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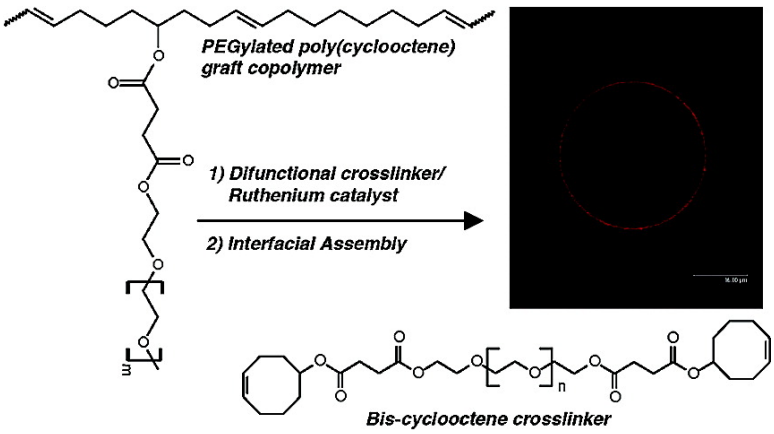

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Novel Polymer Capsules from Amphiphilic Graft Copolymers and Cross-Metathesis

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Polymer self-assembly is of considerable interest for the preparation of well-defined structures and materials. While polymer materials in solution are most commonly polydisperse random coils, advances in polymer synthesis, supramolecular assembly, and interfacial segregation have generated polymer-based materials with structural features that possess unprecedented precision.[1−7] When polymer assemblies contain reactive functionality, opportunities arise for cross-linking, and thus structural solidification, to give materials with wide applicability in both materials science and medicine.

An increased understanding of materials at interfaces offers tremendous opportunities with regard to surfaces, thin films, and nanostructured materials.[8−11] Amphiphilic polymers are particularly useful for mediation of the oil−water interface, as demonstrated by their rich science and commercial utility as polymer surfactants.[12] Amphiphilic block copolymers are very interesting in this regard, as the range of accessible chemistries and molecular weights, for example, in amphiphilic diblock copolymers, leads to polymer assemblies, micelles, and vesicles of considerable interest in encapsulation and controlled release.[13−17] We have been studying the synthesis and interfacial behavior of novel amphiphilic graft copolymers, as the graft copolymer structure provides integration of considerable functionality onto the polymer backbone that can be addressed chemically after the assembly process. Our particular interest in copolymers composed of hydrophobic polyolefin backbones with covalently bound hydrophilic poly(ethylene glycol) (PEG) pendant chains is examined here. We previously reported the preparation of these copolymers by ring-opening metathesis copolymerization[18] of cyclooctene and PEG-substituted cyclooctene macromonomers to give PEGylated poly(cyclooctenamers)[19] that can be tuned considerably in terms of their backbone and graft molecular weights. In addition, a variety of grafted functionality and linker chemistry is accessible.

In this report, we focus on assemblies and capsule formation of PEGylated polyolefins at the oil−water interface, using graft copolymers that contain on average one PEG chain per 16 carbon atoms of the backbone. The combination of interfacial activity and backbone reactivity of the copolymers used in this study makes them amenable to capsule formation. Figure 1 depicts their segregation to the oil−water interface to generate capsules with cross-linked membranes. Indeed, a number of chemistries should be accessible on the unsaturated backbone. We chose ring-opening cross-metathesis chemistry, an extremely useful methodology in small molecule synthesis,[20] to generate the desired cross-linking, as this can be performed under mild conditions that do not disrupt the initial assembly. Samples of bis-cyclooctenyl PEG were prepared for this cross-linking chemistry, by reaction of 2 equiv of carboxylic acid functionalized cyclooctene with α,ω-PEG-diol under carbodiimide coupling conditions. These difunctional molecules are, like the graft copolymers, interfacially active, and upon addition

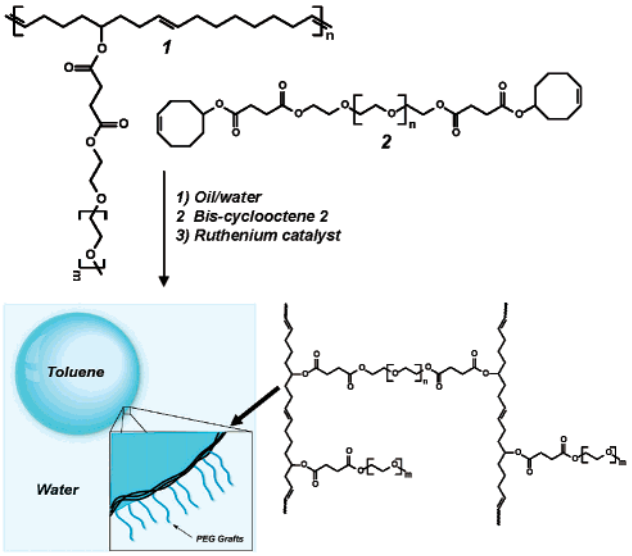

Figure 1. Schematic representation of interfacial activity of PEGylated poly(cyclooctene), and the bis-cyclooctene PEG used for cross-linking at the interface by ring-opening cross-metathesis.

of ruthenium benzylidene catalyst they react with the polymer assembly by ring-opening cross-metathesis.

