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DENDRIMERS AND HYPERBRANCHED POLYMERS: TWO FAMILIES OF THREE-DIMENSIONAL MACROMOLECULES WITH SIMILAR BUT CLEARLY DISTINCT PROPERTIES

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ABSTRACT

Dendrimers and hyperbranched polymers are globular macromolecules that are characterized both by a highly branched structure, in which all bonds converge to a focal point or core, and a multiplicity of reactive chain-ends. Because of the obvious similarity of their building blocks, many assume that the properties of these two families of dendritic macromolecules are almost identical and that the terms "dendrimer" and "hyperbranched polymer" can be used interchangeably. This assumption is incorrect because only regular dendrimers have a precise end-group multiplicity and functionality and exhibit properties that are totally unlike those of all other families of macromolecules. For example, regular dendrimers display a maximum in the relationship between their intrinsic viscosity and molecular weight, but hyperbranched polymers do not. Because of their uniformity in shape, size, and structure, only regular dendrimers spread uniformly at the air–water interface. The chemical reactivity of the chain-ends of dendrimers as well as the inner nanoenvironment that their regularly branched structure provide are unique features of these three-dimensional globular macromolecules. However, the price that has to be paid for these special properties is one of accessibility. Today, regular dendrimers can only be prepared using rather tedious, multistep syntheses that require intermediate purifications. Though processes involving little intermediate purification have been claimed to afford "dendrimers," the molecules that are obtained have varying degrees of chemical and structural regularity and may not possess the ultimate properties of regular dendrimers. In contrast, hyperbranched polymers are easily obtained using a variety of one pot procedures, some of which mimic, but do not truly achieve, regular dendritic growth. As a result, hyperbranched polymers also exhibit fascinating properties such as low solution and melt viscosities, but these properties tend to be intermediate between those of the fully regular dendrimers and those of branched or star-shaped macromolecules.

INTRODUCTION

Since their discovery in the early 1980s by Tomalia [1], Denkewalter [2], and Newkome [3], dendrimers have attracted much interest because of their unique structural symmetry, shape, and branching pattern. These structural features have translated into discoveries of new properties, phenomena, and applications [4].

This report will not attempt to review broadly the large number of families of dendrimers and hyperbranched polymers that have been prepared over the past decade. Instead, it will first examine one family of highly regular dendrimers prepared in the author's laboratories by the convergent growth approach [5, 6], and outline some of their more unusual properties. A comparison will then be made with selected other regular dendrimers, as well as a number of less regular hyperbranched polymers that retain both a globular shape and a high end-group functionality, but have less structural regularity and a lower degree of branching.

PRECISE CONTROL OF DENDRIMER STRUCTURE BY THE CONVERGENT GROWTH APPROACH

In 1989 we pioneered an extremely versatile "convergent" route [5] to dendrimers that affords globular dendrimers of unmatched purity and provides a unique degree of control over the final placement of functional groups at their chain-ends or "periphery" [6]. Figures 1 and 2 outline the concepts that underlie the convergent growth approach [5], a synthetic strategy that is ideally suited for the preparation of uniquely functionalized molecules designed to probe some of the ultimate properties of the "dendritic state." Numerous other research groups have also used elegant

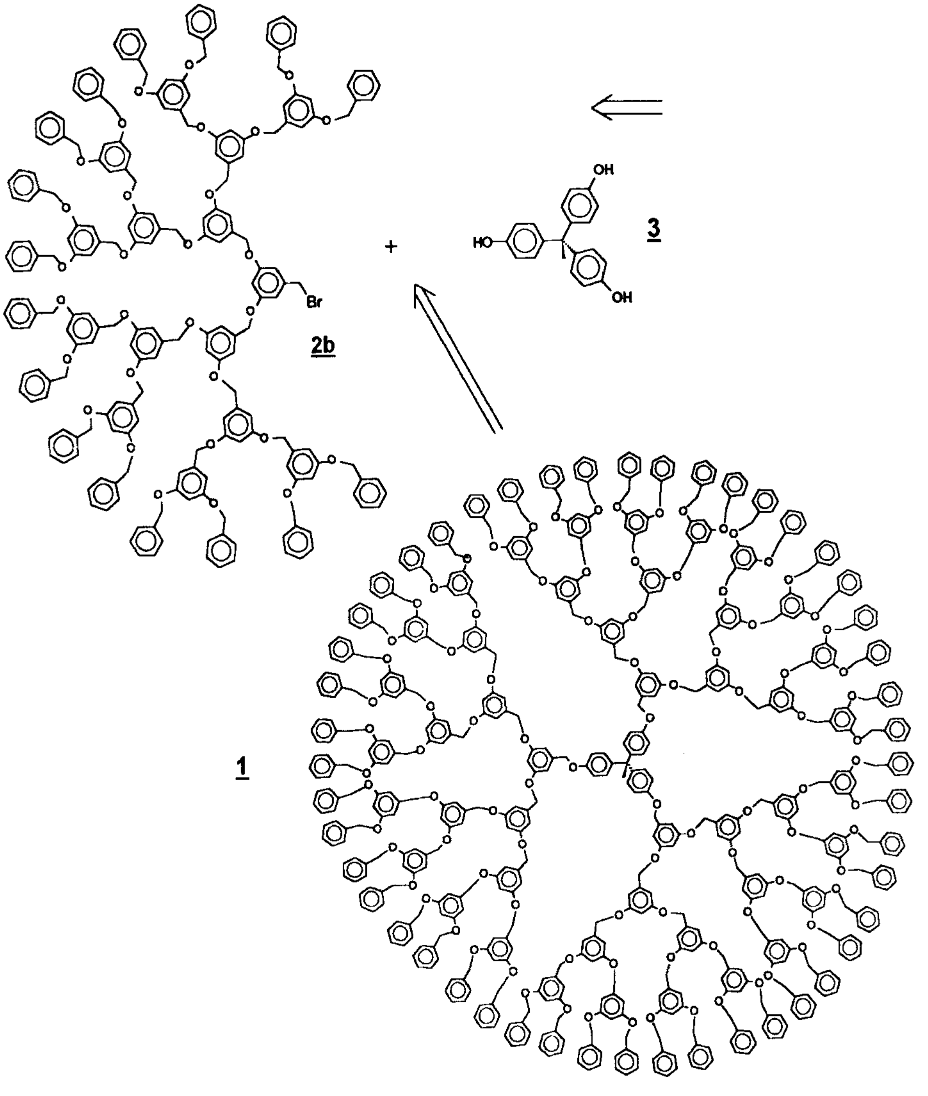


FIG. 1. Retrosynthetic scheme for the preparation of a tridendron dendrimer by the convergent growth approach.

implementations of the convergent growth approach to prepare a variety of novel dendrimers [7].

As a result of its high degree of symmetry, a retrosynthetic disconnection of dendrimer **1** suggests that it may be obtained by the attachment of three smaller monofunctional dendrimers **2b** to a trifunctional core molecule **3** (Fig. 1). Further disconnection of dendrimer **2b** lead to smaller and smaller dendrimers (**4**–**6**) and eventually to the monomer **7** and the chain end unit **8** (Fig. 2). In order to avoid confusion, reactive dendrimers such as **2** that have a unique functional group located at their focal point will be termed “dendrons,” while molecules such as **1**,

