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ARTICLE

Ring-Opening Metathesis Polymers for Biodetection and Signal Amplification: Synthesis and Self-Assembly

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ABSTRACT: The ring-opening metathesis polymerization (ROMP) was used to develop a new class of block copolymers toward biological detection with signal amplification. For this, three classes of ROMP monomers were synthesized: (i) luminescent and electrochemiluminescent transition-metal-containing monomers, with ruthenium, osmium, and iridium bipyridine units, (ii) biologically compatible monomers and macromonomers containing oligothylene glycol units, and (iii) bioconjugatable monomers as well as monomers containing the biorecognition unit biotin. ROMP was used to efficiently combine these monomers into amphiphilic di- and triblock copolymers. Self-assembly of these block copolymers in aqueous media generates micellar spherical assemblies, which contain a large number of luminescent transition-metal centers in their core, a biocompatible and biologically inert protecting shell, and biological recognition units or bioconjugatable groups on their periphery. These micelles can act as luminescent markers for biological molecules with potential for signal amplification. In addition, the monomers and polymers reported here can serve as useful biologically enabled building blocks for a number of applications, including drug delivery and tissue engineering.

Introduction

The development of efficient methods for the detection of biological molecules has gained significant recent interest[1] notably in response to the need for early detection and diagnosis of diseases. Many biosensors have been designed with the focus on proteins[2] and nucleic acids.[3] However, as these biological markers are present in very small quantities in cells, the sensitivity of these methods needs to be increased. The polymerase chain reaction is well established for the amplification of DNA samples; however, processing this requires skilled manpower[4] and sometimes can lead to loss of information.[5] As well, no analogous process for proteins is readily available. Thus, techniques to amplify the signal itself rather than analyte are highly desirable.[6] Some recent examples of protein detection with signal enhancement[7] include enzyme-mediated release of initially self-quenched luminophores[8] or luminescent molecules from gold nanoparticle quenchers,[9] fluorescence resonance energy transfer between chromophores and quantum dots in immunoassays,[10] immobilization of coreactants on nanoparticles to enhance the electrochemiluminescence signal,[11] and attachment of functionalized vesicles[12] or gold nanoparticles[13] to amplify detection with microgravimetric or impedimetric[14] biosensors.

Transition-metal complexes, by virtue of their easily tunable properties and functionalities, provide a unique tool to develop these methods.[15] Ruthenium and iridium polypyridine complexes, in particular, have become the subject of considerable interest.[16] They have long excited-state lifetimes and large Stokes shifts and are chemically inert and resistant toward photobleaching.[17] These properties make ruthenium- and iridium-containing complexes and polymers attractive chromophores, with numerous potential light-harvesting applications in areas such as solar cell development,[18] photosensitizing,[19] photocatalysis,[20] photoconducting,[21] and modeling artificial photosynthetic systems.[22] A large number of these luminescent metal complexes can be confined in a small space without quenching their luminescence, and hence, they offer greater advantage over organic dyes, which self-quench when in close proximity.[23] Indeed, light-emitting properties of ruthenium, iridium, and other metals complexes are very promising in applications such as LED[24] and sensing.[25] Their bipyridine complexes are excellent sources of electrochemiluminescence, a process in which they catalytically generate light near an electrode, resulting in significant signal enhancement.[26]

Given these advantages, a particularly attractive approach toward biological detection with signal amplification would involve the creation of polymeric nanospheres (Scheme 1) that contain a large number of ruthenium or iridium polypyridine units and are capable of specific biological recognition. This would introduce the numerous advantages of these chromophores in bioassays, allowing the labeling of a single bioanalyte molecule with a large number of metal centers and thus potentially resulting in significant lowering of detection limits for these analytes.

This report describes the generation of a toolbox of monomers for biological detection and their incorporation into amphiphilic di- and triblock copolymers using the ring-opening metathesis polymerization (ROMP).[27] Self-assembly of these block copolymers in aqueous media generates micellar spherical assemblies, which contain a large number of luminescent transition metal centers in their core, a biocompatible and biologically inert protecting shell, and biological recognition units or bioconjugatable groups on their periphery (Scheme 1). These micelles can act as luminescent markers for biological molecules with potential for signal amplification. In addition, the monomers and polymers reported here can serve as useful building blocks to access a range

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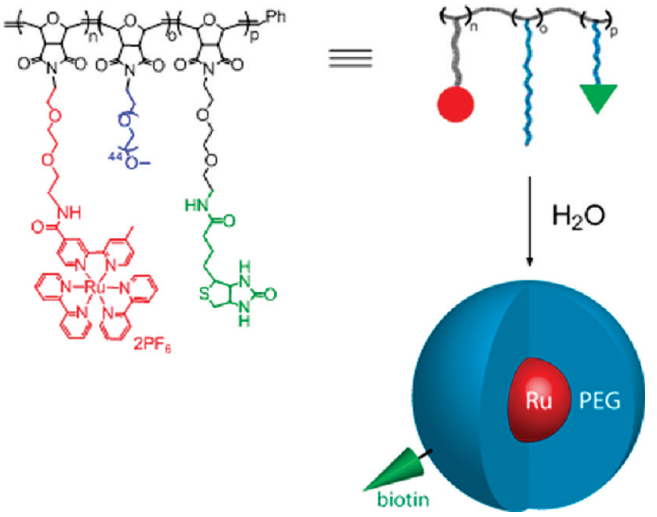
of biologically enabled ROMP polymers for other applications, including drug delivery and tissue engineering.

