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Divergent Approach for Synthesis and Terminal Modifications of Dendritic Polyphenylazomethines

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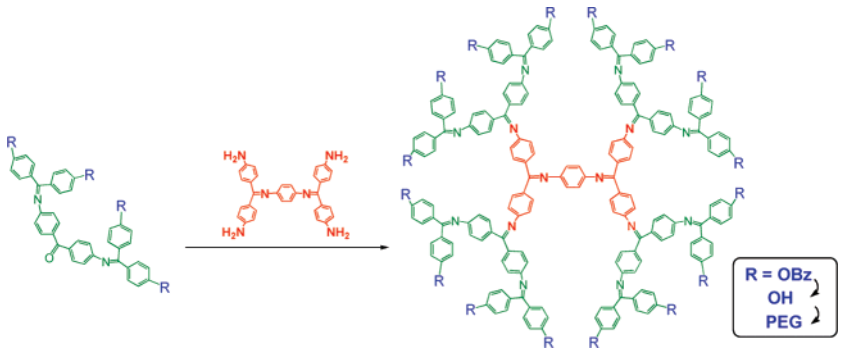
ABSTRACT



In the past, dendritic polyphenylazomethines (DPA) have been synthesized via the convergent method. However, the convergent method has problems such as difficult terminal-group modifications and an increased number of steps. Therefore, we synthesized the terminal-protected DPA to construct the dendritic structure via the divergent method. The combination of the convergent method and the divergent method easily achieved the rapid synthesis of a higher generation dendrimer. Furthermore, we succeeded in the synthesis of the water-soluble PEG-DPA via the divergent method using the ester-DPA.

Dendrimers have a single molecular weight and three-dimensional spreading structure in which the density of the branches increases radially outward.[1] On the basis of these properties, dendrimers have potential use in drug delivery systems,[2] electronic materials,[3] catalysts,[4] molecular recognitions,[5] and charge separation systems.[6] Dendritic polyphenylazomethines (DPA) have π-conjugated rigid backbones, a basicity gradient from the core imines to the terminal imines, and a stepwise complexation property.[7] Due to these properties, DPA was used as the hole-transport material for OLEDs,[8] oxidative polymerization catalyst for fluorophenols,[9] solar cells,[10] and self-assemblies.[11]

DPA has such unique properties, but the end-group modification has rarely been done[12,13] because, to date, DPA

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has only been constructed using the convergent method. The end-group modification with complete control enables the further addition of the functions for DPA and extends the applications of DPA.

In most cases, dendrimers are constructed by the convergent method or the divergent method only. The convergent method forms a dendrimer from outside to inside. With this method, it is easy to change the core group but difficult to change the end group. On the other hand, with the divergent method, it is easy to change the end group but difficult to change the core group. Furthermore, stepwise synthesis only using the convergent method or the divergent method requires a significant number of steps and a long time. Therefore, a combination of the divergent method and the convergent method called the double-stage convergent method is a good approach to alleviate these problems (Figure 1).[14,15]

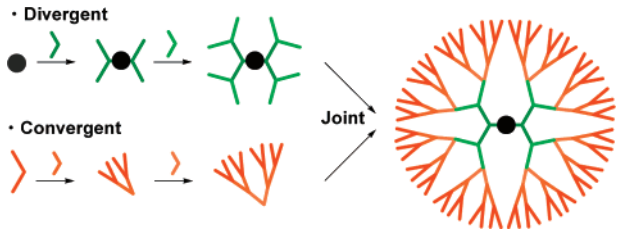


Figure 1. Synthesis of dendrimer via the double-stage convergent method. The divergent method constructs the inner frame, and the convergent method constructs the outer frame. The combination of the divergent method and the convergent method allowed the easy and rapid synthesis of dendrimers with various types of cores, terminal groups, and generations.

We now report the synthesis of DPA using the double-stage convergent method and the synthesis of the water-soluble DPA by the divergent method.

