

Iterative Molecular Assembly Based on the Cation-Pool Method. Convergent Synthesis of Dendritic Molecules

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Iterative processes that are based on multiple use of the same reaction sequence serve as powerful methods for construction of relatively large structurally well-defined organic molecules.¹ Various iterative processes have been developed, and they are widely utilized in the synthesis of organic compounds. To achieve such processes, a method involving generation and accumulation of a highly reactive species (activation) followed by the coupling reaction with a building block, which is equipped with a potential active site for the generation of the reactive species in the next sequence, is quite effective (Figure 1).

The cation-pool method² that involves generation and accumulation of highly reactive organic cations using anodic oxidation³ in the absence of a nucleophile seems to be suitable for the present purpose. Recently we have reported that diarylcarbenium ions **2**⁴ can be generated and accumulated by low-temperature anodic oxidation of diarylmethanes **1** (Scheme 1a).⁵

Based on this finding, the following working hypothesis came to mind. If diarylcarbenium ion **2** reacts with two benzene rings of diphenylmethane derivative **3** in a Friedel–Crafts manner (Scheme 1b), the resulting extended diarylmethane **4** could be used as a precursor of the next activation–coupling sequence (Scheme 1c). Consequently, multiple use of this sequence leads to convergent synthesis⁶ of dendritic molecules⁷ (Scheme 1). This concept works, and we report herein the results of our proof-of-principle study on iterative molecular assembly using the cation-pool method.

Although the anodic oxidation of diphenylmethane led to the formation of a complex mixture, the reactions of substituted diphenylmethanes **1** (Ar = *p*-FC₆H₄, *p*-CH₃C₆H₄, *p*-CH₃OC₆H₄, *p*-ClC₆H₄, etc.) gave rise to effective formation of the corresponding diarylcarbenium ion pools.³ We chose to use di(*p*-fluorophenyl)methane **1a** (Ar = *p*-FC₆H₄) as a starting material because the conversion to diarylcarbenium ion **2a** is very efficient among the examined (Scheme 2). The resulting **2a** was allowed to react with diphenylmethane **3a** (X = H), but the expected 1:2 adduct **4a** (Ar = *p*-FC₆H₄, X = H) was not produced. Instead, the 1:1 adduct **7** was obtained in very low yield (11%).

To solve this problem, a silyl-substituted diphenylmethane, **3b** (X = SiMe₃), was used because the introduction of a silyl group at the benzylic position increases the HOMO level of the benzene ring to increase its reactivity.⁸ Also if the outer-sphere electron transfer takes place, the C–Si bond in the resulting radical cation is readily cleaved.⁹ However, Mayr, Fukuzumi, and co-workers reported that the outer-sphere electron transfer is definitely excluded for the reaction of diarylcarbenium ions with nucleophiles.¹⁰ In fact, the reaction of **3b** (X = SiMe₃) with **2a** proceeded without cleavage of the C–Si bond to give desired **4b** (Ar = *p*-FC₆H₄, X = SiMe₃) [G-1, the first generation] in 79% yield.¹¹

There is another merit in the use of a silyl group. For the oxidation of **4b** to generate diarylcarbenium ion **5** in the next

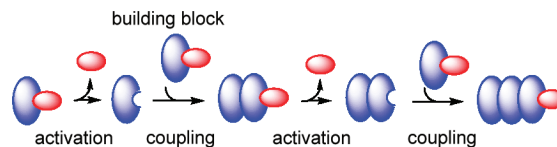
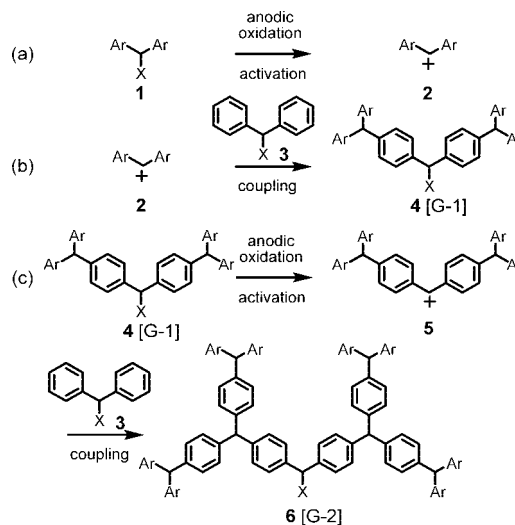
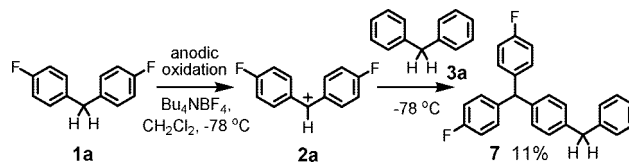


Figure 1. Iterative process based on activation–coupling sequence.

