

Suprasupramolecular chemistry: the chemistry within the dendrimer

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Abstract: Relationships between branched architectures and supramolecular chemistry are examined via development of novel building blocks possessing either molecular recognition, electroactive or ligating moieties. Construction via combinatorial techniques is also reported.

The topic of *supramolecular* chemistry has grown, since its inception by Lehn,^{1,2} to encompass simple host-guest interactions as well as molecular events that extend to the evolution of life and the biosynthesis of contemporary biological systems. The *supermolecular* aspects of this presentation arose with the advent of dendrimers^{3,4} or precisely structured, spherical, oligomeric macromolecules, which possess nanometric dimensions and are also known as arborols,^{3;5;6} starburst,⁴ cascade^{7;8} or cauliflower⁴ polymers. These supermolecular species bridge the gap between traditional unnatural organic molecules (MW < 2,000 amu) and the “classical” polymers, generated from linear monomers. Thus, the melding of supramolecular chemistry *within* these supermolecules,⁹ can then be envisioned as “suprasupramolecular” chemistry.

In order to construct specifically designed supermolecules, one must create a series of well defined polyfunctional monomers, each possessing a branching point as well as an appropriate center where the interaction will eventually occur. Such tailored assemblies can best be constructed by the use of appropriate *branched* building blocks rather than the standard, readily available, linear monomers. Thus, these highly branched macromolecules are synthesized by a simple step-wise approach in order to instill the desired reactive construction center(s) at precise loci within the superstructure. Figure 1 depicts the two different methods for the construction of dendrimers. This iterative or step-wise approach

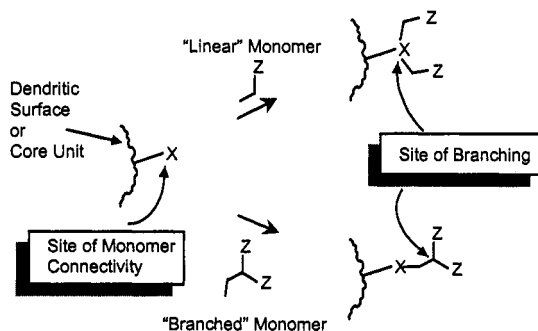


Figure 1. The two general methods for branched architecture construction.

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using branched monomers to synthesize dendrimers provides the opportunity to control the superstructure, molecular weight, and generational properties desired *within* the ultimate product.¹⁰ These fractal-like constructs generally possess excellent solubilities, when compared with classical polymers, since the surface characteristics, dominant in dissolution, can be readily modified by recently demonstrated combinatorial chemistry.¹¹

For years, non-covalent interactions have attracted enterprising chemists to construct receptors capable of binding to biologically important as well as unnatural molecules. Molecular recognition at a *specific* site within a dendrimer can easily be envisioned (Figure 2) by the simple incorporation 2,6-diacylaminopyridine.¹² Titration studies using this dendrimer, possessing this well-studied *H*-bonding moiety, confirm its complementary

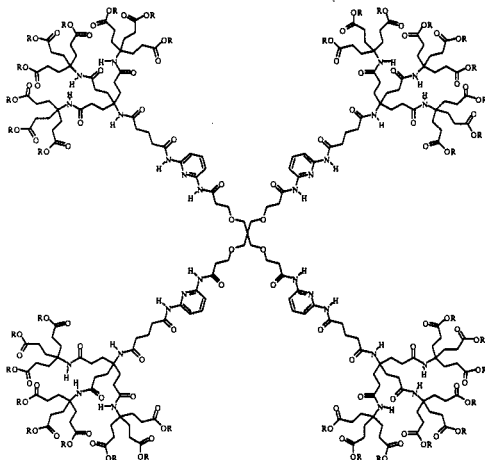


Figure 2. Incorporation of molecular recognition sites within a dendrimer.

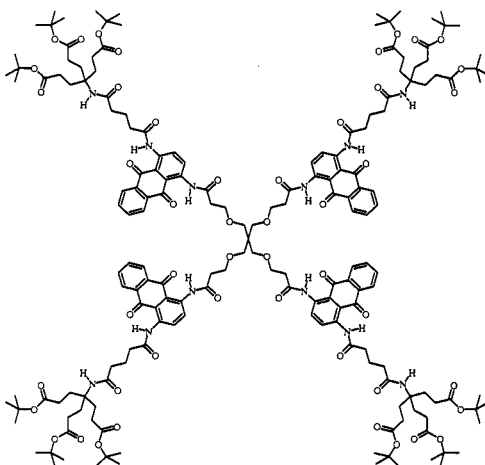


Figure 3. Incorporation of electroactive elements within a dendrimer.

binding of barbituric acid derivatives, such as AZT, within its superstructure. Interestingly, the use of traces of paramagnetic metals again confirms the site of coordination and starts to afford critical information concerning the folding of the limbs into the molecular infrastructure of these ordered polymeric systems.¹³