Experimentally, these polyolefin-*graft*-PEG capsules were produced by dissolving graft copolymer **1** (M_n 15−200 K, PDI 1.8) and cross-linker in toluene, adding Grubbs' Generation II catalyst[21] to the mixture, and transferring aliquots of this mixture into water. This heterogeneous mixture was shaken for 15 min to produce cross-linked capsules that swell in both water and organic solvents, because of their amphiphilic nature, and are elastomeric as a result of the cross-linked membrane. The capsule density is tunable by choice of organic solvent: the toluene-filled capsules float on water, while capsules filled with higher density solvents (i.e., trichlorobenzene) stand on the bottom of the flask.

Fluorescence confocal microscopy (Leica inverted confocal microscope) was used to visualize the segregation of these polymers to the oil−water interface. Only a very faint contrast at the interface was observed on the as-prepared copolymers due to their lack of fluorescence emission. Thus, we prepared a fluorescent cyclooctene derivative through esterification of 5-hydroxycyclooctene with rhodamine B (**3** in Figure 2) and integrated this new monomer into the amphiphilic graft copolymer by copolymerization with cyclooctene and the PEGylated cyclooctene macromonomer. The functional group tolerance of the catalyst proved very valuable for the preparation of this fluorescent polyolefin. Confocal images of the fluorescent amphiphilic graft copolymer in oil-in-water biphasic systems (Figure 2a) reveal a strong preference of the graft copolymer for the interface, as indicated by the emission at 556 nm at the equator of an oil droplet in water. The capsules can be adjusted in size, depending on assembly conditions, and are

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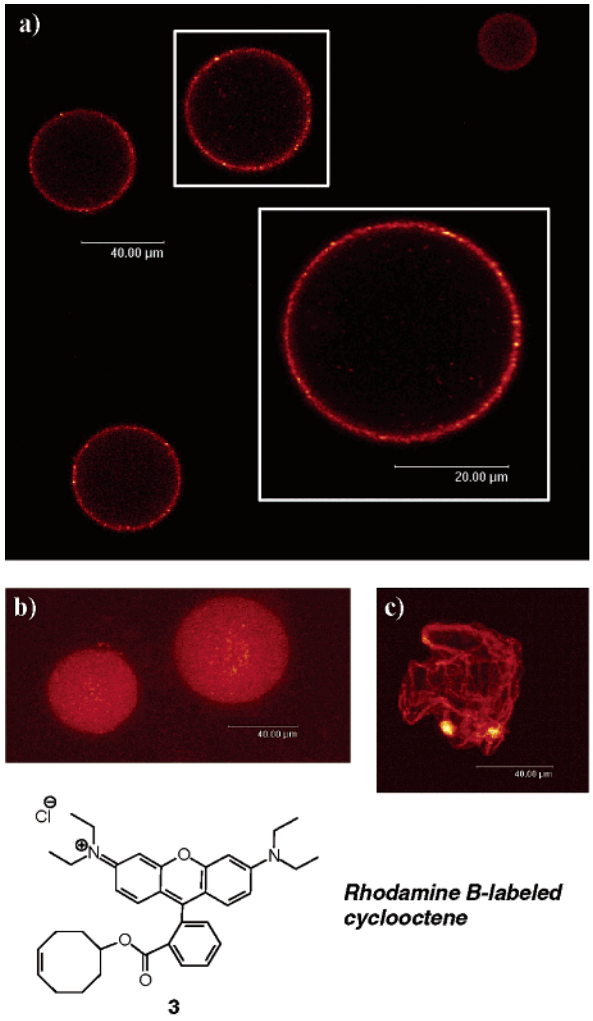

Figure 2. (a) Confocal laser scanning micrograph cross-section of microcapsules using graft copolymer **1** with M_n ca. 55 K; the fluorescence arises from integration of cyclic olefin **3** into the graft copolymer; (b) projection image showing accumulated cross-sections of two capsules; (c) a collapsed capsule membrane after the introduction of ethanol.

presently unoptimized in terms of size dispersity (see Supporting Information for a lower magnification image). The capsules are hollow and can be filled with reagents and polymers of appropriate solubility. A three-dimensional reconstruction of the capsules is illustrated in Figure 2b, to demonstrate their spherical nature and complete coverage by the polymer. Figure 2c confirms the effective cross-linking of the graft copolymer by replacing the two-phase oil/water mixture with the mutually good solvent ethanol. In this case, the capsules do not dissolve away, and the collapsed cross-linked membrane can be isolated and visualized clearly. Preliminary atomic force microscopy (AFM) micrographs, performed on capsules that were dried on silicon substrates, are shown in the Supporting Information and suggest the presence of a thin polymer membrane on the droplet surface; further detailed work in this area is in progress.

In summary, we report novel polymer capsules through ring-opening cross-metathesis of self-assembled amphiphilic PEG-grafted polyolefins at the oil−water interface. The polymer capsules described here are expected to be useful in encapsulation and release, and they benefit from the graft copolymer architecture used in their synthesis. This architecture provides significant opportunity for integration of a large number and diverse range of functional groups onto the capsule surface, provided this does not disrupt the amphiphilicity and thus interfacial assembly. The PEGylated polycyclootene capsules are expected to be biocompatible due to the presence of the PEG grafts. Future reports will include biocompatibility studies, the integration of oligopeptides into these structures, and membrane morphology and permeability.

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Supporting Information Available: Procedures for the synthesis and characterization of rhodamine-B substituted cyclooctene **3** and rhodamine labeled poly(cyclooctene)-*g*-PEG; low magnification confocal micrograph of capsules, AFM imaging height analysis, and dye filled capsules (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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