Results and Discussion

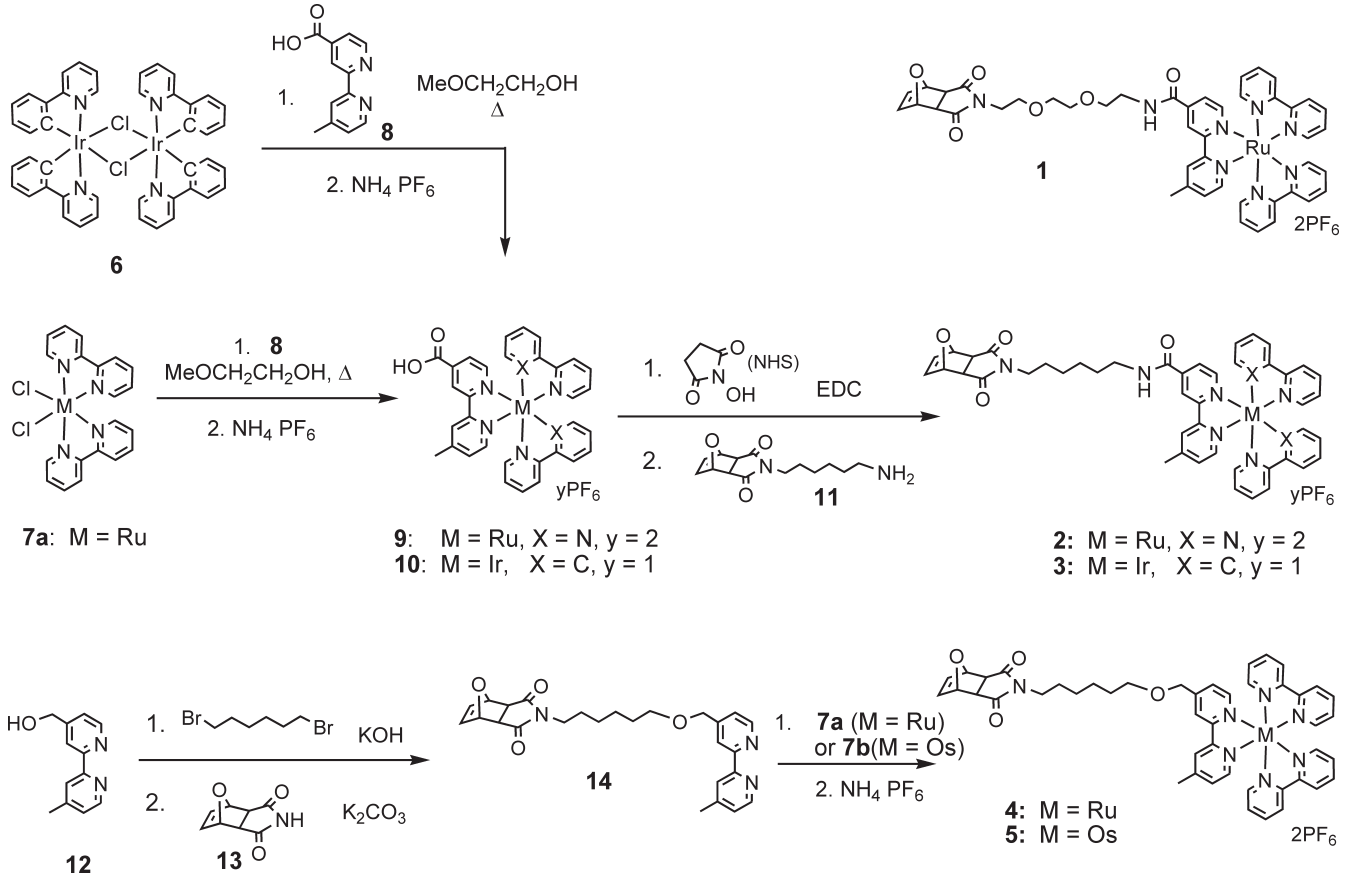
Design. In order to generate polymeric nanospheres for effective biodetection, the synthetic scope of ROMP needed to be expanded to (1) include luminescent ruthenium or iridium centers in the polymer, (2) render the polymers biocompatible and water-soluble and eliminate the possibility of nonspecific binding, (3) make the polymers bioconjugatable and/or attach biological recognition elements, and (4) ensure the correct block architectures and ratios for assembly of spherical star micelle morphologies of uniform sizes. Four classes of ROMP monomers were synthesized which can be incorporated into block copolymers that result in the above features. Specifically, we constructed (a) luminescent monomers containing ruthenium, iridium, or osmium bipyridine centers that are connected to the monomer backbone using various chemistries (this was done to modulate luminescence, hydrophobicity, and metal−metal communication along the polymer backbone); (b) biocompatible monomers that present oligo(ethylene glycol) units of different lengths, in order to protect the luminescent metal centers in the core from the aqueous medium, to eliminate nonspecific binding,[28] and to tune the self-assembly properties of the micellar aggregates; (c) monomers with a number of bioconjugatable groups that are useful for covalent attachment of DNA or protein probes on the periphery of the nanospheres as well as a biotin-containing monomer for specific binding to avidin or streptavidin.[29] Previously, we[30] and others[31] established the living nature of ROMP with polymers containing ruthenium bipyridine centers, and here we show the ready and quantitative incorporation of the above monomers into di- and triblock ROMP copolymers. The copolymers were self-assembled in water to give spherical micelles with luminescent metals located at their core and biorecognition units at the periphery.

