Utilisation of Dendritic Architectures in Molecular Recognition and Self-Assembly Processes

C.R. Yates and W. Hayes*

School of Chemistry, The University of Reading, Whiteknights Reading, Berkshire RG6 6AD, UK

Abstract: This mini-review outlines recent key developments in the use of dendritic architectures in self-assembly processes *via* utilisation of molecular recognition motifs.

Keywords: Dendrimers, molecular recognition, self-assembly, hydrogen bonding interactions.

1. INTRODUCTION

In the last 20 years, synthetic developments in the area of macromolecular science have progressed and diversified rapidly. One of the important developments within this era was hyperbranched materials, most notably dendrimers derived from AB_2 monomers [1-3]. Dendrimers are highly branched, globular, three-dimensional polymers with an architecture that may be highly functionalised whereas in comparison hyperbranched polymers are irregular branched polymers that are polydisperse systems both in terms of molecular weight characteristics and their branching factors [4, 5].

The unique physical characteristics of dendrimers, such as low intrinsic viscosity, increased solubility parameters in a wide range of both organic and aqueous media and good chemical reactivity, render this new class of polymers ideal candidates in a wide scope of applications, including utilisation in new catalysts [6] and pharmaceutical devices [7]. Another aspect of macromolecular science that has received significant attention over the past decade is supramolecular chemistry [8], and dendritic architectures have been employed in supramolecular arrays [9]. The interest in supramolecular chemistry has arisen as chemists endeavour to mimic nature in the search for efficient processes and new functional and potentially 'intelligent' materials. As observed in nature, complex molecular assemblies are formed by a multitude of weak non-covalent interactions, such as hydrogen bonding, aromatic π- π interactions and ion pairing [10]. In this respect, dendrimers are attractive macromolecules for use in host-guest chemistries, as these perfectly branched macromolecules adopt globular three-dimensional structures at higher generation numbers (as a consequence of steric crowding effects), which is analogous to globular proteins [9a], whereas in the case of lower generation number dendritic systems, more open conformations are observed.

Two key phenomenon are of key importance in supramolecular chemistry:- i) *Molecular Recognition*: involves the selective binding of a guest molecule(s) by a (dendritic) host and ii) *Self-Assembly*: the utilisation of numerous weak non-covalent interactions in a directed manner to generate large functional assemblies.

In this short review, notable recent examples (post 1998) of the use of dendritic architectures in the area of supramolecular chemistry will be highlighted. The objective of this article is not only to provide a comprehensive coverage of this rapidly advancing field but the reader is also directed to several excellent reviews and books that have been published in recent times [8, 9].

2. DENDRIMERS AND MOLECULAR RECOGNITION

Molecular recognition plays an important role in biological processes as exemplified by enzymes and antibodies [11]. The exploitation of this phenomenon has led chemists to devise synthetic three-dimensional 'host' structures [12] such as crown ethers, cryptates and cyclophanes [11] for the selective binding of 'guest' molecules. Synthetic polymer chemists have utilised these studies in the formation of dendritic host molecules amongst others, in order to bind specific guests, either at the peripheral surface of the dendritic architectures – *exo receptors*, or utilising the interior cavity – *endo receptors* [9b, 9c].

2.1. Molecular Recognition at the Peripheral Surface of the Dendritic Architecture

The peripheral surface of a dendrimer features a large number of functional groups and can, therefore, act as an ideal host for molecular recognition events. Glycodendrimers [13, 14, 15] have been studied extensively as a consequence of the importance of carbohydrate-protein binding in many cellular processes. In 1996, Stoddart *et al.* studied the formation of dendrimers containing carbohydrate residues at the peripheral surface, which emanated from short peptidic chains joined to a central benzenoid core (see **1** in Fig. **1**) [14]. The dendrimers were synthesised utilising a convergent growth strategy with a repetitive amide bond forming sequence to achieve the desired dendrons, which incorporated glucose as the carbohydrate residue at the surface. Subsequent related studies involved the surface modification of commercially available poly(propylene imine) (PPI), dendrimers with either D-galactose or D-lactose [15].

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*Address correspondence to this author at the School of Chemistry, The University of Reading, Whiteknights Reading, Berkshire RG6 6AD, UK; Tel.: +44(0)118 3786491; Fax: +44(0)118 3786331; E-mail: w.c.hayes@reading.ac.uk

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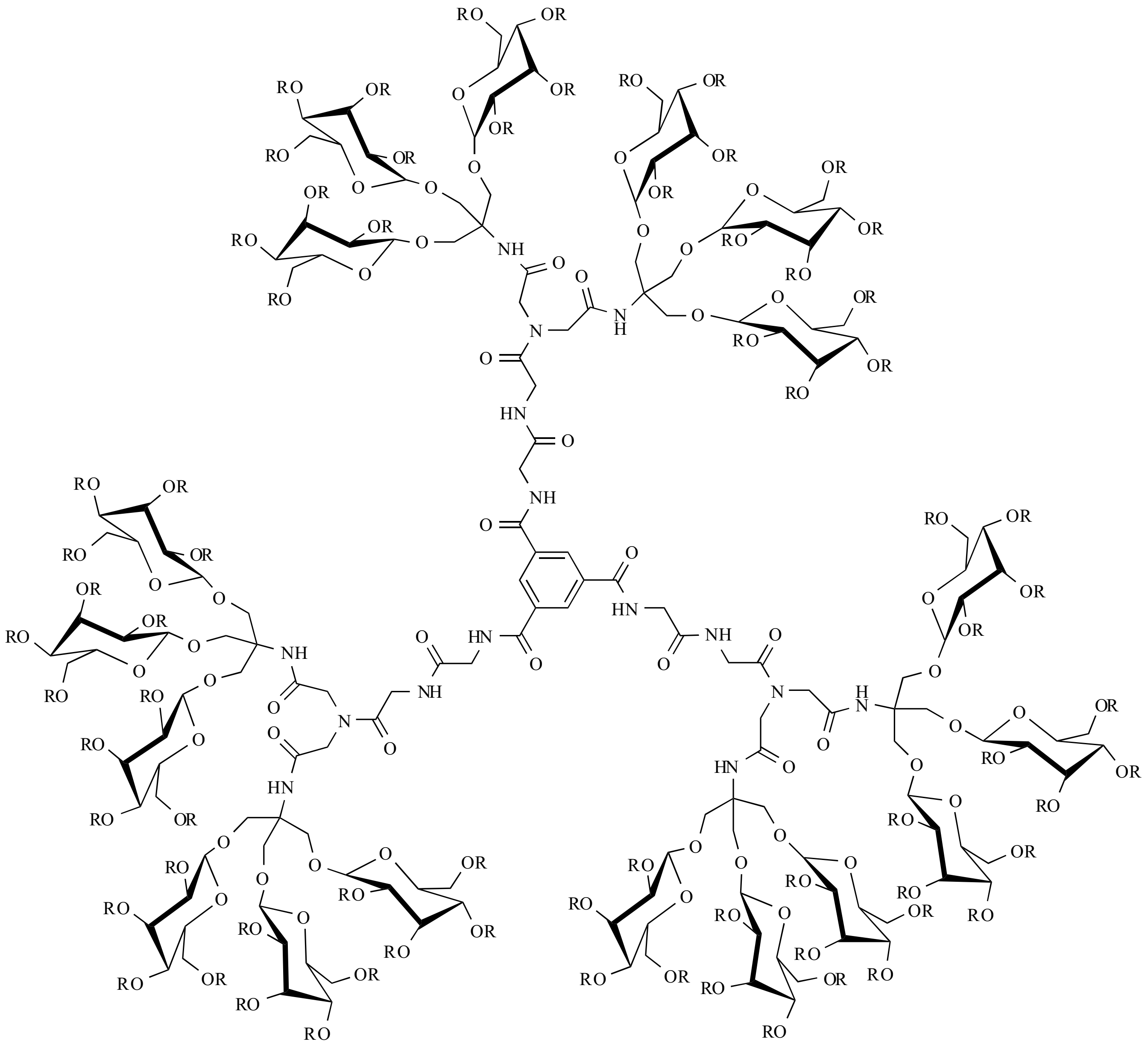

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Fig. (1). Glycodendrimer **1** synthesised by Stoddart and co-workers [14].

It was predicted that these glycodendrimer systems could be used as suitable oligosaccharide candidates in the preparation of neoglycoconjugates, as it was postulated that several sugar residues joined to a central spacer through covalent bonds might be able to form stronger complexes with protein receptors than a single sugar moiety alone. Recent investigations in this field by Cloninger and co-workers involved the study of the strength of lectin binding interactions with mannose/hydroxyl functionalised dendrimers [16]. The dendritic 'supports' synthesised consisted of a poly(amidoamine) (PAMAM) backbone with mannose subunits attached to the dendritic surface *via* *iso*thiocyanate linkages, and by altering the dendrimer size, a relationship between the number of available mannose sites and the binding affinity of the lectin (concanavalin A) was established using a combination of haemaglutination and precipitation assays. From these studies, it was determined that the degree of lectin clustering and the overall activity of the lectin with the dendrimer could be altered by the different mannose loadings of the dendrimers. The maximum activity observed occurred when the mannose loading was ≥ 50 % for all of the dendrimer generations tested. It was envisaged that dendrimer superstructures could be formed with a high degree of control over both the lectin binding affinity and the number of lectins clustered into a specific area on the cell surface. Stoddart and co-workers have also synthesised an array of glycodendrimers that contain a porphyrin unit at the core of the dendrimer architecture [17] *via* formation of amide linkages between four β-D-glucopyranose based dendrons (the sugar moieties are protected with benzoate groups) to a tetrafurcated porphyrin core. The resultant deprotected glycodendrimers were water-soluble, whereas in contrast, the protected species were soluble in common organic solvents. The photophysical properties of the dendrimers incorporating the porphyrin core were assessed and both the protected and deprotected dendrimers were found to exhibit two distinct fluorescence lifetime values in comparison to the porphyrin model system that exhibited only one. This interesting result was accounted for by considering that the dendrimers, when in solution, can adopt two different conformations as a consequence of the bulky β-D-glucopyranose substituents on the peripheral surface. Furthermore, the porphyrin cored dendrimer featuring the protected β-D-glucopyranose units at the periphery exhibited minimal energy transfer from the benzoate groups of the β-D-glucopyranose branch to the porphyrin core.

In an alternative approach, several research groups have studied the effect of metal complexation on the dendritic host systems. A notable example was reported by Meijer and co-workers in 1997 [18], and involved the synthesis of a series of PPI dendrimers, to afford increasing numbers of functional groups at the peripheral surface. The surface was functionalised with *bis*-(3-aminopropyl)amine groups which acted as multiple polydentate ligands for various transition metals such as Cu^{2+}, Zn^{2+} and Ni^{2+}. It was observed that upon addition of metal salts to methanolic solutions of the dendrimers dendritic poly-*bis*-(3-aminopropyl)amine-MCl_2 (where M = Cu, Zn or Ni) complexes were produced. The ability of these dendrimers to complex transition metals in this fashion has led to the construction of metal-containing nanoscopic assemblies of defined structure and size, incorporating a distinct number of transition metal ions (up to 32 metal centres) depending on the generation number of the dendrimer.

PPI dendrimers were employed by the research groups of Kaifer [19] and Astruc [20], who have published independently the studies of dendrimers in redox processes. Kaifer and co-workers described the first example of the use of dendritic terminal groups for the inclusion complexation of cyclodextrins [19]. The PPI dendrimers featured ferrocene functional groups on the peripheral surface connected *via* amide spacer groups. It was observed that upon addition of the cyclodextrins to the ferrocene derivatised dendrimers, the solubility in aqueous solution increased dramatically, which is consistent with the formation of inclusion complexes between the ferrocene on the surface of the dendritic structures and the cyclodextrin units. A major restriction of this study was limited solubility of the higher generation dendrimers in aqueous media, either complexed to or in absence of the cyclodextrins. The limited solubility observed was rationalised by consideration of the significant steric hindrance associated with the complexation of the cyclodextrin moieties. In an alternative approach, Astruc and co-workers added small inorganic anions, such as $H_2PO_4^-$ and Cl^- to ferrocene functionalised dendrimers [20] for use as redox sensors. Upon addition of the anions to the dendrimers, the resultant solutions were monitored by cyclic voltammetry (CV), which revealed that, in the case of the $H_2PO_4^-$ anion, there was formation of an electrostatic interaction between the cationic ferrocenium branch and the $H_2PO_4^-$ anion. In contrast, the addition of HSO_4^-, Cl^- and NO_3^- anions produced weaker effects, as there were no new redox waves observed in the CV analysis. The stable assemblies arose as a consequence of synergistic relationships involving a combination of electrostatic interactions between the ferrocenium cations and hydrogen bonds of the amide NH group of the dendritic backbone and the $H_2PO_4^-$ anions. It was observed that as the generation number of the dendrimers increased steric crowding effects involving the ferrocene termini of the dendritic branches precluded penetration of the anion. Therefore, as the anions used in the study were small, the greatest effect and selectivity was observed for the highest soluble generation dendrimer as a consequence of the formation of 'open' cavities within the dendrimer architecture. For comparative purposes, it is worthy of note that endoreceptors also favour anion inclusion with open cavities where size compatibility plays an important role. In an alternative approach, Astruc and co-workers synthesised a series of redox active metallodendrimers for the specific recognition of $H_2PO_4^-$ anions [21]. PPI dendrimers were utilised to enable the free amine moieties at the dendritic exterior to participate in hydrogen bonding interactions with a range of hydroxyl functionalised dendritic wedges that in turn featured ferrocenyl functionalities at the peripheral surface. Once the hydrogen bonding assembly was formed, this array was able to complex the $H_2PO_4^-$ anions at the amidoferrocene branches. It was established that the cyclic voltamic response of binding of $H_2PO_4^-$ anions to monomeric amidoferrocene was weak, whereas when the amidoferrocene branches were complexed to the PPI dendrimer receptor the CV signal increased. This increase in voltage was consistent as the generation number of the dendrons increased was consistent with a positive dendritic effect, which in turn was indicative of the hydrogen bonding assembly of amidoferrocenyl dendrimers.

