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Self-Assembly Using Dendritic Building Blocks – Towards Controllable Nanomaterials

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Abstract

Dendritic molecules have well defined, three-dimensional branched architectures, and constitute a unique nanoscale toolkit. This review focuses on examples in which individual dendritic molecules are assembled into more complex arrays *via* non-covalent interactions. In particular, it illustrates how the structural information programmed into the dendritic architecture controls the assembly process, and as a consequence, the properties of the supramolecular structures which are generated. Furthermore, the review emphasises how the use of non-covalent (supramolecular) interactions, provides the assembly process with reversibility, and hence a high degree of control. The review also illustrates how self-assembly offers an ideal approach for multiplying up the branching of small, synthetically accessible, relatively inexpensive dendritic systems (*e.g.* dendrons), into highly branched complex nanoscale assemblies.

The review begins by considering the assembly of dendritic molecules to generate discrete, well-defined supramolecular assemblies. The variety of possible assembled structures is illustrated, and the ability of an assembled structure to encapsulate a templating unit is described. The ability of both organic and inorganic building blocks to direct the assembly process are discussed. The review then describes larger discrete assemblies of dendritic molecules which do not exist as a single well-defined species, but instead exist as statistical distributions. For example, assembly around nanoparticles, the assembly of amphiphilic dendrons and the assembly of dendritic systems in the presence of DNA will all be discussed. Finally, the review examines dendritic molecules which assemble or order themselves into

extended arrays. Such systems extend beyond the nanoscale into the microscale or even the macroscale domain, exhibiting a wide range of different architectures. The ability of these assemblies to act as gel-phase or liquid crystalline materials will be considered.

Taken as a whole, this review emphasises the control and tunability that underpins the assembly of nanomaterials from dendritic building blocks, and furthermore highlights the potential future applications of these assemblies at the interfaces between chemistry, biology and materials science.

Keywords: dendrimers, nanotechnology, self-assembly, supramolecular

Contents

- 1 Introduction
- 2 Self-assembly of discrete well-defined supramolecular dendrimers
 - 2.1 Untemplated assemblies
 - 2.2 Assembly directed by organic templates
 - 2.3 Interlocked molecules with dendritic components
 - 2.4 Assembly directed by a single metal ion
 - 2.5 Assembly directed by well-defined metal clusters
3. Self-assembly of discrete nanoscale structures which exist as statistical distributions
 - 3.1 Dendron-stabilised nanoparticles
 - 3.2 Assembly of dendrons and dendrimers in the presence of DNA
 - 3.3 Dendritic nanoclusters and nanotubes
 - 3.4 Assembly of dendrons with surfactant-like properties
4. Self-assembly of extended nanoscale arrays of dendritic building blocks
 - 4.1 Assembly of extended aggregates using multiple recognition events on the dendritic surface
 - 4.2 Assembly of one-dimensional architectures – gel-phase materials
 - 4.3 Self-ordering of dendritic molecules – liquid crystalline materials
 - 4.3.a Supramolecular dendromesogens
 - 4.3.b Mesogen-functionalised dendrimers
5. Conclusions and prospects for the future
6. References

1. Introduction

Self-assembly is an incredibly powerful concept in modern molecular science. The ability of carefully designed building blocks to *spontaneously assemble* into *complex nanostructures* underpins developments in a wide range of technologies – ranging from materials science through to molecular biology [1]. Self-assembly is a *supramolecular* approach which relies on complementary non-covalent interactions, such as electrostatic interactions, hydrogen bonds, van der Waals forces, coordination interactions and solvophobic effects [2]. In self-assembled structures, these temporal intermolecular forces connect the molecular scale building blocks in a *reversible, controllable* and *specific* way. Of particular value are the possibilities offered by self-assembly to generate nanoscale complexity with relatively *little synthetic input*. Furthermore, the ability of assembled superstructures to behave as more than the sum of their individual parts, and exhibit completely new types of behaviour, is of special interest.

Dendrimer chemistry is another key area of nanoscale science – indeed dendritic molecules can be considered to be a unique nanoscale toolkit [3]. However, even though the synthesis of dendritic molecules is iterative and involves simple repetitive synthetic steps, it is still often time-consuming and tedious to generate perfect nanoscale dendritic structures. Self-assembly therefore offers an attractive option by which dendritic building blocks, many of which can be relatively small and synthetically accessible, can be simply assembled into more complex architectures. This has the effect of multiplying up the dendritic branching and generating new supramolecular dendrimers (Figure 1). There are many ways in which supramolecular chemistry can be combined with dendrimer technology (*e.g.* host-guest binding *etc.*) and for a full discussion the reader is directed to a number of excellent reviews [4], however, this article focuses on the *self-assembly of multiple dendritic building blocks* into novel nanoscale architectures. In particular, this review focuses on assembly and ordering processes in solution, and as such, does not describe self-assembly at interfaces (*e.g.* air/water) or on solid surfaces (*e.g.* metals, silicas).

There are a number of fundamentally different ways in which dendrimers can be assembled in solution, and this provides the structure by which this review article is organised. One approach (Section 2) gives rise to *well-defined (monodisperse)* assemblies of dendritic building blocks. The assemblies generated using this approach are generally based on well-

established, specific supramolecular interactions and each assembly consequently contains a precisely defined number of dendritic building blocks. Such supramolecular dendrimers have an equivalent degree of structural definition to a ‘traditional’ covalent dendrimer, however they are held together by reversible non-covalent interactions. The second approach (Section 3) gives rise to less well defined, yet discrete, assemblies such as nanoparticles and micelles. Such systems exist as a *statistical distribution* of different sizes, each of which will contain a slightly different number of dendritic building blocks. The final approach (Section 4) gives rise to *extended* (non-discrete) *arrays* of dendritic molecules. Such systems extend beyond the *nanoscale* into the *microscale* or even the *macroscale* domain. By controlling the inherent structure of the individual dendritic building blocks, and the interactions between them, it is possible to generate a wide diversity of assembled and organised nano-architectures which have intriguing potential applications.

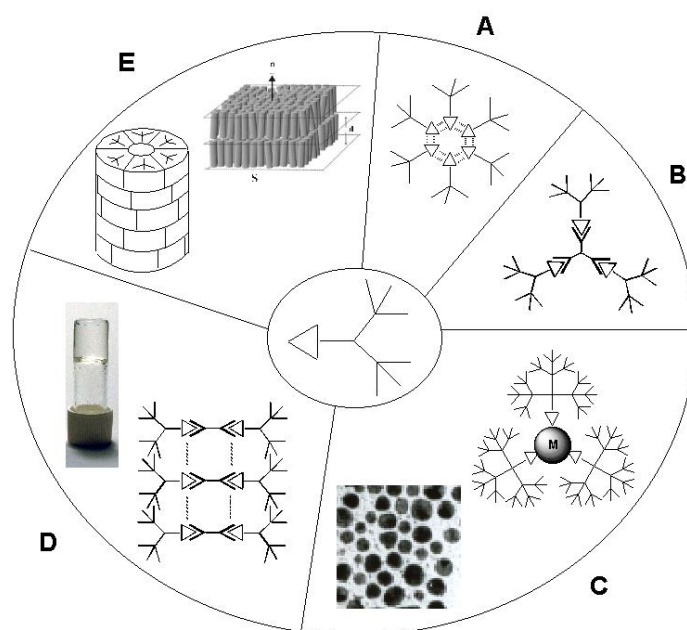


Figure 1. Schematic illustration of the self-assembly of dendritic building blocks. A: Untemplated assembly of dendrons. B: Templated assembly of dendrons. C: Nanoparticles with assembled dendritic surface groups. D: One-dimensional, fibrous, gel-phase assemblies of dendritic molecules. E: Liquid crystalline assemblies of dendritic molecules.

Self-assembled supramolecular dendrimers have wide-ranging novel properties which depend on the *reversibility* and *specificity* of the assembly process, as well as on the *branching* inherent within the dendritic building blocks. As will be illustrated, the self-assembly of

dendritic building blocks in solution potentially has applications in diverse areas; including *controlled release*, *nanoscale electronics*, *gel-phase* and *liquid crystalline* materials, and *biotechnology*. Given the relative simplicity of using self-assembly as a non-covalent synthetic tool, this approach is relatively *cost-effective*, and its potential for genuine future applications is therefore significantly enhanced.

2. Self-assembly of discrete well-defined supramolecular dendrimers

2.1 Untemplated assemblies of dendrons

Perhaps as a consequence of their importance in biology, and their easy visualisation using simple modelling systems, hydrogen bonds have long been prized for their ability to assemble supramolecular architectures. Hydrogen bonds typically possess a high degree of directionality and can be built into arrays. This makes them ideal for the assembly of nanostructures with controlled geometries. The earliest example of a self-assembled discrete supramolecular system using hydrogen bond interactions was reported by Zimmerman and co-workers, and offers an elegant illustration of the way in which *molecular scale information* programmed into the dendritic branches can play a key role in determining the nature of the assembly formed [5]. These workers functionalised the focal point of a Fréchet-type dendron with a carefully designed, rigid tetra-carboxylic acid unit (Figure 2). Such carboxylic acid units have the potential to assemble in two different ways. Firstly, they can assemble into a discrete hexameric rosette, but alternatively, they can assemble into less well-defined linear aggregates (supramolecular polymers). Interestingly, Zimmerman and co-workers reported that the mode of assembly was controlled by the dendritic generation. At lower dendritic generations, this molecule yielded linear aggregates, however, as the size of the dendritic branches was increased, the system was shown (using gel permeation chromatography (GPC), vapour pressure osmometry, laser light scattering and small angle neutron scattering) to exclusively form the desired *hexameric 'rosette' aggregate*. It was argued that the dendritic branches act as a *steric buttress*, disfavours the formation of linear aggregates and providing the assembly process with a high degree of definition.

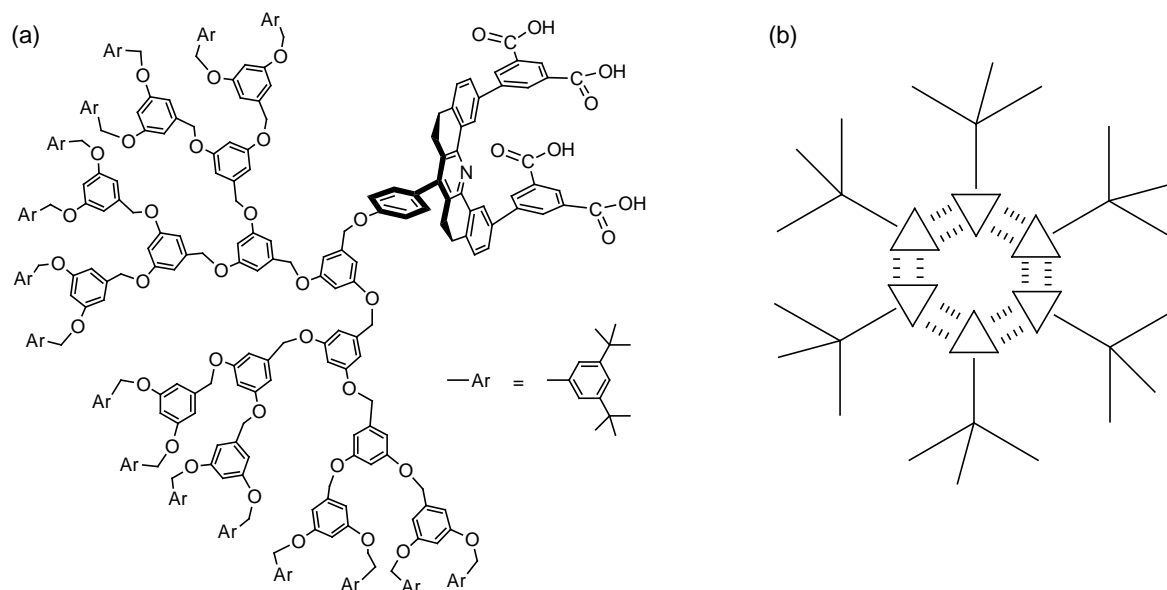


Figure 2. (a) Tetra-carboxylic acid focussed dendron. (b) Assembly of dendrons into a well-defined hexameric rosette structure.

In an attempt to provide this type of assembly with additional specificity and control, Zimmerman and co-workers have also developed supramolecular dendrimers which use a DDA·AAD hydrogen bonding motif (D: hydrogen-bond donor; A: hydrogen bond acceptor) to assemble individual dendrons into hexameric rosettes [6]. All studies were consistent with a cooperative aggregation process, and it was observed that decreasing the concentration, increasing the temperature or adding a competitive solvent shifted the equilibrium back from hexameric rosette towards monomer – clearly illustrating the *reversibility* of this type of assembly process. Most interestingly, a combinatorial library was generated using a 1:1 mixture of first and third generation building blocks. Although this mixture can potentially generate as many as 13 possible hexameric assemblies, only *one* supramolecular dendrimer was observed to any significant degree, in which the first and third generation building blocks alternated around the rosette (Figure 3). It was proposed that steric hindrance between the third generation branches favoured this structure, and this observation indicates the way in which pre-programmed dendritic information can control the assembly process. Zimmerman and co-workers have also reported highly stable, discrete, hexameric assemblies based on AADD·DDAA contacts, and observed that there is no crossover with rosettes based on alternative hydrogen bonding patterns (*e.g.* DDA·AAD) [7].

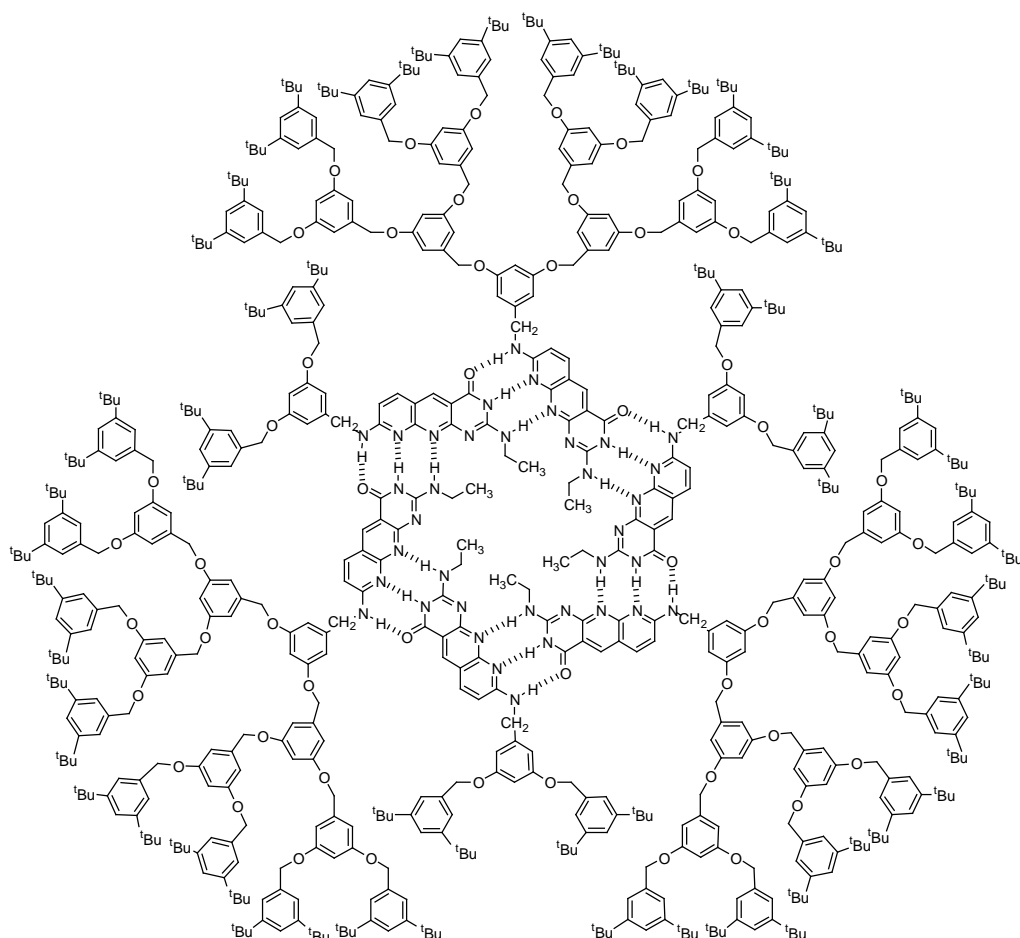


Figure 3. Assembly of a mixture of first and third generation DDA:AAD hydrogen bonding dendrons only gave rise to a single hexameric rosette with alternating dendrons.

Self-assembling hydrogen-bonded rosettes have also been reported by other groups, including those of Reinhoudt [8] and Fréchet [9]. In both of these cases, two *complementary* wedges were used in order to achieve assembly. The two wedges possessed complementary hydrogen-bonding subunits at their focal points – one wedge possessing a melamine unit, the other having either a barbituric or cyanuric acid derivative. Interestingly, in this case, Fréchet and co-workers observed that higher generation (G3 and G4) systems did not give rise to the expected hexameric rosette, whilst lower generation systems did. They argued that this was because steric repulsions between the larger dendritic head groups could dominate over the relatively weak hydrogen-bonding interactions used to construct the rosette.

Recently, Fréchet and co-workers have assembled ‘bow-tie’ shaped molecules, in which two complementary dendrons are connected together in CDCl_3 *via* intermolecular hydrogen bond

and electrostatic interactions at their focal points (Figure 4) [10]. The focal points of these dendrimers were either functionalised with a bis(adamantylurea) group or with a complementary glycinylurea fragment. The authors reported that the *surface groups* of the dendrons, which are distant from the binding event at the core of the supramolecular system, can have a profound impact on the thermodynamics of binding. Removing the acetal protecting groups from the surfaces of one of the dendrons enhanced the binding strength, because the solubility of the deprotected dendron was significantly decreased. However, replacing these acetals with tri(ethylene oxide) groups decreased the binding, possibly as a consequence of backfolding (and steric hindrance) or competition for the hydrogen bonding sites at the core of the supramolecular species.

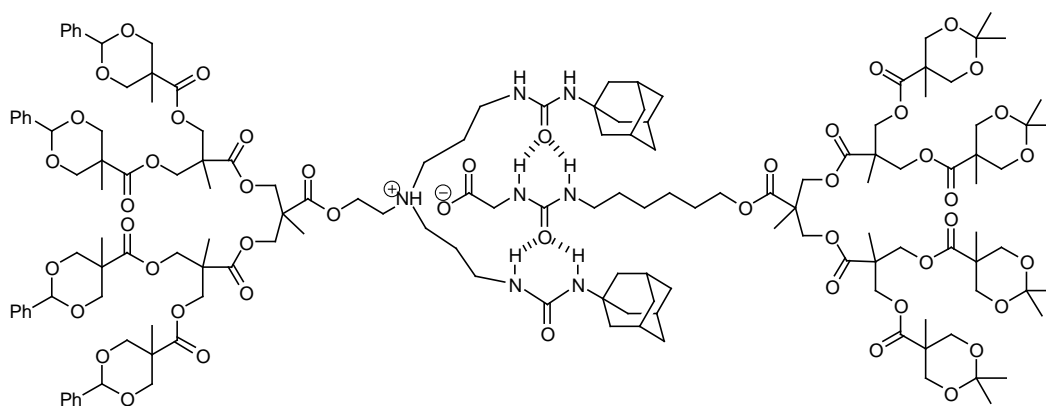


Figure 4. Assembly of two complementary dendrons into a ‘bow-tie’ structure *via* hydrogen bond and electrostatic interactions.

These studies indicate the way in which carefully designed dendrons can spontaneously assemble into more complex, yet well-defined supramolecular structures. By determining the structure-activity relationships in these types of assembly, it should prove possible to assemble even more complex, and ultimately multi-functional, nanoscale structures.

2.2 Assembly directed by organic templates

The systems described above are dendrons which *automatically* assemble into discrete supramolecular dendrimers in an appropriate solvent. However, systems have also been developed in which specific non-covalent interactions are used to assemble individual dendritic branches only in the presence of a suitably functionalised *template*. In many cases,

the template is a metal ion, and such systems are dealt with in more detail later (section 2.3). Firstly, however, we shall consider cases in which the template is an organic molecule.

Zimmerman and co-workers reported the first example of a dendrimer assembled in this way [11]. They used Fréchet-type dendritic wedges functionalised at the focal point with an anthridine unit. Two of these dendrons assembled around a bis-amidinium template (Figure 5) to generate a supramolecular dendrimer with a molecular mass over 10000. The dendritic generation had little effect on the thermodynamics of the assembly process – a result that was expected, given that the receptor is relatively rigid and the dendritic branching is oriented away from the binding site. The bis-amidinium cation used as a template in this case was chosen as it is active against *Pneumocystis carinii* pneumonia – a common opportunistic infection in AIDS patients. As such, this early research indicates the ability of supramolecular dendrimers to encapsulate *active templates* which play medicinally important roles.

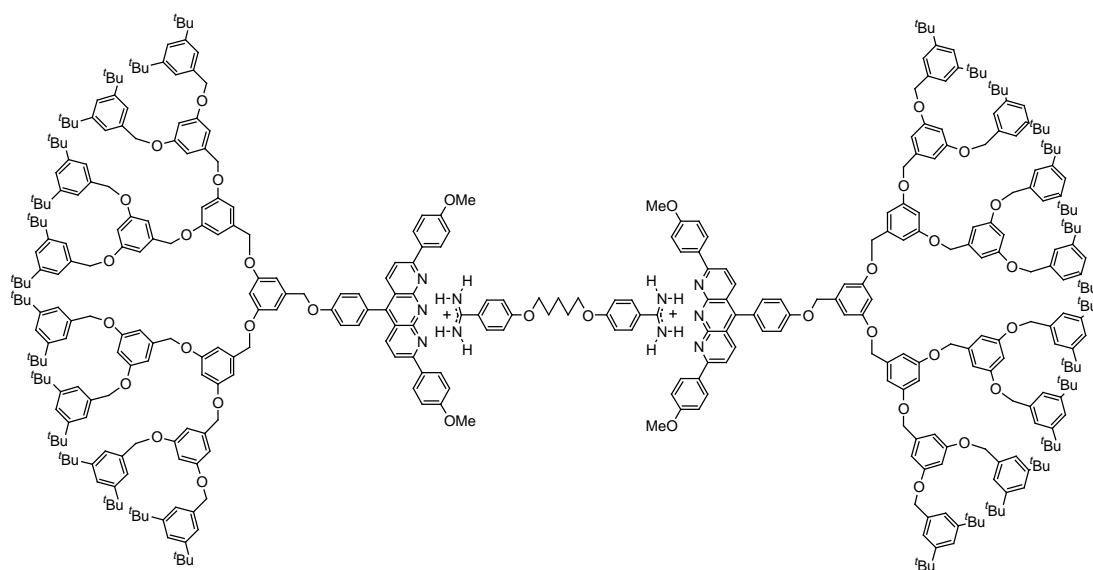


Figure 5. Assembly of anthridine focussed dendrons around a bis-amidinium organic template molecule as a consequence of hydrogen bond interactions.

Smith and co-workers have made extensive use of carboxylic acid-amine interactions to assemble supramolecular dendrimers [12]. Although relatively weak [13], such interactions, which consist of a hydrogen bond with an associated electrostatic interaction (if proton transfer occurs) have the benefit of being very general and hence have *widespread applicability*. In this research, L-lysine based dendrons, with a carboxylic acid at the focal

point were employed, exhibiting a good ability to solubilise hydrophilic amines into apolar solvents. Control experiments indicated that the presence of the carboxylic acid was important for effective solubilisation to occur (although there was also some non-specific binding in the branches). The solubilisation of hydrophilic proflavine hydrochloride into dichloromethane was shown to be generation dependent, with greater uptake occurring at higher generations of growth – presumably a consequence of more effective encapsulation of the template (Figure 6). In addition, the *optical properties* of the templating dye were generation dependent, with a shift in λ_{max} from 440 nm to 461 nm on progressing from using first to fourth generation dendrons. This indicates that the dendritic solubilising agent controls the *microenvironment* experienced by the dye [14]. Transport experiments indicated that these branches could continuously transport dye molecules through an apolar phase and deliver them into an aqueous medium. Furthermore, when using dendritic branches with an amine group at the focal point, it was shown that carboxylic acid functionalised templates could be solubilised and encapsulated [12b].

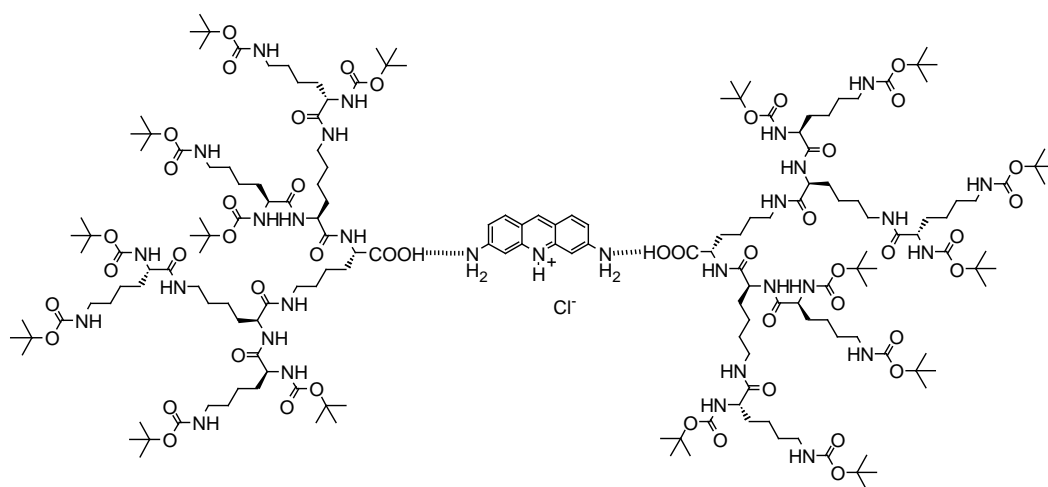


Figure 6. Dendrons encapsulating a hydrophilic dye as a consequence of acid-base interactions.

Given that these acid-base interactions are relatively weak, Smith and co-workers have also reported L-lysine dendrons functionalised at the focal point with a benzo-18-crown-6 derivative [15]. 18-Crown-6 is well-known to bind primary ammonium cations, with which it forms an electrostatic interaction supplemented by three complementary hydrogen bonds. By using di-protonated 1,4-bis-(aminomethyl)benzene, it was possible to assemble two crown-functionalised dendrons around the template, even in competitive methanol solution. As

might be expected, the thermodynamics of the assembly process became less favoured with increasing generation. It was argued that this was due to a combination of steric clashes between the branches and the fact that burial of the dipositively charged template within the dendritic shell, away from the polar solvent, is disfavoured. In this case, the key advantages of a supramolecular system were clearly demonstrated – *control* and *reversibility*. The addition of K^+ cations was used to disassemble the supramolecular dendrimer as a consequence of its ability to bind competitively to the crown ether ring (Figure 7). The template bis-ammonium cation was effectively ‘released’ into solution, a process which could be followed by 1H NMR. This clearly illustrates the potential for supramolecular dendrimers to be used in *controlled release* applications. This use of supramolecular dendrimers would be of particular interest if the templating species was an *active* pharmaceutical or agrochemical.

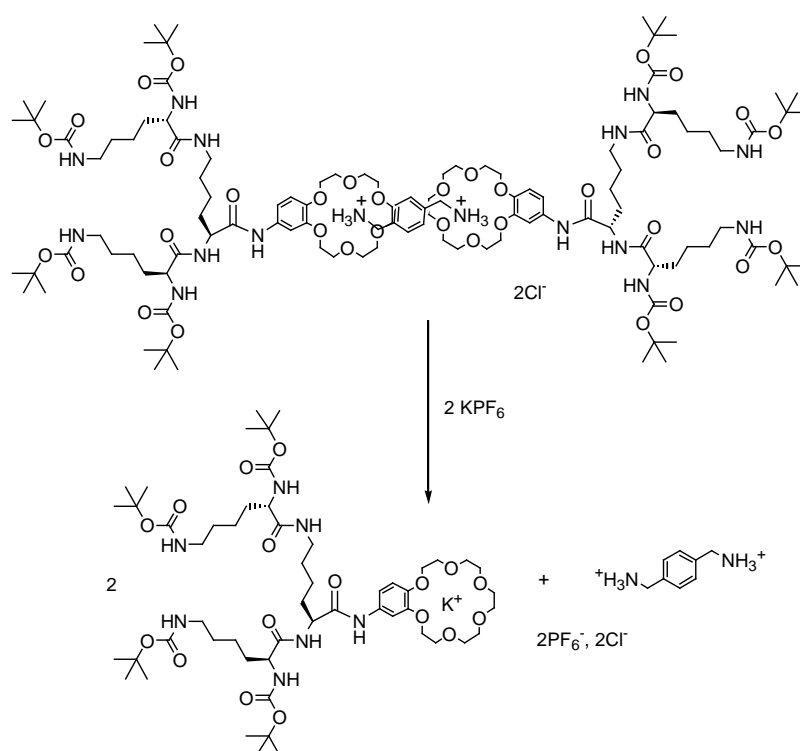


Figure 7. Assembly of crown ether functionalised dendrons around a bis-ammonium cation, and disassembly of the complex triggered by the addition of K^+ ions, which gives controlled release of the template into solution.

Dendrons have also been assembled around functional organic cores using purely *electrostatic* interactions. Anionic tetrakis-sulfonate-functionalised porphyrins have been used as a template for the assembly of dendritic branches which have a positively charged

quaternary ammonium salt at their focal point (Figure 8) [16]. Interestingly, as in the results described above, the authors noted a dendritic effect on the UV-visible properties of the encapsulated template. The λ_{\max} value of the porphyrin Soret band shifted from 415 nm when using first generation dendrons to 426.5 nm when using third generation systems. These results once again indicate the potential of dendritic branches to non-covalently modify the properties of an active core – such effects are well-known in covalent dendrimer chemistry [17], but the application of a supramolecular approach offers considerable *synthetic advantages*.

