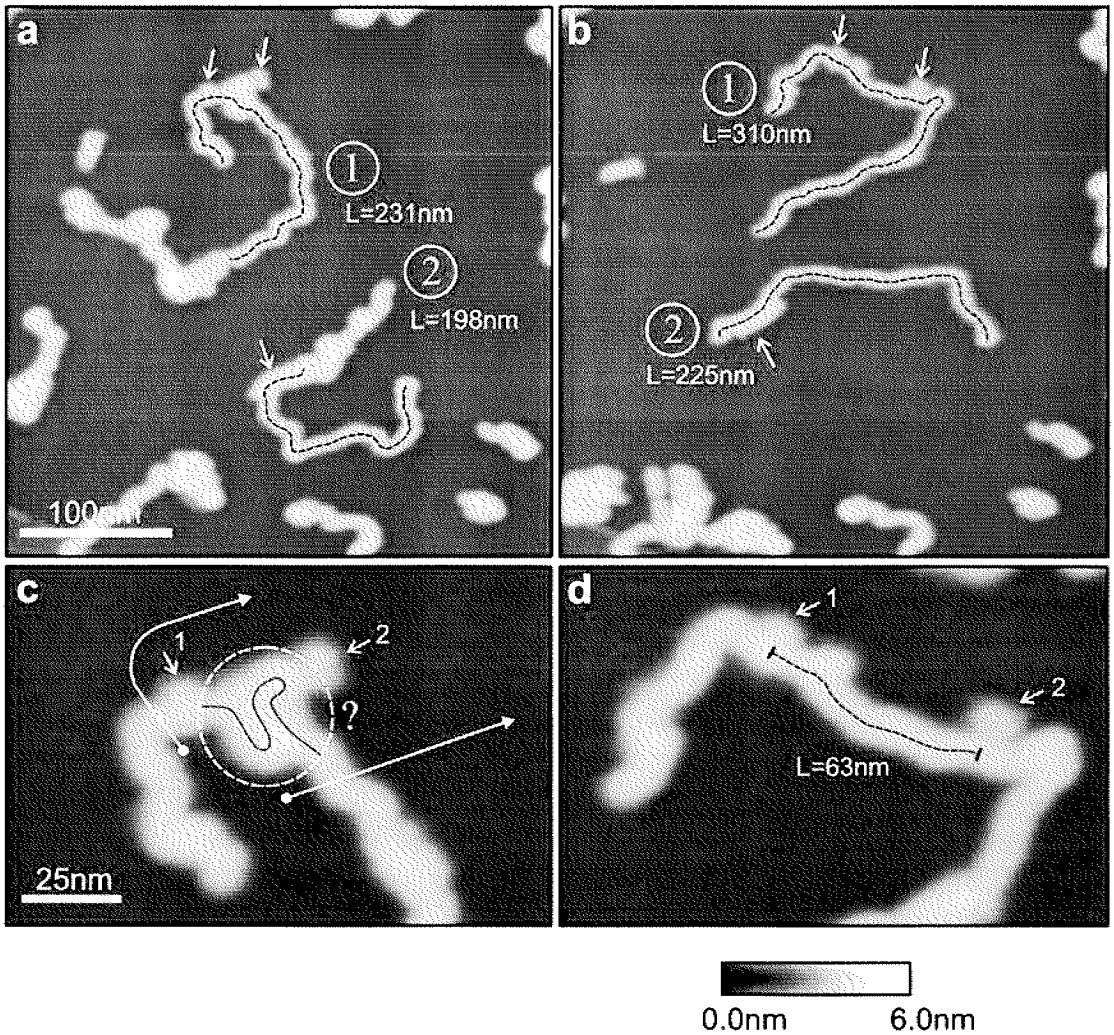



**Figure 33**. Polymer **71c** adsorbed onto a monolayer of $C_{12}H_{25}NH_2$ on HOPG. a) Initial conformation of aggregates 1 and 2 of **71c**; b) extracted single strands 1 and 2 after several manipulation steps; c) and d) corresponding zoom of images a) and b) before and after manipulation, respectively, which display the unfolding of a claw (dashed circle) resulting in a length release of 63 nm. The white arrows in c) indicate the tip motion during contact-mode SFM manipulation.

The single dendronized polymers were used for a move-connect-prove sequence (Figure 34). The linkage between two dendronized polymers could again be induced with UV light, as proven by challenging it mechanically with the SFM tip in contact mode up to chain rupture beside the induced linkage, thus indicating that the linkage between the individual strands was of truly covalent nature.

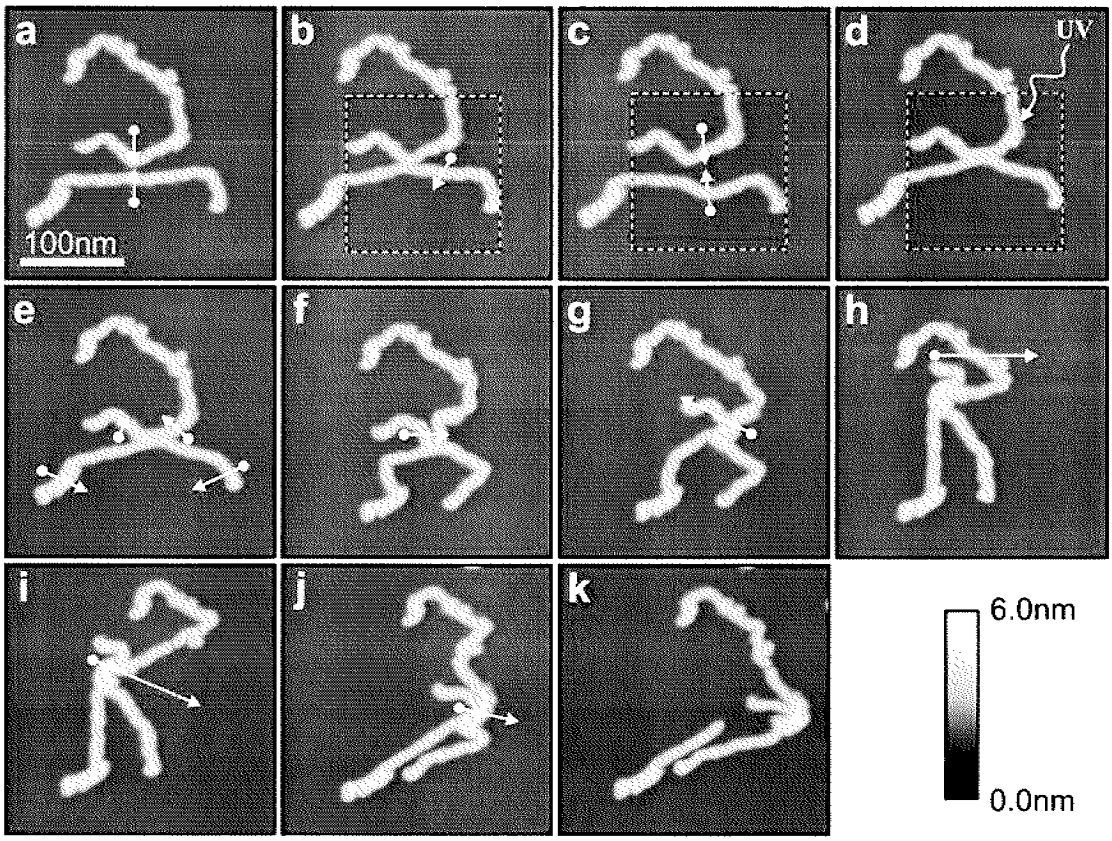



**Figure 34**. Move-connect-prove sequence of **71c** adsorbed onto a monolayer of $C_{12}H_{25}NH_2$ on HOPG. a) Initial conformation as shown in Figure 30b; b) a junction between the two strands is formed and c) opened; d) dendronized polymers are moved back again and illuminated *in-situ* with UV light (254 nm) for 5 min; e)-k) challenging the link mechanically up to strand rupture close to the junction. In images b)-d), local topography was refreshed only inside the dashed square to speed up the manipulation process. The white arrows indicate the tip movement during contact-mode SFM manipulation.

Similar results were obtained for monolayers of $C_{23}H_{47}COOH$, indicating that there is some flexibility in the choice of the organic precoating. This finding opened the possibility, for instance, to co-adsorb these neutral dendronized polymers with either anionic or cationic polyelectrolytes (which require oppositely charged surfaces for their adsorption) in order to form heterojunctions with different macromolecules including biopolymers, DNA, etc. One example is shown in Figure 35. Dendronized polymer **71c** was co-adsorbed with DNA on HOPG surface precoated with a monolayer of $C_{23}H_{47}COOH$ and then, a move-connect-sequence was demonstrated. The preparation of these different macromolecules was achieved by first preparing a monolayer of $C_{23}H_{47}COOH$ on the HOPG surface. Dendronized polymer **71c** dissolved in organic solvent ($CHCl_3$) was then spin coated onto the HOPG surface precoated with $C_{23}H_{47}COOH$. After drying the surface, DNA dissolved in water was

also spin coated onto the surface without influencing the polymer **71c**. The same move-connect-prove sequence as described above was demonstrated here. Dendronized polymer chains and DNA molecules were brought into tight contact. UV irradiation led to a heterojunction between dendronized polymer **71c** and DNA. Another example of the "heterojunction kind" was accomplished between dendronized polymer **71c** and a step-edge of HOPG. The idea is outlined in Figure 36, whereas the real move-connect-prove sequence is demonstrated in Figure 37. A strand of dendronized polymer **71c** was brought into tight contact with the step-edge of HOPG. A step-edge of HOPG usually results from an imperfect cleavage of a basal HOPG layer (Figure 36). This cleavage leads into introduction of different atoms and functional groups, such as, hydroxy, carboxylic acid group, etc. into the step-edge of HOPG at ambient conditions. Upon irradiation with UV, the site where the strand of polymer **71c** and the step-edge of HOPG were in tight contact led to the formation of a covalent connection. However, no covalent connection was observed with the basal HOPG surface which is stable and saturated.

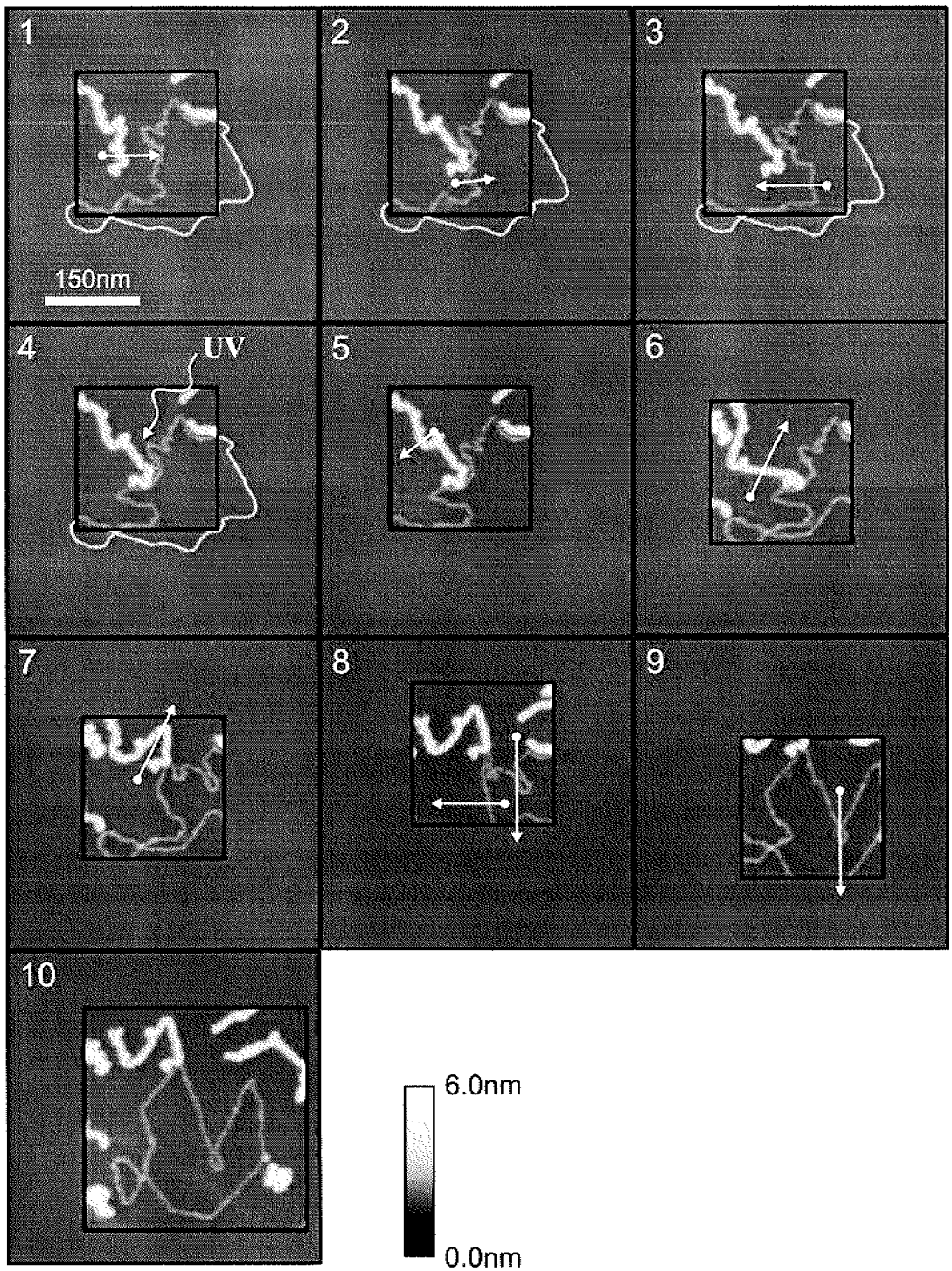



**Figure 35**. Move-connect-prove sequence of **71c** and DNA co-adsorbed onto a monolayer of $C_{23}H_{47}COOH$ on HOPG. 1) Initial conformation of both **71c** and DNA; 2) **71c** was brought into tight contact with DNA; 3) **71c** was separated from DNA to proof there is no junction; 4) DNA and **71c** was moved back again into tight contact and then illuminated *in-situ* with UV light (254 nm) for 5 min; 5)-10) challenging the link by moving the strands away from each other. The white arrows indicate the tip movement during contact-mode SFM manipulation.

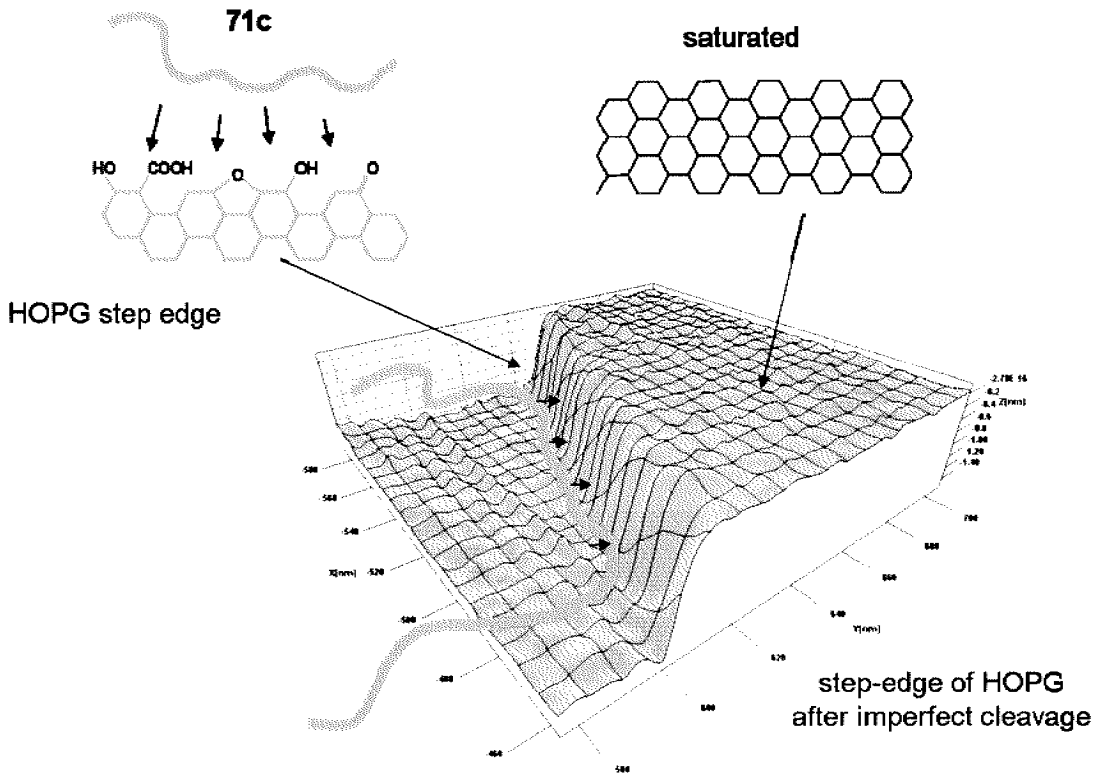



**Figure 36**. A schematic illustration of a strand of dendronized polymer **71c** and step-edge of HOPG.

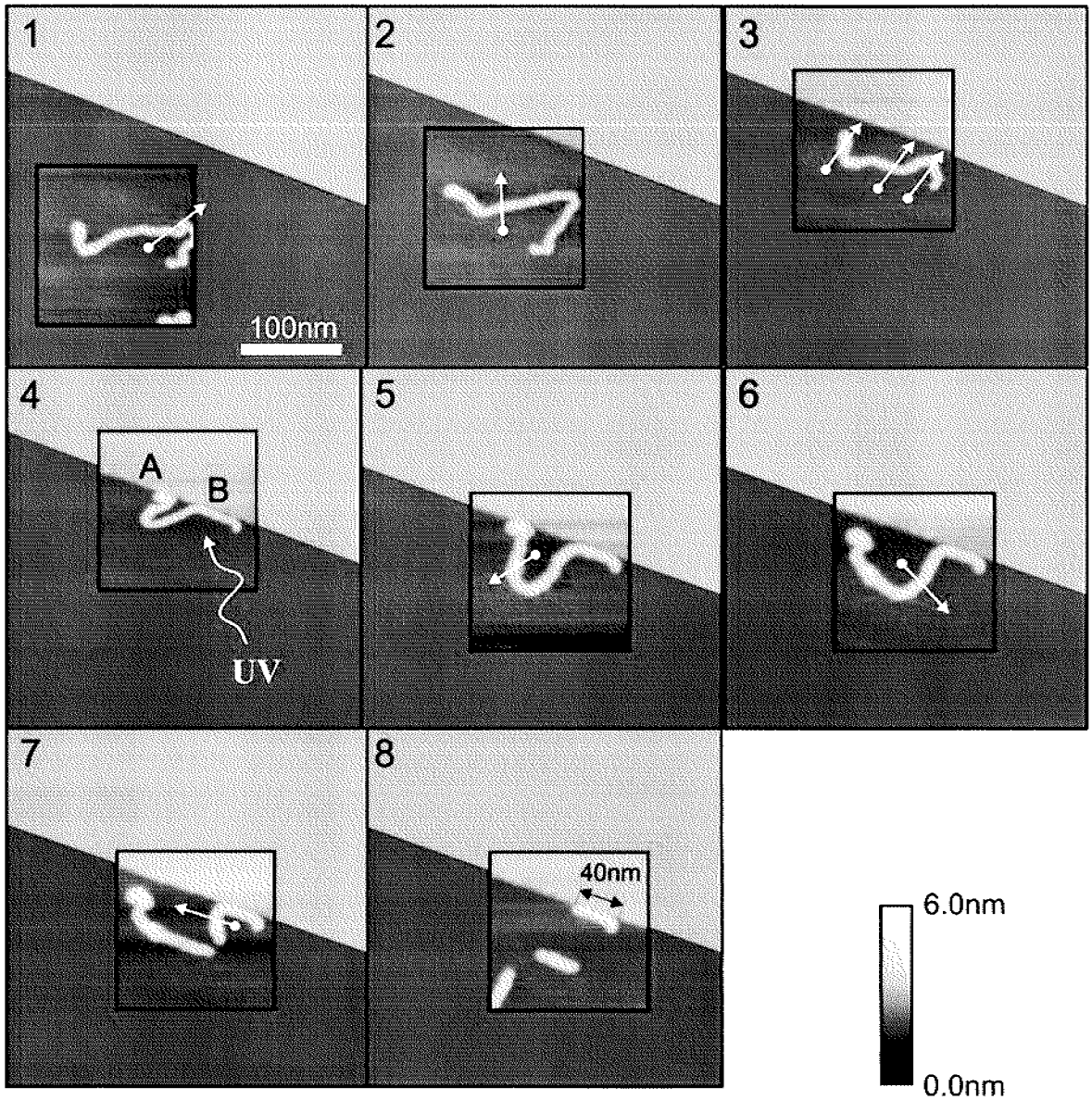



**Figure 37**. Move-connect-prove sequence of **71c** and a step-edge of HOPG. 1) Initial conformation of both **71c** and a step-edge of HOPG; 2)-3) **71c** was brought into tight contact with a step-edge of HOPG; 4) **71c** and the step-edge of HOPG was exposed *in-situ* to UV light (254 nm) for 5 min; 5)-8) challenging the link mechanically up to strand rupture close to the junction with the step-edge of HOPG . The white arrows indicate the tip movement during contact-mode SFM manipulation.

## 3.4 Quantification of Structure Perfection of Third Generation Dendronized Polymers Prepared by the Attach-to-route

Parts of this work have been published in: Helvetica Chimica Acta **2006**, *89*, 2745-2763

As mentioned in paragraph 1.2, dendronized polymers have so far been prepared either by polymerization of macromonomers, which already carried the dendron of the desired generation and peripheral substitution (macromonomer route), or by systematic attachment of G1 or G2 dendrons to an already existing polymer both by the convergent or divergent route (attach-to route). The representatives prepared by the later have the intrinsic disadvantage that their structure will have defects due to an incomplete coverage of the starting polymer with dendrons. Though this coverage could be driven to values above 99%, it still has to be quantified in each case, which is a rather tedious procedure. Up to the present, UV and fluorescence spectroscopy were used for this purpose after appropriate labeling as shown in literature[16] and in paragragh **3.3.2**. Each of these methods has its intrinsic limitations and uncertainties and involves a considerable amount of effort. It was therefore of interest to have a method available that is independent and perhaps easier to perform.

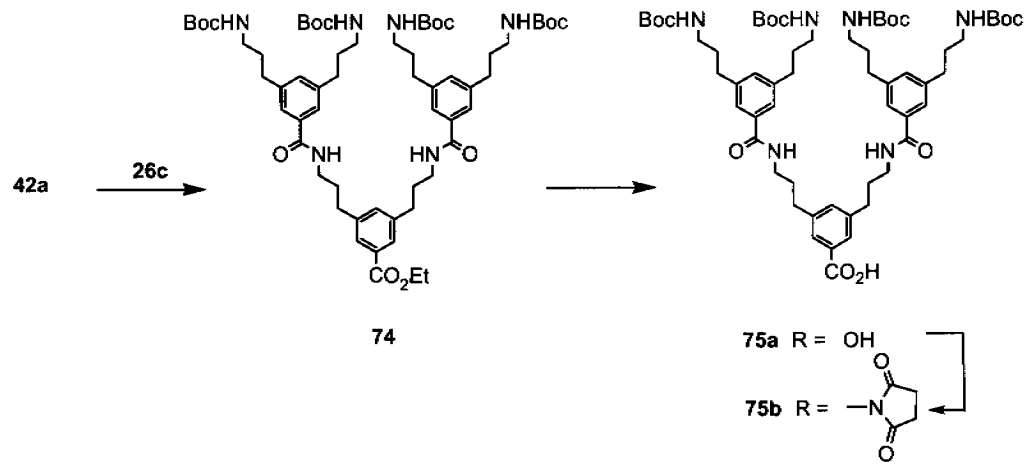
The idea was to prepare a third generation dendronized polymer by using the attach-to route and then to cleave the dendron completely right at the linkage point between dendron and polymer backbone. This would then enable to investigate the structural perfection of the dendrons by high field NMR spectroscopy, a technique which cannot be reasonably applied for such a purpose to G3 dendronized polymers above 1 million molar mass.

In most of the dendronized polymers prepared in Schlüter's group, the dendrons are attached to the polymer backbone through benzylic ester linkages. These linkages were found to be quite sensitive to hydrogenolysis conditions, a commonly used protocol for the removal of the Cbz protecting group. Submission of these dendronized polymers to hydrogenolysis conditions led to the cleavage of the dendrons right at the benzylic position (de-dendronization). This incident was then used for the purpose described here. A G3 dendronized polymer was first prepared by using the attach-to-route. G2 dendrons carrying succinimidyl active ester groups at the focal point were bound to the two amine anchor groups presented per repeat

unit of a G1 dendronized polymers. The reaction was found to be very efficient. The obtained G3 dendronized polymer was then submitted to hydrogenolysis which led to the cleavage of the G3 dendrons from the polymer backbone. The G3 dendrons were then investigated by high resolution NMR spectroscopy to see if there were still free amines in the dendron structure. The investigation was based on the analysis of the $^1$H-NMR chemical shifts of the methylene groups $\alpha$ to the amines. If the dendronization did not lead to a complete coverage of the terminal amines of the G1 dendronized polymer with the G2 dendrons, the product obtained would then contain some unreacted amines next to reacted (amidated) ones. Given the shift difference between the respective $\alpha$ -methylene groups, this was then used to quantify the degree of coverage by NMR integration. Quantification of course is not possible as long as one deals with the entire dendronized polymer. NMR signals are too broad to even consider such a method. The NMR investigation on the cleaved dendrons was then carried out and with a reasonable amount of effort the quantification could also be accomplished. It was found that almost all amine groups have reacted with the second generation dendron. The synthesis and results are discussed in detail in the following.

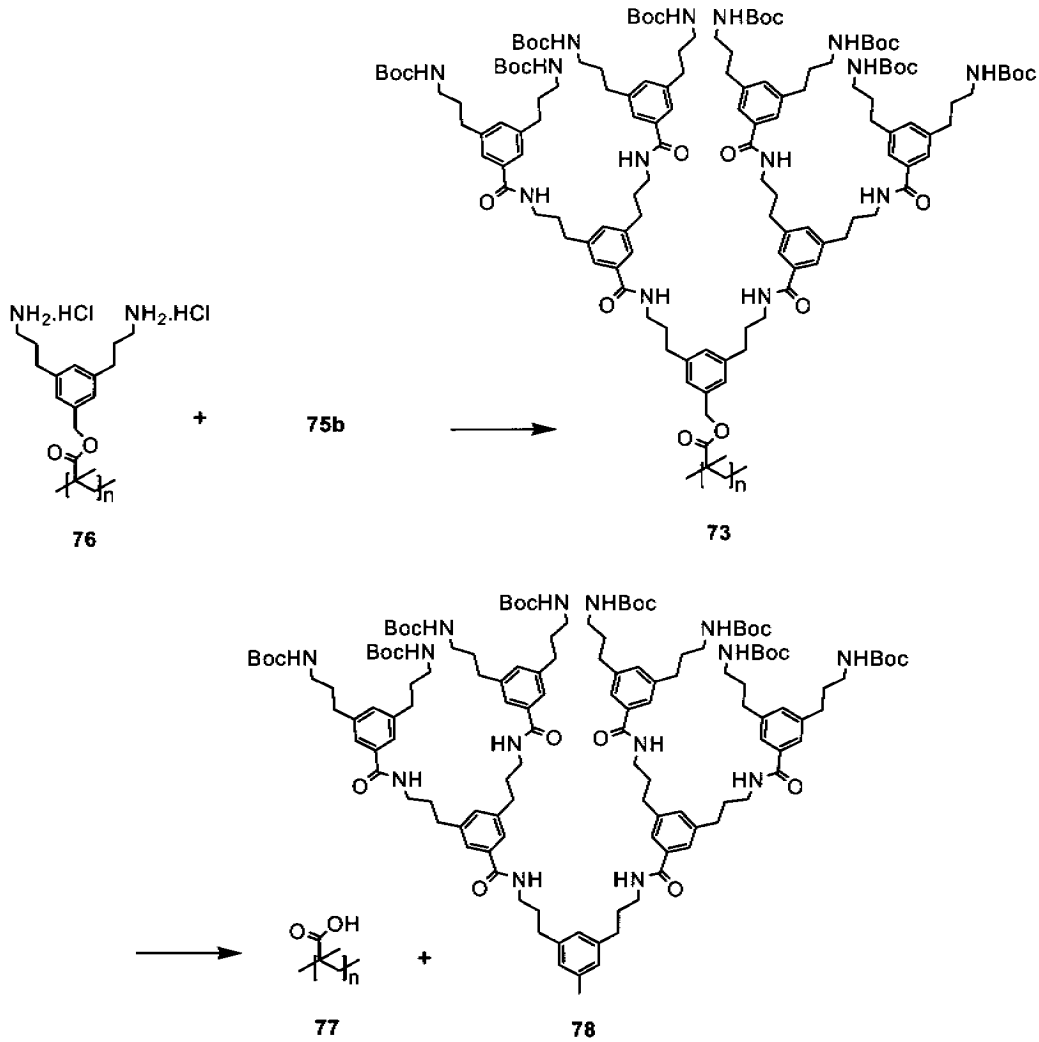
### 3.4.1 Synthesis of a third generation dendronized polymer using the attach-to-route

Schemes 23 and 24 delineate all the synthetic sequences to obtain the target G3 dendronized polymer **73** by the attach-to-route. Scheme 23 describes the synthesis of the G2 succinimidyl ester dendron carrying four Boc amino protecting groups **75b,** which is an important precursor to obtain the target G3 polymer. The starting materials were the dendrons **42a** and **26c**, which had already been synthesized before (Scheme 13 and Scheme 7, respectively). The amide coupling of the free amino groups of dendron **42a** with the carboxylic acid group of dendron **26c** was achieved using the HOBt/EDC system and gave G2 dendron **74** in a yield of 82%. The ester function of dendron **74** was then saponified to give the acid dendron **75a**. By using the HOSu/DCC system, the carboxyl group of dendron **75a** was then converted into the succinimdyl active ester G2 dendron **75b**. This dendron was then isolated on the 10 g scale and was stored under cooled conditions for further reactions.




