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Amphiphilic Carborane-Containing Diblock Copolymers

Yoan C. Simon, Christian Ohm, Melanie J. Zimny, and E. Bryan Coughlin*

Department of Polymer Science and Engineering, University of Massachusetts, Amherst, Massachusetts 01003

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Introduction. Boron-containing polymers were historically commercialized primarily for their chemical and thermomechanical resistance (e.g., Olin's DEXSIL and Union Carbide's UCARSIL).^{1,2} In addition, boron-containing polymers have been used to immobilize catalysts, as sensor materials, separation media, and optical materials.³ For instance, because of their remarkable stability, the icosahedral carboranes have been chiefly viewed as ideal candidates for the chemical/thermal strengthening of polymers.^{1,2,4} However, recently, there has been a growing interest in incorporating these boron clusters into tailored macromolecular structures by means of living or quasi-living polymerizations.^{5–7} This recrudescence stems from the rising awareness that carborane-based macromolecules can span a gamut of applications, for example, nonlinear optical materials,^{8–13} precursors for ceramics,^{14–17} boron neutron capture therapy of cancer (BNCT),^{18,19} etc.

Ober has developed boron-containing polymeric masks for extreme UV lithography beginning with poly(styrene-*b*-1,2-butadiene) diblock copolymers followed by a post-polymerization functionalization approach employing the pendant olefins and a hydroboration/hydroxylation method to attach pendant carborane cages.²⁰ Adronov was the first to report the direct incorporation of carborane moieties in well-defined macromolecules (PDI < 1.2) by controlled radical polymerization and by sequential dendrimer synthesis.^{6,21,22} In their controlled radical experiment, they have demonstrated the possibility of incorporating carboranes in polymers of narrow polydispersity. However, loss of control upon attempted formation of the second block hampered the formation of well-defined amphiphilic structures.^{6,21} Seminal works by Sneddon and co-workers on precursors for boron-containing ceramics have highlighted the use of ring-opening metathesis polymerization (ROMP) to obtain high boron content polymers that can undergo pyrolysis to form a boron carbide/carbon network.^{5,23–26} Building upon this work, Malenfant et al. have recently shown how ROMP can be used for the synthesis of boron-containing diblock copolymers and their subsequent transformation into nano-ordered ceramics.⁷

In this report, the synthesis of a boron-containing monomer based on an oxonornornene-functionalized *o*-carborane and its subsequent ring-opening metathesis polymerization to obtain low-polydispersity (PDI < 1.1) high-molecular-weight carborane-based polymers is described. The formation of amphiphilic block copolymers is demonstrated via sequential monomer addition, followed by deprotection of the second block to generate the amphiphilic copolymers. Initial solution behavior studies by dynamic light scattering (DLS) are also discussed. These copolymers are unique examples of a narrow polydispersity amphiphilic architectures incorporating carboranes that will permit the exploration of potential applications ranging from

nanoscopic templates in thin film applications²⁷ to boron neutron capture therapy for the treatment of cancer.^{18,28}

Results and Discussion. Gomez et al. had previously reported a protocol to synthesize 3-[2-(*tert*-butyldimethylsilyl)-1,2-dicarba-*closo*-dodecaboran(12)-yl]propan-1-ol, **2** (Figure 1).²⁹ The synthesis of this entity was key to the elaboration of the targeted monomer **3**. However, while reproducing their experiments, slight modifications were introduced. The distillation of *o*-(C₂B₁₀H₁₁)SiMe₂tBu (**1**) occurred at higher pressure and lower temperatures than previously reported (Supporting Information).

The oxonornornene derivative **3** was synthesized via Mitsunobu coupling of *exo*-7-oxonornornene imide and **2**.^{30,31} A previous study in our group had demonstrated the difference in polymerization rates between *exo* and *endo* carborane-containing norbornene derivatives,³² corroborating findings by Grubbs and co-workers.³³ In order to maximize the polymerization rates, an isomerically pure *exo* compound was needed. Furthermore, to avoid the problems of head-to-head and head-to-tail additions, a symmetric monomer was desirable. To address these issues, we undertook the synthesis of SONIC (silyl-protected oxonornornene imide carborane), whose symmetry and stereochemistry were specifically designed for fast and controlled polymerization kinetics. This control permits the exploration of well-defined architectures, such as blocky structures. The homopolymerization of SONIC afforded polySONIC **4** in good yields (>82%) and very narrow polydispersity (PDI < 1.1) (Supporting Information). To achieve this task, advantage was taken of the versatility and efficacy of ROMP catalysts, which not only give a living character to the polymerization but also display a greater tolerance to diverse chemical functionalities.³⁴ The reaction happens indeed within minutes and offers good control over molecular weight and molecular weight distribution, with no apparent broadening even for the highest *M_n* (Supporting Information).

