Controlled functional group presentations in dendrimers as a tool to probe the hyperbranched architecture†

Ashootosh V. Ambade, Yangbin Chen and S. Thayumanavan‡

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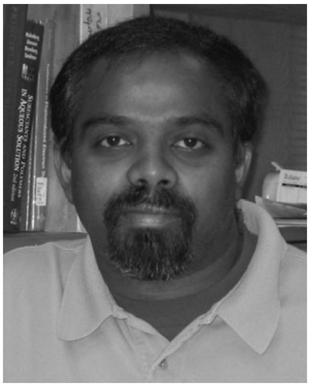
The layer-by-layer incorporation of monomers in the synthesis of dendrimers allows for variations in the functionalities between one layer and the next. However, incorporation of different functionalities in combination with the above would lead to the introduction of sequences in dendrimers. We review the three complementary synthetic methods we have developed for sequencing the dendrimers. We also illustrate the utility of these methodologies in identifying certain fundamental properties of dendrimers. More specifically, we have probed the intermediate layers of the dendrimers by incorporation of spectroscopic probes in precise locations within dendrimers. Similarly, we have utilized this method to identify the true architectural advantages of dendrimers as light harvesters in solar energy applications.

1 Introduction

Exquisite control over shape, size, and functional group presentations are all hallmarks of the most ubiquitous biopolymers in nature, proteins. These molecules utilize these features to fine-tune the properties so as to be very specific in molecular recognition and function. Considering the versatility of proteins in biological function, it is interesting to build artificial mimics of these molecules. Although bioinspired molecular design has been an area of interest for chemists for a long time, these mimics have been mostly focused on building small molecule analogs.[1] It is important to recognize that Nature has chosen macromolecular architectures to build its structural complexity and present its binding sites to various small molecule ligands and other biomacromolecules. Therefore, it is interesting to be able to build structural mimics for proteins using macromolecules.[2] Dendrimers have attracted great interest as possible protein mimics, because these molecules tend to adapt globular conformations at high molecular weights (possible analogs for globular proteins); these molecules can be built with very good precision in molecular weights; and the functionality at the core can be encapsulated by the dendrimer backbone and thus isolating it from the environment.[3] Although there have been excellent contributions to the field of dendrimer-based biomimetic structures, we will primarily focus on the contributions to this field by our research group with appropriate references to only some of the related work from other research groups. More specifically, we will deal with the strategies for placing functionalities in precise locations within dendrimers and their utility in furthering the fundamental understanding on the branched architecture. Our group has also been involved in biomimetic dendrimers based on amphiphilicity at every

Ashootosh Ambade obtained his MSc in organic chemistry from Fergusson College, University of Pune and joined the Indian Institute of Technology, Bombay, India in 1999 to pursue a PhD degree. He worked under the guidance of Prof. Anil Kumar in the area of dendritic macromolecules and received his PhD in 2004. With growing interest in this field he subsequently joined Prof. Thayumanavan's group at the University of Massachusetts, Amherst as a postdoctoral fellow. His research interests include design of amphiphilic dendrimers and polymers that afford tunable and stimuli-responsive assemblies in aqueous media.



S. Thayumanavan ("Thai") obtained his BSc and MSc degrees from The American College, Madurai, India. He obtained his PhD from the University of Illinois at Urbana-Champaign with Professor Peter Beak. After a postdoctoral stint with Professor Seth Marder at the California Institute of Technology, he started his independent career at Tulane University in 1999. His group moved to the University of Massachusetts Amherst in 2003. His research interests include the design and synthesis of macromolecules (dendrimers and polymers) that are of interest in chemistry, materials, and biology.

Department of Chemistry, University of Massachusetts, Amherst, MA 01003, USA. E-mail: thai@chem.umass.edu

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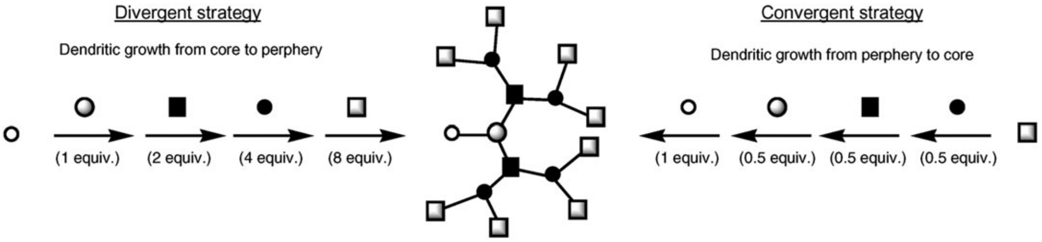
‡ Visiting Professor at the Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India (October–December 2006).



Scheme 1 Divergent and convergent strategies to build dendrimers. Both these strategies allow for variations among the layers.

repeat unit.[4–8] This part of our work is beyond the scope of this review.

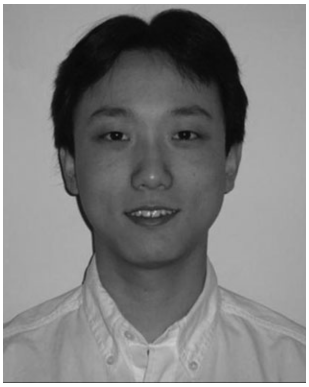
2 Functional group diversity in dendrimers

Synthetic approaches towards dendrimers can be broadly classified into two: divergent strategy[9] and convergent strategy.[10] Dendrimers are built layer-by-layer in both these strategies and therefore one could gain control over functional group placements in one layer with respect to the neighboring layers, as shown in Scheme 1. However, if one has to move dendrimers towards a true structural mimic of biomacromolecules such as proteins, we should be able to differentiate each monomer unit from the other with precision, *i.e.* build sequences within dendrimers. This section will discuss the strategies that we have developed for this purpose.