**Scheme 23**. Synthesis of G2-succinimidyl ester dendron **75b** carrying 4 Boc peripheral amino protecting groups.

The G2 active ester dendron **75b** was then coupled to the free amino groups of the G1 dendronized polymer **76** (Scheme 24).[96] Polymer **76** was first dissolved in methanol which contained 6-8 equivalents of triethylamine per ammonium group of **76**. A solution of 1.75 equivalents of dendron **75b** per amine in MeOH and methylene chloride (1:2) was then added dropwise. After stirring for two days, the solvent of the still homogenous solution was removed in vacuum. The polymeric residue was then taken up in dimethyl formamide (DMF) with some triethylamine and a solution of 0.25 equivalents of dendron **75b** in DMF was added. The mixture was stirred for another 12 hours, and after conventional work-up, polymer **73** was obtained. Subjecting polymer **73** to hydrogenolysis conditions led only to partial de-dendronization. Under certain conditions (10 % formic acid for 4 days at 20 °C), the de-dendronization could however be driven to completion furnishing polymethacrylic acid **77** and the corresponding dendron **78**. The latter carries a methyl group at the focal point, which is indicative for the cleavage process actually being hydrogenolytic and not solvolytic in nature.




**Scheme 24**. Synthesis of G3 dendronized polymethacrylate **73**, and its corresponding dendron **78** which resulted from hydrogenolysis.

### 3.4.2 Quantification of structure perfection

Investigation of the resulting dendron **78** was mainly based on the analysis of the $^1$H-NMR chemical shifts of the methylene groups α to amines or amides. The shifts were large enough to be used here for quantification. If the dendronization of the dendronized polymer **73** does not lead to a complete coverage of the terminal amino groups of polymer **76** with dendron **75b**, the product **73** then should contain some unreacted amines next to the reacted (amidated) ones. The NMR investigation could not be done on dendronized polymer **73** because the NMR signals were too broad. However, the complete de-dendronization of dendronized polymer **73** enabled us to do the NMR investigation on dendron **78** with a reasonable amount of effort, and the quantification could therefore be acomplished. For this purpose, the model

compounds **80b,** and **81** were prepared (Scheme 25). They served as reference points for the relevant α-methylene chemical shifts. The de-dendronization of **73** was performed as described above. When driven to completion it furnished dendron **78** in yields of 80 and 85% (run 1 and 2, respectively) after the raw product had been passed once through a short silica gel column in order to remove impurities. During this simple step, extra care was taken to ensure that any eventually existing incomplete dendron with free amines would not be removed (for details, see the experimental part). For the NMR analysis the spectra of compounds **80b**, **81** and the two samples of **78** which stemmed from independent preparations (runs 1 and 2) were compared (Figure 38).

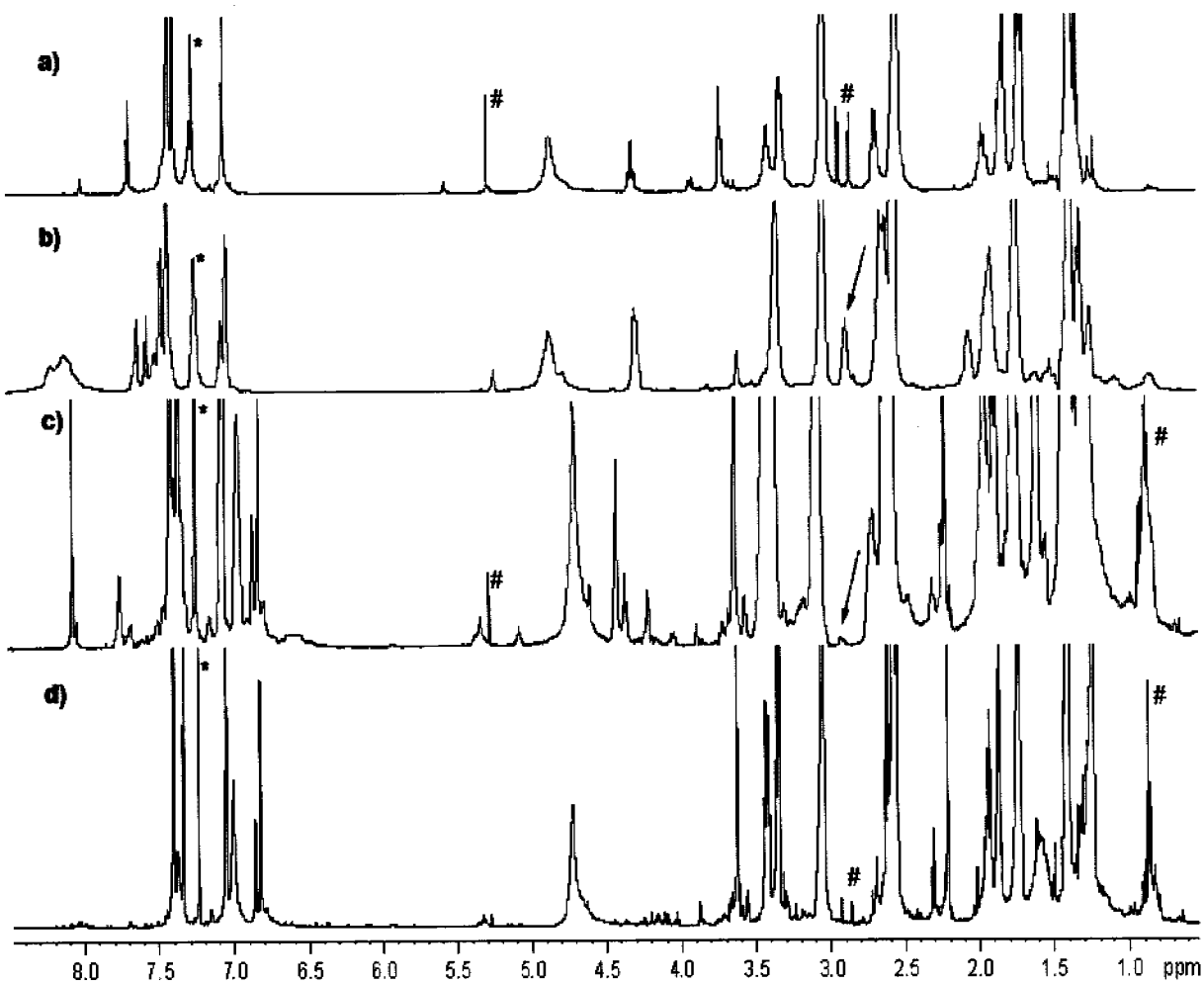
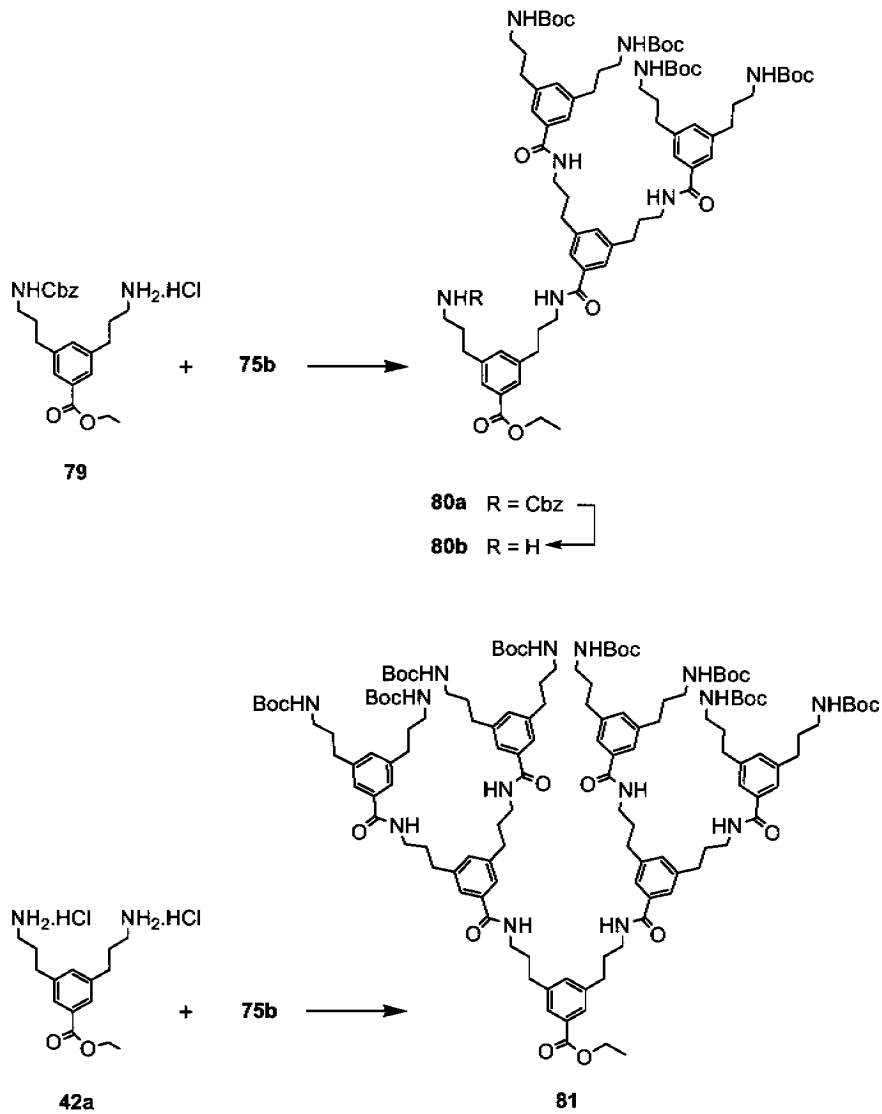



**Figure 38**: $^1$H NMR spectra of model compounds **81** (a), **80b** (b) and raw dendron **78** obtained from two independent experiments [run 1: (c); run 2: (d)]. All spectra were run in $CDCl_3$ which is marked (*). Solvent signals (DMF, $CH_2Cl_2$, grease) are marked (#).

The critical signal is the one of **80b** at $\delta$ = 2.85 ppm which represents the protons of a methylene $\alpha$ to a free amino group. It is marked with an arrow (Figure 38b). This signal does, of course, not appear for model compound **81** (Figure 38a). The spectrum of dendron **78** (run 1) shows a very low intensity signal in the relevant shift range whose intensity was estimated by integration to be 1.5% assuming that it represents two protons (Figure 38c). Given the fact that the samples of **78** used for the study had not been carefully purified it was not clear at this point whether this small signal actually stemmed from an $\alpha$-methylene group. Figure 38d shows the spectrum of dendron **78** (run 2). Virtually nothing was to be seen in the shift range $\delta$ = 2.70-2.90 ppm and the integration was therefore not performed. It was clear from these experiments that one deals with a level of structure perfection which was at or even below the limit of what NMR spectroscopy could provide. Defects amounting to a few percent would certainly be detected. This finding was in good agreement with the other quantification experiments described earlier which underlines that the attach-to route can be a powerful and reliable tool for the synthesis of structurally defined, high molar mass and high generation dendronized polymers.

### 3.4.3 Synthesis of models compound 79b and 80

Scheme 25 describes the synthesis of the model compounds **80b** and **81** which were needed for the NMR investigation of the dendron **78**. The removal of the Boc group of dendron **28a**, which was previously described (Scheme 7), gave dendron **79** which carries only one free amino group at the periphery. The amide coupling of the free amino group of dendron **79** with the active ester dendon **75b** furnished dendron **80a**. Removal of the Cbz group of **80a** by hydrogenolysis gave then dendron **80b**. On the other side, the model compound **81** was obtained by reacting the free amino groups of the dendron **42a**, which was described before (Scheme 13), with the active ester dendron **75b**.




**Scheme 25**. Synthesis of the model compounds **80b** and **81**

Apart from the issue of structure perfection, the observed de-dendronization of **73** opened another interesting possibility which was the determination of the backbone's tacticity. It was still an open question whether there was a preorientation of dendronized monomers prior to their polymerization to dendronized polymers.[105] An eventual occurrence of isotactic or syndiotactic backbones may be caused by such phenomena, though a non-occurrence of tacticity, of course, does not mean that there is no preorientation. The $^{1}$H NMR spectrum of the polymethacrylic acid **77** obtained by de-dendronization of **73** by comparison with literature spectra of highly *iso*-, *syndio*-, and *atactic* polymethacrylic acids (not shown)[106-108] has shown that polymer **77** was mainly atactic with some isotactic units.

# 4. Overview

In the present thesis a set of first (G1) and second generation (G2) orthogonally protected dendrons was first synthesized. The dendrons carry Boc and Cbz protected amino groups in varying ratios. On the G1 level three different dendrons were obtained, **29a**, **30a**, and **30b** carrying 1Boc and 1Cbz, 2Boc, and 2Cbz peripheral amino protecting groups, respectively. On the G2 level five different dendrons were accomplished, **32a**, **32d**, **33a**, **33d**, and **33f**, carrying 3Boc and 1Cbz, 1Boc and 3Cbz, 2Boc and 2Cbz, 4Boc, and 4Cbz groups, respectively. Selective removal of the above protecting groups for all dendrons leaving the other untouched was also achieved.

A set of high molar mass first (G1) and second generation (G2) orthogonally protected, methacrylate-based dendronized polymers was synthesized using the macromonomer route. The polymers carry a predetermined number of Boc and Fmoc* protected peripheral amino groups at each repeat unit. On the G1 level, the polymers **45a** carrying 1Boc and 1Fmoc*, and **48a** carrying 2Fmoc* were obtained. And on the G2 level, the polymers **51a**, **56a**, and **61a**, carrying 2Boc and 2Fmoc*, 3Boc and 1Fmoc*, and 1Boc and 3Fmoc* groups, respectively were obtained. The selective removal of these protecting groups on the polymer level, where easily hundreds of them were present per macromolecule, was proven.

The synthesis of a neutral, high-molar-mass, acrylamide-based, third generation dendronized polymer, **71c** with a defined number of azide groups at its periphery was described. An attach-to-route was used in which a first generation (G1) dendronized polymer, **70b** was reacted with a second generation (G2) dendron, **67b**. The degree of structure perfection of the resulting dendronized polymer, **71a** was quantified as 99.8 %. This value was obtained after the introduction of a fluorescence label (dansyl chloride) at the sites that remained unaffected by the dendronization.

The third generation dendronized polymer, **71c**, was spin-coated onto a highly oriented graphite that was precoated with an ultrathin layer of $C_{12}H_{25}NH_2$, which was introduced to provide a well-defined substrate for dendronized polymer adsorption and manipulation. Scanning force microscopy revealed single dendronized polymers, which could be moved across the surface and welded by covalent cross-linking induced by photochemical decomposition of the azides into highly reactive nitrenes.

The successful formation of covalent bonds between two dendronized polymers was confirmed mechanically challenging the link with scanning force microscopy. More SFM experiments were carried out with dendronized polymer **71c** to form heterojunction bonds. An experiment of this kind was carried out between dendronized polymer **71c** and DNA single strands after they have been co-adsorbed onto the same substrate. Another experiment was carried out also between dendronized polymer **71c** and the step-edge of HOPG to form a heterojunction linkage.

Finally, a method was developed for the quantification of structure perfection of dendronized polymers synthesized according to the attach-to-route. An acrylate-based G3 dendronized polymer, **73**, was first prepared by reacting the first generation acrylate based dendronized polymer, **76**, with the second generation dendron, **75b**. The resulted polymer **73** was then submitted to hydrogenolysis which led to the cleavage of the G3 dendron **78** right at the linkage point to the polymer backbone (de-dendronization). NMR investigation on the cleaved dendron **78** showed that almost all the amino groups of the G1 polymer **76** have reacted with the G2 dendron **75b**.

# 5. Outlook

The set of orthogonally protected dendronized polymers described in this thesis opens the way to a systematic exploration of "surface" modifications for this class of polymers and their possible impact properties. These polymers under certain conditions can be represented as macromolecular objects with cylindrical shape and selectively addressable chemical functionalities as shown in Figure 39. Therefore, the pesent work can be considered as a rational property engineering of complex nanocylinders. Such an endeavor will not only reach far into material sciences but also into the "bio world". Compounds derived like the ones described in section 3.3 and their corresponding SFM experiments may also have a considerable future impact in regard to single molecule chemistry at interfaces which may turn to be useful for the bottom-up approach to the nanosciences.

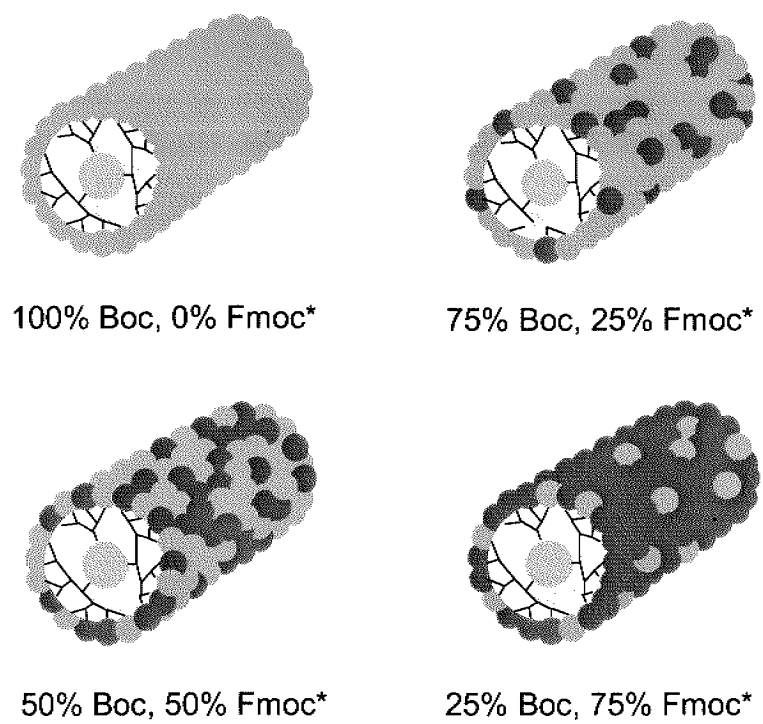



**Figure 39.** Schematic representation of dendronized polymers with selectively addressable chemical functionalities on the surface.

# 6. Experimental part

## 6.1 General

All reagents were purchased from Aldrich, Across or Fluka and used without further purification. Methacryloyl chloride (MAC) was freshly distilled before use. Tetrahydrofuran (THF) and triethylamine ($Et_3N$) were refluxed over Na with benzophenone as indicator, dichloromethane ($CH_2Cl_2$) was dried by distilling over $CaH_2$. The catalyst $Pd(PPh_3)_4$ was synthesized according to literature, stored in a glove box, and used without further characterization. All other reagents and solvents were used as received. All reactions with moisture sensitive reagents were performed under nitrogen atmosphere.

### 6.1.1 Chromatographic Methods

***Analytical TLC:***

Reactions were monitored by thin layer chromatography (TLC) using TLC silica coated aluminium $60F_{254}$ (Merck). Compounds were detected by UV light (254 nm or 366 nm) and/or by treatment with a solution of ninhydrine in ethanol (0.1 %) followed by heating.

***Column Chromatography:***

Column chromatography was run with Silica gel 60 M (Macherey-Nagel, 0.04-0.063 mm/ 230-400 mesh). Usually the crude product was pre-adsorbed onto small amounts of silica gel and thereafter purified by chromatography

***Analytical GPC***

Gel permeation chromatography (GPC) measurements were carried out using PL-GPC 220 instrument with 2x PL-Gel Mix-B LS column set (2 x 30 cm) equipped with RI (refractive index), viscosity and LS (Light Scattering with 15° and 90° angle) detectors [DMF + 1 $gL^{-1}$ LiBr as eluent at 80°C]. Universal calibration was done using PMMA standards in a range of $M_p$ = 2,680 to 3,900,000 (Polymer Labs. Ltd, UK).

### 6.1.2 Analysis

***NMR spectroscopy:***

$^{1}H$ and $^{13}C$ NMR spectra were recorded on Bruker AM 300 ($^{1}H$: 300 MHz, $^{13}C$: 75 MHz), AV 500 ($^{1}H$: 500 MHz, $^{13}C$: 125 MHz), and AV 700 ($^{1}H$: 700 MHz) spectrometers at room temperature (if not otherwise stated) using chloroform-d or methanol-$d^4$ as a solvent. The $^{13}C$ NMR spectra of polymers **71b** and **71c** were not recorded because too long accumulation times would have required in order to getting spectra with sufficient signal-to-noise ratios.

***Mass spectrometry***

Electrospray mass spectrometry (ESI-MS) analyses were performed by the MS-service of the Laboratorium für Organische Chemie, ETH Zürich, on an IonSpec Ultra instrument. High resolution MALDI spectra were run on an IonSpec Ultra instrument.

***Elementel Analysis***

Elemental analyses were performed by the Mikrolabor of the Laboratorium für Organische Chemie, ETH Zürich. The samples were dried rigorously under vacuum prior to analysis to remove strongly adhering solvent molecules.

***Fluorescence Measurements:***

The fluorescence measurements were performed in chloroform at room temperature using a Spex Fluorolog 2, Jobin Yvon (U.K.) with 1cm quartz cells. The intensity of the fluorescence bands was determined by measuring their area. A line shape analysis was not performed.

***SFM Measurements:***

For SFM imaging and lateral manipulation, a home-built SFM based on the Multimode head and Nanoscope III controller of Digital Instruments Inc., (Santa Barbara, CA, USA) was used. Olympus etched cantilevers (OMCL-AC240) with a nominal normal spring constant of 2N/m and a tip radius below 10nm were used. Images were taken by SFM operating in tapping mode.

UV illumination was carried out with a standard spectral Ne-Hg lamb (Pen-Ray 11SC-1, UVP Inc. Upland, CA, USA) with a maximum emission at a wavelength of 254nm.

## 6.2 Syntheses

Compounds **25**,[109] **26(a-d)**,[96,98] **28b**,[78] **30(a-c)**,[14] **42a**,[14] **79**,[110] were prepared according to literature procedures, and gave satisfactory NMR, MS, and elemental analysis data. Polymers **62**,[14] **63**,[14] were already published but in the course of this work were prepared with different molar masses. Compounds **74**,[96] **75a**,[96] **75b**,[96] **76**,[96] were prepared using the same procedure as in the literature.

### 6.2.1 Compounds of Chapter 3.2

**General procedure for monomer synthesis (Procedure A)**

MAC (1.5 eq.) in $CH_2Cl_2$ was added dropwise to a solution of the respective dendron with alcohol focal point , DIEA (2 eq.) and DMAP (catalytic amount) in $CH_2Cl_2$ at 0 °C. The resulting mixture was stirred overnight at r.t. After washing with $NaHCO_3$ and brine, the solvent was removed at r t. and the monomer was purified with column chromatography.

**General procedure for polymerization (Procedure B)**

Into a Schlenk tube was added the monomer and solvent. The mixture was stirred until it turned homogeneous (few minutes). The concentration of the monomer was kept around 75 % (w/w). The mixture was immediately degassed by several freeze-pump-thaw cycles, and then kept at 70 °C for a predetermined time. After polymerization, the polymer was dissolved in $CH_2Cl_2$ and purified by column chromatography (silica gel, $CH_2Cl_2$ as eluent).

**General procedure for Boc deprotection of polymers (Procedure C)**

25 % HCl (8 eq. per amine group) in THF was added dropwise to a solution of the respective polymer in THF at 0°C. The resulting mixture was stirred at r.t. overnight. The solvent was evaporated and the polymer was dried in high vacuum.

**General Procedure for Fmoc* deprotection of polymers (Procedure D)**

25 % Aqueous piperidine (20 eq. per amine group) in DMF was added dropwise to a solution of the respective polymer in DMF at 0°C. The resulting mixture was stirred at r.t. for 48 h. It was then washed with hexane, and the free amine was protonated by

adding 0.1 N HCl. After evaporation of the solvent, the polymer was dissolved in MeOH and precipitated in diethylether.

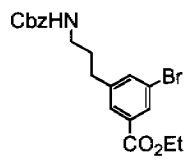
**General procedure for deprotection of the Boc-group of the orthogonally protected second generation dendrons (Procedure E)**

A solution of the G2-dendron in THF was cooled to 0 °C in an ice bath. 25% HCl (4 equiv. per Boc-group) in THF was added dropwise, and the reaction mixture stirred at 0 °C for 1 h and at r.t. for another 2 h. Then, the reaction mixture was evaporated to dryness and vacuum dried at r.t. affording the deprotected dendrons in quantitative yield.

**General procedure for deprotection of Cbz-group of the orthogonally protected second generation dendrons (Procedure F)**

G2-dendron was first dissolved in a mixture of THF/ AcOEt /ethanol (1/1/1). 1,4 cyclohexadiene or 5% formic acid and palladium on charcoal were added, and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. over night. The product was filtered through celite and the solvent was evaporated at r.t. to yield the deprotected dendrons.

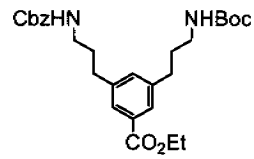
**Ethyl-3-bromo-5-[3-(benzyloxycarbonylamino)propyl]benzoate (27)**




A solution of benzyl propyl-2-enylcarbamate (12.50 g, 65.4 mmol) in dry toluene (150 mL) in a dry schlenk flask under $N_2$ was degassed (3x), and at 0 °C, 9-BBN (8.65 g, 71.5 mmol) was added. The mixture was stirred for 12 h at r.t. The resulting mixture was then transferred to a three necked flask containing 1M KOH (100 mL), **25** (20.00 g, 65.3 mmol) and toluene (50 mL). The solution was again degassed (3x), and then tetrakis(triphenylphosphine) palladium (0) (2.00 g, 1.7 mmol) was added. It was stirred at 60 °C for 48 h under $N_2$. The organic phase was separated from aqueous phase, washed with brine (100 mL), $NaHCO_3$ (100 mL), and dried with $MgSO_4$. Chromatographic separation (silica gel, hexane/AcOEt v/v 15/1 then 8/1), followed by flash chromatography using $CH_2Cl_2$ yielded 16.78 g as a slightly yellow colored oil (66%). $^1$H NMR ($CDCl_3$): δ 1.33 (t, 3 H, $CH_3$), 1.75 (m, 2 H, $CH_2$), 2.60 (t, 2 H, $ArCH_2$), 3.09 (m, 2 H, $NHCH_2$), 4.30 (q, 2 H, $CH_2O$), 4.69 (s, br, 1 H, NH), 5.02 (s, 2 H, $OCH_2Ar$), 7. 31 (m, 5 H, ArH), 7.44 (s, 1 H, ArH), 7.72 (s, 1 H, ArH), 7.92 (s, 1 H,

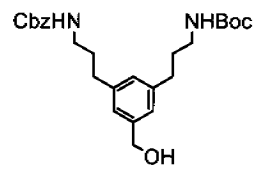
ArH). $^{13}C$ NMR ($CDCl_3$): δ 14.23, 31.32, 32.49, 40.03, 61.24, 66.69, 122.35, 128.09, 128.47, 130.19, 132.43, 135.53, 143.89, 156.39, 165.27. EI-MS. 419 $[M]^+$. Anal. calc. for $C_{20}H_{22}BrNO_4$ (418.8): C, 57.15, H, 5.25, N, 3.33. Found: C 57.30, H 5.27, N 3.23.