Scheme 1. Self-Assembly of Block Copolymers into Spherical Aggregates Containing (i) a Core Rich in Luminescent and Electrochemiluminescent Metal Centers (Red), (ii) a Poly(ethylene glycol) Biocompatible Corona (Blue), and (iii) Bioconjugatable, or Biorecognition Units, Such as Biotin on the Periphery (Green)



Monomers. *a. Metal-Containing Monomers.* Scheme 2 displays the chemical structures and the synthetic routes to the ruthenium, iridium, and osmium-containing monomers. Monomer **1** has an oligoethylene glycol linker connecting the

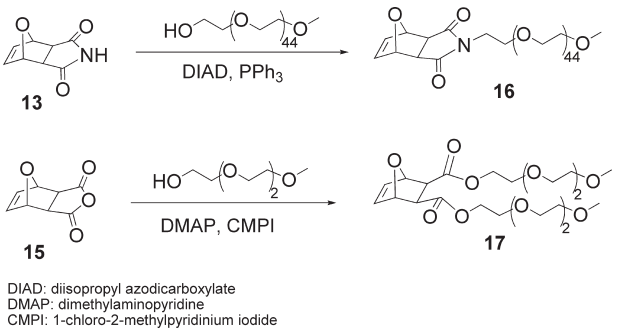
Scheme 2. Luminescent Metal-Containing Monomers and Their Synthesis



luminescent ruthenium unit to the norbornene backbone,[30] whereas monomers **2**−**5** contain a hexyl linker. The use of a long alkyl chain increases the hydrophobicity of the metal-containing units over monomer **1**, thereby increasing the propensity of these units to localize in the core of a micellar aggregate in aqueous media. In monomers **1**−**3**, the metal centers are connected to the oxanorbornene units via an amide linkage, while an ether linkage is used in monomers **4** and **5**. The nature of the linkage of the metal centers to the polymer backbone has been shown by Meyer's group to modulate the rates of metal−metal energy transfer across the polymer backbone, with the amide linkage providing greater rates.[32]

Monomer **1** was synthesized as reported previously.[30] The synthetic route to monomers **2** and **3** starts with the corresponding metal dichloride complexes **6** and **7a** (Scheme 2).[33] Treatment of these dichlorides with 4′-methyl-[2,2′]bipyridinyl-4-carboxylic acid (**8**) yielded the corresponding carboxylic acid complexes **9** and **10**. The carboxylic groups in both ruthenium and iridium derivatives were activated by esterification with *N*-hydroxysuccinimide (NHS). Final products **2** and **3** were then prepared by amide formation with exo-*N*-(6-aminohexyl)-7-oxabicyclo[2.2.1]-hept-5-ene-2,3-dicarboximide (**11**). 4-Methyl-2,2′-bipyridine-4′-methyl alcohol (**12**) is a starting point in the preparation of monomers **4** and **5**. First, **12** was alkylated with 1,6-dibromohexane to create an *n*-hexyl linkage. The remaining bromine atom was then substituted by deprotonated exo-7-oxabicyclo[2.2.1]-hept-5-ene-2,3-dicarboximide (**13**) to give the bipyridine-containing monomer **14**. The latter compound was subsequently converted to its ruthenium- (**4**) and osmium-containing (**5**) derivatives by refluxing with corresponding chloride complexes $Ru(bpy)_2Cl_2$ (**7a**, M = Ru) and $Os(bpy)_2Cl_2$ (**7b**, M = Os) in methanol solution. All monomers **2**−**5** were precipitated as hexafluorophosphate salts.