Recently, the introduction of electro- and photoactive cores into dendrimers has been elegantly demonstrated by several research groups.¹⁴⁻²⁶ We also were interested in the introduction of chromophoric 1,4-diaminoanthraquinone units within the cascade infrastructure.²⁷⁻²⁹ Dendrimers, based on a four-directional pentaerythritol

core, were synthesized using an extended $1 \rightarrow 3$ building block, which was prepared from three components under high dilution conditions; subsequent divergent expansion to the higher generations was utilized^{30,31} (Figure 3). Cyclic voltammetry studies showed an expected positive shift of the reduction potentials of the anthraquinonoid moieties upon incorporation. UV-vis spectroscopy assisted in the monitoring the facile, reversible chemical reduction process of this dendritic series using sodium borohydride. These examples shown in Figures 2 & 3 demonstrated the facility to insert desired chemically interesting

moieties at specific positions within the molecule's superstructure.

Specifically placed metal centers are another approach to probe the chemistry within a macromolecular construct. Balzani et

al. reported early examples of the self-assembly of metallodendrimers by a simple step-wise use of ruthenium(II)-polypyridine type complexes.³² Such complexes possess novel properties and have recently lead to a series of luminescent dendrimers with mixed metal, macromolecular composition.^{33;34}

One of the synthetic challenges in the construction of these large macromolecules is their purity, or better, the ability to ensure the synthetic completeness at each succeeding generation. Although not generally acknowledged, synthetic integrity above generation 3 or 4 can not be guaranteed, since simply having a (mass spectral) peak at the desired mass position need not support overall compositional purity. A simple qualitative approach³⁵ to this issue was the use of a traditional qualitative organic approach in which a reagent can selectively react with residual "loose ends" within the dendrimer. This procedure starts to address the integrity of the construct but also offers an interesting method to randomly incorporate dyes and labeled substrates within the macromolecular protected regime.

An alternative approach was to assemble proven components into a precise construct by means of stable metal ion centers. Such a procedure capitalizes on the easy detection and quantification of the number of metal centers, thus the assembly must be comprised of the macromolecular components based on the presence of these metal centers. To demonstrate the technique, the synthesis of a dendritic "lock and key" complexes, such as shown in Figure 4, is based on well-established *bisterpyridine-ruthenium(II)* [$-\langle Ru \rangle-$] coordination chemistry.³⁶

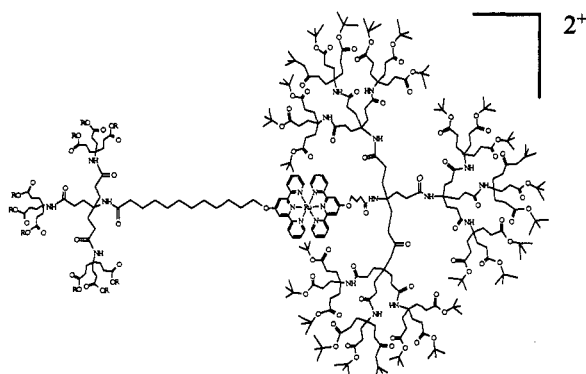


Figure 4. An idealized representation of a dendritic "key" and "lock".

The "key" series of terpyridines, possessing increasing - first through third - generations of proven "molecular trees," was prepared by the aid of $RuCl_3$; the corresponding "lock" portion was similarly prepared.³⁷ Reduction of the "key" in the presence of the appropriate lock afforded an assembly, which can be analyzed by the presence of the metal center. The cyclic voltammetry, interestingly, exhibited irreversible redox processes as the generation number of the lock increased. Ineffective electron transfer due to the isolation of the redox center from the electrode surface by the dendritic surface or destabilization of redox products due to steric hindrance are possible rationale for the experienced irreversibility.

Recently, this procedure was extended to utilize two Ruthenium centers per appendage, for example [$-\langle Ru \rangle-(X)-\langle Ru \rangle-$], in order to evaluate the "inner" versus "outer" aspects of such polycomplexes.³⁸ A combination of divergent and convergent approaches

gave rise to the step-wise construction of tiered metallodendrimers via a controlled metal complexation.

The application of such -<Ru>- connectivity has led to the formation of dendritic methane and to isomeric metallodendrimers³⁹ (Figure 5). Thus, the application of *H*-heterocycles to the preparation of tailored macromolecular structures will start open exciting new frontiers. The “molecular ceiling,” which has constrained chemists for nearly two centuries has now been shattered and the interface between organic and inorganic chemistries will open new vista into the mesomolecular regime.