**Ethyl-3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzoate (28a)**




Into a Schlenk flask, (*N-tert*-butoxycarbonyl) allylamine (8.20 g, 52.3 mmol), and dry toluene (150 mL) under nitrogen were added. The solution was degassed (3x), and at 0 °C, 9-BBN (7.00 g, 57.0 mmol) was added. The mixture was stirred for 12 h at r.t. The solution was then transferred to a three necked flask containing 1M KOH (100 mL), **27** (16.70 g, 39.8 mmol) and toluene (50 mL). The mixture was degassed (3x), and then tetrakis(triphenylphosphine) palladium (0) (1.50 g, 1.3 mmol) was added. Then it was stirred at 100 °C for 14 h under $N_2$. The organic phase was separated from aqueous phase, washed with brine (100 mL), $NaHCO_3$ (100 mL), and dried with $MgSO_4$. Chromatographic separation (silica gel, hexane/AcOEt v/v 8/1 then 3/1) yielded 18.63 g as slightly yellow colored oil (86%). $^1H$ NMR ($CDCl_3$): δ 1,35 (t, 3 H, $CH_3$), 1.44 (s, 9 H, $CCH_3$), 1.78 (m, 4 H, $CH_2$), 2.60 (m, 4 H, $ArCH_2$), 3.09 (2q, 4 H, $NHCH_2$), 4.34 (q, 2 H, $CH_2O$), 4.63 (s, br, 1 H, NH), 4.85 (s, br, 1 H, NH), 5.02 (s, 2 H, $OCH_2Ar$), 7.12 (s, 1 H, ArH), 7.31 (m, 5 H, ArH), 7.62 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 14.23, 28.32, 31.31, 31.47, 32.61, 32.67, 40.24, 60.89, 66.59, 79.08, 127.07, 127.13, 127.99, 128.42, 130.71, 133.09, 141.76, 141.95, 156.39, 156.79, 165.27. FABMS (3kV): m/z (%): 521(5.15) $[M+Na]^+$. Anal. calc. for $C_{28}H_{38}N_2O_6$ (498.61): C, 67.45, H, 7.68, N, 5.62. Found: C 67.32, H 7.48, N 5.25.

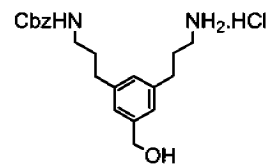
**3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzyl alcohol (29a)**




A solution of **28a** (2.00 g, 4.0 mmol) in abs.THF (30 mL) was added dropwise to a suspension of $LiAlH_4$ (0.36 g, 9.6 mmol) in THF (10 mL) over a period of 30 min under $N_2$ at 0 °C. The mixture was stirred for 8 h below 10 °C and the reaction was quenched by adding acidified water (4 ml, pH = 5). The resulting precipitate was filtered, washed with AcOEt (3x 60 mL), and the solvent was removed in vacuo. Chromatographic

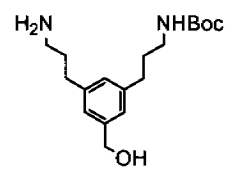
separation (silica gel, AcOEt/hexane: v/v: 1/1) yielded **29a** (1.48 g) as a colorless viscous oil (81%). $^1$H NMR ($CDCl_3$): δ 1.43 (s, 9 H, $CCH_3$), 1.79 (m, 4 H, $CH_2$), 2.45 (t, 4 H, $CH_2Ph$), 3.10 (q, 2 H, $CH_2NH$), 3.20 (q, 2 H, $CH_2NH$), 4.49 (s, 2 H, $OCH_2$), 4.85 (s, br, 2 H, NH), 4.95 (s, 2 H, $OCH_2Ph$), 6.91 (s, 1 H, ArH), 6.99 (s, 2 H, ArH), 7.31 (m, 5 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.19, 31.08, 31.25, 32.54, 32.59, 39.66, 40.12, 64.36, 66.27, 78.85, 124.38, 126.60, 126.99, 127,25, 127.77, 128.10, 128.21, 136.41, 141.39, 141.53, 155.92, 156.38. ESI-MS: 479.3 $[M+Na]^+$. Anal. calc. for $C_{28}H_{38}N_2O_6$ (456.26): C, 68.40, H, 7.95, N, 6.14. Found: C 68.11, H 7.92, N 6.17.

**3-(3-amino-propyl)-5-[3-(benzyloxycarbonylamino)-propyl]benzyl alcohol.HCl (29b)**




A solution of 25% HCl (1.37 mL, 4 equiv) in THF (3 mL) was added slowly to a solution of **29a** (1.20 g, 2.6 mmol) in THF (25 mL) under nitrogen at 0°C. The reaction was monitored with TLC. After the reaction is finished (~3h), the solvent was evaporated at r.t. to yield **29b** as viscous oil (0.97 g, 94%). The product was used for next step without further purification procedures.

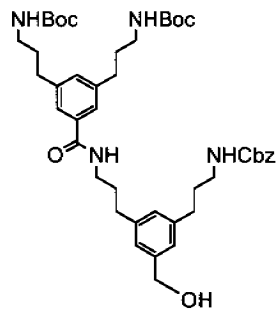
**3-(3-amino-propyl)-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzyl alcohol (29c)**




Into a hydrogenation flask, **29a** (1.00 g, 2.2 mmol) in AcOEt/ethanol (20 mL, 1/1), Pd on charcoal (100 mg, 10% by weight) and 1,4 cyclohexadiene (1.74 g, 22.0 mmol) were added. The mixture was hydrogenated under 3 bar of $H_2$ at r.t. for 4 h. The solution was then filtered through celite and the solvent was evaporated at r.t. to yield **29c** as viscous oil (0.7 g, 92%). The product was used for next step without further purification procedures.

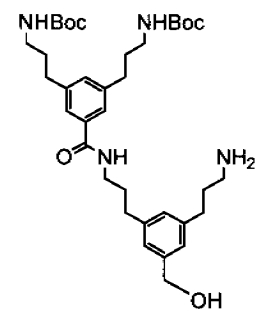
**3-[3-(benzyloxycarbonylamino)-propyl]-5-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]benzoylamino}benzyl alcohol (31a)**

To a solution of the acid dendron **26c** (1.10 g, 2.5 mmol) in $CH_2Cl_2$ (30 mL) were added N-hydroxybenzotriazol (0.39 g, 2.7 mmol) at r.t. After 10 min at -30 °C, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.50 g, 2.6 mmol) was added. The mixture was stirred for 3 h. Then a solution of **29b** (0.82 g, 2.1 mmol) and $Et_3N$ (1.45 mL, 10.4 mmol) in a mixed solvent of $MeOH/CH_2Cl_2$ (15 mL, 1/1) was




added dropwise at -20 °C. The resulting mixture was warmed to r.t. and stirred for 14 h. It was then washed with brine and aqueous $NaHCO_3$. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. Chromatographic separation (silica gel, AcOEt/ hexane, v/v, 2/1 then 3/1) yielded **31a** (2.65, 84%) as a colorless foam. $^1$H NMR ($CDCl_3$): δ 1,45 (s, 9 H, $CCH_3$), 1.66 (m, 6 H, $CH_2$), 1.80 (m, 2 H, $CH_2$), 2.44 (m, 8 H, $CH_2Ph$), 2.97 (m, 6 H, $CH_2NH$), 3.30 (q, 2 H, $CH_2NH$), 4.45 (s, 2 H, $OCH_2$), 4.74 (s, br, 1 H, NH), 4.96 (s, 4 H, $OCH_2Ph$), 5.28 (s, br, 2 H, NH), 6.77 (s, 1 H, ArH), 6.84 (s, 1 H, ArH), 6.88 (s, 2 H, ArH), 6.97 (s, 1 H, ArH), 7.19 (m, 10 H, ArH), 7.27 (s, 1 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.06, 30.55, 30.95, 31.18, 32.45, 32.92, 39.38, 40.18, 64.24, 65.99, 78.60, 124.21, 124.49, 126.98, 127.50, 127.55, 128.03, 131.15, 134.44, 136.37, 141.26, 141.34, 141.41, 141.47, 155.92, 156.34, 167.60. ESI-MS: 797 $[M+Na]^+$. Anal. calc. for $C_{44}H_{62}N_4O_8$ (775.00): C, 68.19, H, 8.06, N, 7.23. Found: C 67.92, H 8.23, N 7.12.

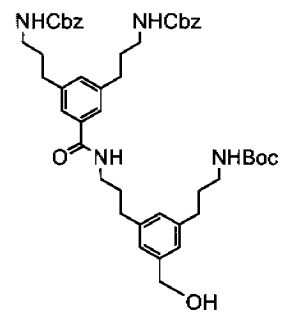
**3-[(3-amino)-propyl]-5-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]benzoylamino} benzyl alcohol (31b)**




According to Procedure F: Into a hydrogenation flask, **31a** (2.15 g, 2.8 mmol) in THF/AcOEt/ethanol (1/1/1, 30 mL), Pd on charcoal (0.22 g, 10% by weight) and 1,4 cyclohexadiene (0.4 mL, 10 equiv.) were added. The mixture was hydrogenated under 3 bar of $H_2$ at r.t. The hydrogenation was controlled with TLC until the reaction was finished (~5 h). The product was filtered and washed with AcOEt (50 mL). Evaporation of the solvent at r.t. yielded **31b** (1.77 g, 99%) as a viscous oil. The product was used for next step without further purification procedures.

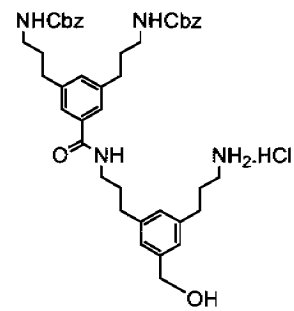
**3-{3,5-bis-[3-(benzyloxycarbonylamino)-propyl]benzoylamino}-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzyl alcohol (31c)**

Into a schlenk flask containing **26d** (1.13 g, 2.2 mmol) and N-hydroxybenzotriazol (0.36 g, 2.4 mmol) in $CH_2Cl_2$ (60 mL) was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.47 g, 2.5 mmol) at -30 °C under $N_2$. The mixture was stirred till the hydrochloride dissolved. Then a solution of **29c** (0.58 g, 1.8 mmol) and $Et_3N$ (0.75 mL, 5.4 mmol) in a mixed solvent of $MeOH/CH_2Cl_2$ (15 mL, 1/1) was



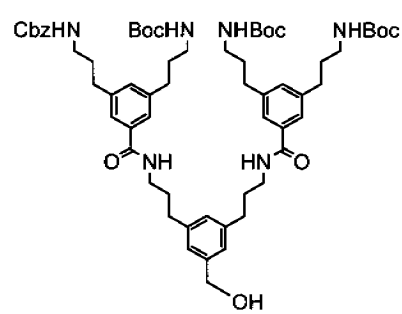

added dropwise at -20°C. The mixture was warmed to r.t. and stirred for 14 h, then washed with aqueous $NaHCO_3$ (50 mL) and brine (50 mL), and dried with $MgSO_4$. Chromatographic separation (silica gel, AcOEt / hexane, v/v, 3/1) yielded **31c** (1.01 g, 69%) as a colorless foam. $^1$H NMR ($CDCl_3$): δ 1,44 (s, 18 H, $CCH_3$), 1.76 (m, 6 H, $CH_2$), 1.92 (m, 2 H, $CH_2$), 2.57 (m, 8 H, $CH_2Ph$), 3.13 (m, 6 H, $CH_2NH$), 3.40 (q, 2 H, $CH_2NH$), 4.58 (s, 2 H, $OCH_2$), 5.2 (s, br, 1 H, NH), 5.06 (s, 2 H, $OCH_2Ph$), 5.29 (s, br, 2 H, NH), 6.89 (s, 1 H, ArH), 6.97 (s, 1 H, ArH), 7.01 (s, 1 H, ArH), 7.07 (s, 1 H, ArH), 7.32 (m, 5 H, ArH), 7.39 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.10, 30.54, 30.76, 31.21, 32.12, 32.57, 32.99, 39.50, 39.80, 64.33, 66.13, 78.66, 124.24, 124.57, 127.04, 127.57, 127.66, 128.11, 131.23, 134.48, 136.30, 141.32, 141.45, 155.90, 156.44, 167.68. ESI-MS 831 $[M]^+$. Anal. calc. for $C_{47}H_{60}N_4O_8$ (809.01): C, 69.78, H, 7.48, N, 6.93. Found: C 69.63, H 7.68, N 6.94.

**3-{3,5-bis-[3-(benzyloxycarbonylamino)-propyl]benzoylamino}-5-(3-amino)-propyl]benzyl alcohol (31d)**




According to Procedure E: To a solution of **31c** (1.20 g, 2.6 mmol) in THF (25 mL) was slowly added a solution of 25% HCl (1.37 mL, 4 equiv.) in THF (3 ml) under nitrogen at 0 °C. The reaction was stirred for 3 h. The solvent was evaporated at r.t. to yield **31d** as viscous oil (1.00 g, 96%). The product was used for next step without further purification procedures.

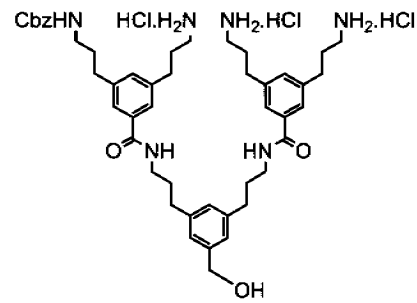
**3-(3-{3-[3-(benzyloxycarbonylamino)-propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl alcohol (32a)**




To a solution of acid dendron **28b** (1.50 g, 3.2 mmol) and N-hydroxybenzotriazol (0.53 g, 3.9 mmol) in $CH_2Cl_2$ (80 mL) was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.7 g, 3.66 mmol) at -20 °C under $N_2$. The reaction mixture was stirred until the hydrochloride was dissolved completely (~3 h). To this solution were added **31b** (1.77 g, 2.7 mmol) and $Et_3N$ (1.4 mL) in $CH_2Cl_2$/MeOH (30 mL, 1/1) at -20 °C. The reaction mixture was stirred for 15 h at r.t. It was then

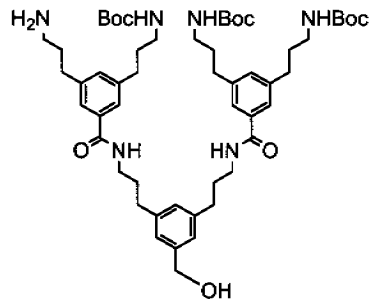
washed with aqueous $NaHCO_3$ (70 mL) and brine (70 mL). The organic phase was dried with $MgSO_4$ and the solvent was evaporated. Chromatographic separation (silica gel, AcOEt/ hexane, 3/1) yielded **32a** (2.4 g, 80%) as a colorless foam. $t_g$= 35.10 °C. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1,43 (s, 27 H, $CCH_3$), 1.71 (m, 8 H, $CH_2$), 1.86 (m, 4 H, $CH_2$), 2.55 (m, 12 H, $CH_2Ph$), 3.06 (q, 6 H, $CH_2NH$), 3.23 (q, 2 H, $CH_2NH$), 3.34 (q, 4 H, $CH_2NH$), 4.50 (s, 2 H, $OCH_2$), 4.85 (s, br, 2 H, NH), 4.99 (s, 2 H, $OCH_2Ph$), 6.90 (s, 1 H, ArH), 6.96 (s, 2 H, ArH), 7.02 (s, 2 H, ArH), 7.27 (m, 5 H, ArH), 7.29 (s, 2 H, Ar), 7.30 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 28.41, 30.77, 31.36, 32.50, 33.29, 39.62, 65.00, 66.59, 78.67, 124.75, 127,66, 128.04, 128.46, 131.48, 134.57, 141.34, 141.41, 141.96, 156.13, 156.35, 167.73. FABMS (3kV): m/z (%): 1115(100) $[M+Na]^+$. Anal. calc. for $C_{62}H_{88}N_6O_{11}$ (1093.41): C, 68.11, H, 8.11, N, 7.69. Found: C 67.92, H 8.25, N 7.51.

**3-(3-{3-[3-(benzyloxycarbonylamino)-propyl]-5-[3-aminopropyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-aminopropyl]-benzoyl}-amino)-propyl-benzyl alcohol. 3HCl (32b)**



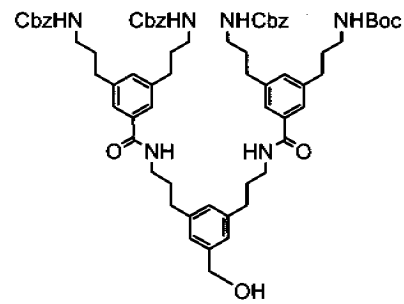

According to Procedure E: **32a** (0.23 g, 0.21 mmol) in THF (10 ml) was cooled to 0 °C in an ice bath. 25% HCl (0.50 mL, 18 equiv.) in THF (6 mL) was added dropwise, and the reaction mixture was stirred at 0 °C for 1 h and at r.t. for another 4 h. Then, the solvent was evaporated at r.t. affording the deprotected dendrons **32b** (0.18 g, 93%) as colorless viscous oil. $^1$H NMR ($CD_3OD$, 500 MHz): δ 1.78 (m, 2 H, $CH_2$), 1.92 (m, 4 H, $CH_2$), 2.01 (m, 6 H, $CH_2$), 2.62 (m, 4 H, $CH_2Ph$), 2.66 (m, 8 H, $CH_2Ph$), 3.08 (t, 2 H, $CH_2NH$), 3.33 (m, 10 H, $CH_2NH$), 4.52 (s, 2 H, $OCH_2$), 5.02 (s, 2 H, $OCH_2Ph$), 6.93 (s, 1 H, ArH), 6.96 (s, 2 H, ArH), 7.18 (s, 2 H, ArH), 7.25 (m, 5 H, ArH), 7.43 (s, 2 H, Ar), 7.48 (s, 2 H, ArH). $^{13}$C NMR ($CD_3OD$, 500 MHz): δ 30.05, 32.20, 33.26, 34.32, 40.29, 40.85, 66.85, 67.33, 126.33, 126.71, 127,80, 128.64, 129.46, 139.02, 142.65, 143.05, 156.35, 170.09.

**3-(3-{3-[3-aminopropyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl alcohol (32c)**




According to Procedure F: **32a** (0.17 g, 0.2 mmol) was dissolved in a mixture of THF/AcOEt/ethanol (20 mL, 2/1/1). 1,4 cyclohexadiene (0.06 mL, 0.6 mmol), and Pd/C (20 mg, 10% by weight) were added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. over night. The product was filtered through celite and the solvent was evaporated at r.t to yield **32c** (0.14 g, 94%) as a slightly pale solid. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1,39 (s, 27 H, $CCH_3$), 1.82 (m, 8 H, $CH_2$), 1.90 (m, 4 H, $CH_2$), 2.52 (m, 8 H, $CH_2Ph$), 2.59 (t, 4 H, $CH_2Ph$), 2.88 (t, 2 H, $CH_2NH$), 3.02 (q, 6 H, $CH_2NH$), 3.29 (q, 4 H, $CH_2NH$), 4.50 (s, 2 H, $OCH_2$), 6.88 (s, 1 H, ArH), 6.93 (s, 1 H, ArH), 6.96 (s, 1 H, ArH), 7.02 (s, 2 H, ArH), 7.31 (s, 4 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.30, 30.63, 31.47, 32.47, 33.03, 39.49, 65.75, 78.67, 124.66 124.76, 127,66, 128.04, 128.46, 131.48, 134.57, 141.34, 141.41, 141.96, 156.35, 167.73.

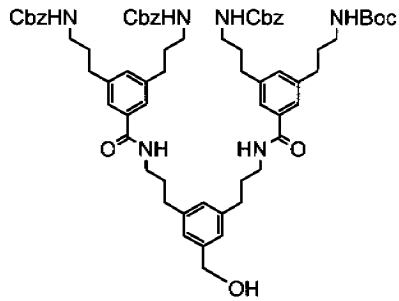
**3-{3-{3-[3-(butyloxycarbonylamino)-propyl]-5-[3-(benzyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(benzyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl alcohol (32d)**




To a solution of the acid dendron **28b** (0.72 g, 1.7 mmol) and N-hydroxybenzotriazol (0.22 g, 1.7 mmol) in $CH_2Cl_2$ (30 mL) was added -20 °C under $N_2$, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.33 g, 1.73 mL). The mixture was stirred for 3 h. Then a solution of **31d** (0.85 g, 1.3 mmol) and $Et_3N$ (0.93 mL, 6.7 mmol) in a mixed solvent of $MeOH/CH_2Cl_2$ (15 ml, 1/1) were added dropwise at -20 °C. The resulting mixture was warmed up to r.t. and stirred for 14 h. It was then washed with brine (50 mL) and aqueous $NaHCO_3$ (50 mlL). The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH v/v, 4/1) yielded **32d** (0.91 g, 69%) as a colorless foam. $t_g$= 33.10 °C. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1,44 (s, 9 H, $CCH_3$), 1.75 (m, 8 H, $CH_2$), 1.88 (m, 4 H, $CH_2$), 2.55 (m, 12 H, $CH_2Ph$), 3.00 (t, 2 H, $CH_2NH$), 3.10 (q, 6 H, $CH_2NH$), 3.34 (t, 4 H, $CH_2NH$), 4.51 (s, 2 H, $OCH_2$), 5.01 (s, 6 H, $OCH_2Ph$), 6.91 (s, 1 H, ArH), 6.97 (s, 2 H, ArH), 7.03 (s, 1 H, ArH), 7.27

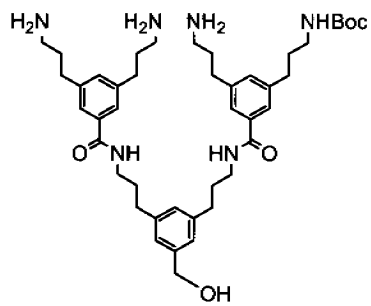
(m, 20 H, ArH). $^{13}C$ NMR ($CDCl_3$, 500 MHz): δ 28.39, 30.64, 31.09, 31.29, 32.44, 33.21, 39.64, 40.14, 64.89, 66.60, 78.60, 124.82, 127.60, 127.93, 128,02, 128.45, 131.53, 134.77, 136.57, 141.50, 141.71, 141.87, 155.92, 156.62, 167.90. FABMS (3kV): m/z (%): 1183(65.15) $[M+Na]^+$. Anal. calc. for $C_{68}H_{84}N_6O_{11}$ (1161.45): C, 70.32, H, 7.29, N, 7.24. Found: C 70.52, H 7.05, N 6.96.

**3-(3-{3-[3-aminopropyl]-5-[3-(benzyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(benzyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl alcohol. HCl (32e):**




**32d** (0.18 g, 0.16 mmol) in THF (10 mL) was cooled to 0°C in an ice bath. 25% HCl (0.12 mL, 6 equiv.) in THF (4 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and at r.t. for 3 h. The solvent was evaporated at r.t. affording the deprotected dendron **32e** (0.16 g, 98%) as colorless solid. $^1H$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 1.70 (m, 8 H, $CH_2$), 1.86 (m, 4 H, $CH_2$), 2.53 (m, 10 H, $CH_2Ph$), 2.75 (t, 2 H, $CH_2NH$), 3.03 (q, 6 H, $CH_2NH$), 3.27 (t, 4 H, $CH_2NH$), 4.51 (s, 2 H, $OCH_2$), 4.96 (s, 6 H, $OCH_2Ph$), 6.86 (s, 1 H, ArH), 6.90 (s, 2 H, ArH), 6.99 (s, 1 H, ArH), 7.27 (m, 20 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 30.64, 31.19, 31.29, 32.47, 33.21, 39.64, 40.14, 66.60, 78.60, 124.82, 127.60, 127.93, 128,02, 128.45, 131.53, 134.77, 136.57, 141.50, 141.71, 141.87, 156.92, 167.90.

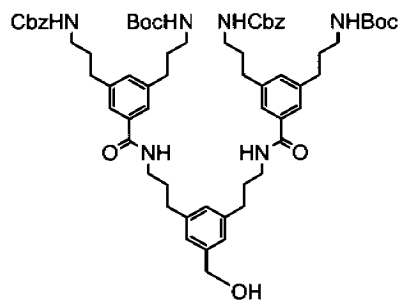
**3-(3-{3-[3-(butyloxycarbonylamino)-propyl]-5-[3-aminopropyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-aminopropyl]-benzoyl}-amino)-propyl-benzyl alcohol (32f)**




According to Procedure F: **32d** (0.20 g, 0.2 mmol) was dissolved in a mixture of THF/ AcOEt /ethanol (15 mL, 1/1/1). 1,4 cyclohexadiene (0.40 g, 5.2 mmol), and Pd/C (50 mg, 10% by weight) were added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. over night. The product was filtered through celite and the solvent was evaporated at r.t. NMR showed that there are still some Cbz-protecting groups. Therefore, the product was

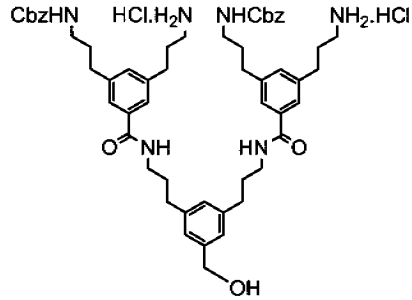
treated for another night with same procedure to yield the product **32f** (0.10 g, 85%) as slightly yellow viscous oil. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 1,44 (s, 9 H, $CCH_3$), 1.78 (m, 2 H, $CH_2$), 1.82 (m, 6 H, $CH_2$), 1.92 (m, 4 H, $CH_2$), 2.68 (m, 8 H, $CH_2Ph$), 2.72 (m, 10 H, $CH_2Ph$, $CH_2NH$), 3.04 (t, 2 H, $CH_2NH$), 3.34 (t, 4 H, $CH_2NH$), 4.51 (s, 2 H, $OCH_2$), 6.95 (s, 1 H, ArH), 6.97 (s, 2 H, ArH), 7.23 (s, 1 H, ArH), 7.26 (s, 1 H, ArH), 7.40 (s, 1 H, ArH), 7.42 (s, 3 H, ArH). $^{13}$C NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 28.39, 31.09, 31.29, 33.90, 34.31, 39.95, 41.78, 65.23, 79.50, 125.77, 125.91, 128.56, 132.77, 132.83, 142.89, 143.21, 143.68, 156.62, 170.30.

**3,5-bis-(3-{3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoylamino}-propyl)-benzyl alcohol (33a)**



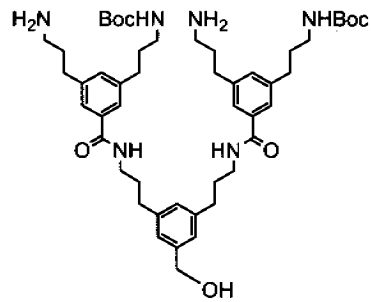

To a solution of acid dendron **28b** (1.20 g, 2.6 mmol) and N-hydroxybenzotriazol (0.35 g, 2.6 mmol) in $CH_2Cl_2$ (30 mL) was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.53 g, 2.8 mmol) at -20 °C under $N_2$. The reaction mixture was stirred until the hydrochloride was dissolved completely (~ 3 h). To this solution was then added **30c** (0.30 g, 1.0 mmol) and $Et_3N$ (0.8 mL) in MeOH (10 mL) at -20°C. The reaction mixture was stirred for 15 h at r.t. It was then washed with aqueous $NaHCO_3$ (40 mL) and brine (40 mL). The organic phase was dried with $MgSO_4$ and the solvent was evaporated. Chromatographic separation (silica gel, AcOEt/ hexane, v/v, 4/1) yielded **33a** (0.98 g, 86%) as a colorless foam. $t_g$= 43.90 °C. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1,43 (s, 18 H, $CCH_3$), 1.71 (m, 8 H, $CH_2$), 1.88 (m, 4 H, $CH_2$), 2.58 (t, 8 H, $CH_2Ph$), 2.69 (t, 4 H, $CH_2Ph$), 3.06 (q, 4 H, $CH_2NH$), 3.23 (q, 4 H, $CH_2NH$), 3.34 (q, 4 H, $CH_2NH$), 4.52 (s, 2 H, $OCH_2$), 4.85 (br, 1 H, NH), 5.01 (s, 4 H, $OCH_2Ph$), 5.12 (s, br, 2 H, NH), 6.85 (s, br, 2 H, NH), 6.90 (s, 1 H, ArH), 6.98 (s, 2 H, ArH), 7.04 (s, 2 H, ArH), 7.27 (m, 14 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 28.15, 30.55, 30.85, 31.03, 32.23, 32.95, 36.19, 39.45, 39.92, 64.38, 66.17, 78.76, 124.35, 124.62, 127.09, 127.62, 127,70, 128.16, 130.51, 131.27, 134.52, 136.40, 141.49, 141.58, 156.02, 156.49, 167.74. FABMS (3kV): m/z (%): 1149(100) $[M+Na]^+$. Anal. calc. for $C_{65}H_{86}N_6O_{11}$ (1127.43): C, 69.25, H, 7.69, N, 7.45. Found: C 69,03, H 7.87, N 7.52.