Another interesting application of dendrimers in molecular recognition was the development of chemical switches. Zhang and co-workers [22] utilised polyether dendrimers with spironaphthoxazine groups at the periphery to afford a unique chemical switch. These spironaphthoxazine groups are able to isomerise photoactively in a reversible fashion when doped with metal ions such as Ag^+, Zn^{2+} and Al^{3+}, and can, therefore, be controlled photochemically and utilised as switches. The dendritic architecture acts as a special microenvironment for the spironaphthoxazine groups that are unable to form stable complexes with the metal ions and therefore isomerisation occurs between the non-ionic and ionic states, unlike the spironaphthoxazine monomers, which form a stable complex with the metal ions and remains in the stable ionic form. Upon irradiation of the dendrimer supported spironaphthoxazine groups the reversible chelating and releasing of the metal ions was observed.

In 2000, Esumi *et al.* [23] described the interactions of carboxylate functionalised PAMAM dendrimers with cationic surfactants. The aqueous properties of mixtures of PAMAM dendrimers featuring peripheral carboxyl groups with cationic surfactants such as dodecyltrimethylammonium bromide (DTAB) and 1, 2-*bis*-(dodecyldimethylammonio)ethane dibromide was studied by surface tension measurements, fluorescence spectra and dynamic light scattering measurements. In the case of the DTAB-dendrimer assembly, it was observed that the surface tension decreased as the DTAB concentration was increased. This decrease in surface tension was explained by the formation of aggregates in which the hydrophilic groups of the DTAB were adsorbed onto the carboxyl groups of the dendrimer, thereby orientating its hydrophobic chains to the aqueous solution. This postulate was viable as the hydrophobicity of the aggregates between the dendrimers and DTAB increased with decreasing dendrimer generations. Following the initial aggregation, a further increase in DTAB concentration led to an increase in the surface tension as the DTAB appeared to adsorb onto the dendrimers as a bilayer that would lower the surface activity than that of the aggregates themselves. The results of dynamic light scattering analysis were concomitant with those obtained from surface tension measurements, thereby reinforcing the hypothesis that adsorption of the surfactant onto the dendrimer surface led to the formation of complex aggregates.

In the quest to find an interesting method for the modification of a dendrimer exterior by non-covalent interactions, Kim *et al*. [24] synthesised a novel pseudorotaxane terminated dendrimer. The PPI dendrimer skeletons possessing amide spacers linked the pseudorotaxane assemblies to the dendritic backbone. To understand the effect of the pseudorotaxane molecules on the conformation of the dendrimers, molecular dynamic simulations were carried out. It was observed that the protonated PPI dendrimer exhibited a degree of backfolding of the terminal groups and following the addition of the cucurbituril macrocycles *via* non-covalent interactions the dendrimer adopted a fully extended conformation with the terminal groups segregated from each other. This conformational change increases the overall size of the dendrimers and the large terminal pseudorotaxane units appear to form a rigid shell at the exterior of the dendrimer, which in turn behaved as a barrier isolating the dendrimer from bulk solvents. These pseudorotaxane terminated dendrimers are both topologically intriguing and also have provided a novel way into the modification of dendrimer exteriors by non-covalent interactions. The application of such dendrimers can be used to inhibit the escape of guest molecules trapped within the dendritic exterior, or could be envisaged as delivery vehicles for the translocation of guests such as drugs if the surface cucurbituril macrocycles could be removed in a reversible fashion.

Meijer and co-workers have expanded the scope of the utility of PPI dendrimers by utilising them as host systems for a range of urea functionalised guest molecules [25]. In this research, the PPI dendrimers were functionalised with either adamantine-*bis*(propylthiourea) or palmityl-*bis*(propylthiourea) molecules on the periphery, which acted as pincer-like hosts for glycine-urea functionalised guest molecules. Infrared spectroscopy was used to assess the degree of hydrogen bonding in the functionalised molecules. It was observed that as the dendrimer generation number increased, the intensity of the non-hydrogen bonded states decreased whilst the intensity of the hydrogen bonded states increased. The host-guest interactions of the thiourea dendrimers were also studied by 1D- and NOESY- nuclear magnetic resonance (NMR) spectroscopy. From the NMR spectral data thus obtained, it was determined that the guest molecules were bound to the dendrimer host molecules *via* thiourea (from the host molecule) to urea (from the guest molecule) hydrogen bonds, and by ionic bonding between the terminal guest carboxylate moiety and the outer shell tertiary amines of the dendrimer.

2.2. Molecular Recognition in the Interior of the Dendritic Architecture

Dendrimers are constructed of a multifunctional core moiety that subsequently is linked to highly branched dendrons that can act as localised microenvironments with internal cavities. Recognition events can, therefore, be tailored to occur at either the core or throughout the branched structure in addition the host-guest interactions at the peripheral surface (*vide supra*).

2.2.1. Molecular Recognition in the Interior Branches of the Dendritic Architecture

The main way in which the branched components of the dendritic architecture are able to participate in host-guest interactions is *via* the accommodation of guest molecules through encapsulation phenomena. A seminal report of this approach was presented by Meijer and co-workers in 1994 [26] and described the divergent synthesis of a 'dendritic box' comprised of a fifth generation PPI dendrimer featuring a chiral shell of *N*-*tert*-butyloxycarbonyl (*t*-Boc) protected amino acids, (for example, L-phenylalanine) on the dendrimer surface. Experimental modelling was carried out on the dendritic host system, and it was determined that the dendrimer architecture consisted of a 'solid shell' and a flexible core, which had internal cavities that were able to accommodate guest molecules. A selection of dyes such as eriochrome black T, 7, 7, 8, 8-tetracyanoquinodimethane (TCNQ) and Rose Bengal were chosen as suitable guest molecules and were introduced into the PPI dendritic core (taking advantage of the affinity of the dye molecules for the tertiary amines). The dyes were allowed to diffuse into the dendrimer until the thermodynamic equilibrium was established between the free and the dendritically encapsulated dyes. Subsequent reaction of the exterior primary amines with the *N*-hydroxy-succinimide ester of the *t*-Boc protected amino acids formed the exterior shell and thus imprisoned the guest molecules. In the case of the encapsulation of Rose Bengal [26-28], it was observed by ultraviolet-visible (UV-vis) spectroscopic analysis revealed that there was an average load of one dye molecule per dendritic box (see **2** in Fig. **2**). The encapsulated dyes could be released by shape-selective liberation by the deprotection of the multivalent dendritic surface [28].

In an alternative approach, Smith and co-workers [29, 30] have studied the solubilisation of hydrophilic dyes using individual dendrons. The dendrons featured L-lysine as the branched repeat unit with either methyl esters or carboxylic acid functionalities at the peripheral surface and a primary amine at the focal point. The solubilisation studies were carried out on two dye systems:- proflavine hydrochloride and aurin tricarboxylic acid. It was envisaged that the proflavine hydrochloride dye would be hydrogen bonded *via* its two available amino groups to the carboxylic acid functionalities on the periphery of the dendritic wedge and the dye uptake by the dendron was monitored by UV-vis spectroscopy. It was observed that when the dye was added to dichloromethane, minimal solubility of the dyestuff in the halogenated solvent occurred, however, when the dye was mixed with the dendron in dichloromethane uptake of the dye was evident. The molecular weight of the dendron played a major role in increasing the solubility of the dye

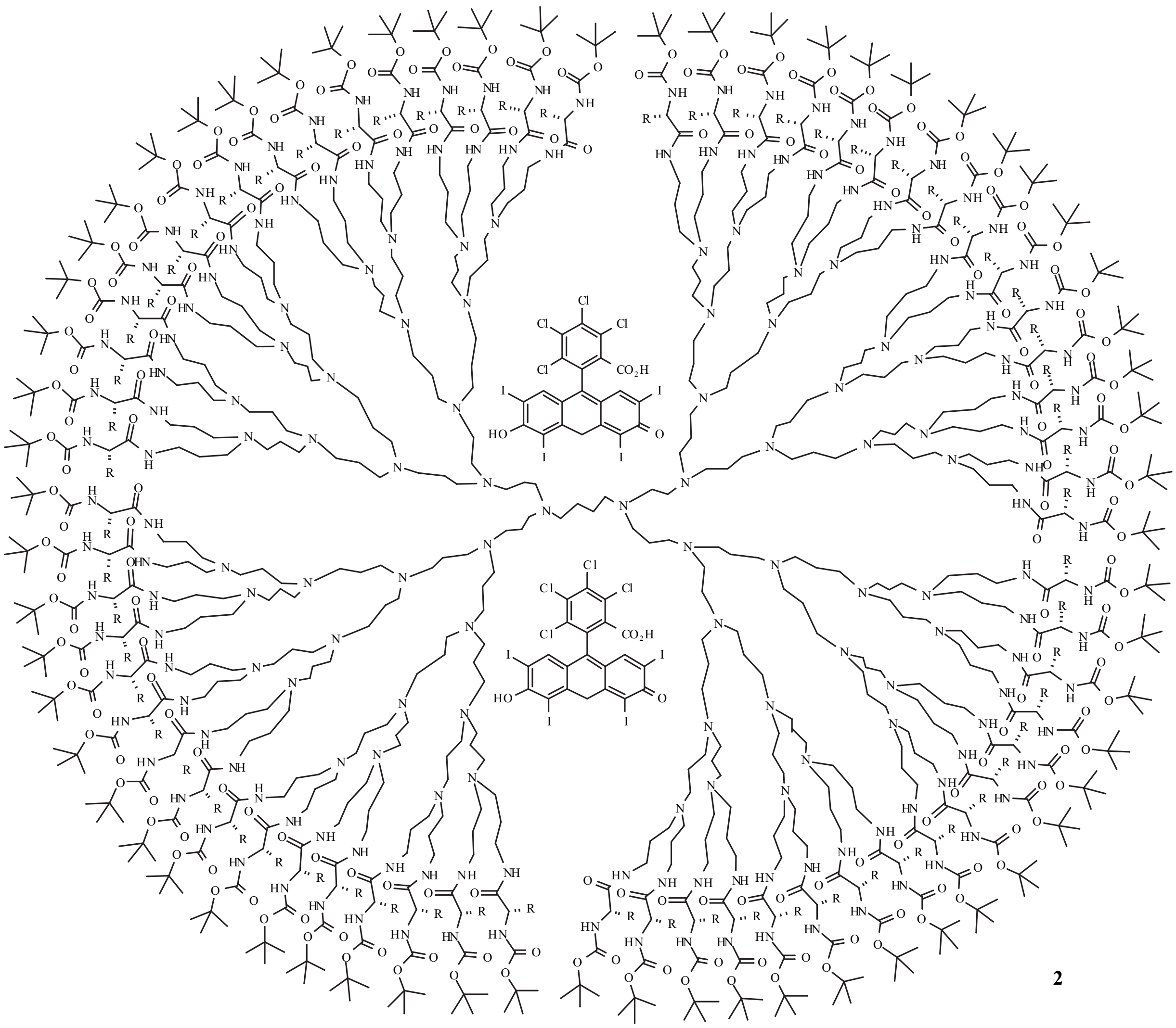

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Fig. (2). PPI dendritic box **2** with encapsulated rose bengal molecules reported by Meijer and co-workers [26-28].

molecules. Increasing the generation number of the branched polyamide receptor from the 1st to the 4th generation resulted in an increase in the amount of dye that was encapsulated within the branches and there was a subsequent bathochromic shift λ_{max} value from 441 to 461 nm in the UV-vis spectrum. For comparative purposes the methyl ester protected dendritic branches were examined for dye uptake. It was observed that the rate of uptake of the dye diminished through the apolar phase which emphasised the importance of complementary acid-amine interactions, however, a proportion of the dyestuff was transported it was concluded that multiple weak secondary interactions within the cavities of the dendritic branches was also an important factor. In order to test this theory, a second dye, aurin tricarboxylic acid, was tested as it features two carboxylic acid functionalities and therefore, would bind strongly to the primary amine at the dendrons' focal point *via* hydrogen bonding interactions. As observed in the case of the proflavine hydrochloride dye, similar bathochromic shifts were observed in the UV-vis spectra of the dendritic complexes. This study exemplified the ability of dendritic branches to encapsulate dye molecules, which in turn could then be transported subsequently through apolar phases by the tailoring of the functionality of the dendritic branches.