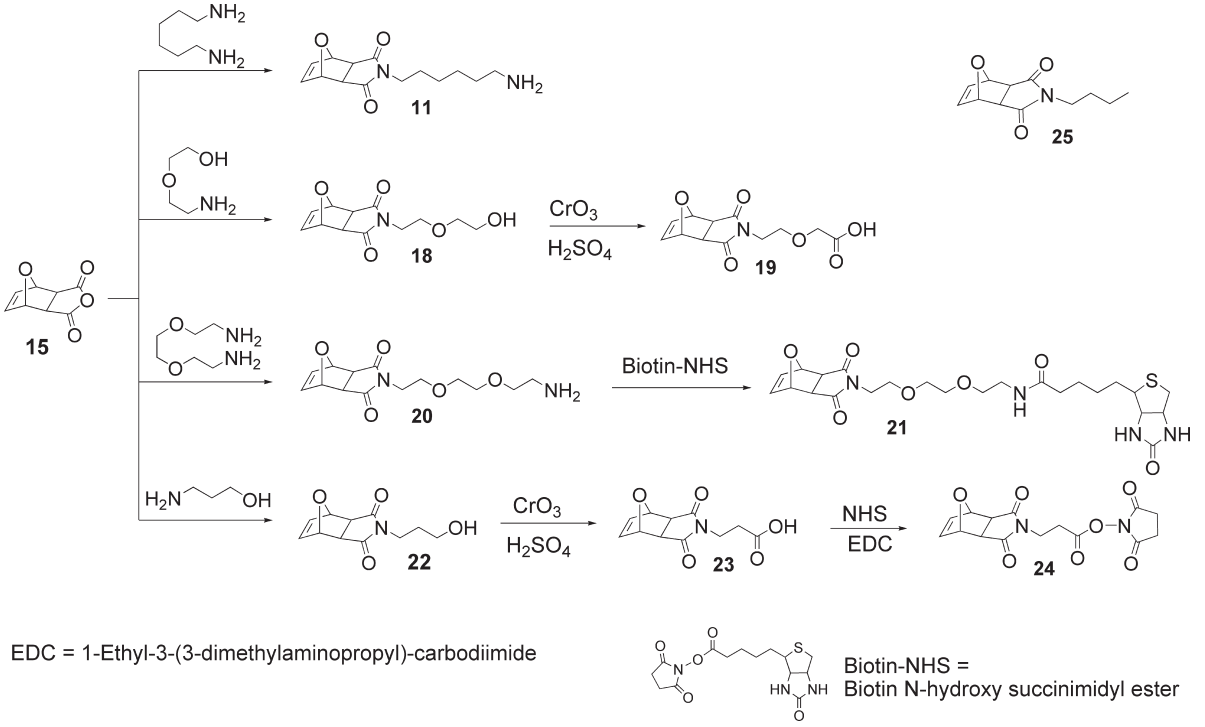
Scheme 3. Synthesis of Biocompatible ROMP Monomers



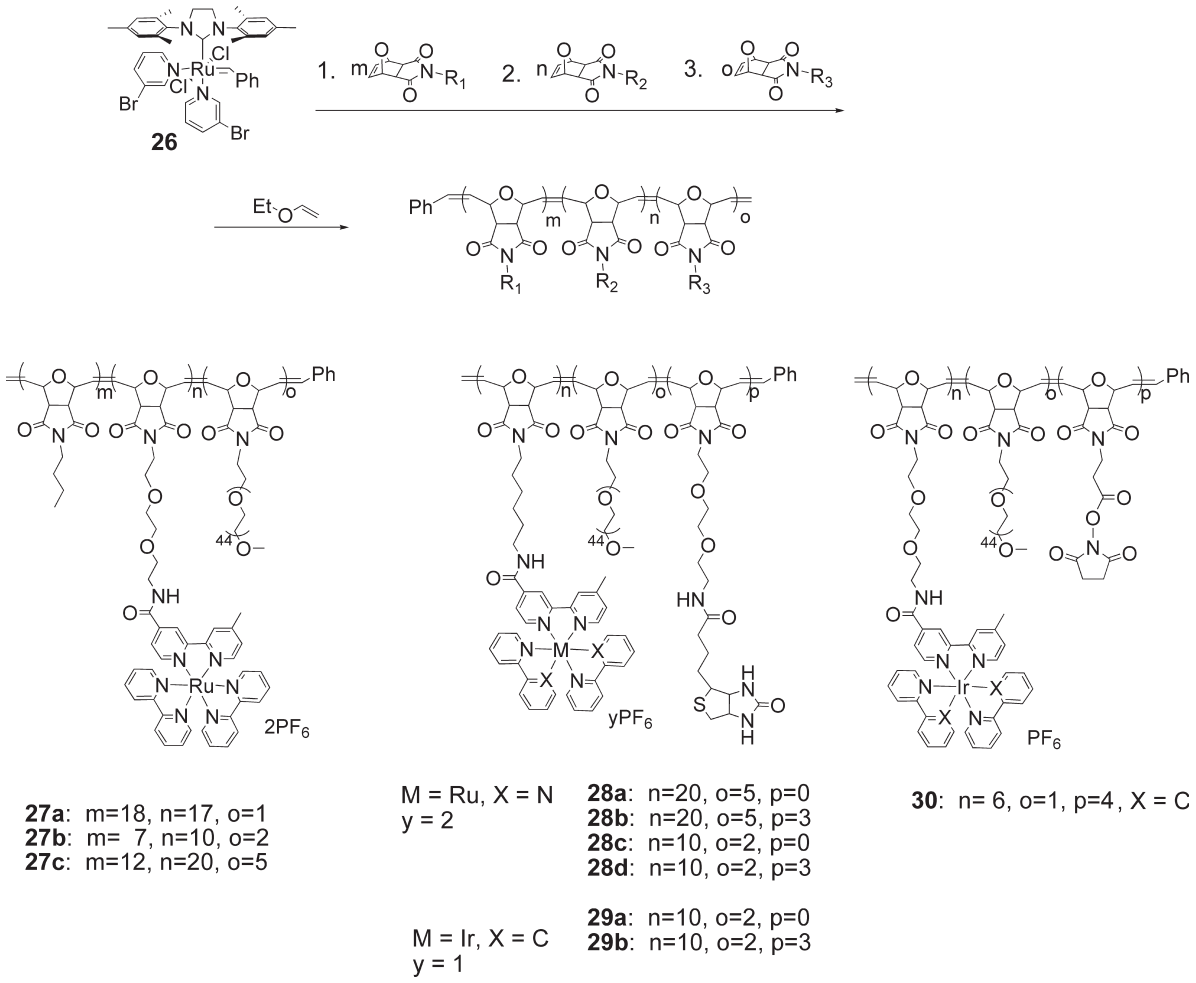
b. Biocompatible, Hydrophilic Monomers. Monomers **16** and **17** were prepared to access hydrophilic blocks in our polymers. These are useful to both isolate the metal centers from the aqueous medium and prevent nonspecific binding of the resulting polymeric nanospheres. As described below, the use of oligo(ethylene glycol) of different lengths allows tuning of the micellar morphologies in the self-assembled block copolymers. Macromonomer **16**, functionalized with a methoxy-terminated poly(ethylene glycol) chain with an average MW = 2000 (average DP = 44), was synthesized by Mitsunobu coupling of exo-7-oxabicyclo[2.2.1]-hept-5-ene-2,3-dicarboximide **13** and methoxyPEG(2000) (Scheme 3). Monomer **17**, with two short hydrophilic triethylene glycol chains, was prepared in a reaction of the corresponding exo-anhydride **15** with an excess of the triethylene glycol monomethyl ether using Mukaiyama's reagent (1-chloro-2-methylpyridinium iodide) to activate OH groups (Scheme 3).

