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From Small Building Blocks to Complex Molecular Architecture

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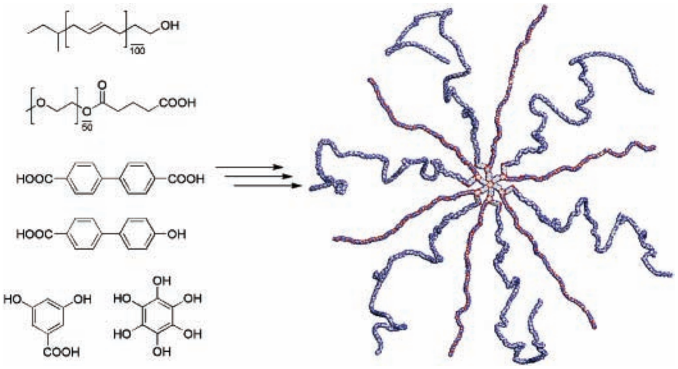
ABSTRACT



We describe a synthesis of a dendrimer-like amphiphile containing a flat rigid core and 12 hydrophobic and hydrophilic arms. We employ a modular approach based on stepwise protection chemistry starting from simple building blocks. The key feature of this approach is the absence of a polymerization step, which makes it applicable for linear monofunctionalized precursors of any kind. This strategy also allows for precise control of the number of arms and ensures their alternating arrangement.

The synthesis of dendritic[1] and starlike[2] molecules is more challenging than the preparation of linear structures, yet these compounds attract greater attention due to their unusual properties. The availability of well-defined branched molecules is still limited, and new synthetic strategies should be found. In principle, any living anionic polymerization from the surface of poly(divinylbenzene) nodules offers a quick one-step synthesis of star-shaped molecules.[3] However, the number and the spatial distribution of arms cannot be controlled in this case, and only indirect methods can estimate these critically important parameters. The use of well-defined cores, such as carbosilane dendrimers,[4] calixarenes,[5] and dendritic-linear hybrid structures,[6] alleviates this limitation but immediately brings another one. The initiator must not have any electrophilic sites in order to survive highly basic anionic conditions. Only a handful of multifunctional initiators can meet this requirement.[7] An alternative is given by the atom transfer radical polymerization (ATRP) and nitroxide-mediated polymerization (NMP), which exhibit much greater functional group tolerance.[8,9] Nonetheless, many

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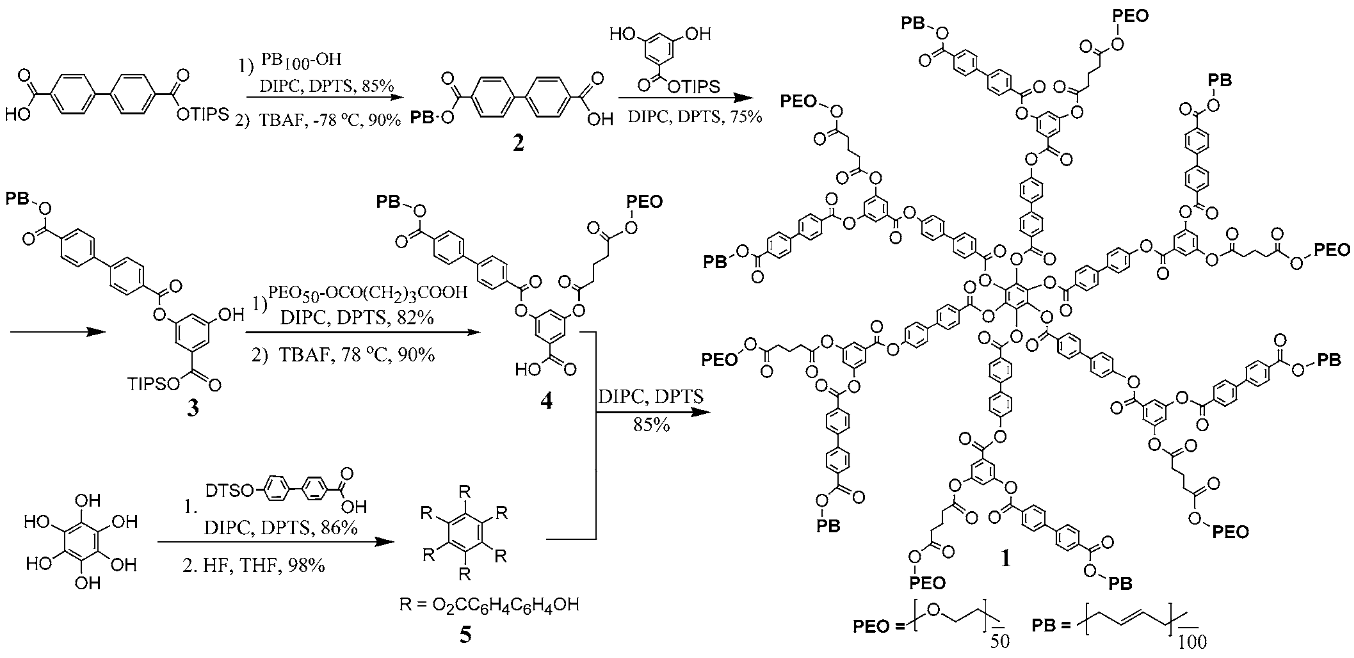
Scheme 1. Synthesis of Starlike Amphiphile **1**