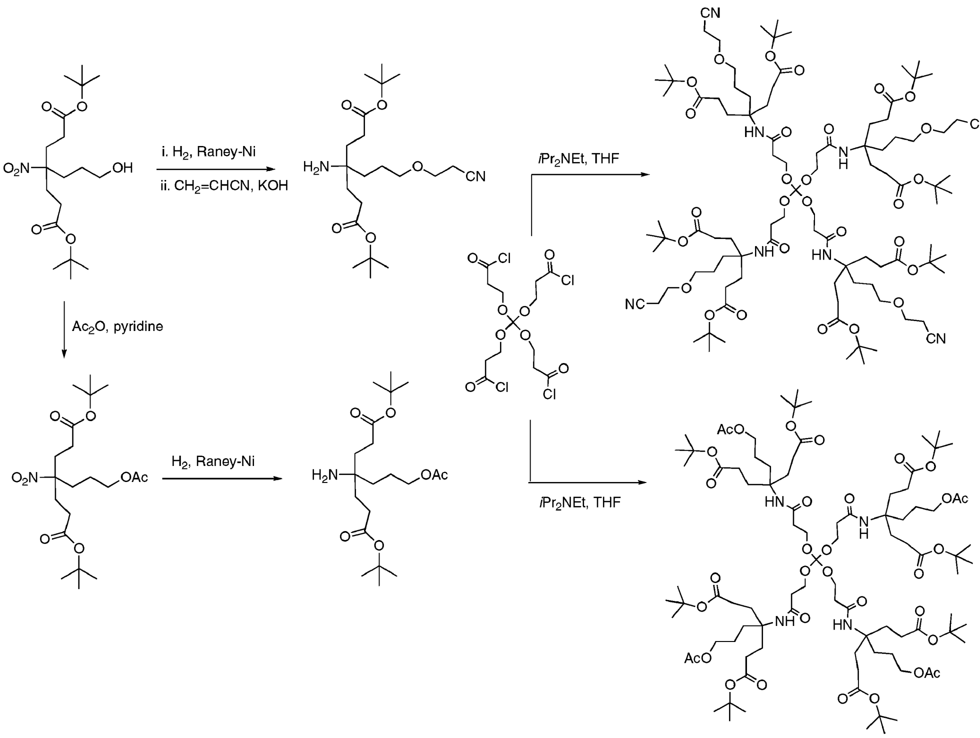
Approach to sequencing dendrimers will work well with a convergent approach, since there is a greater control over the systematic incorporation of the functionalities in higher generation. This is because the number of reactions that is performed with each generation remains the same in the convergent synthesis. However, it should be noted that diversity in the periphery of dendrimers have been brought about using both divergent and convergent strategies. Following divergent approach, the periphery has been functionalized by varied amounts of reactants to obtain a statistical distribution of substituents[11] or by reaction with two different functionalities in stoichiometric amounts so as to afford two functionalities with a predetermined ratio on the periphery.[12] On the other hand, a combination of divergent and convergent strategies has been used to incorporate multifarious peripheral functionalities.[13] In this approach, a dendritic wedge differentially substituted on the periphery—'so-called' 1 → (2 + 1) C-branched monomer—was synthesized and then attached to a core to obtain functional dendrimers as shown in Scheme 2. Similarly, melamine-based dendrimers with only one or two peripheral functionalities were synthesized using convergent approach (Scheme 3). Here, the differential reactivity of trichlorotriazine with aliphatic and aromatic amines at different temperatures was taken advantage of.[14] Benzyl ether dendrimers have also been synthesized with only one nitrile group on the periphery using a convergent approach.[15]

However, the key feature in designing a methodology, where one could vary each monomer from its neighbors using the convergent approach, involves the ability to differentially functionalize the two 'B' moieties in an AB_2 monomer. We show this concept using a cartoon representation in Scheme 4. We have developed three complementary approaches to achieve such differentiation between the two B functionalities: (i) through the stepwise incorporation of two different functional groups to an ABB_p monomer, where one of the B-functionality is protected;[16] (ii) through an ABB' monomer, in which the reactivity of B and B′ with A is significantly different;[17] and (iii) through an ABB_m building block, wherein the masked B-moiety (B_m) can be transformed into a reactive group, once the first reaction between A and B is completed.[18] In the example of the approaches represented in Scheme 4, we show the protection–deprotection strategy to differentiate the B functionalities. In this, after the reaction with unprotected 'B', the second moiety is deprotected and substituted with a different compound. This results in variations in the branching points. Continuation of these variations throughout the synthesis affords the capability for differentially functionalizing the periphery.

We demonstrated this concept by achieving a dendron in which all the peripheral functionalities are different from one another. This demonstration is conceptually similar to sequencing the dendrimers, as far as synthetic strategy is concerned. In this, we used 3,5-dihydroxybenzyl alcohol as the AB_2 monomer unit, in which one of the phenolic B units is protected. The protecting group used involves an allyl moiety or methoxymethyl ether functionality (MOM). The resultant product was treated with one alkylating agent to cleanly afford the mono-substituted compound, which was then treated with sodium borohydride in the presence of a palladium catalyst to afford the deprotection of the allyl group. The resultant phenol was then treated with a second electrophile to afford the differentially substituted **G1** dendron. Conversion of the hydroxymethyl moiety to bromomethyl group and iteration of the above mentioned steps resulted in the synthesis of a **G3** dendron with eight different peripheral functionalities. The



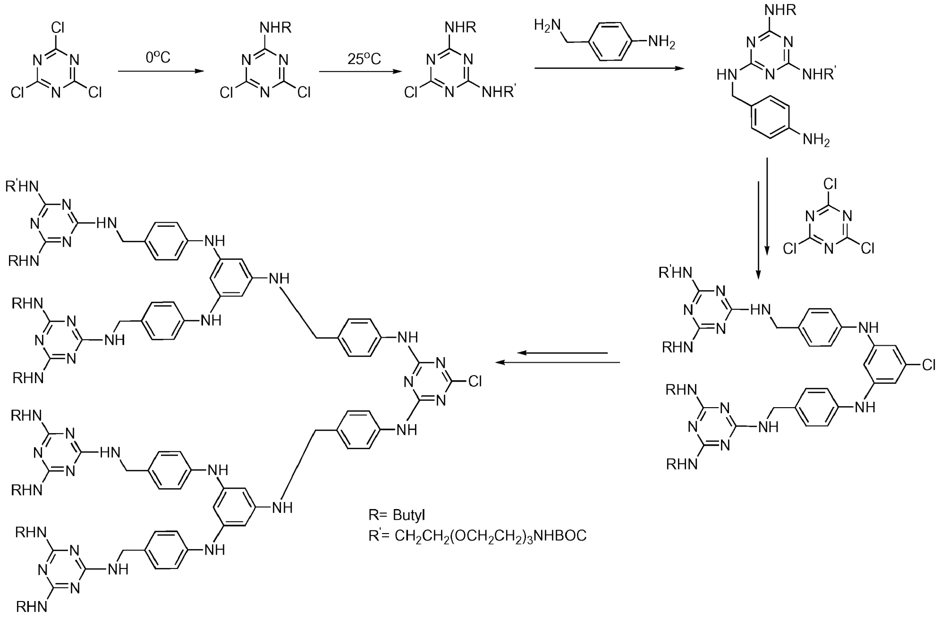
Yangbin Chen was born in Guangdong, China and received his BS degree from the University of Science and Technology of China in 2004. He is currently attending the University of Massachusetts at Amherst as a graduate student under the guidance of Prof. S. Thayumanavan. His current research is focused on synthesis of amphiphilic molecules and their applications via self-assembly and surface modifications.