c. Bioconjugatable Monomers. We have incorporated a number of bioconjugatable and biorecognition units into monomers (Scheme 4). These are useful to access a toolbox of biologically enabled ROMP polymers for a number of applications, including biological detection, drug delivery vehicles, cell growth scaffolds, and chemical biology probes. They include amino (**11**, **20**), alcohol (**18**, **22**), carboxylic acid (**19**, **23**), and *N*-hydroxysuccinimidyl ester (**24**) groups. In addition, biotin was incorporated into monomer **21**. As a

Scheme 4. Synthesis of Bioconjugatable and Biorecognition Monomers and Structure of the Hydrophobic Monomer 25 (Top Right)



Scheme 5. Block Copolymers 27−30 Prepared by Sequential Addition of Monomers to Grubbs' Catalyst 26



biological recognition unit, biotin displays a selective and exceedingly high binding affinity to the proteins avidin and streptavidin ($K_d \approx 10^{-15}$ M) and is widely used for bioassays.[29] Furthermore, (strept)avidin can bind up to four biotin units; thus, it acts as a linker between two or more biotinylated molecules.

Amino-containing monomers **11** and **20** were prepared by reaction of the exo-anhydride **15** with hexamethylenediamine and 2,2′-(ethylenedioxy)bis(ethylamine), respectively. Treatment of amino compound **20** with the *N*-hydroxysuccinimidyl ester of biotin (Biotin-NHS) gave biotin-containing monomer **21**.[34] Monomers **18** and **22**, with hydroxyl groups, were synthesized by reaction of *exo*-anhydride **15** with 2-(2-aminoethoxyethanol) and 3-aminopropanol, respectively. Oxidation of **18** and **22** with chromic acid gave their carboxylic acid derivatives **19** and **23**, respectively. The monomer **23** was then converted to its activated ester derivative **24** by coupling with *N*-hydroxysuccinimide in the presence of 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide (EDC).

Scheme 4 shows also a structure of monomer **25**.[35] The lipophilic properties of the butyl moiety were used to build hydrophobic blocks into the block copolymers, thus favoring microphase separation of the micellar aggregates (vide infra).

Synthesis of the Polymers. Because of its living character and functional group tolerance, ROMP is a powerful tool for the synthesis of block copolymers. Before proceeding to the construction of block copolymers, homopolymers of the monomers as shown in Schemes 2−4 were first synthesized and characterized. This was carried out in degassed dichloromethane, using the third generation Grubbs catalyst **26** (Scheme 5). Polymerization was quenched with excess ethyl vinyl ether. The polymerization was monitored by ^{1}H NMR and showed rapid and quantitative reaction of the monomers. Integration of the peaks corresponding to the repeat units, and comparison with the peaks corresponding to the phenyl group on the chain end (arising from the ruthenium ROMP initiator), showed degrees of polymerization consistent with the monomer-to-initiator ratios in all cases. Most polymerizations were complete in less than 20 min. GPC analysis showed low polydispersity indices for the homopolymers (PDI < 1.1). Interestingly, even the macromonomer containing a long PEG chain polymerized readily, and the crossover from this monomer was facile; similar readiness to polymerize other macromonomers was recently reported.[36] In contrast, polymerization of the ruthenium bipyridine-containing monomers was slower, requiring ∼1 h for completion, and crossover from this monomer was sluggish. This is possibly due to an interaction of this monomer with the ROMP initiator. Metal-containing polymers could only be characterized by spectroscopic methods because of their interaction with the GPC stationary phase. However, we had previously shown that the ROMP reaction of metal-containing monomer **1** was living in character.[30] Using these results, triblock copolymers **27**−**30** shown in Scheme 5 were synthesized. The sequential addition of monomers proceeded with quantitative incorporation into these blocks (^{1}H NMR), and