In a related study, on the ability of dendrimers to encapsulate dye moieties, Vögtle *et al.* monitored the effect of fluorescent guests hosted within fluorescent dendrimers [31]. PPI dendrimers were utilised that incorporated dansyl units on the peripheral surface of the dendrimer and a selection of dye molecules including eosin Y, fluorescein, naphthofluorescein and Rose Bengal were utilised as the guest systems. The excitation characteristics of the resultant host-guest complexes were observed and interpreted in terms of both fluorescence quenching and sensitisation processes. This study revealed that the fifth generation PPI dendrimer could host up to 12 eosin Y molecules and the corresponding fourth generation dendrimer was capable of binding ~25 Rose Bengal moieties. The fluorescence quenching properties of these host-guest complexes was also assessed. It was also calculated that only a single eosin Y guest was sufficient to completely quench the fluorescence of any excited dansyl unit in the dendrimer host and fluorescence lifetime measurements established that the dye molecules could also reside within two different environments of the exterior of the dendritic host. The spectroscopic results thus obtained have revealed avenues for applications of such dendritic hosts ranging from chemical sensors to catalysis as the strong guest selectivity of the

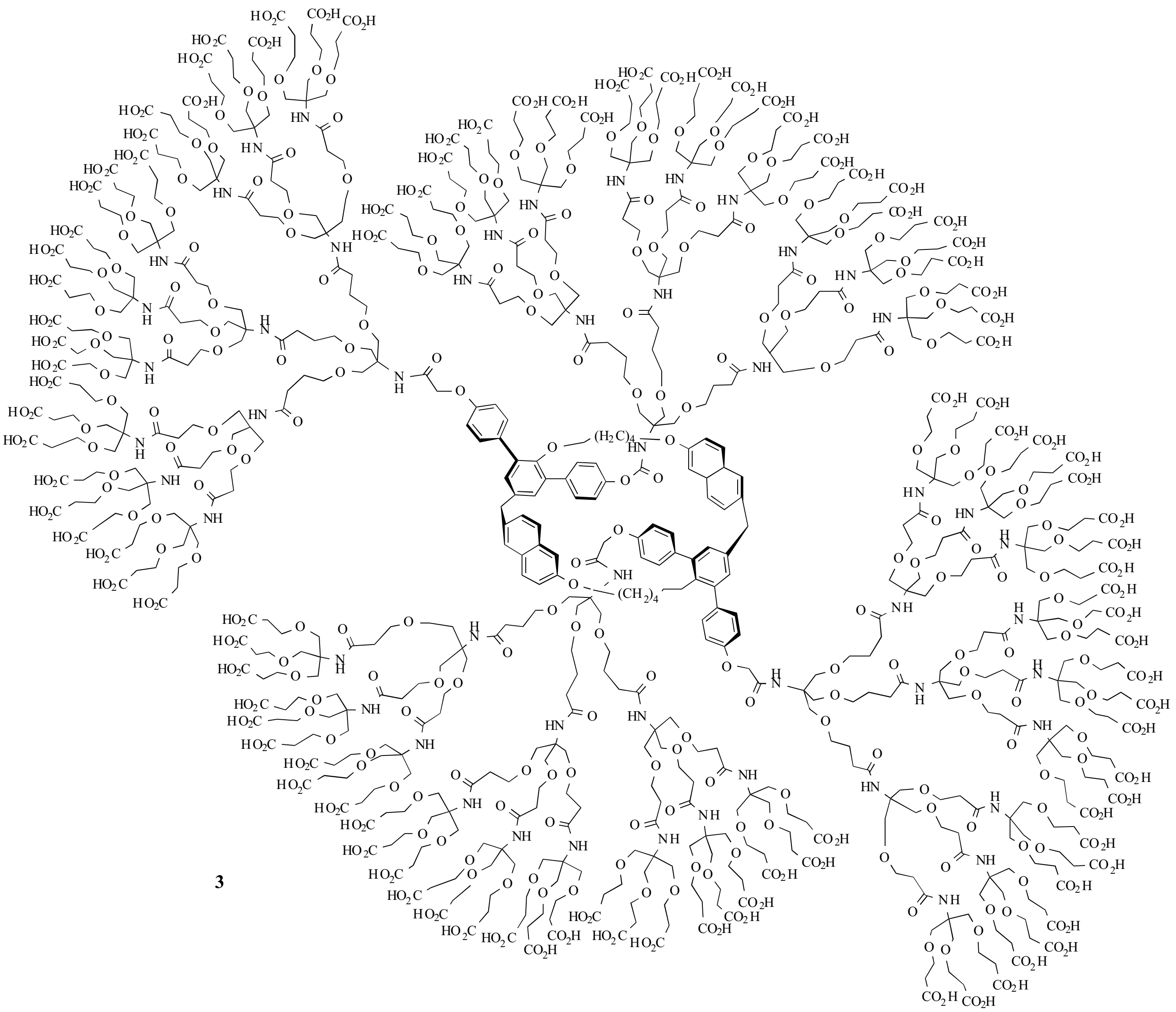

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Fig. (3). Dendrophane receptor **3** reported by Diederich and co-workers [34-37].

dendritic guest of this type is comparable to that exhibited by enzymes.

Smith and co-workers have synthesised dendritic ferrocene derivatives and studied the redox properties of these systems [32, 33]. The ferrocene molecules were encapsulated within a symmetric amide-ether dendritic shell and the redox potential of the host-guest complexes was measured in a range of solvents of varying polarities. It was observed that in apolar non-hydrogen bonding solvents the redox potential of the ferrocene increased when incorporated within the branched dendrimer units, thereby indicating that the oxidation of the ferrocene units to the corresponding ferrocenium species became hindered thermodynamically by the dendrimer architecture. This effect was rationalised by the dendrimer acting as a less polar medium in comparison to that of the surrounding electrolyte solution. For comparative purposes, asymmetric derivatives of the amide-ether dendrimers were also investigated and it was observed that increased branching of the dendrimer encouraged oxidation of ferrocene to occur and thus resulted in a decrease in the redox potential of the encapsulated ferrocene moieties. It was postulated that the dendrimer shell behaved as a non-polar shield, thereby protecting the redox-active ferrocene units from the polar ionic solution hence stabilising the charged form of the dendritic core and is therefore analogous to the properties exhibited by proteins. It was also concluded that in the cases of the symmetrical dendritic systems the polarity of the solvents used also had a marked effect, i.e. when the redox assays were carried out in methanol, the dendritic branches exerted minimal shielding effects and was attributed to complete solvation of the dendritic shell – this behaviour was not observed in less polar media. This study again exemplifies the ability of dendritic architectures as considered as ideal biomimetic models.

2.2.2. Molecular Recognition at the Core of the Dendritic Architecture

The core functionality of the dendrimer is encapsulated within the branched architecture and has been utilised frequently in molecular recognition assays. Pioneering

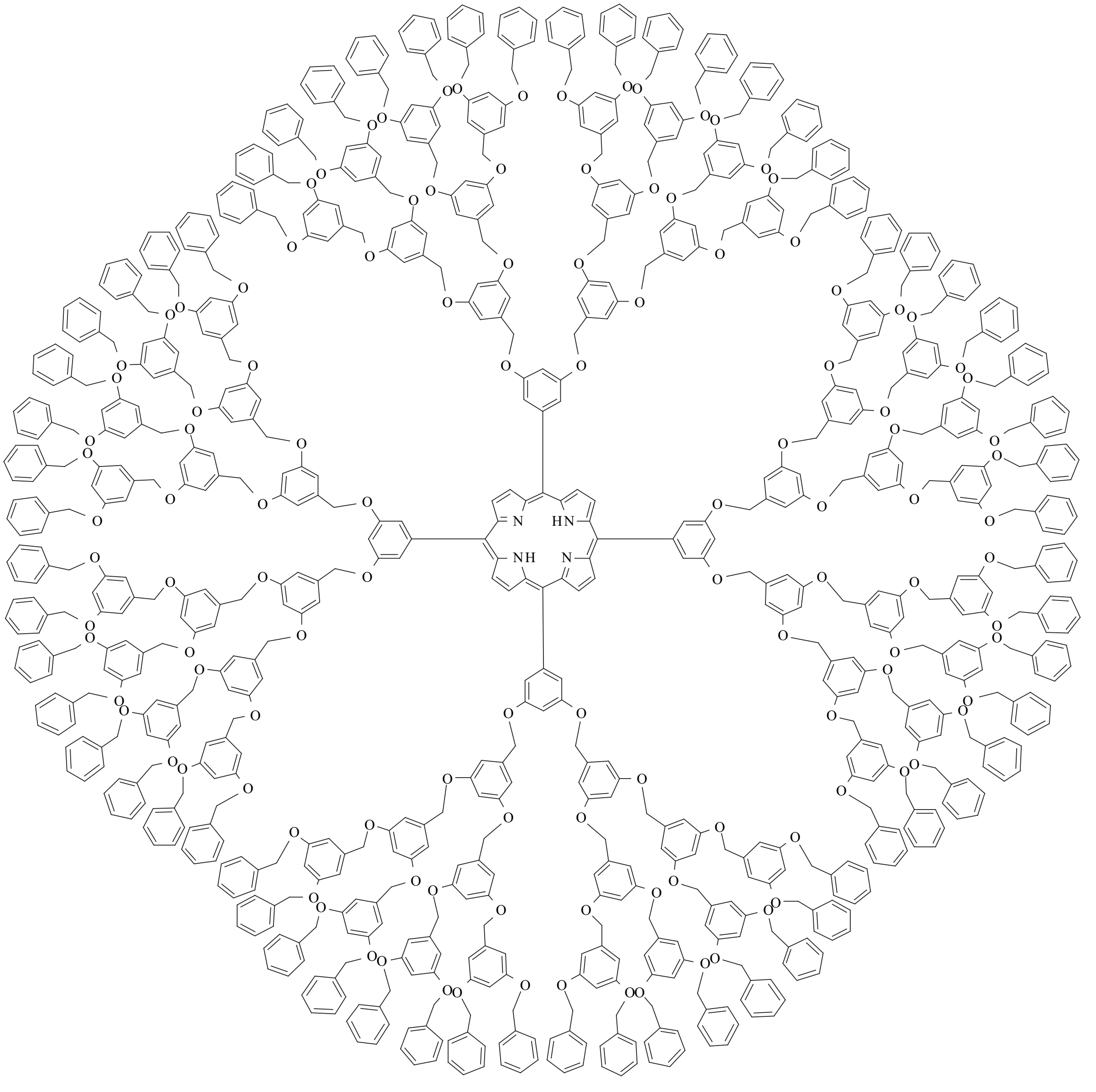

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Fig. (4). Porphyrin cored poly(aromatic ether) dendrimer **4** synthesised by Fréchet and co-workers [40, 41].

studies in this field have been reported by Diederich and co-workers [34] – for example, dendritic receptors were synthesised that featured either as cyclophane-type, *dendrophanes* [34-37] or cleft-type, *dendroclefts* [38, 39] recognition sites at the core. Two types of dendrophane were designed that both incorporated poly(ether amide) branching units with carboxylic acids groups at the peripheral surface. The first series contained a central cyclophane core possessing a binding cavity that was able to complex either benzene or naphthalene guest molecules, whilst the second series incorporated a cyclophane core able to bind large steroidal substrates (see **3** in Fig. **3**). Both series of dendrophanes were found to be water-soluble and were prepared *via* either divergent or semi-convergent fashions up to the third generation.

Both ^{1}H NMR and fluorescence spectroscopic binding titrations were used to investigate the binding properties of the dendrophanes and these studies revealed that the complexation of guest molecules occurred almost exclusively within the cyclophane core moiety – binding processes analogous to that of active sites buried within proteins. The host-guest association constants (K_a) obtained from fluorescence spectroscopic titrations were in close agreement with those obtained from the ^{1}H NMR spectroscopic data, the K_a values obtained for both naphthalene-2, 7-diol and 6-(*p*-toluidino)naphthalene-2-sulfonate were in the order of 10^3 to 10^4 lmol^{-1}. The host-guest exchange kinetics were fast in all of the dendrophanes studied ($K_{\text{decomplexation}} > 10^2$-$10^3$ s^{-1}) and the cyclophane recognition sites proved to be accessible and effective for all of the dendritic generations studied.

Several porphyrin core dendrimer systems have been reported in the literature and the photophysical properties have been studied in the relation to the binding of metal cations [40-43] or as the free-base porphyrins [44]. Preliminary studies on the synthesis and photophysical and hydrodynamic properties of poly(aromatic ether) dendrimers with a porphyrin core moiety that was able to complex zinc