An appropriate protecting group for the amine was required for the divergent synthesis of DPA. The protecting group had to resist harsh, dehydrating conditions such as $TiCl_4$ (Lewis acid) in the presence of DABCO (base) and be removed without breaking the imines. We investigated various protecting groups and found that the amide group has such properties. We investigated the effect of varying the amide substituents on the stability and solubility (Figure 2). Stability during silica gel chromatography decreased when

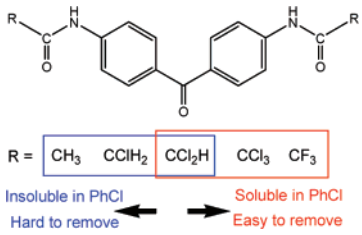
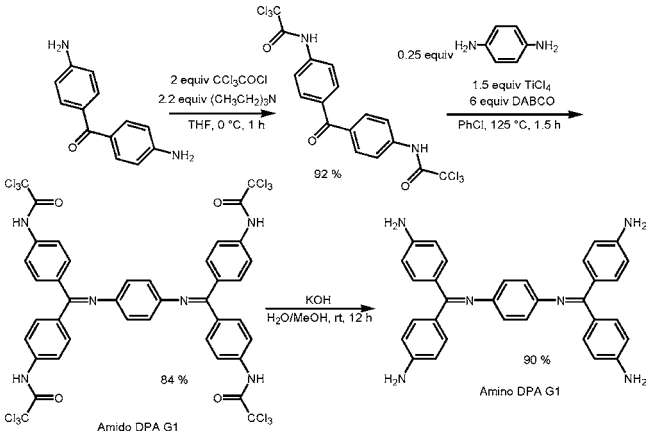


Figure 2. The effect of varying the amide substituents on the stability and solubility. When R is an electron-rich group, the amide becomes too stable for hydrolysis and insoluble in PhCl. On the other hand, when R is an electron-poor group, the amide becomes unstable for hydrolysis and soluble in PhCl. As a result, the trichloroacetamide ($R = CCl_3$) has the appropriate solubility and stability.

the amide was substituted with a CF_3, whereas a CH_3 substituent resulted in decreased solubility in PhCl and was also difficult to remove. As a result, the best approach during the synthesis of DPA was to protect the amine group as a trichloroacetamide.

Amido-DPA G1 was synthesized by the dehydration of *p*-phenylenediamine and 4,4′-trichloroacetoamidobenzophenone (Scheme 1). Under basic conditions, amido-DPA G1

Scheme 1. Synthesis of Amido-DPA G1 and Amino-DPA G1



was hydrolyzed to form amino-DPA G1. The obtained amino-DPA G1 was reacted with DPA dendron G3 to synthesize DPA G4 (Figure 3). The MALDI TOF MS

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spectrum of the reaction mixture showed the generation of DPA G4 via DPA dendron G3. This method was also used

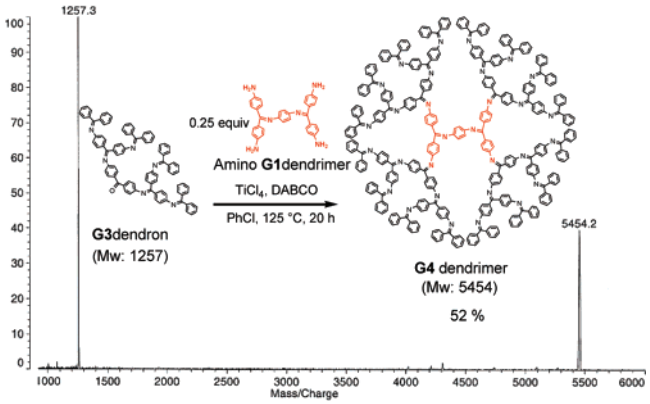


Figure 3. Synthesis of DPA G4 via the combination of amino-DPA G1 and DPA dendron G3.

for the synthesis of DPA dendrons (see Supporting Information).[15] For the DPA synthesis, this combination of the divergent method and the convergent method is a good approach because of the separate construction of DPA from the inside and outside and the control of the number of reaction sites.