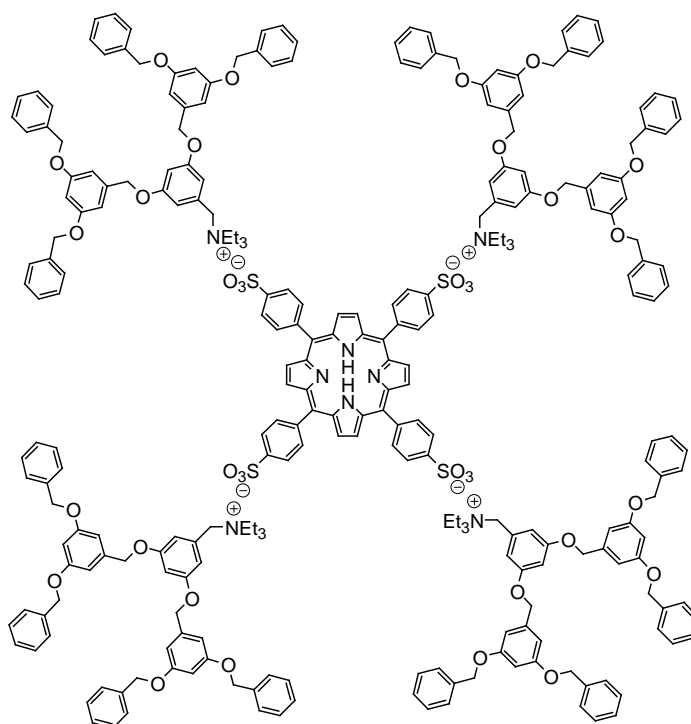


Figure 8. Encapsulation of an anionic porphyrin by cationic dendrons as a consequence of electrostatic interactions.

In addition to assembling dendrons around appropriate template species, fully formed spherical dendrimers possessing a well-defined binding site at the core have also been assembled into higher order complexes. Diederich and Kenda made use of dendritic cyclophane (dendrophane) receptors in this way [18]. Such receptors bind guests as a consequence of *solvophobic* interactions within the cyclophane cavity. This type of binding is particularly strong in water, and hence these assemblies persist even in biologically relevant aqueous conditions. In their investigations, a rigid rod functionalised with two terminal testosterone groups was designed, the length of which could be varied. Steroids such as

testosterone bind to cyclophanes with high binding strengths in water, and consequently one dendropane could bind to each end of the rod. Elegantly, Diederich and Kenda illustrated that the ability to generate a 2:1 assembly in which both ends of the rod become complexed (Figure 9), was dependent on both the *length of the rod* and the *generation of the dendrimer*. With a short spacer chain, the steroid-steroid distance is 4.1 nm, and the second generation dendrimer was only able to bind to one end of the rod. Steric hindrance and electrostatic repulsion presumably prevent the second binding event from taking place. However, with a longer spacer, and a steroid-steroid distance of 5.5 nm, both binding events could be clearly observed with the second generation dendropane. This allows the extension of the dendritic shells to be estimated, and hence means that these rigid rods effectively act as *nano-scale rulers*. The large assembled structure which is generated also illustrates the power of self-assembly to readily synthesise large systems – in this case the molecular mass is over 14000.

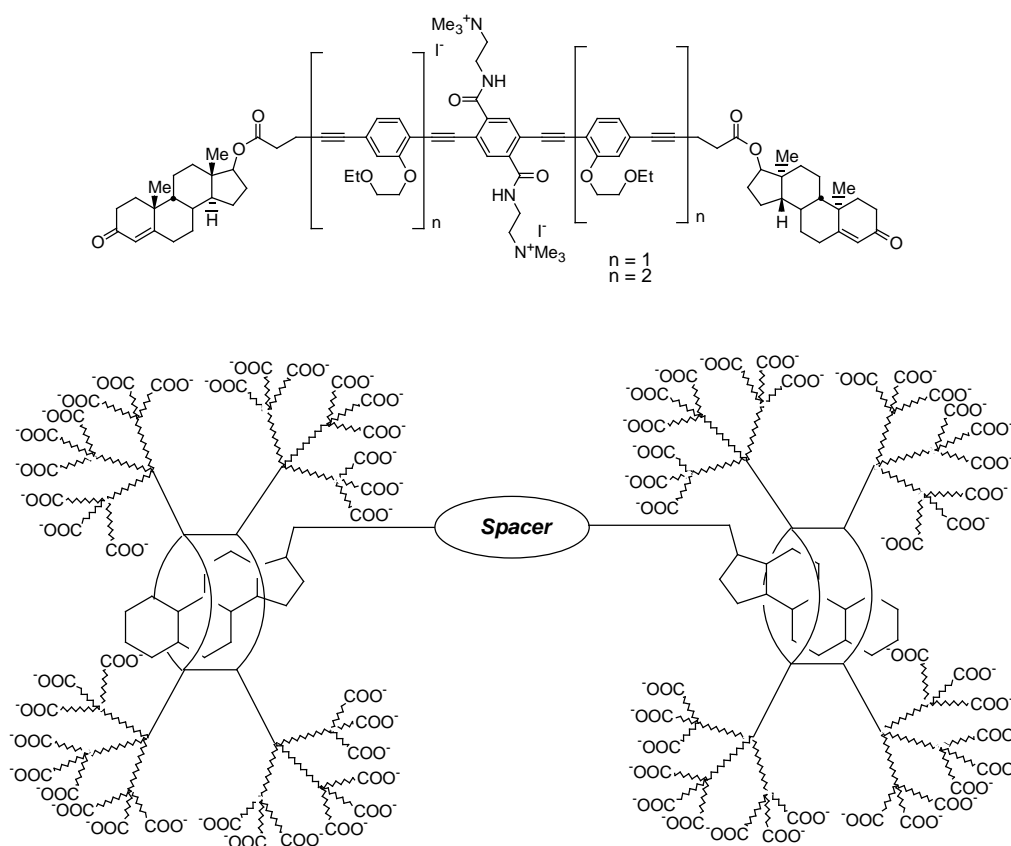


Figure 9. Dendritic cyclophanes (dendrophanes) self-assemble around a rod with steroid termini in aqueous solution. The rigid rod acts as a molecular-scale ruler capable of effectively measuring the extension of dendritic shells of different generations.

Newkome and co-workers also employed a similar strategy to assemble dendritic cyclodextrin derivatives around a bis(adamantane ester) [19]. In contrast to the work described above, the spacer chain on the organic template was flexible, and perhaps as a consequence, no clear dendritic effects on the assembly process were reported.

2.3 Interlocked molecules with dendritic components

In some cases, it is possible that the organic template species can be bound in such a way that the two components end up being interlocked. Indeed, there is intense interest in the ability of self-assembly to generate nanostructures in which the individual components are *interlocked* rather than covalently connected [20]. Such structures offer the potential to act as prototype molecular mechanical devices. It is therefore not surprising that the ability of dendritic groups to play a *pro-active role* in the assembly of interlocked species has been investigated [21].

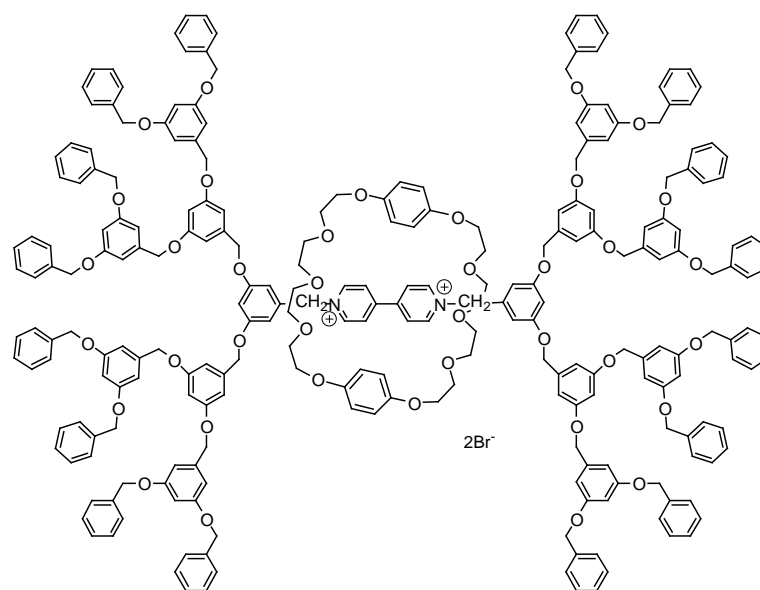


Figure 10. [2]Rotaxane with dendritic stoppering groups.

Stoddart and co-workers used the steric bulk of a dendritic branch to generate an effective stoppering system for a [2]rotaxane (Figure 10) based on the interaction between bis-*p*-phenylene-34-crown-10 (rotor) and functionalised bipyridinium (axle) [22]. By covalently connecting the sterically encumbering third generation dendritic head groups to the axle, *dethreading* of the interlocked architecture was prevented. Rotaxanes containing multiple

bipyridinium units on the axle were synthesised so that dynamic behaviour of the rotor could be investigated. The authors argued that the dendritic stoppering groups, in addition to their obvious steric effects (preventing de-threading), play a pro-active role in *enhancing the solubility* of these systems in common organic solvents, in spite of the high charge on the multi-bipyridinium axle. This allowed the solvent dependence of the shuttling action of this type of rotaxane to be investigated for the first time.

[2]Rotaxanes with dendritic stoppering groups have also been reported by Vögtle and co-workers, who made use of their trapping procedure for templated rotaxane synthesis [23]. Of particular interest in this study was the fact that the authors compared the differences between dendritic head groups and conventional stoppers. Specifically, they used NMR methods to investigate the rate of de-threading at elevated temperatures – a process which is known to occur *via a slippage mechanism*. This mechanism is dependent on the effective spatial demand of the stoppering group (and hence its ability to ‘slip’ through the macrocyclic ring). As expected, higher generation dendrons de-threaded more slowly than their lower generation analogues. Furthermore, the authors were able to make comparisons between Fréchet-type dendrons and more rigid conventional molecules, which provided useful information about the *dynamic spatial demand* of these dendrons – information which was difficult to obtain using other approaches

In the examples above, the dendritic blocks were put into place using *covalent chemistry*, and were not directly involved in the self-assembly step of the synthesis. Jeong and Park, however, have recently reported a [2]rotaxane in which the actual assembling building blocks are already dendritically functionalised before assembly takes place, and in this way, the *dendritic building blocks spontaneously assemble* into an interlocked architecture (Figure 11) [24] Assembly occurs as a consequence of osmium coordination (to form the cyclic rotor) and hydrogen bonding interactions (to stabilise the threaded form of the axle). Even for higher generation systems, de-threading could still occur at ambient temperature, presumably because the coordinate bonds in this system are reversible and hence the ring can fracture to assist the de-threading process. However, increasing the dendritic generation did, to some extent, increase the energy barrier to the de-threading process.

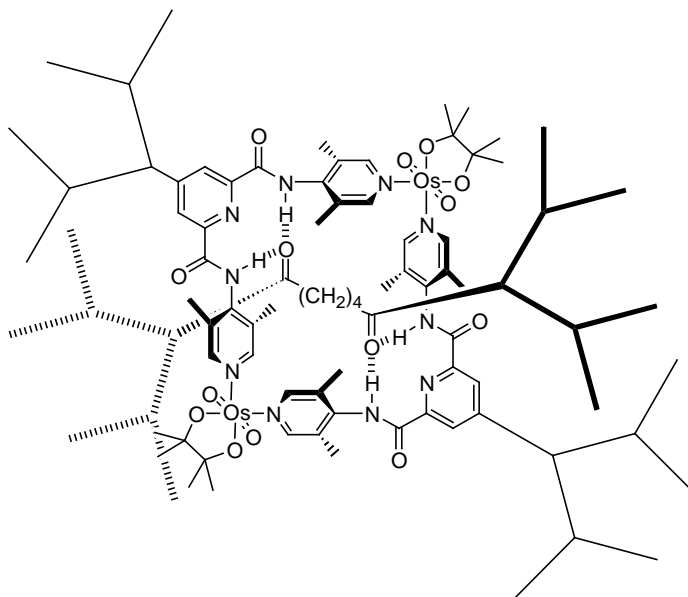


Figure 11. Assembly of a [2]rotaxane using dendritically functionalised building blocks.

Rotaxanes and pseudo-rotaxanes based on the interaction between dibenzo-24-crown-8 derivatives and a secondary ammonium cation have been of considerable use in the development of self-assembling dendritic systems. Gibson and co-workers first reported the innovative use of this chemistry for the assembly of dendritic systems in 1998 [25]. They used Fréchet-type dendrons functionalised at the focal point with a dibenzo-24-crown-8 moiety. This dendron interacted with a trivalent organic template possessing three secondary ammonium cations and solubilised it into chloroform (Figure 12). Using NMR and mass spectrometric methods, it was demonstrated that a 3:1 complex was obtained. Simple CPK modelling indicated that using the third generation dendrons would create an assembly with a diameter of *ca.* 12 nm. In a later, more detailed study [26], Gibson and co-workers reported that in non-polar solvents such as acetone, the binding of the trivalent template with the first, second and third generation dendrons showed strong *cooperativity*. In fact, in chloroform, only 3:1 assemblies were ever observed. Using simple, non-dendritic dibenzo-24-crown-8, however, gave rise to the expected statistical dependence of complex formation, with 1:1, 2:1 and 3:1 complexes all being observed. This indicates that in non-polar solvents such as chloroform, the dendritic branches play a *pro-active role* to encourage the *encapsulation*, and hence *solubilisation* of the polar template.

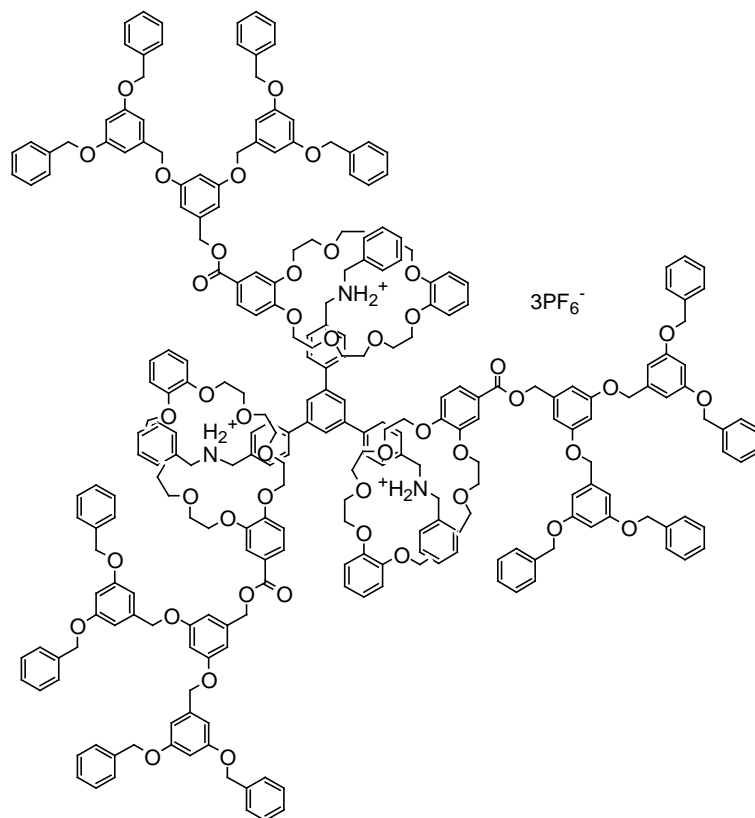


Figure 12. Assembly of dibenzo-24-crown-8 functionalised dendrons around a trivalent organic core yields a pseudo-rotaxane type 3:1 interlocked assembly.

Stoddart and co-workers have also made use of the interaction between crown ethers and secondary ammonium cations to generate interlocked branched systems [27]. However, in this case, the dendritic branching was added using covalent Wittig methodology after the non-covalent interlocking assembly process had taken place. The dendritic branching therefore acts as a stopper, converting the non-covalently held pseudo-rotaxane structure into a permanently interlocked rotaxane. This group has also made use of *slippage* to assemble a supramolecular dendrimer (Figure 13) [28]. They took a Fréchet-type dendron with a secondary dialkylammonium ion at the focal point and firstly investigated its thermally induced slippage into a dibenzo-24-crown-8 macrocycle. The synthesis required 10 days refluxing in dichloromethane, and the assembled structure disassembled itself with a half-life of 7.8 h when dissolved in DMSO solution at room temperature. They then also functionalised the dibenzo-24-crown-8 macrocycle with two Fréchet-type dendrons, and reinvestigated the slippage and deslippage reactions. Slippage was now much slower, requiring 90 days at reflux, whilst the half-life for disassembly of the complex was increased to 17.7 h in DMSO at room temperature. This is presumably a consequence of *steric*

hindrance between all the branched units, which hinders the motion required for interlocking or de-threading to occur. The authors speculate that such systems may have potential applications in *controlled release* technologies, where slow release of an active ingredient is required.

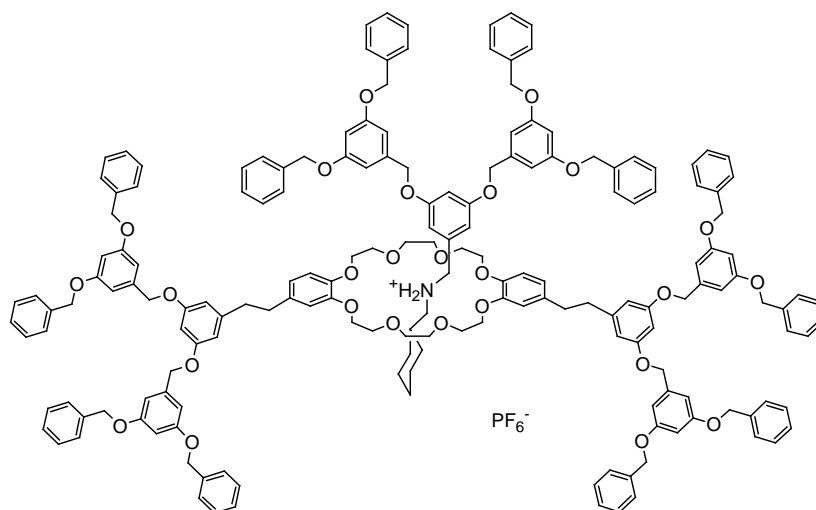


Figure 13. Interlocked branched architecture assembled as a consequence of slippage of the dialkylammonium cation through the dibenzo-24-crown-8 macrocycle.

2.4 Assembly directed by a single metal ion

The use of *metal coordination* is perhaps the most highly developed method for the directed assembly of dendritic superstructures, and the coverage in this article is not intended to be comprehensive. However, we intend to illustrate the different key strategies by which metals have been employed in the assembly of multiple dendritic building blocks.

Balzani and co-workers realised early on in dendrimer chemistry that metal centres could themselves act as *branching points* within a dendritic architecture, and that self-assembly of metal ions with appropriate ligands could generate supramolecular metallo-dendrimers in a single step [29]. However, such examples, although outstanding exemplars of the self-assembly approach to synthesis, do not actually assemble multiple building blocks that are, in their own right, dendritic. Hence, this approach will not be dealt with in detail here.

More relevant to the concept of assembling dendritic building blocks is the pioneering work of Newkome, Constable and co-workers, exploiting metal centres as '*building-block*

connectors' [30]. By using the interaction between ruthenium(II) and dendron-functionalised terpyridine ligands, it was possible to construct dendrimers held together by terpyridine-ruthenium *coordination interactions*. In order to do this, the periphery of a spherical dendrimer was functionalised with multiple terpyridine units, and subsequent reaction with a ruthenium(II) focussed dendron enabled the placement of an additional layer of branching onto the dendritic surface *via* metal coordination interactions (Figure 14). Such structures generally have multiple metal ions within the branches, holding the dendritic structure together. Recently, Newkome and co-workers have varied the structure of the ruthenium(II) focussed dendron in order to yield supramolecular dendrimers with a variety of different surface groups [31]. They have also extended this approach to enable the formation of dendritic systems with internal carboxylate groups which neutralise the dipositive ruthenium cations which are found within the superstructure [32].

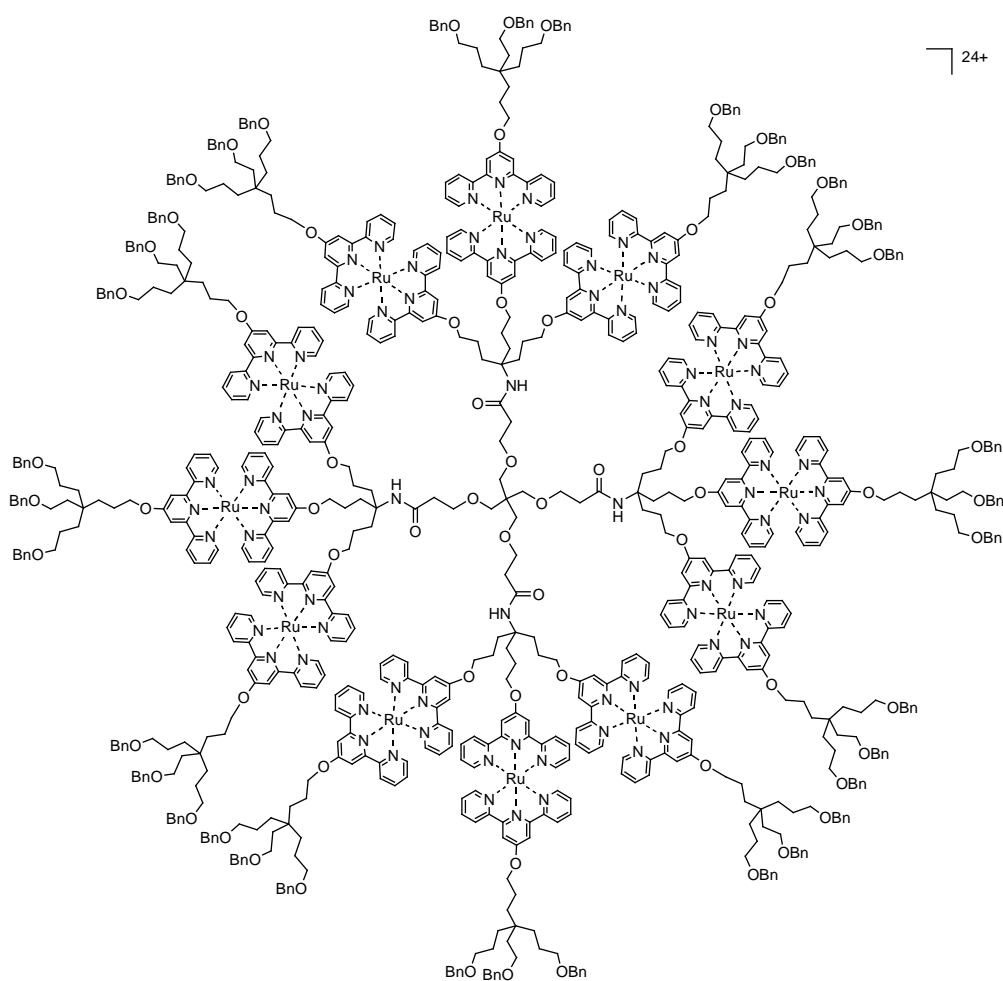


Figure 14. Ruthenium(II) terpyridine complexes can be used as ‘building block connectors’ for the assembly of dendritic architectures.

Most often however, rather than being located in the branches themselves, the metal centre forms the *core* of the supramolecular dendrimer – with dendrons that have ligating groups at the focal point being coordinated around a *single, central metal ion*. A wide range of different coordination chemistry approaches have been employed, and a flavour of these will be provided in the following discussion.

Vögtle and co-workers have made use of dendrons with 2,2'-bipyridine (bipy) ligands at the focal point [33]. Such ligands are well-known to bind metals such as ruthenium(II), and indeed, three dendrons can be coordinated around a single Ru(II) centre (Figure 15). There has been significant interest in investigating the *redox* and *optical* properties of the encapsulated ruthenium(II) ion, as it is often argued that dendritic encapsulation places an active unit in a unique local microenvironment [14]. Vögtle and co-workers have reported that the luminescent excited state of the ruthenium(II) ion at the core of the dendrimer is protected from dioxygen quenching. Indeed, the luminescent lifetime of the largest dendrimer (third generation) was three times longer than that of the first generation analogue in aerated acetonitrile solution.

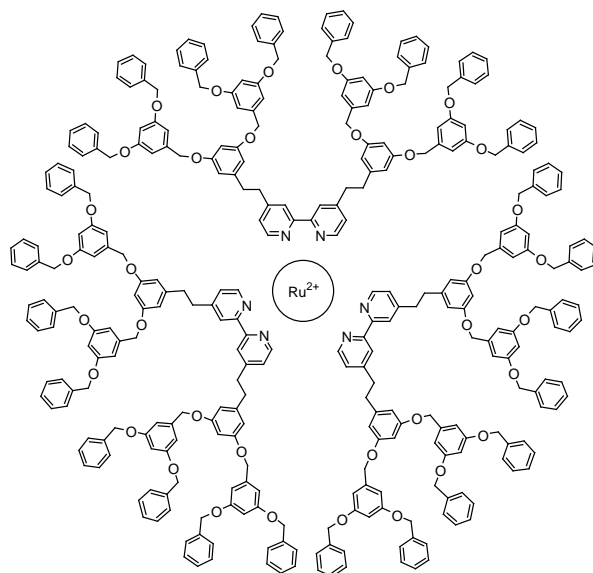


Figure 15. Dendrimer assembled as a consequence of Ru(II)-bipyridine coordination interactions at the core.

There have also been reports of dendrons with a terpyridine unit at the focal point being assembled around metal ions [34]. Once again, the ability of the dendritic shell to *tune* the properties of the encapsulated metal ion, in particular the redox properties of encapsulated

Ru(II), has been of primary interest. Chow and co-workers reported that the redox potential of the metal ion was unaffected by the extent of dendritic functionalisation, however, the redox reversibility could be correlated with the size of the dendrimer (as determined from size exclusion chromatography), because the assembled dendritic shell *hinders effective electron transfer* from the electrode to the metal ion. Meanwhile, Nierengarten and co-workers have employed phenanthroline-copper(II) interactions to assemble dendritic systems functionalised on the periphery with multiple fullerene units [35]. Particularly noteworthy was the high molar extinction coefficient observed for this assembly as a consequence of the large number of fullerene units on the dendritic surface.

Other ligating groups have also been placed at the focal points of dendrons. For example, Narayanan and Wiener prepared dendrons containing an ethylenediamine unit which assembled around a Co(III) metal ion [36]. Meanwhile amino-acids with dendritic side chains have been bound to Zn(II) and Co(II) to give pseudo-tetrahedral complexes [37] and to Cu(II) ions to give square-planar assemblies [38]. As illustrated by this comparison, the *geometric preferences* of different metal ions (as a consequence of their d-electron counts and ligand field stabilisation energies) enables the *controlled assembly* of dendritic supermolecules with *well-defined shapes*. Dendrons with focal phosphine-type ligands have also been reported, and used for assembly around iridium carbonyl complexes, the resultant complex going on to act as a host for C₆₀ [39].

Metals have recently been used to self-assemble dendrimers designed for *direct intervention in biological processes*. Roy and co-workers used bipyridine focussed dendrons with surface saccharide functionalisation (Figure 16) [40]. These ligands were assembled around copper (II) ions, and the lectin binding activity of the saccharide arrays on the surface of the assembled dendrimer was evaluated. Interestingly, the assembled complexes were shown to possess significantly greater activities than the simple uncoordinated dendrons, indicating the power of self-assembly to generate supramolecular dendrimers with *enhanced biological potency*. In a similar approach, Shinkai and co-workers assembled 4,4'-functionalised-2,2'-bipyridine derivatives with first generation 'Newkome-type' branching which had a carboxylate functionalised surface. They monitored the ability of these assemblies to bind to the surface of cytochrome c *via* electrostatic interactions [41]. They found that not only were these dendrimers able to bind to the biological target, but the asymmetric branched derivative was also able to undergo photoinduced electron transfer to the oxidised form of cytochrome c,

hence modulating the redox state of the biomolecule. This indicates how biological systems can be bound by self-assembled dendritic surfaces, with their properties being modified as a consequence.

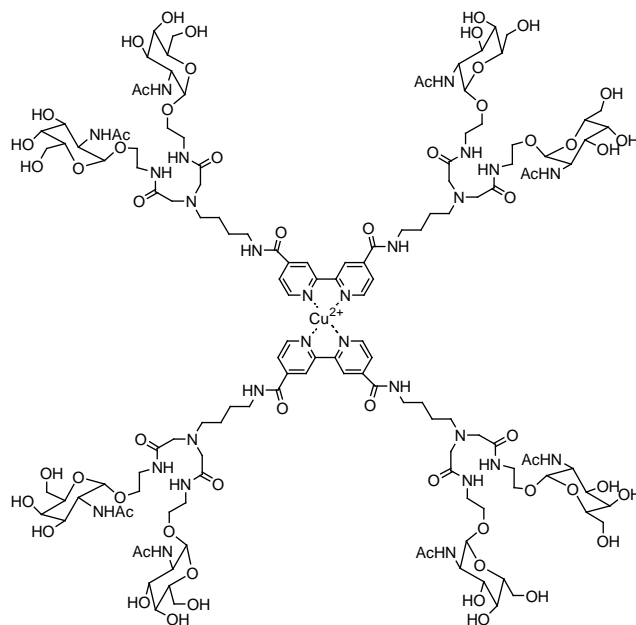


Figure 16. Assembled dendrimer which multiple saccharide groups on the surface exhibits enhanced lectin binding activity when compared with the individual dendron building blocks.

Burn and co-workers have used 2-phenylpyridine and benzothienylpyridyl derived branched ligands to bind iridium(III) [42]. Although the dendrimers employed have generally only been small (mainly first generation), the branched ligands provide the metal with *good solubility* in organic solvents, hence making this system ideal for solution processing methods such as spin coating or ink jet printing. Furthermore, the ligand plays a role in controlling the intermolecular interactions between the metal ions, with higher generation systems exhibiting enhanced photoluminescence quantum yields (PLQY). The PLQY of the second generation system was 150% that for the first generation system, and almost 300% that of the non-dendritic analogue. This research clearly illustrates how relatively small amounts of branching can be *multiplied up* by assembly or coordination processes to give rise to *significant effects*. The branched systems described above have real potential applications in *light emitting devices*.

Lanthanide ions have also been used as template ions for the assembly of supramolecular dendrimers. Due to the core-like nature of the 4f electrons, the binding of ligands to these

metals is considered to be predominantly *electrostatic* in nature, and hence hard anionic ligands have predominantly been employed. In a key paper, Kawa and Fréchet reported the assembly of carboxylate focussed dendrons around erbium(III), terbium(III) and europium(III) cations [43]. In each case, electrostatic considerations (charge neutralisation) require that three dendrons assemble around the central trivalent lanthanide cation (Figure 17). These complexes have interesting luminescent properties as the dendritic branching can act both as an *antenna*, funnelling energy absorbed by the branched shell down to the metal ion, but also as a means of *isolating the metal ion* from its neighbours – hence decreasing quenching and increasing the luminescence intensity [44]. This class of lanthanide complex consequently has potential applications in the development of components for *advanced fibre-optics* [45]. Smith and co-workers have taken a similar approach to encapsulating lanthanides within a dendritic shell using a dendron based on L-lysine which has a carboxylic-acid group at the focal point [46]. These researchers are interested in the potential future applications of these chiral lanthanide complexes as selective Lewis acid catalysts.

