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 and starlike 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. 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, calixarenes, and dendritic-linear hybrid structures, 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. An alternative is given by the atom transfer radical polymerization (ATRP) and nitroxide-mediated polymerization (NMP), which exhibit much greater functional group tolerance. Nonetheless, many

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important monomers, such as dienes, oxiranes, and cyclosi-
loxanes, do not polymerize under ATRP conditions. Here,
we demonstrate how complex macromolecular architectures
can be constructed from small building blocks and com-
mercially available linear precursors. This approach avoids
the polymerization and all of the limitations associated 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 mol-
ecules. 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 carboxy-
lation, and the presence of a significant amount of dead
chains. For that reason, we used OH-terminated polybuta-
diene (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 esterifica-
tion of the resulting compound 2 with excess carboxyl-
protected DHBA (10 equiv) produced functional precursor
3, which was purified by flash chromatography and char-
acterized by 1H NMR and size-exclusion chromatography
(SEC).

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

Scheme 1. Synthesis of Starlike Amphiphile 1

![Scheme 1](image-url)
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 1H NMR, whereas its molecular weight was determined by MALDI-TOF (MW = 7400) and SEC (MW = 13800, PDI = 1.12).

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 1H 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 (CD2Cl2). On the other hand, PB resonances were considerably suppressed (~80% reduction) in NMR spectra collected from D2O solutions of star-shaped amphiphile 1.

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

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