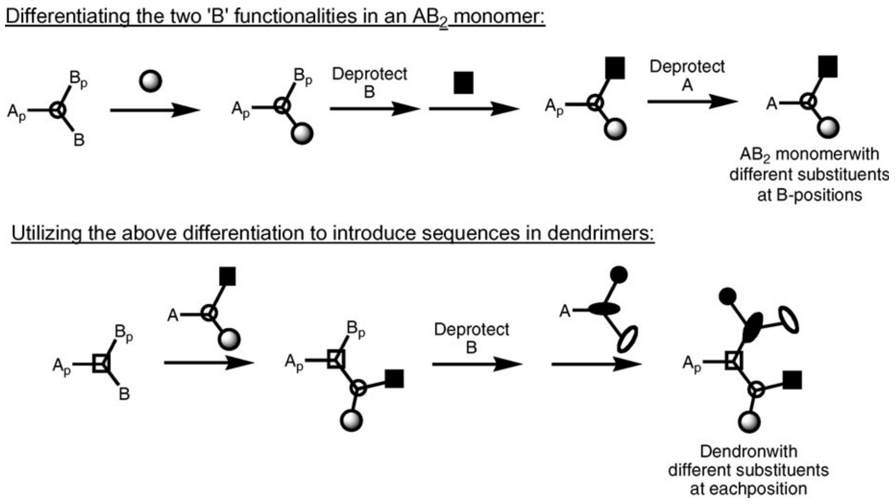
Scheme 2 Synthesis of polyamide dendrimers with a functional periphery.

synthetic strategy is shown in Scheme 5. Since substitution–deprotection–substitution significantly increases the number of steps in the synthesis, we were interested in demonstrating this reaction sequence with a single pot methodology. We were indeed able to do this through the development of a palladium-catalyzed deprotection methodology in the presence of potassium carbonate, which also happens to be the reagent for alkylation.[19]

In the ABB′ strategy for synthesizing similar dendrons, we utilized the differences in reactivity of the phenolic and hydroxyalkyl functionalities with an alkylating agent. In this case, two different reaction conditions had to be employed to preferentially effect the first substitution compared to the second substitution. We used the selective reaction of the phenolic functionality with an alkyl halide in the presence of potassium carbonate; the reaction of the alkanol with the alkyl



Scheme 3 Synthesis of melamine-based dendrimers with only one functional group on the periphery.



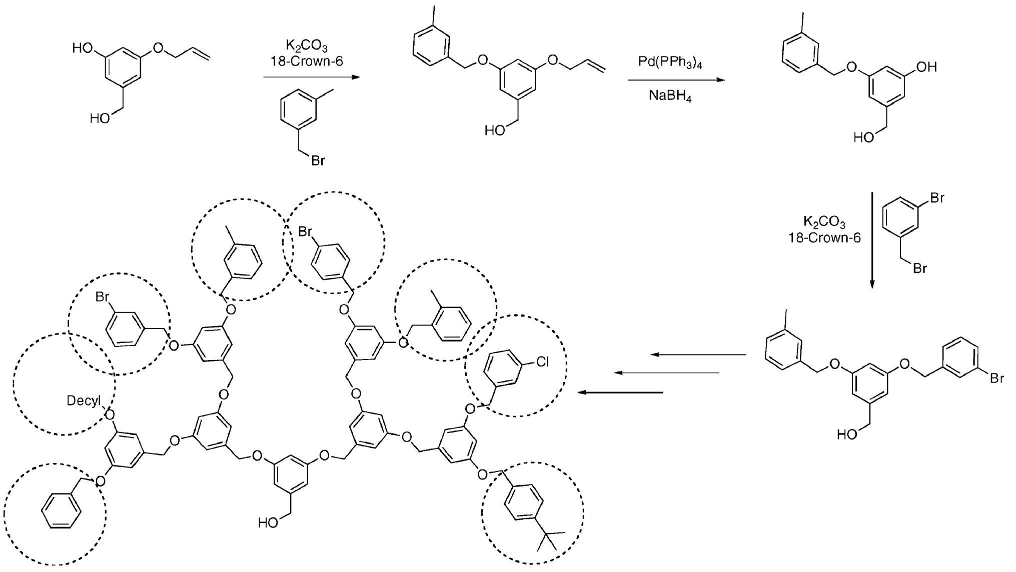
Scheme 4 Cartoon representation for sequencing dendrimers by differentiating the two B-functionalities in an AB_2 monomer.

halide was then achieved using sodium hydride as the base. We have exemplified this approach in Scheme 6 with the synthesis of a **G1** dendron. Again, we have demonstrated that these substitutions can be done in a single pot and that higher generations could also be achieved.[17]

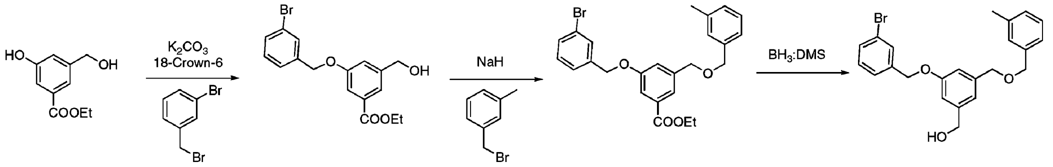
In the third strategy, we mask one of the B-functionalities as an unreactive one. This moiety is unmasked, after the first substitution. There are only subtle differences between this approach and the first one shown above. An example of this approach is shown in Scheme 7. In this case, the alkanol moiety is masked as a double bond initially. Once the substitution of the first phenolic group has taken place, the allyl moiety can be converted to an alkanol functionality that is ready to be alkylated. We have utilized a combination of all these strategies to generate a dendron in which every repeat unit is different from the neighbors.[18] The structure of a **G3** dendron thus synthesized is shown in Fig. 1.

3 Probing every layer in dendrons by controlled placement of fluorescent probes

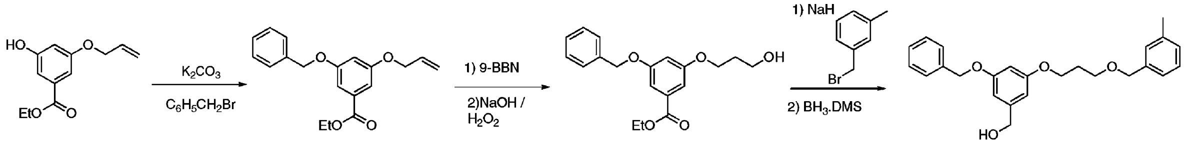
We have utilized the ability to selectively place functionalities to develop a fundamental structure–property relationship in dendrimers. Properties of a dendritic core have been studied quite extensively through encapsulations of photoactive, and electroactive units. However, relatively little is known regarding the properties of functionalities incorporated in the intermediate layers of the dendrimer. This could be mainly due to the fact that the synthetic strategies allow for incorporation of a single functionality at the core with relative ease; whereas placing a single functional moiety in a specific location within the branching units or at the periphery of the dendron is synthetically challenging. Nevertheless, few interesting papers have appeared recently. For example, in the case of benzyl ether dendrimers three **G3** dendrons having a single aromatic



Scheme 5 Synthesis of a dendron with functionally diverse periphery using a protection–deprotection approach.



Scheme 6 Example of the functional diversity using the ABB′ strategy.