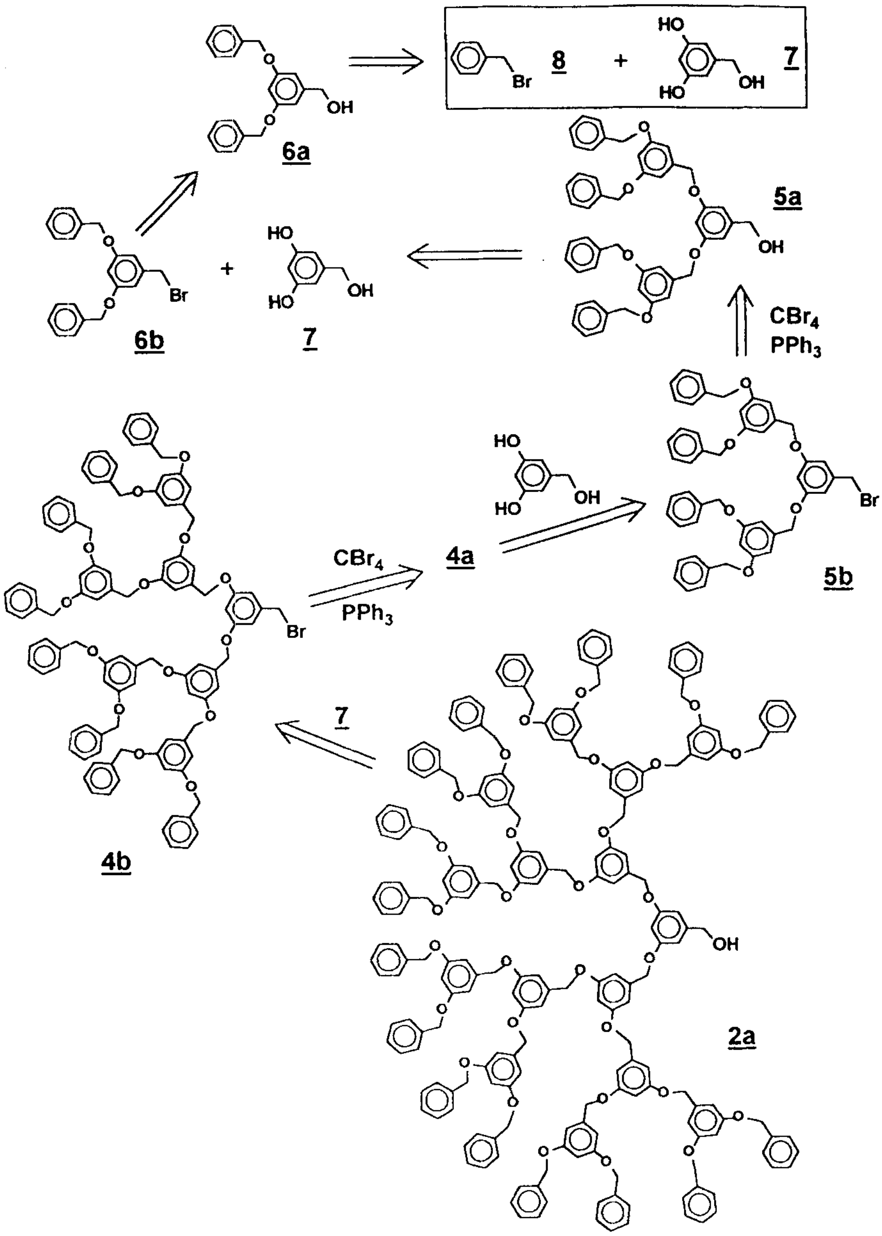


FIG. 2. Retrosynthetic scheme for the preparation of a monodendron by the convergent growth approach.

devoid of focal point reactive group, will be termed dendrimers. This differentiation is purely arbitrary because both moieties are actually regular dendrimers and, when their size is roughly equivalent, they display essentially the same properties. The "generation number" is a useful descriptor for both dendrimers and dendrons. This term will be used to indicate the number of monomer layers in the final macromolecules. Therefore **2a**, with its four layers of monomer units between the benzylic alcohol focal point and the chain ends, is a fourth generation dendron [G-4]-OH, while **1** with four dendrons around a central core is a "tridendron" dendrimer $[G\text{-}4]_3\text{-}C$.

The preparation of the fourth generation dendrons **2a** and **2b** with their four layers of monomer units involves an iterative series of Williamson ether syntheses in which the reactive bromide focal point of each dendron of the previous generation is attached to one of the two phenolic hydroxyls of the monomer. Regioselectivity is preserved due to the difference in reactivity between the phenolic and benzylic alcohol functional groups of the monomer. Once the addition to the monomer has been completed, the focal point of the newly created dendron is activated by bromination to enable further generation growth, again by Williamson coupling to monomer **7**. Therefore, an important characteristic of the convergent growth approach is that each successive generation of dendron (i.e.: **6**, **5**, **4**, **2**) contains a single reactive group (hydroxyl or bromide) at its focal point, while the number of chain-ends increases exponentially as illustrated in Fig. 2. Because coupling to the monomer only involves the focal point of the dendron, the reaction is easily carried out using just a small excess of the dendron (typically 5%, or 2.1 mole per mole of monomer). The chemistry selected for growth of these polyether dendrons is also ideally suited for the purification of all intermediate generations, ensuring that the regularity of the overall structure is preserved throughout growth. In practice, flash chromatography can easily resolve the very simple mixture of products that arise from such Williamson ether coupling reactions.

The high yield Williamson chemistry used in the preparation of the reactive dendrons is also used to effect their attachment to a polyphenolic core using the reactivity of their benzylic bromide focal point (Fig. 1). For example, the tridendron dendrimer **1** is obtained by coupling three dendrons **2b** to the core molecule, 1,1,1-tri(4-hydroxyphenyl)ethane, **3**. Numerous molecules may be selected as cores as long as their coupling sites are readily accessible, and they show at least some solubility in the reaction medium, as is the case with phenol-functionalized C_{60} [8]. Figure 3 shows a retrosynthetic approach to a dendrimer with a C_{60} core obtained from **2b**. As will be seen below, we have used multifunctional cores, termed "hypercores," that are themselves dendrimers containing up to 24 reactive phenolic functionalities at their periphery, for the "double-stage" growth of large dendrimers [9]. The great purity of dendrimers and dendrons obtained by the convergent approach is illustrated by the matrix-assisted laser desorption (MALDI) mass spectrum of a convergent chain-end deuterated [G-4]-OH dendron shown in Fig. 4(a).

In addition to its ability to produce dendrimers that are truly single molecules, rather than polydisperse species, the convergent approach shines in its ability to prepare dendrimers that have precise and, if desired, nonsymmetrical distributions of functional groups [4, 6, 10, 11]. Because assembly of the dendrimers proceeds by attachment of two molecules to the monomer unit, a single dendron may carry more than one type of chain end [6], or different dendrons may be attached to a single

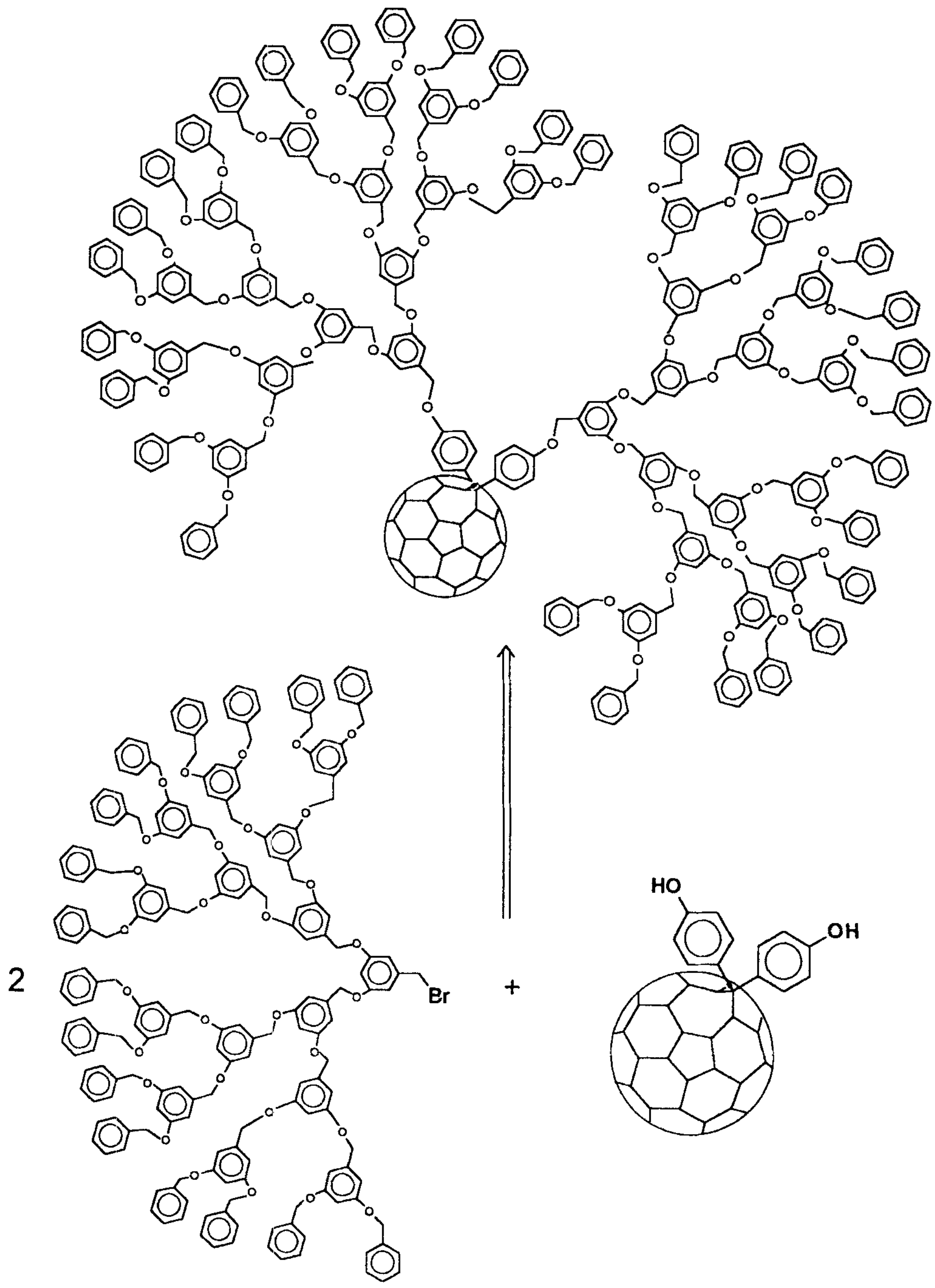


FIG. 3. Synthetic scheme for the preparation of a bidendron dendrimer on a functionalized C_{60} core.

