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Design of Hydrophilic Ruthenium Catalyst for Metal-Catalyzed Living Radical Polymerization: Highly Active Catalysis in Water

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A novel hydrophilic phosphine ligand for ruthenium catalyst was synthesized toward useful living radical polymerization in water. Triethylene glycol (TEG) was introduced at para position of triphenylphosphine and the resultatnt TEG-decorated ligand was combined with Cp*-based ruthenium precursor ($[Cp^*Ru(\mu_3\text{-}Cl)]_4$) to prepare hydrophilic ruthenium complex. The obtained ruthenium complex induced homogeneous controlled polymerization of poly(ethylene glycol) methacrylate (PEGMA) in water: the monomer conversion reached over 90% in 20 min., and the obtained polymers showed narrow MWD ($M_w/M_n < 1.16$). The ruthenium catalyst was active enough to allow decrease in catalyst amount ($[Ru]_0/[Initiator]_0$ = 1/100) or polymerization at low temperature, 0 ˚C [for 2-hydroxyethyl methacrylate(HEMA)]. The catalyst also induced aqueous block copolymerization for the combination of water-soluble monomers: PEGMA/HEMA and PEGMA/2-(dimethylamino)ethyl methacrylate (MeDMA).

Introduction

Water is an ideal solvent for polymerizations in terms of sustainability because it is not only eco-friendly but also much cheaper than organic counterparts. In addition, water solvent is essential when polymer chain is connected with biomolecule via bio-conjugation through controlled polymerization: the inherent functions of biomolecules could be diminished unless water is used as the solvent.

So far, some controlled radical polymerizations have been developed using various methodologies, such as metal-catalyzed (ATRP)[1–9], nitroxide-mediated (NMP)[10,11], reversible addition fragmentation chain transfer (RAFT)[12,13], tellurium-mediated (TERP)[14], and cobalt-mediated (CMRP)[15]. Above all, metal-catalyzed living radical polymerization is user-friendly due to the simple procedure and versatile design of the initiator/catalyst. However, use of metal sometimes incurs limitation of the utility, because the catalyst could suffer from poisoning by polar solvents including water, leading to loss of catalytic activity. Especially, for ruthenium (Ru)[16] and iron (Fe)[17–19] catalysis, an active and useful system in water is still limited, in contrast to copper (Cu)-based[20–38]. Since required compatibility of the central metal of catalyst depends on bioapplications, active catalysis in water is important for each central metal.

Recently, we found that coordination of phenolic phosphine ligand (**P-PhOH**) on Cp*-based (Cp* = pentamethyl-cyclopentadienyl) ruthenium catalyst allowed living radical polymerization of water-soluble methacrylate monomers in water[16] (Figure 1). The catalytic activity was high enough to induce fast controlled radical polymerization even at lower temperature (40˚C). However, the hydrophilicity of the phenol-based ligand was insufficient for the resultant complex to be perfectly soluble in water. The polymerization seems to proceed nearly homogeneously, but indeed the catalyst is just dispersed thanks to liquid monomers of amphiphilic features. Furthermore, the reactive phenoxy anion could coordinate on ruthenium center to deactivate the catalyst, which is described later.

In this paper, we introduced triethylene glycol (TEG) as hydrophilic group from the phenol site of **P-PhOH** via substituent reaction to prepare the TEG-decorated phosphine ligand (**P-TEG**). The hydroxy group of TEG would not affect the ligation of phosphorus (P) or polymerization control, since radical polymerization can be controlled in alcohol solvents using similar phosphine-based ruthenium catalyst. Consequently, coordination of **P-TEG** on ruthenium catalyst allowed very active living radical polymerization in water.

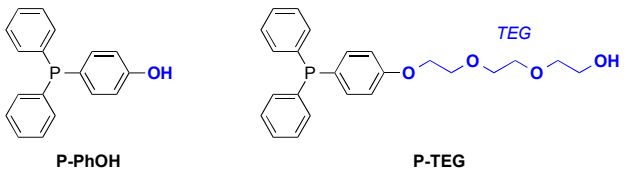

Figure 1. Hydrophilic phosphine ligands for ruthenium catalyzed aqueous polymerization.