Scheme 7 Example of the functional diversity using the ABB_m strategy.

bromide at three different positions[20] and a library of dendrimers with an allyl group at specific generations have been reported.[21] Phosphorus dendrimers have also been post-synthetically modified to introduce allyl, propargyl and dendritic moieties in the internal layers.[22]

The ability to access structures with a single functionality at various locations within dendrimers allows for a fundamental structure–property relationship study concerning the intermediate layers of the dendrimers in comparison with the core and the periphery. There have been limited number of studies that compare the intermediate layers of dendrimers with the periphery and core. In this direction, protonation and complexation with metal ions of internal amines in PAMAM and poly(propylene imine) dendrimers have been reported. Complexation of Cu(II) with PAMAM dendrimers was probed by EPR spectroscopy and it was observed that binding of Cu(II) with the internal layers and the structural changes in dendrimers were a function of pH, temperature and metal ion concentration.[23] Protonation of poly(propylene imine) dendrimers was monitored by ^{15}N NMR and compared with that of oligoamines of similar structures (Fig. 2) to understand the extent of protonation of various internal layers.[24] It was found that protonation behaviour of dendrimers and the linear molecules is similar and follows a two-step process. The primary amines because of high proton affinity are protonated in the first step, followed by the tertiary amines in the second step. This two-step process is however interesting in these dendrimers, because here the outermost shell and the innermost shell (α and δ) are protonated almost simultaneously, followed by the intermediate layers (β and γ).

Although, such non-covalent functionalization provides useful information, it is interesting to covalently attach reporter molecules to the dendritic framework in order to better understand these properties in solution. Indeed, we have investigated the properties of every layer of dendrons by incorporating a single fluorescent probe unit in a specific location.[25] The extent of guest molecule accessibility to each location within a dendrimer is then analyzed using an intermolecular photoinduced electron transfer (PIET) based fluorescence quenching process. In these molecules, anthracene was used as the fluorescent probe and benzyl ether dendrimers

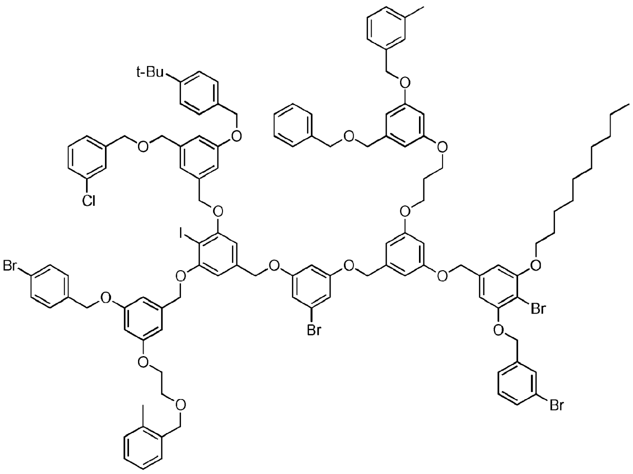


Fig. 1 Structure of a **G3** dendron with all repeat units different from each other.

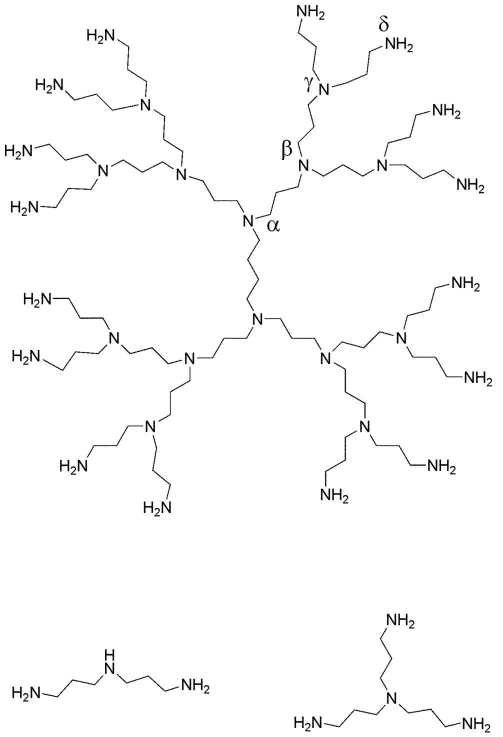
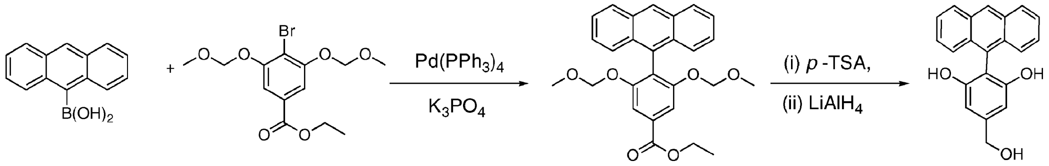


Fig. 2 Poly(propylene imine) dendrimer (left) and the oligoamine analogs (right). Different shells in the dendrimer are denoted by Greek letters.



Scheme 8 Synthesis of the anthracene containing building block unit.