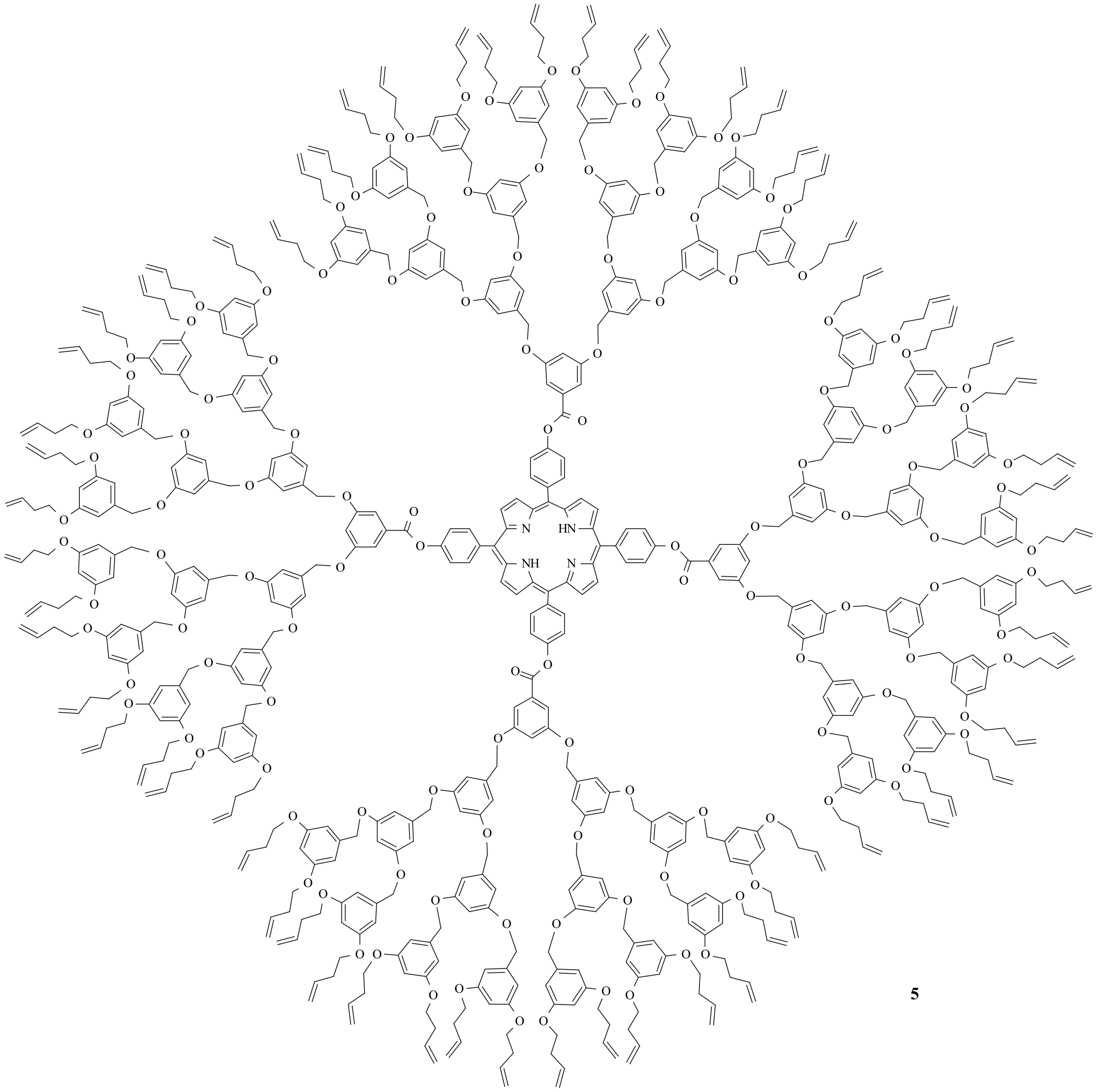

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Fig. (5). Poly(aromatic ether) dendritic template **5** synthesised by Zimmerman and co-workers for the molecular imprinting of porphyrins [51].

cations were reported by Fréchet and co-workers [40, 41] (see **4** in Fig. **4**).

The poly(aromatic ether) dendrimers synthesised featured dendrons from the 1st to 4th generation and contained either a zinc porphyrin (PZn) or a tetraphenylporphyrin (TPP) core moiety (for comparative purposes). Both series of dendrimers did not aggregate in solution or exhibit any intramolecular interactions between the porphyrin unit and the dendrons when in the ground electronic state. Studies of the intrinsic viscosity of the dendrimers revealed that these dendrimers incorporating the PZn core moiety collapsed upon reaching the fourth generation since the hydrodynamic radius decreased. Interestingly, the dendrimers incorporating TPP as the core were never fully extended in solution when compared to the corresponding gas-phase radii thereby indicating a more dense structure in the case of the dendrimers featuring PZn at the core. This phenomenon was rationalised by the consideration that the core moieties possess different structural features:- the TPP core unit featured an extra phenyl group which serves to separate further the branched dendrons from the core moiety and therefore enabling the overall steric constraints of the dendrimer to be reduced.

Aida and co-workers have studied recently the use of cobalt (II) porphyrin dendrimers in the AIBN initiated reaction with alkynes [43]. These studies demonstrated the highly chemoselectivity of AIBN-initiated organic transformations of poly(aryl ester) dendrimer-appended cobalt (II) porphyrins with a variety of alkynes. These novel core-active dendrimers were found to react rapidly and in a chemoselective fashion with an optimum sized dendritic framework, whereas, in contrast if the dendritic component was ≥ the 3rd generation, the reaction was retarded as a consequence of limited access to the active site for the reactive species. Furthermore, it was also observed that this retardation in reaction rate was noticeable for reactions involving propargyl alcohol but not in the case of 1-hexyne. This observation implies that molecular recognition ability within the highly confined dendritic core was taking place and results of this nature afford encouragement for the use of core-active dendrimers as designer catalysts and artificial enzymes.

In 1998, Zimmerman and co-workers described the hydrogen bonding capability of core moieties in dendritic host molecules and in particular, amidinium guests [45]. Zimmerman has expanded recently these studies further in the synthesis of cored dendrimers [46, 47]. These poly(aromatic ether) dendrimers featured homoallyl ether groups at the peripheral surface and a 1, 3, 5-*tris*(hydroxymethyl)benzene core. The peripheral allyl groups were subjected to ring-closing metathesis (RCM) [48] to generate 'cored' dendrimers that could be visualised as polymeric nanospheres, or core-shell nanoparticles. Base hydrolysis removed the core moiety to generate recognition sites within the nanosphere and the resultant products were envisaged as ideal candidates for delivery agents or molecular sensors. Furthermore, Zimmerman and co-workers reported in 2003 [49] the generation of organic nanotubes from porphyrin dendrimers utilising a synthetic approach similar to that employed in the construction of the nanospheres. However, in this case the poly(aromatic ether) dendrimers contained a oligoporphyrin core moiety which was subsequently complexed with tin(IV) prior to RCM to generate the desired nanotube systems. To generate the cored nanotube, the porphyrin moiety was removed by a transesterification reaction to afford organic nanotubes with four complementary binding sites.

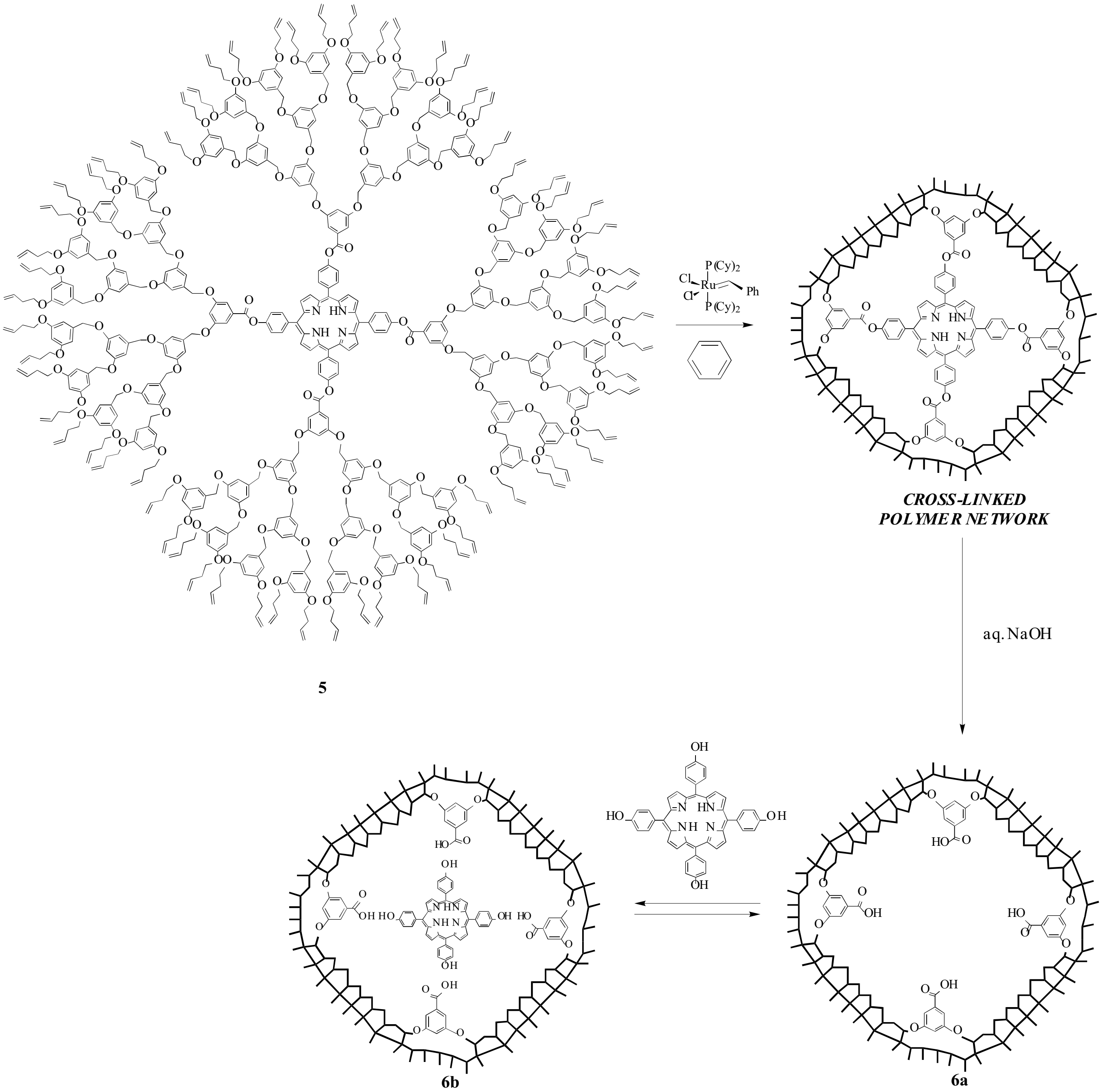
Molecular imprinting [11, 12, 50] utilises molecular recognition phenomena between a template molecule and monomers employed in polymerisation to create stable complexes within rigid macroporous polymer networks**.** Following polymerisation, the template is removed to afford imprinted binding sites that are complementary to the template used. The binding sites are held securely in a three-dimensional environment as a result of the rigidity of the highly cross-linked polymer matrix. The rigid porous nature of the imprinted polymer network, in theory, facilitates efficient rebinding of the template. Zimmerman and co-workers have utilised this molecular imprinting phenomenon in the formation of synthetic dendritic hosts [51]. In order to demonstrate the concept of monomolecular imprinting, a porphyrin system was imprinted within a poly(aromatic ether) dendrimer (see **5** in Fig. **5**).

The molecular imprinted polymers were synthesised from the porphyrin containing poly(aromatic ether) dendrimer that possessed homoallyl functionalities at the peripheral surface and were subsequently exposed to RCM using Grubb's first generation catalyst [52], followed by removal of the porphyrin core moiety by base catalysed hydrolyse to leave four complementary binding sites (see **6a** and **6b** in Scheme **1**) [51]. This study described an efficient route to the formation of synthetic hosts possessing a single imprinted binding site per molecule utilising the well-established technique of molecular imprinting, which are not only soluble but are also sizeable macromolecular hosts ($M_w \approx 10$ KDa). The results obtained indicated a high yield of imprinted sites that exhibited a high selectivity for well-defined porphyrins that were capable of participating in hydrogen bonding, but with only a moderate degree of shape selectivity.

Smith *et al.* have reported recently the synthesis of complexes using terbium (III) ions and dendritic branches based on L-lysine building blocks [53]. These dendritic complexes were bound predominately by electrostatic lanthanide-carboxylic acid interactions, previously reported by Fréchet and Kawa [54] and were utilised as Lewis-acid catalysts in Diels-Alder reactions. However, it was observed that the encapsulated lanthanide species had no effect on the regiochemical outcome of the products, although when terbium (III) acetate was used in the absence of the dendritic host, the lanthanide ions remained bound to the reaction products (as observed by ^{1}H NMR spectroscopic studies). In contrast, the dendritic terbium complexes were separable from the cycloadducts. This observation indicates that the Lewis-acid centre may be inaccessible both to substrate and products in the more highly functionalised dendritic environment. Therefore, for effective Lewis-acid catalysis within an encapsulated environment it is viable to postulate that sufficient space is required to allow diffusion of the substrate and product moieties in and out of the dendritic environment and that there are no donor atoms present in the dendritic branches that may effect unwanted coordination of the Lewis acid.

Vögtle and co-workers have reported the formation of a 2:1 luminescent complex between a dendrimer and a cyclam core with Zn^{2+} cations utilising dendritic branches as ligands [55]. The dendrimers synthesised consisted of a cyclam core with appended 12 dimethoxybenzene and 16 napthyl units, respectively, and the complexation of Zn^{2+} within the core moiety was studied. It was observed that in the case of the cyclam dendritic ligand with Zn^{2+} afforded a 2:1 complex, an unusual stoichiometry as the majority of cyclam complexes are 1:1 complexes in nature. It was postulated that this unusual 2:1 stoichiometry could be attributable to the dendrimer branches favouring the coordination of the cyclam nitrogen atoms to the Zn^{2+} with respect to the coordination of solvent molecules or counter ions. This observed dendritic effect could be envisaged as useful in the design of cyclam containing ligands for the complexation of metal ions in various fields including catalysis and medical therapies.

A notable example of controlled release of encapsulated dendritic molecule by crown ethers was outlined by Smith *et al.* in 2002 [56, 57]. The dendritic framework employed was based upon L-lysine as the repeat unit – in this example the polyamide dendrons' focal point was functionalised with benzo-[18]-crown-6. The dendritic branches were assembled around a *bis*-ammonium cation **7**, thus encapsulating it within a supramolecular dendritic shell, utilising the methodology described by Stoddart and co-workers [58].