**3,5-bis-(3-{3-[3-(benzyloxycarbonylamino)propyl]-5-[3-aminopropyl]-benzoylamino}-propyl)-benzyl alcohol. 2HCl (33b)**



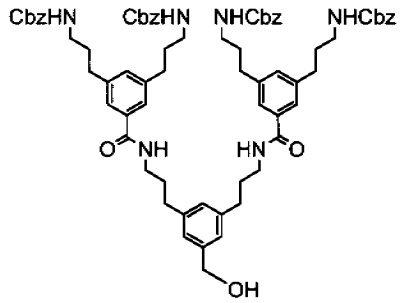

According to Procedure E: **33a** (0.40 g, 0.4 mmol) in THF (15 mL) was cooled to 0 °C in an ice bath. Then, 25% HCl (0.5 mL, 11 equiv.) in THF (5 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 1 hr and at r.t. for another 3 h. The solvent was evaporated at r.t. affording the deprotected dendron **33b** (0.34 g, 97%) as viscous oil. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 1.77 (m, 4 H, $CH_2$), 1.90 (m, 4 H, $CH_2$), 1.98 (m, 4 H, $CH_2$), 2.61 (m, 12 H, $CH_2Ph$), 2.82 (q, 4 H, $CH_2NH$), 3.08 (q, 4 H, $CH_2NH$, 3.34 (q, 4 H, $CH_2NH$), 4.52 (s, 2 H, $OCH_2$), 502 (s, 4 H, $OCH_2Ph$), 6.93 (s, 1 H, ArH), 6.98 (s, 2 H, ArH), 7.09 (s, 2 H, ArH), 7.27 (m, 10 H, ArH), 7.39 (s, 2 H, ArH), 7.42 (s, 2 H, ArH).$^{13}$C NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 30.09, 31.53, 32.60, 38.54, 39.17, 65.84, 78.76, 124.14, 124.79, 127.02, 127.35, 127,82, 128.16, 130.51, 131.27, 134.52, 136.40, 141.33, 141.76, 156.80, 168.21.

**3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]benzoylamino}-5-[3-aminopropyl]benzyl alcohol (33c)**



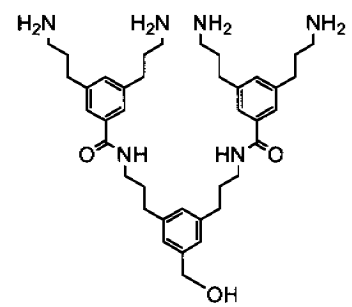

According to Procedure F:**33a** (0.40 g, 0.3 mmol) was dissolved in a mixture of THF/AcOEt/ethanol (21 mL, 1/1/1). 1,4,cyclohexadiene (0.68 mL, 7.01 mmol), and Pd/C (40 mg, 10% by weight) were added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. over night. The product was filtered through celite and the solvent was evaporated at r.t to yield **33c** (0.29 g, 95%) as a pale solid. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1,43 (s, 18 H, $CCH_3$), 1.73 (m, 8 H, $CH_2$), 1.88 (m, 4 H, $CH_2$), 2.60 (m, 12 H, $CH_2Ph$), 2.69 (t, 4 H, $CH_2Ph$), 3.03 (q, 4 H, $CH_2NH$), 3.23 (q, 4 H, $CH_2NH$), 4.52 (s, 2 H, $OCH_2$), 6.93 (s, 1 H, ArH), 7.00 (s, 2 H, ArH), 7.04 (s, 2 H, ArH), 7.29 (s, 2 H, ArH) , 7.46 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.11, 30.46, 31.03, 32.27, 32.54, 32.93, 39.36, 40.45, 64.01, 78.86, 124.28, 124.48, 127.00, 131.14, 134.51, 141.48, 141.81, 156.02, 167.70.

**3,5-(Bis-{3-[3,5-bis[3-(benzyloxycarbonylamino)propyl]-benzoylamino}-propyl)-benzyl alcohol (33f):**




To a solution of the acid dendron **26d** (1.64 g, 3.3 mmol) in $CH_2Cl_2$ (30 mL) was added N-hydroxybenzotriazol (0.45 g, 3.3 mmol) at r.t. After 10 min at -30 °C, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.66 g, 3.4 mmol) was added. The mixture was stirred for 3 h. Then a solution of **30c** (0.4 g, 1.4 mmol) and $Et_3N$ (1.5 mL, 10.8 mmol) in MeOH (10 mL) was added dropwise at -20 °C. The resulting mixture was warmed up to r.t. and stirred for 14 h. It was then washed with brine (50 mL) and aqueous $NaHCO_3$ (50 mL). The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuum. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH, v/v, 20/1) yielded **33f** (1.17 g, 72%) as a white foam. $t_g$= 32.07 °C. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1.58 (m, 8 H, $CH_2$), 1.71 (m, 4 H, $CH_2$), 2.39 (m, 12 H, $CH_2Ph$), 2.90 (t, 8 H, $CH_2NH$), 3.18 (t, 4 H, $CH_2NH$), 4.40 (s, 2 H, $OCH_2$), 4.95 (s, 8 H, $OCH_2Ph$), 6.83 (s, 1 H, ArH), 6.91 (s, 2 H, ArH), 6.99 (s, 2 H, ArH), 7.22 (m, 20 H, ArH), 7.34 (s, 4 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 30.36, 30.74, 30.92, 32.19, 32.29, 32.87, 39.32, 39.47, 39.96, 64.17, 66.25, 78.60, 124.42, 124.49, 127.16, 127.50, 127.70, 128.14, 131.38, 132.00, 134.34, 136.31, 141.14, 141.55, 141.63, 156.82, 168.47. FABMS (3kV): m/z (%): 1217(100) $[M+Na]^+$. Anal. calc. for $C_{71}H_{82}N_6O_{11}$ (1217.25): C, 71.33, H, 6.91, N, 7.03. Found: C 71.07, H 7.16, N 7.30.

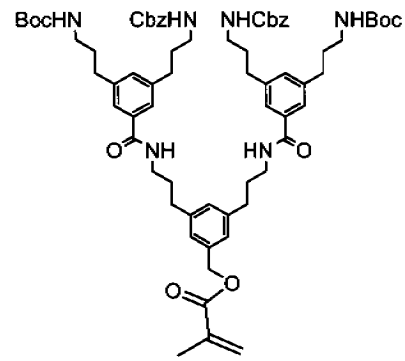
**3,5-(Bis-{3-[3,5-bis[3-aminopropyl]-benzoylamino}-propyl)-benzyl alcohol (33g)**




According to Procedure F: **33f** (0.31 g, 0.3 mmol) was dissolved in a mixture of THF/ AcOEt/ethanol (15 mL, 1/1/1). 5% formic acid (0.5 mL), and Pd/C (70 mg, 10% by weight) was added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. over 48 h. The product was filtered through celite and the solvent was evaporated at r.t. to yield the product **33g** (0.12 mg, 85%) as viscous brown oil. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 1.58 (m, 8 H, $CH_2$), 1.71 (m, 4 H, $CH_2$), 2.39 (m, 12 H, $CH_2Ph$), 2.90 (t, 8 H, $CH_2NH$), 3.18 (t, 4 H,

$CH_2NH$), 4.40 (s, 2 H, $OCH_2$), 4.95 (s, 8 H, $OCH_2Ph$), 6.83 (s, 1 H, ArH), 6.91 (s, 2 H, ArH), 6.99 (s, 2 H, ArH), 7.22 (m, 20 H, ArH), 7.34 (s, 4 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 29.29, 31.63, 31.71, 33.18, 33.39, 33.94, 40.44, 40.53, 78.60, 125.42, 125.76, 128.25, 132.34, 135.70, 142.20, 142.43, 142.73, 169.67.

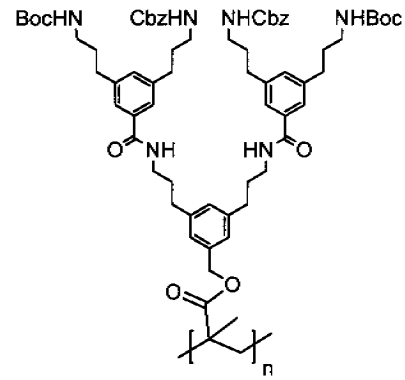
**3,5-bis-(3-{3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoylamino}-propyl)-benzyl methacrylate (34)**




According to procedure A: MAC (0.07 mL) in $CH_2Cl_2$ (5 mL) was added to a solution of compound **33a** (0.50 g, 0.45 mmol), $Et_3N$ (0.19 mL) and DMAP (10 mg) in THF (30 mL). Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 1/2) yielded **34** (0.46 g, 85 %) as white solid. $^1H$ NMR ($CDCl_3$, 500 MHz): δ 1,43 (s, 18 H, $CCH_3$), 1.71 (m, 8 H, $CH_2$), 1.88 (m, 4 H, $CH_2$), 2.02 (s, 3 H, $CH_3$), 2.58 (t, 8 H, $CH_2Ph$), 2.69 (t, 4 H, $CH_2Ph$), 3.06 (q, 4 H, $CH_2NH$), 3.23 (q, 4 H, $CH_2NH$), 3.34 (q, 4 H, $CH_2NH$), 4.52 (s, 2 H, $OCH_2$), 4.85 (br, 1 H, NH), 5.01 (s, 4 H, $OCH_2Ph$), 5.12 (s, br, 2 H, NH), 5.21 (s, 2 H, $CH_2O$), 5.61 (s, 1 H, $CH_2$=), 6.21 (s, 1 H, $CH_2$=), 6.85 (s, br, 2 H, NH), 6.90 (s, 1 H, ArH), 6.98 (s, 2 H, ArH), 7.04 (s, 2 H, ArH), 7.27 (m, 14 H, ArH). $^{13}C$ NMR ($CDCl_3$, 500 MHz): δ 28.15, 30.55, 30.85, 31.03, 32.23, 32.95, 36.19, 39.45, 39.92, 64.38, 66.17, 66.44, 67.02, 78.76, 124.35, 124.62, 127.09, 127.62, 127,70, 128.16, 130.51, 131.27, 134.52, 136.40, 141.49, 141.58, 156.02, 156.49, 167.74. FABMS (3kV): m/z (%): 1216(100) $[M+Na]^+$. Anal. calc. for $C_{65}H_{86}N_6O_{11}$ (1194.66): C, 69.32, H, 7.59, N, 7.03. Found: C 69,13, H 7.87, N 7.12.

**Poly[3,5-bis-(3-{3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxy carbonylamino)-propyl]-benzoylamino}-propyl)-benzyl methacrylate] (35)**

According to procedure B: monomer **34** (0.22 g), DMF (70 μL) were used. Chromatographic separation yielded **35** (0.14 g, 65 %) as a white solid. $^1H$ NMR ($CDCl_3$, 500 MHz): δ 0.83 (br, 3 H, $CH_3$), 1.31 (br, 18 H, $CCH_3$), 1.68 (br, 8 H, $CH_2$), 1.88 (br, 4 H, $CH_2$), 2.49 (br, 8 H, $CH_2Ph$), 2.69 (br, 4 H, $CH_2Ph$), 3.10 (br, 8 H, $CH_2NH$), 3.34 (br, 4 H, $CH_2NH$), 4.52 (br, 2 H, $OCH_2$), 4.85 (br, 2 H, NH), 5.01 (br, 4 H, $OCH_2Ph$), 6.85 ( br, 2 H, NH), 6.90 (br, 3 H, ArH), 7.04 (br, 2 H, ArH), 7.27 (br, 14

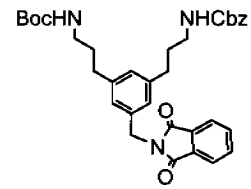



H, ArH). $^{13}C$ NMR ($CDCl_3$, 500 MHz): δ 28.49, 30.84, 31.39, 32.14, 34.66, 39.27, 40.53, 47.33, 66.66, 119.39, 122.16, 124.71, 125.16, 131.68, 134.84, 138.70, 142.24, 144.57, 149.98, 157.58, 168.70. Mn = 3.6 x $10^5$, Mw = 8.3 x $10^5$

**Synthesis of compounds 36a and 36b:**

**35** (0.31 g, 0.3 mmol) was dissolved in a mixture of THF/ AcOEt/ethanol (15 ml, 1/1/1). 5% formic acid (0.5 ml), and Pd/C (100 mg, 10% by weight) was added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. over 36 h. The product was filtered through celite and the solvent was evaporated at r.t. to yield the products **36a** and **36b**. $^1H$ NMR is shown in page 48 which is a mixture of two products.

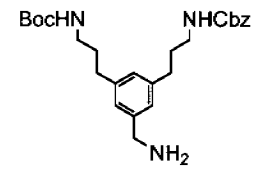
**3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzyl phthalimide (37)**




Mesyl chloride (0.44 mL, 1.25 equ.) in $CH_2Cl_2$ (5 mL) was added to a solution of **29a** (2.07 g, 4.50 mmol) and $Et_3N$ (1.00 mL) in $CH_2Cl_2$ (50 mL) at -30 °C. The mixture was stirred at -20 °C for 2 h and regularly checked by TLC (EtOAc/hexane, 1:1) until **29a** had disappeared. The reaction was then quenched with MeOH and the solution washed four times with cold water and brine. The organic phase was dried over $MgSO_4$, the solvent evaporated at r.t. and the product dried under vacuo. The residue was then dissolved in DMF (40 mL) and potassium phthalimide (1.10 g, 5.9 mmol) added at r.t. The mixture was stirred over night at 100 °C. DMF was then evaporated, the mixture dissolved in $CH_2Cl_2$ (50 mL), washed with 0.5 M NaOH, sat. brine, sat. $NaHCO_3$ and, finally, dried over $MgSO_4$. Chromatographic separation (silica gel, EtOAc/ hexane, 1:1) yielded **37** (2.35 g, 88 %) as a pale solid. $^1H$ NMR ($CDCl_3$): δ 1.44 (s, 9 H, $CH_3$), 1.81 (m, 4 H, $CH_2$), 2.58 (m, 4 H, $ArCH_2$), 3.18 (m, 4 H, $NHCH_2$), 4.66 (s, br, 1 H, NH), 4.79 (s, 2 H, $CH_2$), 5.00 (s, 1 H, NH), 5.11 (s, 2 H, $CH_2$), 6.92 (s, 1 H, ArH), 7.08 (s, 2 H, ArH), 7.36 (m, 5 H, ArH), 7.72 (m, 2 H, ArH), 7.85 (m, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.43, 31.64, 32.88, 40.13, 41.57, 66.72, 79.04, 94.71, 123.36, 126.38, 128.06, 132.14, 133.96, 136.54, 142.21, 156.00, 168.06. ESI-MS 608 $[M + Na]^+$. Anal.

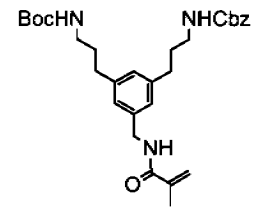
calc. for $C_{34}H_{39}N_3O_6$ (585.28): C, 69.72, H, 6.71, N, 7.17. Found: C 69.35, H 6.55, N 7.07.

**3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzyl amine (38):**




Hydrazine hydrate (0.65 mL, 3.2 equ.) was added to a solution of **37** (2.35 g, 4.1 mmol) in THF/EtOH (60 mL, 1/1). The mixture was stirred at 60 °C for 6 h. After the reaction was finished (TLC), the solvent was evaporated. The precipitate was then dissolved in $CH_2Cl_2$, washed with 0.5 M NaOH, and sat. brine. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH/$Et_3N$, 100:10:1) yielded **38** (1.62 g, 89 %) as a yellowish oil. $^1$H NMR ($CDCl_3$): δ 1.45 (s, 9 H, $CH_3$), 1.77 (m, 4 H, $CH_2$), 2.60 (t, 4 H, $ArCH_2$), 3.14 (m, 4 H, $NHCH_2$), 3.89 (s, 2 H, $CH_2NH$), 4.55 (s, br, 2 H, NH), 4.79 (s, 2 H, $CH_2$), 6.92 (s, 1 H, ArH), 6.98 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.44, 31.67, 31.89, 32.96, 40.13, 46.41, 65.62, 79.05, 124.83, 127.00, 141.96, 143.53, 156.00. ESI-MS 478 $[M + Na]^+$.

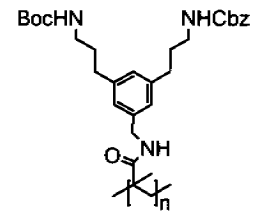
**3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzyl methacrylamide (39)**




Methacryloyl chloride (0.45 mL, 5.8 mmol) in $CH_2Cl_2$ (4 mL) was added dropwise to a solution of **38** (1.77 g, 3.9 mmol) and $Et_3N$ (2.2 mL) in $CH_2Cl_2$ (30 mL) at -30 °C. The mixture was stirred at -20 °C for 30 min and monitored by TLC (EtOAc/hexane, 1/1) until **39** had disappeared. The reaction was then quenched with MeOH. The solution was washed with sat. brine and sat. $NaHCO_3$. The organic phase was dried over $MgSO_4$ and the solvent evaporated at r.t. Chromatographic separation (silica gel, EtOAc/ hexane, 1:1) was done twice to yield **39** (1.9 g, 93 %) as a white solid. $^1$H NMR ($CDCl_3$): δ 1.44 (s, 9 H, $CH_3$), 1.84 (m, 4 H, $CH_2$), 2.01 (s, 3 H, $CH_2$), 2.62 (t, 4 H, $ArCH_2$), 3.14 (q, 4 H, $NHCH_2$), 4.45 (d, 2 H, NH), 4.69 (s, br, 2 H, NH), 5.35 (s, 1H, CH), 5.75 (s, 1H, CH), 6.26 (t, 1 H, NH), 6.93 (s, 1 H, ArH), 6.94 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 18.76, 28.43, 31.62, 31.60, 32.76, 32.85, 40.02, 40.47, 43.74, 66.60, 76.65, 79.09, 103.69, 119.67, 125.72, 125.76, 127.76, 128.50, 136.65, 138.45,

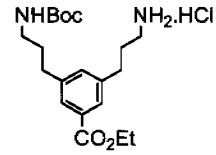
139.95, 142.03, 142.21, 156.00, 168.24. ESI-MS 546 $[M + Na]^+$. Anal. calc. for $C_{30}H_{41}N_3O_5$ (543.3): C, 66.23 H, 8.85, N, 8.58. Found: C 65.95, H 8.87, N 8.49.

**Poly{3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzylmethacryl amide} (40):**



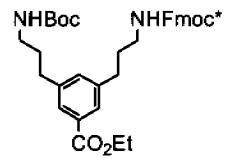

To a Schlenk tube containing monomer **39** (0.60 g, 1.22 mmol) was added a solution of DBPO (0.47 mg, 0.16 mol-%) in DMF (0.2 mL). The resulting mixture was degassed several times by freeze-pump-thaw cycles. Then it was kept at 70 °C for 12 h. After polymerization, the polymer was dissolved in $CH_2Cl_2$ and purified by column chromatography (silica gel, $CH_2Cl_2$ as eluent) to yield **40** (0.42 g, 70 %) as a colorless foam. $^1H$ NMR ($CDCl_3$): δ 0.85 (br, $CH_3$), 1.45 (br, $CH_3$), 1.90 (br, $CH_2$), 2.65 (br, $ArCH_2$), 3.14 (br, $NHCH_2$), 4.05 (br, $CH_2CH_3$), 5.35 (br, NH), 6.94 (br, ArH), 7.12 8br, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.45, 31.62, 32.85, 40.02, 41.24, 66.25, 79.09, 125.73, 127.76, 138.45, 139.95, 142.21, 158.00, 168.24. Mn = 3.5 x $10^5$, Mw = 9.5 x $10^5$.

**Ethyl-3-[3-(amino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzoate (41a)**



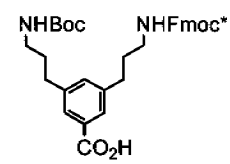

$CF_3COOH$ (7.5 mL, 3.2 eq.) in $CH_2Cl_2$ (130 mL) was added to a solution of **26a** (14.0 g, 30 mmol) in $CH_2Cl_2$ at 0 °C. The mixture was stirred at r.t. for 48 h and the solvent was then evaporated. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH/$Et_3N$: v/v: 10/1/0.1) yielded **41a** (6.8 g, 62 %) as a brown viscous oil. $^1H$ NMR ($CDCl_3/CD_3OD$): δ 1.37 (t, 3 H, $CH_3$), 1.40 (s, 9 H, $CCH_3$), 1.75 (m, 2 H, $CH_2$), 1.99 (m, 2 H, $CH_2$), 2.62 (t, 2 H, $CH_2Ph$), 2.68 (t, 2 H, $CH_2Ph$), 2.99 (q, 2 H, $CH_2NH$), 3.12 (q, 2 H, $CH_2NH$), 4.32 (q, 2 H, $CH_2O$), 4.71 (s, br, 1 H, NH), 7.17 (s, 1 H, ArH), 7.62 (s, 1 H, ArH), 7.66 (s, 1 H, ArH), 8.24 (s, br, 2 H, NH). $^{13}C$ NMR ($CDCl_3/CD_3OD$): δ 14.23, 28.34, 28.68, 31.42, 32.08, 32.64, 39.19, 61.09, 127.04, 127.49, 130.77, 133.04, 140.64, 142.26, 160.42, 166.81. HiRes-MALDI: 365.24 $[M + Na]^+$.

**Ethyl-3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzoate (41b)**




Compound **41a** (0.4 g, 1.1 mmol) and DIEA (0.36 mL, 2.2 mmol) in $CH_2Cl_2$/ MeOH (10 mL, v/v, 1/1) were added dropwise to a solution of (2,7-di-tert-butyl-9-fluorenyl)methyl 2,5-dioxopyrrolidin-1-yl carbonate (0.59 g, 1.32 mmol) in $CH_2Cl_2$ (20 mL) over 15 min at -30 °C. The resulting mixture was warmed to r.t. and stirred overnight. The product was washed with $NaHCO_3$ and brine. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 2/1) yielded **41b** (0.68 g, 89 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3$): δ 1.27 (t, 3 H, $CH_3$), 1.36 (s, 18 H, $CCH_3$), 1.43 (s, 9 H, $CCH_3$), 1.84 (m, 4 H, $CH_2$), 2.65 (t, 4 H, $CH_2Ph$), 3.13 (q, 2 H, $CH_2NH$), 3.24 (q, 2 H, $CH_2NH$), 4.15 (t, 1 H, CHCH$_2$), 4.39 (m, 4 H, $CH_2O$), 4.59 (s, br, 1 H, NH), 4.93 (s, br, 1 H, NH), 7.19 (s, 1 H, ArH), 7.40 (d, 2 H, ArH), 7.58 (dd, 4 H, ArH), 7.69 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 14.41, 28.46, 31.65, 32.72, 32.80, 34.89, 40.03, 40.49, 47.33, 60.96, 67.03, 79.16, 119.22, 121.89, 124.72, 127.18, 127.27, 130.81, 133.19, 138.73, 141.82, 142.02, 144.8, 149.78, 156.04, 156.66, 166.79. HiRes-MALDI: 721.24 [M + Na]$^+$. Anal. calc. for $C_{47}H_{60}N_4O_8$ (698.43): C 73.89, H 8.36, N 4.01. Found: C 73.61, H 8.11, N 3.96.

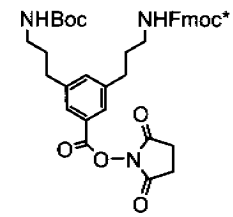
**3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzoic acid (41c)**




Compound **41a** (0.70 g, 1.90 mmol) was heated with KOH (0.43 g, 4 eq.) in THF/MeOH/$H_2O$ (10/10/5, v/v) at 55 °C for 6 h. After the reaction was finished (TLC), water (3 mL) and then acetic acid were added until pH = 5 was reached. The solvent was evaporated. The resulting mixture and DIEA (0.8 mL, pH 8-9) in $CH_2Cl_2$/MeOH (25 mL, 3/2) were added dropwise into a solution of (2,7-di-tert-butyl-9-fluorenyl)methyl 2,5-dioxopyrrolidin-1-yl carbonate (1.10 g, 2.30 mmol) in $CH_2Cl_2$ (20 mL) over 15 min at -30 °C. The resulting mixture was warmed to r.t., and stirred overnight. The product was washed with $NaHCO_3$ and brine. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 1/1) yielded **41c** (0.96 g, 75 %) as slightly yellow solid. $^1$H NMR ($CDCl_3$): δ 1.28 (s, 18 H, $CCH_3$), 1.37 (s, 9 H, $CCH_3$), 1.70 (m, 4 H, $CH_2$), 2.54 (m, 4 H, $CH_2Ph$), 2.99 (q, 2 H, $CH_2NH$), 3.09 (q, 2 H, $CH_2NH$), 4.05 (t, 1 H, CHCH$_2$), 4.32

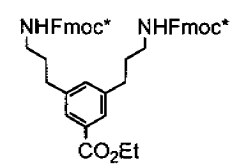
(q, 2 H, $CH_2O$), 7.09 (s, 1 H, ArH), 7.28 (d, 2 H, ArH), 7.50 (dd, 4 H, ArH), 7.59 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.46, 31.66, 31.77, 32.95, 34.90, 40.29, 46.73, 62.17, 67.17, 79.03, 119.20, 121.66, 124.69, 125.40, 126.80, 137.92, 138.80, 141.38, 141.63, 144.09, 144.26, 149.80, 156.12, 156.32, 169.55.

**3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzoic acid 2,5-dioxo-pyrrolidin-1-yl ester (41d)**




*N*-Hydroxy-succinimide (0.33 g, 2.87 mmol) was added into a solution of **41c** (1.55 g, 2.31 mmol) in dry $CH_2Cl_2$ (60 mL) at r.t. After the mixture had been stirred for 15 min dicyclohexylcarbodiimide (0.65 g, 3.15 mmol) was added at -20 °C. The resulting mixture was warmed to r.t. and stirred overnight. After the precipitate had been filtered off, chromatographic separation (silica gel, hexane/ EtOAc: v/v: 3/1) yielded **41d** (1.43 g, 81 %) as slightly yellowish solid. $^1H$ NMR ($CDCl_3$): δ 1.34 (s, 18 H, $CCH_3$), 1.42 (s, 9 H, $CCH_3$), 1.74 (m, 4 H, $CH_2$), 2.64 (t, 4 H, $CH_2Ph$), 2.89 (s, 4 H, $CH_2$), 3.11 (q, 2 H, $CH_2NH$), 3.21 (q, 2 H, $CH_2NH$), 4.11 (t, 1 H, $\underline{CH}CH_2$), 4.39 (q, 2 H, $CH_2O$), 4.71 (s, br, 1 H, NH), 5.11 (s, br, 1 H, NH), 7.01 (s, 1 H, ArH), 7.39 (d, 2 H, ArH), 7.58 (dd, 4 H, ArH), 7.72 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 24.94, 25.69, 28.43, 31.44, 31.61, 32.55, 32.64, 33.86, 34.87, 39.89, 40.35, 47.30, 66.99, 70.19, 79.16, 119.18, 121.89, 124.70, 125.37, 128.05, 128.13, 135.40, 138.70, 142.59, 142.80, 144.05, 149.79, 156.05, 156.67, 169.39, 171.16. HiRes-MALDI: 790.40 $[M + Na]^+$ Anal. calc. for $C_{45}H_{57}N_3O_8$ (767.21): C 70.38, H 7.48, N 5.47. Found: C 70.10, H 7.66, N 5.48.

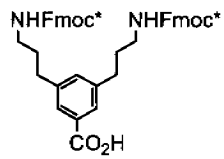
**Ethyl-3,5-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl] benzoate (42b)**




Compound **42a** (0.3 g, 0.90 mmol) and DIEA (0.44 mL, 2.50 mmol) in $CH_2Cl_2$/ MeOH (10 mL, v/v, 1/1) were added dropwise to a solution of (2,7-di-tert-butyl-9-fluorenyl)methyl 2,5-dioxopyrrolidin-1-yl carbonate (1.0 g, 2.22 mmol) in $CH_2Cl_2$ (20 mL) over 15 min at -30 °C. The resulting mixture was warmed to r.t. and stirred overnight. The product was washed with $NaHCO_3$ and brine. Chromatographic separation (silica gel, hexane/ EtOAc: v/v:

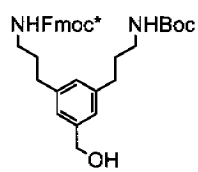
2/1) yielded **42b** (0.6 g, 95 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3$): δ 1.26 (t, 3 H, $CH_3$), 1.37 (s, 36 H, $CCH_3$), 1.87 (m, 4 H, $CH_2$), 2.68 (t, 4 H, $CH_2Ph$), 3.24 (q, 4 H, $CH_2NH$), 4.20 (t, 2 H, CHCH$_2$), 4.45 (m, 6 H, $CH_2O$), 4.95 (s, br, 2 H, NH), 7.22 (s, 1 H, ArH), 7.39 (s, 2 H, ArH), 7.41 (s, 2 H, ArH), 7.64 (d, 8 H, ArH), 7.72 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 14.56, 31.79, 32.84, 35.05, 40.64, 47.46, 61.14, 67.17, 119.36, 122.02, 124.84, 127.40, 138.88, 141.94, 144.19, 149.92, 156.77. HiRes-MALDI: 956.32 $[M + Na]^+$. Anal. calc. for $C_{61}H_{76}N_2O_6$ (933.27): C 78.50, H 8.21, N 3.00. Found: C 78.34, H 8.27, N 2.97.