important monomers, such as dienes, oxiranes, and cyclosiloxanes, do not polymerize under ATRP conditions. Here, we demonstrate how complex macromolecular architectures can be constructed from small building blocks and commercially available linear precursors. This approach avoids the polymerization and all of the limitations assosiated with it and allows for the synthesis of macromolecular branched structures with a broad range of monomeric units. As an example, we used this approach to prepare high molecular weight (MW ~50000 g/mol) starlike amphiphiles containing poly(ethylene oxide) and polybutadiene chains. This is an important synthetic target because *heteroarm* star-shaped PB-PEO structures prepared by polymerization remain unknown, and only one example of a *core*−*shell* PB-PEO star (four arms) synthesized by polymerization has been reported to date.[10]

We previously described the synthesis of starlike molecules containing short hydrophobic chains (20 repeat units, MW = 1000 g/mol).[11] The purpose of this communication is to demonstrate that much larger structures can be constructed using a modular stepwise approach. We employ protection chemistry starting from commercially available linear molecules. In addition, various multifunctional cores can be used in this route because coupling between the presynthesized hairpin-like molecules and the multifunctional core proceeds under mild esterification conditions at room temperature.

The first part of the overall synthesis required the preparation of a hairpin-like PB-PEO diblock molecule **4** with the carboxyl group at the focal point (Scheme 1). Silyl-protected 3,5-dihydroxybenzoic acid (DHBA) can be used as a junction point when COOH-terminated linear polymers are coupled to it using 1,3-diisopropylcarbodiimide and DPTS.[12] However, our attempts to couple commercially available carboxyl-terminated PB resulted in a very poor yield (~20%), which was due to a low degree of carboxylation, and the presence of a significant amount of dead chains. For that reason, we used OH-terminated polybutadiene (MW = 5400 g/mol, PDI = 1.12) and switched its terminus to carboxyl group via attachment of silyl-protected biphenyl dicarboxylic acid (Scheme 1). Incorporation of a biphenyl moiety was also beneficial in terms of NMR analysis because it introduced additional proton resonances that served as highly reliable internal references. Deblocking of the triisopropylsilyl (TIPS) group followed by esterification of the resulting compound **2** with excess carboxyl-protected DHBA (10 equiv) produced functional precursor **3**, which was purified by flash chromatography and characterized by ^{1}H NMR and size-exclusion chromatography (SEC).

The next step involved the reaction with glutaric acid-terminated PEO (MW = 2200, PDI = 1.15), which was

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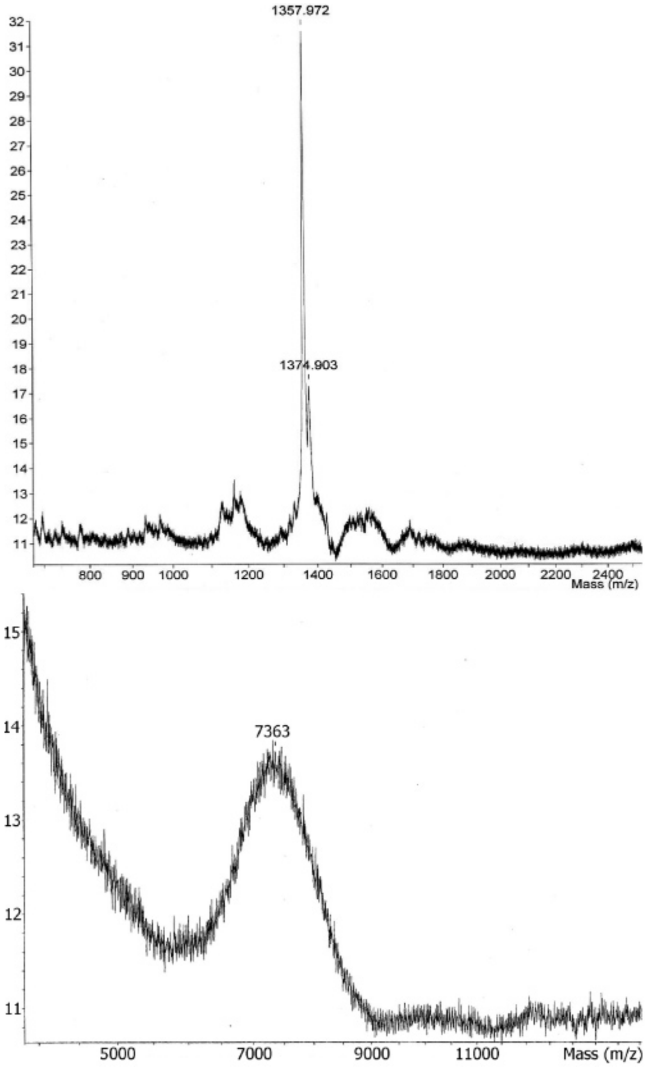