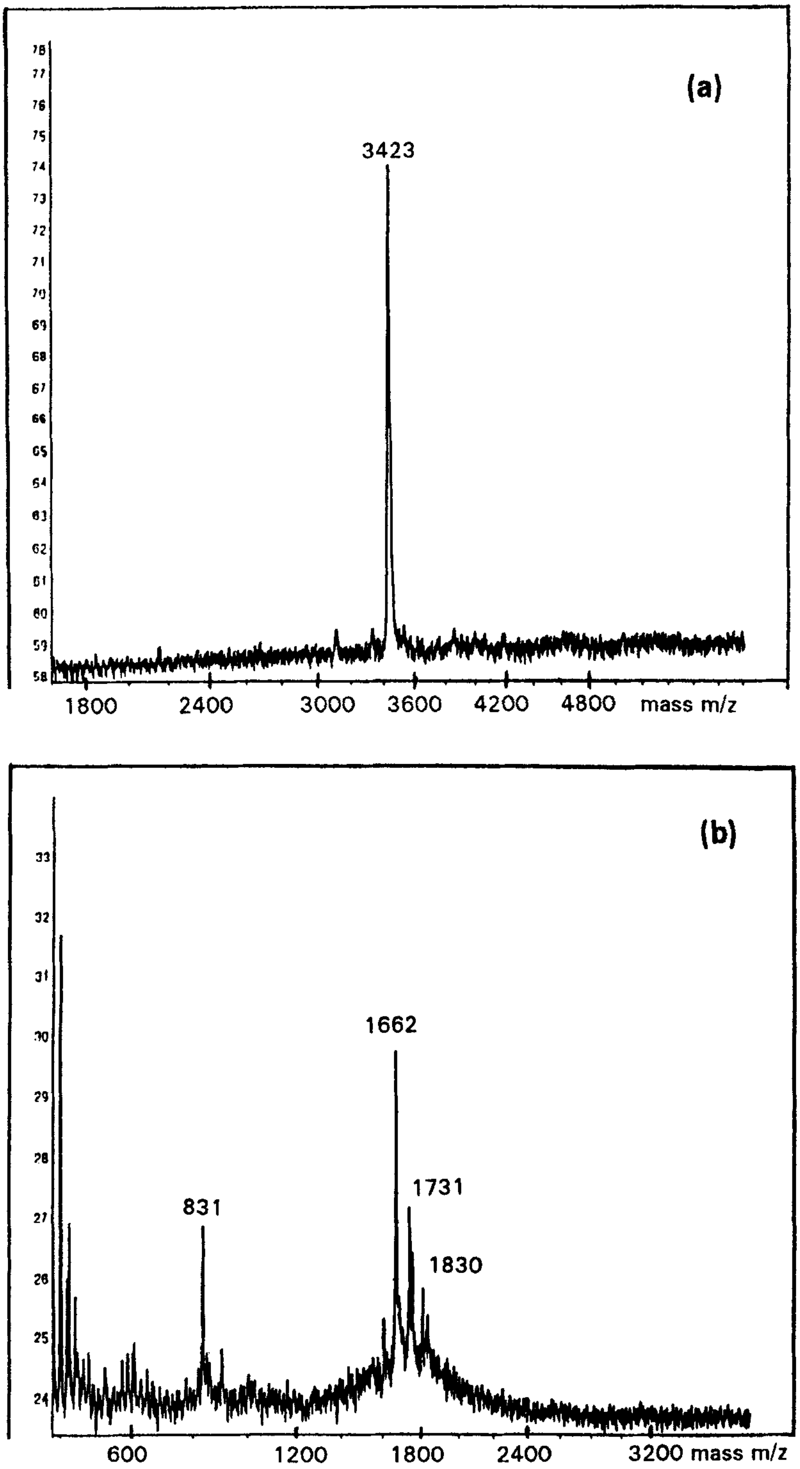


FIG. 4. (a) MALDI spectrum of a convergent chain-end deuterated [G-4]-OH polyether dendrimer. (b) MALDI spectrum of a divergent [G-3] poly(propylene imine).

core [10, 11]. Similarly, the unique functional group at the focal point of the various dendrons may be used for attachment of reactive moieties such as molecular probes [12], photoactive or catalytic species [13], or other macromolecular chains [14, 15].

A COMPARISON OF THE CONVERGENT AND DIVERGENT APPROACHES TO DENDRIMERS

The divergent or Starburst approach to dendrimers pioneered by Tomalia [1] has been used to produce very large poly(amidoamine) PAMAM dendrimers that may also be highly regular [16]. However, because generation growth leads to an exponential increase in the number of chain ends that must *all* react with the low molecular weight building block, the regularity of the final dendrimer will depend both on the conditions used to carry out the reaction and the care taken to purify the product after each step. Tomalia reported [16, 17] that nearly perfect dendrimers can be obtained. He also documented [18, 19] the pattern of irregular features that may develop in a dendrimer if ideal conditions, involving the use of large excesses of reagents and repeated purification steps, are not maintained throughout the synthesis. The problems that may be encountered in the divergent synthesis if reaction conditions and purification steps are not optimized are illustrated in Fig. 5. This figure documents the many side-products which may be obtained in the preparation of polyamine dendrimers using the clever "cascade" approach originally developed by Vögtle [20] for the preparation of low molecular weight polyamines. Although the preparation of analogous families of polyamine dendrimers has later been optimized by several research groups [21] who have claimed high purity products up to generation 5, the materials that are obtained are actually quite difficult to purify. For example, impurities arising from undesired processes, such as incomplete reaction of all the peripheral sites, are evident in the MALDI spectrum of a third generation polyamine dendrimer obtained using the procedure outlined in the recent literature (Fig. 4b).

Despite these shortcomings, the divergent approach has many advantages and it may be the method of choice for the preparation of *very large* dendrimers. This is because the convergent synthesis eventually fails if the dendrons that are to be coupled to the monomer become too large or too hindered. For example, the convergent synthesis of the polyether dendrons shown in Fig. 2 is successful to the sixth generation [5]. These very large dendrons can still be coupled, albeit in much lower yield, to the trifunctional core 1,1,1-tri(4-hydroxyphenyl)ethane to afford $[G\text{-}6]_3$-C with a molecular weight of ca. 40,000. If a larger size dendrimer is desired, the approach selected does not use the seventh generation dendron, because the steric requirements of the sixth generation dendron effectively exceeds the practical limits imposed by the geometry of monomer **7**. Instead, a lower generation dendron such as **2b** may be used in a "double-stage" convergent method [9] with a hypercore also built in dendritic fashion, but with a looser geometry and numerous phenolic chain-ends. For example, **2a** coupled to a hypercore with 24 phenolic hydroxyl chain-ends affords a polyether dendrimer with molecular weights of ca. 160,000. In this instance the steric requirements of the dendrons are lessened by the use of a lower generation material, and the flexibility of the core is increased by the introduc-

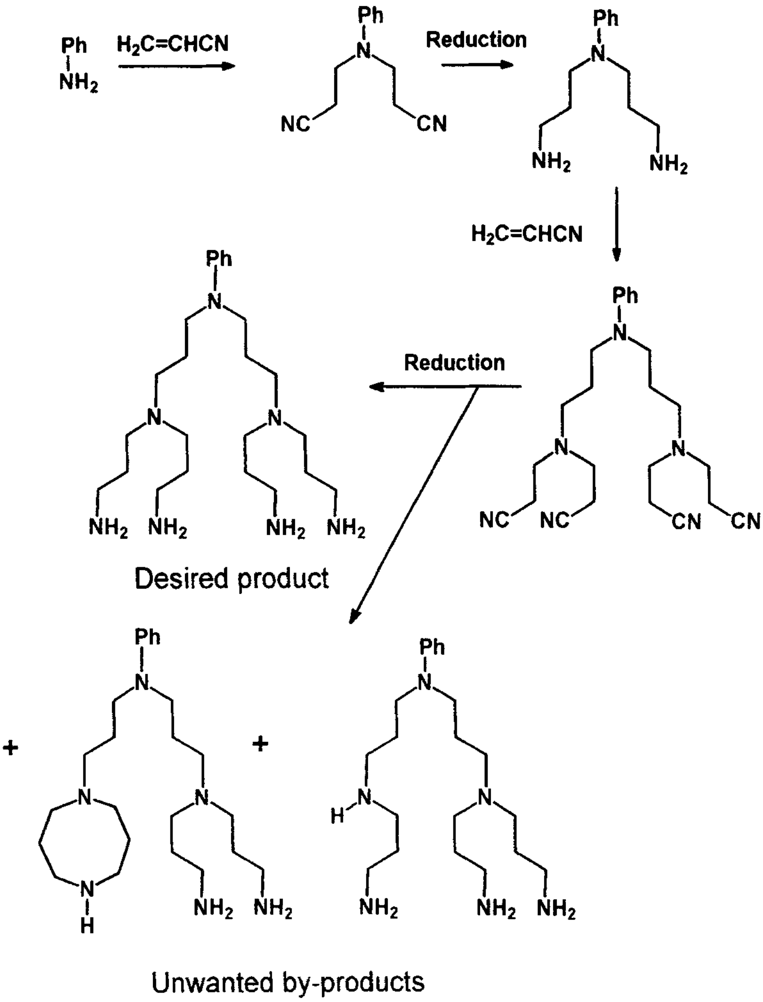
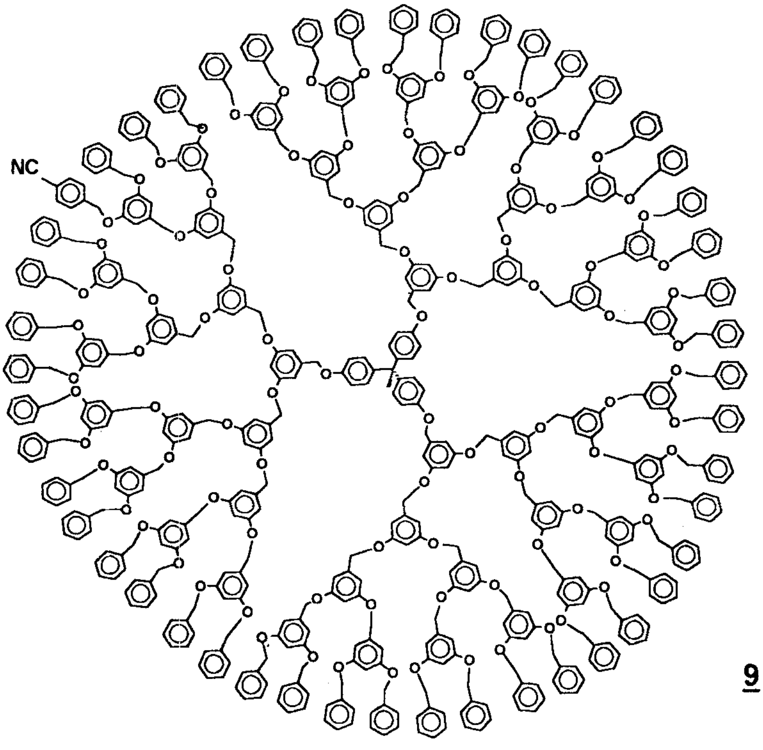