5

6b

6a

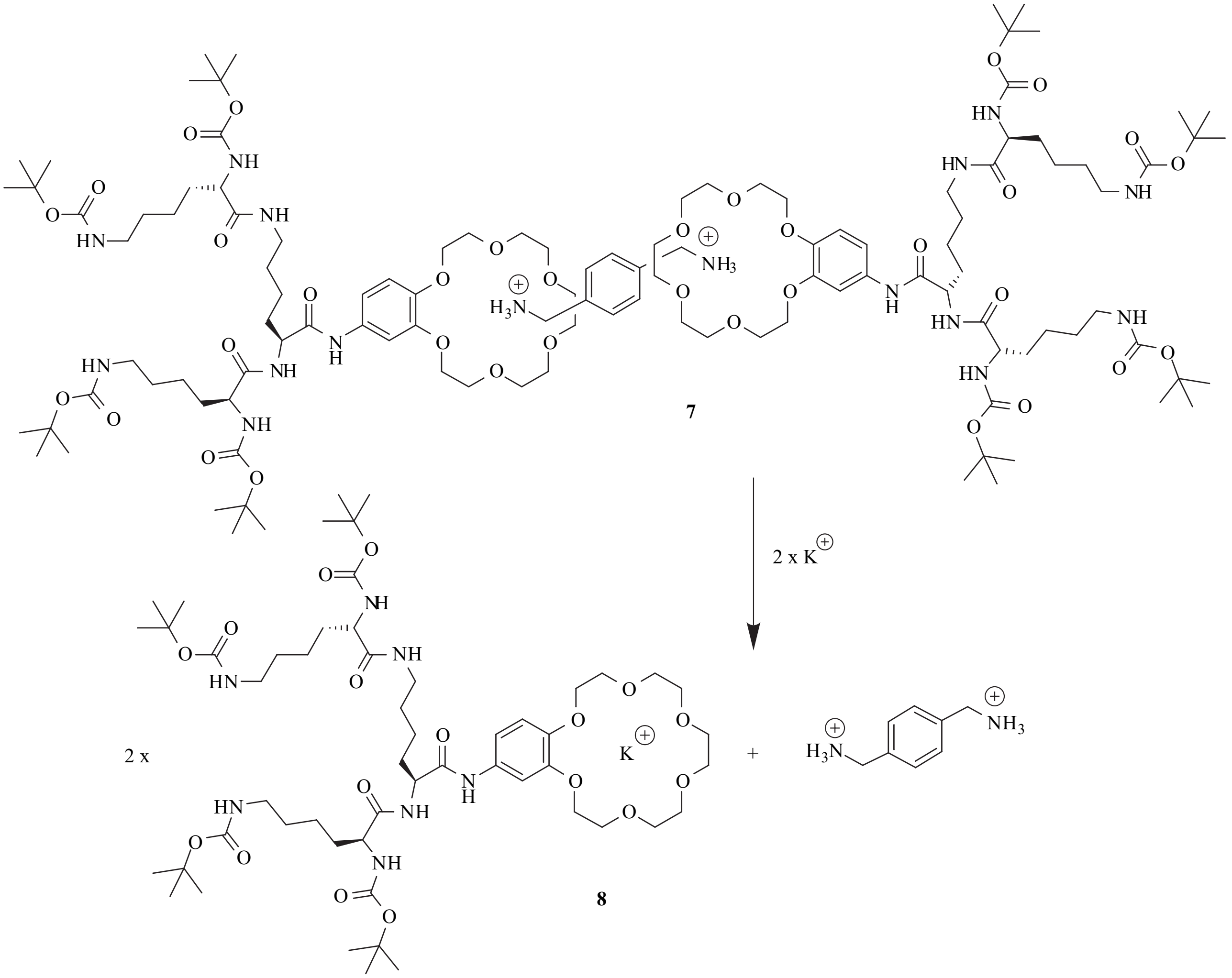
Scheme 1. Monomolecular imprinting approach described by Zimmerman and co-workers [51]; i) poly(aromatic ether) dendritic template **5**, ii) imprinted cavity containing four complementary binding sites **6a**, iii) complexation of a porphyrin guest molecule within the imprinted dendritic host molecule **6b**.

The controlled release of the dendritic molecule was component of the assembly **8** and was achieved by addition of potassium ions to the array (Scheme **2**).

This supramolecular assembly was the first example of the ability to achieve controlled assembly and disassembly of a supramolecular dendrimer in solution, which utilises the focal point of the dendrons as a core molecule.

3. DENDRIMERS AND SELF-ASSEMBLY PROCESSES

Self-assembly applies to reaction pathways in which the final product is produced directly and spontaneously when the correct components are mixed under the appropriate conditions. The pathway must be reversible and the resultant product represents the thermodynamic minimum at equilibrium [59]. The supramolecular chemistry of dendrimers involves selective binding of one or more dendritic species, small molecules, biopolymers and in particular proteins and nucleic acids [60]. In the case of dendrimers, the term *self-assembly* has been used in a very broad sense to include systems that self-organise such as liquid crystalline materials [60]. The concept of self-assembly and dendrimers leads to unique layered architectures, which may require reorganisation of the



Scheme 2. Controlled release of an encapsulated dendritic molecule described by Smith and co-workers [56, 57]; i) dendritic branches are assembled around a *bis*-ammonium cation **7**, ii) release of the dendritic molecule by the addition of K^+ ions **8**.

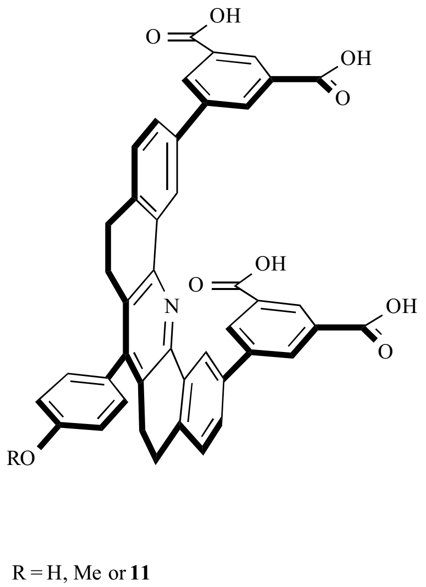
dendrimers' shape or volume and the creation of external and internal microenvironments as these interesting polymeric moieties form defined multimolecular assemblies [61].

3.1. Self-Assembly of Dendrimers Mediated by Hydrogen-Bonding

One of the most important non-covalent interactions in both natural and unnatural systems is hydrogen bonding [10]. Dendrimers have been shown to self-assemble successfully *via* hydrogen bonding interactions – for example, Zimmerman *et al.* reported a self-assembling dendrimer system in 1996 [62]. In this seminal paper, Zimmerman described the self-assembly of a model tetraacid system that featured two isophthalic acid units held in a *syn*-orientation by a rigid 2, 12-dibromo-7-(4-methoxy-phenyl)-5, 6, 8, 9-tetrahydro-dibenzo[*c*, *h*]acridine spacer **9**, which aggregated in either cyclic hexamers **10** or in linear zigzag polymeric aggregates (Fig. **6**). Aromatic polyether dendrons featuring *tert*-butyl groups on the peripheral surface to enhance the dendrons' solubility characteristics were coupled to the hydroxyl functionality of the tetraacid spacer unit. The aggregation properties were studied by ^{1}H NMR spectroscopy, which revealed that the dendritic tetraacids **11** existed as discrete units in polar solvents, and the self-assembly behaviour was assessed using a combination of SEC, laser light scattering and vapour pressure osmometry analyses. The molecular weight data obtained revealed that the dendritic tetraacids assembled into the desired hexameric cyclic arrays (Fig. **7**) [62, 63]. Further analytical studies carried out on the assemblies using small-angle neutron scattering (SANS) [64] also confirmed that the desired cyclic hexameric arrays of the dendritic tetraacids were formed.

In recent times, Zimmerman and co-workers have expanded this work further by incorporating dendrimers that feature heterocyclic 7-amino-3-carbethoxy-1, 8-naphthyridin-2(1*H*)-one units containing complementary donor-donor-acceptor (DDA) and acceptor-acceptor-donor (AAD) hydrogen bonding units maintained at an angle at 60 ° in order to facilitate self-assembly of hexameric arrays [65, 66]. A combination of ^{1}H NMR spectroscopic, SEC and dynamic light scattering (DLC) analyses has shown that these new dendritic systems self-assemble in a cooperative fashion to yield stable hexameric aggregates in apolar organic solvents.

Stoddart and co-workers have created a self-assembled dendrimer system [67] using a technique referred to as *slippage* [68]. This process entailed the introduction of dendrons into a previously interlocked molecular compound



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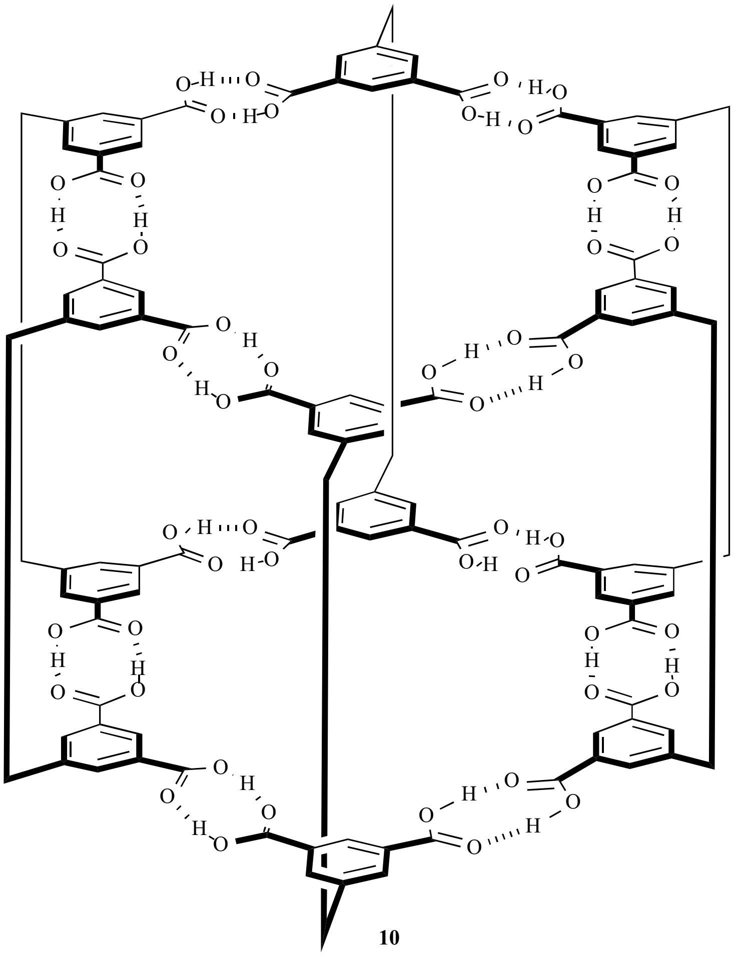

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Fig. (6). The self-assembly of tetraacids by hydrogen bonding described by Zimmerman and co-workers [62]; i) tetraacid unit **9**, ii) cyclic hexamer formation **10**.

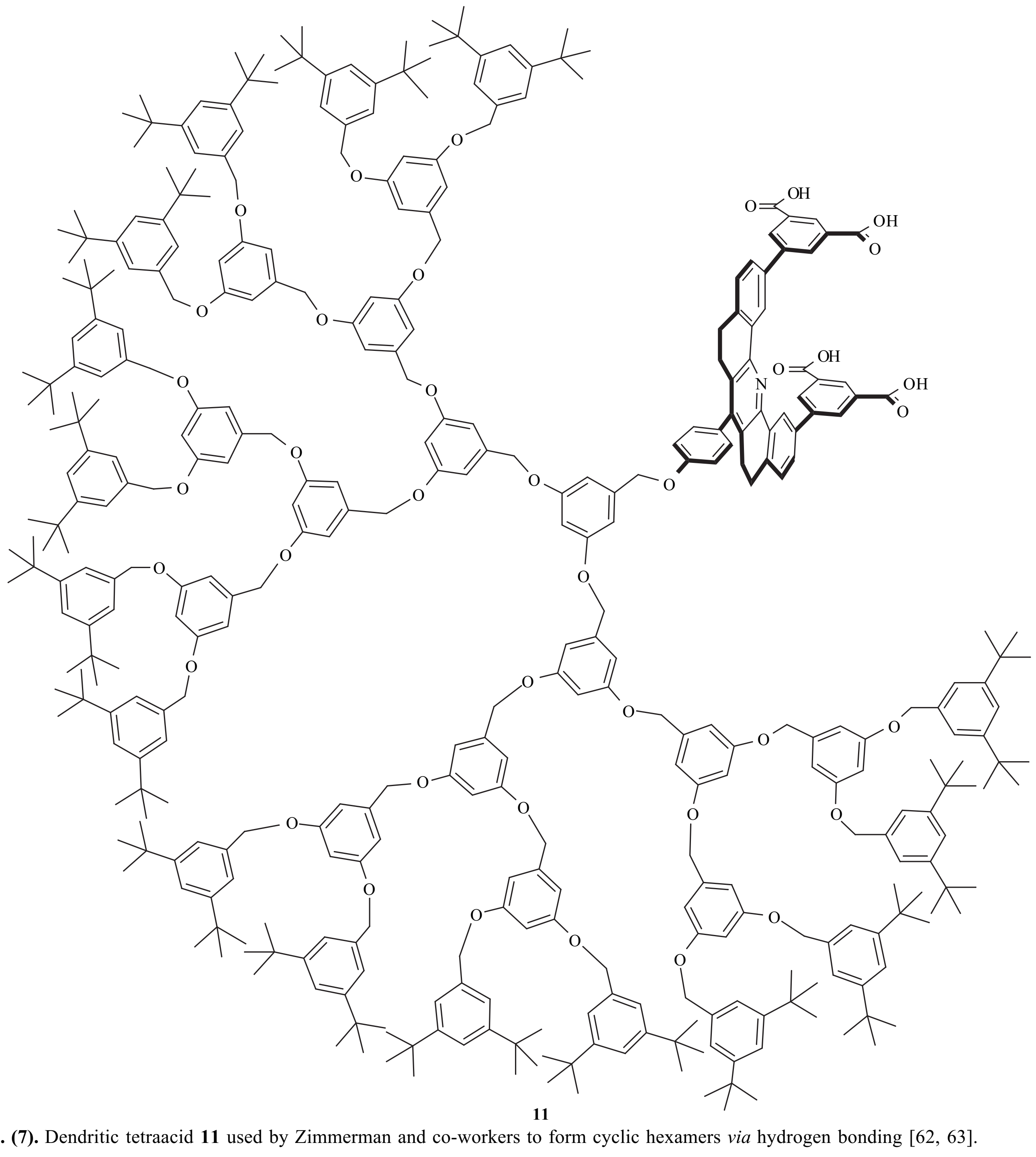
using Wittig chemistries. The slippage methodology provides a bridge between the kinetically stable interlocked compounds and the kinetically labile supramolecular assemblies. Prior studies by the Stoddart research group on novel self-assembly mechanisms had established that secondary dialkylammonium ions, ($(RCH_2)NH_2^+$, where R is a cyclohexyl group) will form a kinetically stable complex [2]-rotaxanes when the dialkylammonium salt and dibenzo-[24]-crown-8 (DB-24-C-8) **12** are combined in CH_2Cl_2 [58]. Utilising this methodology, an aromatic polyether dendrimer featuring a DB-24-C-8 core unit was able to assemble *via* a slippage process with an aromatic polyether dendron **13** that featured an ammonium focal point unit with a cyclohexyl moiety to afford a stable [2]-rotaxane (see **14** in Scheme **3**). Aromatic polyether dendrons were selected in this study as it was predicted that these branched units would be soluble in CH_2Cl_2 and that the phenolic ether functionalities would not interfere with the [N^+–H•••O] hydrogen bonds and the [C–H•••O] interactions that constitute a significant proportion of the non-covalent bonding in the recognition motif. This study has shown that mechanically interlocked dendrimers can be self-assembled under thermodynamic control by utilising the slippage protocol. This methodology could lead ultimately to the development of mechanically linked dendrons that are able to trap guest molecules and then be dissociated in a controlled manner, i.e. for the slow release of drugs in patients.