**3,5-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl] benzoic acid (42c)**




Compound **42a** (0.35 g, 1.05 mmol) was heated with KOH (0.3 g, 5 eq.) in THF/MeOH/$H_2O$ (10/10/5, v/v) at 55 °C for 6 h. After the reaction was finished (TLC), water (3 mL) and then acetic acid were added until pH = 5 was reached. The solvent was evaporated. The resulting mixture and DIEA (0.6 mL, pH 8-9) in $CH_2Cl_2$/MeOH (25 mL, 3/2) were added dropwise into a solution of (2,7-di-tert-butyl-9-fluorenyl)methyl 2,5-dioxopyrrolidin-1-yl carbonate (1.1 g, 2.3 mmol) in $CH_2Cl_2$ (20 mL) over 15 min at -30 °C. The resulting mixture was warmed to r.t., and stirred overnight. The product was washed with $NaHCO_3$ and brine. Chromatographic separation (silica gel, hexane/EtOAc: v/v: 2/1) yielded **42c** (0.90 g, 94 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3$): δ 1.35 (s, 36 H, $CCH_3$), 1.84 (m, 4 H, $CH_2$), 2.65 (t, 4 H, $CH_2Ph$), 3.20 (q, 4 H, $CH_2NH$), 4.16 (t, 2 H, CHCH$_2$), 4.41 (d, 4 H, $CH_2O$), 7.35 (s, 1 H, ArH), 7.38 (s, 2 H, ArH), 7.55-7.66 (m, 12 H, ArH. $^{13}$C NMR ($CDCl_3$): δ 31.43, 32.54, 34.54, 37.87, 40.19, 47.21, 66.81, 119.09, 119.45, 121.71, 123.31, 124.62, 127.44, 127.70, 130.58, 133.32, 138.60, 141.83, 143.92, 149.79, 156.98, 169.05. HiRes-MALDI: 927.52 $[M + Na]^+$.

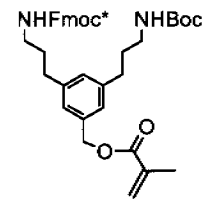
**3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzyl alcohol (43)**




A solution of 2M $LiBH_4$ (2.86 mL, 5.7 mmol) in dry THF (10) was added dropwise to a solution of **41b** (0.5 g, 0.72 mmol) in dry THF (15) at 0 °C. The reaction mixture was stirred overnight at r.t. and then quenched by adding dropwise 5 % HCl (2 mL). The resulting precipitate was filtered

off. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 2/1) yielded **43** (0.43 g, 92 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3$): δ 1.39 (s, 18 H, $CCH_3$), 1.47 (s, 9 H, $CCH_3$),1.82 (m, 4 H, $CH_2$), 2.65 (t, 4 H, $CH_2Ph$), 3.14 (q, 2 H, $CH_2NH$), 3.24 (q, 2 H, $CH_2NH$), 4.20 (t, 1 H, CHCH$_2$), 4.55 (d, 2 H, $CH_2O$), 4.64 (s, 2 H, $CH_2O$), 4.95 (s, br, 2 H, NH), 6.92 (s, 1 H, ArH), 7.02 (s, 2 H, ArH), 7.43 (d, 2 H, ArH), 7.64 (dd, 4 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.46, 29.68, 29.87, 31.66, 31.77, 32.95, 34.90, 40.29, 46.73, 62.17, 67.17, 79.03, 119.20, 121.66, 124.69, 125.40, 126.80, 137.92, 138.80, 141.38, 141.63, 144.09, 144.26, 149.80, 156.12, 156.32. HiRes-MALDI: 679.41 [M + Na]$^+$. Anal. calc. for $C_{41}H_{56}N_2O_5$ (656.42): C 74.97, H 8.59, N 4.26. Found: C 74.99, H 8.63, N 4.21.

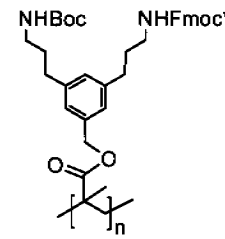
**3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzyl methacrylate (44)**




According to procedure A: MAC (0.11 mL) in $CH_2Cl_2$ (5 mL) was added to a solution of compound **43** (0.47 g, 0.71 mmol), DIEA (0.24 mL) and DMAP (10 mg) in $CH_2Cl_2$ (20 mL). Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 2/1) yielded **44** (0.49 g, 94 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3$): δ 1.41 (s, 18 H, $CCH_3$), 1.48 (s, 9 H, $CCH_3$),1.85 (m, 4 H, $CH_2$), 2.02 (s, 3 H, $CH_3$), 2.65 (t, 4 H, $CH_2Ph$), 3.16 (q, 2 H, $CH_2NH$), 3.28 (q, 2 H, $CH_2NH$), 4.22 (t, 1 H, CHCH$_2$), 4.56 (d, 2 H, $CH_2O$), 4.95 (s, br, 2 H, NH), 5.21 (s, 2 H, $CH_2O$), 5.61 (s, 1 H, $CH_2$=), 6.21 (s, 1 H, $CH_2$=), 7.02 (s, 1 H, ArH), 7.06 (s, 2 H, ArH), 7.43 (d, 2 H, ArH), 7.64 (dd, 4 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 18.25, 28.47, 31.66, 32.85, 32.92, 34.90, 40.14, 40.56, 47.34, 66.44, 67.02, 79.11, 119.24, 121.90, 124.73, 125.80, 125.88, 126.30, 128.44, 136.37, 136.37, 138.74, 141.92, 142.13, 144.09, 149.78, 156.06, 156.69, 167.28. HiRes-MALDI: 747.43 [M + Na]$^+$. Anal. calc. for $C_{45}H_{60}N_2O_6$ (724.25): C 74.55, H 8.34, N 3.86. Found: C 74.29, H 8.31, N 3.83.

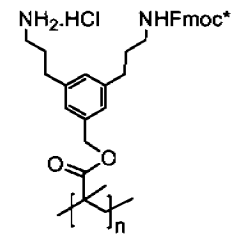
**Poly{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzyl methacrylate} (45a)**

According to procedure B: monomer **44** (0.22 g), DMF (70 μL) were used. Chromatographic separation yielded **6a** (0.14 g, 65 %) as a slightly yellowish solid. $^1$H NMR ($CDCl_3$, 500 MHz): δ 0.83 (br, 3 H, $CH_3$), 1.31 (br, 27 H, $CCH_3$), 1.68 (br, 4 H,



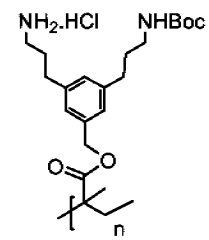

$CH_2$), 2.05 (br, 2 H, $CH_2$), 2.49 (br, 4 H, $CH_2Ph$), 3.00 (br, 2 H, $CH_2NH$), 3.10 (br, 2 H, $CH_2NH$), 4.05 (br, 1 H, CH$CH_2$), 4.25 (br, 2 H, $CH_2O$), 4.83 (br, 2 H, $CH_2O$), 5.19 (br, 1 H, NH), 5.74 (br, 1 H, NH), 6.87 (br, 3 H, ArH), 7.29 (br, 2 H, ArH), 7.52 (br, 4 H, ArH). $^{13}C$ NMR ($CDCl_3$, 500 MHz): δ 28.64, 31.30, 31.73, 32.97, 34.90, 40.35, 40.77, 47.52, 67.20, 78.90, 119.27, 121.95, 124.71, 125.95, 135.57, 138.80, 142.08, 142.33, 144.30, 149.84, 156.18, 156.81.

**Poly{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(amino)-propyl] benzyl methacrylate x HCl} (45b)**



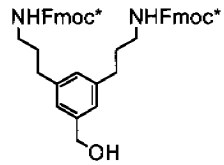

25 % HCl (0.28 mL), THF (10 mL) and **45a** (90 mg) were used. Evaporation of the solvent yielded **45b** (82 mg, 96 %) as slightly greenish solid. $^1H$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.83 (br, 3 H, $CH_3$), 1.28 (br, 18 H, $CCH_3$), 1.70 (br, 2 H, $CH_2$), 1.98 (br, 4 H, $CH_2$), 2.48 (br, 4 H, $CH_2Ph$), 2.89 (br, 2 H, $CH_2NH$), 3.04 (br, 2 H, $CH_2NH$), 4.05 (br, 1 H, CH$CH_2$), 4.25 (br, 2 H, $CH_2O$), 4.83 (br, 2 H, $CH_2O$), 6.94 (br, 3 H, ArH), 7.26 (br, 2 H, ArH), 7.48 (br, 4 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 28.81, 31.35, 32.44, 32.87, 34.68, 39.57, 40.70, 45.36, 57.34, 67.12, 119.21, 121.73, 124.65, 126.02, 128.48, 135.53, 138.70, 141.07, 142.53, 144.10, 149.87, 157.48.

**Poly{3-[3-(amino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzyl methacrylate x HCl} (45c)**



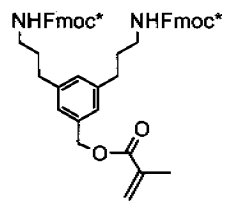

25 % Piperidene (1.2 mL), DMF (10 mL), and **45a** (0.1 g) were used to yield **45c** (50 mg, 80 %) as colorless solid. $^1H$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.85 (br, 3 H, $CH_3$), 1.43 (br, 9 H, $CCH_3$), 1.77 (br, 2 H, $CH_2$), 2.05 (br, 2 H, $CH_2$), 2.59 (br, 2 H, $CH_2Ph$), 2.70 (br, 2 H, $CH_2Ph$), 2.99 (br, 2 H, $CH_2NH$), 3.06 (br, 2 H, $CH_2NH$), 4.92 (br, 2 H, $CH_2O$), 7.09 (br, 3 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 28.73, 30.98, 32.64, 39.19, 39.87, 66.77, 78.66, 126.00, 128.32, 135.54, 141.03, 141.32, 142.65, 157.01.

**3,5-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]benzyl alcohol (46)**



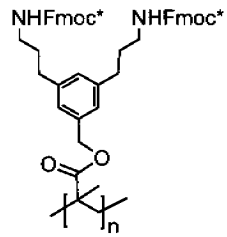

A solution of 2M $LiBH_4$ (3.2 mL, 4.8 mmol) in dry THF (10 mL) was added dropwise to a solution of **42b** (0.45 g, 0.48 mmol) in dry THF (15 mL) at 0 °C. The reaction mixture was stirred overnight at r.t. and then quenched by adding dropwise 5 % HCl (2 mL). The resulting precipitate was filtered off. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 2/1) yielded **46** (0.37 g, 87 %) as greenish solid. $^1$H NMR ($CDCl_3$): δ 1.39 (s, 36 H, $CCH_3$), 1.87 (m, 4 H, $CH_2$), 2.66 (t, 4 H, $CH_2Ph$), 3.24 (q, 4 H, $CH_2NH$), 4.20 (t, 2 H, $CHCH_2$), 4.43 (d, 4 H, $CH_2O$), 4.67 (s, 2 H, $CH_2O$), 4.95 (s, br, 2 H, NH), 6.97 (s, 1 H, ArH), 7.05 (s, 2 H, ArH), 7.42 (s, 2 H, ArH), 7.44 (s, 2 H, ArH), 7.66 (d, 8 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 31.80, 32.95, 35.05, 40.64, 47.46, 65.37, 67.17, 119.37, 122.02, 124.84, 138.88, 141.94, 144.20, 149.93, 156.79. HiRes-MALDI: 914.34 $[M + Na]^+$. Anal. calc. for $C_{59}H_{74}N_2O_5$ (891.23): C 73.89, H 8.36, N 4.01. Found: C 73.61, H 8.11, N 3.96.

**3,5-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]benzyl methacrylate (47)**



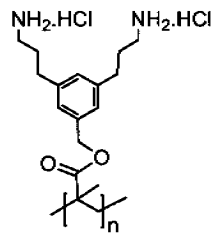

According to procedure A: MAC (0.05 mL) in $CH_2Cl_2$ (5 mL) was added to a solution of compound **46** (0.26 g, 0.29 mmol), DIEA (0.05 mL) and DMAP (8 mg) in $CH_2Cl_2$ (15 mL). Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 3/1) yielded **47** (0.22 g, 78 %) as greenish solid. $^1$H NMR ($CDCl_3$): δ 1.41 (s, 36 H, $CCH_3$), 1.90 (m, 4 H, $CH_2$), 2.02 (s, 3 H, $CH_3$), 2.68 (t, 4 H, $CH_2Ph$), 3.28 (q, 4 H, $CH_2NH$), 4.20 (t, 2 H, $\underline{CH}CH_2$), 4.45 (d, 4 H, $CH_2O$), 5.08 (s, br, 2 H, NH), 5.20 (s, 2 H, $CH_2O$), 5.62 (s, 1 H, $CH_2$=), 6.21 (s, 1 H, $CH_2$=), 7.03 (s, 1 H, ArH), 7.08 (s, 2 H, ArH), 7.43 (s, 2 H, ArH), 7.46 (s, 2 H, ArH), 7.66 (d, 8 H, ArH),. $^{13}$C NMR ($CDCl_3$): δ 18.43, 26.96, 31.66, 31.87, 32.82, 34.90, 40.57, 47.34, 66.43, 67.04, 119.24, 121.89, 124.73, 125.76, 125.89, 128.43, 136.26, 136.44, 138.75, 141.94, 144.08, 149.77, 156.65, 167.28, 175.69. HiRes-MALDI: 982.46 $[M + Na]^+$. Anal. calc. for $C_{63}H_{78}N_2O_6$ (959.30): C 78.88, H 8.20, N 2.92. Found: C 78.63, H 8.20, N 2.92.

**Poly{3,5-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl] benzyl methacrylate} (48a)**



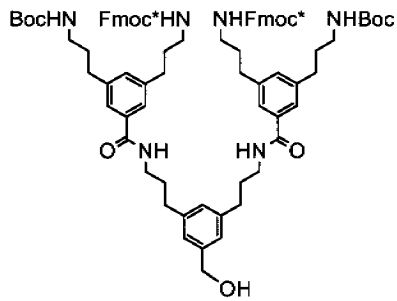

According to procedure B: monomer **47** (0.27 g) and DMF (75 µL) were used. Polymerization at 70 °C for 18 h. Chromatographic separation yielded **48a** (0.17 g, 63 %) as a greenish solid. $^1$H NMR ($CDCl_3$, 500 MHz): δ 0.94 (br, 3 H, $CH_3$), 1.29 (br, 36 H, $CCH_3$), 1.74 (br, 4 H, $CH_2$), 2.52 (br, 4 H, $CH_2Ph$), 3.11 (br, 4 H, $CH_2NH$), 4.00 (br, 2 H, CHCH$_2$), 4.25 (br, 4 H, $CH_2O$), 4.92 (br, 2 H, $CH_2O$), 5.63 (br, 2 H, NH), 6.91 (br, 3 H, ArH), 7.29 (br, 4 H, ArH), 7.52 (br, 8 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 30.82, 31.63, 32.72, 34.75, 40.52, 47.17, 67.02, 119.19, 121.84, 124.60, 125.89, 128.31, 135.61, 138.61, 141.95, 144.03, 144.03, 149.56, 156.74.

**Poly{3,5-[3-(amino)propyl] benzyl methacrylate x 2HCl} (48b)**




According to procedure D: 25 % Aqueous piperidene (3.5 mL), DMF (15 mL) and **48a** (0.15 g) were used to yield **48b** (50 mg, 85 %) as viscous oil. $^1$H NMR ($CD_3OD$, 500 MHz): δ 0.85 (br, $CH_3$), 1.85 (br, $CH_2$), 2.55 (br, $ArCH_2$), 3.11 (br, $NHCH_2$), 4.85 (br, $CH_2CH_3$), 6.94 (br, ArH). $^{13}$C NMR ($CD_3OD$, 500 MHz): δ 31.56, 32.87, 40.20, 125.86, 127.61, 139.18, 141.38, 168.24.

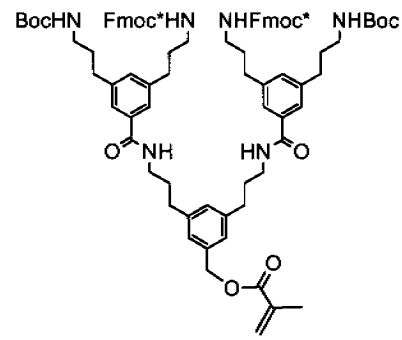
**3,5-Bis-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino) propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoylamino}-propyl)-benzyl alcohol (49)**




Compound **30c** (0.2 g, 0.67 mmol) and DIEA (0.4 mL, 2.4 mmol) in MeOH (10 mL) was added dropwise to a solution of **41d** (1.3 g, 1.7 mmol) in $CH_2Cl_2$ (25 mL) at -30 °C over 10 min. The resulting mixture was warmed to r.t. and stirred for 20 h. The product was washed with $NaHCO_3$ and brine. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 3/1) yielded **49** (0.89 g, 86 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3$): δ 1.41 (s, 36 H, $CCH_3$), 1.48 (s, 18 H, $CCH_3$),1.84 (m, 8 H, $CH_2$), 1.92 (m, 4 H, $CH_2$), 2.64 (m, 12 H, $CH_2Ph$), 3.08 (q, 4 H, $CH_2NH$), 3.20 (q, 4 H, $CH_2NH$), 3.46 (q, 4 H, $CH_2NH$), 4.16 (t, 2 H, CHCH$_2$), 4.40 (d, 4 H, $CH_2O$), 4.58 (s, 2

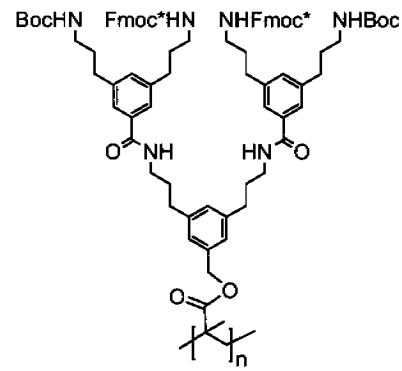
H, $CH_2O$), 4.85 (s, br, 2 H, NH), 5.31 (s, br, 2 H, NH), 6.94 (s, 1 H, ArH), 7.01 (s, 3 H, ArH), 7.09 (s, 3 H, ArH), 7.40 (d 2 H, ArH), 7.43 (d, 2 H, ArH), 7.60 (dd, 8 H, ArH), 7.65 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.44, 30.80, 31.36, 31.62, 32.44, 33.26, 34.87, 39.63, 40.25, 47.28, 64.92, 67.04, 79.19, 119.20, 121.86, 124.73, 127.61, 131.57, 134.92, 138.69, 141.57, 141.75, 141.87, 144.03, 149.79, 156.19, 156.77, 167.83. HiRes-MALDI: 1551.28 $[M + Na]^+$. Anal. calc. for $C_{95}H_{126}N_6O_{11}$ (1528.05): C 74.67, H 8.31 N, 5.50. Found: C 74.39, H 8.30, N 5.38.

**3,5-Bis-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino) propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoylamino}-propyl)-benzyl methaacrylate (50)**



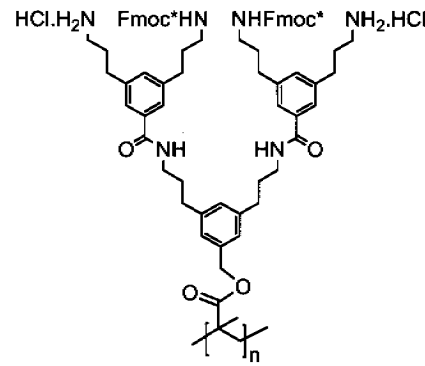

According to procedure A: MAC (0.08 mL) in $CH_2Cl_2$ (5 mL) was added to **49** (0.84 g, 0.55 mmol), DIEA (0.22 mL) and DMAP (20 mg) in $CH_2Cl_2$ (25 mL). Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 2/1) yielded **50** (0.67 g, 77 %) as slightly greenish solid. $^1H$ NMR ($CDCl_3$): δ 1.41 (s, 36 H, $CCH_3$), 1.48 (s, 18 H, $CCH_3$),1.87 (m, 12 H, $CH_2$), 2.02 (s, 3 H, $CH_3$), 2.65 (m, 12 H, $CH_2Ph$), 3.10 (q, 4 H, $CH_2NH$), 3.22 (q, 4 H, $CH_2NH$), 3.46 (q, 4 H, $CH_2NH$), 4.16 (t, 2 H, $\underline{CH}CH_2$), 4.38 (d, 4 H, $CH_2O$), 4.95 (s, br, 1 H, NH), 5.10 (s, 2 H, $CH_2O$), 5.31 (s, br, 1 H, NH), 5.58 (s, 1 H, $CH_2$=), 6.14 (s, 1 H, $CH_2$=), 7.03 (s, 4 H, ArH), 7.10 (s, 3 H, ArH), 7.39 (d, 2 H, ArH), 7.43 (d, 2 H, ArH), 7.47 (s, 2 H, ArH), 7.64 (dd, 8 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 18.29, 28.44, 30.94, 31.28, 31.66, 32.32, 32.49, 33.12, 34.86, 39.51, 39.61, 40.20, 47.28, 66.42, 67.06, 79.12, 119.22, 121.86, 124.73, 124.89, 125.89, 126.05, 128.48, 129.01, 131.59, 134.94, 136.18, 136.29, 138.70, 141.75, 142.06, 144.03, 149.78, 156.20, 156.78, 167.29, 167.91, 169.91. HiRes-MALDI: 1617.96 $[M + Na]^+$. Anal. calc. for $C_{99}H_{130}N_6O_{12}$ (1594.97): C 74.50, H 8.21, N 5.27. Found: C 74.24, H 8.26, N 5.15.

**Poly{3,5-bis-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino) propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoylamino}-propyl)-benzyl methaacrylate} (51a)**




According to procedure B: monomer **50** (0.3 g) and DMF (80 μL) were used. Polymerization at 70 °C for 22 h. Chromatographic separation yielded **51a** (0.25 g, 83 %) as a slightly yellowish solid. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1.30 (br, 54 H, $CCH_3$), 1.67 (br, 8 H, $CH_2$), 1.87 (br, 6 H, $CH_2$), 2.45 (br, 12 H, $CH_2Ph$), 2.91 (br, 4 H, $CH_2NH$), 3.05 (br, 4 H, $CH_2NH$), 3.65 (br, 4 H, $CH_2NH$), 4.06 (br, 2 H, CHCH$_2$), 4.28 (br, 4 H, $CH_2O$), 4.85 (br, 2 H, $CH_2O$), 6.88-6.99 (br, 5 H, ArH), 7.29- 7.61 (br, 16 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 28.59, 31.40, 31.60, 31.72, 32.79, 33.19, 34.90, 40.01, 40.66, 47.49, 50.77, 53.40, 67.23, 78.98, 119.27, 11.37, 121.54, 121.95, 124.75, 124.98, 131.47, 135.10, 138.77, 141.97, 144.26, 149.88, 156.27, 156.86, 168.09.

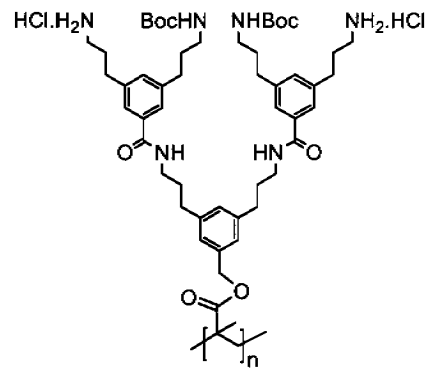
**Poly{3,5-bis-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino) propyl]-5-[3-(amino)-propyl]-benzoylamino}-propyl)-benzyl methaacrylate x 2HCl} (51b)**




According to procedure C: 25 % HCl (0.1 mL), THF (8 mL) and **51a** (60 mg) were used. Evaporation of the solvent yielded **51b** (52 mg, 94 %) as yellowish solid. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.85 (br, 3 H, $CH_3$), 1.22 (br, 36 H, $CCH_3$), 1.65 (br, 8 H, $CH_2$), 1.85 (br, 4 H, $CH_2$), 2.49 (br, 12 H, $CH_2Ph$), 2.97 (br, 8 H, $CH_2NH$), 3.29 (br, 4 H, $CH_2NH$), 3.99 (br, 4 H, CHCH$_2$), 4.37 (br, 2 H, $CH_2O$), 6.95-7.64 (br, 21 H, ArH). $^{13}$C NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 29.47, 31.40, 31.68, 34.68, 41.05, 47.33, 67.23, 119.13, 121.81, 121.54, 122.85, 124.61, 126.07, 127.83, 132.28, 134.90, 135.30, 137.22, 138.53, 140.65, 142.31, 143.90, 149.82, 157.18, 168.65.

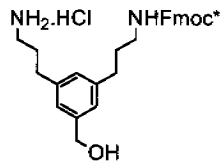
**Poly{3,5-bis-(3-{3-[3-(amino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoylamino}-propyl)-benzyl methaacrylate x 2HCl} (51c)**

According to procedure D: 25 % Aqueous piperidene (0.8 mL), DMF (8 mL) and **51a** (70 mg) were used to yield **51c** (40 mg, 91 %) as colorless solid. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.85 (br, 3 H, $CH_3$), 1.34 (br, 18 H, $CCH_3$), 1.67 (br, 4 H,



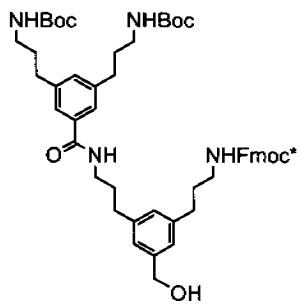

$CH_2$), 1.85 (br, 4 H, $CH_2$), 1.98 (br, 4 H, $CH_2$), 2.52 (br, 12 H, $CH_2Ph$), 2.98 (br, 4 H, $CH_2NH$), 3.12 (br, 4 H, $CH_2NH$), 3.30 (br, 4 H, $CH_2NH$), 4.79 (br, 2 H, $CH_2O$), 6.90 (br, 2 H, ArH), 6.90 (br, 2 H, ArH), 7.44 (br, 5 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 29.08, 29.89, 32.14, 32.49, 33.36, 33.88, 34.36, 34.77, 40.50, 41.04, 47.33, 79.80, 126.14, 126.52, 127.46, 132.83, 136.20, 136.36, 142.39, 142.70, 143.60, 144.29, 156.13, 158.40, 164.86.

**3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)propyl]-5-[3-(amino)-propyl] benzyl alcohol (52)**




To a solution of compound **42** (0.60 g, 0.91 mmol) in THF (25 mL) was slowly added a solution of 25 % HCl (0.55 mL, 4 equiv) in THF (3 mL) under $N_2$ at 0°C. The reaction was stirred for 3 h and controlled with TLC. The solvent was evaporated at r.t. to yield **52** as viscous oil (0.50 g, 94 %). The product was used for next step without further purification procedures.

