

Redesigning strategies in dendrimer syntheses: an “onion peel” approach

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(cette conférence sera présentée en français)

The strategies leading to dendrimer design have been too conservative and restrictive in that chemists have generally used the same repeating units to build dendrimers of higher generations. These approaches have not permitted full controls of their potential biophysical properties. By using: (i) different building blocks in between dendrimer generations in order to expand the scope of their applications; (ii) systematically use the full potential of sugars as multivalent scaffolds together with their inherent diversified stereochemical resources; and (iii) capitalise on the use of functional groups orthogonality, it is possible to change the way dendrimers have been generally constructed. This innovative “onion peel” approach provides much greater flexibility in the synthetic schemes leading to novel dendrimer architectures and properties. One direct outcome will undoubtedly result in improved water-solubility for biological applications and drug delivery.

For instance, when considering the use of carbohydrates as systematic building blocks toward dendrimer syntheses, their great potential can be readily realised. For instance, trioses, pentoses, hexoses, and even disaccharides represent typical cases of A_2B , A_3B , A_4B , and A_7B scaffolds, respectively. Any permutation in their utilization in subsequent dendrimer generation will rapidly lead to an impressive number of surface groups. For example, the use of riboside (an A_3B system) as starting residue, around which is linked three glucosides (A_4B), will provide 12-surface functionalities at the G1 only. The surface groups can be engineered to any functionalities, including sugar themselves that can be used in a wide range of applications, including antibacterial agents, gene transfections, drug delivery, and biosensors. To these exciting features, the stereochemical identities of the individual sugar building blocks also constitute further elements of versatility.

In addition, by not using all hydroxyl groups within a given series, an A_4B hexose system may become equivalent to a pentose corresponding to an A_3B unit. This approach can be strategically used for leaving residual water-soluble OH-groups within the linkage or for the attachment of drugs, probes and the like. Amino acid sugars such as glucosamine and glucuronic acid also represent additional features exploitable for specific applications.

Moreover, the recent photocatalyzed thiol-ene reaction between thiols and alkenes (or alkynes) has been shown to be orthogonal to the base-catalyzed S_N2 reaction between the same thiols but with halomethyl carbonylated derivatives, thus opening novel horizons for this efficient chemistry. Several examples of the above strategies will be illustrated.