3.2. Self-Assembly of Dendrimers Mediated by Metal Complexation Phenomena

Astruc and co-workers have synthesised [69] a series of tri- and nonoferrocenyl thiol dendrons **15** and used them to assemble dendronised gold nanoparticles *via* a Brust-type direct synthesis from a 1:1 mixture of dodecanethiol and the dendronised thiol consisting of AB_9 units (see **16** in Scheme **4**). The gold nanoparticles are surrounded by up to 180 silylferrocenyl units and these assemblies resemble closely large metallodendrimers in which the core is a gold nanoparticle.

These dendronised colloids represented a new type of dendrimers that contained a gold colloidal core and have been used as sensors for selective recognition of $H_2PO_4^-$ anions and adenosine-5'-triphosphate (ATP^{2-}) with a positive dendritic effect. Indeed, selective CV analysis of these anions has proved possible in the presence of other anions such as Cl^- and HSO_4^-. These dendronised colloids have been used to form robust modified electrodes, where the robustness was found to be dependent upon the size of the dendrimer, i.e. the larger the dendron the more robust the electrode. These silylferrocenyl systems are advantageous with respect to amidoferrocenyl systems designed previously [21] as the oxidation process was fully reversible.

In 1999, Abruña and co-workers reported the formation of ordered arrays generated *via* metal-initiated self-assembly

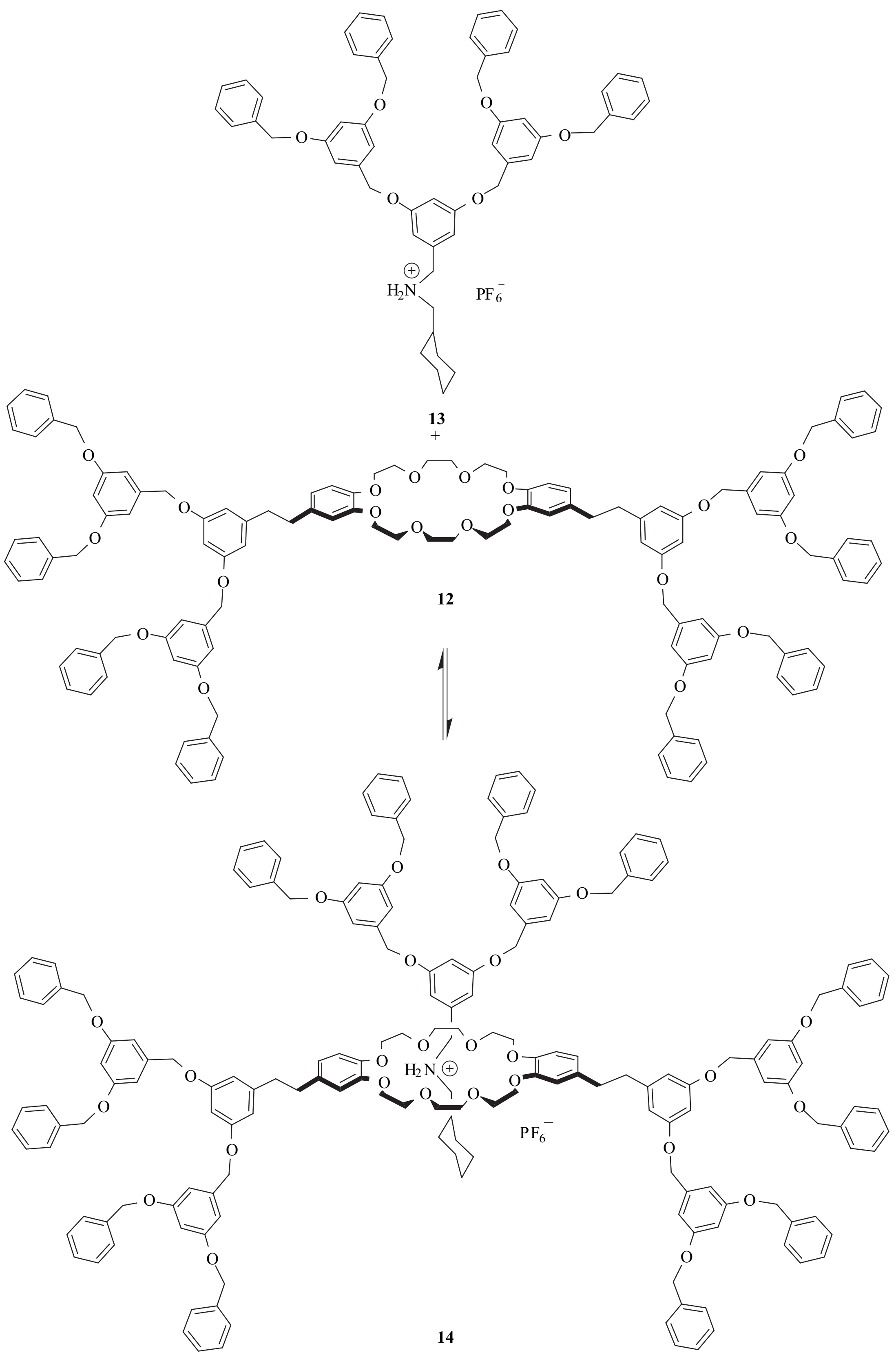


11

Fig. (7). Dendritic tetraacid **11** used by Zimmerman and co-workers to form cyclic hexamers *via* hydrogen bonding [62, 63].

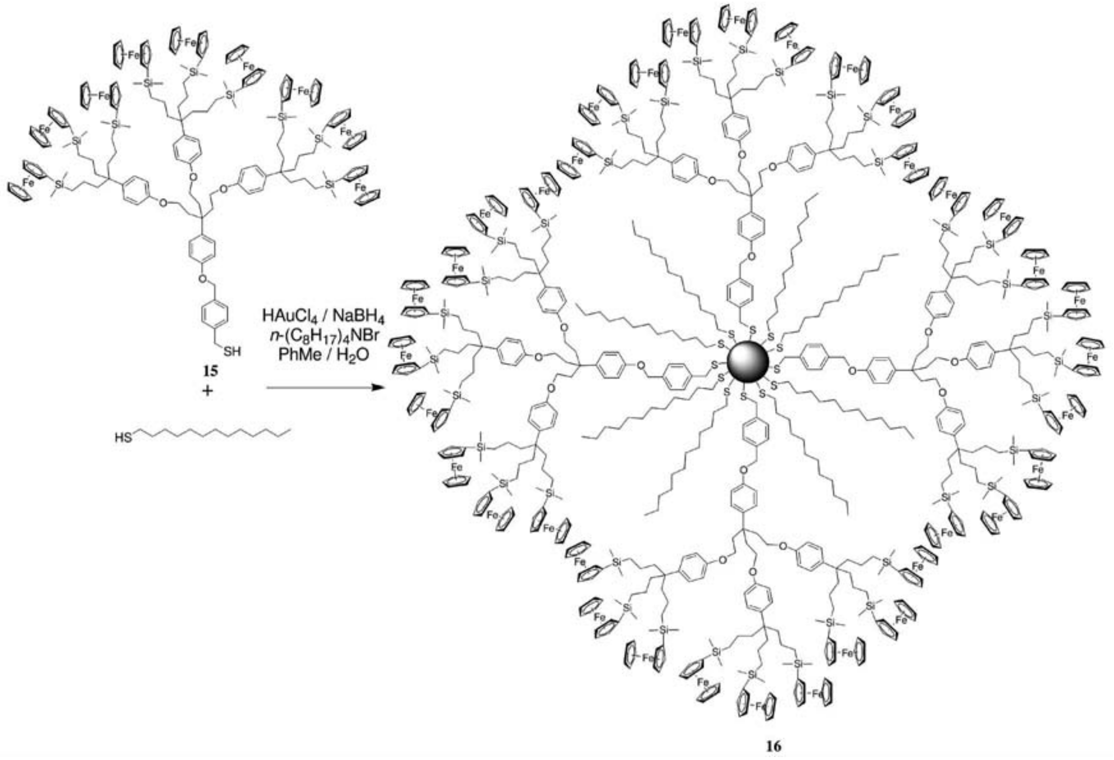
of terpyridine containing dendrimers and bridging ligands [70]. The aliphatic polyamido dendrimers featured 2, 2':6', 2''-terpyridine (tpy) groups on the peripheral surface and were used in the study of the interfacial reaction with the bridging ligand 1, 4-*bis*[4, 4''-*bis*(1, 1-dimethylethyl)-2, 2':6', 2''-terpyridine-4'-yl]benzene (BBDTB) in the presence of aqueous Fe^{2+} or Co^{2+} ions. The molecular recognition between the terpyridine functionalised dendrimers and the bridging ligand with the metal cations enabled the formation of films on highly orientated graphite surfaces. Molecularly resolved scanning tunnelling microscopy (STM) was used to reveal that the films formed highly ordered two-dimensional hexagonal arrays, which were composed of one-dimensional polymeric strands with a repeat unit of $(\text{tpy-dendrimer-tpy-M})_x$ in the case of the dendrimers, or $(\text{tpy-BBDTB-tpy-M})_x$ in the case of the bridging ligand, where M = Fe^{2+} or Co^{2+}. It was observed that in the case of the films derived from the terpyridine pendent dendrimers the ordering was dependent upon the dendrimer generation used and that in all cases the films were electrochemically active and exhibited a reversible electrochemical wave at characteristic potentials that corresponds to the different $[M(tpy)_2]^{2+}$ complexes.

Godínez *et al*. have studied recently the aggregation behaviour of PAMAM dendrimers on the surface of thiol modified gold electrodes [71]. The aggregation of two PAMAM dendrimer molecules was studied on the surface of



Scheme 3. Self-assembly of dendrimer systems **14** by slippage reported by Stoddart and co-workers [67].

both clean and thiol modified gold electrodes from aqueous solution. It was observed that the aggregation behaviour of the dendrimer molecules on the surface of clean gold substrates never attained a surface coverage greater than 9 x 10^{-12} mol/cm^2, whereas the thiol modified gold electrodes exhibited coverage values almost twice as large at a pH of 7. The dendrimer aggregation process was found to be pH dependent and also surface modification dependent. Detailed



Scheme 4. Formation of self-assembled dendronised gold nanoparticles **16** reported by Astruc and co-workers using nonoferrocenyl thiol dendrons **15** [69].

computational analysis of the titration curves obtained using Langmuir and Frumkin isotherm models suggested that the major effect occurring on the thiol modified surface was not an increased overall adsorption energy but a favourable lateral interaction between adjacent adsorbed dendrimer molecules.