FIG. 5. The occurrence of structural irregularities in the cascade synthesis of a tetramine.

tion of spacer groups [9]. Moore and coworkers [22] described an even faster approach for the convergent growth of large dendrimers. This "double-exponential" procedure employs a clever growth scheme with a trifunctional monomer having orthogonally protected functional groups. This approach has allowed the very rapid preparation of pure, well-defined phenylacetylene monodendrons with a mass of ca. 40,000 as confirmed by MALDI analysis.

The convergent approach [5–15] is unmatched in its ability to control ultimate macromolecular architecture. While it may best be used to prepare dendrimers of relatively modest sizes, these may be precisely tailored, not only in terms of exact size and number of chain-ends, but also in the spatial arrangement of diverse functional groups. As was mentioned above, we have prepared the unique "differentiated" dendrimers [6, 10, 11] shown in Fig. 6. For example, **9** is a tridendron den-



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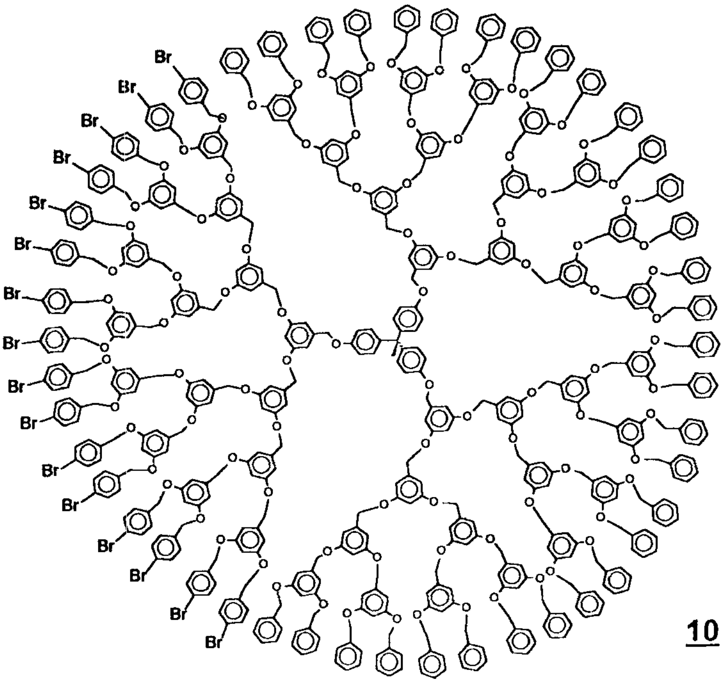

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FIG. 6. Structure of differentiated dendrimer obtained by the convergent growth approach.

drimer in which a single cyano group was built into a large dendron as one of its many chain-ends prior to the attachment of dissimilar dendrons to a core. In structure **10**, different dendrons were again coupled to the core to afford a dendrimer with a non-uniform pattern of chain ends. Numerous other differentiated dendrimers that may act as molecular dipoles, globular amphiphiles, reactive macromonomers, etc. have been prepared by the convergent growth approach. Hybrid linear-dendritic structures such as **11** and **12** (Fig. 7) are readily obtained either by attachment of a linear chain onto [14, 15] – or growth [23] of a linear chain from – the focal point of a convergent dendrimer. Similar structures can also be accessed via a divergent procedure [24] in which the linear chain is used as the core in a divergent Denkewalter-type [2] synthesis.

PROPERTIES OF DENDRIMERS

Perhaps the best documented property of dendrimers is their unusual viscosity behavior [25, 26]. In contrast to linear, and indeed most other polymer architectures, the relationship between intrinsic viscosity and molecular weight for dendri-

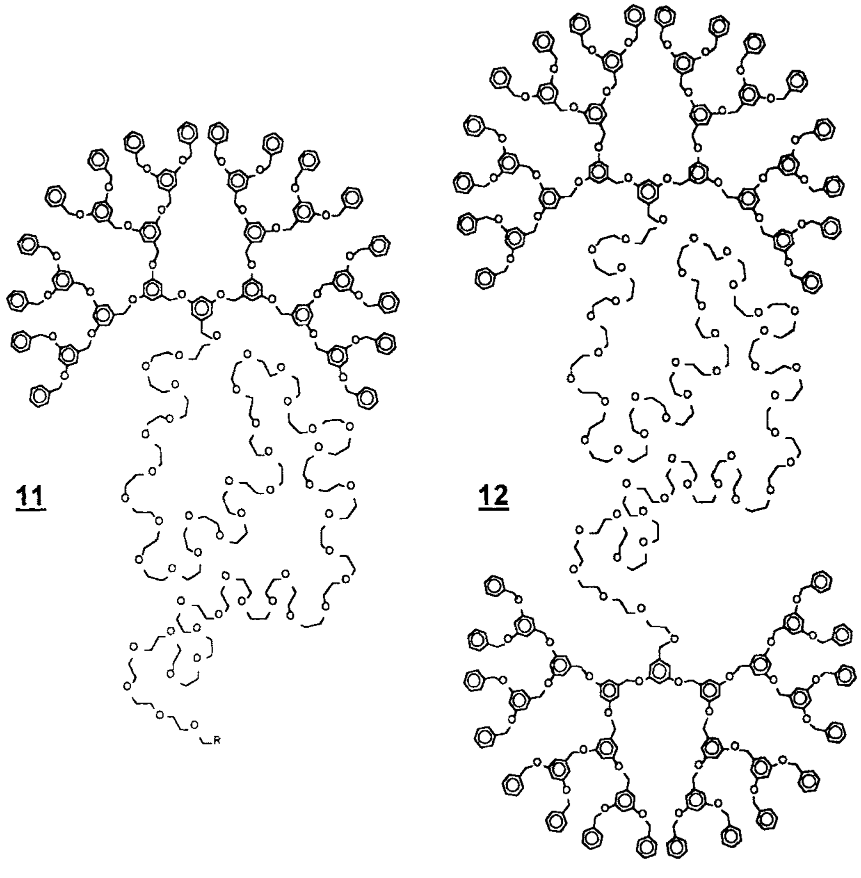

FIG. 7. Hybrid linear-dendritic macromolecules obtained by Williamson coupling of dendron **2b** with linear poly(ethylene oxide) or poly(ethylene glycol).

mers does not follow the classical Mark-Houwink-Sakurada equation: $[\eta] = KM^a$. Instead of the rapid increase in intrinsic viscosity with molecular weight that is predicted from this relationship and is observed for most polymers, the intrinsic viscosity of dendrimers prepared by the convergent approach [5] increases to reach a maximum, then decreases [25] as the molecule becomes larger (Fig. 8). The maximum in the intrinsic viscosity profile is reached at relatively low generation number for both the tridendron polyether dendrimers such as **1** and the monodendrons such as **2**. We believe that this deviation from Mark-Houwink-Sakurada behavior is due to the shape transition that occurs once a size threshold is reached. At low generation number (G = 1-3 for the monodendrons, 1-2 for the tridendrons) the molecules are very flexible and can adopt elongated shapes. As the generation number and steric requirements increase, a transition to a more globular shape is observed [25]. Additional experimental evidence for this shape change has been provided by other studies [1, 12, 27]. The unusual bell-shaped curve, depicting the relationship between intrinsic viscosity and molecular weight, is easily justified if one considers the physical basis of intrinsic viscosity. Because solution viscosity is concentration-dependent, intrinsic viscosities are obtained by extrapolating inherent