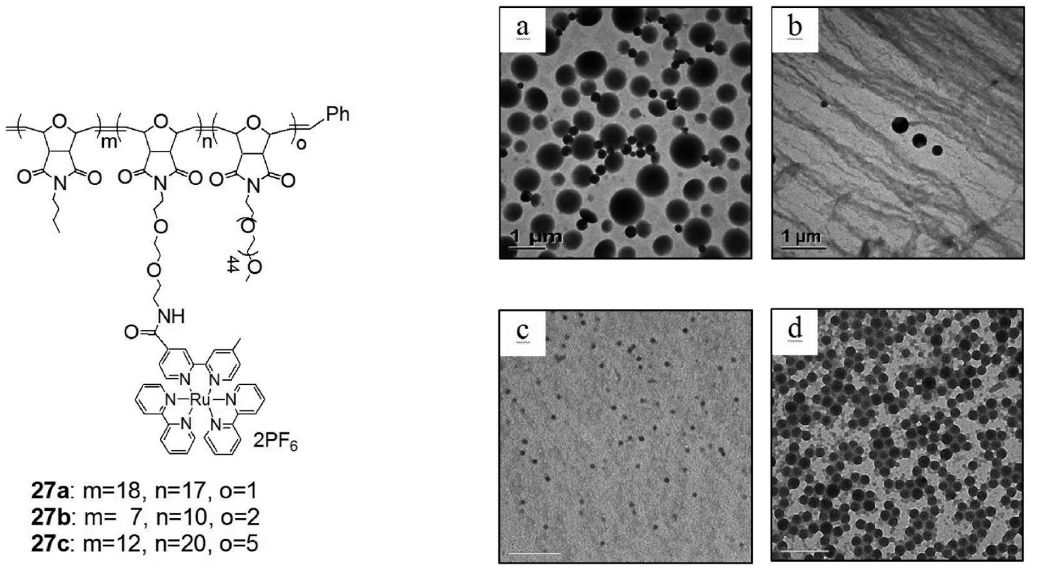


Figure 1. TEM images of (a) polymer **27a** at 50% water in acetonitrile (scale bar is 1 μm), (b) **27a** in 80% water in acetonitrile (1 μm), (c) **27b** (200 nm), and (d) **27c** (200 nm).

GPC analysis of the nonmetal containing block copolymers showed narrow molecular weight distributions in all cases.

Self-Assembly of Block Copolymers in Aqueous Media. An attractive morphology for biological detection with signal amplification is a spherical star micelle, in which the luminescent metal centers reside at the core and are separated from the analyte by a biocompatible and biologically inert corona. The biological recognition groups would reside at the periphery of these polymeric nanospheres (Scheme 1).

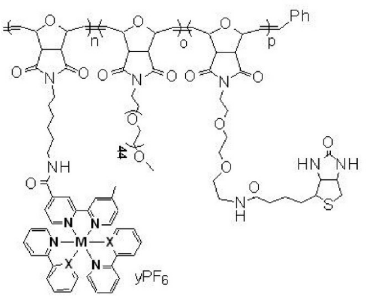
Encapsulated ruthenium bipyridine units inside polystyrene microspheres,[37] liposomes,[38] and silica nanoparticles[39] have been used to create bioassay platforms with signal amplification. However, because of their large sizes, microspheres and liposomes cannot bind in a 1:1 ratio to analytes. In addition, $Ru(bpy)_3^{2+}$ containing silica particles are not readily opened to release the metal centers for efficient electrochemiluminescence detection. In contrast, polymeric star micelles assembled from block copolymers **27**−**30** shown in Scheme 5, if formed, would contain a uniform number of ruthenium centers and would be small enough to bind in a 1:1 ratio to bioanalytes. Because they are self-assembled, they would also be potentially opened with specific solvents to release their constituent polymers for electrochemiluminescence detection.

The block copolymers synthesized are completely soluble in the organic solvents acetonitrile and acetone. Their oligo(ethylene glycol) containing blocks are water-soluble, but their transition-metal-containing blocks are not. Thus, addition of water to their acetonitrile or acetone solutions is expected to produce micellar aggregates, with water-incompatible blocks assembled in the core. The optimal polymer concentrations for aggregation (5 mg/mL in acetonitrile for ruthenium-containing polymers and 2 mg/mL in acetone for iridium-containing polymers) were determined for the self-assembly experiments. Water was added dropwise, with continuous stirring until a water content of 80% of the total volume was reached. The obtained solutions were dialyzed overnight against water to remove the organic solvent. Samples were then drop-cast onto carbon-coated transmission electron microscopy (TEM) grids. No staining was necessary since cores of the micelles containing ruthenium or iridium complexes are dark under the TEM conditions. All measured micelle dimensions given in this work refer to the diameters of their cores.

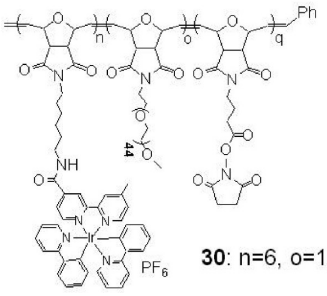
Initially, the self-assembly of block copolymers was examined with oligoethylene glycol-containing monomer **17** as the repeat unit in the biocompatible block. However, self-assembly of these copolymers generated large compound micelles (LCMs), a morphology which likely contains surface-exposed ruthenium centers. This is possibly a result of the large size of the ruthenium bipyridine units in the solvent-incompatible block, preventing the formation of star micelles in favor of "crew-cut" morphologies (such as LCMs).