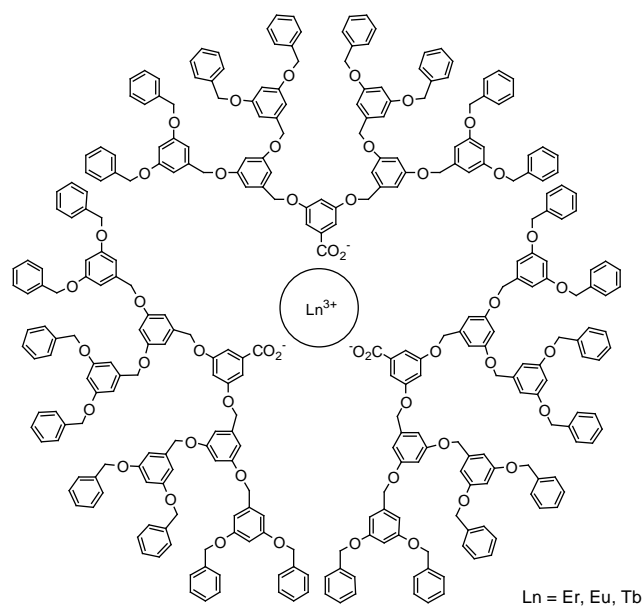


Figure 17. Dendrons which have a carboxylate group at the focal point assemble around trivalent lanthanide cations as a consequence of electrostatic interactions.

2.5 Assembly directed by well-defined metal clusters

All of the systems described above rely on the assembly of a dendritic structure around a single metal ion. However, *clusters of metals* can also be used as a core for the assembly of

dendritic structures. Perhaps the most extensively reported system is that of Gorman and co-workers who have assembled dendritic structures around iron-sulfur (Fe_4S_4) clusters [47]. Iron-sulfur clusters play key roles in biological electron transfer processes and therefore their encapsulation is of considerable *biomimetic* interest. In this case, the ligands employed are Fréchet-type dendrons with a thiolate group at the focal point. The thiolate group binds to vacant sites on the iron atoms in the cluster and gives rise to supramolecular dendrimers in which four dendrons are held around the iron-sulfur cluster by Fe-S coordination interactions (Figure 18). Investigation of the redox properties of these clusters has indicated that the presence of the dendritic branching plays a pro-active role in controlling both the kinetics and thermodynamics of the redox process. For example, in a recent study [48], this group prepared iron-sulfur clusters encapsulated by dendrons which were constitutional isomers – having either *ortho* or *meta* type linkages. They reported that the *ortho*-linked dendron encapsulated the metal cluster more effectively, hence slowing down the rate of electron transfer and making its reduction thermodynamically more difficult. These observations were consistent with the core being located in a more hydrophobic environment as a consequence of the greater degree of backfolding (and more effective encapsulation) generated by the *ortho*-linked dendrons. This same research group has also reported dendrimers based on the assembly of six dendrons with a phenoxide group at the focal point around a molybdenum chloride (Mo_6Cl_8) cluster core [49]. Meanwhile, Zheng and co-workers have described the coordinative synthesis of dendrimers using dendrons with nitrile ligands at the focal point which bind six times to rhenium selenide (Re_6Se_8) clusters [50].

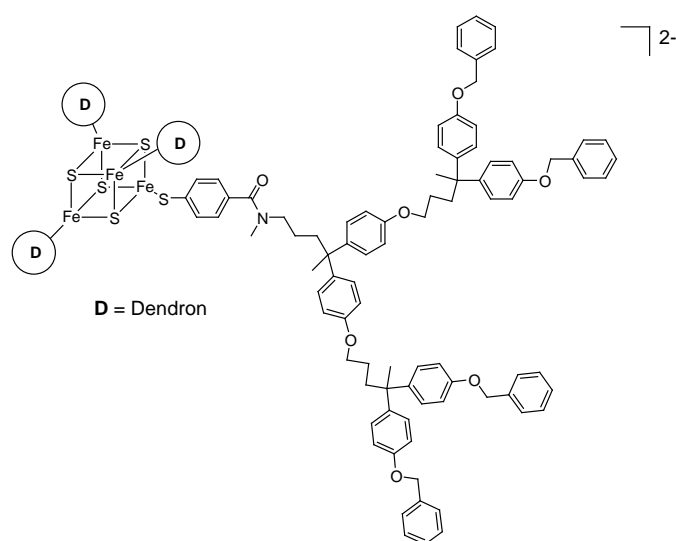


Figure 18. A dendritic iron-sulfur (Fe_4S_4) cluster.

Dendron encapsulated heteropolytungstate clusters possessing an $[(\text{Mn}(\text{H}_2\text{O}))_3(\text{SbW}_9\text{O}_{33})_2]$ core have also been reported [51]. This type of core is of interest because it exhibits excellent *homogeneous catalytic* properties for the epoxidation of dienes. The dendrons chosen were small Fréchet-type branches, with a quaternary ammonium cation at the focal point (Figure 19). These branches assemble around the polyanionic core as a consequence of electrostatic attraction, yielding a stable supramolecular entity. The dendron was capable of *extracting* the heteropolytungstate cluster from an aqueous phase into trichloromethane solution – indicating that binding of the cluster does indeed take place. Using a combination of modelling and small angle neutron scattering (SANS), a spherical structure with a diameter of approximately 3.5 nm was proposed for the assembly. Meanwhile, elemental analysis indicated that approximately 12 positively charged dendrons were associated with each of the dodeca-anionic clusters. Studies are ongoing to generate a range of assemblies using different dendrons so that the impact of the dendritic structure on the catalytic proficiency of the cluster can be fully evaluated.

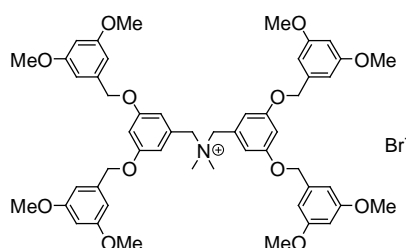


Figure 19. Positively charged dendron used for the encapsulation of a heteropolytungstate cluster $[(\text{Mn}(\text{H}_2\text{O}))_3(\text{SbW}_9\text{O}_{33})_2]$ *via* electrostatic interactions.

In each of the examples above, the cluster is a *preformed* entity, to which the dendrons bind, hence giving rise to encapsulation. However, dendrons can also encourage the *spontaneous formation of metal clusters*. In a particularly noteworthy example, Enomoto and Aida reported a ‘Fréchet-type’ dendrimer with a triazacyclononane ligand at the core [52]. Two of these dendritic ligands assemble around a bis(μ -oxo)dicopper(III) core to generate a supramolecular dendrimer containing two copper ions and bound oxygen (Figure 20). Dioxygen therefore acts as a *reactive template* for the assembly of the di-copper ‘cluster’. On warming these complexes, decomposition occurs as a consequence of the oxidative cleavage of N-C bonds within the dendron, and interestingly the rate of decomposition was observed to be generation dependent. For the unbranched compound, $t_{1/2}$ was 7 s, whilst for the second generation compound the half-life rose to 24 s, and for the third generation there was a

remarkable *increase in stability* with $t_{1/2}$ being 3075 s. It was argued that the larger, more hindered supramolecular dendrimers are less conformationally mobile, and hence the reactive core is unable to access the N-C(dendron) bonds as easily, hence increasing their stability. This type of reactive di-copper centre is of great interest as it *mimics biological systems* such as methane monooxygenase. Such encapsulated di-copper units can be difficult to synthesise using more traditional approaches, indicating the advantage of using dendritic self-assembly. These workers have used a similar approach to encapsulate di-iron(III) complexes as biological mimics [53].

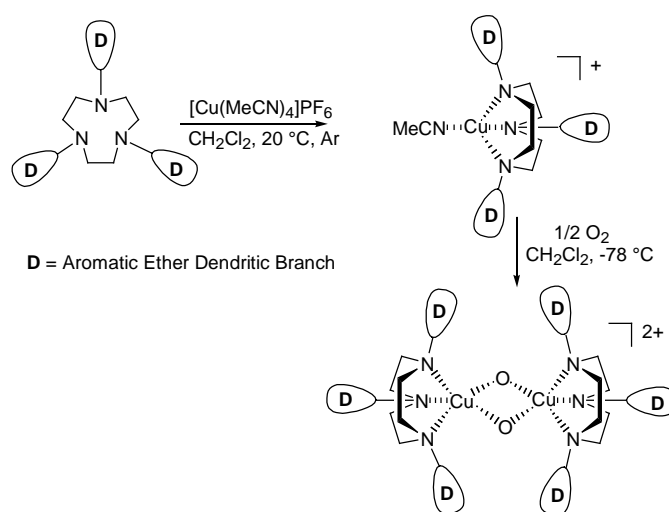


Figure 20. Assembly of a dendritic system with an encapsulated bis(μ -oxo)dicopper(III) complex core, the structure of which mimics enzymes such as methane monooxygenase.

In a recent paper, dendrons have also been designed which are able to assemble metal ions into an even more complex cluster. It is well-known that certain ligands encourage the assembly of large metallo-clusters, and Saalfrank and co-workers have exploited this knowledge in the design of dendritically modified diethanolamine type ligands which assemble metallodendrimers, with a ‘ferric wheel’ motif containing six iron(III) or indium(III) ions encapsulated within an assembled dendritic shell (Figure 21) [54]. This is a particularly powerful strategy by which multiple dendritic building blocks can be assembled around a functional core, which itself is assembled due to the pre-organisation of the ligand system, with the net result being well-defined, discrete, nanoscale assemblies.

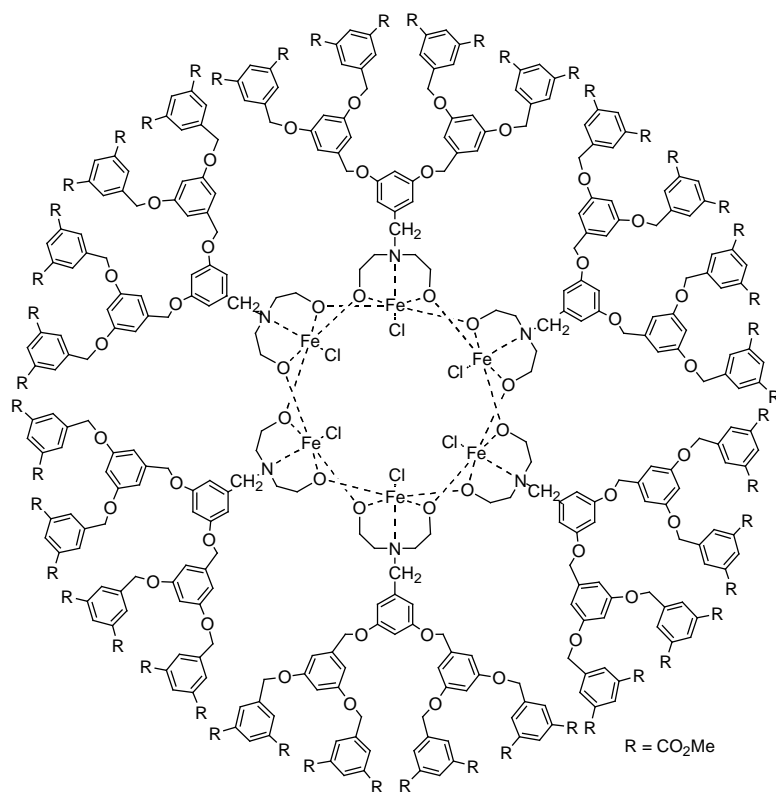


Figure 21. The assembly of a ‘ferric wheel’ using dendritically functionalised ligands results in an encapsulated well-defined metal cluster.

3. Self-assembly of discrete nanoscale structures which exist as statistical distributions

In the examples described in Section 2, the supramolecular dendrimers had *well-defined, monodisperse* structures, possessing an equivalent degree of structural definition to a molecule constructed using a traditional covalent approach. However, it is also possible to use the self-assembly of dendritic building blocks to generate structures that, whilst still *discrete entities*, are not monodisperse, and exist as a *statistical distribution of slightly different structures*, which make use of varying numbers of dendritic building blocks. Interestingly, the information programmed into the dendritic building blocks often plays a direct role in controlling the size, structure and/or polydispersity of the assemblies generated.

3.1 Dendron-stabilised nanoparticles

The reduction of gold(III) gives rise to gold(0) and it is well-established that in the presence of stabilising ligands the precipitation of bulk gold metal can be prevented, and instead the

gold forms discrete *nanoparticles*, surrounded by a stabilising shell of organic ligand (Figure 22) [55]. Sulfur containing ligands are frequently used for the stabilisation of gold(0) due to the high strength of the Au-S interaction. A number of research groups have pioneered the use of dendritic ligands to generate gold nanoparticles, with the aim of using the branching to control the synthesis and enhance the stability of the resultant assemblies. In 2001, the groups of Kim [56] and Zheng [57] both reported dendron stabilised nanoparticles. Kim and co-workers used Fréchet-type dendrons possessing a single thiol group at the focal point (Figure 23a), and found that the assembled nanoparticles had small cores (2.4-3.1 nm) with narrow size distributions and *remarkable stabilities*. Zheng and co-workers on the other hand, used a 4-pyridone ligand at the focal point of an aromatic ether triply-branched dendron (Figure 23b). Interestingly, UV-Visible and transmission electron microscopy (TEM) studies indicated that the size to which the nanoparticles grew was dependent on the dendritic generation, with first generation dendrons yielding nanoparticles with 2.0 nm diameters, whilst second and third generation dendrons gave rise to particles with diameters of 3.3 nm and 5.1 nm respectively – clearly indicating the possibility of *dendritic control of nano-architecture dimensions*. However, these particles had broader size distribution ranges than those reported by Kim and co-workers, perhaps a consequence of the fact that 4-pyridone is a less effective stabilising ligand than a thiol.

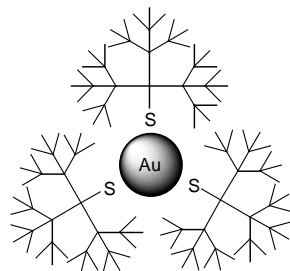


Figure 22. Schematic illustration of a dendritically stabilised gold nanoparticle.

Torigoe and co-workers have also used Fréchet-type dendrons of varying dendritic generation with a thiol group at the focal point for the assembly of gold nanoparticles [58]. These authors reported relatively *narrow size distributions* for the nanoparticles, and they observed that the diameter of the nanoparticles formed increased with increasing dendritic generation (from 1.46 nm using the first generation dendron to 3.77 nm with the fourth generation analogue). Once deposited on carbon film, these nanocomposites appeared to form a *regular assembly*, with the particles laying-down in one-dimensional ‘stripes’. Fox and co-workers

have also used Fréchet-type dendrimers, but in this case with a disulfide at the centre. During the nanoparticle synthesis, the disulfide bond is cleaved and individual dendrons are bound to the nanoparticle surface [59]. The resultant nanoparticles were analysed using TEM and thermal gravimetric analysis (TGA) as well as by UV-Vis, IR and NMR spectroscopic methods. Although the nanoparticle size distributions were relatively broad, the authors reported that the number of dendrons attached per square nanometre of core surface area decreased from 2.18/nm² for the second generation system to 0.27/nm² for the fifth generation analogue. This is due to the steric hindrance of the branching, and indicates that for higher generation stabilising ligands, fewer of the gold atoms on the nanoparticle surface are passivated by the formation of a Au-S bond. This has interesting potential applications in the development of nanoparticles in which the surface of the nanoparticle is catalytically active. With this goal in mind, Fox and co-workers also reported dendron stabilised palladium nanoparticles [60]. As with the gold nanoparticles, much of the metal surface remained *unpassivated* when using higher generation dendrons. Indeed for the third generation system, nearly 90% of the surface is theoretically available for catalysis. Preliminary investigations indicated that although third generation stabilised palladium nanoparticles were not proficient in hydrogenation reactions, they could catalyse Heck and Suzuki reactions. However, no special effects of the dendritic shell other than *solubilisation* of the nanoparticle have been reported yet, and it remains to be seen whether dendron stabilisation can control, for example, the ingress and egress of reagents and products from the catalytic surface.

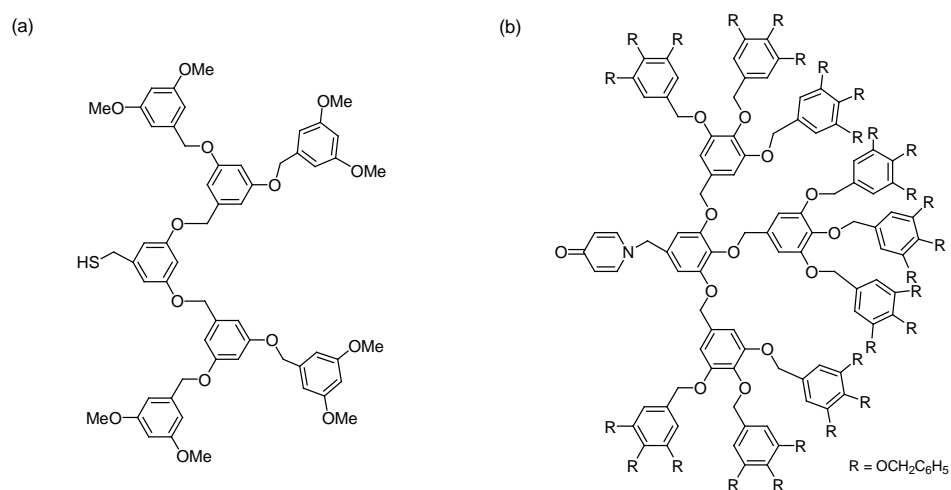


Figure 23. Dendrons which have been used for the stabilisation of gold nanoparticle surfaces.

Instead of using Fréchet-type dendrons, Smith, Chechik and co-workers have developed gold nanoparticles in which the dendritic stabilising ligand is based on an L-lysine repeat unit [61]. The use of this type of branching in self-assembling systems is of considerable interest as a consequence of its *biocompatibility* [62]. A series of disulfide cored dendrimers was prepared (Figure 24) and their effect on the assembly of gold nanoparticles was determined. It was noted that the dendritic generation controlled the diameter of the resultant nanoparticles, as determined using TEM and UV-Vis spectroscopy methods. In this case, as the size of the dendritic unit increased, the diameter of the nanoparticles formed decreased (G1 – 2.9 nm; G2 – 2.4 nm; G3 – 1.8 nm). Interestingly, it was found that the nanoparticles had remarkable thermal stability in solution, being stable even for prolonged periods of time at 100°C. Once heated to 120°C, however, the nanoparticles began to evolve through a ripening process, and became larger in size. In this way, larger particles with diameters of ca. 8 nm could be generated. The nanoparticle growth process could be visualised both by the naked eye, but also using UV-Vis spectroscopic methods. These larger particles were *stable for extended periods* and could be evaporated to dryness and re-dispersed. Interestingly, the dendritic branching controlled the rate of particle growth, and in most solvents the dendritic shell acted by retarding the rate of thermal ripening. This illustrates how information programmed into the dendritic branches can directly *influence the properties and reactivity of supramolecular assemblies* – one of the key advantages of using branched molecules in the assembly of nanoscale materials.

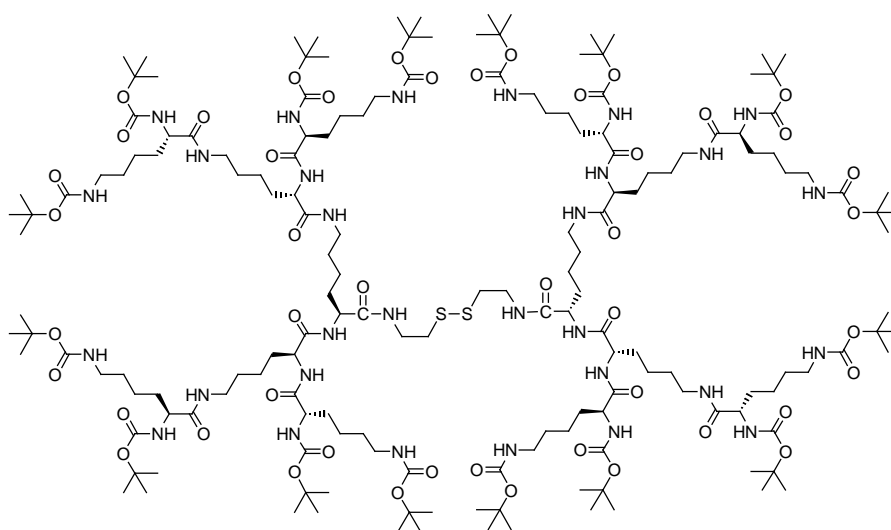


Figure 24. Third generation dendritic disulfides constructed using biocompatible L-lysine building blocks and used in the controlled assembly of gold nanoparticles.

Fox and co-workers have reported dendron-stabilised gold nanoparticles with peripheral carboxylate groups [63]. Aqueous solutions of these nanoparticles exhibited *micellar properties*. For example, pinacyanol chloride was solubilised increasingly well by increasing generations of the dendritic nanoparticle, with its UV-Vis spectrum being consistent with it being within a micellar microenvironment. Pyrene was also solubilised, however in this case there was no dendritic effect.

Astruc and co-workers have reported functional dendritic gold nanoparticles, capable of *sensing anionic species* [64]. They employed dendrons with a focal thiol group and ferrocenyl groups on the surface (Figure 25). Such redox-active groups are capable of electrochemically detecting anions *via* a shift in their redox waves as determined using cyclic voltammetry. This redox shift is a consequence of the positively charged oxidised ferrocenium form of the nanoparticle having a greater affinity for anionic guests than the neutral reduced ferrocene. Increasing the extent of the dendritic branching led to enhanced anion sensing (*i.e.* a more pronounced redox shift). These nanoparticles were used to fabricate reusable modified electrodes which showed selective sensing of phosphate anions (H_2PO_4^- and ATP^{2-}), even in the presence of competitive anions such as HSO_4^- and Cl^- . Interestingly, the non-dendritic analogues of these modified electrodes were not sufficiently stable, whilst employing dendritic branching clearly *enhanced electrode stability*. This example therefore indicates how dendritic assemblies can possess useful materials properties which will enable the fabrication of new *devices* for nanotechnology.

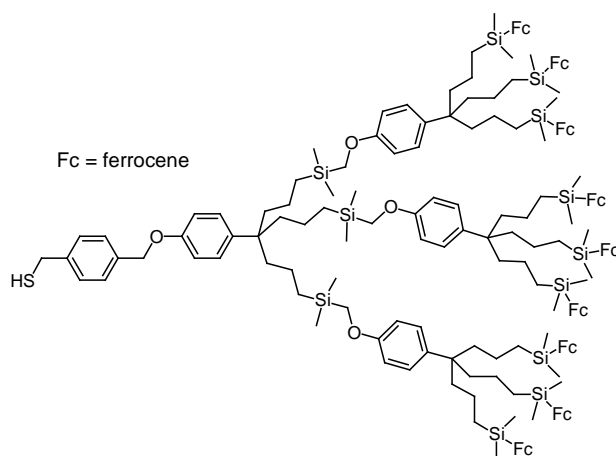


Figure 25. Dendritic ligands used for the assembly of functional gold nanoparticles which have anion sensing groups on the periphery.

In addition to the stabilisation of gold nanoparticles with dendron ligands, a similar strategy has also been applied to the synthesis of cadmium selenide (CdSe) nanocrystals. These semiconductor nanocrystals are of great interest for both their *electronic* and *fluorescent* properties, and are widely regarded as having important applications in the emerging field of nanotechnology. Peng and co-workers employed hydrophilic dendrons with a thiol group at the focal point [65]. The thiol group provides the point of attachment to the surface of a pre-formed CdSe nanoparticle, with ligand exchange being used to achieve the dendritic functionalisation. The ligand shell assembled around the CdSe nanoparticle was closely packed and about 1-2 nm thick. The presence of this ligand shell significantly enhanced the *stability* of the nanocrystal relative to simple long chain thiol ligands, and enabled further chemistry to be performed on the *surface* of the assembly – for example an ester functionalised surface was hydrolysed to the carboxylic acid or alternatively converted into an amide by addition of an amine under EDC coupling conditions. Being able to perform this type of chemistry on the surface of modified CdSe nanocrystals is of great importance for applications in *bio-nanotechnology*.

In an extension of this research, Peng and co-workers reported dendron stabilized CdSe nanocrystals in which the surface of the dendrons could be *cross-linked* using ring closing metathesis with Grubbs' catalyst (Figure 26) [66]. The dendritic branching plays a key role in this system, as without a sufficient degree of branching, it would not be possible to achieve effective cross-linking of the dendron shell. This concept, in which a reversible, self-assembled superstructure is *permanently 'captured'* using a *covalent 'fixing step'* is a key theme in self-assembly. It allows the advantages of using reversible supramolecular chemistry to generate remarkable assembled superstructures to be coupled with the advantages of having a permanent irreversible molecular skeleton. In this case, the surface cross-linked CdSe nanocrystals exhibited significantly *higher stabilities* than their non-cross-linked analogues – for example, surviving sintering at 100°C for 1 h. Given that many colloidal nanocrystals suffer from problems of poor stability, it was postulated that such assembled, cross-linked systems had sufficient stability for a wide range of technical applications to become possible. Interestingly, Peng and co-workers also illustrated that it was possible to remove the CdSe core using HCl and generate empty boxes (capsules). This approach to generating nanoscale *hollow capsules* is of potential significance in the field of *host-guest chemistry*.

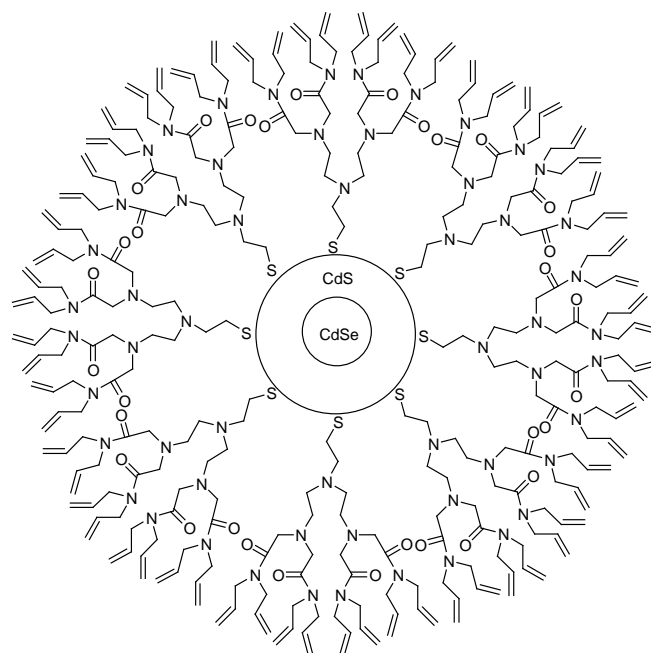


Figure 26. Stabilisation of CdSe nanoparticles by dendritic ligands, with cross-linking of the surface groups being used to permanently capture and stabilise the assembled architecture.

In order to enhance the *biocompatibility* of their cross-linked semiconductor dendron-box nanocrystals, Peng and co-workers have also employed an alternative cross-linking strategy to generate box-nanocrystals (Figure 27) [67]. In this approach a hydroxylated dendron-stabilised CdSe nanocrystal was activated and then cross-linked using small multivalent amine terminated spherical dendrimers. This gave rise to a cross-linked system with peripheral amine groups that could readily be coupled using reliable and mild methods. To demonstrate this, the surface of the nanocrystals was biotinylated and shown to give quantitative and reproducible precipitation of picomole quantities of avidin. These systems were observed to be fully biocompatible with the tested system, and exhibited no non-specific binding.

PAMAM dendrimers have also been used for the stabilisation of CdSe nanocrystal surfaces [68]. When hydrophilic full-generation PAMAM dendrimers were employed, aggregation of the CdSe particles occurred. However, using amphiphilic PAMAM derivatives modified with hydrophobic aliphatic chains, stabilised the CdSe nanocrystals and allowed their dissolution in chloroform. It was found that both amine groups (to interact with CdSe) and hydrophobic chains (to provide solubility) were required for the optimum stabilising effect. Furthermore, the extent of hydrophobic functionalisation controlled the stability of the nanoparticles, with

more highly functionalised systems showing greater resistance to oxidation processes. Controlling the *air stability* of CdSe nanoparticles in this way is of great importance in the development of their *electronic applications*.

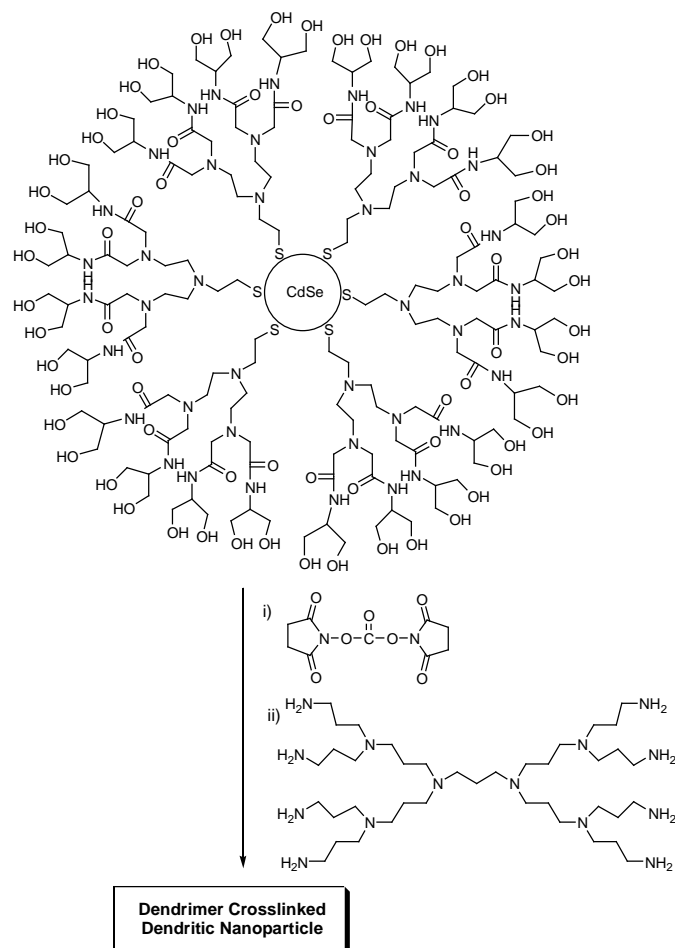


Figure 27. Cross-linking of dendritically stabilised CdSe nanocrystals using dendrimers with multivalent amine surface groups.

It should be pointed out at this point, that there are extensive accounts of metal nanoparticles being assembled within a *single* covalent spherical PAMAM dendrimer [69]. However, this alternative approach to nanoparticle stabilisation is beyond the scope of this article, as it does not rely on the assembly of multiple dendritic building blocks.