The diblock copolymers were obtained by sequential addition of SONIC and BONIA (Boc-protected oxonornornene imide amine) (Figure 1). These copolymers were obtained in good yields (>80%) and with molecular weights ranging from 17 to 65 kg/mol. Also, the favorable comparison, between estimated and measured molecular weights, suggests that the polymers obtained behave like random coils in tetrahydrofuran. Even at high molecular weights, the polydispersity remains very narrow (Figure 2; Table 1, entry 6v). The gel permeation chromatogram illustrates the increase in molecular weight upon addition of the second block (Figure 2). In addition, the molar feed and incorporation ratios are within 5% of one another as determined by ¹H NMR spectroscopy.

Homopolymers of BONIA had previously been reported by our group as potential antibacterial polymers.³⁵ Their low toxicity to red blood cells opens the prospects of medical applications for the synthesized diblock copolymers. The amphiphilicity, necessary to the formation of micelles that can be used as boron neutron capture therapy agents,¹⁸ was achieved through a postpolymerization cleavage of the *t*Boc protecting group in the second block. In so doing, the copolymers obtained are a unique example of a well-defined (PDI < 1.15) amphiphilic copolymer containing carborane. The deprotection can be monitored by the disappearance of the characteristic N–H carbamate peak at δ = 6.89 ppm integrating for 1H and the disappearance of the 9H from the *tert*-butyl protons at δ = 1.35

* Corresponding author. E-mail: Coughlin@mail.pse.umass.edu.

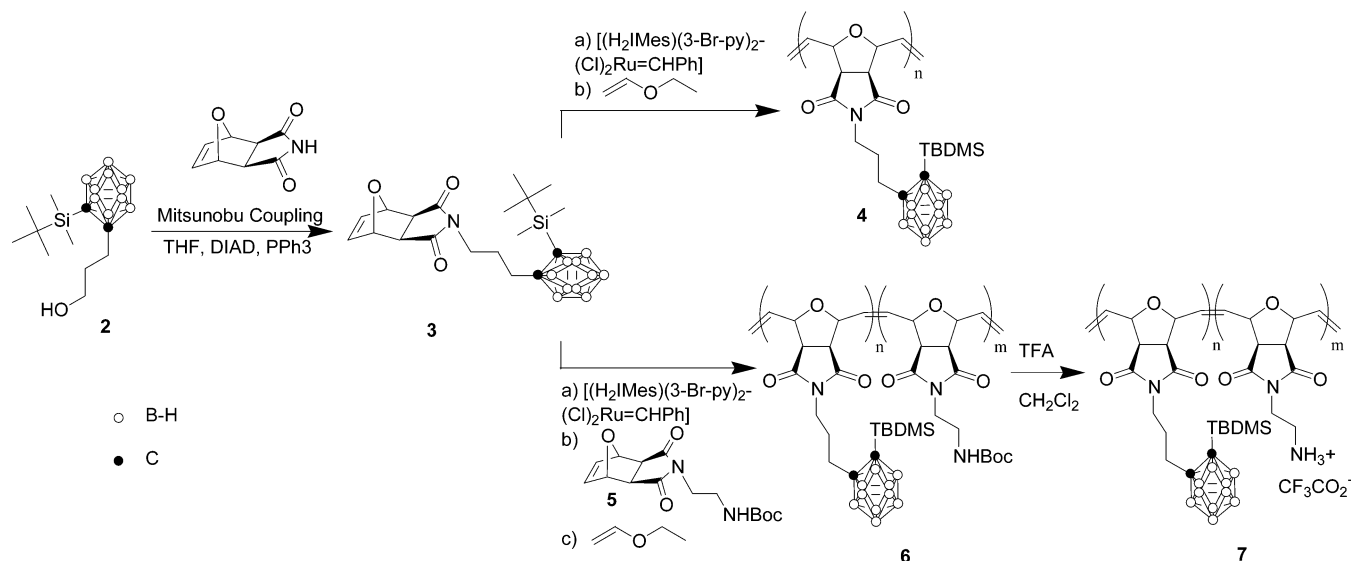


Figure 1. Monomer and polymer syntheses. Synthesis of **3**, **4**, **5**, and **6** (DIAD = diisopropylazodicarboxylate, TBDMS = *tert*-butyldimethylsilyl, TSH = *p*-toluenesulfonhydrazide, TFA = trifluoroacetic acid).

