Properly Assembled Dendrons Can Be Immobilized into Dendrimers by *in situ* Cross-Link

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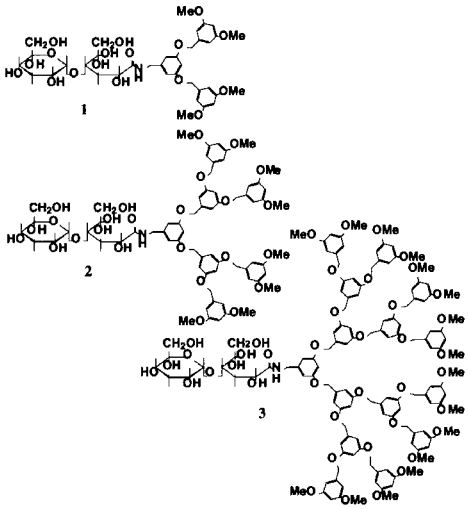
Aggregates obtained from saccharide-containing dendrons were immobilized by *in situ* cross-link with 1,3-phenylene diisocyanate. Characterizations of the resultant oligomers by dynamic light scattering and MALDI-TOF Mass have established that the higher generation dendrons which tend to aggregate into a spherical structure result in a dendritic polymer whereas the lower generation dendrons which tend to aggregate into a disordered large particle cannot result in such a dendrimer-shaped oligomer.

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] In these construction strategies, the hydrogen-bonding and metal-coordination interactions have played a crucial role. Originally, dendrimers were designed by using a core covalently-linked to dendrons. 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? Solution to this proposition would be to use a "nonspecific" aggregative group for the construction of the core.

As an answer to this question, we previously synthesized new dendrons containing a saccharide pivot (**1**, **2**, and **3**).[7] 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. Here, it occurred to us that if these hydrogen-bond-based, "unstable" aggregates can be immobilized by *in situ* cross-link, one may obtain the "stable" covalently-linked dendrimers which precisely reflect the aggregate architectures in solution. In general, secondary-valence forces frequently utilized in supramolecular chemistry play a key role in creation of various supramolecular architectures, but they frequently become "unstable" in different media. One may consider, therefore, that this is a concept to convert "temporary" architectures into "permanent" architectures by post-modification. There are only a few preceding examples in which this concept has successfully been applied to organogel systems.[8,9] We here report the *in situ* cross-link of self-assembled dendrons formed from **1**-**3** by 1,3-phenylene diisocyanate (PDI). This is the first example to apply the above concept to a dendrimer system.



The syntheses of dendrons **1**-**3** were reported previously.[7] Immobilization of dendrons was carried out as follows: the dendron was dissolved in chloroform with the aid of sonication. PDI was added to this solution, which was sonicated again. The solution was left at room temperature under a nitrogen atmosphere for 5 days. At this stage, we analyzed the aliquot of the reaction mixture by FT-IR spectroscopy to confirm that the absorption band of PDI (2270 cm^{-1}) has disappeared. The precipitate formed owing to 3-dimensional cross-link was filtered off with a membrane (Advantec, Cismic-13JP, 0.50 μm), the filtrate being subjected to GPC analyses. The sample was separated into the unreacted product and the polymerized product. The results are summarized in Table 1. It is seen from Table 1 that the amount of precipitated products obtained from **2** (Run 3) and **3** (Run 5) is much lower than that obtained from **1** (Run 1) whereas the amount of the polymerized products obtained from **2** (Run 3) and **3** (Run 5) is higher than that obtained from **1** (Run 1). It is known that **2** and **3** can form dendritic aggregates by saccharide-saccharide hydrogen-bonding interactions whereas **1** tends to form disordered large aggregates.[7] The results therefore imply that in **2** and **3** the cross-link by PDI predominantly occurs within the aggregates. The increase in PDI (compare Runs 1 and 3 with Runs 2 and 4, respectively) did not induce the significant increase in the polymerized and the precipitated products. The results were somewhat different from our expectation but the reason is not yet clear.