In addition to the assembly of dendritic systems on metal nanoparticles, Sakhivel and Florence have also reported the ability of *amphiphilic* dendrons to stabilise polystyrene latex nanoparticles with approximate diameters of 200 nm [70]. The dendrons possessed three (hydrophobic) C-14 chains coupled to a peptide at the focal point of an L-lysine dendron

which had 8, 16 or 32 (hydrophilic) terminal amine groups (Figure 28). These dendrons assembled around hydrophobic latex nanoparticles in phosphate buffered saline solution, a process which is not driven by specific interactions between the nanoparticle and the dendron ligand. Instead, it is the surface-activity of the dendron which encourages it to assemble around the hydrophobic latex nanoparticle, and hence achieve effective *phase separation*, with the hydrophobic components being shielded from the aqueous solvent medium by the dendritic shell. The number of dendrons absorbed per nanoparticle was found to vary with dendritic generation – approximately 4400 first generation dendrons were adsorbed on the nanoparticle surface, while only *ca.* 430 third generation dendrons were adsorbed (as a consequence of steric bulk). These supramolecular nanocomposites are of interest for potential applications in drug delivery. For a discussion of the untemplated assembly of amphiphilic dendrons, see Section 3.4.

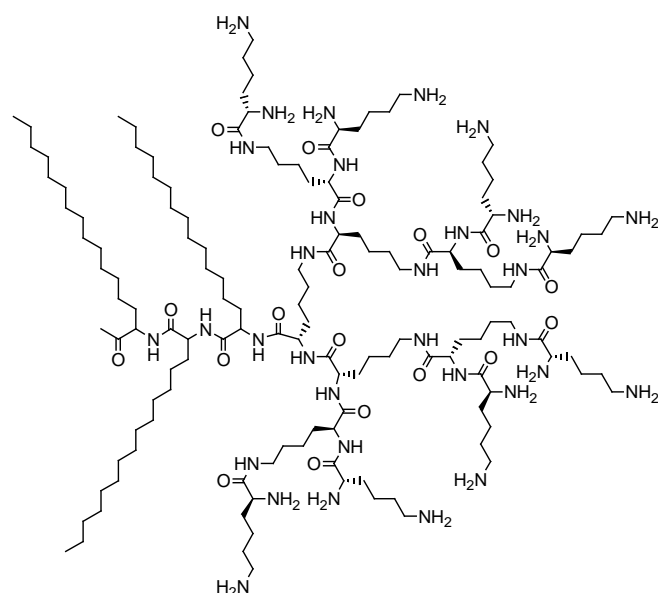


Figure 28. Dendron with surfactant-type properties used for assembly around hydrophobic polystyrene latex nanoparticles.

3.2 Assembly of dendrons and dendrimers in the presence of DNA

Perhaps the most important nanoscale template, at least in terms of its biological relevance, is *deoxyribonucleic acid* (DNA). The discovery of the structure of DNA is a key scientific achievement of the 20th century, and of particular importance is the understanding that many diseases depend on only a single fault within a gene. Consequently, scientists have become increasingly concerned with genetic manipulation. In order to treat genetic disorders in this

way, it is necessary to deliver healthy copies of the genetic material into cells, a process termed *gene therapy* [71]. There are two complementary approaches to solving this problem – viral delivery vehicles, and non-viral (or synthetic) delivery vehicles. Viral delivery systems have been trialled, and significant problems with, for example, immune response, have led to an increasing focus on the development of non-viral gene delivery systems. Since the mid 1990s, dendrimers have seen considerable development as *non-viral delivery vehicles* [72]. PAMAM dendrimers in particular have seen extensive study as a consequence of their positively charged polyamine surface, which is capable of interacting with the polyanionic phosphate backbone of DNA. This major area of dendrimer research was pioneered by insightful work from the groups of Szoka and Tomalia [73]. In this article, we will place particular emphasis on examples in which dendritic building blocks have been proven to assemble around the DNA double helix to generate *characterisable nanostructures* with gene transfection ability.

Interestingly, in early work, Szoka and co-workers indicated that the precise structure of the PAMAM dendrimer could play an important role in controlling the DNA delivery process. They reported that heating the dendrimers, which leads to fracturing of the three-dimensional spherical structure, led to significant enhancements in DNA transfection [74]. They referred to their systems as *fractured dendrimers*, and postulated that it was the enhanced flexibility of these systems which gave rise to their enhanced DNA delivery profiles, suggesting that this flexibility enabled the fractured dendrimer to be compact when complexed with DNA and to swell when DNA was released from the assembled superstructure. Electron microscopy methods were used to determine the morphologies of the assembled nanostructures [75]. It was discovered that all the complexes had *toroidal morphologies* (Figure 29), however, those formed using intact PAMAM had a tendency to aggregate further in solution, whilst those based on fractured PAMAM did not. Szoka and co-workers then went on to show that this kind of dendrimer-DNA complex can be applied both *in vitro* and *in vivo* [76]. Sixth generation fractured PAMAM dendrimers exhibited the highest *in vivo* gene transfer efficiency.

In parallel with Szoka's studies, Tomalia, Baker and co-workers were also investigating the nanoscale structures which were assembled when DNA was treated with PAMAM dendrimers. To this end, they applied a combination of electron paramagnetic resonance (EPR), circular dichroism (CD), UV and melting profile investigations on the DNA

complexes formed by second and sixth generation PAMAM dendrimers [77]. On increasing the concentration of the dendrimer relative to DNA they discovered that initially, minor stabilization of the double helix was detected. On increasing the concentration of dendrimer further, precipitation occurred as a consequence of charge neutralisation – reflecting the formation of high density, high molecular weight complexes. In the presence of excess dendrimer, however, the DNA was resolubilised and stable supramolecular structures were formed. These soluble complexes had a lower density, and Baker and co-workers reported that the majority of transfection (>90%) was being performed by these complexes, even though they only accounted for approximately 10-20% of the total DNA present [78]. In another study, it was proposed that for higher generation PAMAM dendrimers, the DNA effectively wrapped around the spherical dendrimer [79].

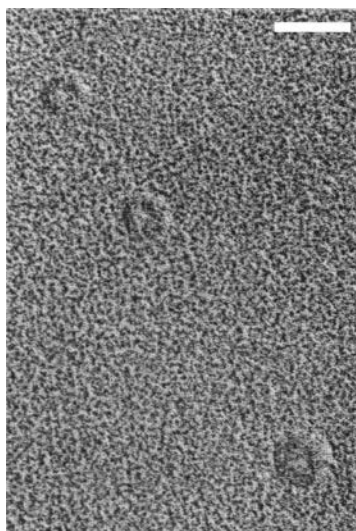


Figure 29. Complexes formed between fractured PAMAM dendrimers and DNA have toroidal morphologies as imaged here by TEM methods. Image reproduced from reference [75] with permission from Nature publishing group. Scale bar = 100 nm.

It is worth noting that the ability of PAMAM dendrimers to transfect DNA efficiently into cells is one of the *current commercial applications of dendrimer technology*. It is possible to purchase ‘Superfect™’ (a fractured PAMAM dendrimer) for use as a transfection agent. Superfect™ has been proven to be competitive with many other *in vitro* gene delivery agents in terms of its transfection activity and, in particular, has been shown to be less toxic than lipid transfection reagents, as well as avoiding their problems with serum dependence [80].

The exciting potential applications of these nanoscale DNA-PAMAM assemblies encouraged other groups to become involved and highlights of this research are discussed below. It is a pre-requisite for gene therapy that the DNA is effectively *protected from in vivo degradation* within the delivery vector, and Roberts and co-workers have used atomic force microscopy (AFM) to visualise the effect of DNase I (a DNA degrading enzyme) on fourth generation PAMAM complexed with DNA [81]. The formation of the nanoscale complex was observed to provide a degree of *protection* to the DNA, although the complex was dynamic in nature, with addition and loss of dendrimers to and from individual self-assembled complexes. The protection was found to be related to the nanoscale morphology of the complex. In particular, at high dendrimer:DNA ratios, spherical particles were formed (diameter measured as ca. 69 nm by AFM) which were still protected after 2 h, with no significant degradation being observed. It was also found to be important that the dendrimer:DNA complex was allowed to incubate for a sufficient period of time, so that stable nano-assemblies could be formed, affording maximum protection to the DNA.

One well-known general strategy for enhancing the activity of bioconjugates is the attachment of a *polyethylene glycol* (PEG) unit. PAMAM derivatives with ‘PEGylated’ surfaces have been reported and applied to DNA delivery [82]. Intriguingly, generation 5 PAMAM modified with PEG ($M_n = 3400$) was 20 times more effective at transfection than fractured PAMAM controls. Only approximately 10% of the surface amine groups were modified with PEG chains. The reason for the enhanced transfection ability has not been fully elucidated in structural terms, although it was proposed that the PEG chains enhanced the flexibility of the dendrimers. In addition, these modified PAMAMs exhibited very low cytotoxicities, although unfortunately high dendrimer:DNA ratios were required for effective transfection.

Park and co-workers have synthetically modified PAMAM dendrimers in a different way – methylating the internal amine groups of hydroxyl surfaced PAMAM dendrimers in order to provide the systems with a *permanent positive charge* across the whole pH scale (Figure 30) [83]. Dendrimers with distinct degrees of quaternisation could be produced by controlling the amount of methyl iodide employed in the methylation. As the degree of methylation (and hence permanent positive charge) was increased, more highly condensed nanoparticles were formed with DNA, with the fully quaternized system forming very small round assemblies with a diameter of ca. 53 nm. This was confirmed by AFM studies (Figure 30b). Furthermore, similar to the ‘PEGylated’ PAMAMs described above, the cytotoxicity of these

systems was much lower than that of the analogous PAMAMs with polyamine surface groups, although the transfection efficiency was also decreased by an order of magnitude. It was suggested that the partial shielding of the interior positive charges by the surface groups may be the reason for both of these decreases.

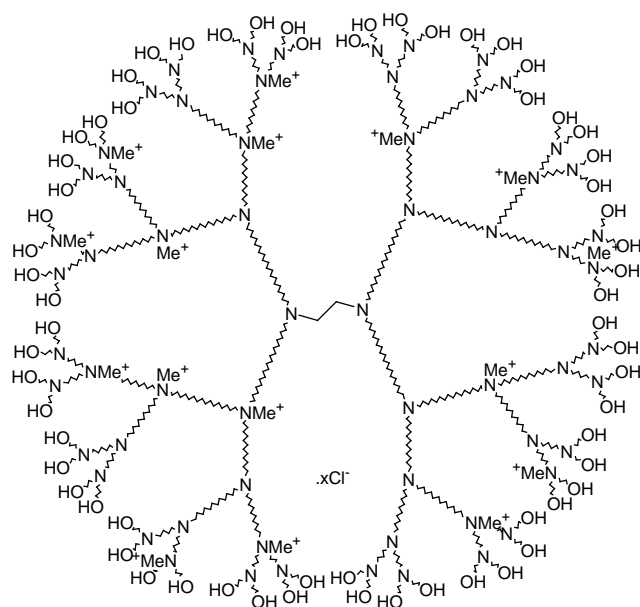


Figure 30. Partially methylated PAMAM dendrimers have a permanent positive charge for binding the phosphate groups on the DNA backbone as a consequence of electrostatic interactions.

The principles which underpin the interactions between DNA and PAMAM dendrimers can also be applied to the assembly of other anionic polymers with PAMAM. Sodium poly(L-glutamate) has been bound to PAMAM dendrimers, with TEM indicating that globular aggregates were formed, which were significantly larger than a single poly(L-glutamate) molecule [84]. Similarly, the interaction between a dendrimer with anionic carboxylate groups on the surface, and a cationic polymer (poly(dimethyldiallylammonium chloride)) has also been investigated, with the importance of pH in controlling the electrostatic assembly process being emphasised in this study [85].

It is not only PAMAM dendrimers that have been of interest for their ability to assemble with and transfect genetic material. One of the systems used as a standard in gene transfection studies is linear poly(L-lysine), and therefore it is not surprising that dendritic poly(L-lysine) has also been of interest in gene delivery applications. Niidome and co-workers have used

dendritic poly(L-lysine) for *in vitro* gene transfection studies [86]. Agarose gel electrophoresis and ethidium bromide displacement assays indicated that spherical dendrimers of the third generation and above constructed from L-lysine building blocks with a 1,6-diaminohexane core formed complexes with plasmid DNA. Ethidium bromide binding assays indicated that the degree of compaction of the DNA into a tight nanoscale assembly was increased with increasing dendritic generation. Indeed, fifth and sixth generation derivatives showed effective gene transfection ability with low cytotoxicity, even in the presence of 50% serum, whereas third and fourth generation dendritic systems did not exhibit significant activities. AFM and dynamic light scattering (DLS) studies on these systems indicated that after mixing for 15 min, 1-2 μm assemblies of complex (composed of several 50-200 nm particles) were formed, in addition to individual small complexes (50-500 nm) [87]. After incubation for 2 h, however, only the large complexes were present. Further studies indicated that in this case, it was these large complexes which were predominantly responsible for transfection *in vitro*. This is therefore an interesting example in which the *biological activity can be related to the nanoscale structure* of the assembled system, and indicates the importance of controlling the self-assembly process in order for the most effective biological activity profile to be obtained.

Simple *synthetic modifications* to dendritic L-lysine derivatives have also been made, offering a useful approach to generating advanced gene delivery properties. For example, the terminal lysines have been replaced with arginine and histidine units in order to observe the effect on transfection ability [88]. The dendritic systems with terminal arginine groups showed 3-12 fold higher transfection abilities than simple dendritic poly(L-lysine), whilst histidine terminated dendrimers did not transfect DNA. However, if the histidine terminated dendrimers were mixed with DNA at pH 5 (to ensure histidine protonation), a spherical complex with a diameter of 1-2 μm was formed which remained relatively stable when placed in neutral conditions. In a recent study, Vlasov and co-workers have used L-lysine type dendrimers and reported that the *chemical architecture* of the dendrimer plays a key role in controlling the structure and properties of its self-assembled complex with DNA – in particular, grafting lipophilic palmitoyl residues onto the dendrimer appeared to enhance DNA binding and compaction [89].

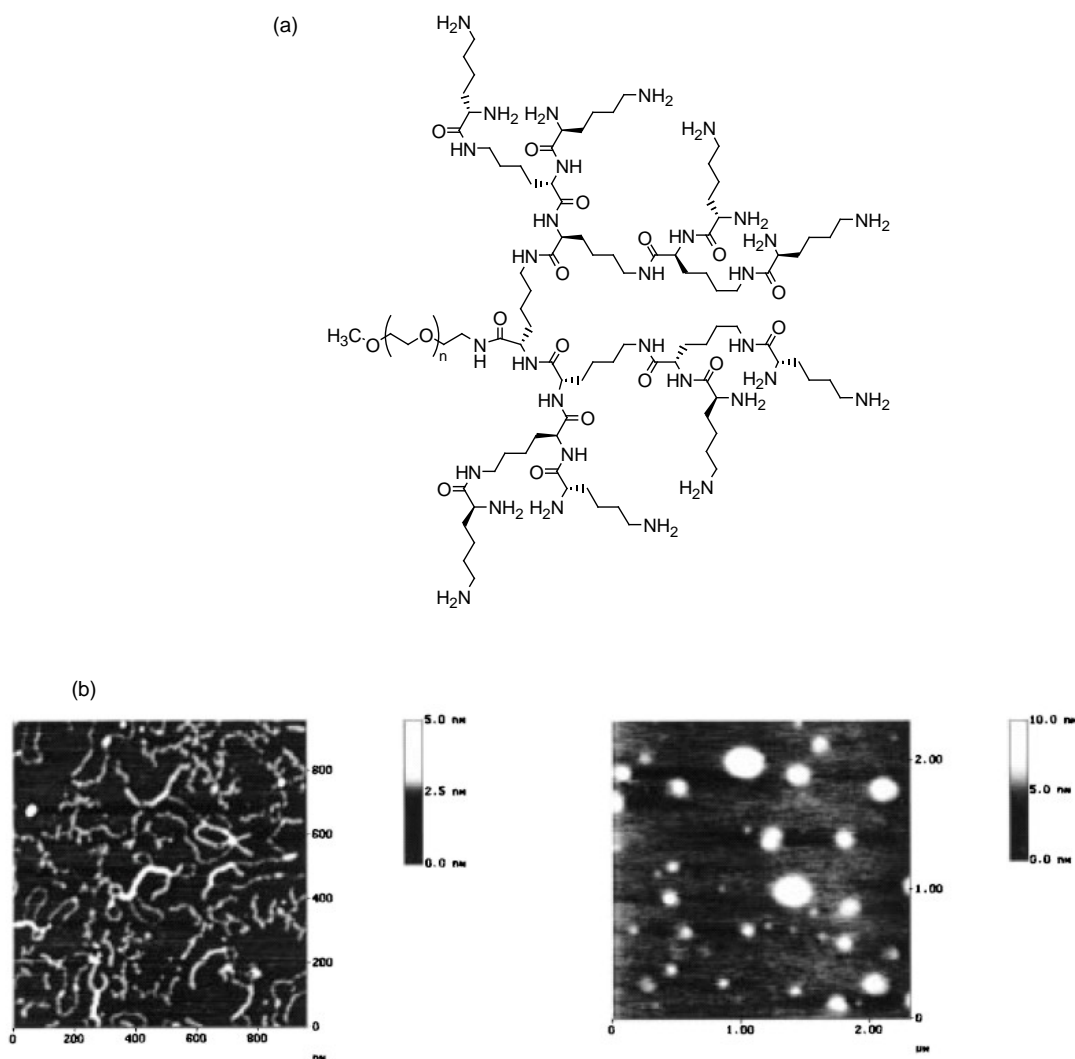


Figure 31. (a) Dendritic poly(L-lysine) and PEG block co-polymers form complexes with DNA which have enhanced solubility. (b) Globular nanostructures are generated on assembly of fourth generation dendrimer with DNA as visualised using AFM techniques. Image reproduced from reference [90] with permission from Elsevier.

Park and co-workers have been pioneers in this area, making excellent use of *block co-polymers* containing both dendritic poly(L-lysine) [A] and PEG [B] blocks (Figure 31a). They have reported both AB [90] and ABA [91] co-polymers and characterised their ability to self-assemble in the presence of plasmid DNA. They used agarose gel electrophoresis and DNase I protection assays to show that the AB polymers formed a water-soluble complex with DNA, with a *globular nanostructure* as determined by AFM (Figure 31b). Interestingly, this is different to co-polymers based on linear poly(L-lysine), which form extended *toroidal nanostructures* with DNA – indicating that the dendritic architecture can play a direct role in

controlling the structure of the nanoscale assembly. The solubility of these complexes is in contrast to many other polyelectrolyte DNA complexes which precipitate as a consequence of charge neutralisation, and it was proposed that the PEG chain plays a pro-active role in *enhancing complex solubility*. Similar techniques were also applied to ABA (barbell-like) triblock co-polymers. Interestingly, comparison of the self-assembling behaviour of the third and fourth generation dendrimers indicated that only the fourth generation system formed spherical assemblies with DNA and could hence protect the encapsulated DNA from DNase I induced degradation. This is perhaps what would be expected on the basis of the higher cationic surface charge of the fourth generation system in comparison to its third generation analogue. Cytotoxicity measurements (using NIH3T3 cells) indicated that the triblock ABA copolymer was significantly *less cytotoxic* than commonly used gene delivery agents such as poly(L-lysine) and poly(ethylene imine). Even at very high concentrations (400 $\mu\text{g/mL}$), no toxicity towards NIH3T3 cells was observed.

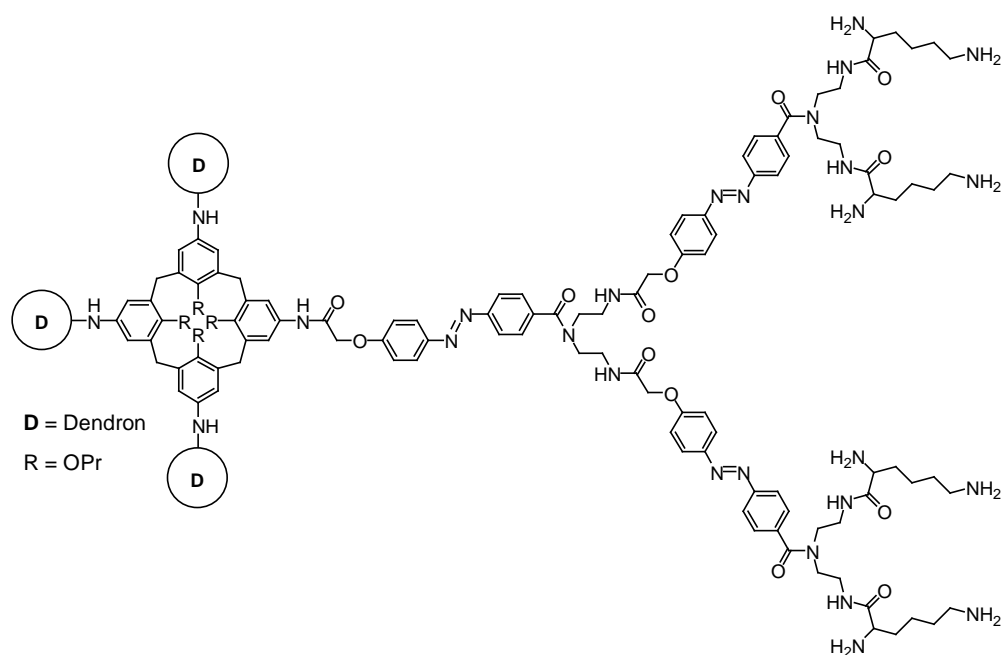


Figure 32. Polyazobenzene dendrimer functionalised with L-lysine building blocks which binds DNA to form complexes with UV-switchable behaviour.

A polyazobenzene dendrimer based on a calix[4]arene core has been functionalised with peripheral L-lysine units and shown to bind plasmid DNA (Figure 32) [92]. Intriguingly, the azobenzene dendrimer provides a *UV-switchable framework*. It was shown that the zeta potential of the dendrimer, as well as its apparent size (as monitored by GPC) could be

switched using UV light. Given that UV irradiation controlled the zeta potential of the dendrimer (which is a useful measure of surface charge), it was then shown that the more highly charged system had a higher affinity for DNA, and hence, the affinity of the system towards DNA could be *controlled* using UV irradiation. Engineering this kind of control into a nanoscale supramolecular assembly is an important achievement. These results clearly indicate the way in which synthetic manipulation can give rise to dendritic constructs with different *functional gene transfection properties*, and is one of the important ways in which this area of science is currently developing.

Dendritic poly(propylene imine) (PPI) derivatives have also been of interest for their assembly properties with DNA. It has been reported that the larger PPI dendrimers have significantly greater cytotoxicity (against the A431 cell line), however transfection efficiency does not necessarily require the largest dendrimers [93]. Therefore it was reported that a second generation PPI dendrimer was actually *optimal* for transfection applications in this case.

A sophisticated *ternary complex* approach to gene delivery has also been reported using a complex between PPI-DAB dendrimers, DNA and cucurbituril (Figure 33) [94]. Cucurbituril (CB) is a cylindrical host molecule composed of glycoluril units, which shows strong pseudorotaxane-type binding to diaminoalkane chains. In the ternary complex, PPI-DAB binds to DNA in the usual manner (electrostatic attraction) then cucurbituril binds with the DAB functionalised dendritic surface forming multiple pseudorotaxane-type complexes. Dialysis was used to remove any excess CB from the complex. The ternary complex (including CB) was found to be larger (151 nm) than the simple PPI-DAB:DNA complex (83.5 nm). It was shown that the presence of CB decreased the affinity of the dendrimer for DNA binding, however, the ternary complexes were still effective at gene transfection. This paper provides an example of how a supramolecular approach can be used in order to achieve additional *nanoscale control* of dendrimer/DNA complexes in an attempt to control the gene delivery process.

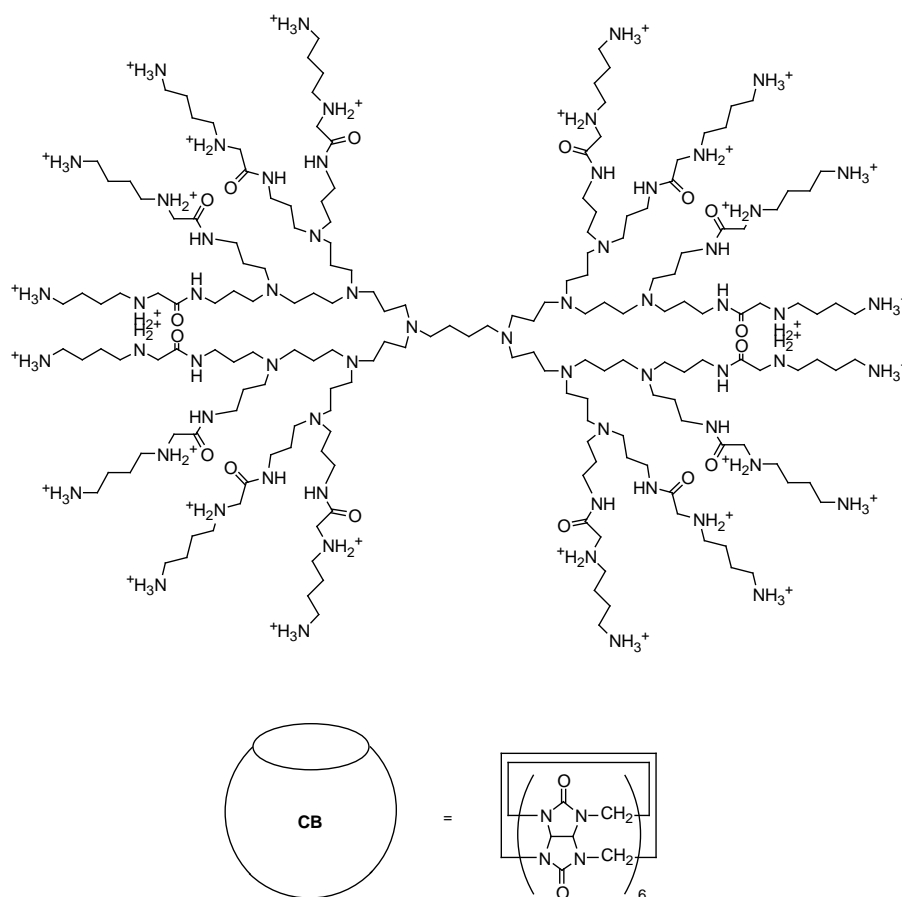


Figure 33. A ternary complex is formed between PPI-DAB dendrimers, cucurbituril (CB) and DNA. The binding of CB to the DAB surface of the dendrimer controls the dimensions of the nanoscale assembly.

With the move toward more *tailored systems* for gene delivery, rather than just using simple unfunctionalised dendrimers, Diederich and co-workers have reported an interesting class of amphiphilic dendrimers which act as self-assembling vectors for gene delivery [95]. Their rational design process led to the use of a polyamine surfaced dendron (to favour DNA binding and endosomal escape once internalised into the cell) attached via a phenylacetylene rigid rod segment to a branched unit with long aliphatic dodecyl chain surface groups (to enhance self-assembly processes) (Figure 34). DNA binding experiments indicated that, as expected, the number of ammonium cations plays a role in controlling DNA binding, however, more interestingly, the number of alkyl chains also has an important influence on the DNA binding ability. The structure with three lipophilic chains (rather than 1 or 9) clearly showed enhanced DNA binding ability. This was attributed to the importance of *self-assembly* of the amphiphilic dendrons for effective DNA binding. Even with only relatively basic optimisation of the molecular structure, the transfection abilities of these compounds

exceeded that of Superfect™ by a factor of around three, with all compounds showing low cytotoxicities. Tapping-mode AFM was used to visualise the dendrimer-DNA complexes and structures resembling flattened spheres (height 5-10 nm, diameter 60-80 nm) were observed – a clear indication of efficient DNA condensation by these dendritic systems. It was particularly interesting that these systems were able to bind and transfect DNA even though they were relatively small (unlike PAMAM dendrimers where an optimum M_w greater than 116000 is required). It is possible that this is a consequence of the *inherent self-assembling potential* of these amphiphilic systems – illustrating the way that dendritic systems can be designed to exhibit enhanced self-assembly with DNA for gene transfection applications.

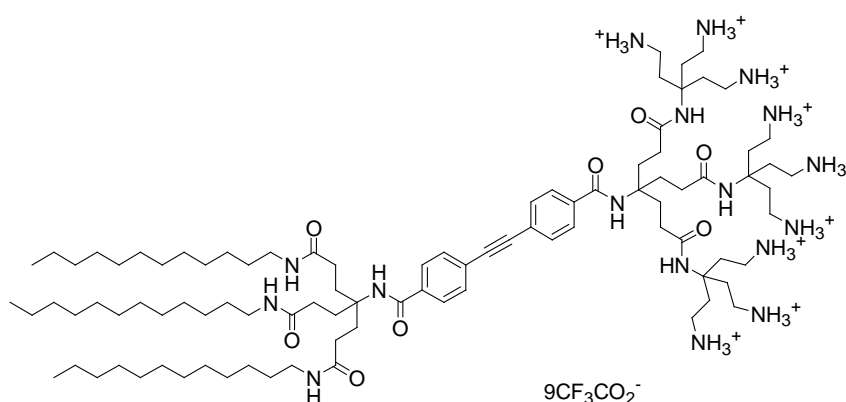


Figure 34. Rationally-designed self assembling dendritic systems which exhibit efficient gene transfection behaviour. The molecules possess groups to bind DNA (polyamines) as well as groups which encourage the self-assembly of the system (hydrophobic alkyl tails).

There are a wide-range of other *bioorganic* applications of dendritic systems – not least those relying on multivalent molecular recognition processes at the dendritic surface (for example lectin binding and antiviral activity). However, given that these other applications do not generally self-assemble multiple dendritic building blocks, they are not discussed further here – however, the interested reader is directed towards some excellent review articles [96].

3.3 Dendritic nanoclusters and nanotubes

In fascinating recent work, approaches to discrete nanoscale clusters of dendrimers have been reported. Tomalia and co-workers have reported their so called *core-shell tecto(dendrimers)* which are generated using a self-assembly step [97]. The authors make use of carboxylate- and ammonium-functionalised PAMAM dendrimers, which have negatively and positively

charged surfaces respectively. It might be expected that mixing these dendritic building blocks together in a 1:1 ratio would yield an *infinite extended assembly* (see Section 4.1), however, by employing an excess of the anionic dendrimer in the presence of LiCl in water, and using dilute dendrimer solutions, the formation of an extended lattice can be minimised and a core-shell dendrimer assembly can be generated (Figure 35a). Subsequent addition of 1-(3-dimethylaminopropyl)3-ethylcarbodiimide hydrochloride can *covalently fix* the assembled superstructure. In this way, a fifth generation cationic dendrimer core was assembled with third generation anionic dendrimers and subsequently cross-linked. GPC and polyacrylamide gel electrophoresis (PAGE) indicated that the *nanoscale dimensions* of the product were similar to those of an eighth generation dendrimer. The products could also be characterised by MALDI-TOF mass spectrometry and AFM. Perhaps surprisingly, the inverse assembly (using an excess of the cationic dendrimer to surround an anionic dendrimer) could not be generated in this work.

