A Novel Attempt to Control the Aggregation Number of Dendrons with a Saccharide

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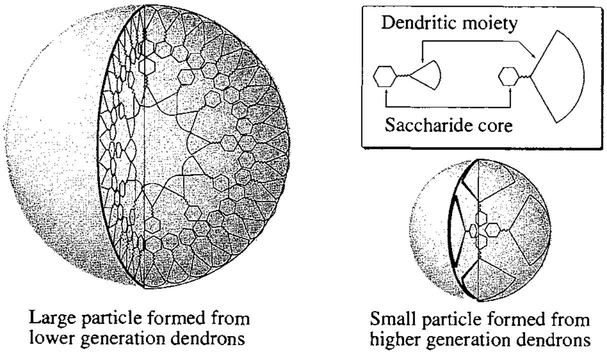
New dendrons containing a saccharide core were synthesized. In organic solvents these dendrons formed self-assembled particles due to the hydrogen-bonding interaction and the particle size decreased with the increase in the generation of dendrons. In this system the saccharide moieties provide a driving-force for aggregation whereas the dendritic moieties provide steric crowding for deaggregation. These two opposing effects balance with each other to control the particle size.

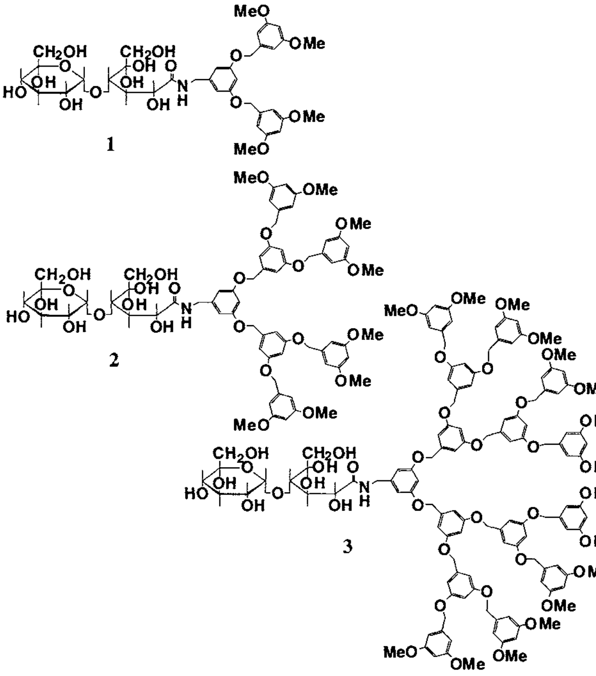
Supramolecular architectures constructed with non-covalent interactions have provoked a great deal of interest in building up novel nanostructures. Indeed, numerous articles have been devoted to syntheses of nanometer size components using non-covalent bonds; for example, self-assembled capsules,[1] nanotubes,[2] catenanes,[3] and helical polymers.[4] Originally, dendrimers were designed by using a core covalently-linked to dendrimers. It was later known, however, that well-defined self-assembled dendrimers can be also prepared from dendrons with a core constructed by metal-coordination[5] and hydrogen-bonding interactions.[6] The dendron aggregation number (DAN) of these assemblies depends on the specific coordination number of the metal or the specific hydrogen-bonding number in the core: by accurately controlling these numbers it is now possible to design the higher generation dendrimers.[5,6] In the foregoing systems, however, the interactions used in the core are so strong and so specific that DAN is primarily governed by the core structure but not by the dendron structure or the dendron generation. It is unclear, therefore, whether or not the dendrimer inside is sterically filled up with dendrons. Is there any other method by which the steric bulkiness of dendrons governs DAN and the resulting dendrimer inside is probably filled up with dendrons? One possible solution to this proposition would be to use a "nonspecific" aggregative group for the construction of the core. The purpose of this paper is to control the dendrimer size by steric bulkiness of branched dendritic moieties according to a self-assembled manner (Figure 1). Therefore, we designed compounds **1**-**3** bearing a polyethereal dendron to fill up the resultant dendrimer inside and a saccharide group to form a core by "nonspecific" hydrogen-bonding interactions. We have found that in the higher generation compound (*e.g.*, **3**), the dendrimer size becomes smaller because of steric bulkiness arising from the bulky dendron wedges (Figure 1). To the best of our knowledge, this work is the first example for the control of DAN by the dendron bulkiness.



Large particle formed from lower generation dendrons

Small particle formed from higher generation dendrons

Figure 1. Structures presumed for self-assembling dendrimer.