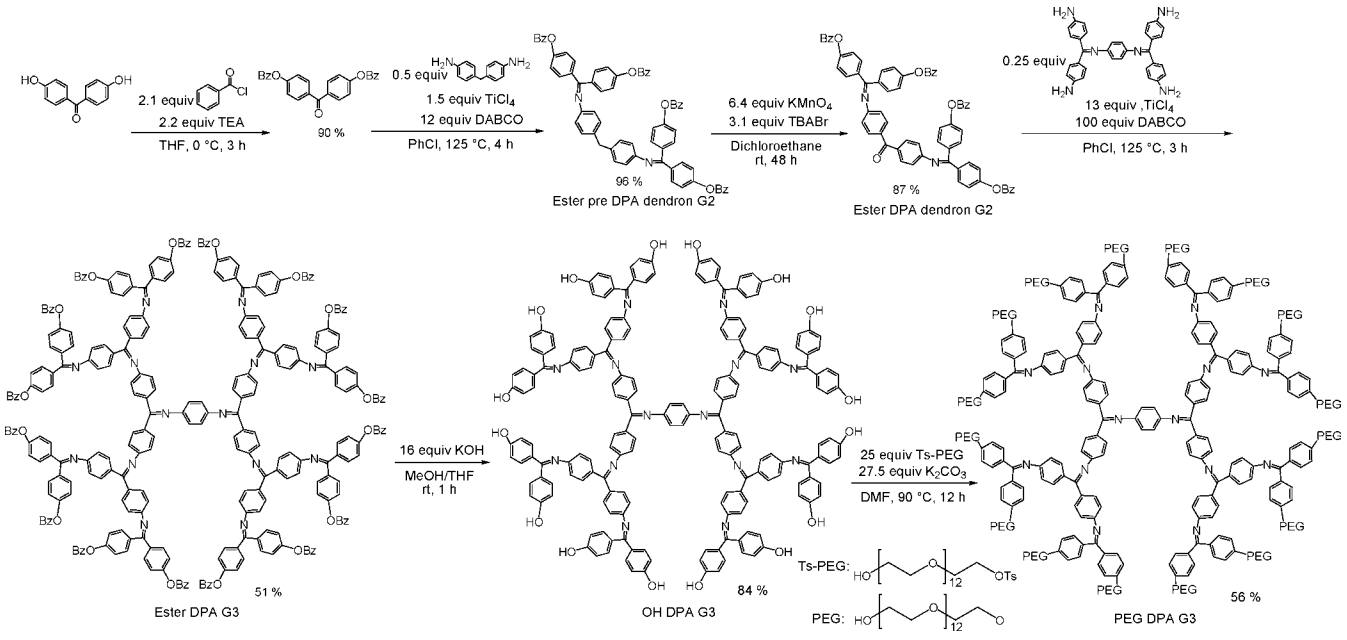
Initially, for the end-group modification of DPA, only the substituents that were resistant to dehydrating and oxidizing conditions were used. Furthermore, the convergent approach prevents easy modification of the end group. However, if the modification was performed as in the divergent approach, various end-group modifications are possible. Because the amide group is a good protecting group for such conditions, the ester group was also expected to be successful for this purpose. The ester is a protecting group for carboxylic acid and hydroxyl groups. These groups are useful for the end-group modification. In these, we selected the phenolic hydroxyl group because of its reactivity toward the etheration under mild conditions and the stability of the formed ether bond. Therefore, we used the ester as a protecting group for the phenolic hydroxyl group and performed the end-group modification through the etheration of the phenolic hydroxyl group on the terminal of the DPA.