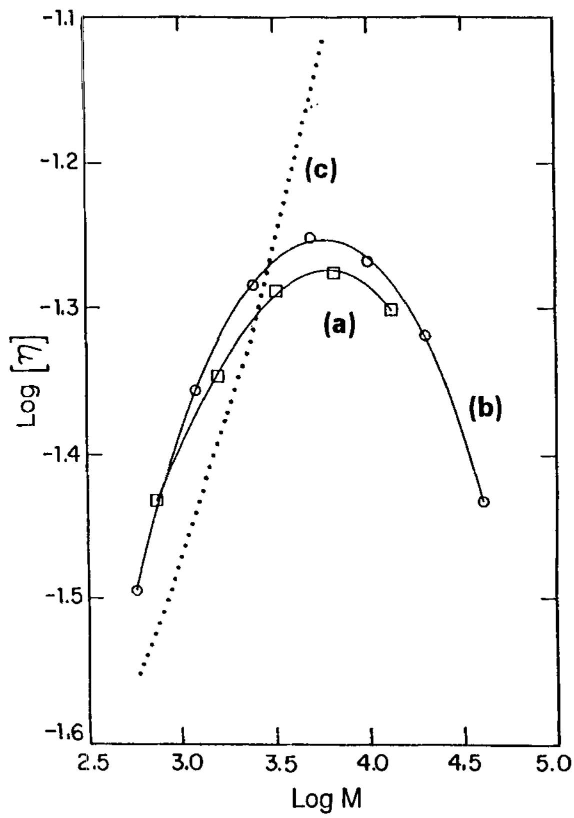

FIG. 8. Intrinsic viscosity-molecular weight relationship for a family of convergent polyether dendrimers: (a) monodendrons, (b) tridendrons, and a comparison with (c) polystyrene.

viscosities to zero concentration. The value of [η] is therefore expressed in inverse concentration units, i.e., a volume divided by a mass. If the globular shape of a dendrimer in solution is approximated to a sphere, the volume of the dendrimer increases cubically with its radius while its mass (which doubles each time a generation is added) increases exponentially. Therefore, as one progresses from low to higher generations, the mass term dominates the expression and a bell-shaped curve indeed results [1, 25].

Experimental evidence gathered by Tomalia in the preparation of very large PAMAM dendrimers [16, 17] tends to support the spherical model first proposed by De Gennes [28] which predicts that "close packing" would inhibit regular growth at high generation. This concept is supported both by the molecular modeling work of Goddard [16, 29] and by experimental data obtained for a very compact polyether structure for which growth appears to be curtailed very early on [30]. Other studies have questioned the concept of close packing [31, 32], and a definitive proof is still lacking.

The radius of gyration r_h of convergent polyether dendrons and dendrimers, measured in solution, shows the expected regular increase with increasing generation number. An excellent correlation [25] between calculated and measured values of r_h is obtained as shown in Fig. 9.

Enlightening results have also been obtained from melt viscosity measurements with the convergent polyether dendrimers such as **1** and **2** as well as others obtained by coupling **2** to hypercores. Once again, the profile that is obtained for the relationship of viscosity vs molecular weight is unlike that for other polymers. Dendrimers show only a very modest increase in their viscosity as their molecular weight increases within a homologous series [26]. The slope of the plot is approximately 1.1 as predicted by the Rouse model [33], but the sharp increase in slope, that normally correlates with the onset of chain entanglement in other polymers, is not seen. This data is important because it confirms that dendrimers are nonentangled macromolecules and therefore their properties are well differentiated from those of other polymers.

DENDRIMERS AT THE AIR–WATER INTERFACE

In collaboration with White and coworkers, we recently performed detailed studies involving convergent polyether dendrimers [G-*x*]-OH analogous to those shown in Figs. 1 and 2, as well as similar molecules with deuterated terminal benzyl groups, spread as monolayers at the air–water interface [34, 35]. For a homogeneous series of dendrimers in which the generation number increases, a change in behavior is seen as one proceeds from the fourth generation convergent dendron to its larger fifth generation analog. The smaller [G-3]-OH and [G-4]-OH dendrons exhibit surfactant-like behavior that results from the strong interaction of their single focal point hydroxyl group with the water surface. As the pressure of the movable Langmuir–Blodgett (LB) barrier is increased, nucleation is observed and a second layer is formed. Larger [G-5]-OH and [G-6]-OH dendrons as well as all tridendron dendrimers, that are devoid of hydroxyl functionality, do not display this surfactant-like behavior and do not undergo the type of nucleation that would lead to a regular multilayer when the pressure of the LB barrier is increased [35].

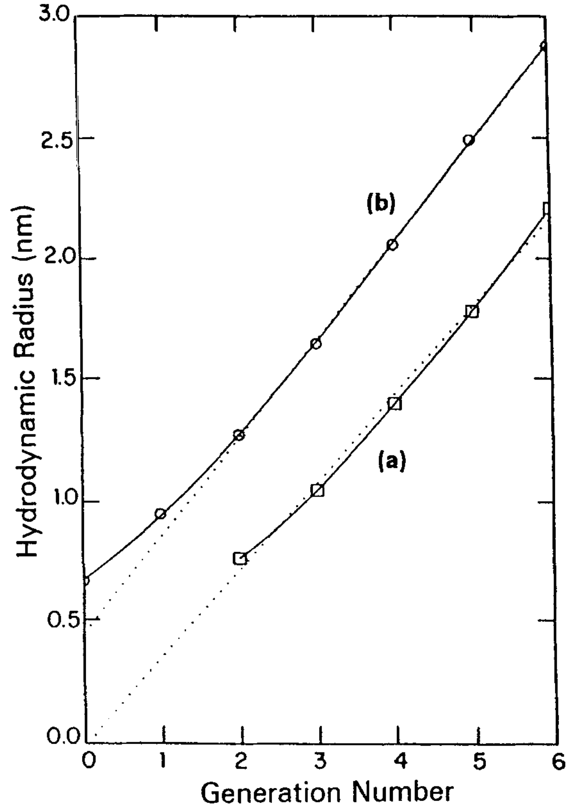

FIG. 9. Radius of gyration vs generation number for a family of convergent polyether dendrimers (see Figs. 1 and 2): (a) monodendrons, (b) tridendrons. The dotted lines are linear fits of the data for generations 2 to 6.

Even more interesting results are obtained when the solvent-free monolayers obtained with the fourth generation dendron, [G-4]-OH, are used in neutron reflectivity experiments [35]. These experiments have confirmed that, at low barrier pressures, the collapsed, solvent-free dendrimers are roughly spherical with diameters of about 2.1 nm. When pressure is applied, nucleation occurs and a second layer is formed. The overall thickness of the bilayer structure varies from 4.4 to 5.7 nm depending on the applied pressure. Because the top layer is only partially filled, its thickness remains constant at 2.1 nm and only the lower layer is compressed. Individual molecules in this layer adopt an ovoid shape in which height is approximately twice the width. Studies with dendrimers deuterated at their benzylic chain ends spread on H_2O further indicate that the lower portion of the bottom layer contains much water, while the upper portion is enriched in deuterium. This finding is consistent with a flexible globular shape for [G-4]-OH in which the original unstressed collapsed globule has enough flexibility to allow the hydroxyl group to position itself at the water surface upon compression. On further compression, reorganization of the internal bonds of the dendrimers occurs within the elongated ovoids to locate the polar hydroxyl and neighboring ether bonds close to the water surface, while the free energy of the system is lowered by placing the deuterated aromatic ends away from the water. The next generation dendron [G-5]-OH is already so large that conformations in which the hydroxyl group is allowed to remain at the periphery of the dendrimers to interact with the water surface are energetically disfavored. However, it must be emphasized that the Langmuir films are delicate to handle and therefore these results should not be overinterpreted. The energy differences that regulate conformational preferences are quite small, and low generation dendrimers, such as the polyethers used in this study, retain much flexibility even as their size increases. This is demonstrated by the fact large dendrimers can be built even from fifth and sixth generation dendrons (albeit with long reaction times), confirming the accessibility of their focal points.

THE NANOENVIRONMENT WITHIN DENDRIMERS

Due to their geometry that allows extended globular or even almost spherical conformations in solution, dendrimers can act as a host "cavity" to accommodate small molecules in their interior. As a result, they may function as a reservoir for small molecules, providing them with a unique nanoenvironment determined by the polarity and local interactions of the dendrimer's internal building elements. This interesting property of dendrimers may be of critical value in the design of nanoscopic reactors, micellar and reverse micellar structures, drug or other delivery systems, devices, catalysts, etc.

The existence of a special nanoenvironment within dendrimers has been confirmed by the solvatochromic probe experiments of Hawker et al. [12]. In these experiments a solvatochromic probe is attached to the focal point of a series of convergent dendrons of increasing sizes (Fig. 10). The UV spectra of solutions of these dendrimer-bound probes are then examined in different solvents, revealing that, as the size of the dendrons increases, the probe becomes more and more influenced by the dendrimer rather than the solvent. This is easily understood if one considers that as one proceeds to higher generations, the probe, which is attached at the dendrimers' focal point, soon becomes totally engulfed by the globular dendrimer and therefore has little opportunity to escape the influence of its building blocks. These experiments have allowed us to determine that at higher generation number, the internal polarity within convergent polyether dendrimers such as **1** or **2** may be roughly equivalent to that of dimethylformamide [12].