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Experimental

Materials

PEGMA [$CH_2C(CH_3)COO(CH_2CH_2O)_nCH_3$; n = 8.5 (number-average)] (Aldrich) and HEMA (Aldrich; > 99%) were purified by passing through an inhibitor-removal column (Aldrich) and were subsequently degassed by three-time vacuum-argon bubbling cycles before use. The ruthenium tetramer precursor $[Cp^*Ru(\mu_3\text{-}Cl)]_4$[39,40] and $H(MMA)_2\text{–}Cl$[41] initiator [$H(CH_2CMeCO_2Me)_2Cl$; an MMA dimer chloride] were prepared according to the literature. (4-Hydroxyphenyl)diphenylphosphine and materials for preparation of $[Cp^*Ru(\mu_3\text{-}Cl)]_4$, listed below, were used as received without further purification and handled in a glovebox (MBraun Labmaster 130, M. Braun Inertgas-Systeme GmbH, Garching, Germany) under a moisture- and oxygen-free argon atmosphere (H_2O < 1 ppm; O_2 < 1 ppm): ruthenium(III) chloride hydrate (Wako; > 99.9%); 1,2,3,4,5-pentamethylcyclopentadiene (TCI; > 93%); and lithium triethylhydridoborate (Aldrich, 1.0 M solution in THF). Toluene (Kishida Kagaku; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, SG Water USA, Nashua, NH; Glass Contour) and bubbled with dry nitrogen for more than 15 min immediately before use. Water (Wako; distilled), buffer solutions (TCI) and ethanol (Wako; super dehydrated) were bubbled with dry nitrogen for more than 15 min immediately before use. 1,2,3,4-tetrahydronaphthalene (tetralin; internal standard for ^{1}H NMR) was dried over calcium chloride and distilled from calcium hydride. MeDMA (methyl chloride-quaternized 2-(dimethylamino)ethyl methacrylate) (Wako; >97.0%), 2-[2-(2-Chloroethoxy)ethoxy]-ethanol (TCI; >96%), K_2CO_3 (Wako; > 99.5%), NaCl (Wako; > 99.5%), DMF (Wako; super dehydrated), diethyl ether (Wako; > 99.5%), hexane (Wako; > 96.0%), ethyl acetate (Wako; > 99.5%), silica gel (Wako; Wakogel® C-200) are used as received.

Ligand synthesis (P-TEG)

A suspension of (4-hydroxyphenyl)diphenylphosphine (913 mg, 3.28 mmol), 2-[2-(2-chloroethoxy)ethoxy]ethanol (580 mg, 3.44 mmol) and K_2CO_3 (544 mg, 3.94 mmol) in DMF (15 mL) was stirred at 90 ˚C for 40 h under argon. After evaporation of DMF at 50 ˚C, diethyl ether (80 mL) was added to the residue. The organic layer was washed with water (1 × 60 mL) and brine (1 × 60 mL), and then the aqueous layer was extracted by diethyl ether (2 × 60 mL). The combined organic layer was dried over anhydrous Na_2SO_4. After filtration, the filtrate was evaporated under vacuum. **P-TEG** was isolated by silica gel column chromatography using hexane/ethyl acetate (50/50) as an eluent in 70% yield (947 mg). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.44-7.33 (m, 6H), 7.26-7.15 (m, 6H), 7.00 (d, J = 7.7 Hz, 2H), 4.56 (t, J = 5.4 Hz, 1H), 4.10 (t, J = 4.6 Hz, 2H), 3.74 (m, J = 4.6 Hz, 2H), 3.61-3.56 (m, 2H), 3.56-3.51 (m, 2H), 3.48 (dt, J = 5.4, 5.2 Hz, 2H), 3.41 (t, J = 5.2 Hz, 2H). ^{13}C NMR (125 MHz, methanol-d_4): δ 161.2, 139.3, 139.2, 136.7, 136.5, 134.5, 134.3, 129.6, 129.5, 129.4, 129.2, 129.1, 116.0, 115.9, 73.7, 71.8, 71.4, 70.8, 68.5, 62.2. ^{31}P NMR (202 MHz, toluene-d_8): δ -6.1. ESI-MS: m/z 433.23 ($[M+Na]^+$; calcd. 433.15).