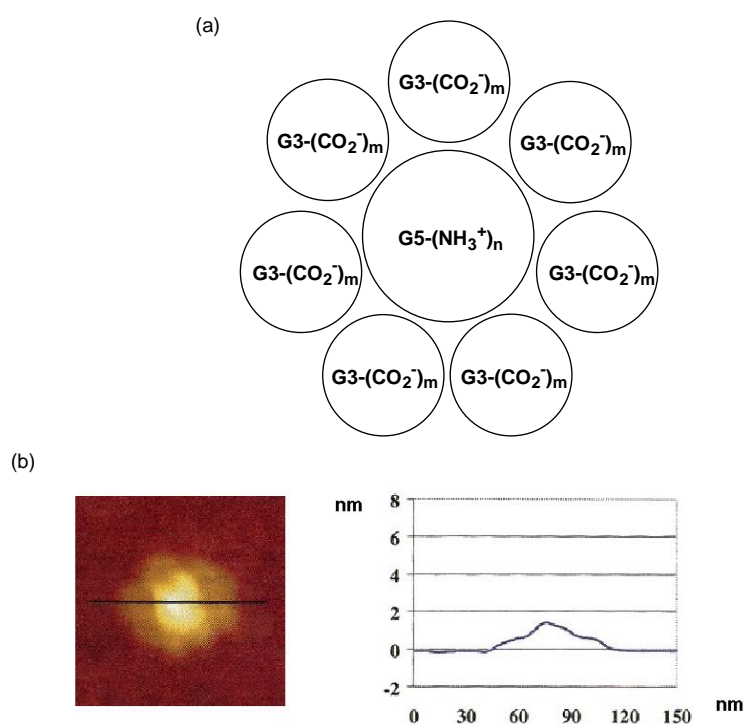


Figure 35. (a) Core-shell tecto(dendrimers) assemble as a consequence of controlled electrostatic interactions. (b) AFM image and cross-section of a (G7)(G5)₁₁₋₁₂ core-shell tecto(dendrimer) reproduced from reference [98] with kind permission of the American Chemical Society.

In a subsequent paper, a detailed investigation of core-shell tecto(dendrimers) assembled using a core G7 dendrimer and peripheral G5 dendrimers was made using tapping-mode AFM with a carbon nanotube tip (Figure 35b) [98]. The average volume of the assembly generated using these building blocks was $893 \pm 70 \text{ nm}^3$, while the volumes for the G5 and G7 building blocks are 62 ± 3 and $187 \pm 10 \text{ nm}^3$, respectively. This indicates a composition consistent with $(G7)(G5)_{11-12}$, although imperfect structures and aggregates were also observed in the AFM images.

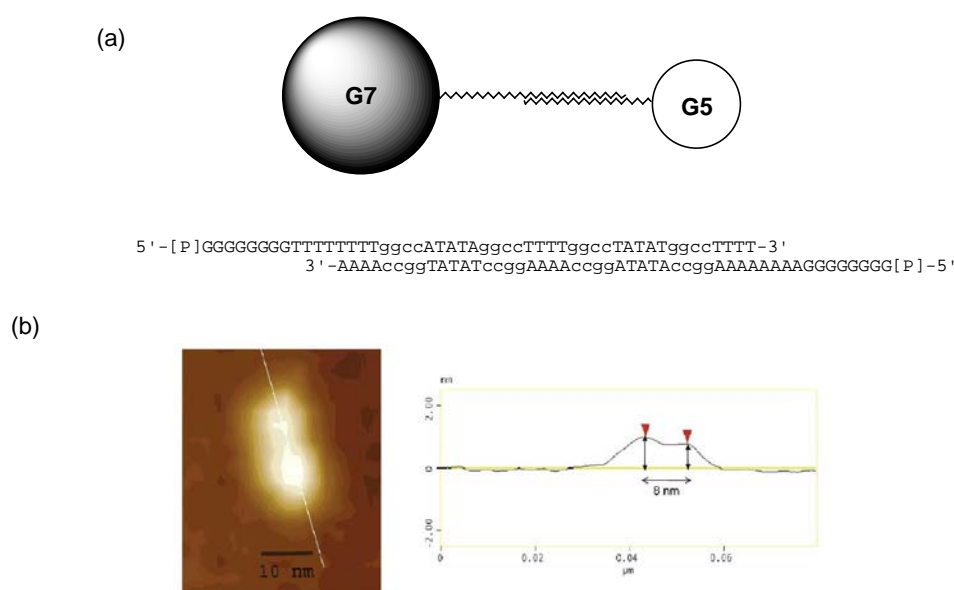


Figure 36. (a) Assembly of G7 and G5 DNA-functionalised PAMAM dendrimers as a consequence of complementary base-pairing interactions. (b) The dumbbell-shaped complexes formed as visualised by AFM techniques. Image reproduced from reference [99] with kind permission of the American Chemical Society.

In order to generate nanoclusters with more *specificity and control*, Baker and co-workers have combined DNA with PAMAM dendrimers [99]. They functionalised the surface of G5 and G7 PAMAM dendrimers with single strand oligonucleotides, having previously capped 90% of the dendrimer surface by acetylation (Figure 36a). The sequence of the oligonucleotide was designed such that the first nucleotides would act as a spacer unit, while the remaining nucleotides would be available for complementary base pairing. It was concluded that on average, the G7 dendrimers were functionalised with at least two 66-base-long oligonucleotides, whilst the G5 analogues had at least one 66-base-long oligonucleotide attached, which was complementary to the oligonucleotides attached to the G7 dendrimer.

The G5 and G7 oligonucleotide functionalised systems were *hybridised* and analysis performed by DLS and AFM. Some large aggregates were observed, but in addition, some smaller *dumbbell-shaped clusters* could be visualised (Figure 36b). The dimensions of these objects were consistent with the connection of a G7 dendrimer to a G5 dendrimer held together non-covalently *via* a base paired DNA fragment. This work offers a very interesting approach to the controlled assembly of *multi-dendrimer arrays*.

Zimmerman and co-workers have applied a dendrimer-dendrimer self-assembly approach to the assembly of novel *cylindrical structures* [100]. They made use of a porphyrin-cored dendrimer with a bound Sn(II) ion in the centre of the porphyrin ring. On the addition of succinic acid, which can act as a bridging ligand connecting two tin centres, a cylindrical oligomeric structure was assembled (Figure 37). Subsequent to this assembly step, the supramolecular nanostructure was covalently fixed by performing Grubbs' metathesis on the peripheral alkene groups. The dendritic branching plays a key role in this fixing step by ensuring that there are enough alkenes for effective cross-linking of the surface of the nanoassembly to take place. GPC indicated that at this stage, the compound was mostly present as a pentamer, although given the limits of GPC calibration for dealing with oligomers with unusual architectures, it is possible the cylinder was longer. The cylinder could then have its core removed via a transesterification reaction, and this gave rise to a *hollow nanotubular structure*. An M_n value of ca. 35000 was estimated for this hollow nanotube using GPC methods. This paper provides an outstanding example of how supramolecular assembly can be used to generate a unique self-assembled architecture in such a manner that a covalent-fixing step can then be used to capture the architecture permanently. It seems likely that this type of approach will, in the future, be used to generate a wide variety of different nanoscale architectures which have intriguing potential *applications* in host-guest chemistry and nanotechnology.

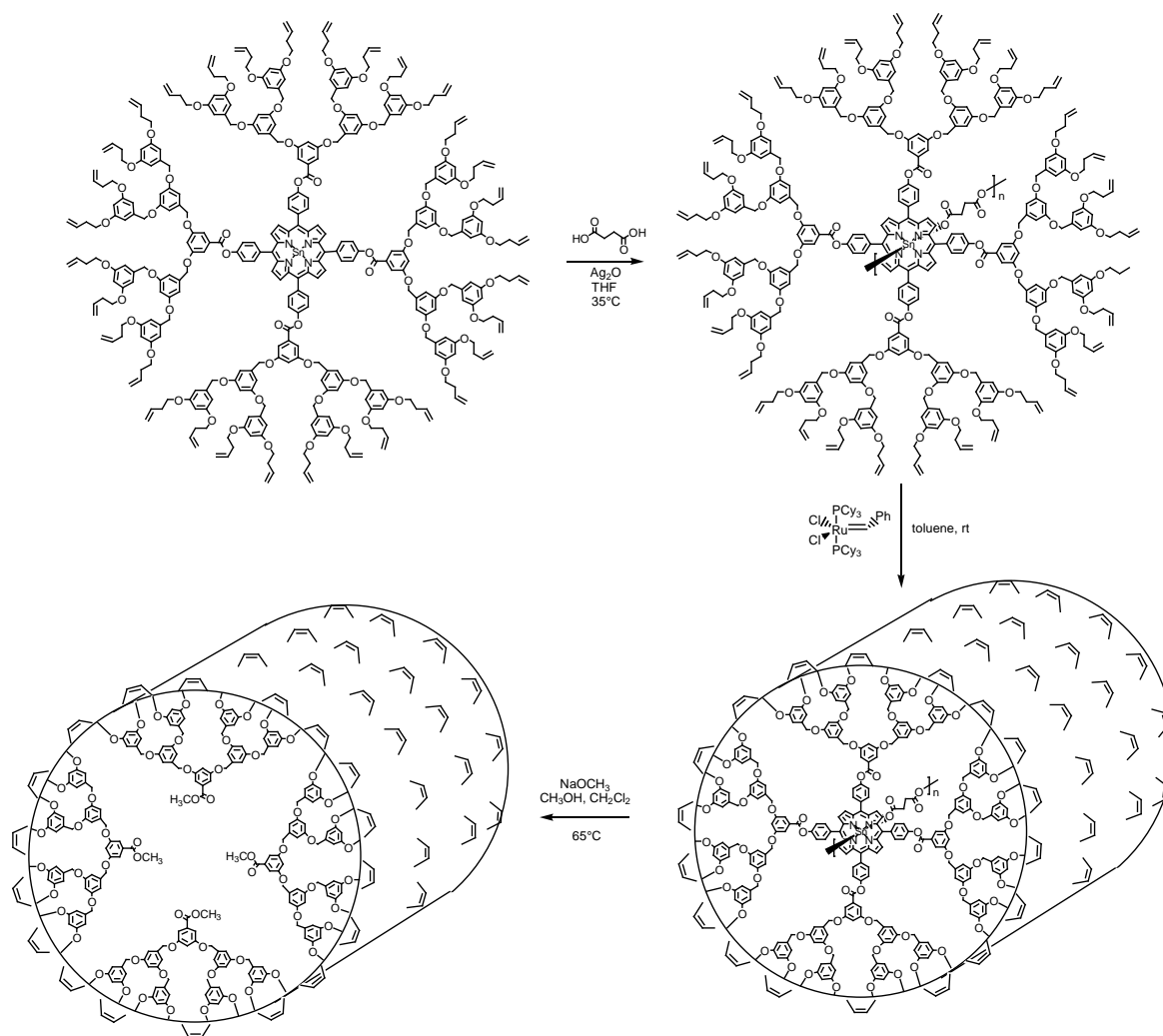


Figure 37. Cylindrical nanostructures assembled from dendritic porphyrins using a dicarboxylate linking group to coordinate to the metal ions and encourage porphyrin stacking. The structure can subsequently be cross-linked, and have the porphyrin groups removed by hydrolysis, leaving a hollow nanotube structure.

3.4 Assembly of dendrons with surfactant-like properties

Surface-active molecules are well-known to assemble into discrete structures such as *micelles* and *vesicles* in aqueous solution. Dendritic systems are no exception to this rule, and a range of dendrimers with surfactant-like assembly properties have been reported. Some of these will be discussed in Section 4, which focuses on the assembly of extended nanoscale arrays, however, those systems which generate *discrete* supramolecular structures will be outlined here.

It is worth noting that a number of groups have reported spherical dendrimers as effective *unimolecular micelles* [101]. These unimolecular micelles use symmetric spherical dendrimers with apolar and polar regions separated between the interior and exterior of the dendrimer. Such systems behave like micelles, yet have no concentration dependence to their behaviour, as they do not require any self-assembly for their formation. As such, they are beyond the scope of this article. On the other hand, for asymmetric *phase separated* systems *e.g.* individual dendrons, the apolar and polar regions will attempt to *phase-separate* via *self-assembly* into structures such as micelles. It is worth noting that only in some cases does the aggregation process give rise to micellar structures. This process occurs at concentrations greater than a *critical micelle concentration* (CMC), which is one of the key parameters in surfactant self-assembly. In other cases, however, aggregates with a variety of different non-micellar structures (which are sometimes ill-defined) are formed. In this article, such nanostructures are discussed in terms of a *critical aggregation concentration* (CAC).

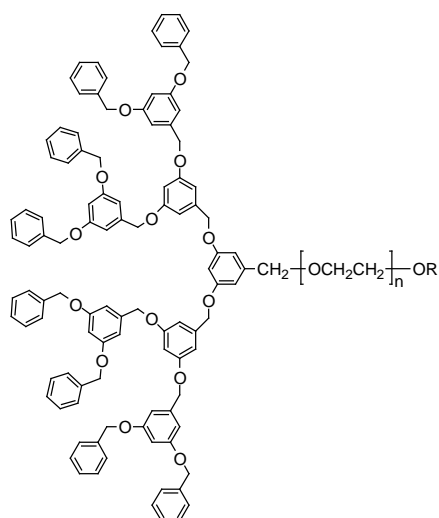


Figure 38. Hybrid linear-dendritic block co-polymers self-assemble in mixed methanol-water to give micellar structures. In this case, the dendritic head group is less polar than the linear polymer segment.

It was Fréchet and co-workers who first realised the possibilities of using asymmetrically functionalised dendritic blocks to generate molecules with interesting surfactant properties. They generated hybrid *linear-dendritic block co-polymers* (Figure 38) [102], in which the linear chain was polar poly(ethylene glycol) (PEG), while the dendritic head group was relatively apolar (based on Fréchet-type branching). They reported that these AB dendritic-linear co-polymers formed micelles in mixed methanol-water solution. They estimated that

the second generation system formed a micelle which consisted of approximately 7 or 8 molecules of the AB co-polymer and had a densely packed apolar dendritic core – shielded from the polar solvent. They also reported symmetric ABA block co-polymers with sufficient flexibility to phase separate and form micellar-type aggregates [103]. The self-assembly of these systems was reported to be strongly solvent-dependent.

Chapman and co-workers also reported linear-dendritic block co-polymers which they referred to as *hydraamphiphiles* [104]. Their system made use of a hydrophilic poly(ethylene oxide) (PEO) linear block and a dendritic block based on L-lysine with hydrophobic *tert*-butoxycarbamate (Boc) protecting groups on the surface (Figure 39). Although equilibration in solution was slow, surface tension measurements could be used to determine a CMC of 8×10^{-5} M. The surfactant properties of the fourth generation system were investigated further, with aqueous solutions being able to solubilise hydrophobic orange-OT dye. Hammond and co-workers also generated linear-dendritic amphiphilic systems, in their case based on a combination of a PEO linear chain and a PAMAM dendritic block [105]. This type of system has also been applied for self-assembly with DNA, with the PEO chain enhancing the solubility of the dendrimer-DNA complex [106].

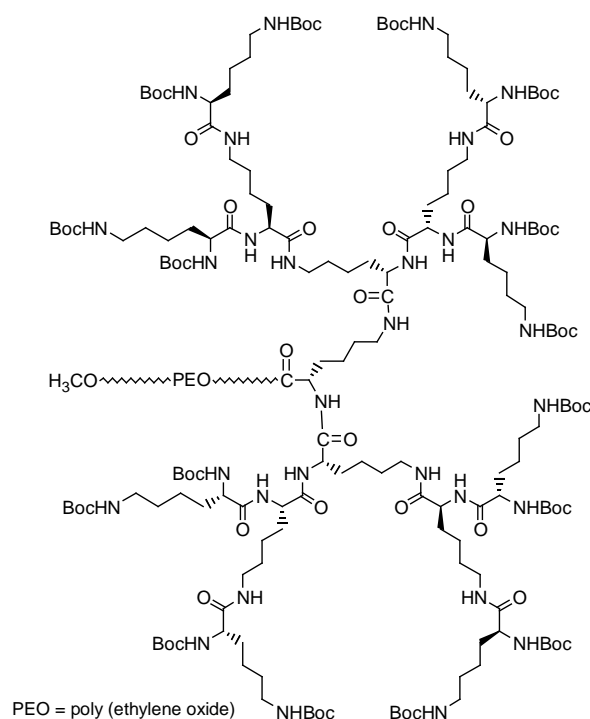


Figure 39. Linear dendritic block co-polymer hydraamphiphile based on L-lysine.

In a series of excellent papers, Meijer and co-workers also reported amphiphilic linear-dendritic block co-polymers [107]. They were the first to postulate that linear-dendritic block co-polymers could exhibit *superamphiphile behaviour*. Their amphiphilic systems were based on hydrophobic linear poly(styrene) blocks functionalised with a hydrophilic dendritic poly(propylene imine) head unit (Figure 40). These dendritic systems showed aggregation at *very low concentrations*, with CACs being as low as 5×10^{-7} M. These *stable aggregates* could be observed using TEM. It was even possible to characterise the assemblies using GPC. This indicates the stability of the aggregates, given that GPC normally disassembles any aggregates which are only weakly bound. Five different generations of dendritic branching were employed and DLS experiments indicated a degree of agreement with Israelachvili's *theories* on surfactant assembly [108]. These theories explain the way in which aggregate morphology varies with the volume of the polar head group and the apolar tail of a surfactant-type molecule. Meijer observed that on increasing the dendritic generation, and hence the volume of the polar head group, the aggregation type changed from an inverted micellar structure through vesicles and rodlike micelles to spherical micelles – in agreement with the theoretical predictions.

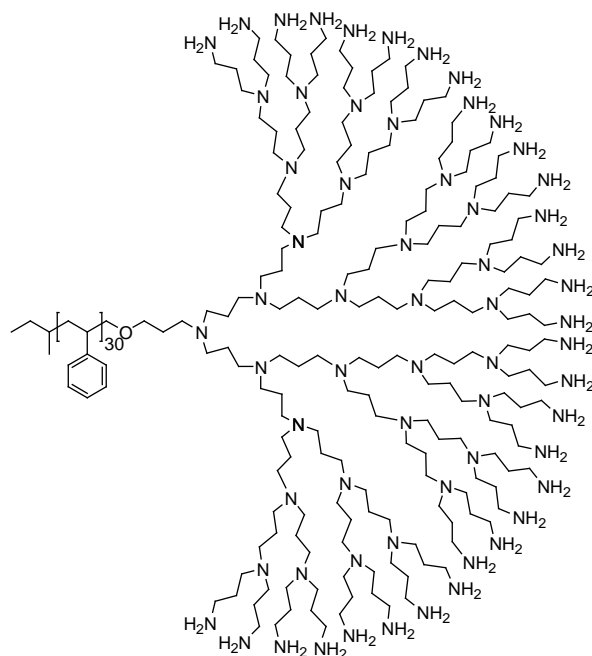


Figure 40. Hybrid linear-dendritic block co-polymers which exhibit superamphiphile behaviour. In this case the dendritic head group is the polar segment while the linear polymer is hydrophobic.

Dendritic-linear block copolymers with carboxylate surface groups have also been reported [109]. In this case, the linear portion was a hydrophobic poly(styrene) unit ($M_n = 3.2 \times 10^3$, polydispersity = 1.05), whilst the dendritic block was a hydrophilic poly(propylene imine) dendron with carboxylic acid groups on the periphery. NMR investigations indicated that the molecules formed a reverse micellar assembly in organic solvents such as chloroform, whilst in water the higher generation amphiphiles showed good solubility, but the long relaxation times and broad peaks clearly indicated that the polystyrene block was encapsulated within an aggregated structure. TEM indicated that large network structures were being formed – extreme clustering which was not observed for the amine functionalised amphiphiles, showing that surface groups can play a role in controlling assembly. Only for third generation branching could the aggregation structures be clearly visualised as curved worm-like micelles. CACs were once again low – typically 10^{-6} - 10^{-7} M. Overall, Meijer's studies clearly indicate the potential of dendritic systems to offer *powerful surfactant and detergent-like behaviour*. Interestingly, the concept that dendritic branching can improve amphiphilicity, connects nicely with work by Zhong and Eisenberg [110], who reported that dicarboxylate terminated polystyrene acted as a superamphiphile in terms of its ability to form reverse micelles in cyclohexane. The CMC was too low to determine, whilst the monocarboxylate terminated analogue was a relatively normal amphiphile (CMC ca. 1×10^{-5} M).

Kim and co-workers synthesised amphiphilic linear poly(ethylene oxide) (PEO) – dendritic carbosilane block copolymers [111]. In this case, the linear polymer is hydrophilic, whilst the dendritic group is hydrophobic. The surfactant properties of these molecules were highly dependent on dendritic generation. The third generation material could not be dispersed in water, as the apolar block was too large, however first and second generation systems both dispersed effectively, with the apolar dendritic head group being on the interior of the assembly in this case. CMCs were determined, and it was found that the second generation system was more effective at forming micelles (CMC = 2.3 mg/L) than the first generation analogue (CMC = 82.6 mg/L). This indicates that the *size of the apolar dendritic group plays a key role in controlling the self-assembly process*. Furthermore, the mean diameters of the micelles (as determined by dynamic light scattering) were generation dependent – being 120 nm for the first generation system and 170 nm for the more sterically demanding second generation dendron, with both systems having narrow unimodal distributions. Interestingly, the authors measured the steady-state fluorescence anisotropy values of 1,6-diphenyl-1,3,5-hexatriene, which provided evidence that the microviscosity of the dendritic core of the

micelle is lower than that of standard polymeric micelles. It is well-known that in bulk media, dendrimers exhibit lower viscosities than their polymeric analogues [112], but this was the first report that indicated that such effects could also be determined within self assembled supramolecular structures, and indicates that assembled aggregates with *dendritic interiors* may behave differently to traditional micelles.

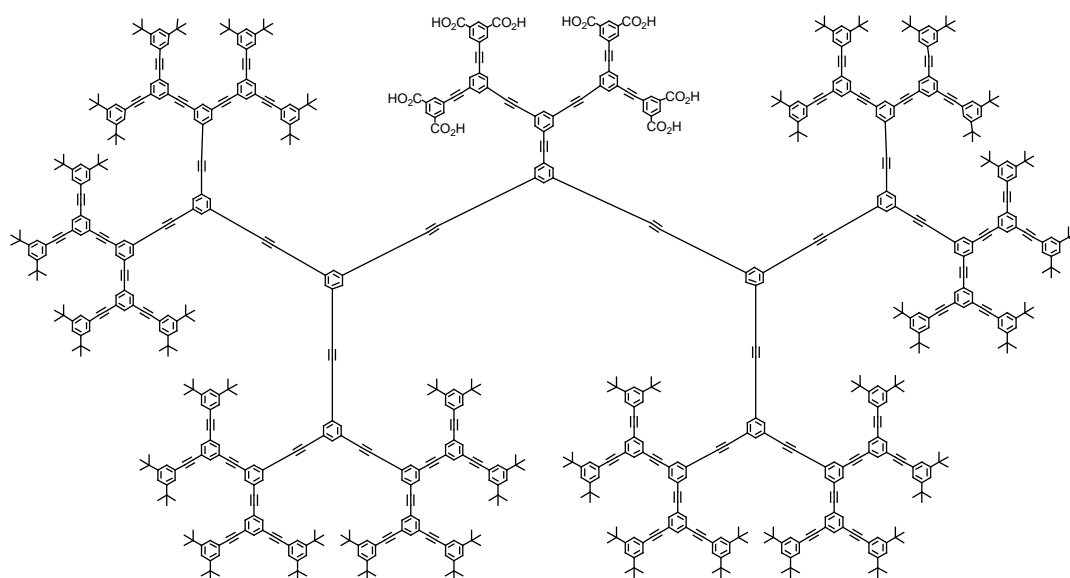


Figure 41. Rigid, shape-persistent amphiphilic dendrimers in which the relative sizes of the hydrophobic and hydrophilic blocks can be varied.

Using a different approach to amphiphilic branched molecules, Pesak and Moore generated a series of *rigid, shape persistent dendrons* based on phenylacetylene building blocks [113]. These systems had a hydrophobic phenylacetylene-type dendron, with a second dendritic unit attached at the focal point. This second dendritic unit had *tert*-butyl esters on the periphery, which could readily be converted to carboxylic acid groups *via* simple thermolysis to provide the dendrimer with a hydrophilic segment (Figure 41). Interestingly, this approach generates rigid amphiphilic dendrons with both polar and apolar surface groups in *precisely defined locations*. The authors were also able to vary the size of the hydrophilic dendron block to generate amphiphiles with different hydrophobic/hydrophilic ratios. GPC in tetrahydrofuran indicated assembly of the structures to form higher mass aggregates (presumably due to contact between the hydrophilic blocks of different dendrimers in order to shield them from this apolar solvent). There was, however, some doubt about whether the thermolytic deprotection conditions could also induce some covalent cross-linking (in addition to the non-covalent aggregation process which take place). Nonetheless, treatment of this aggregate with

diazomethane (to convert the carboxylic acid groups back into esters) largely removed the aggregates and regenerated a peak corresponding to individual dendrimer molecules.

In a recent paper, Kobayashi and co-workers provided an elegant example of how a supramolecular approach can be used to generate micellar aggregates [114]. They synthesised a series of phthalocyanines with a silicon bound in the macrocyclic ring, and in which one of the axial ligands was a Fréchet-type dendron with hydrophilic terminal carboxylic acid groups, whilst the other axial ligand was a long hydrophobic chain (Figure 42). In this way, an asymmetric amphiphilic system was created. The ability of these dendritic systems to self-assemble into spherical micelles was investigated using GPC and cryo-TEM. It was estimated that each aggregate contained 10 ± 3 molecules, providing each micelle with a radius of 3.6-3.9 nm. It was postulated that the CMC of these systems was much lower than that of conventional anionic surfactants as a consequence of the molecular shape of the dendron. It was also illustrated that organic guests, such as perylene, could be encapsulated within the micellar interior.

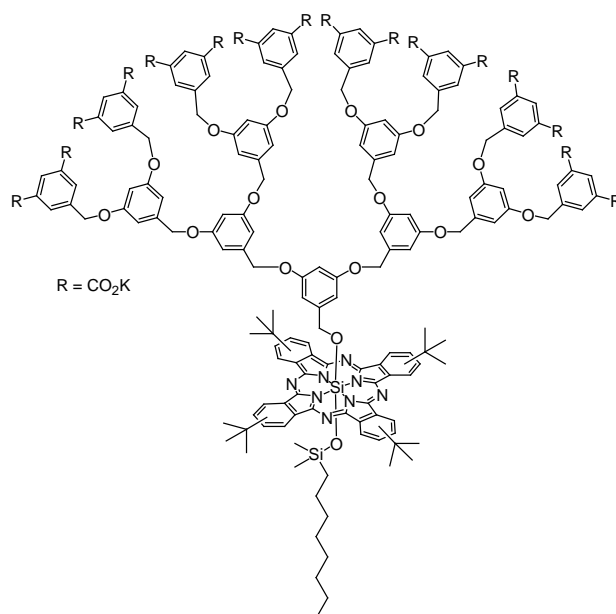


Figure 42. Dendritic molecule with surfactant-like properties which is itself assembled around a silicon-bound phthalocyanine.

Hirsch and co-workers have used a dendritic fullerene as an amphiphile, with the C₆₀ unit providing the hydrophobicity, and Newkome-type dendritic branches with peripheral carboxylic acid groups acting as the hydrophilic head group [115]. On its own, this molecule

does not aggregate in aqueous solution, however when mixed with tetradecyl-trimethylammonium hydroxide (a co-surfactant which normally forms simple micelles), it assembled into spherical bilayer vesicles with diameters ranging from 30 to 340 nm. This vesicular structure could be imaged using freeze-fracture TEM. This use of *dendrimers as co-surfactants* therefore offers an interesting method by which the formation of *new nanostructures* can be induced.

More recently, Hirsch and co-workers have developed a dendritic amphiphile based on a calix[4]arene skeleton [116]. The upper rim was functionalised with hydrophilic dendritic branches, whilst the lower rim was functionalised with hydrophobic alkyl tails. Assembly into micelles was observed in aqueous solution (pH = 7.2) and cryo TEM was used to provide evidence that these micelles were remarkably well-defined. The authors argued that seven individual dendritic molecules assembled into each single micelle. It was even possible to model the internal structure of the micelle using image processing procedures. This indicates that it is possible to use relatively general phase separation processes, in combination with dendritic amphiphiles, to generate remarkably well-defined assemblies with low polydispersities.

Shinkai and co-workers have illustrated that surfactant-type dendrons can, once they have been assembled, be immobilised into covalent dendritic structures [117]. As described previously, the concept of *covalent capture* is an important one in supramolecular chemistry, as it allows the self-assembly process to do the difficult synthetic work. Shinkai's dendrons had apolar Fréchet-type branching with saccharide units attached to the focal point (Figure 43). These dendrons assembled in chloroform solution as a consequence of saccharide-saccharide hydrogen bonding interactions, and the authors then cross-linked the saccharide units by the addition of 1,3-phenylene diisocyanate. The resultant aggregates were investigated before and after cross-linking using DLS in different solvents (chloroform and tetrahydrofuran). Of particular interest was the fact that the aggregates formed using the third generation dendron did not significantly change in size during the cross-linking process (ca. 6 nm). MALDI-TOF mass spectrometry showed peaks corresponding to a system constructed from between one and five dendrons. For smaller generation dendrons the results were less clear, and the assembly process appeared to give rise to ill-defined aggregates. The authors argue that this is because the assembly of the dendrons depends on two terms – a favourable set of hydrogen bond interactions between saccharide units, and an unfavourable steric

repulsion between dendritic head blocks. For the self-assembly process to be effective in forming discrete assembled structures rather than ill-defined, extended arrays, these two factors should be in balance with each other.