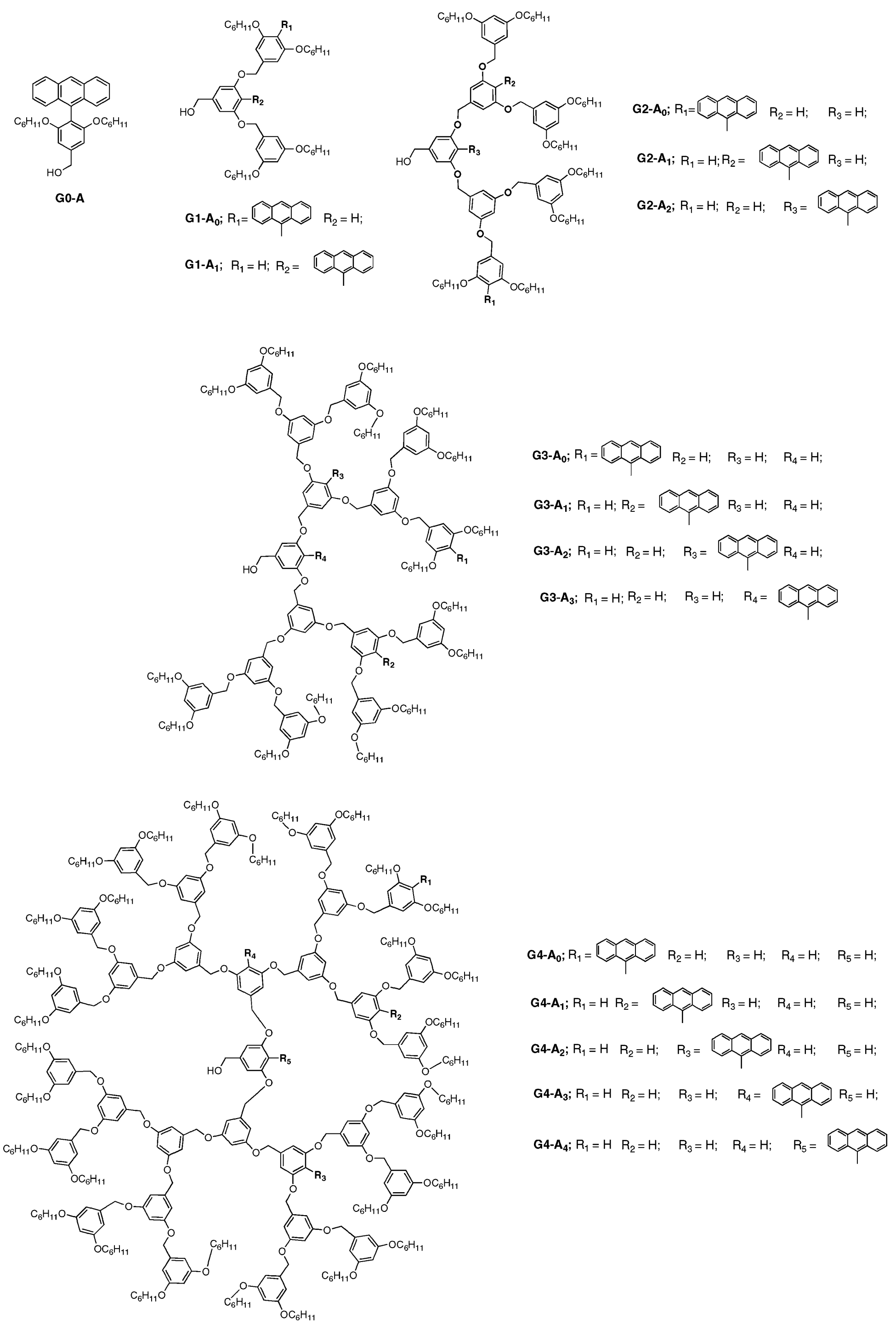


Fig. 3 Structures of dendrimers with anthracene as the fluorescent probe in specific locations.

were used as the scaffold. In order to incorporate this fluorescent moiety in specific locations of a dendrimer, we first synthesized an anthracene containing monomer unit. The monomer was synthesized from anthracene boronic acid and the bromoarene derived from 4-bromo-3,5-dihydroxybenzoic acid, as shown in Scheme 8.

Structures of the dendrons containing anthracene at the specific locations are shown in Fig. 3. The dendrimers are labeled as **G*n*-A*m***, where anthracene is in the *m*th layer of the *n*th generation dendron—the 0th layer being the periphery. The fluorescence quenching was used as the measure of the interaction between this fluorophore and an externally added quencher *viz*. tren-Me_6. The extent of fluorescence quenching is related to the concentration of the quencher through the Stern–Volmer equation: $I_0/I = 1 + K_{SV}[Q]$, where I_0 and I are the fluorescence intensities in the absence and presence of quencher, [Q] is the concentration of the quencher, and K_{SV} is the Stern–Volmer quenching constant. The constant K_{SV} is a product of the bimolecular quenching rate constant k_q and fluorescence lifetime of anthracene dendrimer in the absence of the quencher (t_0), *i.e.* $K_{SV} = k_q t_0$. The k_q values could be considered as a measure of the accessibility of a quencher to a fluorophore.[26]

Table 1 Stern–Volmer quenching constants and bimolecular-quenching rate constants for the anthracene-labeled dendrons

Dendron	K_{SV}	$10^8 k_q/s^{-1}$
G1-A$_0$	13.3	23.6
G1-A$_1$	15.2	22.8
G2-A$_0$	9.99	17.7
G2-A$_1$	14.5	18.0
G2-A$_2$	14.0	15.5
G3-A$_0$	11.2	15.5
G3-A$_1$	11.2	16.6
G3-A$_2$	9.61	13.1
G3-A$_3$	7.68	8.96
G4-A$_0$	8.91	12.4
G4-A$_1$	9.68	12.5
G4-A$_2$	6.76	7.44
G4-A$_3$	6.12	6.60
G4-A$_4$	4.81	5.01
G0	13.3	22.7

From the values of K_{SV} and k_q as shown in Table 1, it can be seen that (i) the steepest change in accessibility occurs in the middle layers; the difference between the periphery (**A$_0$**) and the next layer (**A$_1$**) of the dendrons is negligible in all dendrons; from the first to second layer, *i.e.* from **A$_1$** to **A$_2$**, there is a significant difference in accessibility; (ii) there is significant difference in generation-dependent accessibility even in the peripheral layers of dendrons: for example, periphery of **G4** is about 48% more encapsulated than that of **G2**—k_q decreases from 17.7×10^8 s^{-1} for **G2** to 12.4×10^8 s^{-1} for **G4**; (iii) beyond the first layer of a dendron, the accessibility of a layer within a dendron seems to be similar to the next layer of the previous generation. For example, the first layer compound of the third generation compound **G3-A$_1$** exhibits a similar k_q value (16.6×10^8 s^{-1}) as the second layer compound of the second generation **G2-A$_2$** (15.5×10^8 s^{-1}). Similar trends can also be noted by comparing **G3-A$_2$** with **G4-A$_1$** and **G3-A$_3$** with **G4-A$_2$**. (iv) it is noteworthy that the steepest change occurs in the second layer (0th layer is periphery) *i.e.* at **A$_2$** in all dendrons and hence the difference in accessibility of **A$_2$** in all dendrons is most prominent. Also, K_{SV} values determined by both steady-state and time-resolved spectroscopy were the same indicating that it is a dynamic quenching process. This type of a fundamental understanding could not have been easily envisaged without the sequencing methodologies developed by us. In tune with this theme, incorporation of solvatochromic probes in the interior of dendrimers to understand the polarity gradient of the dendritic interior has been reported recently.[27]

The difference in encapsulation of periphery in the above dendrons can be attributed to the 'backfolding' effect in dendrimers.[28] More recently, we have studied this effect using heterogeneous electron transfer as well—note that the photo-induced electron transfer in anthracene-labeled dendrons described above is a homogeneous electron transfer. We have used dendrimers with electroactive triarylamine moiety on the periphery to study the heterogeneous electron transfer.[29] Three types of molecules were studied and compared—dendrimers with the periphery fully decorated by the electroactive moiety, difunctionalized dendrimers *i.e.*, only two electroactive moieties on the periphery and their corresponding linear analogues. Structures of all these molecules are shown in Fig. 4. In the fully decorated dendrimers, the number of functionalities and so the number of redox reactions doubles at every generation, which makes it difficult to calculate the heterogeneous electron transfer rate constant (k^0). The difunctionalized dendrimers, where the number of electroactive functionalities remains the same at all generations are thus useful for this study. The diffusion coefficient (D_0) and rate constant (k^0) values were obtained for all the derivatives using microelectrodes. The 'backfolding' effect at higher generations could be easily seen in difunctionalized dendrimer **G3-D**, for example, k^0 for **G3** (3.7×10^{-4} cm s^{-1}) was four times lower than for **G1** and **G2** ($\sim 1.4 \times 10^{-3}$ cm s^{-1}). However, for linear analogs no significant difference was seen for all generations (k^0 for **G1-L–G3-L** $\approx$ 1.7–2.1 $\times 10^{-3}$ cm s^{-1}) as expected. Thus, we have unambiguously demonstrated that encapsulation of the periphery does occur in dendrimers using homogeneous as well as heterogeneous electron transfer. An example of the implications that this study could have involves biomolecular recognition involving polyvalent interactions and periphery functionalized sensors using dendrimers. These studies reveal that the periphery encapsulation will have to be taken into account during data interpretation.