Polymerization procedures

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with a three-way stopcock or in sealed glass vials. An example for PEGMA polymerization with the H-MMA_2-Cl/$[Cp^*Ru(\mu_3\text{-}Cl)]_4$/**P-TEG** in water is given below. $[Cp^*Ru(\mu_3\text{-}Cl)]_4$ (2.2 mg, 0.0020 mmol), 100 mM **P-TEG** in toluene (0.16 mL, 0.016 mmol), and toluene (1.0 mL) was placed in a Schlenk tube. The solution was heated to 60 ˚C for 2 h to prepare ruthenium complex. After cooling the mixture to room temperature and removal of toluene under vacuum, PEGMA (0.88 mL, 2.0 mmol), buffer solution (TCI B0178; pH 8.0) (3.02 mL) and 200 mM H-MMA_2-Cl in ethanol (0.10 mL, 0.020 mmol) were added; the total volume was 4.0 mL. Immediately after mixing, aliquots (0.50−1.0 mL each) of the solution were injected into baked glass tubes, which were then sealed (except when a stopcock was used) and placed in an oil bath kept at 40 ˚C. In predetermined intervals, the polymerization was terminated by adding methanol containing air to the reaction mixture and cooling it to −78 °C in dry ice−methanol. Monomer conversion was determined by ^{1}H NMR from the integrated peak area of the olefinic protons of the monomer with ethanol as an internal standard. Obtained polymer solutions were evaporated under vacuum and dissolved in DMF (1.0 wt%). After filtration of the solutions, the filtrates were analysed with SEC.

Another example for HEMA polymerization with the H-MMA_2-Cl/$[Cp^*Ru(\mu_3\text{-}Cl)]_4$/**P-TEG** in water-ethanol mixed solvent (1/1 v/v%) is also given below. $[Cp^*Ru(\mu_3\text{-}Cl)]_4$ (2.2 mg, 0.0020 mmol), 100 mM **P-TEG** in toluene (0.16 mL, 0.016 mmol), and toluene (1.0 mL) was placed in a Schlenk tube. The solution was heated to 60 ˚C for 2 h to prepare ruthenium complex. After cooling the mixture to room temperature and removal of toluene under vacuum, HEMA (0.97 mL, 8.0 mmol), ethanol (1.36 mL), water (1.52 mL) and 500 mM H-MMA_2-Cl in ethanol (0.16 mL, 0.080 mmol) were added; the total volume was 4.0 mL. Immediately after mixing, aliquots (0.50−1.0 mL each) of the solution were injected into baked glass tubes, which were then sealed (except when a stopcock was used) and placed in an oil bath kept at polymerization temperature (40 ˚C or 0 ˚C). In predetermined intervals, the polymerization was terminated, and the monomer conversion was determined, followed by SEC analysis in the same way as mentioned above.

For synthesis of PEG–*block*–PHMEA with $[Cp^*Ru(\mu_3\text{-}Cl)]_4$/**P-TEG** in water is given below. $[Cp^*Ru(\mu_3\text{-}Cl)]_4$ (5.4 mg, 0.0050 mmol), 100 mM **P-TEG** in toluene (0.40 mL, 0.040 mmol), and toluene (1.0 mL) was placed in a Schlenk tube. The solution was heated to 60 ˚C for 2 h to prepare ruthenium complex. After cooling the mixture to room temperature and removal of toluene under vacuum, 0.75 mL of ethanol was added, leading to 27 mM solution in ethanol. PEG-Cl (M_n ~ 4500) (0.36 g, 0.080 mmol), HEMA (0.97 mL, 8.0 mmol) and water (2.73 mL) were placed in another Schlenk tube and the 27 mM catalyst solution in ethanol (0.30 mL, 0.0080 mmol) was added (total volume: 4.0 mL). Immediately after mixing,

aliquots (0.50−1.0 mL each) of the solution were injected into baked glass tubes, which were then sealed (except when a stopcock was used) and placed in an oil bath kept at 40 ˚C. In predetermined intervals, the polymerization was terminated, and the monomer conversion was determined, followed by SEC analysis.