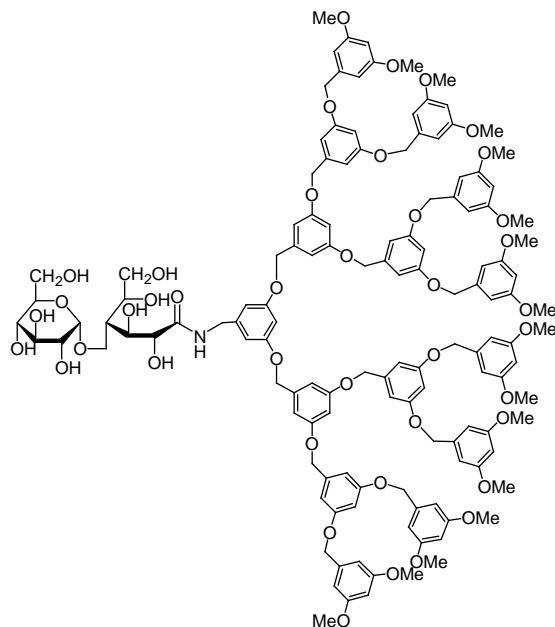


Figure 43. Assembly and subsequent covalent capture (cross-linking) of individual dendrons functionalised with saccharide units at the focal point. This process is generation-dependent.

Overall, given the *commercial importance of surfactants* in a wide range of applications, and the ability of dendritic systems to exhibit *powerful self-assembly properties*, it seems likely that research will continue to focus on the assembly of dendritic structures which possess polar and apolar regions. In particular, the synthetic flexibility which is possible should enable the development of a range of interesting tunable and multi-functional assemblies composed of surfactant-like dendritic building blocks.

4. Self-Assembly of extended nanoscale arrays of dendritic building blocks

In addition to assembling *discrete* nanoscale structures as described above, it is also possible to use dendritic building blocks to generate *extended arrays*. In such systems, multiple branched molecules assemble into structures such as fibres and sheets as a consequence of *multiple, highly directional, non-covalent interactions* in solution. This type of assembled superstructure often has interesting *materials properties*, as the assembly process gives rise to extended structures which are ultimately expressed on a *macroscopic scale*.

In addition to self-assembly mediated by non-covalent interactions in solution, dendrimers can also ‘order’ themselves, particularly when in the bulk solid/liquid state. Self-ordering occurs predominantly as a consequence of *long range packing interactions*, and is often dependent on molecular shape. Many self-ordering dendritic systems *exhibit liquid crystalline behaviour* as a consequence of the introduction of partial long-range order. For the purposes of this review, extended aggregates will be discussed in terms of self-assembling and self-ordering systems – although it should be pointed out that there is a degree of overlap between these different categories.

4.1 Assembly of extended aggregates using multiple recognition events on the dendritic surface

One approach to the assembly of extended arrays is to make use of multiple molecular recognition events on the dendritic surface. In this way, the dendrimer acts as a *cross-linking* unit, and when assembled with another multifunctional system, has the potential to generate an extended (‘infinite’) array. Aida and co-workers used an *electrostatic* approach to assemble dendrimers in this way [118]. They employed dendrimers with central porphyrin units surrounded by Fréchet-type branching with either anionic carboxylate or cationic polyalkylammonium surface groups (Figure 44). When the two solutions were mixed in equimolar concentrations, large fluorescent aggregates (10-20 μm) were observed, and if the mixture was allowed to stand for a day, the aggregates continued to grow until precipitation occurred. The authors used the free-base anionic dendritic porphyrin, and the metallated (Zn(II)) cationic dendrimer, and therefore fluorescence techniques could be used to investigate the energy transfer from the metallated to the free-base porphyrin in the assembled network. In the 1:1 assembly, the fluorescence bands for the metallated porphyrin decreased in intensity, whilst those for the free base porphyrin increased – suggestive of singlet energy transfer from one to the other – the rate of which was consistent with a model in which the anionic and cationic dendrimers were in *direct contact* with one another. It should be pointed out that if an excess of anionic or cationic dendrimer was employed, the growth of an extended array was retarded and smaller discrete clusters of dendrimers were generated. This is directly analogous to the approach used by Tomalia and co-workers to generate core-shell tecto(dendrimers) (Section 3.3) [97].

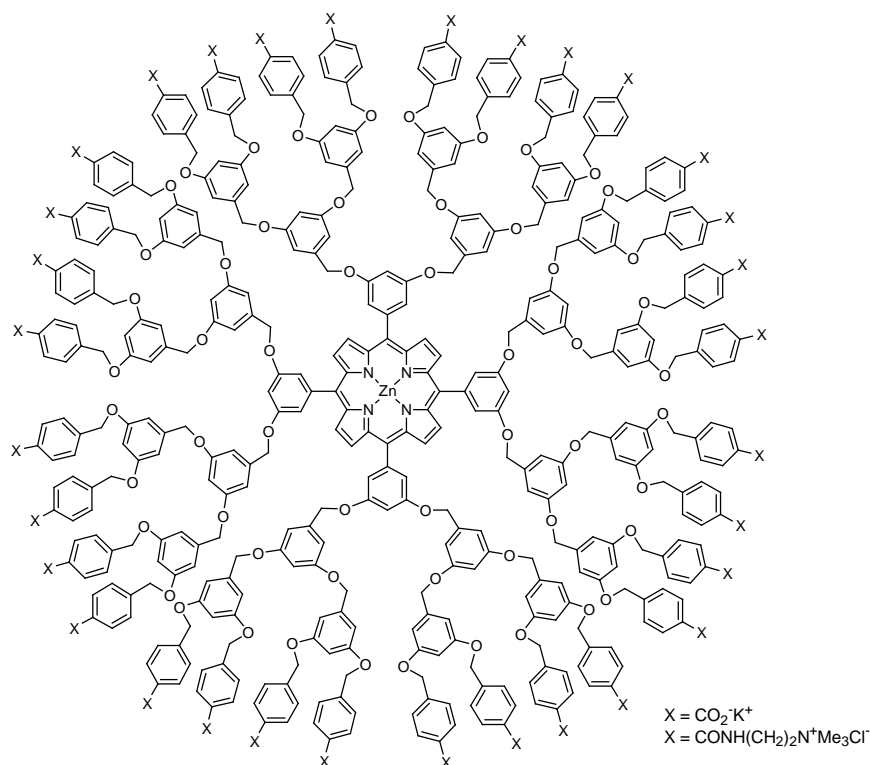


Figure 44. Extended arrays are generated by mixing anionic and cationic dendrimers in a 1:1 ratio.

Dendrimers with multivalent thiolated surfaces have been used for the construction of nanoscale arrays in combination with multivalent gold clusters and nanoparticles. Müllen and co-workers have modified the periphery of poly(phenylene) dendrimers with disulfides [119] and thioethers [120] in order to give rise to assembled arrays of dendrimers and gold nanoparticles (Figure 45). In the case of the disulfide functionalised dendrimers, the assemblies were formed by ligand exchange with dodecylamine-stabilised nanoparticles (diameter ca. 4 nm). Films of the cross-linked extended structure were assembled in a layer by layer process with 14 deposition cycles – the cross-linking nature of the dendritic multivalent ligand endowed the films with additional mechanical strength. These films were of interest for potential vapor sensing applications. The poly(phenylene) dendritic structure gave the advantage of enhanced sensitivity to volatile organics, and decreased interference from moisture. Indeed, the films showed high sensitivity for tetrachloroethylene and toluene vapours with rapid response times. The systems based on thioether ligands also formed aggregates as a consequence of the cross-linking ability of the dendritic system. Furthermore, the dendritic system appeared to encourage the formation of arrays of Au nanoparticles which had an unusual bimodal size distribution, with average diameters of 4 and 20 nm.

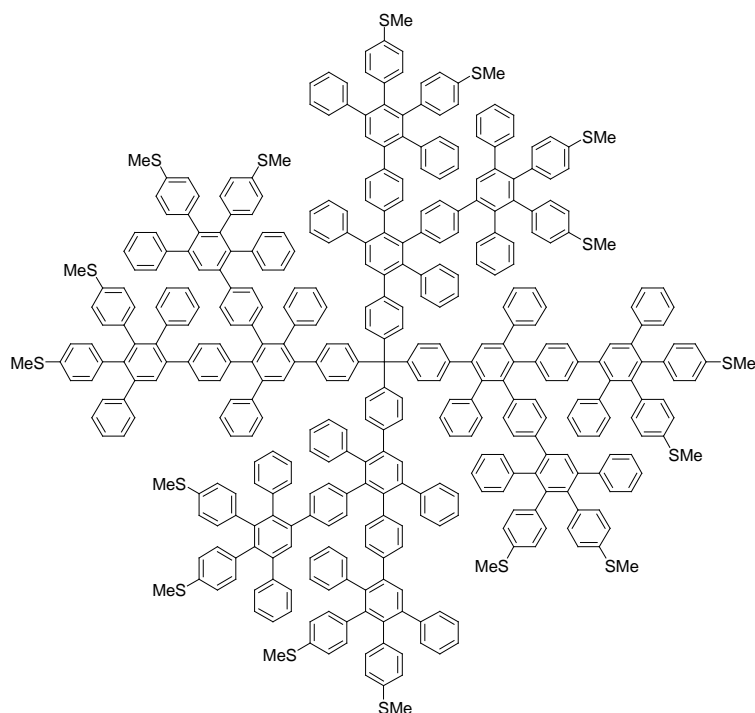


Figure 45. Thioether-functionalised poly(phenylene) dendrimer which forms extended nanoscale arrays with gold nanoparticles.

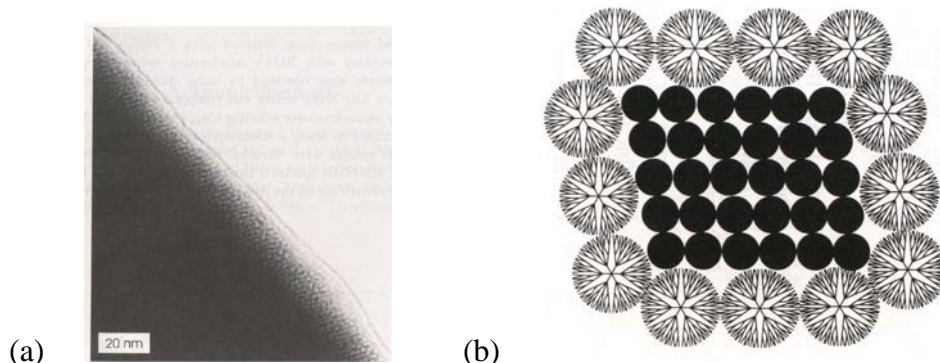


Figure 46. Extended arrays of Au_{55} nanoclusters as imaged by TEM were generated when a stabilising thiolated phosphorus based dendrimer was employed. The TEM image shows the edge of one of the $(Au_{55})_{\infty}$ microcrystals and the schematic illustrates how dendrimers stabilise multiple Au_{55} clusters. Images reproduced from reference [121] with kind permission of Wiley-VCH.

Schmid and co-workers reported the use of thiolated phosphorus based dendrimers (prepared by Majoral and co-workers) as stabilisers for Au_{55} clusters [121]. By treating $Au_{55}(PPh_3)_{12}Cl_6$ with the thiolated dendrimer in a 1:3 ratio, it was possible to replace the phosphine ligand

with thiols, and this gave rise to an insoluble black material. Unexpectedly, TEM, as well as small angle and wide-angle X-ray diffraction experiments indicated the formation of superstructures of Au₅₅ clusters to form perfect microcrystals (Au₅₅)_∞ (Figure 46). The authors proposed that the gold clusters, rather than being stabilised as individual entities by the dendritic ligand, were actually stabilised as a ‘cluster of clusters’ within an enveloping dendritic shell – TEM images indicated the presence of an amorphous shell of material surrounding the gold microcrystals (Figure 46b). It was argued that the clustering of Au₅₅ is thermodynamically favoured on the basis of Au⋯Au interactions.

This type of dendrimer assembly process can clearly give rise to interesting *solid-phase aggregates* with potential applications in materials science and nanotechnology. However, it is also possible to generate extended assemblies which are still compatible with the solvent in which they are formed. In many cases, these assemblies will have a one-dimensional (or fibrous) nanoscale architecture, and such systems are described in detail in the following section.

4.2 Assembly of one-dimensional architectures using multiple recognition events

The supramolecular assembly of *one-dimensional architectures* (such as fibres) is of intense current interest [122], partly as a consequence of the biological relevance of such fibrillar aggregates in the pathways of *neurodegenerative diseases* such as Alzheimer’s and CJD [123]. When fibrillar assemblies become entangled within a solvent, the solvent effectively becomes immobilised within pockets in a network of one-dimensional assemblies – giving rise to a *gel-phase (soft) material*. The assembly of such materials using small molecules, rather than traditional covalent polymeric systems, is one of the most important and active frontiers of current *supramolecular chemistry* (Figure 47) [124]. One feature of gelation is that very small quantities of organic material are able to immobilise relatively large volumes of solvents (ca. 1% wt/vol). The challenge of controlling multiple supramolecular interactions over macroscopic length-scales has encouraged chemists to develop innovative building blocks for the assembly of these intriguing soft materials. In terms of their molecular size, dendritic architectures lie somewhere between small-molecule organogelators, and the covalent polymers traditionally used in gel formation – but given that dendrimers are discrete, well-defined building blocks, which must be assembled through *multiple non-covalent interactions* to form fibrous architectures, they have more in common with small organic

molecules. Given that dendritic architectures contain a *multiplicity of functional groups*, their application in gel phase materials is logical yet challenging – as these potential interacting groups must be *organised* in an appropriate manner to encourage the formation of a *supramolecular fibrillar architecture*.

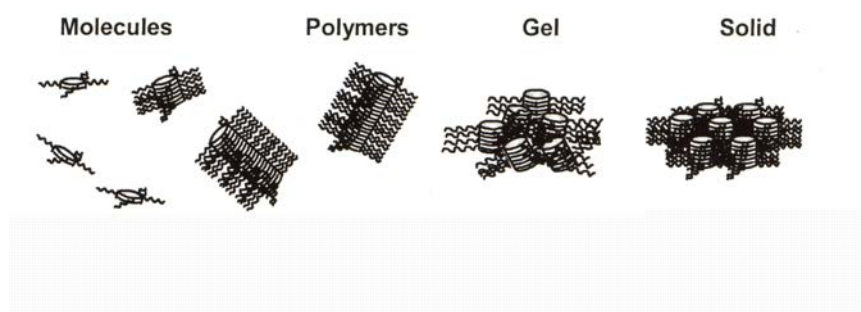


Figure 47. Schematic illustration of the assembly of individual small-molecule building blocks to generate fibrous supramolecular polymers and hence gel-phase materials. Image reproduced from reference [125] with the kind permission of the American Chemical Society.

In the early 1990s, Newkome and co-workers initiated the field by reporting dendritic *bola-amphiphiles* with hydrophilic polyalcohol surfaces and hydrophobic alkyl interiors that acted as effective hydrogelators (Figure 48) [126]. The primary driving force for hydrogelation in this case was provided by phase-separation of the hydrophobic and hydrophilic domains, and the authors proposed that these dumbbell-shaped molecules formed a one-dimensional network that maximised *hydrophobic* and *hydrophilic* contacts. This can be achieved by effectively stacking the dumbbell-shaped molecule one on top of the next. Electron microscopy clearly indicated the presence of a fibrous aggregate in the gel-phase material. A hydrophobic dye (chlorotetracycline, CTC), which only fluoresces in a hydrophobic *microenvironment* was employed, and CTC fluorescence was only observed in the presence of the gel. It was argued that CTC was intercalated within the hydrophobic regions of the one-dimensional aggregate. On the other hand, the addition of potassium borate inhibited gel formation – it is well-known that borates form complexes with polyols, and it was therefore proposed that this process was occurring on the hydrophilic surface of the dendritic molecule, and was hence inhibiting the assembly of fibres. Newkome and co-workers synthesised a range of dumbbell shaped molecules with different spacer units [127]. They found that flexible spacers were generally more successful in encouraging gelation than more rigid analogues with similar chain lengths.

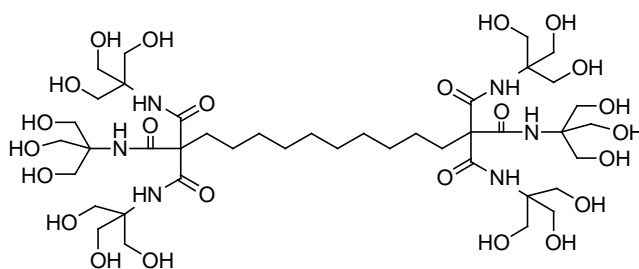


Figure 48. Dendritic bola-amphiphiles which act as effective hydrogelators.

Aida and co-workers were one of the first groups to report dendritic molecules capable of forming physical gels with *organic solvents* [128]. They made use of Fréchet-type dendrons functionalised at the focal point with a dipeptide (Tyr-Ala) building block (Figure 47 – category 1). They found that relatively extensive second or third generation dendritic branching was required for effective gelation, which then occurred at very low concentrations (ca. 1.0 mM). Indeed, they calculated that one molecule of gelator could effectively ‘immobilise’ almost 20000 solvent molecules (it should, however, be pointed out that in gel phase materials, the individual solvent molecules actually do retain their mobility within pockets in the gel phase matrix, but the overall flow of the fluid is inhibited as a consequence of capillary forces). In contrast, lower generation analogues only gave a crystalline solid, rather than a gel-phase assembly.

In a subsequent excellent paper, Jang and Aida uncovered the structural parameters required for effective gelation in more detail by synthesising a series of different dendrons (Figure 49) [129]. Three different categories of potential gelator were reported, in which the Fréchet-type dendron was attached either to the tyrosine side chain of the dipeptide (category 1), the *N*-terminus of the dipeptide (category 2) or the *C*-terminus of the dipeptide (category 3). The key conclusions of this study were as follows:

- (i) dipeptides are required for effective gelation (rather than mono-peptides),
- (ii) ester functionalities (rather than methoxy groups) on the surface of the dendron assist the gelation process,
- (iii) peptides in categories 1 or 2 are required for gel formation,
- (iv) higher generation dendrons give more effective gelation.

The gels were investigated after drying using scanning electron microscopy (SEM) techniques. Some gelators exhibited a fibrous nanostructure whilst others showed relatively wide (30-60 nm) self-assembled nanoribbons. X-ray diffraction on the dried gels combined

with the other results helped the authors to propose potential assembly modes for the different categories of dendritic gelators, and these are illustrated in Figure 50. In each case, it is *well-organised complementary supramolecular interactions* which give rise to the *directional assembly* process.

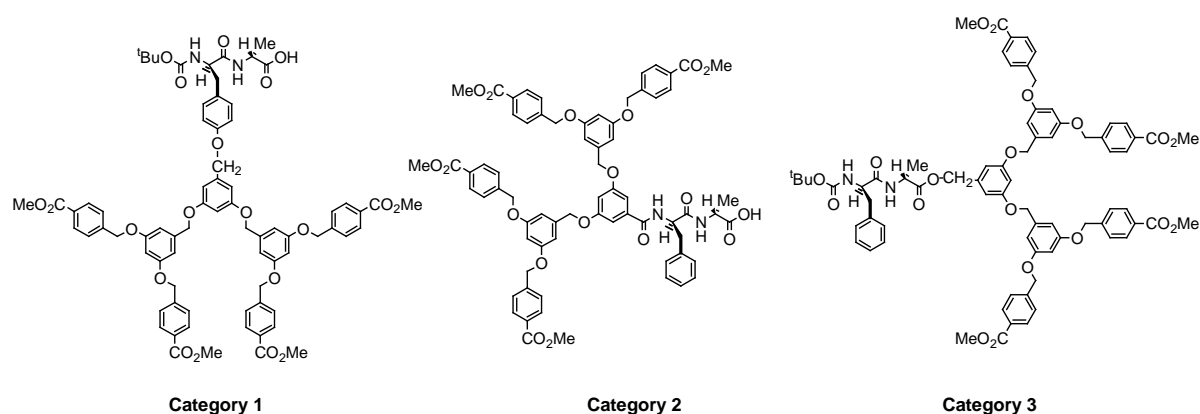


Figure 49. Three categories of molecules, some of which are capable of forming gel-phase materials in organic solvents (see discussion).

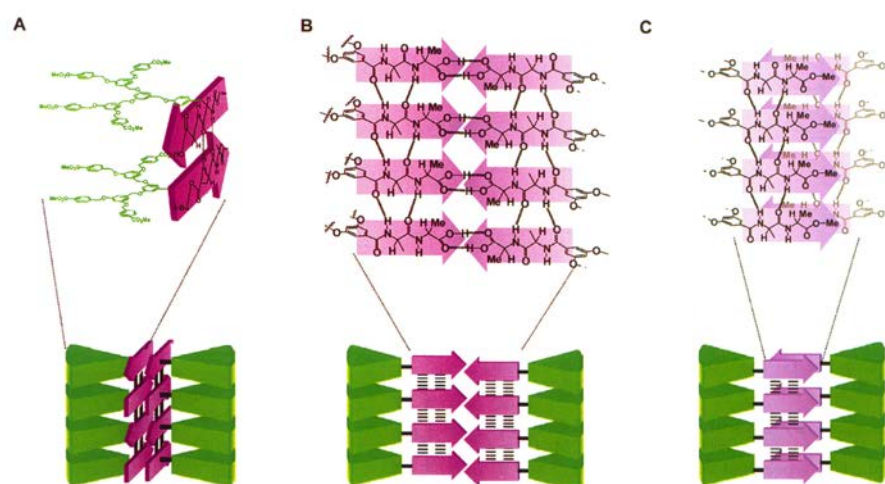


Figure 50. Proposed assembly modes for the organogelators depicted in Figure 49. This image is reproduced from reference [129] with kind permission of the American Chemical Society.

Kim and co-workers have also reported dendritic molecules capable of acting as gelators [130]. They employed both *dendrons* and *symmetric dendrimers* constituted from repeating amide units with peripheral hydrophobic chains (Figure 51). Gel-phase materials were formed at relatively high organic loadings (5-8% wt/vol) and interestingly, the presence of

additional dendritic branching appeared to have a negative impact on the gel-sol transition temperature – both for the dendrons and the symmetric dendrimers. TEM and XRD studies indicated a lamellar structure. Interestingly, some of these asymmetric phase-separated dendrons also possess *amphiphilic properties* and were observed to form discrete *vesicles* (diameter ca. 160 nm) in the aqueous phase.

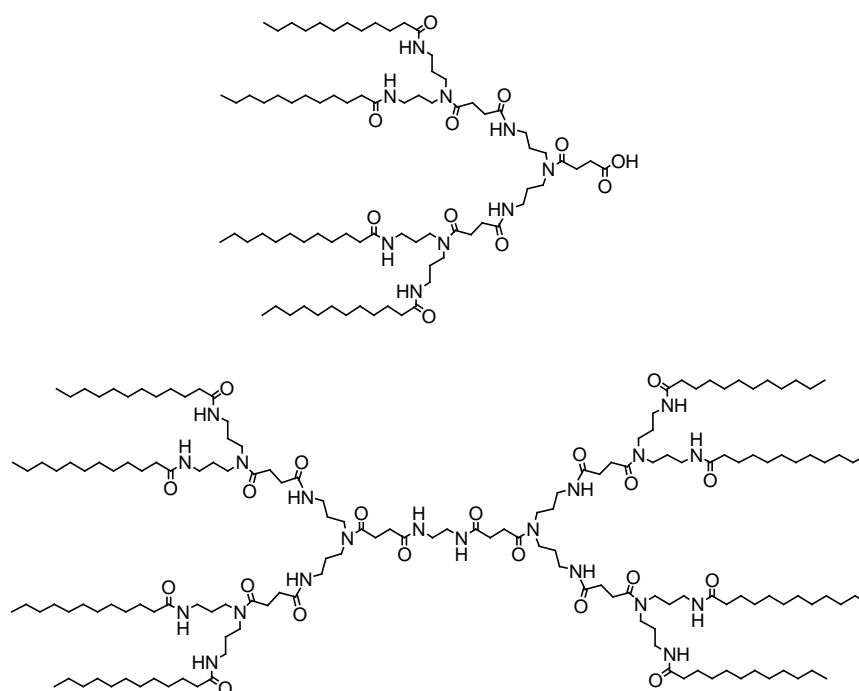


Figure 51. Dendrons and symmetric dendrimers capable of gelling organic solvents.

In an extension of this work, *alkyne* functionalities were incorporated into the long hydrophobic tails on the periphery of the dendritic structure [131]. TEM images of the second generation dendron indicated the presence of fibrous bundles, and X-ray diffraction (XRD) of the dried gels indicated that these fibres had a hexagonal columnar structure. An attempt was then made to *covalently capture* the assembled superstructure using *in situ* photopolymerisation of the triple bonds. UV irradiation of the assembled structures in toluene led to a colour change, with the samples becoming deep red. After irradiation for 2 h, part of the sample became insoluble in organic solvents, with this product maintaining its *columnar hexagonal* packed structure as indicated by XRD. The first generation dendron assembled into a lamellar structure, which could also be covalently captured. In water, these dendrons both formed *vesicle assemblies* (ca. 200 nm), which once again could be polymerised.

Other dendritic gelators have been reported by Simanek and co-workers, who made use of a small library of triazines with a variety of surface and interior linking groups [132]. They ascertained that those dendrimers which incorporated interior and surface groups capable of donating hydrogen-bonds (*e.g.* using a N-H group) were more effective gelators than those that did not. TEM confirmed the presence of fibres in the assembled structure. Furthermore, the authors developed a useful *gel permeation chromatography assay* which offered predictive ability for gelation below the gelation threshold concentration – the authors observed that for gel-forming systems, the *retention times were significantly different* in acidified and neutral chloroform. Given that gelation properties can often be difficult to predict *ab initio*, such an assay may be of more general use in the high-throughput screening of libraries of potential gelator systems.

Majoral and co-workers have reported that some of their phosphorus derived dendrimers functionalised with alkylammonium (or pyridinium) cations on the surface behave as *hydrogelators* (Figure 52) [133]. Gelation was a very *slow process*, with heating at 60-65°C for 11-13 days being required for the synthesis of optimal gel-phase materials – although intriguingly, the authors noted that gelation times were shortened (by 10-30%) in the presence of water soluble additives (*e.g.* buffer, metal salts, acids *etc.*). It was proposed that supramolecular association of hydrophilic and hydrophobic regions of the dendrimer provided the driving force for gelation in this case, although a full model for the unidirectional assembly process was not developed. Small molecule hydrogelators are of interest as a consequence of their potential *biomedical applications* in areas as diverse as *drug delivery* and *tissue engineering*.

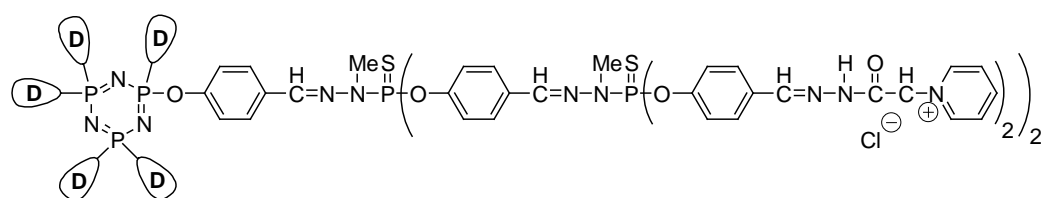


Figure 52. Hydrogelators based on ammonium-functionalised phosphorus based dendrimers.

Smith and co-workers have taken a different approach to the assembly of fibrous architectures – one which relies not on the simple assembly of a dendrimer into a nanostructure, but instead requires the presence of *two components* in solution for the assembly process to take place.

Such two-component gelator systems are rare, and are of considerable importance due to their high degree of *tunability*. For a two-component gelator, the individual components must initially interact to form a well-defined *supramolecular complex*, and subsequently, this *complex can self-assemble* in order to generate a fibrous nanoscale architecture. In this way, the supramolecular assembly process works on *multiple levels*, and is hence highly tunable and controllable. Smith and co-workers first reported this two-component dendritic gelator early in 2001 – one of the first dendritic gel-phase materials [134]. The two components required for gelation are a dendritic poly(L-lysine) which has a carboxylic acid group at the focal point, combined with an aliphatic diamine (Figure 53).

The proposed mode of gelation is the initial formation of a 2:1 complex between dendritic acid and aliphatic diamine (as a consequence of *acid-base interactions*) [12-13]. It is then argued that this complex goes on to assemble into a fibrous structure (as illustrated by SEM and AFM studies) as a consequence of anisotropic hydrogen bond interactions between the dendritic peptides. Smith and co-workers have recently reported that the acid-amine interaction which forms the two-component complex prior to hierarchical assembly can be replaced by the interaction between a *crown ether* and a *protonated amine*, and gel-phase materials behaviour is still observed [15b].

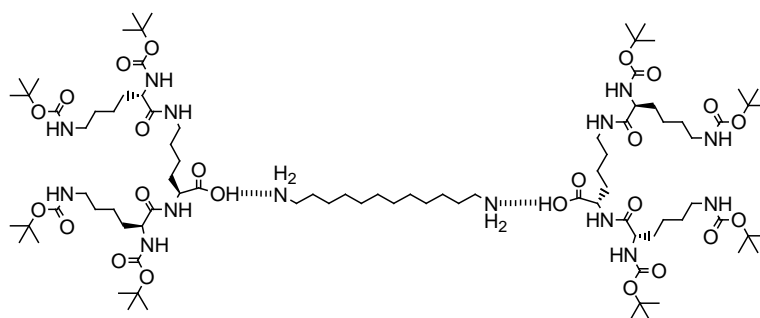


Figure 53. Two-component gelation system. The initial supramolecular complex forms as a consequence of acid base interactions between dendritic L-lysine and an aliphatic diamine. This complex then goes on to assemble into one dimensional aggregates in organic solvents.

In recent work [135], it has been discovered that the length of the aliphatic spacer chain directly controls the thermal stability of the gel, with each extra carbon atom adding approximately 15-20°C to the T_{gel} value – the temperature at which a transition from gel to sol is observed. Circular dichroism studies have indicated that the spacer chain must be of a

sufficient length in order for the dendritic peptide units to interact efficiently with one another and form nanofibres with a *helical organisation*. Dendritic branching of second generation is optimum for the formation of the gel [136]. First generation branching does not gelate, whilst third generation branches form thermally less-stable gels. The effect of solvent on the assembly of fibrous one-dimensional architectures using these building blocks has also been investigated [137]. It was found that the thermal behaviour of the gel can be correlated with a solvent polar solubility parameter. However, the ability of the solvent to donate hydrogen bonds (as given by the Kamlet-Taft α parameter) directly interferes with this correlation. This reinforces the importance of amide-amide hydrogen bonding in the fibrous assembly.

In a key study, Smith, Hirst and co-workers reported that the morphology of the nanoscale aggregates formed could be directly controlled using the ratio of dendrimer:diamine (Figure 54) [138]. A 2:1 ratio gave rise to the expected fibrillar aggregates. However, increasing the amount of diamine employed led to a dramatic change to a platelet-type morphology (platelets were 1-2 μm in diameter). It is believed that in this case, the excess diamine forms *microcrystalline domains*, which are capped with the small amount of dendritic branch that is present in an attempt to stabilise the hydrophilic amine groups as best as possible in the apolar solvent medium.