Using carboxylate-terminated dendrimers that act as unimolecular micelles in water, we also demonstrated [10] that dendrimers can accommodate small molecules within their "cavity." This property may be used to extract contaminants such as toxic polynuclear aromatic compounds from water [10]. The recent work by Meijer and coworkers exploited this property in an even more spectacular way with the trapping of a variety of small molecules within a "dendritic box" that may subsequently be "closed" by the attachment of bulky substituents at its chain ends [36]. More recently, Tomalia and coworkers successfully utilized dendrimers as carriers of genetic material in gene transfection experiments [37]. However, with the notable exception of the use of dendrimers to extract hydrophobic molecules from aqueous media [10], none of these experiments actually made full use of the special nanoenvironment within dendrimers.

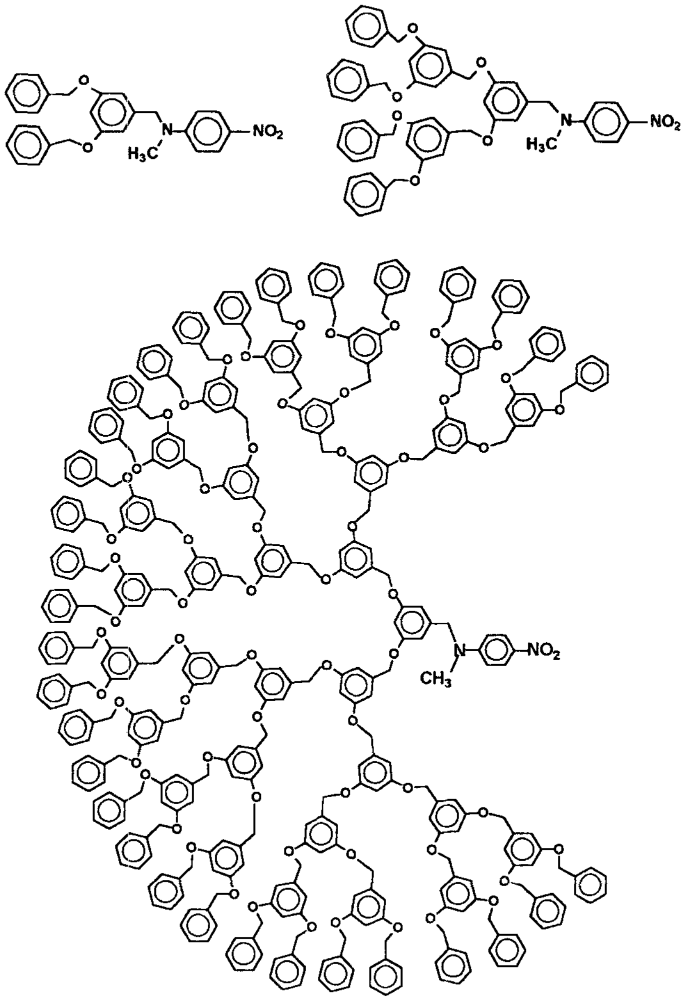

FIG. 10. Structure of the solvatochromic probes fixed at the focal point of different generation dendrimers.

We have recently demonstrated that this nanoenvironment can be used to perform reactions that normally do not proceed satisfactorily in solution. For example, the anionic polymerization of ϵ-caprolactone is a notoriously difficult process that, in many cases, only leads to low molecular weight oligomeric products due to the extensive occurrence of backbiting reactions. Therefore, a dendritic macroinitiator may be obtained by transforming the hydroxyl focal point of the fourth generation convergent dendron **2a** into its potassium alkoxide derivative. Use of this dendritic alkoxide in the polymerization of ϵ-caprolactone affords a quantitative yield of a high molecular weight linear polyester totally free of low molecular weight oligomers [23]. In contrast, both potassium *t*-butoxide or an analogous potassium alkoxide derived from the first generation dendrimer, **6a**, used in the same polymerization under otherwise identical conditions, only lead to low molecular weight oligomers. Figures 11(a) and 11(b) show the SEC chromatograms obtained using a small alkoxide or the fourth generation dendritic alkoxide, respectively. We speculate that the drastically different outcome of these two reactions is entirely due to the fact that polymerization is carried out within the cavity of the larger dendrimer in the second case. The highly coordinating environment within the polyether dendrimer is ideal for the potassium counterion that remains within the dendritic cavity throughout the polymerization process. Because monomer can easily penetrate the open cavity, polymerization proceeds readily. The polyester that is formed is expelled from the polyether dendrimer for which it has little affinity, and therefore backbiting is prevented.

Such experiments are important because they provide conclusive proof that architectural control in synthetic macromolecules is a most efficient tool for the design of unique molecules that perform tasks normally reserved for complex natural systems such as enzymes. It is likely that concepts such as those used in the design of these simple dendrimers will prove invaluable in the development of highly specific biological delivery systems [37] and catalysts [13, 38].

IRREGULAR DENDRITIC STRUCTURES: HYPERBRANCHED POLYMERS

While dendrimers easily attract much attention because of the unique relationship between their structure and their properties, their tedious preparation by a repetitive stepwise process remains an obstacle to their broad availability. Even the "commercial" poly(amidoamine) and poly(propyleneimine) dendrimers offered by Dendritech and DSM, respectively, are only available at high cost. It is possible to envision more rapid, less controlled, and therefore less costly syntheses for these materials, but the influence of increasing amounts of structural imperfections in the products that would be obtained is yet to be determined.

Highly branched and generally irregular dendritic structures have been known for some time, being found, for example, in polysaccharides such as amylopectin, glycogen, and some other biopolymers. In the area of synthetic structures, Flory discussed, as early as 1952 in his Baker Lectures text *Principles of Polymer Chemistry* [39, 40], the theoretical growth of highly branched polymers obtained by the polycondensation of AB_x structures in which x is at least equal to 2. Such highly branched polymer structures are now known as "hyperbranched polymers," a term that was coined in 1988 by Kim and Webster [41] to describe the soluble polyphenylenes they obtained by the Pd-catalyzed polycondensation of the AB_2 monomer 3,5-dibromobenzene boronic acid. The growth of a hyperbranched polymer from an AB_2 monomer is shown schematically in Fig. 12. Such a molecule grows by a kinetic process controlled both by local instantaneous differences in reactivity and accessibility. Therefore, at any given instant, one B group might react while a neighboring B group is temporarily shielded and therefore remains unreacted. Polymer growth involves the condensation of monomeric, oligomeric, and larger species that all contain a single A group and several B groups, located both at unreacted sites and at chain-ends. As the polymerization progresses, the bulk of the growth process involves the self-condensation of AB_x units in which the average value of x increases rapidly.