For synthesis of PEG–*block*–PMeDMA with [Cp*Ru(μ_3-Cl)]$_4$/**P-TEG** in water is given below. Ruthenium catalyst solution (27 mM in ethanol) was prepared in the same way as for PEG–*block*–PHEMA synthesis. PEG-Cl (M_n ~ 4500) (0.36 g, 0.080 mmol), MeDMA (0.83 g, 4.0 mmol), water (3.60 mL), ethanol (0.10 mL) and 27 mM ruthenium catalyst solution in ethanol (0.30 mL) were placed in a Schlenk tube; the total volume was 4.0 mL. The polymerization was performed in the same way as for PEG–*block*–PHEMA synthesis. Obtained polymer solutions were evaporated under vacuum and dissolved in water (0.1 wt%). After filtration of the solutions, the filtrates were analysed with aqueous GPC equipped with columns specific to cationic water-soluble polymers.

Measurements

For neutral (co)polymers of PEGMA or HEMA, M_n and M_w/M_n were measured by size exclusion chromatography at 40 °C in DMF containing 10 mM LiBr as an eluent on three polystyrene-gel columns (Shodex KF-805L; exclusion limit =4 × 10^6; particle size =10 μm; pore size =5000 A; 0.8 cm i.d. × 30 cm; flow rate, 1.0 mL min^{-1}) connected to a PU-2080 pump and a RI-1530 refractive-index detector, and a UV-1570 ultraviolet detector (all from Jasco). The columns were calibrated against 13 standard poly(MMA) samples (Polymer Laboratories; M_n = 630−1 200 000; M_w/M_n = 1.02−1.30) as well as the monomer. For PEG-*block*-PMeDMA, M_n and M_w/M_n were measured by size exclusion chromatography at 40 ˚C in H_2O containing 100 mM $NaNO_3$ as an eluent on one polystyrene-gel columns (TOSOH TSK-GEL® G3000PW$_{XL}$-CP; exclusion limit = 1 × 10^5; particle size = 7 μm; 7.8 mm I.D. × 30 cm; flow rate, 1.0 mL min^{-1}) connected to a PU-1580 pump, a RI-930 refractive-index detector, and a UV-970 ultraviolet detector (all from Jasco), similarly calibrated against standard PEO samples. ^{1}H NMR and ^{31}P NMR spectra were measured at room temperature on a JEOL JNM-ECA500 spectrometer operating at 500.16 and 202.47 MHz, respectively. For the ^{31}P NMR analyses, a capillary of diethyl phosphite solution (50 mM in toluene-d_8) was used as an internal chemical shift standard (7.08 ppm for the phosphite).

Results and discussion

Ligation of P-TEG on Cp*-Based ruthenium complex

The TEG-decorated phosphine, **P-TEG**, was mixed with a tetrameric precursor of pentamethylcyclopentadienyl (Cp*) ruthenium complexes ([Cp*Ru(μ_3-Cl)]$_4$) [ref] in toluene at 60 ˚C to prepare corresponding phosphine complex [Cp*RuCl(**P-TEG**)$_n$] (Figure 2). Here, to study the coordination number of the phosphine ligand, they were mixed on three different ratios, [Ru]$_0$/[**P-TEG**]$_0$ = 1/1, 1/2 and 1/3 molar ratios, and ^{31}P NMR was directly measured for the resultant solutions. In the case of the ratio of 1/1 or 1/2, no peak derived from "free" or non-coordinated phosphine was observed at around –6 ppm, and instead a new peak appeared at 40 ppm, likely derived from coordinated phosphine. In sharp contrast, when more than two equivalents of phosphine was used ([Ru]$_0$/[**P-TEG**]$_0$ = 1/3), both peaks from free and coordinated phosphine ligands. These results indicated that two phosphine ligands were coordinated on ruthenium center to give [Cp*RuCl(**P-TEG**)$_2$] via the aging process.