Table 1. Immobilization of dendrons by PDI

Run	Dendron (mg)	PDI (eq. to dendron) / mg	Products		
			Unreacted / mg	Ploymerized / mg	Precipitated (%) / mg
1	**1** (21.8)	4.5 (1.0)	6.8	1.6	17.9 (68.0)
2	**1** (9.9)	10.1 (5.0)	15.6	1.5	2.9 (14.5)
3	**2** (24.7)	3.0 (1.0)	18.9	2.7	6.1 (22.0)
4	**2** (23.4)	14.0 (5.0)	34.1	4.1	2.7 (7.2)
5	**3** (13.3)	0.9 (1.0)	7.8	2.5	27.5 (27.5)

The particle size of the aggregates present in the filtrates was estimated by dynamic light scattering (DLS; 25 °C, Ar laser; Otsuka Electronics DLS-7000). The results are summarized in Table 2. In chloroform where one can expect the aggregation due to the saccharide-saccharide hydrogen-bonding interaction, the particle size decreased in the order of **1** > **2** ≈ **3**. In THF where the contribution of such a hydrogen-bonding interaction is scarcely expected, only the particle size of **1** decreased drastically and the particle size decreased in the order of **3** ≈ **2** > **1**. The results indicate that the oligomer obtained from **1** can grow up to the larger aggregate because of the saccharide moiety being exposed to the surface whereas the oligomers obtained from **2** and **3** cannot aggregate intermolecularly because of the saccharide moiety being shielded in the core. In particular, the particle size of **3** is nearly constant before and after the cross-linking treatment. One may regard, therefore, that the **3** aggregate is immobilized as it is by *in situ* cross-link with PDI.

Table 2. Particle size as estimated by DLS

Sample	Solvent	Dendron size/nm		
		1	**2**	**3**
Before cross-link	$CHCl_3$	128-186	56-82	6-8
After cross-link	$CHCl_3$	34-48	4-9	4-7
After cross-link	THF	1-2	3-5	3-6

From examination of CPK molecular models the long axis (including the saccharide moiety) is estimated to be 2.5 nm, 3.0 nm, and 3.4 nm for **1**, **2**, and **3**, respectively. The results in Table 2, together with the fact that the saccharide moiety is shielded, suggest that the oligomers obtained from **2** and **3** should have a spherical, dendritic structure consisting of several dendrons. In contrast, the oligomer obtained from **1** should be still insufficient to take such a dendritic conformation. This difference was further corroborated by MALDI-TOF Mass spectroscopy [PerSeptive Voyager RP, matrix: *trans*-3-indoleacrylic acid (IAA) or dithranol]. Examination of the results (Table 3) reveals that the oligomer obtained from **3** consists of cross-linked 2-5 dendrons. These numbers are large enough to unimolecularly construct a dendrimer. In contrast, the major products obtained from **1** are the dimers, which further aggregate in chloroform owing to the intermolecular hydrogen-bonding interaction. The result obtained from **2** is not so clear as that obtained from **3** and shows the intermediary character.

Table 3. Mass spectral analyses[a]

Run[c]	Sample after cross-link	Peaks		Assignment
		m/z	Relative intensity	
1	**1**-PDI	945	25000	987 [(**1**+PDI+H_2O+Na)$^+$]
		1730	2500	1773 [(2·**1**+PDI+H_2O+Na)$^+$]
3	**2**-PDI	1491	12000	1494 [**2**+PDI)$^+$]
		1651	6000	1649 [(2·**2**+PDI)$^+$]
		2981	1800	2984 [(2·**2**+2·PDI)$^+$]
5	**3**-PDI	2582	3500	2583 [(**3**+PDI)$^+$]
		5000	2000	5043 [(2·**3**+PDI)$^+$][b]
		7580	1300	7580 [(3·**3**+2·PDI)$^+$][b]
		10160	1000	10216 [(4·**3**+3·PDI)$^+$][b]
		12741	900	12823 [(5·**3**+4·PDI)$^+$][b]

[a] IAA or dirhranol was used as a matrix. [b] The numbers indicate peak-top values. [c] The runs correspond to those in Table 1.

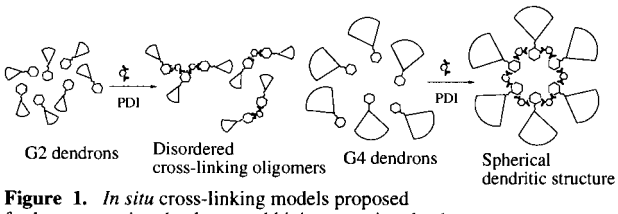


Figure 1. *In situ* cross-linking models proposed for low generation dendrons and high generation dendrons.

Based on the foregoing spectral evidence, one may propose the *in situ* cross-linking mode as shown in Figure 1: that is, **3** which can keep a spherical aggregate structure is cross-linked as it is because of the ordered structure and the high local saccharide concentration in the core site, whereas **1** which exists as a disordered aggregate cannot be cross-linked so efficiently. In conclusion, we have here shown a general strategy for conversion of "unstable" uncovalent aggregates into "stable" covalently-linked aggregate by *in situ* cross-link. We believe that this concept is very crucial to extend the field of supramolecular chemistry to the peripheral fields.

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