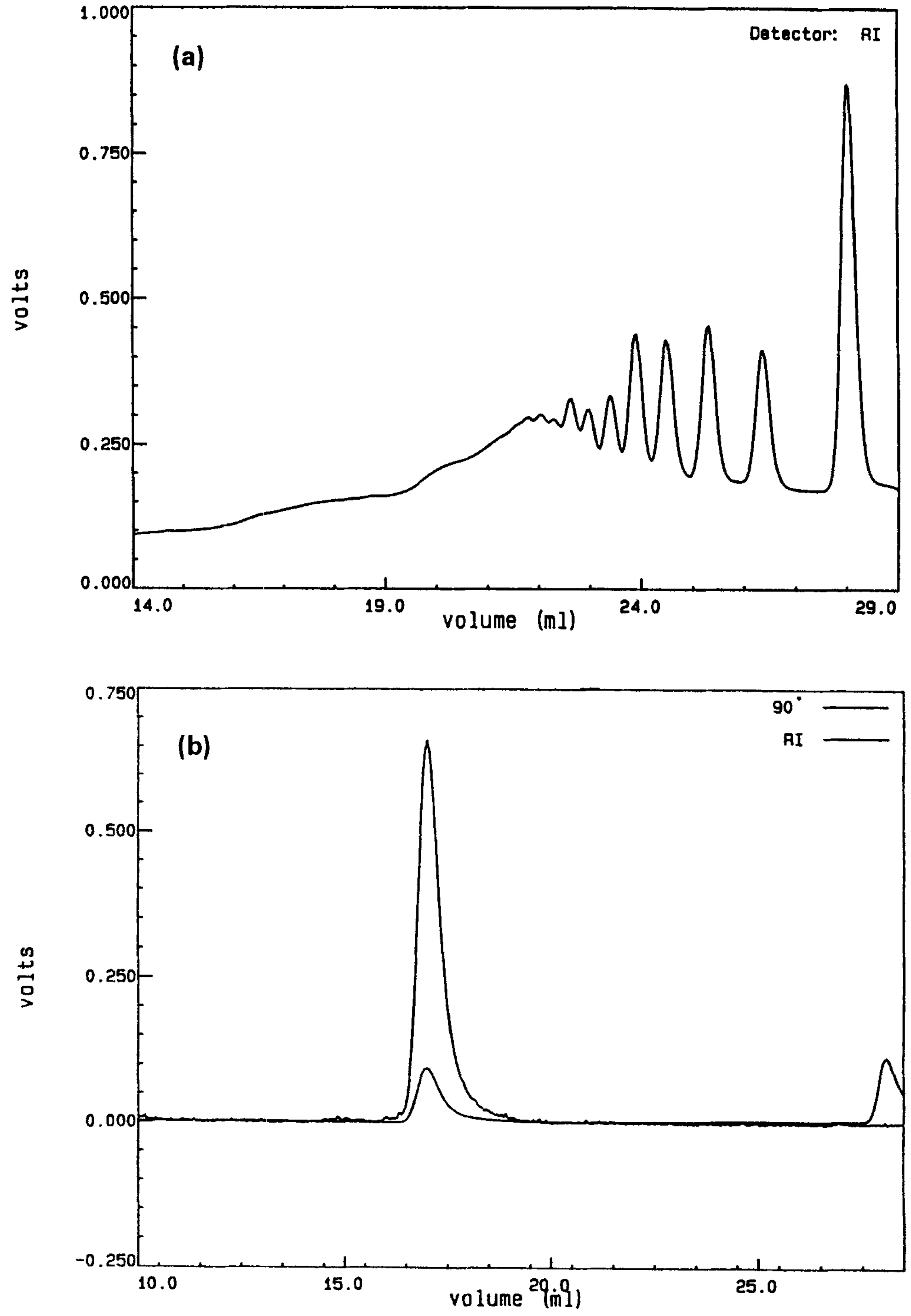

FIG. 11. (a) Size exclusion chromatogram (SEC) of the product obtained by initiation of caprolactone with a small molecule alkoxide. (b) SEC of poly(caprolactone) obtained by polymerization initiated with the alkoxide of **2a**. The polymer has M_n = 307,000 and a polydispersity of 1.07.

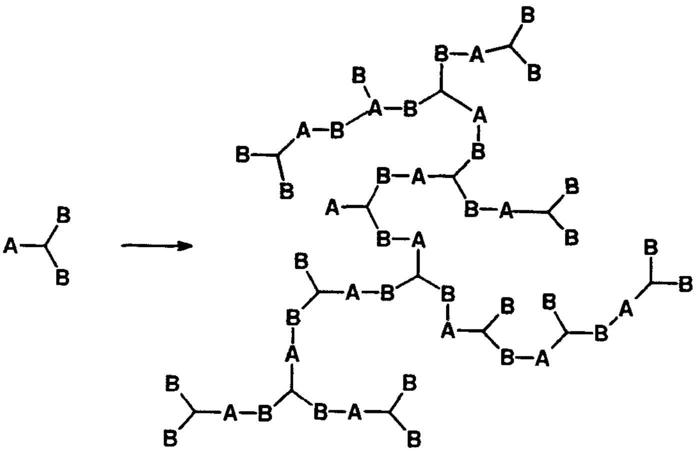

FIG. 12. Schematic growth of a hyperbranched polymer from an AB_2 monomer.

While this description of the growth processes is consistent with Flory's prediction, it is somewhat oversimplified because the occurrence of other reactions such as cyclization or side-reactions is ignored. Clearly, the formation of rings by intramolecular reaction of an A group with a B moiety does not terminate growth because reaction with another A-containing molecule is still possible. Nevertheless, this effect, if dominant, would severely limit the ultimate molecular weight of hyperbranched polymers. It may be predicted, for example, that internal cyclizations would be very important both at high conversion, due to the great paucity of A groups, or in instances where an internal template moiety may assist with this intramolecular reaction. In actual fact, the occurrence of intramolecular cyclization side-reactions has not been a dominant process for the AB_2 hyperbranched structures prepared to-date. Hawker et al. carried out elegant studies [42] to monitor the occurrence of such cyclizations in typical polycondensations and found that intermolecular reactions are favored for most stages of the polycondensation.

The original studies of Kim and Webster [41] on hyperbranched polymers provided some tantalizing, if somewhat misunderstood, clues to their unique properties. For example, it has been reported that, despite their polyphenylene structure, the hyperbranched polymers are very soluble in a variety of solvents. This effect may be attributed not only to the highly branched structure with a 1,3,5 pattern of ring substitution, but also to the presence of numerous remaining bromo groups located both at the chain ends and throughout the structure. As a result of their good miscibility with other polymers, the hyperbranched polyphenylenes may be used as viscosity-modifying additives in blends. For example, additions of amounts as low as 1–3% to polystyrene results in a drastic lowering (50–80%) of the melt viscosity of the blend when compared to unblended polystyrene.

We have also observed that fully aromatic polyesters obtained from 3,5-dihydroxybenzoic acid are readily dissolved even at very high concentrations [43]. Turner and coworkers showed that similar hyperbranched aromatic polyesters with a molecular weight of over 1 million have a very low intrinsic viscosity of only ca. 0.4 dL/g [44]. In addition to their high solubility, the hyperbranched polymers have functional groups that are easily accessed by small molecules. For example, we routinely analyze the phenolic-terminated dendritic polyesters by size-exclusion chromatography after treatment with hexamethyldisilazane to ensure that they do not adhere to the column packing. Other functionalizations are also possible [43], at least when homogeneous reaction medium is used. For example, Kim and Webster [41] lithiated the remaining aromatic bromide sites of their hyperbranched polyphenylenes, then carboxylated them to produce carboxylate-terminated water-soluble polyphenylenes.

The degree of branching [1, 43] of hyperbranched polymers is, of course, always lower than that of true dendrimers. Many of the structures that have been prepared from 1,3,6 substituted aromatic rings have been found to possess a degree of branching of about 50–60% [41–44]. Hawker has shown very elegantly that the structure of the monomer unit can be manipulated to regulate the degree of branching of the hyperbranched polymer [42].

In contrast, the very interesting aliphatic polyesters reported by Hult and coworkers [45] reach a degree of branching as high as 80%. This achievement results from a novel preparation process involving the use of a polyfunctional B_3 core, 2-ethyl-2(hydroxyethyl)-1,3-propanediol, to which the AB_2 monomer, 2,2-bis(hydroxymethyl)propionic acid, is added in successive portions, using a stoichiometry that mimics the growth of a regular dendrimer (Fig. 13). We had attempted in 1991 a somewhat similar preparation involving the slow addition on monomer in the preparation of our aromatic polyesters, but this approach did not yield the desired effect, in part because of the easy occurrence of equilibrating transesterification reactions. It is virtually certain that the low solubility of the monomer in the molten core is a strong contributor to the high degree of branching that is achieved for these aliphatic hyperbranched polyesters. In effect, the monomer is slowly "metered into" the molten core with which it reacts preferentially. As a result of the low concentration of dissolved monomer, statistical self-condensation that would lower the ultimate degree of branching is greatly reduced. In other words, because of its low solubility in the reaction medium, the monomer benefits from "physical protection" (as opposed to the use of chemical protecting groups) that reduces the occurrence of self-condensation. The aliphatic polyesters of Hult and coworkers are now being commercialized by Perstop. They appear to hold great promise for widespread use in coatings and other applications where low viscosity and high functionality are desirable features.

Despite their low viscosity, globular shape, high solubility, and high functionality that resemble those of dendrimers, hyperbranched polymers are clearly distinct from dendrimers in terms of their ultimate properties.

As mentioned above, Turner and coworkers claimed that, unlike regular dendrimers, hyperbranched polymers obey the Mark–Houwink–Sakurada relationship $[\eta] = KM^a$, albeit with rather low "a" values. Key measurements were obtained using a detailed SEC analysis of a single sample of very high molecular weight, highly polydisperse, aromatic polyester [44]. Viscosity measurements were performed on the various fractions eluting from the SEC columns with parallel measurement of absolute molecular weight by low-angle laser light scattering. While the data obtained are very significant, some uncertainty remains because the structure of the various hyperbranched fractions may not be uniform. In particular, density changes would be expected to significantly affect the data [46]. Nevertheless, be-

