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Ring-Opening Metathesis Polymerization by a Ru Phosphine Derivative of Cyclodextrin in Water

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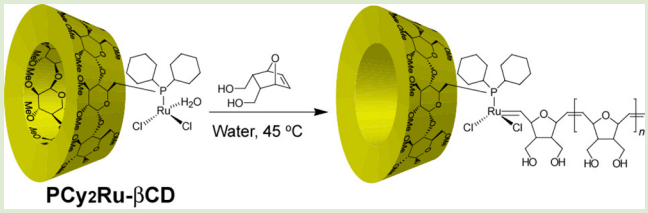
Supporting Information

ABSTRACT: Trimethylated cyclodextrins with a phosphine ligand and ruthenium (PCy_2Ru-CDs) realize supramolecular polymerization catalysts for ring-opening metathesis polymerization (ROMP). Although PCy_2Ru-βCD shows a low polymerization activity for 7-oxanorbornene dimethanol (7-ONorOH_2) in organic solvents, it exhibits a high ROMP activity for 7-ONorOH_2 in aqueous solutions. The ROMP activity of PCy_2Ru-βCD is higher than that of PCy_2Ru-αCD. The addition of competitive guest molecules decreases the polymer yield, indicating that complexation between PCy_2Ru-CD and 7-ONorOH_2 in water plays an important role in the increased polymer yield.



At ambient temperature, enzymes in nature selectively and efficiently form products from substrates.[1−3] Biological enzymes have a precise substrate-recognition site, and the deft reaction site controls the flexible structure due to noncovalent bonds. We hypothesized that supramolecular complexes with catalytic activities, well-known supramolecular catalysts,[4,5] may act in a manner similar to biological enzymes and realize new transformations of matter. Inspired by nature's enzymatic catalysts (e.g., cytochrome P450,[6,7] processive enzymes,[8,9] including cellulases[10,11] and DNA polymerases[12−18]), supramolecular catalysts have been designed not only to mimic but also to transcend the catalytic ability of biological enzymes.[19]

Supramolecular catalysis initially focused on the hydrolysis of activated phenyl esters using cyclodextrins (CDs) as enzymatic models.[20−22] The CD cavity was regarded as a binding pocket for substrates like enzymes.[23−28] Recently, research has shifted to enhancing the catalytic activity and selectivity using host−guest interactions where the host molecules attract substrates into the catalytically active site. Host−guest interactions have been employed in hydrolysis reactions,[29,30] C−H bond activation,[31,32] epoxidation of olefins,[33−35] Diels−Alder reactions,[36−39] 1,3-dipole cycloadditions,[40,41] etc.

Selective molecular recognition and substrate activation are the foundation of supramolecular catalysis. Although supramolecular catalysts for substrate conversions have been frequently reported in organic chemistry, there are fewer reports for polymerization reactions. Previously, we reported that CDs can include and activate lactones, yielding a polymer with a single CD at the end of the polymer chain.[42,43] CD dimers efficiently initiate the polymerization of lactones to produce polyesters. One CD moiety in the dimer acts as the active site for ring opening and converts the monomer to produce a polymer chain.[44] It should be noted that the active sites and the substrate-combining sites are located at the end of the growing polymer chain, demonstrating a highly controlled polymerization behavior. Supramolecular catalysts that resemble a biological system may realize an ideal polymerization system if a supramolecular organometallic catalyst capable of binding, activating, and inserting the monomer between the active and binding sites can be designed. Although water-soluble ring-opening metathesis polymerization (ROMP) catalysts have been reported,[45−50] herein we focus on a supramolecular polymerization catalyst that can bind substrates (monomers) for ROMP in water. Because bicyclo monomers insert between the metal center and growing polymer chain in the polymerization mechanism of ROMP, CD acts as the molecular recognition site located adjacent to the catalytic metal center.

We designed ROMP catalysts, which consist of CD and a phosphine ligand. Figure 1 shows the preparation of trimethylated βCD (TM-βCD) with dicyclohexyl phosphine (PCy_2-βCD) and a ruthenium (Ru) complex with PCy_2-βCD. The tosylated TM-βCD was prepared by a reaction with tosylated βCD and methyl iodide under basic conditions. The lithiation of the protected dicyclohexyl phosphine ($PCy_2H{\cdot}BH_3$) with *n*BuLi gave $PCy_2Li{\cdot}BH_3$. Treatment with an excess of $PCy_2Li{\cdot}BH_3$ at −78 °C synthesized the protected $PCy_2{\cdot}BH_3$-βCD. Deprotection of the BH_3 group with morphorine afforded PCy_2-βCD in 22% yield. Treatment of $RuCl_3{\cdot}3H_2O$ with PCy_2-βCD in ethanol (EtOH) under reflux gave crude PCy_2Ru-βCD, which was purified by washing with pentane to afford PCy_2Ru-βCD in 32% yield. PCy_2Ru-αCD was prepared via the same method as PCy_2Ru-βCD. In the ^{31}P NMR spectra, the ^{31}phosphine (^{31}P) signals of $PCy_2{\cdot}BH_3$-βCD,