3.3. Self-Assembly of Dendrimers into Mono- and Multi-Layers

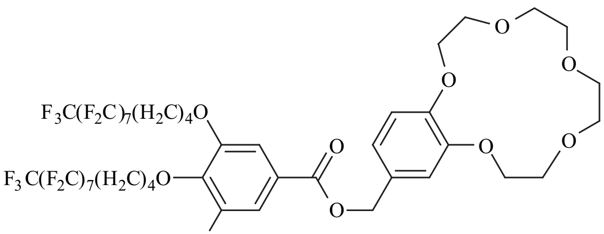
Zhang and co-workers have studied the formation of self-assembled mono-layers of surface bound dendrons [72]. A series of both symmetric and asymmetric poly(aromatic ether) dendrons with thiol functionalities at the focal points were synthesised and the surface of the symmetrical dendrons featured either heptane (hydrophobic) or oligo(ethylene oxide) (hydrophilic) chains, or a combination of the two in order to generate dendrons possessing varying degrees of hydrophobicity characteristics. The dendrons were used to form self-assembled monolayers on a gold surface that were then analysed using STM. In the case of the symmetrical dendrons with aromatic rings on the periphery, a highly ordered striped pattern was observed - the stripes were approximately 3.1 ± 0.3 nm in width. The long-range order was ascribed to the chemisorption between the thiol group and the gold surface and aromatic π-π stacking interactions between the benzene rings of the dendrons. When an asymmetrical dendritic element was introduced into the symmetrical dendritic monolayer, random pore structures were observed that were attributed to the formation of defects as a consequence of the asymmetrical nature of the dendrons. For comparison, the symmetrical dendrons possessing hydrophobic heptane peripheries displayed linear striped patterns with the width of the stripes being approximately 4.0 ± 0.5 nm in a fashion similar to those observed when the symmetrical dendrons. This effect was ascribed to the hydrophobic interactions between the peripheral heptane chains and the chemisorption between the aromatic π-π stacking units thus contributing to the expansion of the stripe width and to some extent the long-range order of the stripes. The dendrons possessing complete hydrophilic peripheries exhibited a homogeneous pattern, which was accounted to the conformation of the ethylene oxide chains weakening the interaction between the aromatic rings. It was also noted that the hydrogen bonding between the oxygen atoms of the ethylene oxide and the water molecules present led to a more densely packed structure. The dendrons that possessed a mixture of hydrophobic and hydrophilic functionalities at the periphery led to the formation of extended honeycomb structures. The formation of structures of this type was attributed to the local aggregation behaviour of the hydrophobic and hydrophilic peripheries based upon a ‘like attracts like’ principle. It was concluded that in the case of the unfunctionalised dendrons, it was the symmetrical structure that played an important role in the formation of the observed striped patterns – for the hydrophobic and hydrophilic dendrons, the aromatic π-π stacking and chemisorption associations were quite similar and therefore, it was the peripheral substituents that contributes to the variation of the surface morphologies observed.

In an alternative approach, van Veggel, Reinhoudt and co-workers [73], devised a system to perform non-covalent chemistries on surface confined, isolated dendrimers. The approach involved the insertion of aromatic polyether dendrons that featured peripheral pyridine functionalities and a dialkylsulfide chain at the focal point into self-assembled mono-layers of decanethiol on a gold surface in order to spatially isolate the branched species. The peripheral dendritic pyridine moieties of the resultant monolayer were reacted with a solution of dendrons that featured SCS Pd (II) pincer moieties at the focal points. The isolated surface-confined dendrimers exhibited an average height of 3.3 nm as determined by atomic force microscopy (AFM) and upon Pd^{2+} – pyridine coordination, an increase in the size in the individually resolved molecules to an average height of 3.1 – 7.5 nm was observed. The diversity of the dimensions of the assembled dendritic species implied that not all of the dendritic adsorbates had been exhaustively coordinated to the four dendrons possible. This methodology allowed the creation of surface-confined architectures and potentially provides a viable complement to 'top-down' methods in nanofabrication.

The literature is replete with examples of the use of dendrimers in the self-assembly of mono- and multi-layer arrays – the reader is directed to an excellent review article published recently by Fréchet and Tully [74] that provides a detailed background to this area.

3.4. Dendrimers and Self-Assembly into Liquid Crystalline Phases

Initial research in the area of the self-assembly of dendrons or dendrimers into liquid crystals has been carried out by Percec *et al.* [75]. This study involved the synthesis of an array of tapered monodendrons containing crown ethers (see **17** in Fig. **8**).

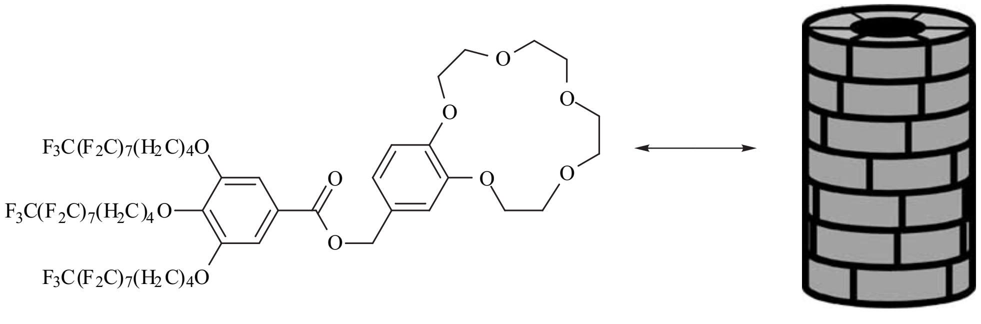


17

Fig. (8). Tapered monodendrons, featuring crown ether moieties **17** reported by Percec and co-workers [75].

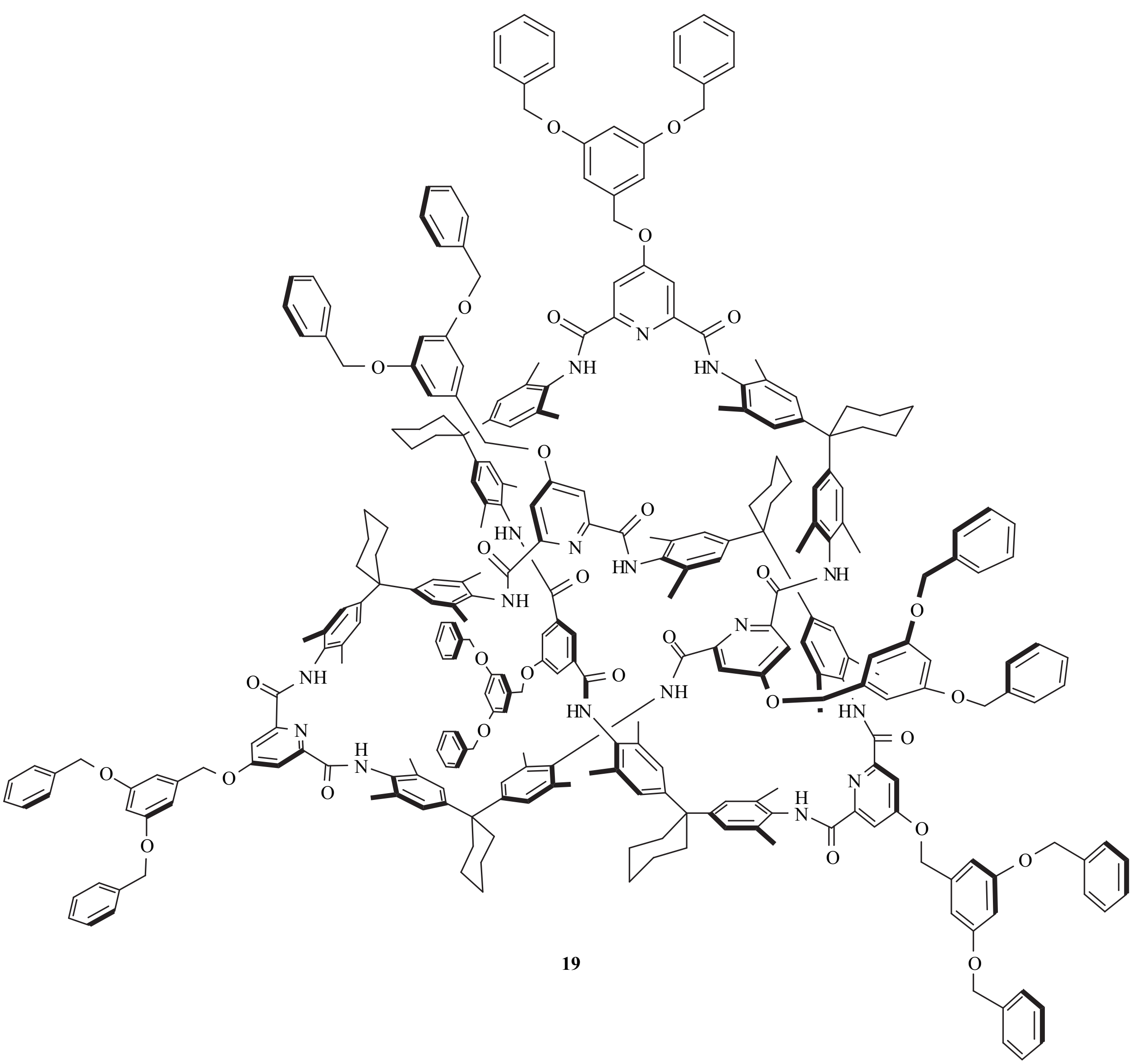
These tapered monodendrons were allowed to self-assemble *via* the complexation with metal cations (Li, Na and K trifluoromethanesulfonates) within the appended crown ether moieties to afford cylindrical or rod-like supramolecular dendrimer arrays (see **18** in Scheme **5**). The assembly process was in part attributed to fluorophobic effects as a consequence of the appended semi-fluorinated dodecyl groups at the dendritic periphery. This result was unusual as previous studies upon related systems relied upon hydrogen bonding and ion-mediated assemblies *via* attachment to a polymer backbone.

The rod-like supermolecules thus formed in turn assembled into thermotropic hexagonal columnar liquid crystalline phases, which aligned homeotropically, i.e. on untreated glass slides the molecule forms a single crystal with the columns orientated with their long axes perpendicular to the glass surface. Percec and co-workers have studied subsequently the formation of self-assembled liquid crystals by using constitutional isomers of AB_2 based monodendrons constructed of either 3, 4, 5-trisubstituted benzyl ether monodendrons [76a] or 3, 4- or 3, 5-disubstituted benzyl ether monodendrons [76b] with dodecan-1-yloxy units located at the peripheral surface. In the case of the disubstituted series of dendrons, the 3, 4-series assembled to yield three-dimensional cubic lattices with a cone-like shape, whereas the 3, 5-substituted series generated two-dimensional hexagonal column lattices that resembled disks. The trisubstituted series the monodendrons also assembled to afford a cubic lattice in a manner similar to the 3, 4-substituted monodendron derivatives. The difference between the 3, 4-disubstituted and the 3, 4, 5-trisubstituted monodendrons was that the trisubstituted series contained fewer monodendrons in its self-assembled state. In all of the three monodendrons series, the structure of the internal repeat unit determined the shape of the monodendron and also the resultant supramolecular dendrimer constructed. Percec and co-workers have extended recently research on the trisubstituted benzyl ether monodendron systems to create monodendrons employing a gallic acid building block [77]. These monodendrons possessed three dodecyl groups attached *via* ether linkages and were allowed to self-organise *via* a host-guest approach. The monodendrons were used as the hosts, and the guest system employed was methyl-3, 5-dihydroxybenzoate. It was observed that liquid crystallinity was induced in the host molecules if the volume of the alkyl tails was increased. Liquid crystallinity was not observed in the case of the monodendron host system on account of strong



17 **18**

Scheme 5. The self-assembly of tapered monodendrons **17** into cylindrical **18** supramolecular dendrimers as described by Percec and co-workers [75].



19

Fig. (9). Tri-dendroknot **19** synthesised by Vögtle and co-workers [82].

aromatic π-π interactions between the head groups of the host dendrons. When the host monodendron was extended to form the corresponding second generation monodendron, the strong π-π interactions were no longer possible and liquid crystals were observed with a thermotropic cubic phase. The cavities of the host molecules in the core were able to complex the small guest molecules thereby affording an insight into the possibility of using these systems as supramacromolecular dendrimer systems as nanoreactors.

Meijer and co-workers [78] studied the liquid crystalline properties of PPI dendrimers that featured peripheral cyanobiphenyl mesogens. Three different generations of mesogenic dendrimer were synthesised with either 4, 16 or 64 available end groups. It was revealed by a combination of differential scanning calorimetry, polarisation spectroscopy and X-ray scattering analyses that all of the dendrimers exhibited smectic A mesophases. The PPI dendrimers orientated themselves into an anti-parallel arrangement which afforded an interdigitated bilayer. This study showed that PPI dendrimers are able to undergo significant conformational changes in the presence of external stimuli (i.e. end group functionalisation) and also the flexibility of the functionalised PPI dendrimers was significantly higher than that had been observed in previous studies.