Figure 1. MALDI-TOF spectra of hexabiphenyl core **5** (top) and PB-PEO diblock **4** (bottom).

found to be a rapid conversion, although the isolation of the amphiphilic product was quite challenging and resulted in some losses upon purification on silica gel eluting with methanol/chloroform (11:89 v/v) mixture. We also found that partial reesterification takes place in the presence of excess methanol at temperatures above 50 °C.

To activate the focal point of the amphiphile **4**, we used TBAF deprotection at subambient temperature (−78 °C), which allows for a selective cleavage of the silyl group in the presence of alkyl aryl esters that remain intact under these mild basic conditions. The resulting hairpin-like PB-PEO amphiphile **4** was purified by column chromatography, and its structure was confirmed by ^{1}H NMR, whereas its molecular weight was determined by MALDI-TOF (MW = 7400) and SEC (MW = 13800, PDI = 1.12).

The diblock PB-PEO molecule **4** offers an opportunity to produce an amphiphilic heteroarm star in just one step provided the coupling with a complementary multifunctional core is highly efficient. On the other hand, the separation of diblock **4** from a target starlike structure can be rather cumbersome since the affinity of PB-PEO to silica gel (R_f) may not change appreciably upon such transformation. This was indeed observed in our initial experiments. To avoid the tedious separation, we used only a slight excess of starting material (6.3 equiv) with respect to a hexabiphenyl core **5**, which was synthesized separately. Accurate estimation of the reagents weight ratio was possible due to availability of the absolute molecular weights of both PB-PEO amphiphile **4** and the hexafunctional core **5** as determined by MALDI-TOF (Figure 1).

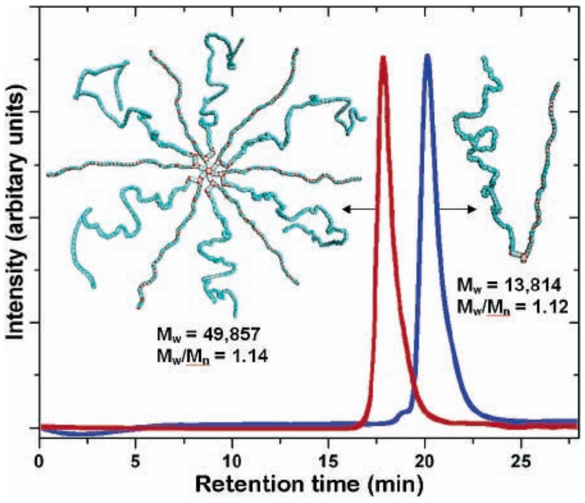

Figure 2. SEC traces of diblock precursor **4** (blue) and the star-shaped PB-PEO amphiphile **1** (red).

The esterification was found to proceed very rapidly, and only a trace amount of starting compound **4** was observed in the SEC trace of the reaction mixture after 1 h (Figure 2). The appearance of a high molar mass peak with MW = 49.8 kDa and PDI = 1.14 suggested that the reaction was nearly complete and that mainly hexa-substituted product formed because the polydispersity of the new peak was as low as that of the starting material (1.14 vs 1.12). The structure of the product was confirmed by ^{1}H NMR as the new resonances from the core biphenyls appeared in the spectrum and their integration was consistent with the expected numbers. Thus, there is no steric limitation in this final step even though the degree of polymerization of the diblock compound **4** is greater than 150.

Our preliminary observations show that the star-shaped amphiphile **1** forms translucent solutions in hexane and water which is indicative of large micellar aggregates present at exceedingly low concentrations (~0.3 wt %). Nearly complete disappearance of the PEO signal at 3.6 ppm was observed in deuterated hexane, whereas PB signals at 5.4 and 2.1 ppm did not change in comparison with spectra obtained in a nonselective solvent (CD_2Cl_2). On the other hand, PB resonances were considerably suppressed (~80% reduction) in NMR spectra collected from D_2O solutions of star-shaped amphiphile **1**. Hexane and water are selective solvents for **1,** and these experiments indicate the self-assembling behavior and the formation of both regular and reverse micelles.

In conclusion, we developed an efficient route to high molecular weight PB-PEO star-shaped amphiphiles. The modular approach employed here is very versatile and may allow for the synthesis of star-shaped molecules with various types of arms as long as the monofunctional linear precursors are available. This synthetic strategy may help overcome classical limitations of living polymerization techniques and serve as a complementary tool to construct complex macromolecular architectures.

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

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