4 Comparison of dendrimers with linear analogs as light harvesters

Another area in which these methodologies have been made useful involves the evaluation of dendritic architectures in light harvesting applications. The need for efficient light harvesting materials is obvious, because it provides a method for effectively using renewable energy sources. The placement of chromophores relative to charge transport units plays a crucial role in the high efficiency of this light harvesting process. Nature's photosynthetic apparatus involves two key steps: (i) electronic energy transfer (EET) where the solar energy is funneled to a single reaction center and (ii) a sequence of

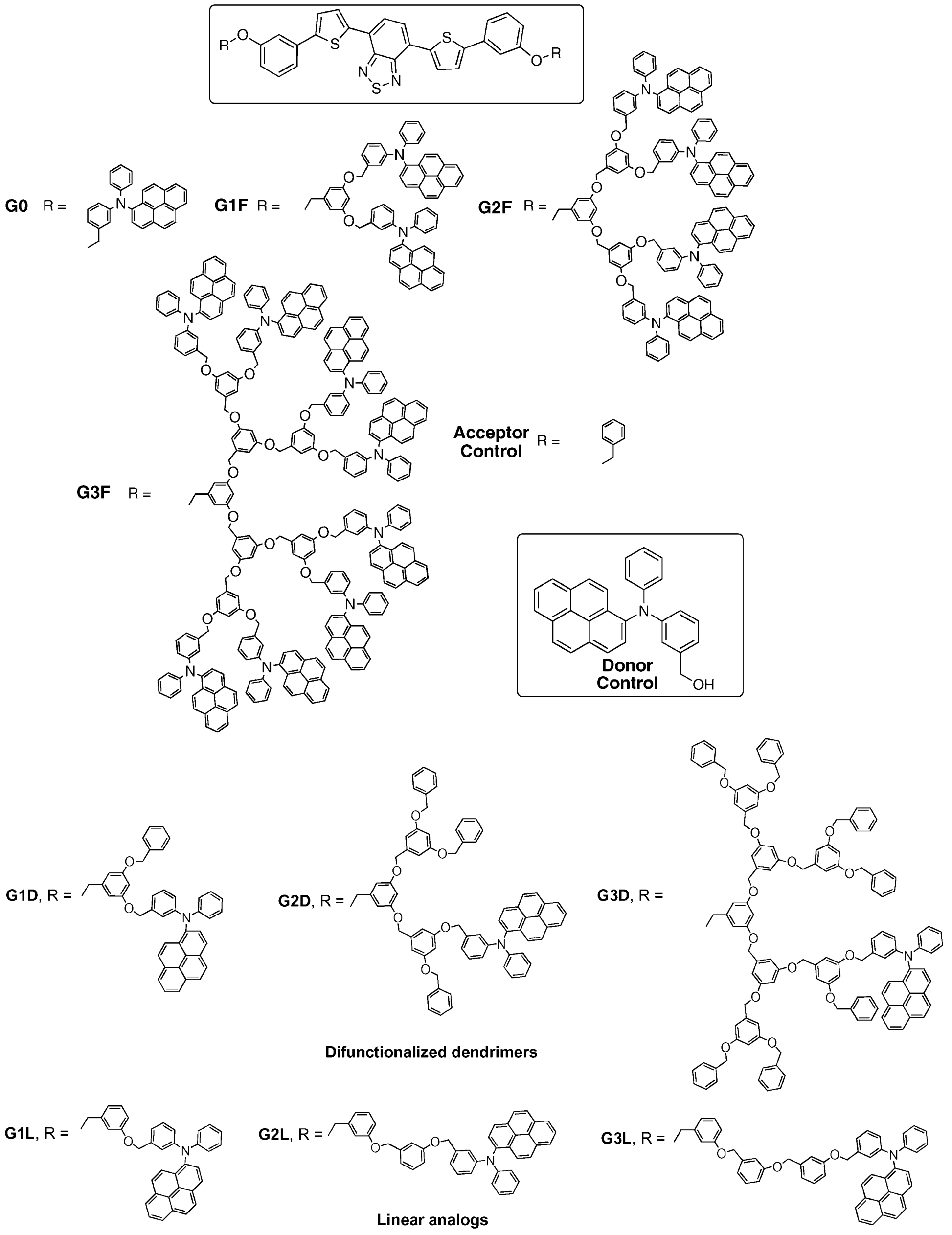


Fig. 4 Structures of the fully functionalized dendrimers, difunctionalized dendrimers, linear analogs and model compounds for photoinduced electronic energy transfer (EET) and charge transfer (CT) studies.

charge transfer (CT) events from the excited state of the reaction center that ultimately results in chemical energy. While Nature's light harvesting systems are extremely efficient in their native conditions, these systems are neither cheap nor robust enough to be widely useful as components of solar cells. Therefore, developing artificial light harvesting systems containing multichromophore arrays is of great interest.

Dendrimers are interesting scaffolds for this purpose. The decreasing number of functionalities from the periphery to the core of the dendrimer makes these molecules excellent candidates for light harvesting antenna (Fig. 5). The periphery of the dendrimers is functionalized with chromophores that collect the light and then funnel the energy to a lower energy acceptor at the core. As mentioned before here, since dendrimers are assembled layer-by-layer, control over the relative placement of photoactive units can be easily achieved. Considering this possibility, several groups have utilized dendrimers as light harvesting antennae, in which efficient energy transfer from the periphery to the core of the dendrimer has been observed.[30] Similarly, considerable effort was also devoted to design dendrimers with favorable electron transfer properties.[31] However, there has been only a limited number of reports on combining these two steps. This sequence of events is outlined in Fig. 5, where a donor molecule first transfers its energy to the core acceptor, which then is able to oxidize the donor and form a charge-separated state. In such a system, the donor fulfils two roles: as energy harvester and electron donor. There have been reports on energy/