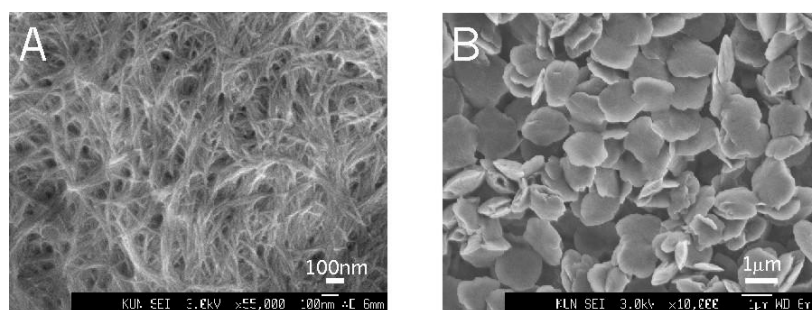


Figure 54. The nanoscale morphology observed using SEM for the two-component gelation system illustrated in Figure 53 can be controlled by changing the ratio of the two-components. A = 2:1 dendron:diamine. B = 1:4 dendron:diamine.

It has also been demonstrated that the *chirality* of the lysine building blocks plays a key role in modulating the mesoscale morphology and materials properties of the gel-phase assembled state (Figure 55) [139]. When using dendrons constructed from all L, or all D lysine, gels are obtained with identical materials properties (*e.g.* T_{gel} values) and equal and opposite CD spectra, indicating the formation of identical fibrous assemblies, but with opposite *helicities*.

However, on making a 50:50 mixture of the two stereoisomers, the degree of macroscopic gelation was significantly reduced. Furthermore, this nanomaterial possesses a new mesoscale morphology – flattened woven ribbons. This indicates the importance of stereochemistry in controlling the precise alignment of the hydrogen bond interactions within the fibrous assembly. This was reinforced by investigating the behaviour of the L,D,D and D,L,L dendrons, which also showed reduced T_{gel} values and formed fibres with different dimensions as observed by SEM. This indicates that subtle changes in the *molecular-scale dendritic architectures* can have a direct impact on the *nanoscale features* of the gel-phase assembled state – effects which are then transcribed into the *macroscopic properties* of the gel. This is one of the reasons dendritic systems are of particular interest as novel gelation systems. Such materials have potential applications in the development of new *chiral separation media* or as *matrices for supported catalysis*.

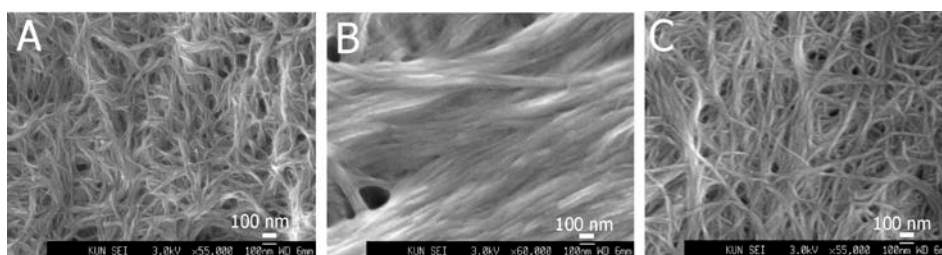


Figure 55. Effect of chirality on the nanoscale morphology of the two-component gelation system illustrated by the SEM images in Figure 53. A = L,L,L. B = 50% D,D,D, 50% L,L,L. C = D,D,D.

Smith, Chechik and co-workers have also recently shown that the two-component approach to dendritic gelators can be mimicked with an analogous *one-component* system in which the dendron units are covalently connected to the diamine spacer (for the structure of the dendrimer, see Figure 24) [140]. These dendrimers gelled non-polar organic solvents, and interestingly exhibited a quantifiable *dendritic effect on materials properties*, with the T_{gel} value of the gel increasing from 45°C for the first generation system to 70°C for the second and 107°C for the third.

Aida and co-workers have also reported what is effectively a *two-component approach* to a fibrous (columnar) assembled nanostructure [141]. They synthesised dendrons with a pyrazole unit at the focal point. Pyrazole is an exobidentate ligand capable of binding group

11 univalent metal ions (Cu(I), Ag(I) and Au(I)), and appropriately functionalised pyrazoles are capable of forming metal pyrazolate *coordination triangles* (Figure 56). Heating a paraffin suspension of the dendron-metal complexes at 200°C and then cooling gave rise to a fibrous precipitate. In this case, the materials does not show gel-phase properties due to its poor solubility in paraffin. It was argued that metal-metal interactions were responsible for holding the assembled superstructure together. These interactions increase in strength with atomic number as orbital mixing (which favours *metal-metal interactions*) becomes more important for heavier elements in the same group – in agreement with the observation of melting temperatures at 197.3°C, 193.7°C and 179.6°C for Au(I), Ag(I) and Cu(I) respectively. The fibres were intensely luminescent, and the dendritic ligand was capable of acting as an antenna and transferring energy to the interior metal ion cluster. On dissolution in CH₂Cl₂, the characteristic luminescence disappeared as the fibre became dissociated into individual metallacycles. Interestingly, a certain level of *dendritic branching* was required for the assembly process to take place indicating that unfavourable steric repulsion and favourable van der Waals forces between dendron units are in balance within the stacked superstructure. On investigation by SEM, it was found that remarkably, even though the system does not contain any chiral centres, the fibres were helical – being made up of a bundle of several loosely twisted fibrils.

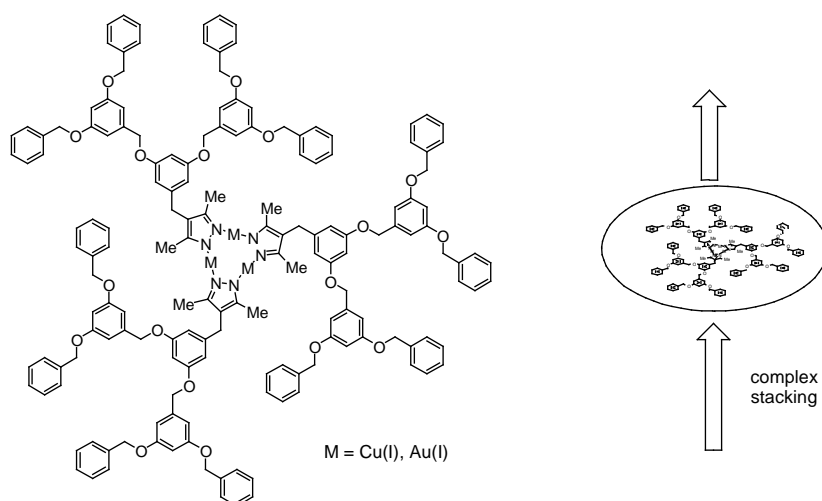


Figure 56. Two-component approach to fibrous assemblies in which the initial complex is assembled as a consequence of coordination interactions between dendritic pyrazole ligands and metal ions. These complexes go on to assemble into a columnar fibrous superstructure which precipitates from solution and exhibits interesting optical properties.

Excellent work investigating the assembly of *fibrillar* and *ribbon-like aggregates* has been performed by Stupp and co-workers. For a number of years, this group has been investigating the intriguing self-assembly properties of block co-polymers with the blocks having very specific functionality (*e.g.* flexibility, rigidity, amphiphilicity) and using this approach they have assembled a number of spectacular nanoscale architectures [142]. It was therefore perhaps not surprising that they turned their attention to the incorporation of a dendritic unit as one of the blocks within their assembling polymers. To this end, they have investigated the assembly properties of *dendron rodcoil* molecules (Figure 57) [143]. These dendron rodcoils are effectively tri-block copolymers, which have a *flexible (coil)* polymer unit attached to a linear *rigid rod* unit, which is, in turn, grafted to a *dendritic head* unit. The synthesis of a whole range of different dendritic generations of dendron rodcoil has been reported [144], but those molecules used most frequently for self-assembly, contain a relatively small dendron block, and can be synthesised in a respectable overall yield. Interestingly, even extremely dilute solutions (as low as 0.2% wt/vol) of these systems in various organic solvents undergo spontaneous gelation to produce *birefringent soft solids*. TEM imaging indicated the formation of one dimensional fibrous objects with a uniform width of 10 nm, which could be consistent with bimolecular packing. Strands as long as 10 μm could be isolated – indicating the high aspect ratio of the assembled superstructure. In order to probe the *structural requirements for assembly*, a range of analogues have been prepared and their assembly properties investigated. It was found that:

- (i) at least four hydrogen bonding OH groups were required on the surface of the dendron block for effective gelation, indicating the importance of hydrogen bond interactions,
- (ii) the rigid rod segment required a sufficient number of biphenyl-ester units for assembly to occur – indeed the more biphenyl-ester units, the greater the mechanical strength of the gel, suggesting a role for π - π interactions in the assembly,
- (iii) a sufficiently long coil was found to be essential for gelation,
- (iv) dendrons of higher generation were not effective in forming gels – possibly a steric effect of the bulky head group inhibiting one-dimensional assembly.

AFM imaging indicated a uniform thickness of 2 nm and this led the authors to propose a *ribbon-like structure* – a proposal backed up by light scattering studies [145]. The *crystal structure* of an analogous small organic molecule was determined, and this allowed the authors to propose a structural model for the assembled nanoribbon structure (Figure 58).

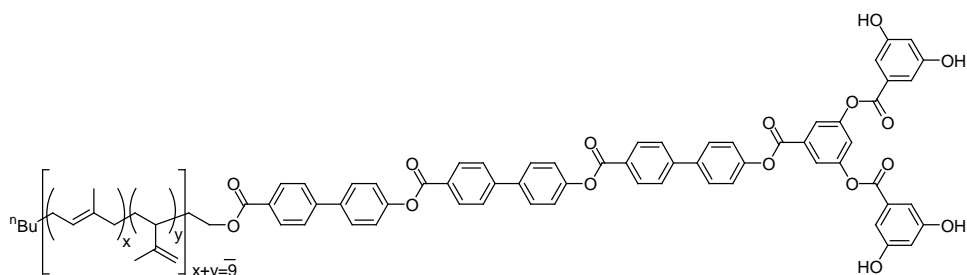


Figure 57. Dendron rodcoil molecule used for the self-assembly of a one-dimensional nanoscale architecture, hence leading to the formation of gel-phase materials.

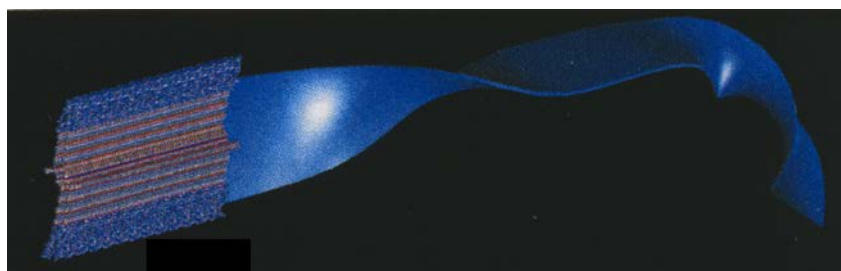


Figure 58. Structural model for the assembled nanoribbons formed by the dendron rodcoil molecule illustrated in Figure 57. This image is reproduced from reference [145] with kind permission of the American Chemical Society.

One fascinating application of these assembled nanostructures has been in the *scaffolding and toughening of polymers* [146]. By choosing a solvent which is capable of both supporting self-assembly *and* being polymerised, the polymerisation reaction can essentially take place around the nanoscale assembled structure generated by the dendron rodcoil. Styrene based gels retain the birefringence associated with the gel, even after polymerisation of the styrene. Small angle x-ray scattering (SAXS) studies indicated that the polymer retained reflections corresponding to the fibrous scaffold, and furthermore, the polystyrene generated in this way had a significantly higher impact strength. Indeed, the impact strength increased from 8 Jm^{-1} for unscaffolded polytyrene to ca. 13.5 Jm^{-1} for the sample of polystyrene formed in the presence of 0.5% wt/vol of dendron rodcoil. It was argued that the supramolecular structure within the polymer may act as an *impact absorbing skeleton* to dissipate strain energy. The nanostructuring of polymers in this way may generate a new generation of advanced polymeric materials and is an exciting frontier of materials science.

Stupp and co-workers have also used these dendron rodcoils for the preparation of CdS nanohelices (Figure 59) [147]. Cadmium nitrate was added to THF and then mixed with a dendron rodcoil gel. The gel was aged for one week and then exposed to $\text{H}_2\text{S}(\text{g})$. The sample was aged for a further week, and the solid inorganic product was isolated. TEM analysis indicated the formation of right and left handed *helices of CdS*, which had been *templated* on the twisted nano-ribbon architecture assembled by the dendron rod-coil. This study clearly indicates how the power of self-assembly can be harnessed to yield new materials with intriguing morphologies that might have interesting *electronic* and *photonic* properties suitable for applications in nanotechnology. These workers have also utilised their dendron rod-coils for the assembly of ZnO nanocrystals [148]. When these organic-inorganic assemblies were placed in an electric field, a degree of alignment occurred (as determined using UV-Vis spectroscopy and second harmonic generation measurements). Most notably, these aligned nanocomposites had a lower threshold for lasing behaviour than pure ZnO nanocrystals – the authors propose that this is a consequence of the greater organisation of the assembled ZnO nanocrystals. These results indicate the way in which self-assembly using dendritic building blocks can be used to generate *hybrid nano-materials* with potential photonic applications.

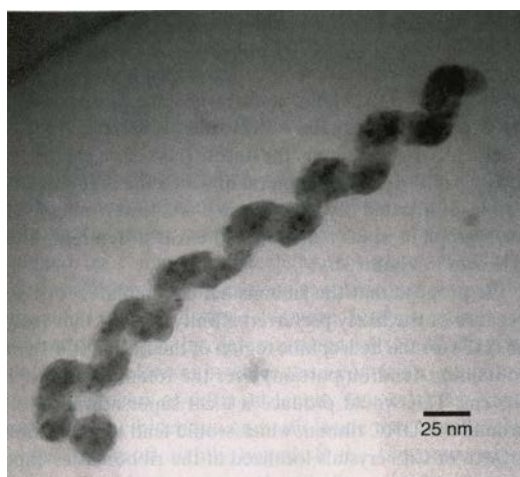


Figure 59. TEM image of the CdS nanohelices generated using assemblies of dendron rodcoils as a templating matrix. This image is reproduced from reference [147] with kind permission of Wiley-VCH.

Stupp and co-workers have also reported a different type of block co-polymer containing dendritic blocks. They took an L-lysine dendron and attached the focal point (*via* a short

aromatic spacer) to an poly(L-lactic acid) chain, which had a cholesterol unit on the other end (Figure 60) [149]. Hydrated samples were found to assemble into lamellar structures, whilst the third generation system actually assembled into discrete nanosized aggregates (oval shaped objects with diameters of ca. 30-35 nm as estimated by AFM and DLS). Of particular interest was the use of an L-lactic acid block, which provides these systems with a degree of *biodegradability*, making them of interest for *biomaterials applications*.

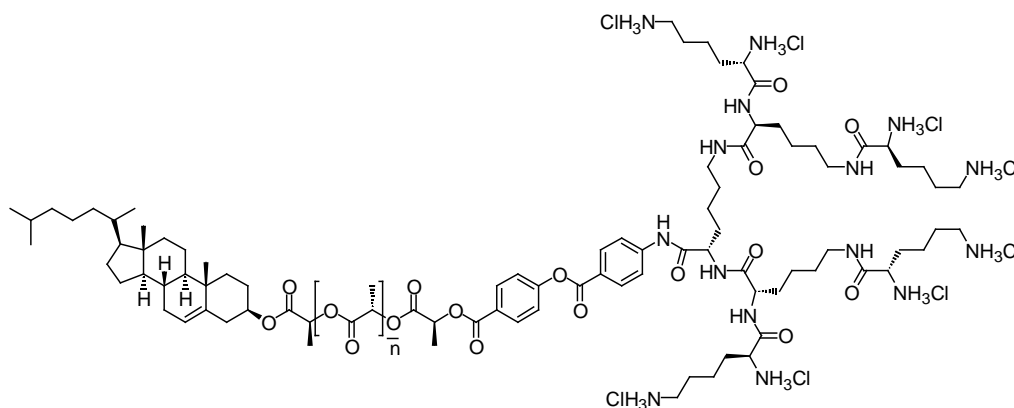


Figure 60. Block co-polymer based on an L-lysine dendron, a biodegradable L-lactic acid polymer chain and a cholesterol unit.

It seems clear that the generation of one-dimensional nanostructures is a rapidly developing frontier of self-assembly. In each case, the dendritic branching appears to play an *essential and pro-active role* in assisting the assembly process, with the specific advantage of using dendritic structures being the degree of control and tunability which can be achieved by simple *synthetic manipulations* of the molecular structures. It is also worth noting that only relatively *small amounts* of dendritic branching are used to generate such assemblies, meaning that the building blocks required are not prohibitively expensive and hence have real *commercial viability*. It is anticipated that in the coming years, an increasing range of novel nano-materials will be generated using this approach, and their applications as functional biomaterials or in electronic/photonic devices will be more widely studied and exploited.

4.3 Self-ordering of dendritic molecules – liquid crystalline materials

In contrast to self-assembly, which depends on a combination of individually weak non-covalent interactions, *self-ordering is a longer range effect* (similar to crystal packing) which encourages molecular building blocks to organise themselves into a more ordered assembly.

Typically the forces that drive this self-ordering process are: molecular shape, space filling effects, deformation ability, chirality, minimal interfacial curvature and microphase separation. The materials generated in this way typically have *liquid crystalline behaviour* (Figure 61) – in which the degree of ordering is intermediate between that found in a crystal (completely ordered) and that observed in a liquid (disordered/isotropic) [150]. Unlike the gel phase assemblies described above, *self-ordering* is often a phenomenon of the concentrated regime, because in the absence of solvent, long-range packing forces are of greater importance (although it should be pointed out that solvent does play a role in the formation of lyotropic liquid crystals).

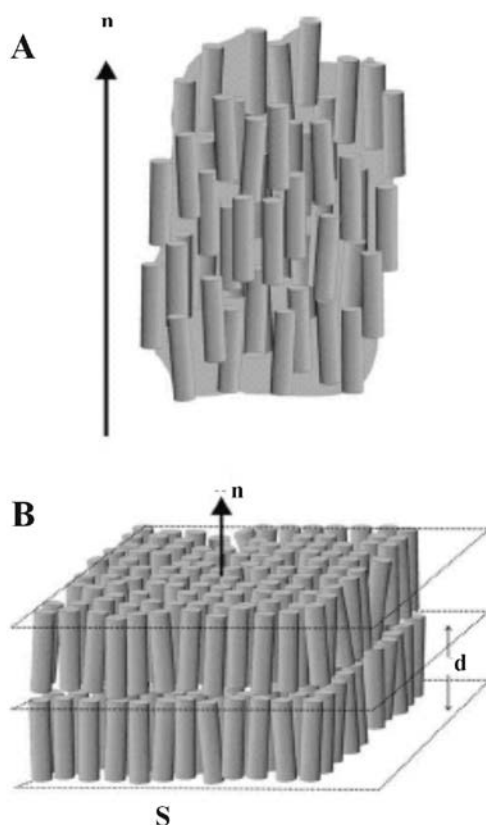


Figure 61. Schematic figure of the ordering of different types of liquid crystalline materials – smectic (S) and nematic (N) are two of the most common liquid crystalline phases. This image is taken from reference [151] with the kind permission of Elsevier.

There has been extensive development of *liquid crystalline dendrimers*, and a comprehensive review is beyond the scope of this article. However, this article will focus on different ordering strategies that have been employed, the different nanoscale assemblies that can be generated, and in particular, will highlight advantages of using dendritic systems for liquid

crystalline applications. There are two distinct approaches to developing dendritic liquid crystals. It is possible to develop dendrons which act as novel mesogens in their own right, and have the ability to assemble into mesophases as a consequence of their inherent molecular structure – such systems will be referred to as *supramolecular dendromesogens*. Alternatively, well-established mesogenic units can be simply attached to the periphery of dendritic molecules in order to endow them with liquid-crystalline behaviour – such systems will be referred to as *mesogen-functionalised dendrimers*.

4.3.a Supramolecular dendromesogens

The ability of dendritic structures, in particular dendrons, to express mesogenic properties has been successfully exploited by Percec and co-workers. In 1995, they first reported a dendron which exhibited calamitic, nematic and smectic thermotropic liquid-crystalline phases (Figure 62) [152]. In this case, the transition temperatures were dependent on the *generation* number of the dendritic branch. The observations made in this paper laid the foundations for the impressive body of work regarding the characterisation of nanoscale structures, which can be generated by dendritic self-ordering.

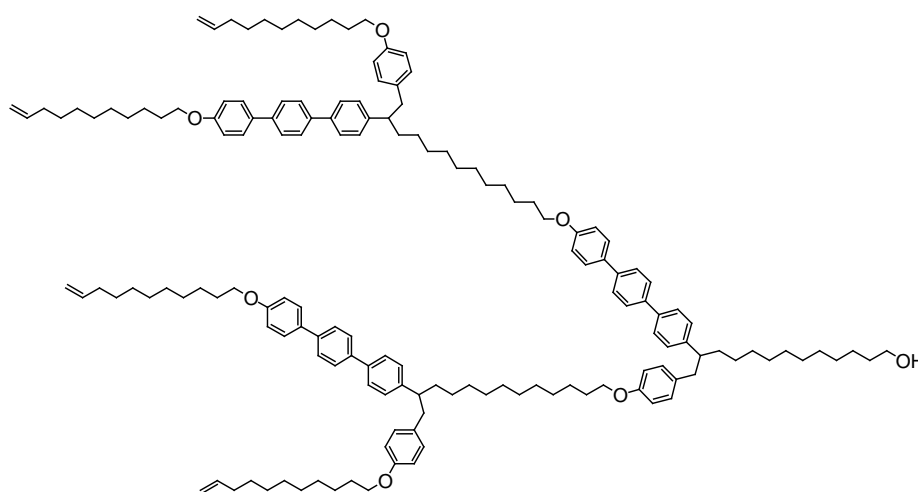


Figure 62. Supramolecular dendromesogen which self-orders to generate liquid-crystalline phases which have generation dependent thermal properties.

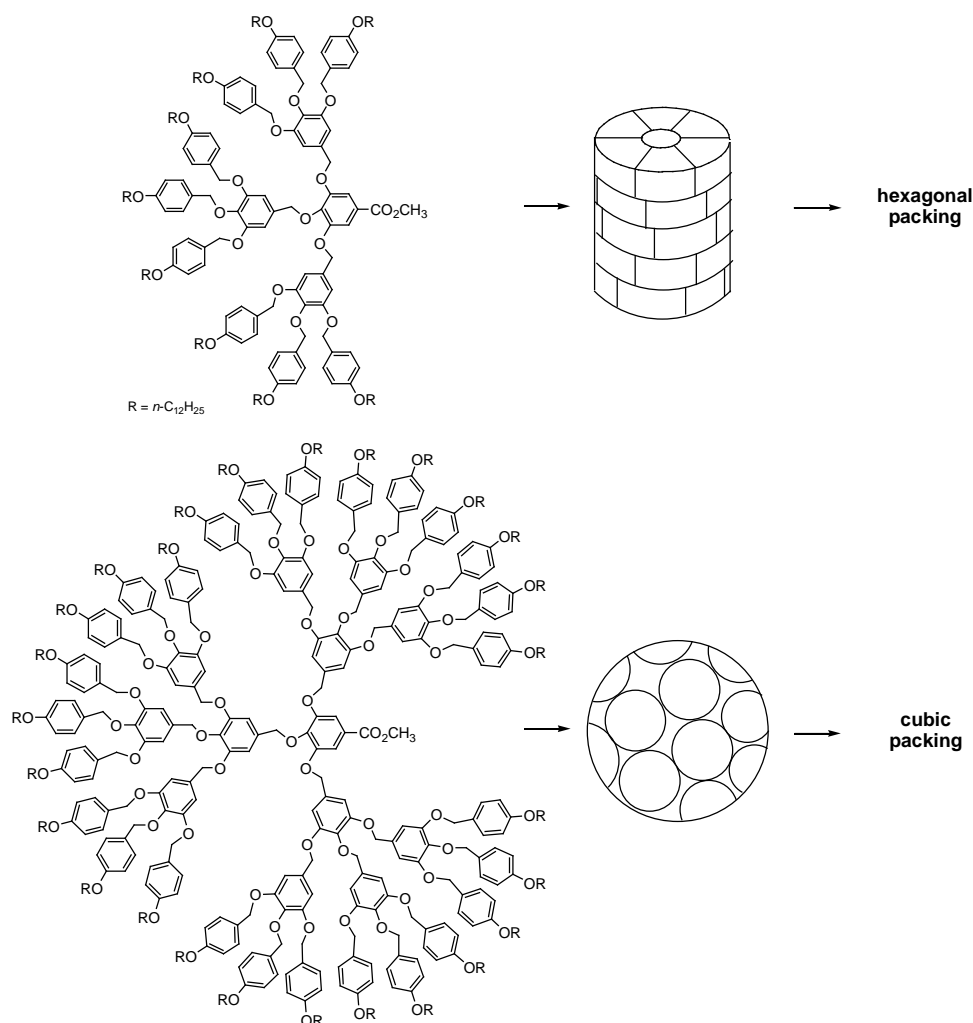


Figure 63. Supramolecular dendromesogens with different structures give rise to different assembled superstructures (cylindrical or spherical) which can pack in different ways (hexagonal or cubic).

In 1997, Percec and co-workers reported a series of dendrons of different generation which assembled into cubic arrays resembling spherical micelles – with larger dendrons exhibiting LC behaviour [153]. These dendrons were functionalised with a polar group at the focal point and long-chain aliphatic groups on the periphery, which help the assembly process as a consequence of *phase separation*. A key breakthrough came, when systems were developed in which the individual building blocks could control the shape of the assembled architecture (Figure 63) [154]. First and second generation tapered dendrons were reported, which assembled into *cylindrical* structures that then packed *hexagonally*, however, the third generation dendron, which is significantly more sterically demanding, cannot be supported within a cylindrical structure, and hence drove the assembly of *spherical* structures which

ordered themselves further and packed in a *cubic* manner. In this way, information can be considered to be ‘programmed-in’ on the molecular scale and transcribed up to the nanoscale assembly. This concept of *generation-controlled supramolecular ordering* has been reinforced in later publications from the group dealing with different dendron architectures [155]. Furthermore, this group has synthesised spherical dendrimers which self-organise into superlattices [156].

In addition to the effect of dendritic generation on the self-ordering process, it has also been illustrated that a number of other structural factors play an important role in controlling the nanoscale architecture.

- (i) The nature of the *linking group*. Using 3,4- and 3,5-disubstituted Fréchet-type branches indicated that the 3,4-disubstituted system formed spherical assemblies, whilst the 3,5-disubstituted analogue formed cylinders (Figure 64) [157]. This is a direct consequence of the impact that linkage isomerism has on the shape of the dendron.
- (ii) The nature of the *polar group at the focal point* [158]. Dendrons with benzo-15-crown-5 groups at the focal point have also been reported to self-order, and in the presence of Na⁺, complexation within the crown ether cavity modifies the ordering process [159].
- (iii) The *functional groups on the periphery* of the dendrimer. The diameter of the assembled cylindrical and spherical nanostructures depends on the peripheral functionalisation [160]. Dendrons with long fluororous tails on the periphery (Figure 65) have been shown to organise themselves as a consequence of the fluorophobic effect [161]. Furthermore, peripheral groups are able to modify the assembly mode of dendrons – for example transforming a spherical assembly built up from multiple dendron cones into a stacked pyramidal columnar array [162]. Similar effects of fluororous groups on assembly processes have also been reported by other workers [163].
- (iv) *Temperature*. Higher temperatures encourage the formation of spherical assemblies, whilst lower temperatures favour cylinders – this is a consequence of the relative entropic costs of forming such architectures [158,164].

Goddard and co-workers have recently modelled the organisation of this type of supramolecular ordering using molecular dynamics simulations at the atomistic level [165].

In particular, their predicted X-ray intensities showed excellent agreement with experimental data.

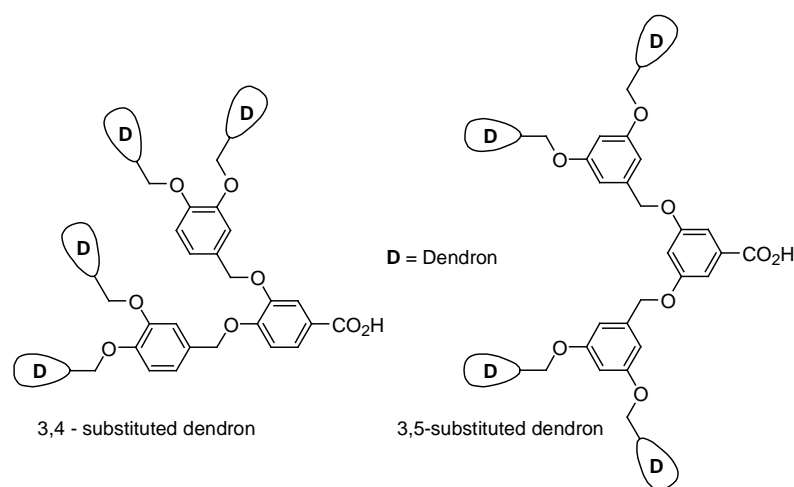


Figure 64. Different constitutional isomers of the dendrons (3,4- substituted or 3,5- substituted) give rise to ordered structures with different geometries.

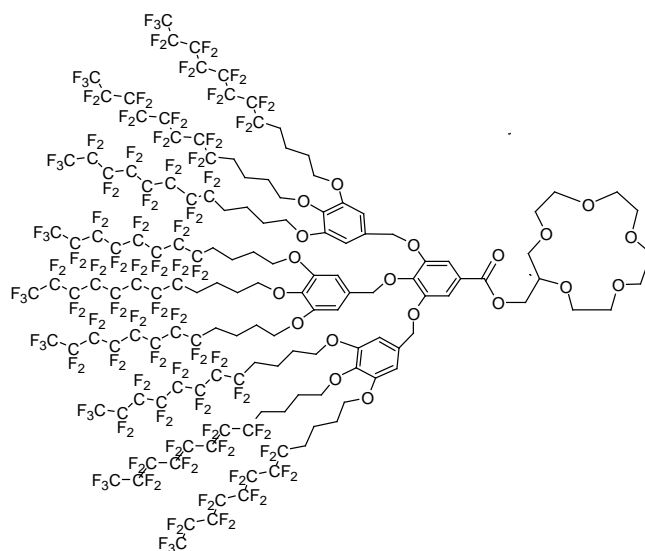


Figure 65. Fluorinated dendrons self-order as a consequence of the fluorophobic effect.