3.5. Amphiphilic Dendrimers from Self-Assembly Processes

The use of amphiphilic dendrimers as building blocks for supramolecular assemblies has been studied by Meijer and co-workers using PPI dendrimer derivatives [79]. The PPI dendritic backbones were modified with long hydrophobic chains at the peripheral surface to achieve the desired hydrophilic PPI core and hydrophobic hydrocarbon outer shell. The aggregation behaviour of these dendritic amphiphiles was studied at the air-water interface utilising Langmuir experiments. It was observed that the molecules arranged themselves into layers in which the hydrophilic PPI dendrimer component of the molecule was in contact with the water subphase and the hydrophobic alkyl chains were aligned away from the water towards the air, thereby forming a parallel packed hydrophobic layer. The organisation of the amphiphilic PPI dendrimers was also assessed in acidic media. Under these experimental conditions, the dendrimers formed smaller spherical aggregates as a consequence of protonation of the PPI amine groups, therefore resulting in an extended conformation in which the dendritic interior and the peripheral hydrophobic tails compress to afford densely packed layers where all the alkyl chains orientate themselves parallel to each other. It was assumed that the amphiphilic dendrimers within the aggregates form the same cylindrical shape as that observed at the air-water interface. Meijer *et al.* have also utilised these amphiphilic dendrimers to template the formation of the different phases of calcium carbonate [80]. The amphiphilic dendrimers were mixed with various single chain surfactants to form stable aggregates that had tuneable surface chemistries. The use of amine-based surfactants led to the generation of different metastable phases of calcium carbonate, whereas when sulfate derived

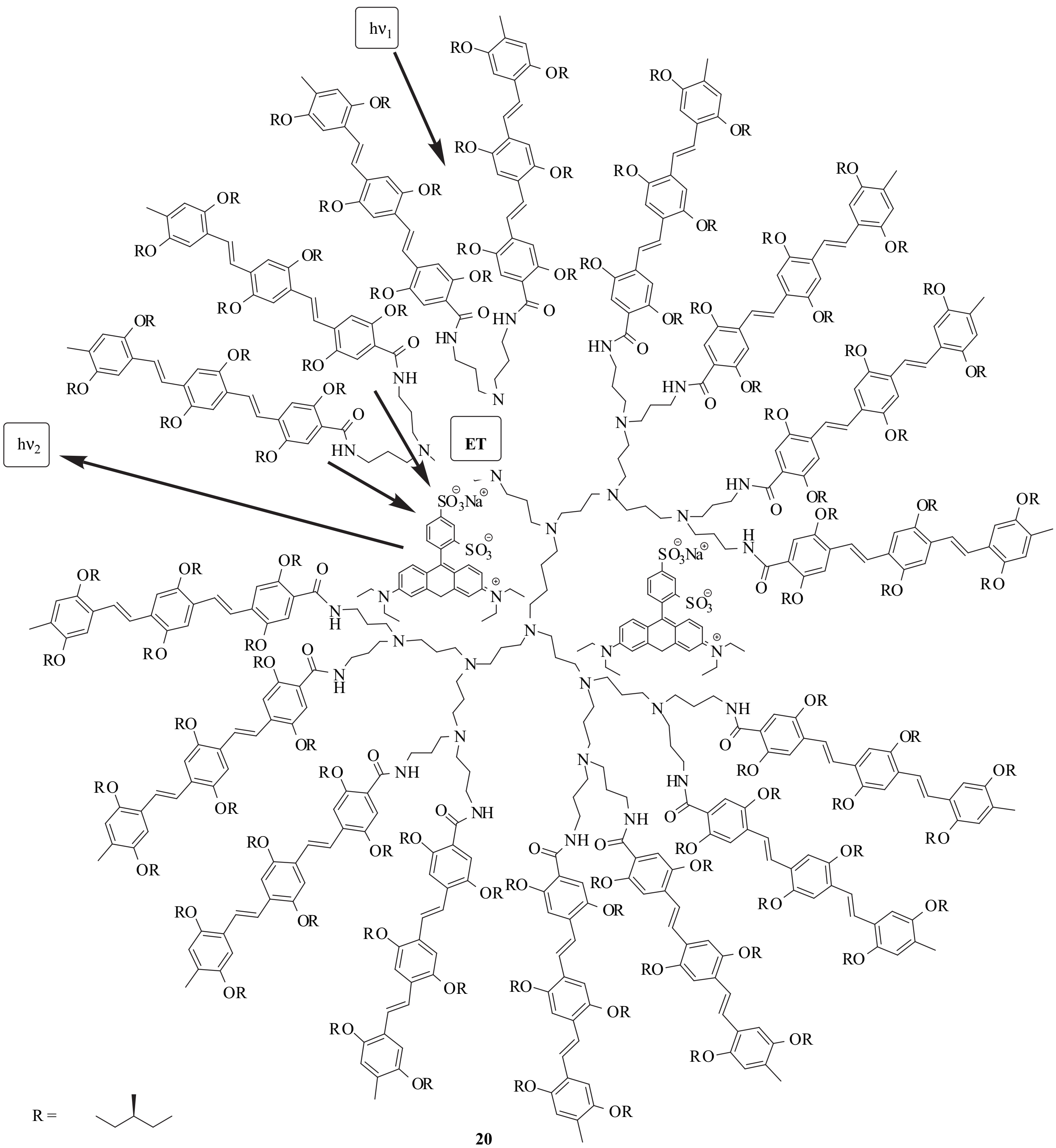


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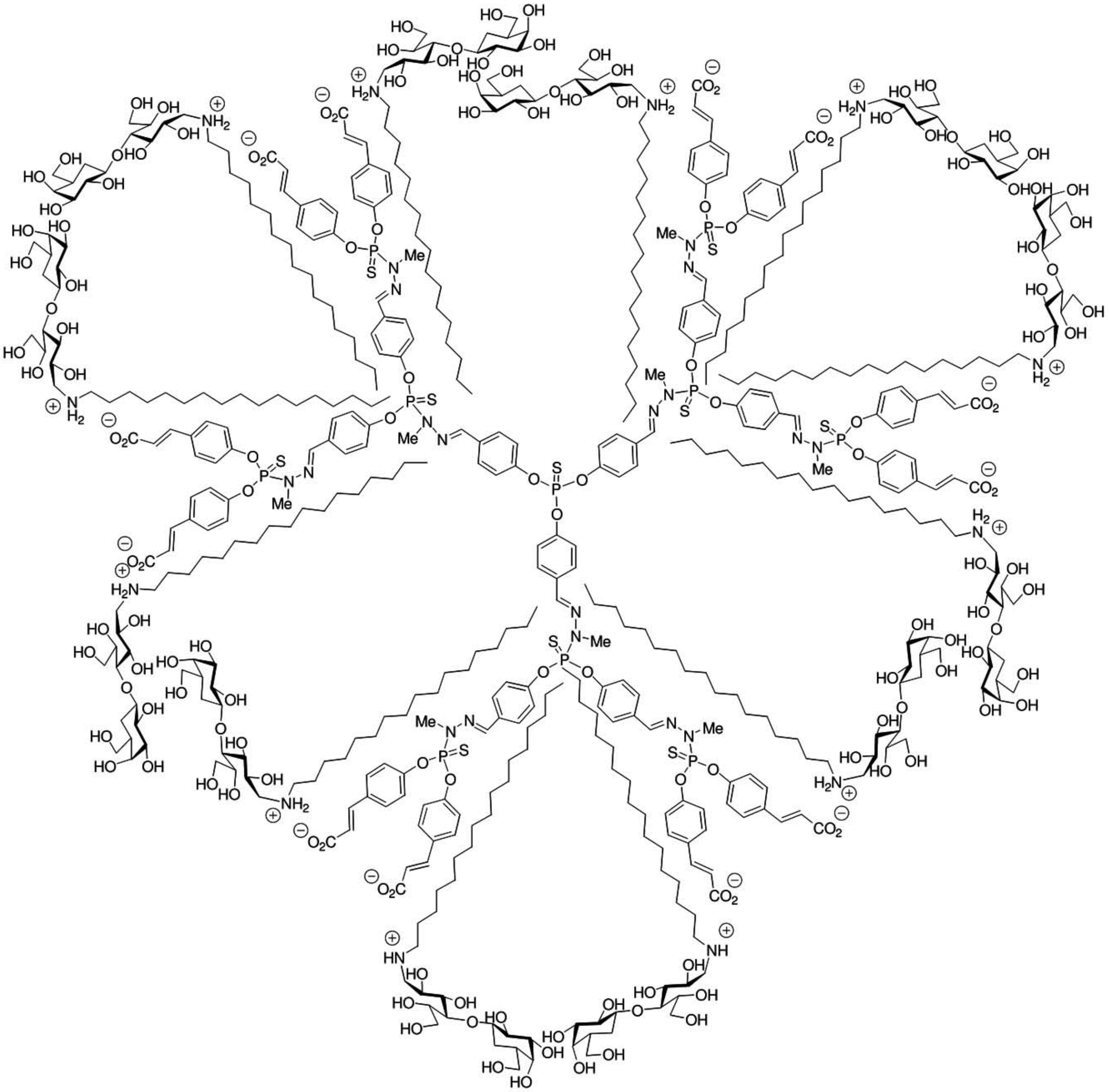
Fig. (10). PPI dendrimer featuring OPV units on the peripheral surface **20** designed by Meijer and co-workers to encapsulate Sulforhodamine B [83].

surfactants were used, retardation of calcium carbonate growth was observed as a consequence of the strong interaction of the sulfate and calcium ions. The blending of amorphous and crystalline phases has been demonstrated to enhance significantly the toughness of materials, which could lead to the generation of new dendrimer composites with improved material properties.

In an alternative approach, Imae *et al.* have utilised amphiphilic PAMAM dendrimers to form organised adsorption films [81]. The PAMAM dendrimers were designed to behave as amphiphilic surface-block dendrimers and therefore half of the dendrimer surface was functionalised with hydroxyl functionalities, whereas the other half of the dendrimer was coated with *n*-hexyl chains. The surface block dendrimers were adsorbed onto mica substrates and the surface was examined by AFM. It was observed that the adsorption surface of a PAMAM dendrimer in its hydrochloride salt form was relatively flat and no particular ordering of the dendrimers was apparent; however, in the case of the amphiphilic dendrimers, adsorption layers were formed. The layers were formed in bilayers by the hydrophilic tails of the dendrimer interacting with the mica surface, and the hydrophobic tails were exposed to enable interaction of the hydrophobic tails with another dendrimer, thereby leaving the hydrophilic tails oriented towards the solution in preparation for the addition of the next bilayer. It was also observed that the amount of adsorption was greatest



21

Fig. (11). Phosphorous dendrimer bearing galβ1cer analogues **21** described by Majoral and co-workers [84].

in the case of the third generation dendrimer system and exceeded the adsorption of the fourth generation, which can be rationalised by the increased number of hydroxyl groups on the fourth generation, and which therefore increases the extent of hydrogen bonding amphiphilic dendrimers.

3.6. Miscellaneous Self-Assembly Dendrimer Systems

Vögtle *et al.* have synthesised successfully a complex dendronised molecular knot using assembly directed by amide groups [82]. The synthesis involved the cyclisation of aromatic polyether dendrons that featured pyridine-2, 6-dicarbonyl dichlorides at the focal point with an 'extended diamine' to yield directly in a one-step process the 'tri-dendroknots' (see **19** in Fig. **9**). The synthesis of the dendroknots was achieved successfully by supramolecular template reactions that were assisted by hydrogen bonds between the host and guest amide groups. This synthesis was an improvement on existing knot syntheses as no external templating agent was required and the knot precursors reacted using an 'internal templating' process. From detailed X-ray crystallographic analysis, it was elucidated that the progression of assembly proceeds initially with the formation of a helical loop followed by threading of the guest amide molecules through the loop. The remaining two chloride functionalities then react subsequently with the terminal amino groups to 'seal' the knot. This molecular knot is an excellent example of a pre-organisation mechanism, and serves to provide an understanding of the threading mechanism in hydrogen bond assisted supramolecular template syntheses. It is envisaged that molecular knots of this type could be utilised as anchoring groups to accommodate additional functionalities that would increase solubility or facilitate crystallisation or even the carriage of chromophoric or light harvesting groups for a wide variety of applications.

In 2000, Meijer *et al.* [83] reported the use of supramolecular assemblies of oligo(*p*-phenylene vinylene)s (OPV's) terminated PPI dendrimers as energy transfer devices. The PPI dendrimers are surface modified with π-conjugated OPV's to afford macromolecules that were able to self-assemble at the air-water interface forming stable layers, which in turn exhibited the ability to encapsulate dye molecules, such as sulforhodamine B. The host-guest complexes formed between the dendrimers and the dye molecules enable energy transfer from the OPV units to the dye molecules (see **20** in Fig. **10**). Energy transfer occurred as there was an overlap of the emission spectrum of the OPV dendrimer and the adsorption spectrum of the encapsulated dye. When the OPV units of the PPI-based dendrimer were excited at a wavelength of 420 nm, the fluorescence (λ_{em} = 492 nm) was quenched and the emission of the sulforhodamine B dye ($\lambda_{em,\ max}$ = 593 nm) was observed thereby indicating that energy transfer from the OPV trimers to the complexed dye molecules had been facilitated. These systems are not ordered *via* intramolecular hydrogen bonds between the amide linkages and were able to extract dye molecules efficiently from aqueous phases into non-polar solvents. Furthermore, these supramolecular systems were able to compatiblise ionic dyes with organic semi-conducting polymers and energy transfer was observed from the organic polymer to the dye molecules.

Phosphorous containing dendrimers bearing galactosylceramide (gal$\beta_1$cer) analogues have been synthesised by Majoral *et al.* [84] and the self-assembly properties of these hybrid dendrimers investigated. The dendrimers synthesised were monodisperse cationic hyperbranched architectures that bear amphiphilic gal$\beta_1$cer analogues on the periphery (see **21** in Fig. **11**). These phosphorous containing dendrimers self-assemble *via* electrostatic interactions in between the acidic terminal groups of the dendritic branches and the aminolactitol group in water at room temperature in a strict stoichiometric ratio. The amphiphilic behaviour of the self-assembled structures was determined by ^{1}H NMR spectroscopy and confirmed further by dynamic light scattering studies, which showed that aggregates formations was spontaneous. The cationic dendrimers arrange themselves in the form of a bilayer, as the stability of cationic surfactants was dependent on the hydrophobic effects between the alkyl chains. In this example, the dendritic skeleton allows inter-dendrimer chain interactions and therefore vesicles were formed. Hydrogen bonding within the dendritic framework enhanced the assembly of the sugar moieties and therefore contributes to the overall stabilisation of the supramolecular assemblies that are formed. Current investigations are underway to test these cationic dendrimers as a possible therapeutic agents in anti-HIV therapies.

CONCLUSIONS

It is apparent from this review that the recent developments in the use of dendritic architectures in self-assembly processes has led to the discovery of a wide range of fascinating macromolecular assemblies that would have proved virtually impossible to create *via* 'traditional' synthetic techniques. The key step in the development of this field is however, the translation of these unique stable dendritic assemblies into functional materials. Significant progress in this direction has been made (as evident by notable examples highlighted in this review), but the application of these fascinating supramolecular architectures still represents a major challenge to synthetic chemists and polymer scientists alike.

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