We selected a benzoyl ester as the protecting group. First, 4,4′-dihydroxybenzophenone was reacted with benzoyl chloride to obtain 4,4′-dibenzoyloxybenzophenone (Scheme 2). This ester benzophenone and 4,4′-diaminodiphenylmethane were dehydrated to form the precursor of ester-DPA dendron G2. The precursor was then oxidized to ester-DPA dendron G2 by $KMnO_4$ in the presence of TBABr. The obtained ester-DPA dendron G2 was reacted with amino-DPA G1 to form ester-DPA G3. Furthermore, the ester-DPA G3 was hydrolyzed under basic conditions to form OH-DPA G3.

As various functions were possible by modification, we tried the synthesis of the water-soluble DPA. For addition of the hydrophilic property to DPA, a sulfonic acid salt, carboxylic acid salt, ammonium salt, and polyethyleneglycol (PEG) were considered. For these salts, we used PEG as an additional modification group because it makes handling of the DPA easier during reaction and purification.

To obtain a sufficient water solubility, we used dodecaethyleneglycol. First, the PEG was monotosylated using

Scheme 2. Synthesis of Ester-DPA G3 via Amino-DPA G1 and Ester-DPA Dendron G2 and Synthesis of PEG-DPA G3 via Ester- and OH-DPA G3



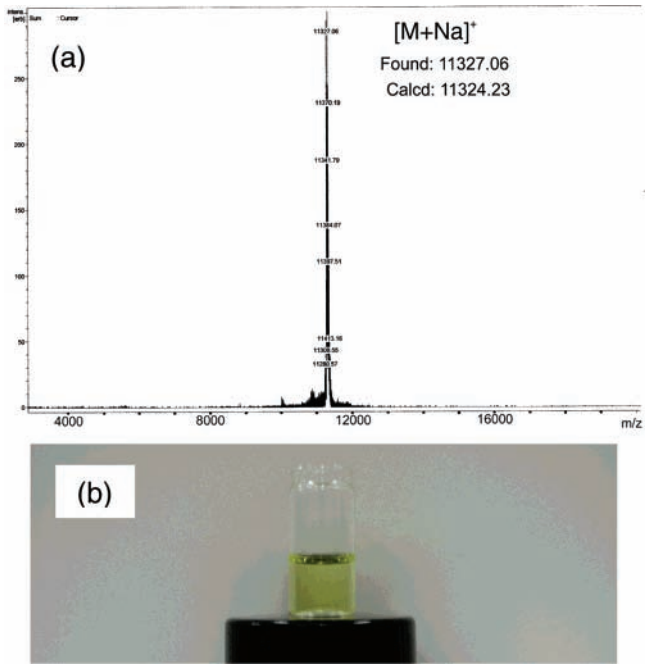


Figure 4. (a) MALDI TOF MS spectrum of PEG-DPA G3 and (b) PEG-DPA G3 dissolved in water.

Ag_2O (see Supporting Information).[16] This monotosylated PEG was reacted with the OH-DPA G3 to obtain PEG-DPA G3 as an oil. The MALDI TOF MS spectrum showed a single peak, and the observed molecular weight agreed with the calculated one (Figure 4a). The water solubility of the PEG-DPA G3 was also confirmed (Figure 4b). We are studying the applications of the water-soluble dendrimer for drug delivery systems, MRI, self-assembling, and organic molecules and metal ion assembling.

In conclusion, we synthesized DPA by a combination of the divergent method and the convergent method. This combination allowed an easy and rapid synthesis of DPA. Further, we tried the end-group modification by the divergent method. The water-soluble PEG-DPA was synthesized from the ester-DPA G3.

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Note Added after ASAP Publication. Reference 7c was added shortly after ASAP publication on November 13, 2007.

Supporting Information Available: Detailed experimental procedures and characterization data of the dendrons and dendrimers. This material is available free of charge via the Internet at http://pubs.acs.org.

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