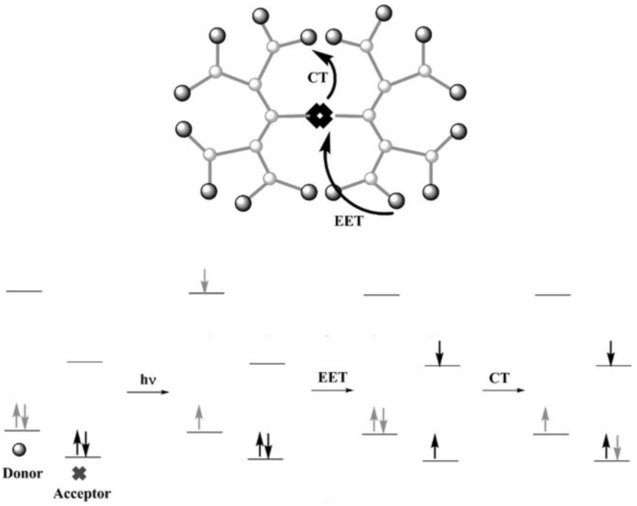


Fig. 5 Schematic of dendrimers for both EET and CT in a single scaffold; (b) relative energy levels for these photoinduced processes.

electron transfer combination in conjugated dendrimers, where the backbone serves as a vehicle for the through-bond communication both for electron and energy transfer.[32] However in non-conjugated dendrimers, the role of the backbone is only structural and not functional. Therefore, studying these dendrimers should be useful in analyzing the architectural advantages of dendrimers in these light-induced processes. In addition, a non-conjugated backbone also provides the ability to independently tune the energy levels of the donors and acceptors within a single molecule. It is also easy to imagine that dendrimers are interesting scaffolds for photoinduced charge transfer for another reason, especially from the core to the periphery. As one moves from the core to the periphery of dendrimers, the number of units at least doubles with each layer. Therefore, dendrimers could provide an entropic driving force for charge separation from the core to the periphery. Our molecular system consists of benzyl ether dendrons functionalized with diarylaminopyrene units in the periphery attached to benzthiadiazole core, structures are shown in Fig. 4.[33]

Through a set of steady state and time-resolved photophysical studies, in collaboration with Professor Christopher Bardeen at the University of California at Riverside, we found that this series of dendrimers exhibits energy transfer from the periphery to the core on a picosecond time scale, which increases from 21.2 ps for **G0** to 162 ps for **G3**. The rapid EET times were consistent with the Förster mechanism. However the EET efficiency was observed to scale only as $1/r^3$, instead of the typical $1/r^6$ Förster relationship. This was attributed to the ability of the flexible arms of the dendrimers to backfold and thus decrease the average distance between donor and acceptor. It has been generally accepted that the distance between two points in a random coil polymer scales as $\sqrt{N}$, as opposed to N (where N is the number of intervening bonds);[34] therefore, the above explanation is reasonable. The EET efficiency decreases with the generation but only slightly, for **G1** it is 0.95 and for **G3** it is 0.89. The most likely origin of this effect is the ability of the benzyl ether backbone to fold back upon itself and reduce the effective acceptor–donor distance in the dendrimer.

The EET was followed by nanosecond charge transfer from the core to the periphery; the lifetime of the charge-separated state was found to be in the microsecond time scale. The CT efficiency was essentially independent of generation but was dependent on solvent polarity as anticipated. For example, CT efficiency in **G3** dendrimer was 0.0042 in toluene, 0.518 in dichloromethane and 0.805 in DMF. The lack of generation dependence of CT efficiency can be explained as follows—the overall CT rate only depends on the distance of the closest ground state electron donor and due to backfolding in higher generation dendrimers at least one donor will be closer to the core. If the distance of this closest donor is nearly the same in all generations then the CT efficiency will also be the same.

In order to test this hypothesis and in general understand the fundamental architectural advantages of dendrimers in EET and CT processes, it is interesting to compare dendrimers with the corresponding linear analogs. To our knowledge, there has been no study that compares dendrimers with the corresponding linear analogs in the context of both intramolecular electronic energy transfer (EET) and charge transfer (CT). We utilize the combination of donors and acceptors shown above (Fig. 4), since these provide a unique opportunity to investigate the advantages that dendrimers provide in both EET and CT processes. We have synthesized the linear molecules containing the diarylaminopyrene-based donors and benzthiadiazole-based acceptors, along with the corresponding dendrimer analogs for a straightforward comparison.[35]

Comparison of dendrimers with linear analogs has been previously done in the context of their physical properties.[36] However, similar comparison in light harvesting dendrimers is more complicated. There are only a couple of reports in this direction. Benzyl ether dendrons and their perfectly linear analogs were attached to a free base porphyrin core (Fig. 6) and the energy transfer process from benzyl ether moieties to porphyrin core was studied.[37] The dendrimers were found to be most efficient in energy transfer compared to other branched and linear analogs—an observation that we also made in our system. The energy transfer efficiency was found to be almost independent of generation in the porphyrin-cored dendrimers whereas it decreased significantly in linear molecules, indicating a morphology change in higher generation dendrimers, *viz*. backfolding. In another example, random copolymers containing coumarin-based donor and acceptor chromophores in a ratio similar to that in corresponding dendrimers have been synthesized.[38] Energy transfer efficiencies were found to be higher in polymers but the quantum yield was poor due to excimer formation and thus it was concluded that overall light harvesting performance of dendrimers was superior.

As mentioned above, to compare both EET and CT properties, classical dendrimers with the periphery fully decorated by donor moieties and a single acceptor unit at the core were synthesized and are represented by **F** in Fig. 4. Comparison of **F** with the linear analog **L** (in Fig. 4) accounts for the donor–acceptor distances that dendrimers and the linear oligomers provide, but fails to provide the equivalent chromophore densities (number of EET/CT donors *vs*. acceptor). However, comparison of the dendrimer **D** having a

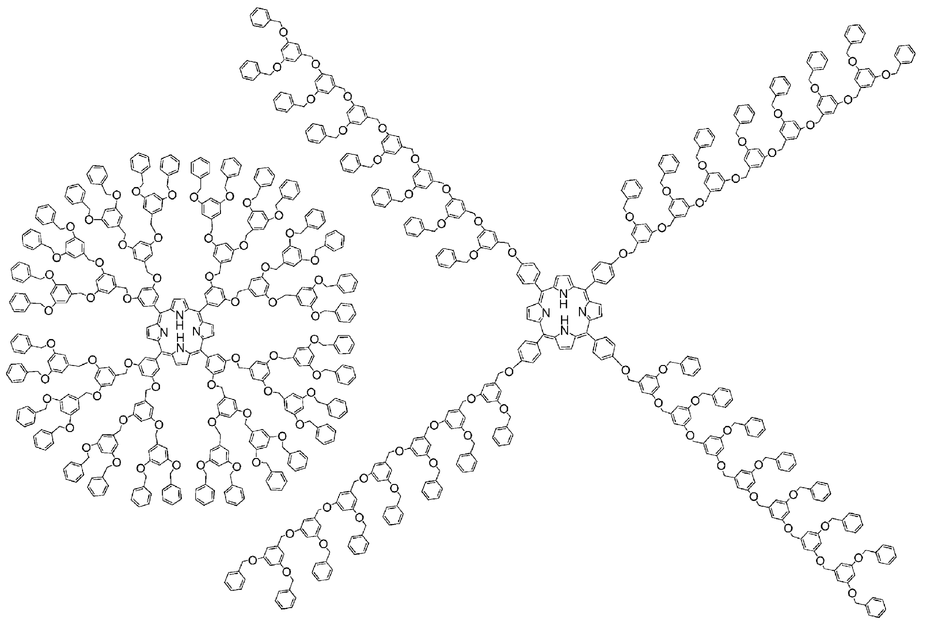


Fig. 6 Structures of porphyrin-cored benzyl ether dendrimer (left) and corresponding linear analog.