In order to demonstrate the usefulness of their approach to liquid crystalline dendritic systems, Percec and co-workers functionalised the focal point of their dendrons with organic donor or acceptor groups [166]. They found that this led to nanometre scale columns, the cores of which contained π stacks of donors, acceptors or donor acceptor complexes, which exhibited high charge carrier mobility. The authors argued that such assembled materials, in

which a π stack is encapsulated within a dendron shell, could have interesting electronic and optoelectronic applications.

In recent papers, Percec and co-workers have begun to focus on trying to control the higher level organisation of their assemblies of dendrons. For example, they have reported that they can design dendrons which assemble into globular supramolecular dendrimers, which then assemble further into an unusual complex tetragonal liquid crystal phase, with 30 globular supramolecular dendrimers within the repeat unit [167]. Furthermore, it has recently been reported that quasi-periodic structures can be generated which do not obey the basic rules of crystallographic symmetry, and hence represent a new mode of organisation in soft matter [168]. In an interesting recent paper, Percec and co-workers investigated the ability of an extensive library of dendron structures to exhibit self-ordering properties and thereafter further organisation into nanoscale superlattices [169]. All of these studies emphasise the way in which supramolecular self-ordering can be a multi-level process with subtle changes on the molecular level being transcribed up to the assembled architectures.

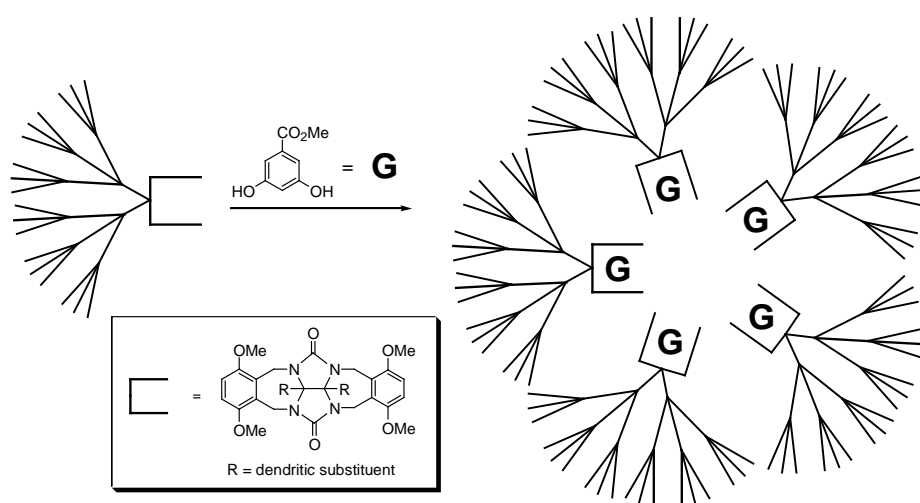


Figure 66. A supramolecular dendromesogen functionalised with a receptor unit at the focal point is capable of self-ordering into supramolecular architectures which retain the potential to bind specific guest molecules within their interiors.

In a particularly interesting approach, Percec collaborated with Nolte and co-workers to functionalise the focal point of self-organising dendrons with a U-shaped *receptor* [170]. In some cases, self-assembly of the dendromesogen still occurred, to yield spherical supramolecular assemblies, in which the receptor was buried in the core, with hydrocarbon

tails decorating the periphery (Figure 66). Furthermore, the 1:1 host:guest complex of the dendromesogen with methyl 3,5-dihydroxybenzoate still self-organised into a liquid crystalline phase, with the *guest included at the core of the assembly*. This illustrates how another level of supramolecular control can be introduced, and furthermore, indicates how potentially *functional molecules* can be incorporated into a nanoscale liquid crystalline array using host-guest chemistry. This approach offers considerable potential for the development of functional nanoscale materials from these simple self-organising dendritic building blocks.

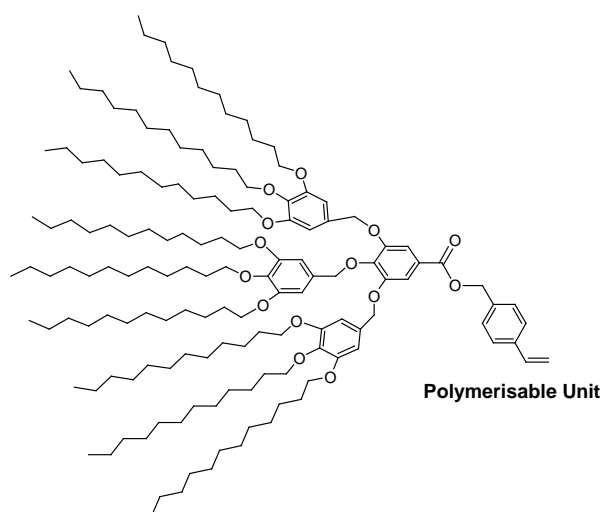


Figure 67. Self ordering dendritic groups can be used to control polymer conformation – enforcing a specific folded organisation onto the polymer.

Having developed their understanding of self-organising dendrons which exhibit LC-type phases, Percec and co-workers have also applied this knowledge to the development of polymeric systems in which the polymer backbone is functionalised with pendant dendritic groups (Figure 67). As a consequence of the self-ordering of the dendritic side groups, the *polymer conformation* or shape can be controlled. For example, when attached to short flexible backbones, the dendrons can produce a spherical polymer conformation, whilst when attached to long polymer chains, the self-ordering pattern of the monodendrons gives rise to a cylindrical system [171]. The structure of the dendritic groups plays a role in controlling the conformation and stiffness of the polymer backbone [172]. The ability to control the conformation of polymeric molecular systems using this type of approach is of considerable current interest, with designed folding systems being referred to as *foldamers* [173]. Such systems are of considerable interest because they mimic the way that proteins fold themselves into well-defined secondary and tertiary structures as a consequence of directed interactions.

Percec and co-workers have also utilised hydrogen-bonding dendritic groups as polymer side chains in order to control polymer architecture, with the resultant systems being capable of hierarchical self-ordering to generate LC phases [174].

Other workers have also developed dendromesogens capable of self-ordering. For example, Wiesner and co-workers have employed *amphiphilic* dendritic-linear block co-polymers with long hydrophobic tails on the periphery of the dendron and a PEO linear block at the focal point (Figure 68) [175]. Under certain conditions, this type of amphiphile can exhibit LC behaviour, driven by phase separation of the polar and apolar segments. The authors made use of these assembled superstructures to generate nanostructured aluminosilicate based hybrid materials. This indicates how non-covalently assembled architectures can be captured using *inorganic materials* synthesis. Stupp and co-workers have reported dendron-rod and dendron-rod-dendron type molecules, in which one or two dendritic units based on 3,4,5 tris(*n*-dodecyloxy)benzoate units are attached to a biphenyl ester rigid segment [176]. These molecules showed the ability to self-organise into smectic, columnar or cubic phases, with the rigid rod playing the dominant role in controlling the organisation process.

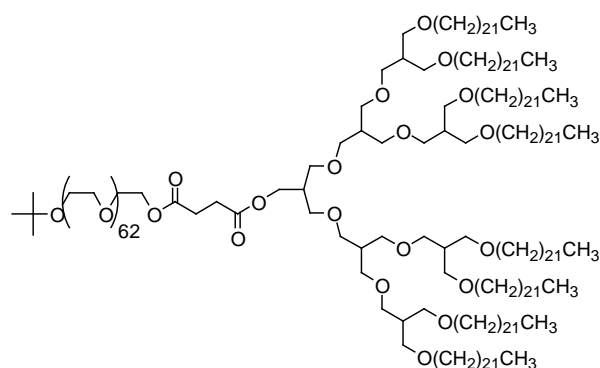


Figure 68. Amphiphilic dendron capable of ordering into liquid-crystalline phases.

Symmetric dendrimers have also been employed as inherent mesogenic units. Pesak and Moore reported *shape persistent, flat, circular dendrimers* constructed using phenylacetylene building blocks and with peripheral oligo(ethylene oxide) chains (Figure 69) [177]. Three generations of dendrimer were prepared and on cooling from the isotropic state, all three dendrimers formed columnar discotic liquid crystalline phases. It was postulated that the well-defined shapes of these dendrimers were important in controlling their ability to self-order into a columnar structure. For the higher generation dendrimers, the liquid crystalline phases existed over a temperature range of ca. 250°C. In a similar approach, Meier and co-

workers reported a series of planar conjugated stilbenoid dendrimers which exhibited LC behaviour [178]. Five generations of dendrimer were prepared, with the first two generations having disc-like shapes, whilst higher generations of dendrimer became cylindrical. All the dendrimers had a high tendency to aggregate (which increased with increasing dendritic generation), however ordered columnar mesophases were only observed for generations 1 and 2, with steric hindrance preventing this type of ordering for the higher generation systems. The photochemical behaviour of these assemblies of stilbenoid dendrimers is of considerable interest – for example, *photochemical reactivity* of the double bonds is only observed in the liquid crystalline state [179].

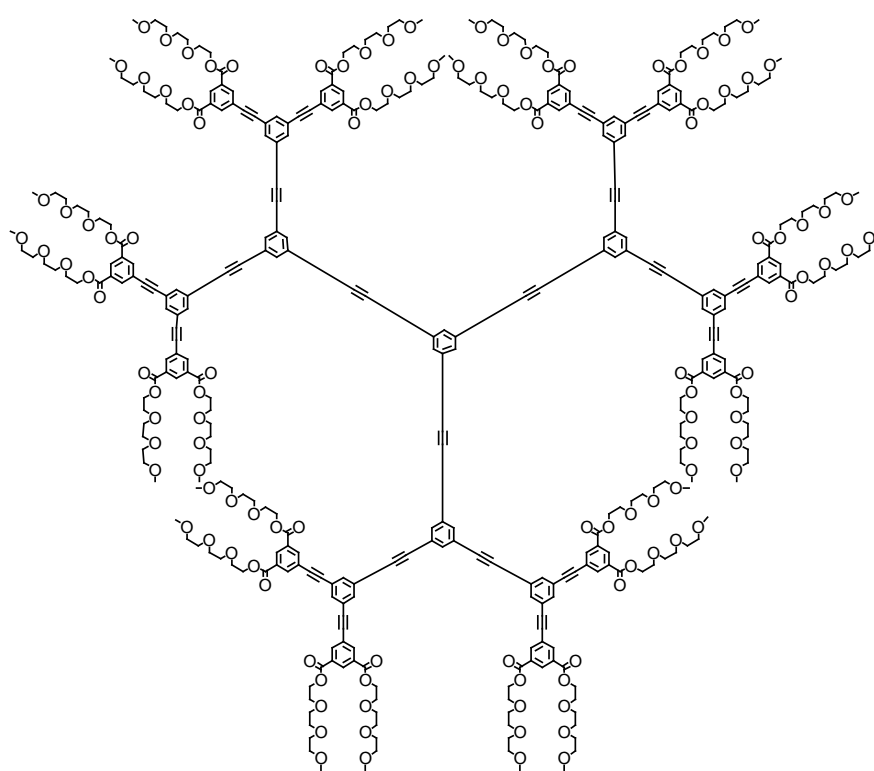


Figure 69. Rigid, shape-persistent dendrimers capable of self-ordering into a columnar mesophase with LC properties over an extended temperature range.

Lattermann and co-workers reported a dendritic system based on tris(aminoethyl)amine (tren), with peripheral hydrophobic tails [180]. These molecules are capable of binding a metal ion at the centre of the dendritic structure (*e.g.* Cu(II), Co(II) or Ni(II)) and subsequently, the metallated dendrimers exhibit LC behaviour. A range of different mesophases could be accessed at relatively low temperatures. Such metallated LC systems are of interest as a consequence of their magnetic properties (the bound transition metal ions

often have unpaired d electrons and are therefore paramagnetic). Controlled ordering of metallomesogens can therefore provide access to *magnetic materials* with nanoscale organisation.

4.3.b Mesogen-functionalised dendrimers

The second approach to the self-ordering of dendritic molecules into liquid crystalline materials is relatively straightforward, and utilises well-known *mesogenic* groups to encourage ordering of dendritic molecules. The ordering process is predominantly driven by the mesogenic groups (the behaviour of which is well-known from extensive LC investigations). As a consequence of this, the following discussion will focus principally on systems in which the dendritic structure itself also has a significant, or *pro-active* effect on the self-ordering process.

A whole range of different dendrimer scaffolds have been employed in order to attach different mesogenic groups. Some of the earliest reports of this class of liquid crystal employed carbosilane dendrimer scaffolds [181]. It was reported that using cyanobiphenyl, methoxyphenyl benzoate or cholesteryl groups as mesogenic fragments gave rise to LC behaviour when appended to first or second generation dendritic scaffolds. In further work, a systematic study of the influence of dendritic generation on the phase behaviour of these LC dendrimers was made [182]. First to fifth generations of cyanobiphenyl functionalised carbosilane dendrimers were synthesised (Figure 70). Smectic-type mesophases were observed over a wide temperature range, and it was shown that with increasing dendritic generation the *temperature* required to convert the LC phase into an isotropic liquid was increased – in particular for fourth and fifth generation dendrimers. The authors commented on two competing effects in the organisation of mesogens on a dendritic surface:

- (i) as dendritic generation increases, there are increasing numbers of *cooperative interactions* between terminal mesogenic groups (favourable interaction),
- (ii) as dendritic generation increases the scaffold becomes more *rigid* and closer to spherical, hence decreasing the interaction strength and ability of mesogenic groups to self-organise.

For the fifth generation dendrimer, unusual columnar superstructures were observed, with smectic-like arrangement of mesogenic groups combined with self-ordering of the dendrimers into columns, (the fifth generation system was investigated using AFM methods) [183].

Similar investigations have been reported for carbosilane dendrimers with different mesogenic surface groups – once again the fifth generation system exhibited more complex phase behaviour than the simple smectic organisation of first to fourth generation systems [184].

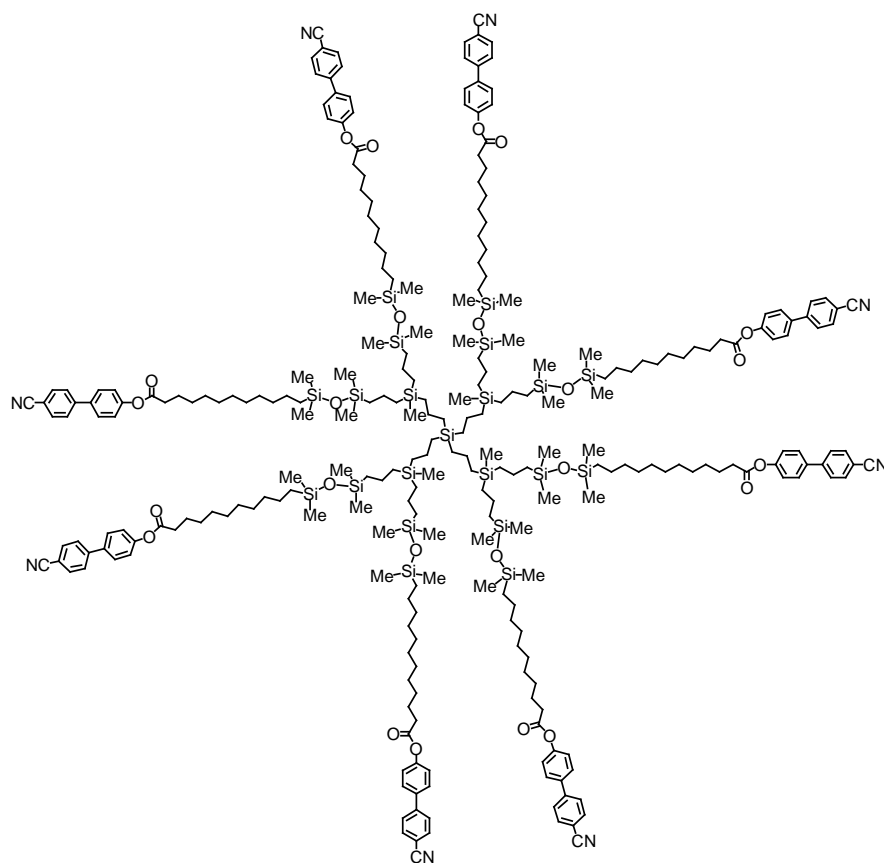


Figure 70. Cyanobiphenyl functionalised carbosilane dendrimers show LC behaviour.

It is worth noting that Zhang and co-workers, publishing only in the Chinese literature, have made extensive study of mesogen functionalised carbosilane dendrimers, and built up a useful database of LC behaviour and the different types of phases that can be generated from dendritic systems. They have also investigated functional LC dendrimers, such as those exhibiting *photochromic* properties [185].

Poly(propylene imine) (PPI) dendrimers have been functionalised with mesogenic groups at the periphery, with the first preliminary report in 1996, in which a library of small first generation dendrimers was compared with linear polymer analogues, indicating that LC phases were formed (Figure 71) [186]. In 1998, Meijer and co-workers reported that the

temperature range of the LC mesophase increased with increasing *dendritic generation*, and that the length of the spacer chain connecting the cyanobiphenyl mesogen to the dendrimer framework played an important role in controlling the phase transitions (a longer spacer encouraged mesophase formation) [187]. Interestingly, the spacings between mesogen layers in the LC phase were found to be independent of both dendritic generation and spacer chain, indicating it is the *ordering of the mesogens* which drives the assembly process and that the dendritic framework can be considered to be completely *distorted* in this case. Yonetake and co-workers also reported that the temperature range of LC smectic phases increased with the increasing dendritic generation of their mesogen functionalised PPI derivatives [188].

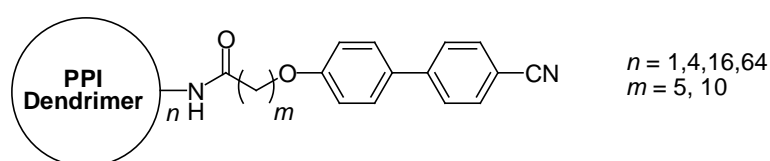


Figure 71. Mesogen-functionalised PPI dendrimers exhibit generation dependent LC thermal properties.

Serrano and co-workers have also made use of PPI dendrimers [189]. They employed the mesogen functionalised polyamine dendritic framework to bind copper ions. EPR studies have been performed to investigate the effects arising from the paramagnetism of Cu(II) [190]. These workers have also compared the relative LC behaviours of PPI derived and PAMAM derived dendritic systems. Having previously reported [191] that mesogen functionalised PAMAM derivatives were in some ways similar to those based on PPI – exhibiting a high degree of flexibility and adopting the most convenient shape for liquid crystalline behaviour – this group went on to perform a more detailed series of comparisons [192] They argued that internal hydrogen bonds within the structure of the PAMAM series of LC dendrimers contributed to the *rigidity* of the internal core, making it more rigid than the PPI analogues, which lack such hydrogen bonds. As a consequence, it was reported that the PAMAM dendrimers exhibited *improved LC properties* – including wide mesophase temperature ranges. These authors also reported that the number of chains on each mesogenic unit contribute significantly to the nature of the LC ordering. It was argued that increasing the aliphatic chain density imposes a curved interface and forces radial arrangement and hence the formation of *columnar mesophases* [193].

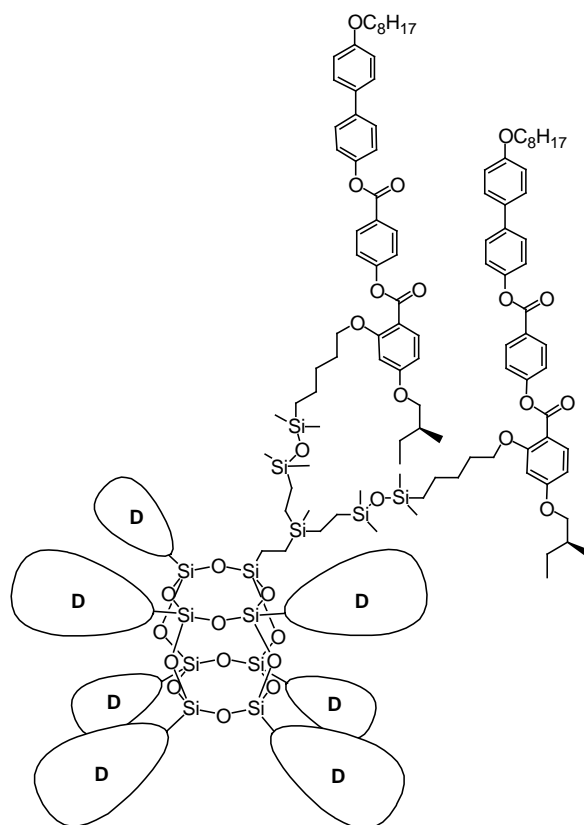


Figure 72. Dendrimers based on a silsesquioxane core functionalised on the surface with mesogenic groups exhibit LC behaviour in which the dendritic framework clearly plays a pro-active role.

Goodby, Saez, Mehl and co-workers have also investigated dendritic liquid crystalline structures in some detail. They have reported dendrimers derived from carbosilazane linkages which are functionalised with peripheral mesogenic groups [194]. They found, in this case, that increasing the dendritic generation had minimal effect on the thermal behaviour of the LC phases. Consequently, the mesogenic behaviour was the dominant force in this ordering process, *negating any effect of the dendritic architecture*. These workers, however, also reported dendritic systems based on silsesquioxane cores appended with chiral mesogens (Figure 72) [195]. These cubic cores were chosen as they have eight branching points, and furthermore have rigid structures – in contrast to many of the other dendritic frameworks investigated for LC activity. Interestingly, in this case, it was reported that the dendritic systems exhibited different liquid crystalline phases (chiral nematic, disordered hexagonal columnar and disordered rectangular columnar) relative to the non-dendritic mesogen (only a chiral nematic phase). This indicates that the dendritic structure is clearly playing a *pro-active role* in the liquid crystal ordering process. In recent work, this group has reported

spherical dendrimers analogous to AB block co-polymers, as the two hemispheres of the structure have markedly different structures [196]. One hemisphere was functionalised with chiral, laterally appended mesogens, whilst the other was appended with achiral terminally appended mesogens (Figure 73). They refer to these systems as ‘Janus’ supramolecular liquid crystals as a consequence of their ability to have two different ‘faces’. It was reported that if only the achiral mesogenic ‘face’ was present, these branched molecules formed achiral smectic phases. However, on addition of the second ‘face’ to the structure, chiral nematic and tilted chiral smectic LC phases were observed.

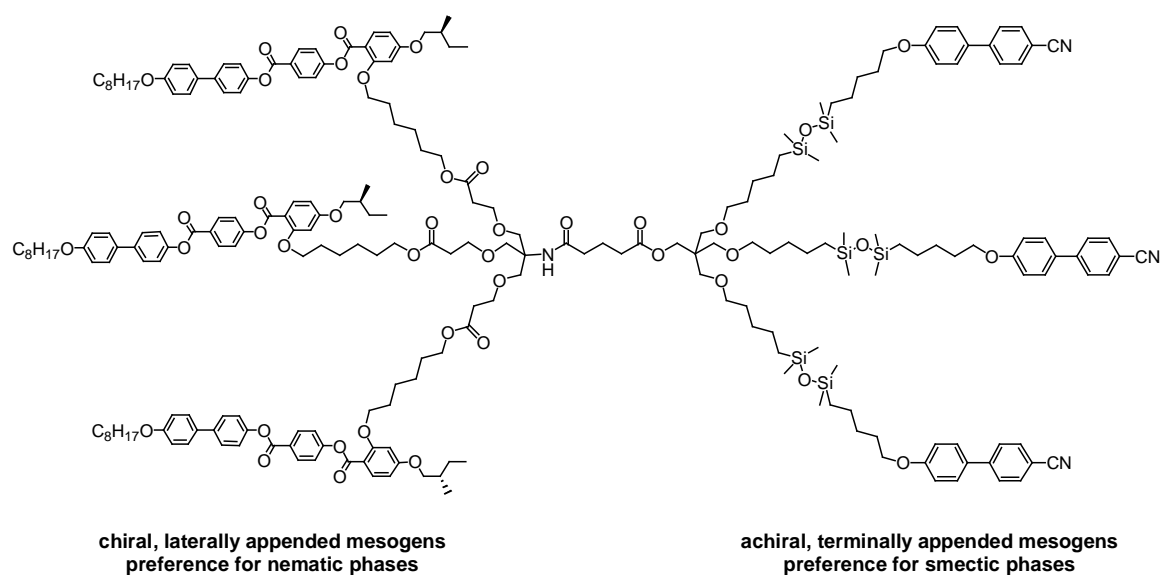


Figure 73. ‘Janus’ supramolecular liquid crystalline dendrimer.

Perhaps the most exciting aspect of liquid crystalline dendritic systems is the fact that LC materials have such widespread and *important technological applications* – in particular in *display screen technology*. With these applications in mind, Hult and co-workers reported dendritic liquid crystalline materials exhibiting *ferroelectric* properties – in other words, where the application of an electric field induces liquid crystalline behaviour [197]. The authors reported that the ferroelectric properties were independent of the generation number of the dendritic scaffold. Fullerene containing liquid crystalline dendrimers which exhibit electrooptical behaviour have also been reported, with the location of the C₆₀ unit within the dendrimer playing a role in controlling the LC behaviour [198]. Tschierske and co-workers have used bent (‘banana-shaped’) mesogenic units at the periphery of a small carbosilane dendrimer, and indicated that it formed a new mesophase type with unique properties (Figure 74) [199]. The authors argued that their dendritic framework stabilised the LC phase by

providing a permanent connection between some of the bent mesogenic units. Secondly, it decoupled the layers of the mesogens, cancelling the polar order in the ground state but allowing external electric fields to switch the structure into the ferroelectric organisation, with this ferroelectric state being stable, and able to be switched between different polarisation states. This type of system, in which the dendritic structure plays a pro-active role in mediating optoelectronic properties offers considerable promise for application as unique nanoscale materials.

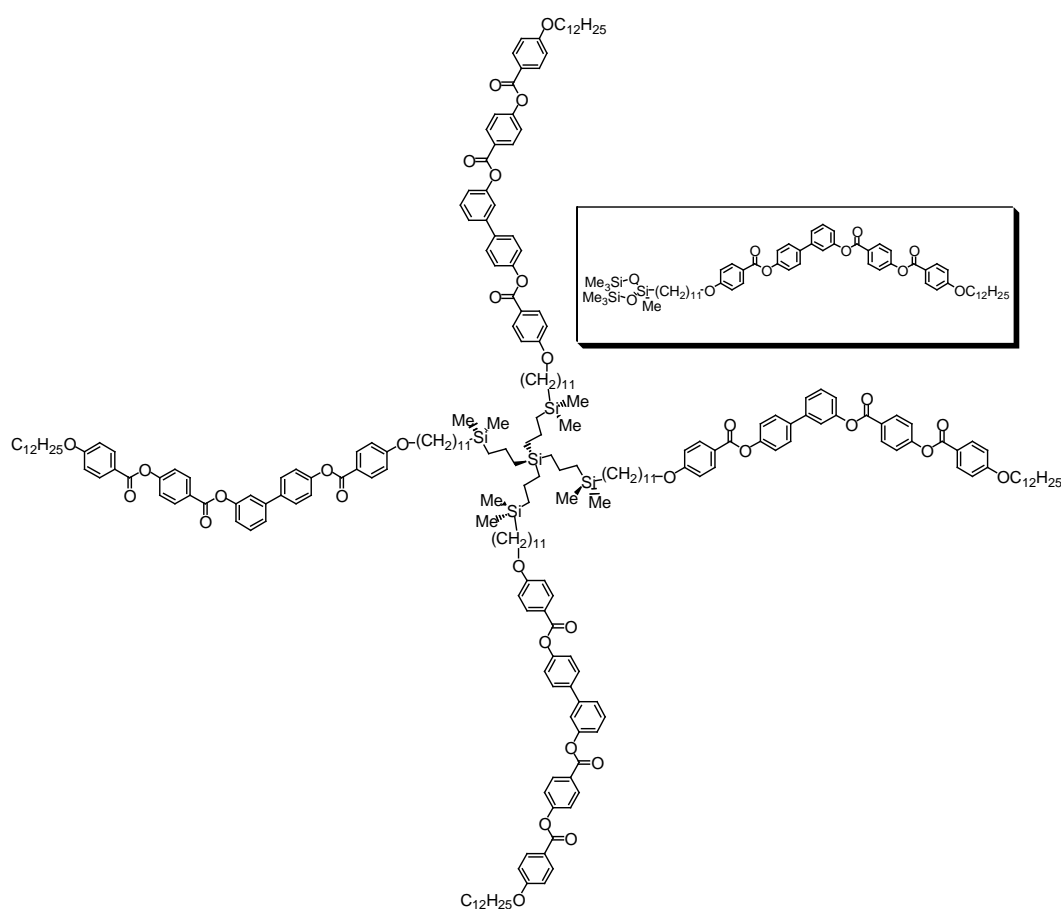


Figure 74. Ferroelectric branched structure with bent mesogenic units at the periphery.

It is clear from this brief overview that mesogen functionalised dendrimers behave in different ways. In some cases the dendritic framework has a pro-active role on the LC properties, whilst in other cases, mesogen ordering is the dominant factor. It is clear that careful design is required in order to fully optimise the combination of *LC behaviour* with a well-defined *dendritic advantage*. However, given the importance of the applications of LC systems, it is evident that further work in this area has the potential to yield novel types of functional nanoscale materials.

5. Conclusions and prospects for the future

In summary, the self-assembly/ordering of dendritic molecules has been an area of explosive growth over the past 10 years. Until the mid 1990s, dendrimer chemistry was predominantly concerned with new methods for the covalent synthesis of branched architectures. Given the painstaking nature of covalent synthetic methods, it has rapidly become clear that a short-cut to achieving real nanoscale functional systems, is to allow dendritic building blocks to self-assemble into more complex architectures. Using organic and inorganic synthetic methods, the individual dendritic building blocks can be constructed/programmed with an almost infinite range of potential architectures, and this provides a huge variety in the nature and behaviour of the nanoscale structures which can be assembled from them.

As illustrated in this article, one-, two- and three-dimensional, discrete and extended superstructures can all be generated using dendritic self-assembly, and these systems have extremely wide-ranging potential for applications – from controlled release, to materials chemistry, and even biotechnology. Given the importance of ‘bottom-up’ fabrication in the development of nanotechnology for the new millennium, it is evident that dendritic molecules are a unique and fascinating molecular-scale toolkit, which can be used to very rapidly access nanoscale structures through self-assembly fabrication methods. As a consequence, the future for this eye-catching and fascinating field appears to be very bright indeed.

6. References

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