**3-{3,5-Bis-[3-(tert-butyloxycarbonylamino)-propyl]benzoylamino}-5-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]benzyl alcohol (53a)**

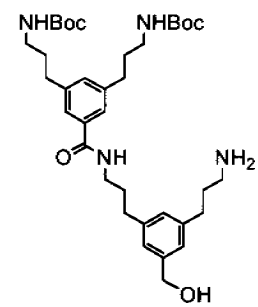



To a solution of the acid dendron **26c** (0.48 g, 1.02 mmol) in $CH_2Cl_2$ (25 mL) were added N-hydroxybenzotriazol (0.15 g, 1.10 mmol) at r.t. After 10 min at -30 °C, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.22 g, 1.15 mmol) was added. The mixture was stirred for 3 h. Then a solution of **52** (0.50 g, 0.85 mmol) and DIEA (0.3 mL, 1.68 mmol) in a mixed solvents of methanol/$CH_2Cl_2$ (15 mL, 1/1) were added dropwise at -20 °C. The resulting mixture was warmed to r.t. and stirred for 14 h. It was then washed with brine and aqueous $NaHCO_3$. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuum. Chromatographic separation (silica gel, AcOEt/ hexane, v/v, 1/1) yielded **53a** (0.67, 82 %) as a slightly yellowish solid. $^1H$ NMR ($CDCl_3$): δ 1.36 (s, 18 H, $CCH_3$), 1.44 (s, 18 H, $CCH_3$), 1.77 (m, 2 H, $CH_2$), 1.86 (m, 4 H, $CH_2$), 1.96 (m, 2 H, $CH_2$), 2.58 (t, 2 H, $CH_2Ph$), 2.70 (m, 6 H, $CH_2Ph$), 3.10 (q, 2 H, $CH_2NH$), 3.22 (q, 4 H, $CH_2NH$), 3.42 (q, 2 H, $CH_2NH$), 4.16 (t, 1

H, CHCH$_2$), 4.40 (d, 2 H, CH$_2$O), 4.59 (s, 2 H, CH$_2$O), 5.09 (s, br, 1 H, NH), 6.96 (s, 1 H, ArH), 7.00 (s, 2 H, ArH), 7.16 (s, 1 H, ArH), 7.38 (s 2 H, ArH), 7.43 (d, 2 H, ArH), 7.60 (dd, 4 H, ArH). $^{13}$C NMR (CDCl$_3$): δ 28.34, 30.81, 31.56, 31.59, 32.48, 32.90, 33.48, 34.88, 39.80, 40.15, 47.28, 65.18, 67.05, 79.15, 119.24, 121.90, 124.71, 127.61, 134.90, 138.73, 141.57, 141.78, 142.14, 144.07, 149.81, 156.11, 156.68, 168.73. HiRes-MALDI: 997.22 [M + Na]$^+$. Anal. calc. for $C_{59}H_{82}N_4O_8$ (974.61): C 72.66, H 8.47, N 5.74. Found: C 72.45, H 8.55, N 5.68.

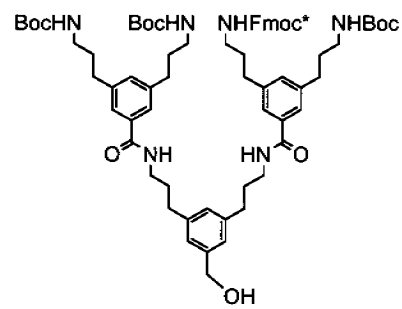
**3-{3,5-Bis-[3-(tert-butyloxycarbonylamino)-propyl]benzoylamino}-5-[3-(amino)-propyl]benzyl alcohol (53b)**

20 % Aqueous piperidene (7 mL, 20 equiv.) was added dropwise to a solution of **53a** (0.67 g, 0.69 mmol) in DMF (25 mL). The mixture was stirred for 14 h and the reaction was controlled with TLC. The mixture was washed three times with hexane. The solvent was evaporated to yield **53b** (0.42 g, 95 %) as slightly brown oil. The product was used for next step without further purification.



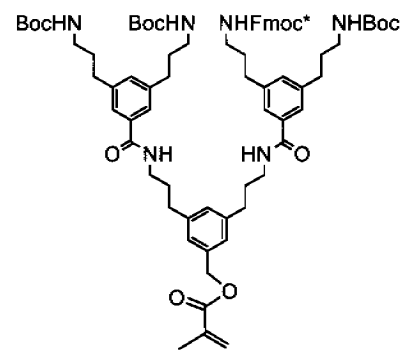

**3-(3-{3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl alcohol (54)**

Compound **53b** (0.73 g, 1.14 mmol) and DIEA (0.3 mL, 1.9 mmol) in CH$_2$Cl$_2$/MeOH (15 mL, 2/1) was added dropwise to a solution of **41d** (1.0 g, 1.3 mmol) in CH$_2$Cl$_2$ (25 mL) at -30 °C over 10 min. The resulting mixture was warmed to r.t. and stirred for 20 h. The product was washed with NaHCO$_3$ and brine. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 1/2) yielded **54** (1.28 g, 87 %) as slightly yellowish solid. δ 1.40 (s, 18 H, CCH$_3$), 1.47 (s, 27 H, CCH$_3$), 1.87 (m, 8 H, CH$_2$), 1.94 (m, 4 H, CH2), 2.67 (m, 12 H, CH$_2$Ph), 3.06 (q, 6 H, CH$_2$NH), 3.19 (q, 2 H, CH$_2$NH), 3.44 (q, 4 H, CH$_2$NH), 4.15 (t, 1 H, CHCH$_2$), 4.38 (d, 4 H, CH$_2$O), 4.59 (s, 2 H, CH$_2$O), 4.85 (s, br, 3 H, NH), 6.95 (s, 3 H, ArH), 7.04 (s, 2 H, ArH), 7.09 (s, 2 H, ArH), 7.37 (m, 4 H, ArH), 7.59 (m, 4 H, ArH). $^{13}$C NMR (CDCl$_3$): δ



18.57, 30.98, 31.49, 31.72, 32.73, 33.44, 34.95, 39.81, 47.57, 65.00, 79.24, 119.29, 121.92, 124.79, 124.92, 127.65, 131.54, 138.85, 142.06, 142.09, 144.25, 150.29, 156.20, 156.78, 167.27. HiRes-MALDI: 1315.79 $[M + Na]^+$. Anal. calc. for $C_{77}H108N_6O_{11}$ (1292.81): C 71.49, H 8.41, N 6.50. Found: C 71.20, H 8.48, N 6.41.

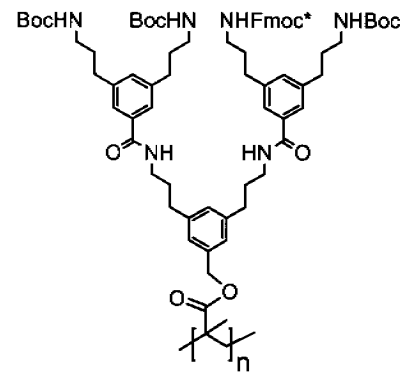
**3-(3-{3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate (55)**




According to procedure A: MAC (0.05 mL) in $CH_2Cl_2$ (5 mL) was added to a solution of compound **54** (0.43 g, 0.33 mmol), DIEA (0.11 mL) and DMAP (10 mg) in $CH_2Cl_2$ (15 mL). Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 1/2) yielded **55** (0.43 g, 95 %) as slightly yellow solid. $^1H$ NMR ($CDCl_3$): δ 1.41 (s, 18 H, $CCH_3$), 1.48 (s, 27 H, $CCH_3$), 1.87 (m, 12 H, $CH_2$), 2.02 (s, 3 H, $CH_3$), 2.65 (m, 12 H, $CH_2Ph$), 3.06 (q, 6 H, $CH_2NH$), 3.18 (q, 2 H, $CH_2NH$), 3.46 (q, 4 H, $CH_2NH$), 4.16 (t, 1 H, $\underline{CH}CH_2$), 4.38 (d, 4 H, $CH_2O$), 4.95 (s, br, 2 H, NH), 5.08 (s, 2 H, $CH_2O$), 5.37 (s, br, 1 H, NH), 5.57 (s, 1 H, $CH_2$=), 6.12 (s, 1 H, $CH_2$=), 7.01 (s, 3 H, ArH), 7.07 (s, 1 H, ArH), 7.09 (s, 1 H, ArH), 7.14 (s, br, 2 H, NH) 7.39 (d, 2 H, ArH), 7.40 (s, 4 H, ArH), 7.64 (dd, 4 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 18.29, 28.42, 30.98, 31.32, 31.60, 32.42, 33.13, 34.84, 39.61, 40.22, 47.27, 66.41, 67.03, 79.05, 119.19, 121.85, 124.71, 124.89, 125.87, 125.96, 128.45, 128.59, 131.57, 134.85, 135.07, 136.16, 136.26, 136.48, 138.67, 141.77, 142.06, 142.09, 144.02, 149.77, 156.20, 156.78, 167.27, 167.92. HiRes-MALDI: 1383.80 $[M + Na]^+$. Anal. calc. for $C_{81}H_{192}N_6O_{12}$ (1360.83): C 71.44, H 8.29, N 6.17. Found: C 71.34, H 8.37, N 6.03.

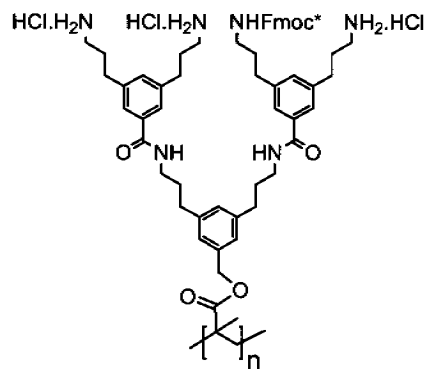
**Poly{3-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate} (56a)**

According to procedure B: Monomer **55** (0.32 g) and DMF (60 μL) were used. It was polymerized at 70 °C for 20 h. Chromatographic separation yielded **56a** (0.24 g, 75 %)




as a slightly yellowish solid. $^1$H NMR ($CDCl_3$, 500 MHz): δ 1.32 ( br, 45 H, $CCH_3$), 1.62 (br, 8 H, $CH_2$), 1.86 (br, 4 H, $CH_2$), 2.44 (br, 12 H, $CH_2Ph$), 2.95 (br, 6 H, $CH_2NH$), 3.07 (br, 2 H, $CH_2NH$), 3.36 (br, 4 H, $CH_2NH$), 4.07 (br, 1 H, CHCH$_2$), 4.30 (br, 2 H, $CH_2O$), 5.11 ( br, 4 H, NH), 7.00 (br, 5 H, ArH), 7.32 (br, 3 H, ArH), 7.45 (br, 2 H, ArH), 7.54 (br, 8 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 18.29, 28.60, 29.77, 31.39, 31.72, 32.77, 34.91, 40.12, 47.54, 66.42, 78.91, 119.25, 121.97, 124.73, 125.16, 135.15, 138.79, 142.01, 144.30, 149.91, 156.31, 156.88, 168.08.

**Poly{3-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(amino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(amino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate x 3HCl} (56b)**

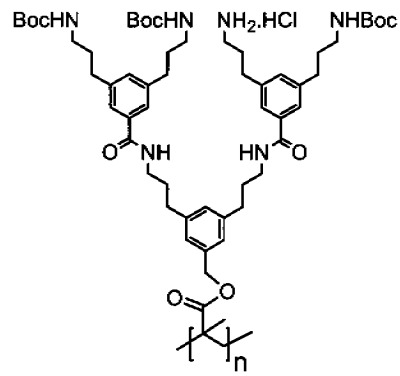



According to procedure C: 25 % HCl (0.8 mL), THF (10 mL) and **56a** (0.1 g) were used. Evaporation of the solvent yielded **56b** (80 mg, 92 %) as slightly yellowish solid. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.78 (br, 3 H, $CH_3$), 1.25 (br, 18 H, $CCH_3$), 1.79 (br, 2 H, $CH_2$), 1.87 (br, 4 H, $CH_2$), 1.98 (br, 6 H, $CH_2$), 2.58 (br, 12 H, $CH_2Ph$), 2.87 (br, 8 H, $CH_2NH$), 3.04 (br, 2 H, $CH_2NH$), 3.29 (br, 4 H, $CH_2NH$), 4.05 (br, 1 H, CHCH$_2$), 4.26 (br, 2 H, $CH_2O$), 6.91 (br, 3 H, ArH), 7.12 (br, 1 H, ArH), 7.19 (br, 1 H, ArH), 7.28 (br, 2 H, ArH), 7.52 (br, 8 H, ArH). $^{13}$C NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 28.49, 30.84, 31.27, 32.14, 34.66, 39.27, 40.01, 47.33, 67.05, 119.18, 121.72, 124.65, 125.38, 131.68, 134.84, 138.71, 141.27, 142.30, 142.59, 144.11, 149.96, 157.58, 168.65.

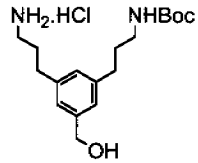
**Poly{3-(3-{3-[3-(amino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate x HCl} (56c)**

According to procedure D: 25 % Aqueous piperidene (1.5 mL), DMF (20 mL) and **56a** (0.12 g) were used to yield **56c** (75 mg, 82 %) as colorless solid. $^1$H NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.82 (br, 3 H, $CH_3$), 1.32 (br, 27 H, $CCH_3$), 1.64 (br, 6 H,

$CH_2$), 1.79 (br, 4 H, $CH_2$), 1.96 (br, 2 H, $CH_2$), 2.48 (br, 12 H, $CH_2Ph$), 2.95 (br, 4 H, $CH_2NH$), 3.12 (br, 2 H, $CH_2NH$), 3.30 (br, 4 H, $CH_2NH$), 4.79 (br, 2 H, $CH_2O$), 7.03 (br, 4 H, ArH), 7.43 (br, 5 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 28.37, 31.44, 32.72, 40.00, 79.02, 125.18, 142.25, 142.70, 156.88, 168.76.

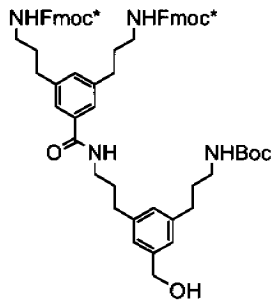



**3-[3-(Amino)propyl]-5-[3-(*tert*-butyloxycarbonylamino)-propyl] benzyl alcohol (57)**




20 % Aqueous Piperidene (9 mL, 18.3 mmol) was added dropwise to a solution of compound **43** (0.40 g, 0.61 mmol) in DMF (20 mL). The mixture was stirred for 14 hours and the reaction was controlled with TLC. It was washed two times with hexane. The solvent was evaporated to yield **57** (0.20 g, 94 %) as slightly brown oil. The product was used for next step without further purification.

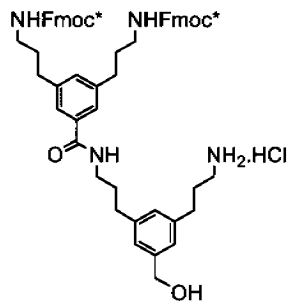
**3-{3,5-Bis-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]benzoylamino}-5-[3-(tert-butyloxycarbonylamino)-propyl]benzyl alcohol (58a)**




To a solution of the acid dendron **42c** (1.21 g, 1.34 mmol) in $CH_2Cl_2$ (30 mL) were added N-hydroxybenzotriazol (0.19 g, 1.40 mmol) at r.t. After 10 min at -30 °C N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.28 g, 1.56 mmol) was added. The mixture was stirred for 3 h. Then a solution of **57** (0.20 g, 0.56 mmol) and DIEA (0.3 mL, 1.68 mmol) in a mixed solvents of methanol/$CH_2Cl_2$ (15 mL, 1/1) were added dropwise at -20 °C. The resulting mixture was warmed up to r.t. and stirred for 14 h. it was then washed with brine and aqueous $NaHCO_3$. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuum. Chromatographic separation (silica gel, AcOEt/ hexane, v/v, 1/1) yielded **58a** (0.55, 83 %) as a slightly greenish solid. $^1H$ NMR ($CDCl_3$): δ 1.37 (s, 36 H, $CCH_3$), 1.41 (s, 9 H, $CCH_3$), 1.78 (m, 2 H, $CH_2$), 1.84 (m, 4 H, $CH_2$), 1.96 (m, 2 H, $CH_2$), 2.58 (t, 2 H, $CH_2Ph$), 2.68 (m, 6 H, $CH_2Ph$), 3.08 (q, 2 H, $CH_2NH$), 3.22 (q, 4 H, $CH_2NH$), 3.46 (q, 2 H, $CH_2NH$), 4.16 (t, 2 H, $\underline{CH}CH_2$), 4.42 (d, 4 H, $CH_2O$), 4.59 (s, 2 H, $CH_2O$), 5.09 (s, br, 1 H, NH), 6.94 (s, 1 H, ArH), 7.00 (s, 2

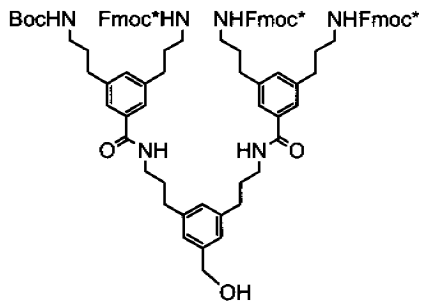
H, ArH), 7.13 (s, 1 H, ArH), 7.38 (s 2 H, ArH), 7.43 (d, 4 H, ArH), 7.60 (dd, 8 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.44, 30.80, 31.33, 31.62, 32.44, 32.90, 33.48, 34.88, 39.77, 40.15, 47.28, 65.15, 67.05, 79.19, 119.20, 121.86, 124.73, 127.61, 134.92, 138.69, 141.57, 141.75, 142.04, 144.03, 149.79, 156.01, 156.73, 168.83. HiRes-MALDI: 1232.75 $[M + Na]^+$. Anal. calc. for $C_{77}H_{100}N_4O_8$ (1209.65): C 76.45, H 8.33, N 4.73. Found: C 76.15, H 8.37, N 4.36.

**3-{3,5-Bis-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]benzoylamino}-5-[3-(amino)-propyl]benzyl alcohol (58b)**




To a solution of **58a** (0.60 g, 0.50 mmol) in THF (25 mL) was slowly added a solution of 25 % HCl (0.65 mL, 4 equiv) in THF (3 mL) under nitrogen at 0°C. The reaction was stirred for 3 h and controlled with TLC. The solvent was evaporated at r.t. to yield **58b** as slightly greenish oil (0.57 g, 98 %). The product was used for next step without further purification procedures.

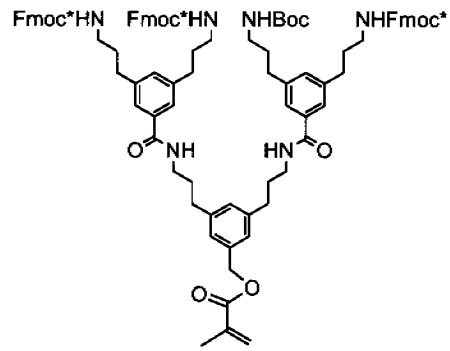
**3-(3-{3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl alcohol (59)**




Compound **58b** (0.55 g, 0.49 mmol) and DIEA (0.12 mL, 0.75 mmol) in $MeOH/CH_2Cl_2$ (15 mL, 1/1) was added dropwise to a solution of **41d** (0.46 g, 0.59 mmol) in $CH_2Cl_2$ (20 mL) at -30 °C over 10 min. The resulting mixture was warmed to r.t. and stirred for 20 h. The product was washed with $NaHCO_3$ and brine. Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 1/2) yielded **59** (0.80 g, 90 %) as slightly greenish solid. $^1H$ NMR ($CDCl_3$): δ 1.35 (s, 54 H, $CCH_3$), 1.42 (s, 9 H, $CCH_3$), 1.76 (m, 8 H, $CH_2$), 1.93 (m, 4 H, $CH_2$), 2.62 (m, 12 H, $CH_2Ph$), 3.07 (q, 2 H, $CH_2NH$), 3.18 (q, 6 H, $CH_2NH$), 3.41 (q, 4 H, $CH_2NH$), 4.16 (t, 3 H, $\underline{CH}CH_2$), 4.37 (d, 6 H, $CH_2O$), 4.55 (s, 2 H, $CH_2O$), 5.10 (s, br, 3 H, NH), 6.94 (s, 1 H, ArH), 6.98 (s, 2 H, ArH), 7.13 (s, 2 H, ArH), 7.38 (d, 9 H, ArH), 7.60 (dd, 12 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.44, 30.80, 31.33, 31.62, 32.44, 32.90, 33.48, 34.88, 39.77, 40.15,

47.28, 64.87, 67.05, 79.09, 119.20, 119.66, 121.86, 122.10, 124.68, 124.82, 127.54, 131.43, 135.15, 138.72, 141.67, 141.75, 144.09, 149.82, 156.15, 156.74, 167.78. HiRes-MALDI: 1785.08 $[M + Na]^+$. Anal. calc. for $C_{113}H_{144}N_6O_{11}$ (1762.41): C 77.01, H 8.24, N 4.77. Found: C 76.24, H 8.25, N 4.59.

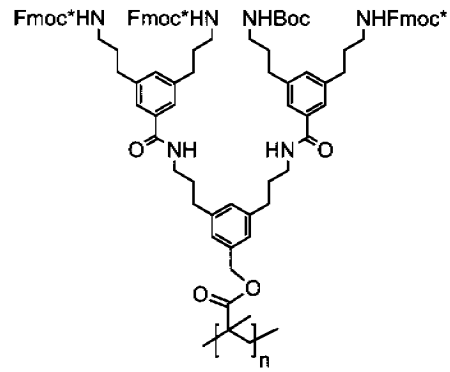
**3-(3-{3-[3-(2,7-Di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate (60)**




According to procedure A: MAC (0.05 mL) in $CH_2Cl_2$ (5 mL) was added to a solution of compound **59** (0.55 g, 0.30 mmol), DIEA (0.08 mL) and DMAP (10 mg) in $CH_2Cl_2$ (15 mL). Chromatographic separation (silica gel, hexane/ EtOAc: v/v: 1/2) yielded **60** (0.50 g, 87 %) as slightly greenish solid. $^1H$ NMR ($CDCl_3$): δ 1.36 (s, 54 H, $CCH_3$), 1.41 (s, 9 H, $CCH_3$), 1.76 (m, 8 H, $CH_2$), 1.93 (m, 4 H, $CH_2$), 1.98 (s, 3 H, $CH_3$), 2.58 (m, 12 H, $CH_2Ph$), 3.01 (q, 2 H, $CH_2NH$), 3.14 (q, 6 H, $CH_2NH$), 3.41 (q, 4 H, $CH_2NH$), 4.16 (t, 3 H, $\underline{CH}CH_2$), 4.37 (d, 6 H, $CH_2O$), 4.84 (s, br, 1 H, NH), 5.01 (s, 2 H, $CH_2O$), 5.48 (s, 1 H, $CH_2$=), 6.12 (s, 1 H, $CH_2$=), 6.94 (s, 4 H, ArH), 7.06 (s, 2 H, ArH), 7.39 (d, 6 H, ArH), 7.41 (s, 2 H, ArH), 7.60 (dd, 12 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 18.30, 28.44, 30.80, 31.33, 31.62, 32.44, 32.90, 33.48, 34.88, 39.77, 40.15, 47.28, 64.87, 67.02, 119.19, 121.81, 124.68, 124.90, 128.43, 131.51, 134.94, 136.30, 141.99, 142.04, 144.02, 149.73, 156.16, 156.77, 167.20, 167.88. HiRes-MALDI: 1853.11 $[M + Na]^+$. Anal. calc. for $C_{117}H_{150}N_6O_{12}$ (1830.46): C 76.77, H 8.15, N 4.59. Found: C 76.35, H 8.23, N 4.40.

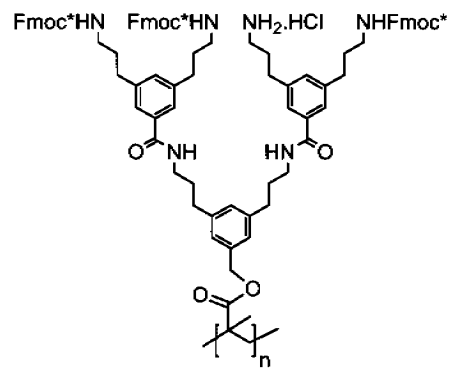
**Poly{3-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate} (61a)**

According to procedure B: monomer **60** (0.30 g) and DMF (75 μL) were used. Polymerization at 70 °C for 14 h. Chromatographic separation yielded **61a** (0.25 g, 83 %) as a slightly greenish solid. $^1H$ NMR ($CDCl_3$, 500 MHz): δ 0.92 (br, 3 H, $CH_3$), 1.28




(br, 63 H, $CCH_3$), 1.68 (br, 8 H, $CH_2$), 1.87 (br, 4 H, $CH_2$), 2.46 (br, 12 H, $CH_2Ph$), 3.05 (br, 8 H, $CH_2NH$), 3.37 (br, 4 H, $CH_2NH$), 4.02 (br, 3 H, CHCH$_2$), 4.26 (br, 6 H, $CH_2O$), 4.86 (br, 4 H, NH), 7.01 (br, 5 H, ArH), 7.25 (br, 6 H, ArH), 7.49 (br, 16 H, ArH). $^{13}C$ NMR ($CDCl_3$, 500 MHz): δ 28.58, 31.29, 31.71, 32.78, 34.88, 40.08, 40.64, 47.50, 67.26, 79.80, 119.27, 121.58, 121.90, 124.72, 125.15, 131.43, 135.21, 138.77, 141.99, 144.24, 145.05, 149.86, 156.24, 156.81157.58, 168.65.

**Poly{3-(3-{3-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino]-5-[3-(amino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(2,7-di-*tert*-butyl-9-fluorenylmethoxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate x HCl} (61b)**

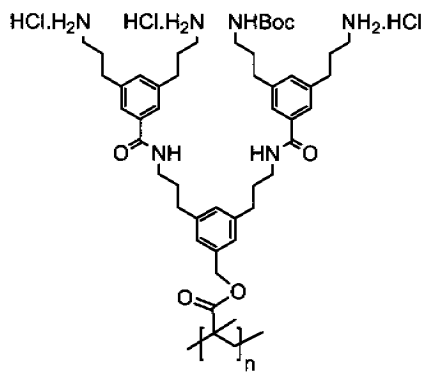



According to procedure C: 25 % HCl (0.3 mL), THF (10 mL) and **61a** (0.10 g) were used. Evaporation of the solvent yielded **61b** (80 mg, 85 %) as slightly greenish solid. $^1H$ NMR (d-DMF, 500 MHz): δ 0.78 (br, 3 H, $CH_3$), 1.26 (br, 54 H, $CCH_3$), 1.77 (br, 6 H, $CH_2$), 1.92 (br, 4 H, $CH_2$), 2.02 (br, 2 H, $CH_2$), 2.58 (br, 12 H, $CH_2Ph$), 2.87 (br, 2 H, $CH_2NH$), 3.10 (br, 6 H, $CH_2NH$), 3.29 (br, 4 H, $CH_2NH$), 4.10 (br, 3 H, CHCH$_2$), 4.26 (br, 6 H, $CH_2O$), 7.04 (br, 6 H, ArH), 7.32 (br, 6 H, ArH), 7.61 (br, 15 H, ArH). $^{13}C$ NMR (d-DMF, 500 MHz): δ 28.49, 30.84, 31.39, 32.14, 34.66, 39.27, 40.53, 47.33, 66.66, 119.39, 122.16, 124.71, 125.16, 131.68, 134.84, 138.70, 142.24, 144.57, 149.98, 157.58, 168.70.

**Poly{3-(3-{3-[3-(amino]-5-[3-(*tert*-butyloxycarbonylamino)-propyl]-benzoyl}-amino)-propyl-5-(3-{3,5-bis-[3-(amino)-propyl]-benzoyl}-amino)-propyl-benzyl methacrylate x 3HCl} (61c)**

According to procedure D: 25 % Aqueous piperidene (2.0 mL), DMF (20 mL) and **61a** (0.10 g) were used to yield **61c** (60 mg, 85 %) as viscous oil. $^1H$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 0.82 (br, 3 H, $CH_3$), 1.35 (br, 9 H, $CCH_3$), 1.70 (br, 2 H, $CH_2$), 1.88 (br, 4 H, $CH_2$), 2.01 (br, 6 H, $CH_2$), 2.57 (br, 12 H, $CH_2Ph$), 2.92 (br, 4 H, $CH_2NH$), 3.12 (br,

2 H, $CH_2NH$), 3.30 (br, 6 H, $CH_2NH$), 4.82 (br, 2 H, $CH_2O$), 6.97 (br, 4 H, ArH), 7.48 (br, 5 H, ArH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 28.48, 30.77, 31.10, 31.98, 33.02, 39.11, 39.70, 78.73, 124.72, 125.17, 128.37, 131.48, 134.79, 140.96, 141.24, 142.21, 142.60, 157.04, 162.50, 168.70.




### 6.2.2 Compounds of Chapter 3.3

***Fluorescence measurements:***

The fluorescence measurements were performed in chloroform at room temperature using a Spex Fluorolog 2, Jobin Yvon (U.K.) with 1cm quartz cells. The intensity of the fluorescence bands was determined by measuring their area. The fluorescence intensity of the non-dansylated polymer was negligible.