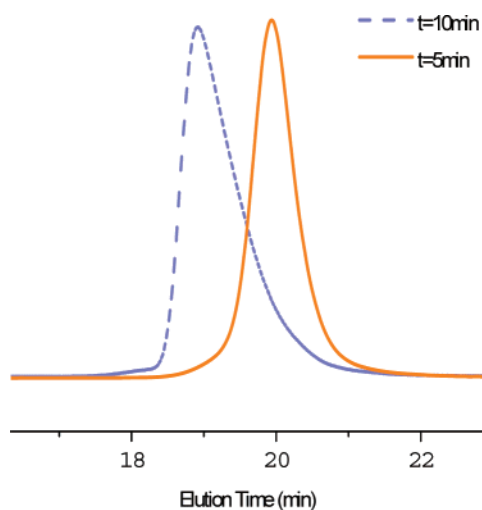


Figure 2. GPC chromatograms in THF of poly(SONIC) (solid line, PDI = 1.08, M_n = 37 kg/mol) and poly(SONIC-*b*-BONIA) (dashed line, entry 6v, PDI = 1.11, M_n = 65 kg/mol).

Table 1. Tabulated Data for the Copolymerization of SONIC 3 and BONIA by ROMP

entry	molar ratios		target				
	SONIC	BONIA	DP _n (S)	DP _n (B)	M_n^a	$M_n^{a,b}$	PDI ^b
6i	4	5	22	28	18 835	17 300	1.09
6ii	2	1	50	25	30 894	32 995	1.10
6iii	8	5	54	34	35 523	33 800	1.12
6iv	4	5	54	68	46 006	45 500	1.15
6v	4	5	86	108	73 178	65 100	1.11

^a In g mol⁻¹. ^b As measured by GPC vs polystyrene standards.

ppm. At the same time, the appearance of the ammonium peak at δ = 8.01 ppm integrating for 3H is observed. As observed by ¹H NMR spectroscopy, the cleavage is quantitative (Supporting Information).

In addition, solution studies in water, using DLS, show the propensity of these polymers to aggregate. This phenomenon can be imputed to the formation of micelles where the charged hydrophilic block constitute the corona and the carborane containing block the core. These aggregates have an average hydrodynamic radius (R_h) of 41 nm (Figure 3). By combining the features attributed to polymer drugs and the efficacy of BNCT, the newly synthesized amphiphilic polymers will have

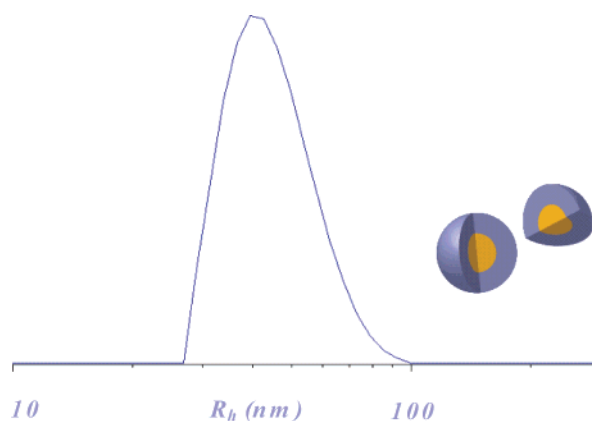


Figure 3. Distribution of sizes of micellar aggregates measured by dynamic light scattering profile (entry 6v).

potential applications in the delivery of high boron content micelles for BNCT. The solution behavior of the amphiphilic block copolymers is currently being investigated as well as the development of relevant models in vitro.

Expanding upon the findings of Malenfant et al.,⁷ it can be anticipated that the amphiphilic systems described here can find applications in the development of nanotemplated films as precursors for ceramics. In this quest to form regular features at the nanoscale, controlling the molecular architecture, and more specifically the polydispersity of the polymers, will be of paramount importance. Moreover, with the push for green chemistry,³⁶ and thanks to the amphiphilicity of the block copolymers, the potential to use water-based systems in the fabrication of templated assemblies is a definite asset.

Conclusions. We have successfully developed a new monomer, SONIC, that enabled us to synthesize a unique example of an amphiphilic diblock copolymer containing carborane. The newly synthesized monomer was homopolymerized using ROMP, yielding materials with low PDI (<1.1). This report paves the way for the design of controlled architectures containing icosahedral carboranes. Further studies are underway to understand the structure–property relationship of these novel hybrid materials. Owing to their propensity to self-assemble, block copolymers have imposed themselves as one of the preferred methods for the design of nanoscopic features. Therefore, we hope to take advantage of the ability to design

controlled macromolecular architectures containing carboranes to extrapolate it to high value applications, including nano-medicine, ceramic thin films, and radiation shielding materials.

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Supporting Information Available: Experimental procedures, additional GPC traces, and spectral data for different compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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