difunctionalized periphery with the linear analog **L** accounts for both these factors. In other words, comparison of **D** and **L** eliminates the chromophore density variable and directly addresses the advantages of dendritic scaffold in light harvesting. On the other hand, comparison of **F** and **D** provides information on the advantages of chromophore density in dendrimers. We were able to access these difunctionalized **D** dendrimers, where only one of several peripheral functionalities in the dendritic arm is photoactive, primarily because of the methodologies mentioned above for selective functionalization within dendritic architectures.

Comparison of these three classes of molecules using steady-state and time-resolved photophysical studies suggests that the fully functionalized **F** dendrimers are indeed advantageous for both EET and CT processes.[39] In the case of EET, although the dynamics is not different in these architectures, the advantage of the **F** dendrimers primarily emanates from the number density of the energy donors that one could decorate equidistant from the acceptor core, a feature that is not available in linear molecules. In the case of CT process, the advantages arise from the fact that in the fully functionalized dendrimers, there are always a reasonable number of CT units present in close proximity to the core chromophore in the excited state to affect the electron transfer. In the case of the difunctionalized dendrimers, such a luxury is not available. For example, the charge transfer time (τ_{CT}) for third

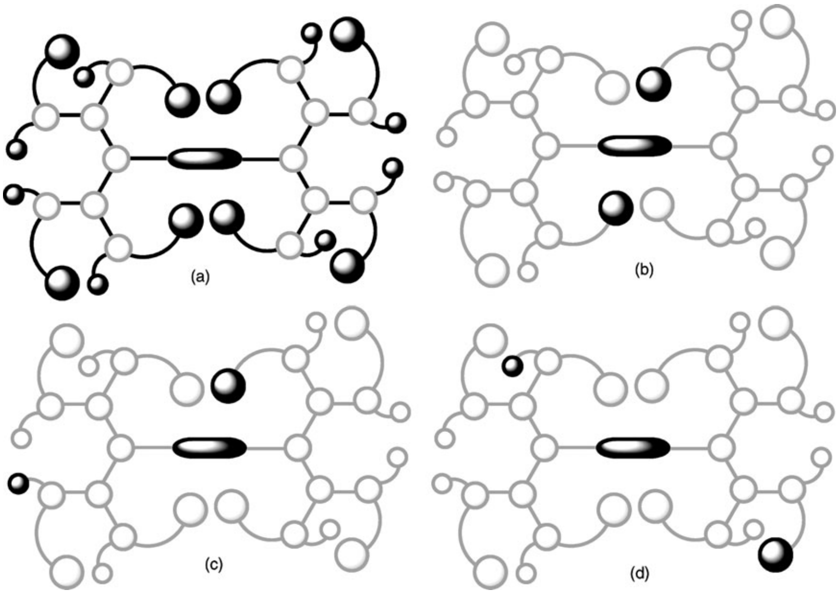


Fig. 7 (a) Hypothetical conformation of a fully decorated dendrimer. (b–d) Various possible conformations of difunctionalized dendrimers similar to the one in (a).

generation linear and difunctionalized molecules is almost same, about 3.8 ns but for fully functionalized **G3** dendrimer it decreases to 1.28 ns. It further decreases with temperature—0.8 ns at 100 °C, suggesting, due to conformational fluctuations at higher temperature, donor molecules interact more rapidly with the core. This difference and therefore the advantages of fully decorated dendrimers are schematically represented in Fig. 7. The difunctionalized dendrimers are likely to be representative of the average of the conformations shown in Fig. 7(b)–(d). Thus, the average distance between the donor and acceptor will increase with generation. However, even when one attempts to draw the different conformations with the fully functionalized dendrimers as in Fig. 7(b)–(d), there would be a certain number of donor units close to the core. This could be sufficient to enhance CT efficiency in higher generations, when fully decorated.

5 Summary and perspective

The outlook on dendrimers has clearly changed in the past decade and it is not surprising today to see dendrimers being applied in entirely new and unexpected ways. We have experienced this transformation in our own laboratories where we started with synthetic strategies and later used these novel architectures in different ways, from studying surface chemistry[8] to protein binding events.[7] For dendrimers to be highly applicable it is important that dendrimer synthesis becomes fairly simple and less time consuming, but without affecting their monodisperse nature. The so-called 'one pot synthetic strategy' has been used towards this goal, but only a handful of examples exist that require specially designed repeat units.[40] The task becomes even more challenging when one attempts to incorporate functionalities at different layers in a dendrimer. Several research groups have tried to address this issue; although we have focused in this review on our work related to dendrimers with absolute control over the placement of functionalities at specific locations, we have made references to others' efforts as well. We have developed three complementary methodologies using the convergent strategy to achieve the specific functional group placements. Such controlled functional presentations in dendrimers will be of special interest in designing new drug delivery vehicles. For example, one could imagine a dendrimer featuring the targeting functionality attached on the periphery and a cleavable prodrug attached to another intermediate layer. The choice of the intermediate layer could be judiciously chosen based on the need for protection of the dendrimer–drug bond from being cleaved prematurely, while still preserving a high loading capacity. This balance is needed because the periphery is the most exposed, but this location also has the maximum loading capacity in a dendrimer because of the number of functional groups.

Another interesting application is in charge transport materials, where the redox gradient from the periphery to the core can be tuned by incorporation of the functional groups at appropriate layers.[41] Developing a fundamental understanding of the behavior of intermediate layers is crucial for these applications, however. In this direction, we have outlined our findings where we incorporated spectroscopic probes at precise locations within the dendrons. Similarly, we have also briefly described the utility of these methodologies in the comparisons of dendrimers with exact linear analogs to develop an understanding of the advantages of dendrimers in light harvesting applications. An insight into the differences in properties of linear and dendritic molecules will be broadly applicable for the creation of the next generation of highly functional materials. Such materials will integrate favorable attributes of linear polymers, such as easy synthesis and good mechanical properties, with those of dendrimers such as well-defined placement of functionalities and highly branched architecture. We believe that new synthetic methods for dendrimers will provide an impetus to fundamental structure–property relationship factors in the ongoing research in our laboratories and elsewhere, and will lead to new materials with exciting properties.

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