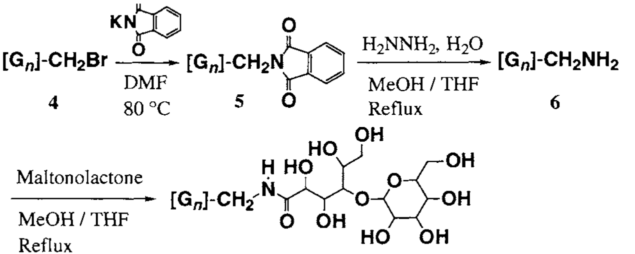
1

2

3

Compounds **1**-**3** were synthesized as shown in Scheme 1. We utilized Fréchet's convergent approach method for the synthesis of dendritic parts ($[G_n]$-CH_2Br **4**).[7] Parts **4** were converted into $[G_n]$-CH_2NH_2 **5** and then saccharide (maltonolactone) was introduced by the reaction with the amino group.[8] The products **1**-**3** were isolated as oil in 10-19% yield. Compounds **1**-**3** were identified by IR, ^1H NMR, and Mass [TOF-MS (dithranol, $NaClO_4$): **1**, *m/z* 819 ($M + Na^+$); **2**, *m/z* 1350 ($M + Na^+$); **3**, *m/z* 2452 ($M + Na^+$)] spectral evidence and elemental analyses.

To obtain direct evidence for the formation of self-assembled dendrimers, we measured the molecular-weight in solution by a dynamic light-scattering method (DLS: Otsuka Electronics DLS-7000). In $CHCl_3$ the formation of such aggregated dendrimers was confirmed for **1**-**3**. As summarized in Table 1, the average particle size decreased and the distribution became narrower with increasing dendron generation. Especially, the particle size for **3** (7.9 nm) was much smaller and showed a narrower distribution than others. The particle sizes as measured



1 (n = 2), **2** (n = 3), **3** (n = 4)

Scheme 1.

Table 1. Particle size and molecular weight determination by DLS[a]

Dendrons	DLS [Particle size (nm)] [b]	
	[Dendron] = 1.0 mmol dm^{-3}	[Dendron] = 20.0 mmol dm^{-3}
1	157.4 ± 28.8	114.5 ± 13.0
2	68.9 ± 12.7	71.4 ± 10.1
3	7.7 ± 1.1	7.9 ± 0.0

[a] 25 °C, $CHCl_3$, [dendron] = 1.0 or 20.0 mmol dm^{-3}. [b] The error range indicate the distribution of the particles

by the transmission electron micrograph (TEM) ranged between 60 and 250 nm for **1**, 50 and 100 nm for **2**, and 4 and 8 nm for **3** (Figure 2) and are comparable with those of DLS. We attempted to estimate the size of a dendron from surface pressure-area (π-A) isotherm and atomic force microscope (AFM), but the reliable monolayer useful for the computation was not obtained from these methods. Hence, we employed CPK molecular models. Examination with CPK molecular models suggests that the particle size of **3** (7.9 nm) is comparable with 2-fold of the molecular size of **3** (*ca.* 3.4 nm). The result strongly supports the view that the aggregate holds a dendrimer structure with the saccharide moieties in the core and the methoxy groups on the exterior surface. By a computational method (Discover 97), we simulated the stable DAN value of **3**. The results showed that it is difficult to assemble more than 10 dendrons of **3** to from a dendrimer. The optimum DAN values are 6–8. It is also seen from Table 1 that in these dendrimers, the particle diameter is smaller in the lower concentration than in the higher one whereas the distribution is conversely wider. Presumably, these dendrimer systems are subject, to some extent, to an aggregation-deaggregation equilibrium.[9]

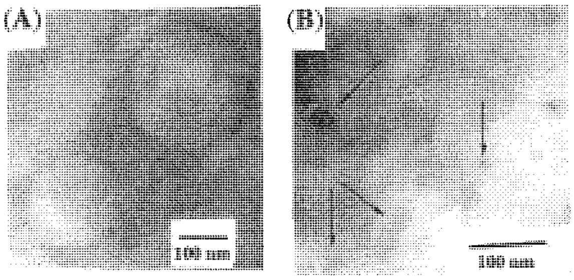


Figure 2. TEM images of aggregates formed by **1** (**A**) (negative staining, × 1.0 × 10^5), **3** (**B**) (negative staining, × 1.6 × 10^5)

In conclusion, we have here shown a general strategy for the control of the aggregation number according to a self-assembled manner. This novel method implies that in supramolecular chemistry the dendritic moieties can govern the aggregation number of self-assembled dendrimers. Now we continue to extend this study to the different dendron shape and difference core structure to create novel self-assembled dendrimers.

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9 To estimate DAN, vapor pressure osmometry (VPO: Knauer & co.) of **1**, **2**, and **3** was measured in $CHCl_3$: the apparent MW values were 11800±600, 12500±1500, and 5900±300, respectively. These results show that the DAN values are 15±3-mer for **1**, 9.5±1.5-mer for **2**, and 2.5±0.5-mer for **3**. These DAN values seem somewhat smaller than the dendrimer size obtained from the DLS measurements and the computational studies. Presumably, the present system is partially influenced by a monomer-aggregate equilibrium.