To counter this effect, we have tested block copolymers containing macromonomer **16** with long PEG chains on each repeat unit, which would make the micelle corona significantly larger. The first examined self-assembled copolymer **27a** possesses a relatively hydrophilic triethylene glycol linker binding the ruthenium tris(bipyridine) moiety to the polymer backbone. To add lipophilic character to the core of the micellar aggregates, we incorporated a hydrophobic monomer **25**, containing an *n*-butyl unit (Scheme 4), into the first block. The ruthenium- and PEG macromonomer-containing blocks were then added sequentially. Polymer **27a** aggregated in water−acetonitrile at water concentrations as low as 10%. Analysis of the TEM images revealed formation of large compound micelles (LCM) with polydisperse diameters (Figure 1a), and only sheets and lamellar structures were observed after dialysis (Figure 1b). This is again likely due to an insufficient volume ratio of the hydrophilic PEG corona-forming block to hydrophobic core.

To increase the volume ratio of the corona-forming block and enhance star micelle formation,[40] block copolymers **27b** and **27c** (Figure 1) with a larger hydrophilic PEG block, relative to the ruthenium block, were then synthesized and assembled in a water−acetonitrile solution. Both **27b** and **27c** gave spherical micellar aggregates with uniform average core diameters of 15 and 43 nm, respectively (Figure 1c,d). With an estimated monomer unit length of 0.6 nm,[41] these diameters are consistent with star micelle morphologies. For both polymers **27b** and **27c**, some smaller spherical aggregates of 4.2 and 16.6 nm average diameters were observed and were attributed to unassembled unimers. In order to decrease the hydrophilicity of the ruthenium-containing block and further confine the ruthenium units to the micelle core, we prepared two pairs of polymers **28a**,**b** and **28c**,**d** where the ruthenium complex was attached with a hexyl



28c: n=10, o=2, p=0, M=Ru, X=N, y=2
28d: n=10, o=2, p=3, M=Ru, X=N, y=2
29b: n=10, o=2, p=3, M=Ir, X=C, y=1



30: n=6, o=1, q=4

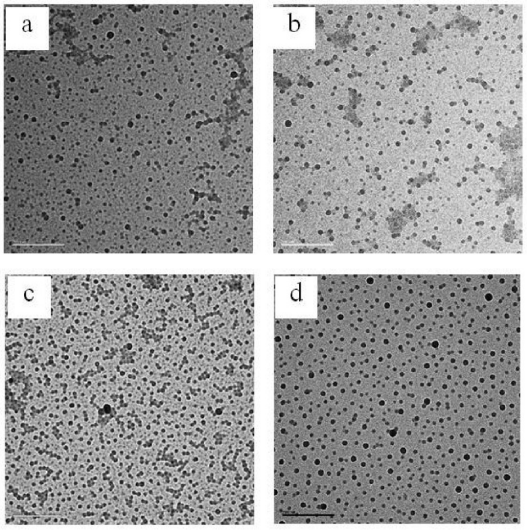


Figure 2. TEM images of self-assembled in water (a) **28c**, (b) **28d**, (c) **29b**, and (d) **30**. Scale bars are 200 nm.

linker instead of diethylene glycol (Scheme 5). The hydrophobicity of the hexyl linkers resulted in microphase separation in aqueous media without the need for the hydrophobic butyl block from **25**. **28a** and **28c** are diblock copolymers with ruthenium and PEG blocks, while **28b** and **28d** are their corresponding triblock copolymers containing an additional biotin block (Scheme 5). All of these block copolymers gave spherical micelles upon self-assembly in water. Longer copolymers **28a**,**b** gave spherical micelles with a somewhat higher proportion of the smaller aggregates (see Supporting Information). However, shorter copolymers **28c**,**d** were better behaved, with a significant proportion of micelles (Figure 2a,b).

As iridium tris(bipyridine) derivatives are known to have advantageous spectroscopic properties,[26] we explored the self-assembly of polymers **29a**,**b**, which have size and block ratios analogous to those in **28c**,**d**. A uniform micelle population of an average diameter 20 nm was observed (Figure 2c). Finally, a shorter copolymer **30**, possessing similar block ratios as **29** but end-terminated with bioconjugatable *N*-hydroxysuccinimide (NHS) block, was used. The self-assembly of this polymer resulted in formation of spherical aggregates that possess readily functionalizable NHS units at their periphery. The average diameter of these aggregates of 10 nm was consistent with a star micelle morphology (Figure 2d) as the estimated iridium block length is ca. 4 nm. This was accompanied by some larger micelles with an average diameter of 20 nm; morphologies consistent with unimers were not observed. We are currently investigating the origin of this second population of larger micelles. Overall, these results show the potential for creating spherical micelles from these luminescent and bioconjugatable polymers by adjustment of the architecture and ratios of the different blocks in the copolymers.

For any use of micelles in biodetection applications, a method to control the number of the accessible biotin units is required. If too many biotin units are present on the micellar surface, they would bind to more than one streptavidin functionalized analyte, resulting in lower sensitivity. To address this, we have mixed biotin-containing polymer **28d** with its biotin-free analogue **28c** (Scheme 5). The 1:9 mixture of both polymers gave micelles with an average diameter of 15 nm (Supporting Information), suggesting that mixing these polymers to control the number of surface biotin units does not negatively affect the self-assembly of these micellar aggregates.