Scheme 1



Scheme 2



sequence, the silyl group works as an electroauxiliary,¹² which activates the molecule toward oxidation and controls the reaction pathway. In fact, the oxidation potential of **4b** (1.25 V) was found to be much less positive than those of **1a** (1.77 V) and **3a** (1.81 V). The anodic oxidation of **4b** took place smoothly, and the C–Si bond was cleaved selectively¹³ without affecting other C–H bonds at benzylic positions. The resulting **5** (Ar = *p*-FC₆H₄) was allowed to react with **3b** (X = SiMe₃) to give **6** (Ar = *p*-FC₆H₄, X = SiMe₃) [G-2, the second generation] in 75% yield.¹⁴

The anodic oxidation of **6** was accomplished in a similar manner. The resulting solution of diarylcarbenium ion **8** exhibited a single set of ¹H NMR signals at –78 °C (Figure 2). A signal at 9.87 ppm (singlet) is assigned to the proton adjacent to the cationic carbon (H^a). The solution also exhibited a ¹³C NMR signal at 193.7 ppm

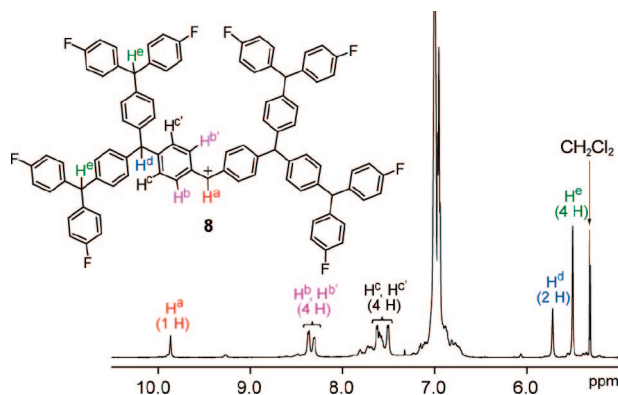


Figure 2. ^1H NMR spectrum of dendritic diarylcarbenium ion **8**.

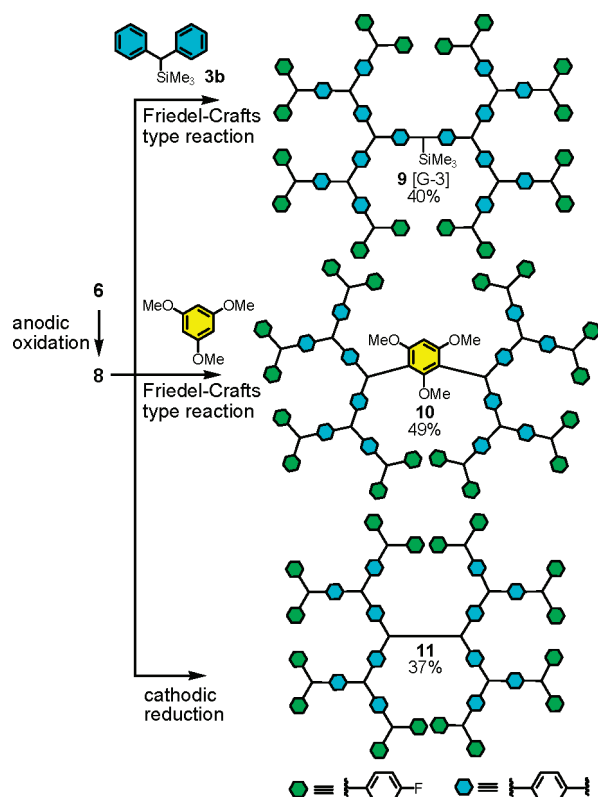


Figure 3. Dendritic molecules synthesized from cation **8**.

from the cationic carbon. These chemical shifts are very similar to those of **2a** (^1H NMR: 9.90 ppm, ^{13}C NMR: 192.6 ppm) and **5** (^1H NMR: 9.92 ppm, ^{13}C NMR: 194.4 ppm).

Dendritic diarylcarbenium ion **8** has sufficient reactivity for further transformation. In Figure 3, the reaction with **3b** proceeded to give **9** [G-3, the third generation] (40%, FAB-MS: m/z calcd for $\text{C}_{198}\text{H}_{144}\text{F}_{16}\text{Si}$: 2853.0764, found: 2853.0782), which can be utilized for the next sequence. The Friedel–Crafts type reaction with 1,3,5-trimethoxybenzene gave the disubstituted product **10** in 49% yield (FAB-MS: m/z calcd for $\text{C}_{191}\text{H}_{136}\text{O}_3\text{F}_{16}$: 2781.0234, found: 2781.0198), suggesting that dendritic molecules having various core structures can be synthesized in a similar manner. Cation **8** is also useful as a precursor for free radical reactions.¹⁵ For example, cathodic reduction gave homocoupling product **11**, although the

yield was not optimized (37%, FAB-MS: m/z calcd for $\text{C}_{182}\text{H}_{126}\text{F}_{16}$: 2614.9604, found: 2614.9590).

In summary, we have developed a new iterative and convergent method for making dendritic molecules based on the cation-pool method. The silyl-substituted diphenylmethane serves as a useful building block. Development of new building blocks and applications to synthesis of dendrimers that have various cores and functional groups exhibiting a variety of functions¹⁶ are under way in our laboratory.

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Supporting Information Available: Experimental procedures and spectroscopic data of compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>

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