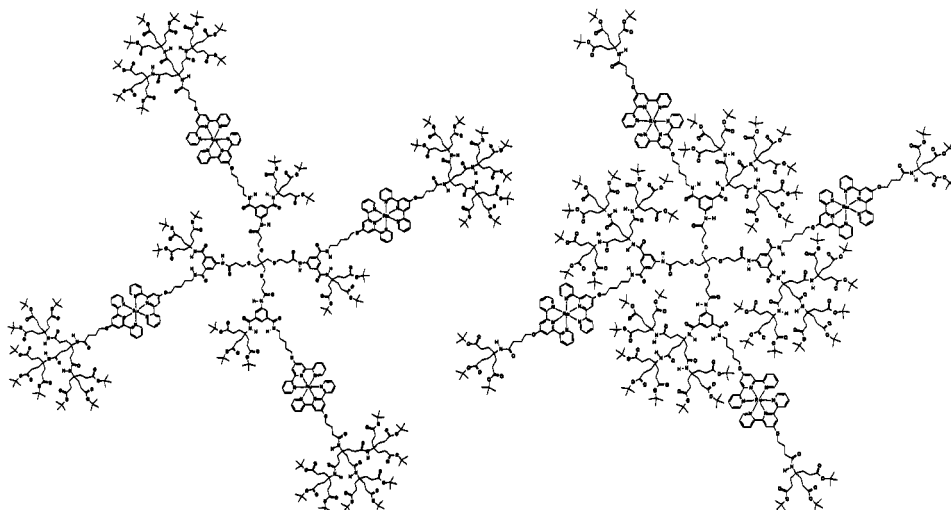


Figure 5. Dendritic constitutional isomers.

These monodisperse, multicomponent macromolecules, prepared from predetermined monomers, are interesting hosts for supramolecular chemistry. The creation of catalytic sites within these structures offers opportunities to evaluate the homo-/heterogeneous interface. The easy manipulation of the surface of materials, such as commercial DSM dendrimers, with mixtures of isocyanate monomers⁴⁰⁻⁴² in a combinatorial manner give rise to novel, dissymmetric architectures, that we have termed “polycelles”, in view of their relationship to poly(micelles)¹¹ (Figure 6). The concept of supramolecular self-assembly of small AB_n -type monomers will prove to be an interesting linkage between small molecules and novel “new age” materials.

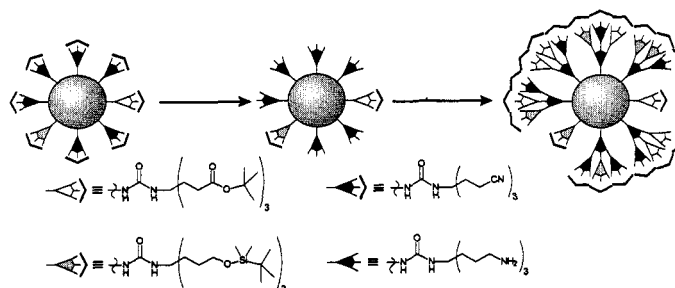


Figure 6. “Combinatorial” methods lead to new materials.

The synthesis of β -cyclodextrin-based dendrimers was accomplished⁴³ by the utilization of these easily prepared 1 \rightarrow 3 C branched isocyanates; this can be envisioned as a facile “dendrimerization” of a polyfunctional substrate. Using phenolphthalein as a UV-vis active probe, it was readily shown that the β -CD cavity of these modified receptors retained their molecular recognition properties and can be employed, convergently, as polyfunctionalized monomers in molecular self-assembly, as demonstrated in the generation of the two-directional “arborol” shown in Figure 7.

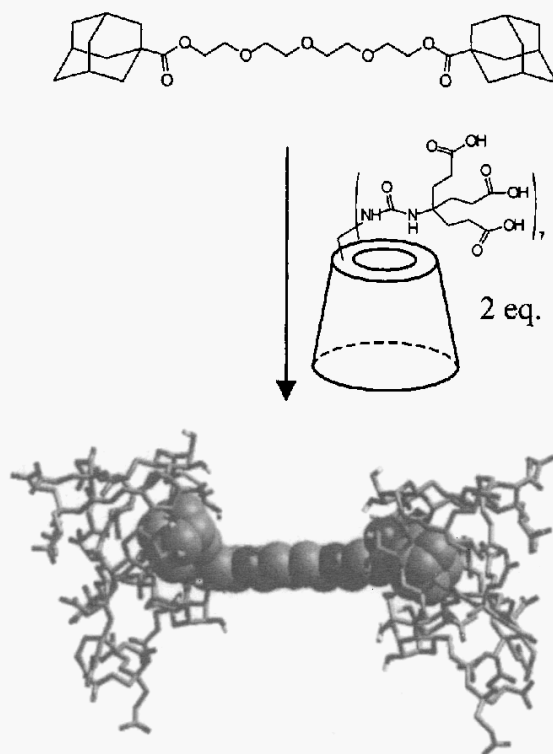


Figure 7. An idealized representation of “dendrimerized” β -CDs coordinated to a *bis*(adamantane-terminated) tetraethylene glycol chain.

The application of these branched monomers offers a convenient tool to construct diverse polyfunctional material possessing predetermined cavity shapes or internal catalytic sites and diverse exterior régimes, thus instilling the desired degree of dissolution.

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