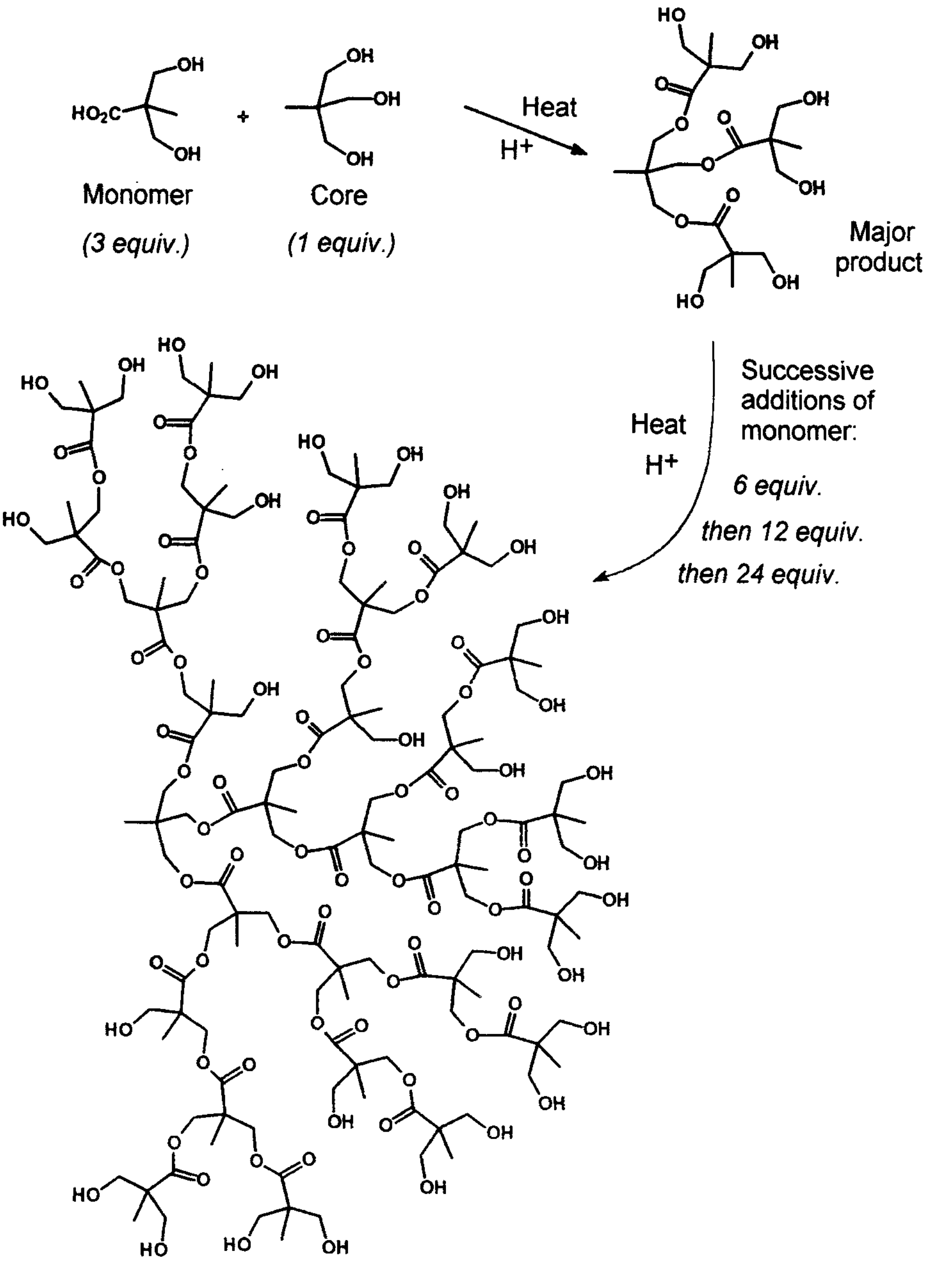

FIG. 13. Aliphatic hyperbranched polymer prepared by the staged addition of a sparingly soluble monomer to a core molecule.

cause loop formation by intramolecular cyclization is intrinsically limited to a maximum of one loop per molecule, the validity of the data, at least in terms of the trends it reveals, is not in doubt.

Figure 14 shows the relationship between [η] and molecular weight for three families of polymers: linear, dendrimer, and hyperbranched. This plot confirms that a fundamental difference exists between dendrimers and hyperbranched polymers: only the former display the unusual bell-shaped relationship that results from their regular globular structure. Unlike dendrimers, hyperbranched polymers have an irregular structure, and the positioning of their functional groups, both at the chain ends and throughout their building blocks, has a great effect on their overall properties. Because their growth is a kinetic process affected by fugitive steric inhibitions, their globular structure is more elongated than spherical, affording less hindered access to their single A group than is the case for the focal point of a high generation dendrimer. At the present time, the melt viscosity behavior of dendrimers, which indicates that these macromolecules are nonentangled [26], has not been matched by similar studies with hyperbranched polymers. It is expected that significant differences will be observed with various hyperbranched polymers depending on their degrees of branching. At high degrees of branching, the influence of chain entanglements on the melt viscosity is not expected to be significant, while at low degrees of branching, the importance of chain entanglements is expected to be more important. However, current data already indicate that hyperbranched polymers have rather low melt viscosities when compared to linear polymers [44]. A very interesting recent review by Voit [47] outlines some of the potential applications of hyperbranched polymers in the modification of the physical properties of various polymer blends.

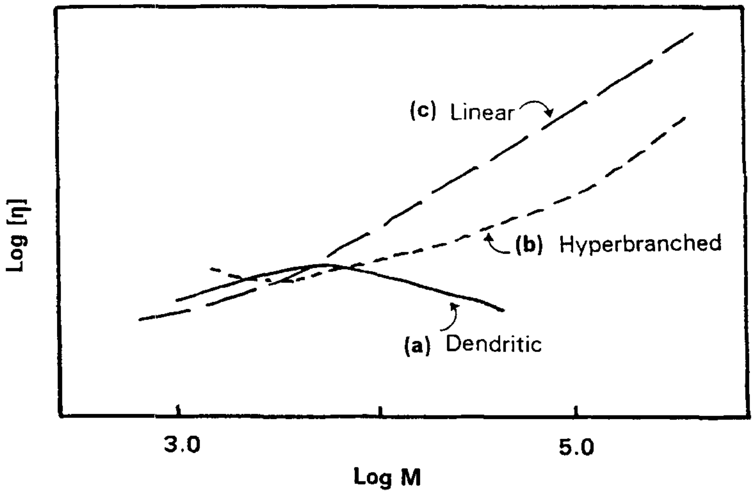

FIG. 14. A comparison of the intrinsic viscosity vs molecular weight relationship for three different polymer architectures: (a) convergent polyether dendrimer; (b) hyperbranched polyester; (c) linear polystyrene.

THE REACTIVITY OF FUNCTIONAL GROUPS IN DENDRITIC POLYMERS

The conformation of dendrimers and the placement of their functional groups in solution or in the solid state has remained a topic of some controversy. Conflicting predictions have been made on the basis of simplified models. De Gennes and Hervet [28] used a spherical model to predict a gradient of density with a minimum at the center of the dendrimer and regular growth until a "dense-packed" state is achieved. Goddard and coworkers [29] used molecular modeling to show that the structure of PAMAM dendrimers evolves from open structures at low generations to close spheroids, with well-developed surfaces and internal hollows, at high generation number. In contrast, Lescanec and Muthukumar [31] used a very simplified kinetic model to predict maximum density at the core of the dendrimer and inward folding of the end groups, leading to their distribution throughout the globular macromolecule. Unfortunately, this model ignores so many structural, thermodynamic, and medium-related factors that it must be considered of limited significance. In particular, solvation phenomena, or the existence of attractive, repulsive, interfacial, or other forces, will strongly affect the conformation of dendrimers. The preparation of carboxylate-terminated dendritic polymers that behave as unimolecular micelles confirms that their chain ends may indeed prefer to be directed outward to minimize the free energy of the system. Similarly, our neutron reflectivity experiments with regular polyether dendrons and dendrimers [35] showed that, while the structures collapse in a solvent-free environment, the chain-ends or focal points of the macromolecules are still able to acquire preferred orientations in response to the thermodynamic demands of the system. The very interesting liquid crystalline polyether dendrimers of Percec et al. [48] have structures in which the liquid crystallinity of the building blocks, as well as the geometry of the linkers used, clearly control the relative placement of chains.

Finally, several dendrimers in which the chain-ends are very different from the inner building blocks have been prepared. Unless specific interactions such as H-bonding or π-stacking exist, these dendrimers are likely to prefer conformations in which the chain-ends are segregated from the inner building blocks. This is confirmed in a study of the reactivity of benzyl ether groups attached to different polyester architectures. Aromatic polyester dendrimers terminated with benzyl ethers are readily debenzylated by hydrogenolysis at the surface of a Pd/C catalyst. In contrast, analogous linear and hyperbranched polyesters containing a comparable amount of benzyl ether groups distributed throughout their structures do not undergo debenzylation at the surface of the solid catalyst. This finding [49] supports the assumption that the benzyl ether groups that have little affinity for the polyester building framework of the dendrimer prefer to reside at—or close to—the surface, in sharp contrast to the situation that prevails with most other molecular architectures.

CONCLUSION

It is now obvious that there are differences between dendrimers and hyperbranched polymers. The important question is: Are these differences significant or only cosmetic? We believe that the answer to this question must take into account the applications that are contemplated for the dendritic polymers. Using living systems as a model, one must anticipate that the regular placement of reactive groups at a precise location, as opposed to throughout a structure, has great importance in terms of ultimate performance when surface and interfacial properties are involved. Therefore, just like Langmuir-Blodgett films, dendrimers belong to a special class of well-defined molecular architectures where exact structure and ultimate performance are intimately related. It is likely that regular dendrimers will continue to draw much attention in specialized applications that take advantage of their precise architecture: drug delivery, catalysis, nanoreactors, molecular devices, etc. In contrast, hyperbranched polymers will join other interesting functional polymers in applications that involve commodity materials: from coatings and adhesives to lubricants, compatibilizers, and carriers. Today, the frontiers in the chemistry of dendritic polymer are in the search for rapid methods of synthesis involving, for example, vinyl polymerizations [46, 50], the preparation of "engineered" dendritic structures, and the discovery of new properties and applications [1, 47].

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