(a) (b)

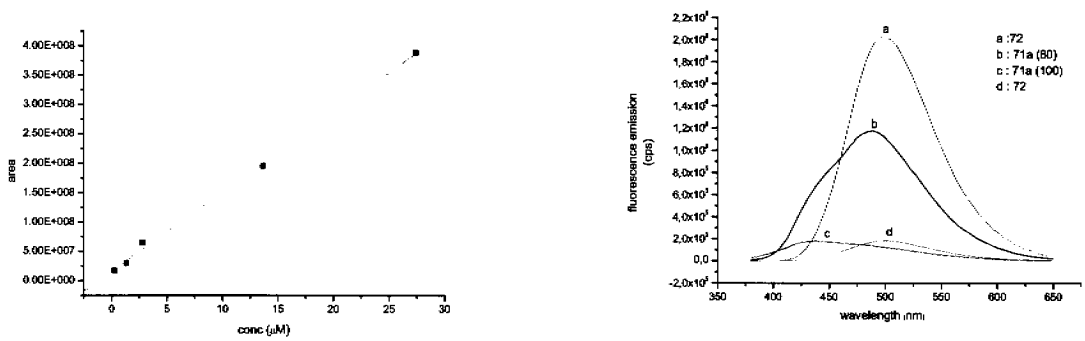



**Figure 41.** (a) Concentration of the dansylated model compound **72** in chloroform (in μM) against fluorescence intensity as obtained from signal areas at room temperature. (b) Fluorescence curves of model **72** as well as polymers **71a(100)** and **71a(80)** both after having been reacted with dansyl chloride.

In the following the procedure is delineated according to which the degrees of coverage were determined for **71a(100)** and **71a(80)**:

*A*: Area of fluorescence signal

*m*: weighed-in mass of polymer

$M_{ru}$: Molecular weight of repeating unit

*V*: Volume of chloroform solution of labelled polymer

$C_{da}$: Concentration of dansyl units in polymer

$n$: Number of mole repeating units

$n_{da}$: Number of mole dansylated repeating units

**71a (100)**: Assuming no free amine groups gives: $M_{ru}$ = 2604 g /mol. With this in 1 g/L of polymer is obtained: $n = 3.84 \times 10^{-4}$ mol. With $m$ = 1.9 mg and $V$ = 2 mL from Figure 1b is obtained: $C_{da} = 4.8 \times 10^{-7}$ M. Normalizing this value to 1g/L ($1.9 \times 10^{-3}$ g / ($2 \times 10^{-3}$), L = 0.95 g/L) it follows: $n_{da} = 4.8 \times 10^{-7}$ mol.L$^{-1}$/ 0.95 g.L$^{-1}$ = $5.05 \times 10^{-7}$ mol. With this value the ratio of dendronized over dansylated repeating units is calculated as $n/n_{da} = 3.84 \times 10^{-4}$/ ($5.05 \times 10^{-7}$) = 760. Since it will not be so that two dansyl groups are attached to the same repeat unit, this value corresponds to on average 1 dansyl unit at every 380$^{th}$ repeat unit.

**71a (80)**: Assuming that 20 % of the repeating units are dansylated gives: $M_{ru}$ = 2235 g /mol. With this in 1 g/L of polymer is obtained: $n = 4.47 \times 10^{-4}$ mol and with $m$ = 0.25 mg and, $V$ = 2 mL from Figure 1b: $C_{da} = 8.7 \times 10^{-6}$ M. Normalizing this value to 1 g/L ( $0.25 \times 10^{-3}$ g / ($2 \times 10^{-3}$), L = 0.125 g/L) it follows: $n_{da} = 8.7 \times 10^{-6}$ mol.L$^{-1}$ / 0.125 g.L$^{-1}$ = $6.96 \times 10^{-5}$ mol. From this value the ratio of dendronized over dansylated repeating units is calculated as $n/n_{da} = 4.47 \times 10^{-4}$ / ($6.96 \times 10^{-5}$) = 6.4 which corresponds to on average 1 dansyl unit every 3.2 repeat units.

***Scanning force microscopy***:

For SFM sample preparation, dendronized polymers were either directly spin-coated from chloroform solution onto highly oriented pyrolytic graphite (HOPG) or spin-coated onto pre-coated HOPG (monolayer of $C_{23}H_{47}COOH$ or $C_{12}H_{25}NH_2$). For direct deposition of dendronized polymers onto HOPG, dendronized polymers (10µL) dissolved in chloroform (c=0.5mg/mL) was spin-coated at 50 rps onto freshly cleaved HOPG and dried under ambient conditions for half an hour for subsequent SFM investigation.

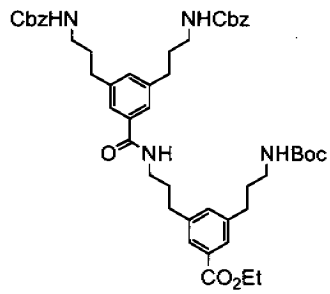
For deposition of dendronized polymers onto pre-coated HOPG, in a first step a solution of $C_{23}H_{47}COOH$ or $C_{12}H_{25}NH_2$ (10µL, Sigma Aldrich) in chloroform (0.1 mg/mL) was spin-coated at 50 rps onto freshly cleaved HOPG to yield a monolayer. The sample was dried for half an hour under ambient conditions. In a second step, dendronized polymer (10 µL) dissolved in chloroform (0.04 mg/mL) was spin-coated at 50 rps onto the pre-coated HOPG. The result is an incomplete

monolayer of individual strands of dendronized polymers. The sample was dried for half an hour before SFM imaging and manipulation.

As every step in manipulation requires verification of the resulting object position and shape, that is, position and conformation of the dendronized polymer, a complete global image had to be recorded; this procedure slowed down the overall manipulation process. To bypass this problem a fast object-tracking procedure was integrated into the SFM-setup, in which only the small area of interest (dashed, white square in Figure 34) was scanned with lower resolution than the global image, but with the same tip velocity. A global SFM-image of 512x512 pixels was recorded in several minutes, whereas local fast object-tracking with a resolution of, for example, 64x64 pixels gave the topographic result on a time scale of a few seconds, thus significantly speeding up the manipulation process.

During manipulation in the contact mode, the SFM tip was moved with a velocity of 500nm/s, whereas the deflection was kept constant at 10nm, which corresponds to a normal Force of about 20nN.

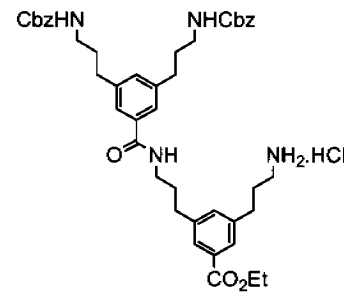
**Ethyl 3-{3,5-bis-[3-(benzyloxycarbonylamino)-propyl]benzoylamino}-5-[3-(*tert*-butyloxycarbonylamino)-propyl]benzoate (64)**




N-Hydroxybenzotriazole (0.30 g, 2.28 mmol) was added to a solution of **26d** (1.10 g, 2.18 mmol) in $CH_2Cl_2$ (60 mL). After 10 min at -30 °C, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.46 g, 2.38 mmol) was added. The mixture was stirred until the hydrochloride had dissolved (~ 3 h). Then a solution of **41a** (0.59 g, 1.83 mmol) and $Et_3N$ (1.03 mL, 7.33 mmol) in $MeOH/CH_2Cl_2$ (10 mL, 1/1) was added dropwise at -20 °C. The mixture was warmed to r.t. and stirred over night. It was then washed with sat. $NaHCO_3$ (50 mL), brine (50 mL), and dried over $MgSO_4$. Chromatographic separation (silica gel, EtOAc/hexane, v/v, 2/1) yielded **64** (1.56 g, 63 %) as a colorless foam. $^1$H NMR ($CDCl_3$): δ 1.38 (t, 3 H, $CH_3$), 1.44 (s, 9 H, $CCH_3$), 1.86 (m, 6 H, $CH_2$), 2.00 (m, 2 H, $CH_2$), 2.64 (m, 6 H, $CH_2Ph$), 2.74 (t, 2 H, $CH_2Ph$), 3.13 (m, 6 H, $CH_2NH$), 3.45 (q, 2 H, $CH_2NH$), 4.38 (q, 2 H, $OCH_2$), 4.75 (s, br, 1 H, NH), 5.06 (s, 4 H, $OCH_2Ph$), 5.12 (s, br, 2 H, NH), 6.89 (s, br, 1 H, NH), 7.09 (s, 1 H, ArH), 7.22 (s, 1 H, ArH), 7.30 (m, 10 H, ArH), 7.41 (s, 2 H, ArH), 7.68 (s, 1 H, ArH), 7.73 (s, 1H, ArH). $^{13}$C NMR ($CDCl_3$): δ 14.36, 28.43, 31.04, 31.14, 31.59, 32.38, 32.77, 33.20, 39.75,

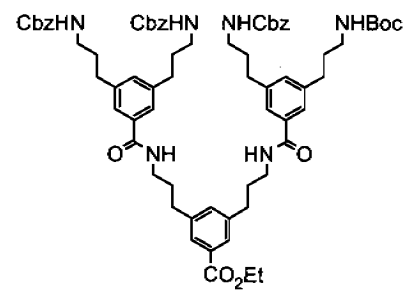
40.06, 60.96, 66.63, 79.22, 124.87, 127.17, 127.18, 127.99, 128.09, 128.51, 131.65, 133.20, 134.93, 136.56, 141.68, 142.04, 142.07, 156.06, 156.58, 1.66.81, 167.91. ESI-MS 873 $[M + Na]^+$. Anal. calc. for $C_{49}H_{62}N_4O_9$ (851.04): C, 69.15, H, 7.34, N, 6.58. Found: C 69.24, H 7.49, N 6.56.

**Ethyl-3-{3,5-bis-[3-(benzyloxycarbonylamino)-propyl]benzoylamino}-5-(3-amino)-propylbenzoate (65)**




Aqueous 25 % HCl (0.75 mL, 5 equiv) in THF (3 mL) was added slowly to a solution of **64** (0.98 g, 1.15 mmol) in THF (25 mL) at 0 °C. The mixture was stirred for 3 h. The solvent was evaporated at r.t. to yield **65** as viscous oil (0.87 g, 96 %). The product was used for the next step without further purification and structural analysis.

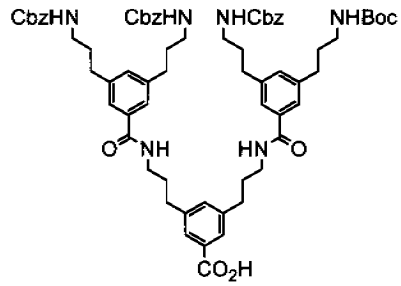
**Ethyl-3-(3-{3,5-bis-[3-(benzyloxycarbonylamino)propyl]-benzoylamino}-propyl)-5-(3-{3-[3-(benzyloxycarbonylamino)-propyl]-5-[3-(*tert*-butyloxy carbonylamino)-propyl]-benzoylamino}-propyl)-benzoate (66)**




N-Hydroxybenzotriazole (90 mg, 0.66 mmol) was added to a solution of **28b** (0.30 g, 0.63 mmol) in $CH_2Cl_2$ (20 mL) at r.t. After 10 min at -30 °C, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimid hydrochloride (0.13 g, 0.68 mmol) was added and the mixture stirred for 3 h. Then a solution of **65** (0.40 g, 0.51 mmol) and $Et_3N$ (0.57 mL, 4.1 mmol) in $MeOH/CH_2Cl_2$ (15 mL, 1/1) was added dropwise at -20 °C. The resulting mixture was warmed to r.t. and stirred for 14 h. It was then washed with brine (40 mL) and sat. $NaHCO_3$ (40 mL). The organic phase was dried over $MgSO_4$ and the solvent removed in vacuum. Chromatographic separation (silica gel, EtOAc/hexane, v/v, 3/1) yielded **66** (0.48 g, 78 %) as a colorless foam. $^1H$ NMR ($CDCl_3$): δ 1.37 (t, 3 H, $CH_3$), 1.43 (s, 9 H, $CCH_3$), 1.75 (m, 8 H, $CH_2$), 1.97 (m, 4 H, $CH_2$), 2.58 (m, 8 H, $CH_2Ph$), 2.69 (m, 4 H, $CH_2Ph$), 3.08 (q, 2 H, $CH_2NH$), 3.13 (q, 6 H, $CH_2NH$), 3.42 (t, 4 H, $CH_2NH$), 4.33 (q, 2 H, $CH_2$), 5.05 (s, 6 H, $OCH_2Ph$), 6.85 (s, br, 2 H, NH ), 7.05 (s, 2 H, ArH), 7.25 (s, 2 H, ArH), 7.30 (m, 15 H, ArH), 7.38 (s, 3 H, ArH), 7.70 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 14.73, 28.43, 30.66, 31.01, 32.35, 32.95, 39.42, 40.05, 66.64, 79.24,

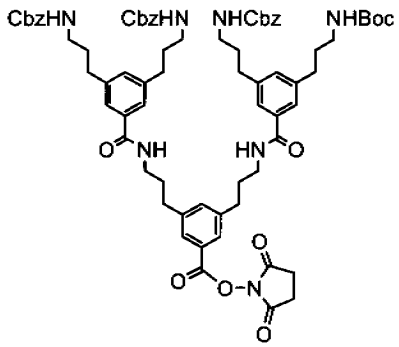
124.86, 125.17, 127.88, 128,04, 128.11, 128.52, 136.56, 141.65, 141.99, 156.55, 162.23, 168.77. ESI-MS 1226 $[M + Na]^+$ Anal. calc. for $C_{47}H_{60}N_4O_8$ (1203.46): C, 69.86, H, 7.20, N, 6.98. Found: C 69.66, H 7.12, N 7.02.

**3-(3-{3,5-Bis-[3-(benzyloxycarbonylamino)propyl]-benzoylamino}-propyl)-5-(3-{3-[3-(benzyloxycarbonylamino)-propyl]-5-[3-(*tert*-butyloxy carbonylamino)-propyl]-benzoylamino}-propyl)-benzoic acid (67a)**




Compound **66** (0.39 g, 0.32 mmol) was heated with KOH pellets (0.07 g, 1.24 mmol) in THF/MeOH/$H_2O$ (24 mL, 2/3/1) at 55 °C for 6 h. After the reaction was finished (TLC), water (3 mL) and then acetic acid was added until pH = 5 was reached. The solvent was evaporated and the G2-acid **67a** extracted with $CH_2Cl_2$. The organic phase was dried over $MgSO_4$. After evaporation of the solvent, 0.33 g (87 %) of the acid **67a** were obtained as a white solid. $^1$H NMR ($CDCl_3$): δ 1.42 (s, 9 H, $CCH_3$), 1.75 (m, 8 H, $CH_2$), 1.88 (m, 4 H, $CH_2$), 2.57 (m, 8 H, $CH_2Ph$), 2.70 (m, 4 H, $CH_2Ph$), 3.07 (t, 2 H, $CH_2NH$), 3.14 (q, 6 H, $CH_2NH$), 3.34 (t, 4 H, $CH_2NH$), 5.01 (s, 6 H, $OCH_2Ph$), 5.15 (s, br, 2 H, NH), 6.83 (s, 1 H, ArH), 7.04 (s, 2 H, ArH), 7.27 (m, 19 H, ArH), 7.73 (s, 2 H, ArH),. $^{13}$C NMR ($CDCl_3$): δ 28.39, 31.23, 31.29, 32.58, 33.16, 39.72, 40.14, 66.79, 125.03, 127.79, 128,15, 128.24, 128.65, 131.84, 134.55, 135.59, 136.64, 141.93, 142.96, 156.87, 175.80. ESI-MS 1198 $[M + Na]^+$.

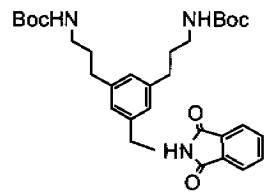
**3-(3-{3,5-bis-[3-(benzyloxycarbonylamino)propyl]-benzoylamino}-propyl)-5-(3-{3-[3-(benzyloxycarbonylamino)-propyl]-5-[3-(*tert*-butyloxy carbonylamino)-propyl]-benzoylamino}-propyl)-benzoic acid 2,5-dioxo-pyrrolidin-1-yl ester (67b)**




N-Hydroxy-succinimide (46 mg, 0.39 mmol) was added to a solution of **67a** (0.33 g, 0.27 mmol) in dry $CH_2Cl_2$ (10 mL) at r.t. After 15 min, dicyclohexylcarbodiimide (85 mg, 0.41 mmol) was added at -20 °C. The resulting mixture was warmed to r.t. and stirred over night. The precipitate was filtered off and the solvent evaporated at r.t. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH v/v, 4/1) yielded **67b** (0.29 g, 83 %) as a white foam. $^1$H NMR ($CDCl_3$):

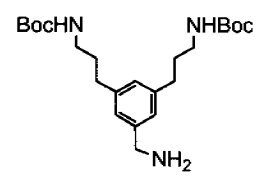
δ 1.37 (s, 9 H, $CCH_3$), 1.73 (m, 8 H, $CH_2$), 1.92 (m, 4 H, $CH_2$), 2.58 (m, 8 H, $CH_2Ph$), 2.69 (m, 4 H, $CH_2Ph$), 2.85 (s, 4 H, $CH_2$), 3.00 (t, 2 H, $CH_2NH$), 3.08 (q, 6 H, $CH_2NH$), 3.35 (t, 4 H, $CH_2NH$), 5.01 (s, 6 H, $OCH_2Ph$), 7.07 (s, 2 H, ArH), 7.27 (m, 15 H, ArH), 7.35 (s, 3 H, ArH), 7.37 (s, 2 H, ArH), 7.75 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.35, 30.66, 31.18, 32.47, 32.93, 39.49, 40.01, 66.57, 79.24, 124.90, 125.17, 127.88, 128.08, 128.51, 131.84, 134.55, 135.59, 141.93, 142.95, 157.11, 162.23, 168.77, 169.99. ESI-MS 1295 $[M + Na]^+$. Anal. calc. for $C_{72}H_{85}N_7O_{14}$(1272.62): C, 67.96, H, 6.73, N, 7.71. Found: C 67.53, H 7.05, N 7.56.

**3,5-Bis-(3-*tert*-butyloxycarbonylamino-propyl)benzyl phthalimide (68a)**




Mesyl chloride (1.77 mL, 22.8 mmol) in $CH_2Cl_2$ (5 mL) was added to a solution of **30a** (8.4 g, 19.9 mmol) and $Et_3N$ (8.5 mL, 59.7 mmol) in $CH_2Cl_2$ (150 mL) at -30 °C. The mixture was stirred at -20 °C for 2 h and regularly checked by TLC (EtOAc/hexane, 1:1) until **30a** had disappeared. The reaction was then quenched with MeOH and the solution washed four times with cold water and brine. The organic phase was dried over $MgSO_4$, the solvent evaporated at r.t. and the product dried under vacuo. The residue was then dissolved in DMF (100 mL) and potassium phthalimide (4.05 g, 21.8 mmol) added at r.t. The mixture was stirred over night at 100 °C. DMF was then evaporated, the mixture dissolved in $CH_2Cl_2$ (70 mL), washed with 0.5 M NaOH, sat. brine, sat. $NaHCO_3$ and, finally, dried over $MgSO_4$. Chromatographic separation (silica gel, EtOAc/ hexane, 1:1) yielded **68a** (10 g, 91 %) as a pale solid. $^1H$ NMR ($CDCl_3$): δ 1.44 (s, 18 H, $CH_3$), 1.78 (m, 4 H, $CH_2$), 2.58 (t, 4 H, $ArCH_2$), 3.14 (m, 4 H, $NHCH_2$), 4.66 (s, br, 2 H, NH), 4.79 (s, 2 H, $CH_2$), 6.92 (s, 1 H, ArH), 7.08 (s, 2 H, ArH), 7.72 (m, 2 H, ArH), 7.85 (m, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 28.43, 31.64, 32.88, 40.13, 41.57, 79.04, 94.71, 123.36, 126.38, 128.06, 132.14, 133.96, 136.54, 142.21, 156.00, 168.06. ESI-MS 574 $[M + Na]^+$. Anal. calc. for $C_{47}H_{60}N_4O_8$ (551.67): C, 67.49, H, 7.49, N, 7.62. Found: C 67.54, H 7.50, N 7.57.

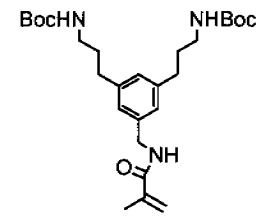
**3,5-Bis-(3-*tert*-butyloxycarbonylamino-propyl)benzyl amine (68b)**




Hydrazine hydrate (2.64 mL, 54.3 mmol) was added to a solution of **68a** (10 g, 18.1 mmol) in THF/EtOH (80 mL, 1/1). The mixture was stirred at 60 °C for 6 h. After the reaction was finished (TLC),

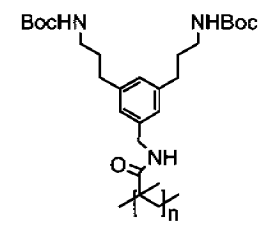
the solvent was evaporated. The precipitate was then dissolved in $CH_2Cl_2$, washed with 0.5 M NaOH, and sat. brine. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH/$Et_3N$, 100:10:1) yielded **68b** (6.66 g, 87 %) as a yellowish oil. $^1$H NMR ($CDCl_3$): δ 1.45 (s, 18 H, $CH_3$), 1.77 (m, 4 H, $CH_2$), 2.60 (t, 4 H, $ArCH_2$), 3.14 (q, 4 H, $NHCH_2$), 3.89 (s, 2 H, $CH_2NH$), 4.79 (s, br, 2 H, NH), 6.92 (s, 1 H, ArH), 6.98 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.44, 31.67, 31.89, 32.96, 40.13, 46.41, 79.05, 124.83, 127.00, 141.96, 143.53, 156.00. ESI-MS 422 $[M + Na]^+$.

**3,5-Bis-(3-*tert*-butyloxycarbonylamino-propyl)benzyl methacrylamide (69)**




Methacryloyl chloride (2.05 mL, 21.2 mmol) in $CH_2Cl_2$ (4 mL) was added dropwise to a solution of **68b** (7.45 g, 17.7 mmol) and $Et_3N$ (3.72 mL, 26.5 mmol) in $CH_2Cl_2$ (60 mL) at -30 °C. The mixture was stirred at -20 °C for 30 min and monitored by TLC (EtOAc/hexane, 1/1) until **68b** had disappeared. The reaction was then quenched with MeOH. The solution was washed with sat. brine and sat. $NaHCO_3$. The organic phase was dried over $MgSO_4$ and the solvent evaporated at r.t. Chromatographic separation (silica gel, EtOAc/ hexane, 1:1) was done twice to yield **69** (7.95 g, 92 %) as a white solid. $^1$H NMR ($CDCl_3$): δ 1.45 (s, 18 H, $CH_3$), 1.77 (m, 4 H, $CH_2$), 1.98 (s, 3 H, $CH_2$), 2.60 (t, 4 H, $ArCH_2$), 3.14 (q, 4 H, $NHCH_2$), 4.45 (d, 2 H, NH), 4.69 (s, br, 2 H, NH), 5.35 (s, 1H, CH), 5.75 (s, 1H, CH), 6.26 (t, 1 H, NH), 6.93 (s, 1 H, ArH), 6.94 (s, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ 18.76, 28.43, 31.62, 32.85, 40.02, 43.74, 79.09, 119.67, 125.73, 127.76, 138.45, 139.95, 142.21, 156.00, 168.24. ESI-MS 512 $[M + Na]^+$. Anal. calc. for $C_{27}H_{43}N_3O_5$ (489.65): C, 66.23 H, 8.85, N, 8.58. Found: C 65.95, H 8.87, N 8.49.

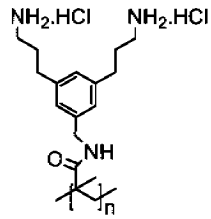
**Poly[3,5-bis-(3-*tert*-butyloxycarbonylamino-propyl)benzylmethacryl amide] (70a)**




To a Schlenk tube containing monomer **69** (0.60 g, 1.22 mmol) was added a solution of DBPO (0.47 mg, 0.16 mol-%) in DMF (0.2 mL). If the monomer did not completely dissolve, somewhat more DMF was added until a homogeneous solution was achieved which was then concentrated up to approximately the initial amount of DMF by evacuation with visible inspection. An exact concentration can therefore not be given for all polymerizations. The resulting mixture was

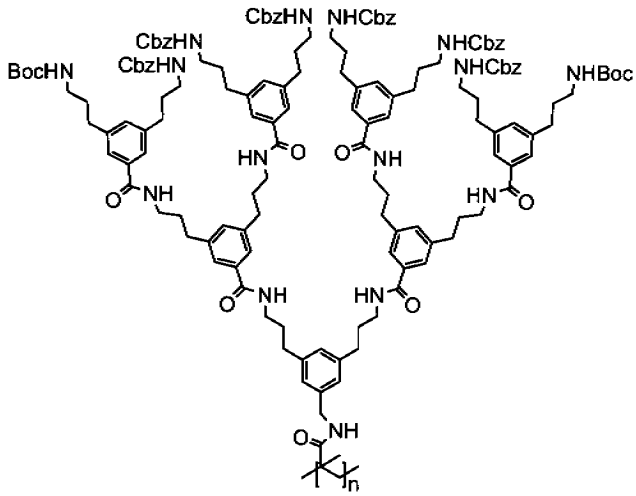
degassed several times by freeze-pump-thaw cycles. Then it was kept at 70 °C for 18 h. After polymerization, the polymer was dissolved in $CH_2Cl_2$ and purified by column chromatography (silica gel, $CH_2Cl_2$ as eluent) to yield **70a** (0.42 g, 70 %) as a colorless foam. $^1$H NMR ($CDCl_3$): δ 0.85 (br, $CH_3$), 1.45 (br, $CH_3$), 1.85 (br, $CH_2$), 2.55 (br, $ArCH_2$), 3.11 (br, $NHCH_2$), 4.05 (br, $CH_2CH_3$), 5.35 (br, NH), 6.94 (br, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.45, 31.62, 32.85, 40.02, 41.24, 79.09, 125.73, 127.76, 138.45, 139.95, 142.21, 158.00, 168.24. Anal. calc. for $(C_{27}H_{43}N_3O_5)_n$ $(489)_n$: C, 66.23, H, 8.85, N, 8.58. Found: C 65.63, H 9.01, N 8.33.

**Poly [3,5-bis-(3-amino-propyl)benzylmethacrylamide x 2 HCl] (70b)**




To a solution of **70a** (0.30 g, 0.61 mmol) in THF (6 mL) was added dropwise aqueous 25 % HCl (0.95 mL, 6 eq. per Boc group) in THF (2 mL) at 0 °C. The mixture was stirred for 14 h. Evaporation of the solvent at r.t. yielded **70b** (0.21 g, 96 %) as a colorless solid. $^1$H NMR ($CD_3OD$): δ 0.85 (br, $CH_3$), 1.85 (br, $CH_2$), 2.55 (br, $ArCH_2$), 3.11 (br, $NHCH_2$), 4.05 (br, $CH_2CH_3$), 6.94 (br, ArH). $^{13}$C NMR ($CD_3OD$): δ 19.18, 32.55, 39.61, 126.60, 127.61, 139.18, 141.38, 168.24.

**Poly{3,5-bis-[3-(3-{3-[3,5-bis(3-{benzyloxyamino}propyl)benzoylamino] propyl}-5-{3-[3-(3-{benzyloxyamino}propyl)-5-(3-{*tert*-butyloxyamino} propyl)benzoylamino]propyl}benzoylamino)propyl]benzylmethacrylamide} (71a)**

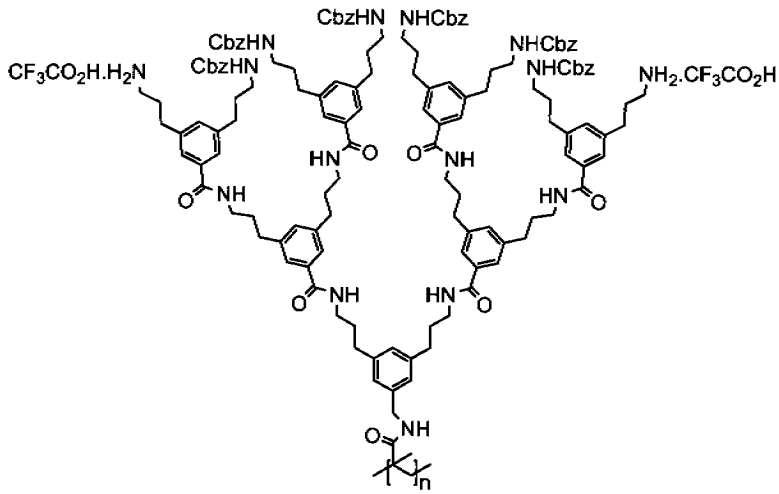



To a solution of **70b** (20 mg, 0.055 mmol) and $Et_3N$ (0.05 mL) in $MeOH/CH_2Cl_2$ (5 mL, 2/1) was added dropwise a solution of **67b** (0.25 g, 1.5 equiv. per amine group) in $CH_2Cl_2$ (6 mL) at -20 °C. The mixture was stirred at r.t. for 18 h. The solvent was evaporated and then another portion of **67b** (25 mg) and $Et_3N$ (0.05 mL) in $CH_2Cl_2$ (3 mL) was added and the mixture stirred for further 12 h. The polymeric product was then washed with brine, the solvent evaporated and purified three times by dissolving it into $CHCl_3$ followed

by precipitation into EtOAc/hexane(1/1) until all excess of **67b** had been completely removed. This furnished **71a** (0.13 g, 74 %) as a colorless solid.
$^1$H NMR ($CDCl_3$): δ 1.35 (br, $CH_3$), 1.65 (br, $CH_2$), 2.35 (br, $ArCH_2$), 2.89 (br, $NHCH_2$), 4.85 (br, $CH_2$), 6.21 (br, NH), 6.94 (br, ArH), 7.11 (br, ArH), 7.28 (br, ArH). $^{13}$C NMR ($CDCl_3$): δ 28.23, 31.42, 32.95, 40.58, 66.69, 79.29, 125.27, 128.03, 128.25, 128.73, 132.08, 135.05, 137.15, 142.41, 157.06, 157.50, 168.86.