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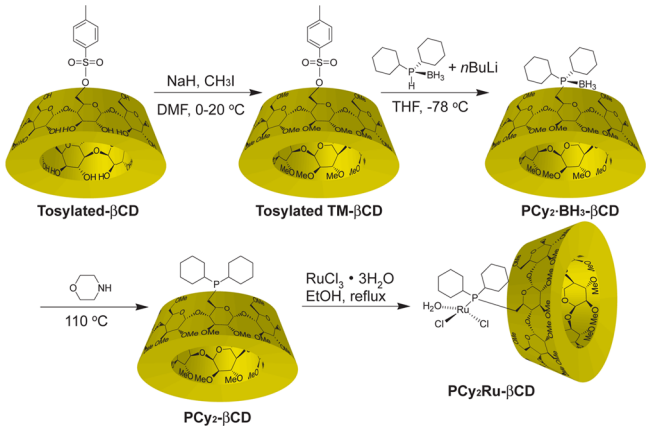
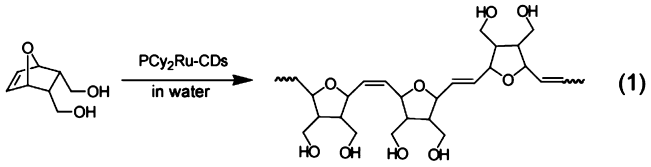


Figure 1. Preparation scheme of PCy_2Ru-βCD.

PCy_2-βCD, and PCy_2Ru-βCD appeared at 24.6, 23.4, and 53.2 ppm, respectively. Similarly, the phosphine signals of $PCy_2{\cdot}BH_3$-αCD and PCy_2Ru-αCD appeared at 26.6 and 59.0 ppm in ^{31}P NMR, respectively.

We initially studied the polymerization activity of PCy_2Ru-CDs for 7-oxanorbornene dimethanol (7-$ONorOH_2$). Polymerization of 7-$ONorOH_2$ initiated by PCy_2Ru-CDs was carried out by stirring in water at 45 °C under an Ar atmosphere (eq 1). The resulting poly(7-$ONorOH_2$) was collected as a



precipitate. Table 1 shows the results of ROMP of 7-$ONorOH_2$ initiated by various Ru complexes. Although $RuCl_3/3H_2O$ and $RuCl_2$ (TPPTS) (TPPTS: 3,3′,3″-phosphinidynetris-(benzenesulfonic acid) trisodium salt), which are well-known water-soluble catalysts, did not initiate polymerization of 7-$ONorOH_2$ (Runs 1−2 in Table 1), PCy_2Ru-αCD afforded poly(7-$ONorOH_2$) in 31% yield (Run 3 in Table 1). PCy_2Ru-βCD was much more active as it produced poly(7-$ONorOH_2$) in 80% yield (Run 6 in Table 1). On the other hand, the yield of ROMP of 7-$ONorOH_2$ in organic solvents, such as tetrahydrofuran (THF) and toluene (Runs 4−5 and 7−8 in Table 1), was much poorer compared to that in an aqueous solution. Furthermore, the molecular weight (M_n) of the poly(7-$ONorOH_2$) obtained by PCy_2Ru-βCD in an aqueous solution was higher than those obtained in organic solvents.

In an aqueous solution, water molecules typically occupied the apolar CD cavity, which is energetically unfavorable (polar−apolar interaction). Consequently, the water molecules were readily substituted by the appropriate "hydrophobic guest molecules". We speculated that the initiation efficacy of PCy_2Ru-βCD is similar to that of PCy_2Ru-αCD due to the same catalytic metal center. In reality, however, the polymerization activity of PCy_2Ru-βCD was higher than that of PCy_2Ru-αCD. These results indicate that complexation between PCy_2Ru-CD and 7-$ONorOH_2$ in water increases the polymer yield.

To confirm that complexation between PCy_2Ru-CD and 7-$ONorOH_2$ on ROMP is significant, we investigated the association constants (K_a) of PCy_2Ru-CDs with 7-$ONorOH_2$ in water. The K_a's of PCy_2Ru-αCD and PCy_2Ru-βCD with 7-$ONorOH_2$ were 170 ± 20 and 460 ± 60 M^{-1}, respectively, indicating that PCy_2Ru-βCD effectively forms an inclusion complex with 7-$ONorOH_2$ in water instead of with PCy_2Ru-αCD. The difference in the complexation ability is responsible for the different polymer yields in the polymerization of 7-$ONorOH_2$ initiated by PCy_2Ru-CDs in aqueous solutions.

