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Tetrahedron 59 (2003) 3797–3798

TETRAHEDRON

Preface

Recent developments in dendrimer chemistry

The field of dendrimer chemistry currently stands at a crucial point in its development. For some time, dendrimers have received much hype as controllable tunable nanoscale materials, yet a question mark still remains. Will they deliver on their early promise, or are they nothing more than aesthetically pleasing curiosities?

Perhaps the greatest asset of dendritic molecules is the vast array of structures which could in principle be synthesised. It is through the synthesis of the widest possible range of branched superstructures that potentially useful new molecules will be generated. Dendrimer synthesis provides a stern test of any synthetic methodology, as reactions must occur multiple times, with high yields, otherwise the branched structures generated will be largely defective, having missing repeat units. It is hoped that this special issue of *Tetrahedron* will go some way towards encouraging more 'synthetic' chemists to test their mettle against challenging dendritic targets.

This symposium-in-print presents some of the interesting ways in which dendrimers are being constructed, as well as the properties and applications of the superstructures that are generated. Some syntheses apply tried and trusted peptide methodology, known as a reliable method for constructing dendrimers with interesting properties. Others adapt 'classic' organic reactions such as S_NAr or hydrosilylation reactions. Solid supported dendrimer synthesis and the application of combinatorial-style methods has great potential, as such an approach provides access more rapidly to a wide range of superstructures. Finally, dendrimer synthesis is not limited to covalent bond construction, coordinative (or supramolecular) interactions can be used to construct higher order architectures. With this goal in mind, the synthesis of dendritic ligands is of considerable current interest.

Although the synthesis of dendritic systems is a crucial aspect of their development, it is also important to ask where the future applications of these molecules lie, and what their unique properties are. There are a huge variety of potential uses of dendritic structures, and this introduction only highlights those that are explored in this special issue. In fact, reading the articles in this collection, it becomes clear that dendrimer chemistry is itself 'branching out' in two directions, that is towards biological and materials chemistry.

First, dendrimers are molecules on a biological scale, and, as such, they are of great interest both for **modelling biological molecules and intervening in biological processes**:

- The simple size analogy between dendrimers and proteins makes dendrimers interesting standards against which to compare biological molecules.
- The interior of a dendrimer (its core) experiences a unique microenvironment generated by the dendritic branching, rather like that experienced by the active site of an enzyme. Current research is bringing us closer to a full understanding of dendritic encapsulation, which in turn should enhance our understanding of the remarkable behaviour of proteins and enzymes. Such investigations also generate dendritic species that may have useful biological applications, such as oxygen imaging in vivo.
- Non-covalent encapsulation of small molecules (e.g. pharmaceuticals) within dendritic architectures offers a potential approach to drug delivery. This is particularly true when the encapsulation process can be controlled using external stimuli.
- The multivalent surface of a dendrimer has a large surface area and is the most accessible region of the superstructure. Consequently, the dendritic surface is of great interest for its ability to interact with biological molecules and surfaces. Several papers in this issue report recent approaches to the functionalisation of dendritic structures with sugars, which are well-known to interact with cell surfaces.
- One of the great 'biological' challenges now facing dendrimer chemists is to control the conformation of dendritic structures analogously to the way in which nature can pre-program protein structure. To this end, dendritic structures with unique conformational properties, which manifest themselves through the optical and chiroptical behaviour of the dendrimer, are extremely exciting.

In addition to biological behaviour, however, the interesting three dimensional structures of dendrimers offer a unique entry into **materials properties**:

- Many dendrimers, some of them conjugated, show interesting optical and electrochemical properties. Dendrimers may avoid some of the processability problems associated with traditional conjugated polymers and also offer

doi:10.1016/S0040-4020(03)00429-0

new forms of functional behaviour suitable for materials applications.

- The attachment of multivalent dendritic branches to a polymer support generates a polymer which has significantly higher loading, enabling relatively large quantities of material to be synthesised on a single bead. This is of great interest in the general development of high-throughput chemistry.
- By controlling supramolecular interactions between dendritic molecules it is possible to control the properties of the material itself. For example, the ability of individual dendritic molecules to generate higher-order mesoscale liquid-crystalline or gel-phase assemblies is of increasing interest. The potential to vary the molecular structure should enable the creation of materials with truly tunable properties.
- Increasingly, investigations are underway to discover differences and similarities between perfect dendritic structures, and their synthetically more accessible imperfect (or 'hyperbranched') analogues. Such investigations will be of importance for the development of new materials based on branched molecules in the most efficient manner.

Obviously the differentiation between biological and materials applications is somewhat artificial, but it does provide a useful framework for considering the applications of these molecules. It should be pointed out, however, that many future applications of dendritic systems will probably lie in the rapidly developing area of 'biomaterials' chemistry. For example, a conjugated dendrimer with interesting materials properties can be surface functionalised with peptides in order that it may interact with biological systems. In both biological and materials chemistry, it is ultimately the tunability of the dendritic structure that offers the key advantage of this fascinating class of molecule. Surface groups, branching groups and core can all be modified in order to tune the desired properties of the dendrimer to the maximum effect.

So, back to the opening question mark—will dendrimers deliver? With potential commercial exploitations of dendrimers currently underway (e.g. multivalent dendritic gadolinium chelates for MRI angiography), and with the huge variety of possible dendritic structures enabling many different types of molecular behaviour, the future should certainly be viewed optimistically.

Finally a few 'thank-yous'! Most importantly, many thanks to all the authors and co-authors (around 100 of you!) who contributed such interesting papers for this special issue. Reading and editing your papers was a pleasure, and from your inspiration, this introduction wrote itself. Thanks also to Richard Taylor and Harry Wasserman for suggesting the project in the first place, and for their support during its progress. Finally, thanks to Janet and Kay, the ever-reliable *Tetrahedron* support team here in York, who kept me on track with all the pink folders and made sure that all the letters went out to the right people at the right time.

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