**Poly{3,5-bis-[3-(3-{3-[3,5-bis(3-{benzyloxyamino}propyl)benzoylamino] propyl}-5-{3-[3-(3-{benzyloxyamino}propyl)-5-(3-{amino}propyl)benzoyl amino]propyl}benzoylamino)propyl]benzylmethacrylamide x 2 $CF_3COO$ H} (71b)**

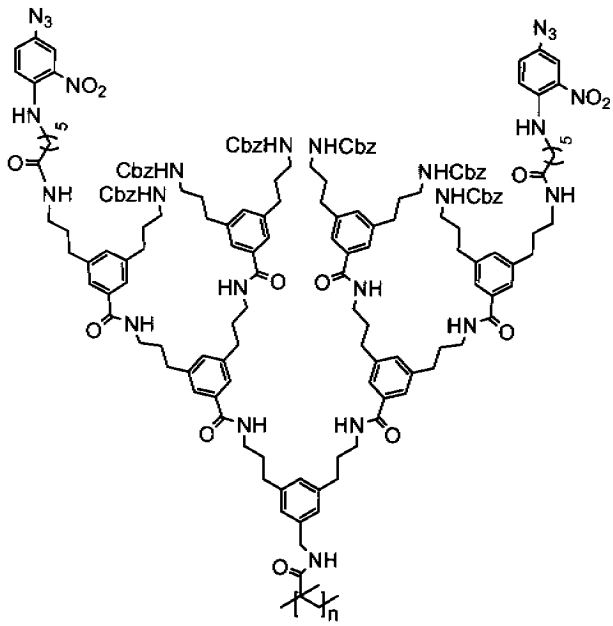
To a solution of **71a** (50 mg, 0.019 mmol) in $CH_2Cl_2$ (3 mL) was slowly added a solution of $CF_3COOH$ (0.11 mL, excess) in $CH_2Cl_2$ (2 mL) at 0 °C. The mixture was stirred for 14 h and then the solvent evaporated at r.t. The polymer was purified by dissolving it in $CHCl_3$ followed by precipitation into EtOAc/hexane (1/2) to yield **71b** (45 mg, 90 %) as slightly yellow solid. $^1$H NMR ($CDCl_3/CD_3OD$): δ 1.65 (br, $CH_2$), 2.40 (br, $ArCH_2$), 2.94 (br, $NHCH_2$), 4.85 (br, $CH_2$), 6.94 (br, ArH), 7.11 (br, ArH), 7.28 (br, ArH).




**Poly{3,5-bis-[3-(3-{3-[3,5-bis(3-{benzyloxyamino}propyl)benzoylamino] propyl}-5-{3-[3-(3-{benzyloxyamino}propyl)-5-(3-{6-(4-azido-2-nitroanilino )hexanoylamino}propyl)benzoyl amino]propyl}benzoylamino) propyl] benzylmethacrylamide} (71c)**

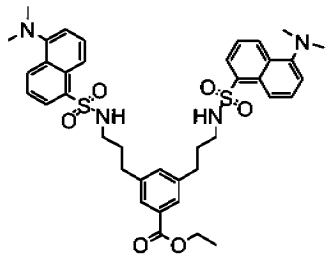
To a solution of **71b** (17 mg, 0.0065 mmol) and $Et_3N$ (0.01 mL) in $CH_2Cl_2$ (2 mL) was added dropwise a solution of N-succinimidyl-6-(4-azido-2-nitroanilino)hexanoate (7.5 mg, 3 eq. per repeating unit) in $CH_2Cl_2$ (2 mL) at -20 °C in the dark. The mixture was stirred for 14 h and the solvent evaporated. The polymer was dissolved in $CHCl_3$ and precipitated into EtOAc/hexane (1:2) to yield **71c** (16 mg, 85 %) as a slightly red

colored solid. $^1$H NMR ($CDCl_3/CD_3OD$): δ 1.55 (br, $CH_2$), 1.75 (br, $CH_2$), 2.01 (br, $CH_2$), 2.40 (br, $ArCH_2$), 2.55 (br, CH2), 2.94 (br, $NHCH_2$), 3.05 (br, $NHCH_2$), 4.85 (br, $CH_2$), 6.7 (br, ArH), 6.95 (br, ArH), 7.11 (br, ArH), 7.55 (br, ArH). IR: ν = 2118 cm$^{-1}$



***Dansylated model compound 72 and polymers 71a(80) and 71a(100):***

**Ethyl-3,5-bis-[3-(5-dimethylamino-1-naphthalinesulfonamide)-propyl]benzoate (72)**



Dansyl chloride (0.13 g, 0.48 mmol) in $CH_2Cl_2$ (4 mL) was added dropwise to a solution of **42a** (68 mg, 0.20 mmol) and $Et_3N$ (0.34 mL, 12 equ.) in $CH_2Cl_2$/ MeOH (15 mL, 2/1) at -30 °C. The mixture was stirred at -30 °C for 20 min and monitored by TLC ($CH_2Cl_2$/ MeOH/ $Et_3N$, 100/10/1) until **42a** had disappeared. The reaction was then quenched with MeOH. The solution was washed with sat. brine and sat. $NaHCO_3$. The organic phase was dried over $MgSO_4$ and the solvent evaporated. Chromatographic separation (silica gel, EtOAc/ hexane, 1:2) was done to yield **72** (0.14 g, 96 %) as a yellowish solid. $^1$H NMR ($CDCl_3$): δ = 1.38 (t, 3 H, $CH_3$), 1.68 (m, 4 H, $CH_2$), 2.48 (t, 4 H, $ArCH_2$), 2.88 (s, 12 H, $CH_3$), 2.92 (q, 4 H, $NHCH_2$), 4.35 (q, 2 H, $CH_2$), 5.26 (t, 2 H, $NHCH_2$), 6.85 (s, 1 H, ArH), 7.16 (s, 1 H, ArH), 7.18 (s, 1 H, ArH), 7.52 (m, 12 H, ArH), 8.24 (d, 2 H, ArH), 8.35 (d, 2 H, ArH), 8.52 (d, 2 H, ArH). $^{13}$C NMR ($CDCl_3$): δ = 14.23, 31.05, 32.25, 42.61, 45.42, 60.95, 115.22, 118.79, 123.24, 127.01, 128.46, 129.61, 129.64, 129.86, 130.42, 130.65, 133.16, 134.80, 141.42, 152.00, 166.68. ESI-MS 752.8 $[M+Na]^+$. Anal. calc. for $C_{39}H_{46}N_4O_6S_2$ (730.81): C, 64.09, H, 6.34, N, 7.66. Found: C 64.05, H 6.49, N 7.51.

**71a (80)**

Dansyl chloride (5.50 mg, 20.00 μmol) in $CH_2Cl_2$ (2 mL) was added dropwise to a solution of **71a (80)** (15 mg, 6.71 μmol) and $Et_3N$ (21 μL, 12 equ.) in $CH_2Cl_2$ (4 mL) at -30 °C. The mixture was stirred at -10 °C for 2 h. The reaction was then quenched with MeOH. The solvent was evaporated and the polymer was purified by dissolving it in $CHCl_3$ followed by precipitation into EtOAc/hexane (1/2), and also by dissolving it in DMSO followed by precipitation into ethyl ether. This procedure was done several times till the bluish color on the TLC had disappeared. Compound **71a (80)** (11 mg) was produced as a greenish solid.

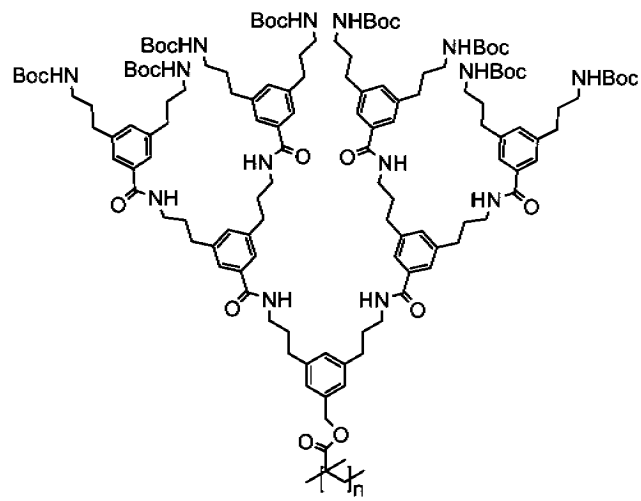
**71a (100)**

Dansyl chloride (5.00 mg, 18.5 μmol) in $CH_2Cl_2$ (2 mL) was added dropwise to a solution of **71a** (10 mg, 3.84 μmol) and $Et_3N$ (10 μL, excess) in $CH_2Cl_2$ (2 mL) at -30 °C. The mixture was stirred at -10 °C for 2 h. The reaction was then quenched with MeOH. The solvent was evaporated and the polymer was purified by dissolving it in $CHCl_3$ followed by precipitation into EtOAc/hexane (1/2), and also by dissolving it in DMSO followed by precipitation into ethyl ether. This procedure was done several times till the bluish color on the TLC had disappeared. Compound **12a (100)** (8 mg) was produced as a slightly grey solid.

### 6.2.3 Compounds of Chapter 3.4

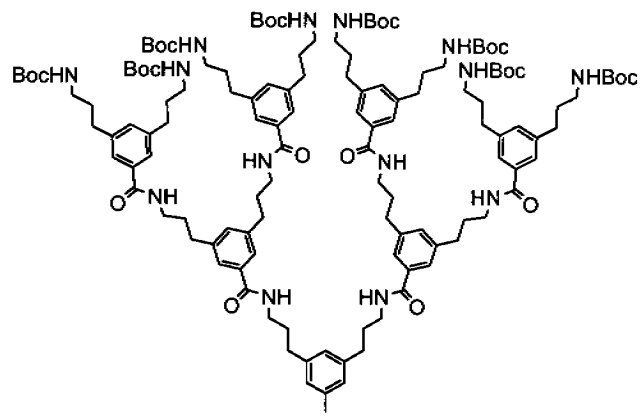
**Poly (3,5-bis-{3-[3,5-bis-(3-{3,5-bis(tert-butyloxyamino-propyl)-benzoylamino}-propyl)-benzoylamino]-propyl}-benzyl methacrylate) (73)**

A solution of **76** (0.04 g, 0.1 mmol) and $Et_3N$ (0.23 mL) in MeOH (5 ml) was added dropwise to a solution of **75b** (0.23 g, 0.2 mmol, 1.75 equiv. per amine group) in $CH_2Cl_2$/MeOH (15 mL) at -20 °C. The mixture was stirred at r.t. for 48 h. The solvent was evaporated and then another portion of **75b** (0.03 g, 0.03 mmol) and $Et_3N$ (0.20 mL) in



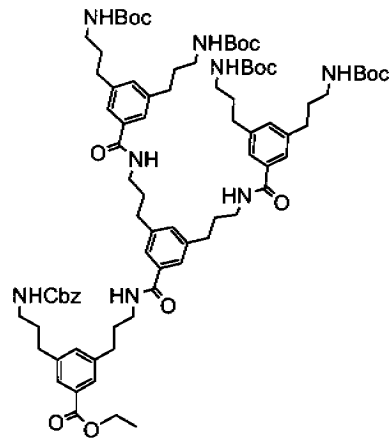
DMF (10 mL) was added and the mixture stirred for further 12 h. The polymeric product was then washed with brine, the solvent was evaporated and the crude product was purified 3 times by dissolving it into $CHCl_3$ followed by precipitation into EtOAc/hexane (1/1) until all excess of **75b** had been completely removed. This furnished **73** (0.25 g, 93%) as a colorless solid. $^1$H NMR ($CDCl_3$, 700 MHz): δ 0.66 (br, 3 H, $CH_3$), 0.80 ( br, 2 H, $CH_2$), 1.35 (br, 72 H, $CH_3$), 1.65 (br, 28 H, $CH_2$), 2.35 (br, 28 H, $ArCH_2$), 2.89 (br, 28 H, $NHCH_2$), 4.85 (br, 10 H, $CH_2O$ + NH), 7.11 (br, 10 H, ArH), 7.28 (br, 11 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 28.23, 31.42, 32.95, 40.58, 66.69, 79.29, 125.27, 128.03, 128.25, 128.73, 132.08, 135.05, 137.15, 142.41, 157.06, 157.50, 168.86. GPC Results: Mn: 3.9 x $10^6$, PDI: 3.23

**Methyl-{3,5-bis-{3-[3,5-bis-{3-{3,5-bis(*tert*-butyloxyamino-propyl)-benzoylamino}-propyl)-benzoylamino]-propyl}-benzene (78)**



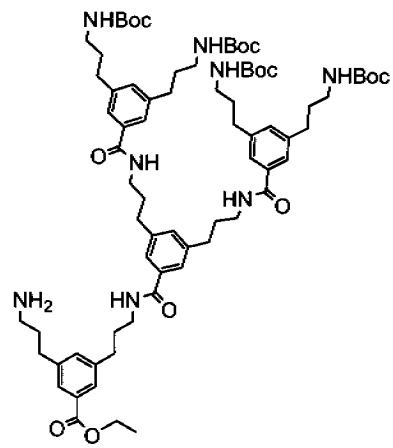

**73** (0.04 g, 0.02 mmol) was dissolved in a mixture of THF/AcOEt/ethanol (32 mL, 1/1/1). 10% formic acid (1 mL) and Pd/C (80 mg, 10% by weight) were added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. for 4 d. The product was filtered and the solvent was evaporated at r.t. the product was washed through column chromatography (silica gel, 7.5 % MeOH/$CH_2Cl_2$) to yield **78** (0.03 g, 84%) as a pale solid. $^1$H NMR ($CDCl_3$, 700 MHz): δ 1.39 (s, 72 H, CH3), 1.76 (m, 18 H, $CH_2$), 1.87 (m, 8 H, $CH_2$), 1.95 (m, 4 H, $CH_2$), 2.22 (s, 3 H, $CH_3$), 2.52 (m, 24 H, $CH_2Ph$), 2.68 (t, 4 H, $CH_2Ph$), 3.08 (q, 18 H, $CH_2NH$), 3.37 (q, 8 H, $CH_2NH$), 3.42 (q, 4 H, $CH_2NH$), 4.30 (q, 2 H, $OCH_2$), 4.21 (br, 8 H, NH), 4.78 (br, 6 H, NH), 6.82 (s, 2 H, ArH), 6.85 (s, 1 H, ArH), 7.04 (s, 2 H, ArH), 7.06 (s, 4 H, ArH), 7.36 (s, 4 H, ArH), 7.41 (s, 8 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 23.09, 28.85, 30.10, 31.15, 31.75, 32.11, 32.32, 32.87, 34.80, 37.04, 37.53, 40.03, 79.53, 125.31, 128.90, 132.07, 133.43, 135.11, 142.20, 156.57, 168.03.

**Ethyl-(3-bis-{3-[3,5-bis-(3-{3,5-bis(*tert*-butyloxyamino-propyl)-benzoylamino}-propyl)-benzoylamino]-propyl}-5-[3-(*tert*-butyloxycarbonylamino)-propyl])benzoate (80a)**




A solution of **79** (0.05 g, 0.1 mmol) and $Et_3N$ (0.12 mL) in $CH_2Cl_2$/MeOH (5 mL, 1/1) was added dropwise to a solution of **75b** (0.16 g, 0.1 mmol) in $CH_2Cl_2$ (20 mL) at -20 °C. The mixture was stirred at r.t. over night. It was then washed with brine (30 mL) and aqueous $NaHCO_3$ (30 mL). The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuum. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH, v/v, 20/1) yielded **80a** (0.14 g, 83%) as a white foam. $^1$H NMR ($CDCl_3$, 700 MHz): δ 1.32 (t, 3 H, $CH_3$), 1.38 (s, 36 H, CH3), 1.72 (m, 8 H, $CH_2$), 1.87 (m, 4 H, $CH_2$), 1.95 (m, 2 H, $CH_2$), 2.52 (t, 8 H, $CH_2Ph$), 2.59 (t, 6 H, $CH_2Ph$), 2.68 (t, 2 H, $CH_2Ph$), 3.01 (q, 8 H, $CH_2NH$), 3.11 (q, 2 H, $CH_2NH$), 3.35 (q, 4 H, $CH_2NH$), 3.43 (q, 2 H, $CH_2NH$), 4.29 (q, 2 H, $OCH_2$), 4.90 (br, 4 H, NH), 5.01 (s, 2 H, $OCH_2$), 5.38 (br, 2 H, NH), 7.03 (s, 2 H, ArH), 7.07 (s, 1 H, ArH), 7.16 (s, 1 H, ArH), 7.26 (m, 5 H, ArH), 7.38 (s, 4 H, ArH), 7.41 (s, 2 H, ArH), 7.61 (s, 1 H, ArH), 7.66 (s, 1 H, ArH). $^{13}$C NMR ($CDCl_3$, 500 MHz): δ 14.58, 28.83, 31.05, 31.37, 31.72, 32.87, 33.06, 33.20, 34.03, 39.55, 39.60, 40.00, 40.88, 66.85, 79.45, 125.28, 127.48, 127.59, 128.36, 128.39, 128.84, 131.02, 131.94, 132.02, 133.68, 135.15, 135.15, 137.07, 142.15, 142.19, 142.29, 142.53, 156.58, 156.99, 167.22, 168.37, 168.45. HR-MALDI: 1575 $[M + Na]^+$.

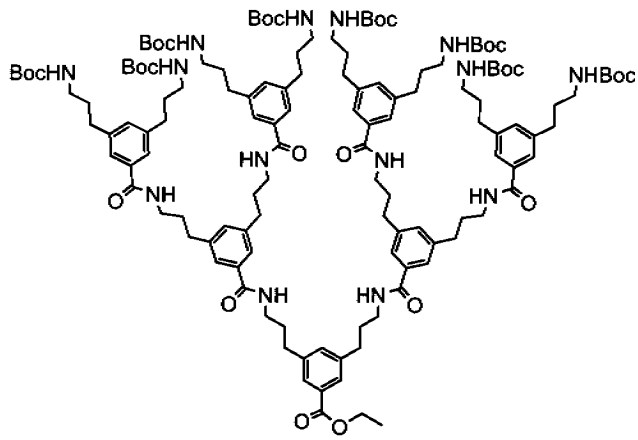
**Ethyl-(3-bis-{3-[3,5-bis-(3-{3,5-bis(*tert*-butyloxyamino-propyl)-benzoylamino}-propyl)-benzoylamino]-propyl}-5-[3-aminopropyl])benzoate (80b)**




**80a** (0.08 g, 0.055 mmol) was dissolved in a mixture of THF/ethanol (15 mL, 2/1). 10% HCOOH (0.5 mL) and Pd/C (80 mg, 10 % by weight) were added and the solution was transferred into a hydrogenation flask. The mixture was hydrogenated under 3.5 bar of $H_2$ at r.t. for 48 h. The product was filtered through celite and the solvent was evaporated at r.t to yield **80b** (60 mg, 83%) as a slightly pale solid. $^1$H NMR ($CDCl_3$/$CD_3OD$, 700

MHz): δ 1.32 (t, 3 H, $CH_3$), 1.39 (s, 36 H, CH3), 1.74 (m, 8 H, $CH_2$), 1.91 (m, 6 H, $CH_2$), 2.05 (m, 2 H, $CH_2$), 2.56 (m, 8 H, $CH_2Ph$), 2.65 (m, 8 H, $CH_2Ph$), 2.88 (q, 2 H, $CH_2NH$), 3.04 (q, 8 H, $CH_2NH$), 3.35 (q, 6 H, $CH_2NH$), 3.37 (q, 4 H, $CH_2NH$), 4.29 (q, 2 H, $OCH_2$), 4.95 (br, 4 H, NH), 7.03 (s, 2 H, ArH), 7.07 (s, 1 H, ArH), 7.25 (s, 1 H, ArH), 7.43 (s, 4 H, ArH), 7.51 (s, 2 H, ArH), 7.57 (s, 1 H, ArH), 7.63 (s, 1 H, ArH), 8.12 (br, 4 H, NH). $^{13}C$ NMR ($CDCl_3/CD_3OD$, 500 MHz): δ 14.56, 28.68, 30.68, 30.81, 31.52, 32.29, 32.89, 33.18, 34.03, 39.23, 39.60, 39.91, 79.10, 125.20, 127.53, 128.08, 131.04, 132.14, 132.28, 133.52, 134.65, 134.81, 140.74, 142.29, 142.39, 142.58, 156.92, 167.29, 169.05, 169.22.

**Ethyl-3,5-bis-{3-[3,5-bis-(3-{3,5-bis(*tert*-butyloxyamino-propyl)-benzoylamino}-propyl)-benzoylamino]-propyl}-benzoate (81)**




A solution of **42a** (15 mg, 0.05 mmol) and $Et_3N$ (0.07 mL) in $CH_2Cl_2$/MeOH (5 mL, 1/1) was added dropwise to a solution of **75b** (0.13 g, 0.1 mmol) in $CH_2Cl_2$ (15 mL) at -20 °C. The mixture was stirred at r.t. over night. It was then washed with brine (25 mL) and aqueous $NaHCO_3$ (25 mL). The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. Chromatographic separation (silica gel, $CH_2Cl_2$/MeOH, v/v, 15/1) yielded **81** (94 mg, 89%) as a white foam. $^1H$ NMR ($CDCl_3$): δ 1.30 (t, 3 H, $CH_3$), 1.38 (s, 72 H, CH3), 1.71 (m, 18 H, $CH_2$), 1.83 (m, 8 H, $CH_2$), 1.96 (m, 4 H, $CH_2$), 2.52 (m, 24 H, $CH_2Ph$), 2.68 (t, 4 H, $CH_2Ph$), 3.08 (q, 18 H, $CH_2NH$), 3.31 (q, 8 H, $CH_2NH$), 3.37 (q, 4 H, $CH_2NH$), 4.30 (q, 2 H, $OCH_2$), 4.95 (br, 8 H, NH), 7.03 (s, 6 H, ArH), 7.25 (s, 1 H, ArH), 7.36 (s, 4 H, ArH), 7.40 (s, 8 H, ArH), 7.66 (s, 2 H, ArH). $^{13}C$ NMR ($CDCl_3$): δ 14.32, 25.58, 28.49, 30.56, 30.61, 31.33, 32.50, 32.80, 32.92, 36.42, 39.26, 39.41, 39.67, 67.93, 79.10, 124.88, 124.96, 127.24, 130.68, 131.50, 131.50, 131.62, 133.43, 134.70, 141.74, 141.83, 142.04, 156.14, 166.82, 167.95, 168.03. HR-MALDI: 2397 $[M + Na]^+$.

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[100] Fmoc* is normally removed under basic conditions which leads to 2,3-di(tert-butyl)dibenzofulvene and is stable under even more acidic conditions than the once applied here. The products of an eventual decomposition under the conditions applied were not investigated but may either be the same fulvene or 2,7-di(tert-butyl)fluorenylmethanol, both of which could be easily detected by TLC and were not observed. Actually there was no low molar mass product observed at all.

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[103] During the synthesis of model compound 68 it was observed that if the reaction was performed at 0 °C, the amine were doubly dansylated to a small extent (NMR spectroscopy). This is why, under the more forceful conditions, the temperature was not elevated above -10 °C.

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# Appendix

## *Symbols and Abbreviations*

| | |
|---|---|
| Boc | *tert*-Butyloxycarbonyl |
| 9-BBN | 9-borabicyclo[3.3.1.]nonan |
| Cbz | Benzyloxycarbonyl |
| $CF_3COOH$ | Trifluoroacetic acid |
| DP | Degree of polymerisation |
| DSC | Differential scanning calorimetry |
| DCC | *N, N'*-dicyclohexylcarbodiimide |
| DBPO | Dibenzoylperoxide |
| DMF | dimethylformamide |
| DMSO | dimethyl sulphoxide |
| EA | Elemental Analysis |
| EI | Electron Ionisation (MS) |
| ESI | ElectroSpray Ionization (MS) |
| $Et_3N$ | Triethylamine |
| EDC | *N, N'*-(3-dimethylaminopropyl)-ethylcarbodiimide hydrogen chloride |
| Fmoc* | 2,7-Di(*tert*-butyl)-9-fluorenyloxycarbonyl |
| Fmoc | 9-Fluorenylmethyleneoxycarbonyl () |
| G1 | First generation |
| G2 | Second generation |
| G3 | Third generation |
| GPC | Gel permeation chromatography |
| g | gram |
| HOPG | Highly oriented pyrolitic graphite |
| HOBt | Hydroxyl-benzotriazole |
| HOSu | Hydroxyl-succinimide |
| h | hour(s) |
| HRMS | High Resolution Mass Spectrometry |
| Hz | Hertz ($sec^{-1}$ or cycles per second) |

| | |
|---|---|
| *J* | coupling constant, in Hz |
| λ | wave length |
| $LiAlH_4$ | Lithium aluminium anhydride |
| Mn | Number average molar mass |
| Mw | Weight average molar mass |
| m | multiplet (NMR) |
| M | molar |
| $[M]^+$ | molecular peak (MS) |
| MALDI | Matrix Assisted Laser Desorption/Ionization (MS) |
| MALDI-TOF | Matrix Assisted Laser Desorption/Ionization - Time Of Flight (MS) |
| *m/z* | mass-to charge ratio in mass spectrometry |
| $CH_3OH$ | methanol |
| mg | milligram |
| MHz | megaHertz $\equiv 10^6$ Hz |
| min | minute |
| ml | milliliter |
| mmol | millimol |
| MS | Mass Spectrometry |
| µl | microliter |
| nm | nanometre |
| NMR | Nuclear Magnetic Resonance |
| PG1 | First generation dendronized polymer |
| PG2 | Second generation dendronized polymer |
| PG3 | Third generation dendronized polymer |
| $Pd[PPh_3]_4$ | Tetrakis-(triphenylphosphan)-palladium |
| PDI | Polydispersity index |
| ppm | parts per million (NMR) |
| r.t. | room temperature |
| SFM | Scanning force microscopy |
| SMCC | Suzuki-Miyaura cross-coupling reaction |
| s | singlet (NMR) |
| t | triplet (NMR) |
| THF | tetrahydrofurane |
| TLC | Thin Layer Chromatography |

| | |
|---|---|
| UV | UltraViolet |
| $\delta$ | chemical shift downfield from TMS, given as ppm |

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- **Sonstige Kenntnisse**

***Sprachen*** Deutsch (gut in Wort und Schrift), Englisch (fließend), Arabisch (Muttersprache)

***EDV*** Microsoft Office (Word, Excel, Power Point, Outlook)
Chemistry Software (ChemDRAW, WinNMR, Mestrec)
Literature Software (Beilstein Crossfire, Scifinder)
Drawing (Corel Draw 11, Adope Photoshop)

- **Veröffentlichungen**

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- **Konferenzbeiträge**

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[4] *Material Science Days in ETH-Zürich*, Poster, Zürich, Schweiz, **März 2005**, und **März 2006**
[5] *American Chemical Society 228$^{th}$ National Meeting and Exposition*, Poster, Philadelphia, USA, **Aug. 2004**
[6] *20th Anniversary Meeting of Polymer Group of Switzerland*, Poster, ETH-Zürich, Zürich, Schweiz, **Nov. 2004**
[7] *SFB 448-Mesoskopisch strukturierte Verbundsysteme*, Poster, Technische Universität Berlin, Berlin, Deutschland, **März 2003**
[8] *3$^{rd}$ International Dendrimer Symposium*, Poster, Freie Universität Berlin, Berlin, Deutschland, **Sept. 2003**

- **Auszeichnungen**

[1] **Aug. 2004**, *American Chemical Society 228$^{th}$ National Meeting and Exposition*, Philadelphia, USA
"Award for Best Posters".
[2] **Sept. 2003**, *3$^{rd}$ International Dendrimer Symposium*- Freie Universität Berlin, Deutschland "Award for Best Posters".
[3] **Apr. 2002**, *Berlin Brandenburg Society for Polymer Science*
Stipendium Apr. 2002- Dec. 2002, "In recognition for excellent performance within the MSc. program in Polymer Science program".