Next we investigated the inhibition of ROMP of 7-$ONorOH_2$ using a competitive guest such as *tert*-butanol, 3-chloro-phenol (3-Cl-phenol), or adamantane (Ad). Ad derivatives exhibited $K_a \approx 10^4$ M^{-1} for βCD.[51] An NMR titration measurement determined that K_a of 3-Cl-phenol with PCy_2Ru-βCD was 660 ± 70 M^{-1}, which is larger than that of 7-$ONorOH_2$. Actually, 100 equivalents of the competitive guest were mixed with PCy_2Ru-CDs. The PCy_2Ru-CDs with competitive guests exhibited a low polymerization activity for 7-$ONorOH_2$ (Runs 9−12 in Table 1). If PCy_2Ru-CDs initiated polymerization regardless of molecular recognition for 7-$ONorOH_2$, PCy_2Ru-CDs with and without competitive guests would be indistinguishable. On the contrary, competitive guests included in the CD unit of PCy_2Ru-CD inhibited monomer recognition of PCy_2Ru-CDs in water. Because these hydrophobic competitive guest molecules inhibited complexation of 7-$ONorOH_2$/PCy_2Ru-CDs, the competitive guest molecules

Table 1. Polymerizations of 7-Oxanorbornene Dimethanol (7-$ONorOH_2$) Initiated by PCy_2-Ru-CDs in Various Solvents[a]

entry	catalyst	solvent	competitive guest	conversion/%	$M_n/10^3$[b]	M_w/M_n[b]
1	$RuCl_3{\cdot}3H_2O$	water	——	<1	——	——
2	$RuCl_2(TPPTS)_2$	water	——	<1	——	——
3	PCy_2Ru-αCD	water	——	31	11	1.7
4	PCy_2Ru-αCD	THF	——	2	——	——
5	PCy_2Ru-αCD	toluene	——	3	——	——
6	PCy_2Ru-βCD	water	——	80	13	1.3
7	PCy_2Ru-βCD	THF	——	13	8.1	2.0
8	PCy_2Ru-βCD	toluene	——	29	5.3	1.7
9	PCy_2Ru-αCD	water	*t*-butanol[c]	24	12	1.5
10	PCy_2Ru-αCD	water	3-Cl-phenol[c]	20	12	1.5
11	PCy_2Ru-βCD	water	adamantane[c]	12	11	1.2
12	PCy_2Ru-βCD	water	3-Cl-phenol[c]	11	13	1.3

[a][7-$ONorOH_2$]/[PCy_2Ru-CD] = 100. PCy_2Ru-CD and 7-$ONorOH_2$ are heated at 45 °C for 14 h. [b]M_n and M_w/M_n are determined by GPC calibrated by polystyrene standards. Eluent is dimethylformamide with lithium bromide. [c]Competitive guest molecules are added to PCy_2Ru-CD prior to initiation of polymerization ([Competitive guest]/[PCy_2Ru-CD] = 100).

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decreased the polymer yield. These observations confirm that the CD unit plays an important role in recognizing the monomer and initiating of 7-ONorOH$_2$.

In conclusion, we demonstrated that water-soluble CD−Ru complexes behave as a ROMP catalyst for 7-ONorOH$_2$ without a cocatalyst in aqueous solutions. Figure 2 shows a proposed

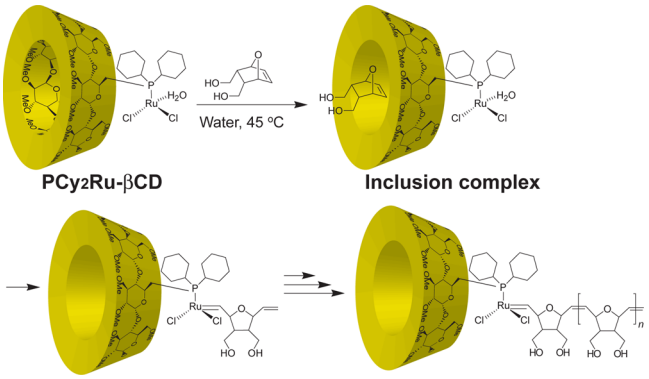

Figure 2. Proposed ROMP mechanism of 7-ONorOH$_2$ initiated by PCy$_2$Ru-βCD in aqueous solutions.

ROMP mechanism of 7-ONorOH$_2$ initiated by PCy$_2$Ru-βCD. The first step is the complexation of 7-ONorOH$_2$ with the TM-βCD unit to give a 1:1 inclusion complex. Then the Ru metal center of PCy$_2$Ru-βCD attacks the double bond of the included 7-ONorOH$_2$ to form a PCy$_2$Ru-βCD−7-ONorOH$_2$ complex. The TM-βCD moiety in PCy$_2$Ru-βCD acts as a molecular recognition site to pass to the Ru catalytic metal center, and the metal center converts the monomer to produce a polymer chain. Continuous inclusion and insertion of 7-ONorOH$_2$ yield linear poly(7-ONorOH$_2$). The polymerization activities of PCy$_2$Ru-CDs depend on the monomer recognition properties. The proper TM-CD with a monomer recognition property displays a high polymerization activity. In contrast, the inhibition of the monomer recognition on the site of TM-CD suppresses the ROMP activity. We have successfully demonstrated the effect of a host−guest interaction in ROMP. Previously, we have reported the ring-opening polymerization of lactones initiated by CD dimers.[44] We suppose that host molecules with polymerization active species will improve the initiation and propagation steps in other polymerization reactions. We are currently investigating the effect of the monomer recognition site in polymerization reactions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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