Physicochemical Properties of the Micelles. Since most biological assays are performed in buffer solutions, it was crucial that the micelles be stable in buffer solutions. Dynamic light scattering (DLS) of the micellar aggregates suspended in phosphate buffer was used to monitor micelle stability over time. DLS data consistently showed the presence of micelles in all samples. The micelles were stable in a phosphate buffer for a period of at least 5 days, making possible their use in the buffer conditions required for biological assays. Additionally, the mechanical stability of micelles was tested and they readily survived 30 min centrifugation and sonication.

Photophysical Studies. Preliminary photophysical studies were carried out on monomer **4** and block copolymers **28c** and **28d** (Scheme 5) both in acetonitrile, in which they are unassembled free chains, and in acetonitrile:water (20:80 v:v), a solvent that favors micelle formation (Table 1). The absorbance spectra in the range of approximately 400−500 nm are very similar for monomer **4** and polymers **28c** and **28d**, with no obvious changes in the band shape or absorbance maximum of the metal-to-ligand charge-transfer (MLCT) absorption.[30,42] As well, the steady-state emission wavelengths and band shapes are similar for the three samples, indicating that the $Ru(bpy)_3^{2+}$ units on the polymer chains essentially behave as individual chromophores. Monomer **4** has a quantum yield of 0.068 in acetonitrile, comparable to the reference compound $Ru(bpy)_3^{2+}$ ($\Phi = 0.062$).[42b]

Table 1. Absorbance and Luminescence Properties of $Ru(bpy)_3^{2+}$-Based Monomer, Diblock, and Triblock Copolymers

		absorbance	emission	
sample	solvent	λ_{max}, nm (ε, M^{-1} cm^{-1})	λ_{max}, nm	quantum yield
4	acetonitrile (ACN)	453 (16 142)	625	0.068
4	80% water in ACN	457 (14 766)	639	0.024
28c	ACN	457 (12 725)	626	0.064
28c	80% water in ACN	457 (15 932)	642	0.021
28d	ACN	457 (11 205)	626	0.060
28d	80% water in ACN	457 (14 362)	642	0.021

Polymers **28c**,**d** have similar quantum yields (Φ = 0.064 and 0.060, respectively) in acetonitrile, suggesting that incorporation into the polymer results in near complete retention of the $Ru(bpy)_3^{2+}$ luminescence intensity (Table 1). Addition of water to the acetonitrile solution of monomer **4** results in red-shifted emission maxima, consistent with the stabilization of the MLCT excited state in this more polar medium. An observed reduction in emission intensity (Φ = 0.024) is consistent with the decrease in quantum yield of $Ru(bpy)_3^{2+}$ with increasing solvent polarity (Table 1).[30,42] The photophysical behavior of block copolymers **28c**,**d** in this aqueous medium is similar to that of monomer **4**, with red-shifted emission maxima and reduced quantum yields (Table 1). In this solvent, these block copolymers are expected to aggregate into micellar structures with the ruthenium units residing in their core. These preliminary studies thus indicate that the core-based ruthenium centers are still exposed to the aqueous medium, possibly due to their short chain lengths and their block ratios (e.g., polymer **28d** is poly(**4**)$_{10}$(**16**)$_2$-(**21**)$_3$; see Scheme 5). However, these studies also indicate that localization of multiple ruthenium centers in the micellar core does not cause quenching of their luminescence. While $Ru(bpy)_3^{2+}$ has a low emission quantum yield,[30,42] its electrochemiluminescence is known to result in very strong signals and is responsible for highly sensitive commercial biological detection systems.[26] Thus, these ruthenium-containing, biologically enabled micelles will potentially find applications for the amplification of biological detection using electrochemiluminescence. We are currently carrying out a detailed photophysical study of the ruthenium-, iridium-, and osmium-containing polymers as a function of their block composition, solvents, and bound biological molecules.

Conclusion

In conclusion, we have developed a number of biologically enabled ROMP monomers, homopolymers, and block copolymers, with the potential for sensitive biological detection, but also for other applications, such as drug delivery and tissue engineering. We synthesized a class of luminescent and electrochemiluminescent transition metal-containing ROMP monomers, with ruthenium, osmium, and iridium bipyridine units. We constructed biologically compatible monomers containing oligoethylene glycol units and a macromonomer containing a long poly(ethylene glycol) chain. We prepared bioconjugatable monomers, including alcohol, amine, carboxylic acid, and succinimide ester-containing molecules, as well as a monomer containing the biorecognition unit biotin. Finally, we used ROMP[27] to combine these monomers into triblock copolymers, and we optimized their self-assembly in aqueous media into star micelles with multiple luminescent metal units in their interior, biocompatible units to protect this core, and bioconjugatable or bioconjugation units in their corona. These micellar aggregates are stable in the buffer aqueous conditions required for biological detection. We are currently optimizing the biological platform that will allow the use of these micelles for electrochemiluminescence detection of proteins with high sensitivity.

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Supporting Information Available: Synthetic procedures, experimental details for the self-assembly and photophysical studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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