When the ratio was 1/2, only one peak was observed likely from coordinating phosphine (*b*) in the ^{31}P NMR spectrum, though a minor one was from the oxidized phosphine. On the other hand, when the phenolic ligand (**P-PhOH**) was employed, another peak was clearly observed in addition to the peak from coordinating phosphine (Figure S1). This peak is probably derived from phosphine ligand whose phenoxy group is ligating on ruthenium. Therefore, P-TEG would be more suitable than **P-PhOH** as the ligand selectively giving the two phosphine-coordinating complex [Cp*RuCl(phosphine)$_2$]. In the following polymerizations, we heated the solution of [Cp*Ru(μ_3-Cl)] and 2 equivalents of **P-TEG** before polymerization and the resultant complex was used as the catalyst without purification.

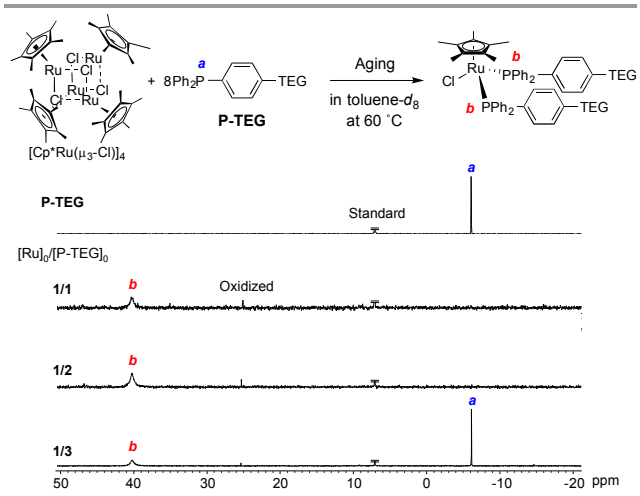

Figure 2. Ligation scheme of P-TEG on Cp*-based ruthenium complex and ^{31}P NMR spectra of P-TEG and complexes prepared with 1:1, 1:2 or 1:3 ratio ([Ru]$_0$:[Ligand]$_0$) in toluene-d_8 at r.t.: [P-TEG]$_0$ = 8.0 mM; [[Cp*Ru(μ_3-Cl)]$_4$]$_0$ = 1.0 mM, [**P-TEG**]$_0$ = 4.0 mM; [[Cp*Ru(μ_3-Cl)]$_4$]$_0$ = 1.0 mM, [**P-TEG**]$_0$ = 8.0 mM; [[Cp*Ru(μ_3-Cl)]$_4$]$_0$ = 1.0 mM, [**P-TEG**]$_0$ = 12.0 mM.

Aqueous living radical polymerization of PEGMA

The *in situ* synthesized **P-TEG** ruthenium catalyst was used for living radical polymerization of PEGMA in water at 40˚C, in conjunction with a chloride-type initiator [H–(MMA)$_2$–Cl] (Figure 3). Note that amine cocatalyst was not employed, although it is usually necessary for ruthenium-catalyzed system in organic solvent. Nevertheless, the monomer was smoothly consumed and the conversion reached over 90% in less than half hour (91%, 20 minutes). SEC analyses of obtained polymers showed the polymerization was fairly controlled:

molecular weight was increased with conversion and molecular weight distributions (MWDs) were narrow (M_w/M_n ~ 1.16–1.22) through polymerization. By contrast, when **P-PhOH** was used, the polymerization was slower and MWDs of obtained polymers were broader (M_w/M_n ~ 1.32–1.40). Thus, faster polymerization with better control was possible through modification with TEG chain for the phenol site of **P-PhOH**.

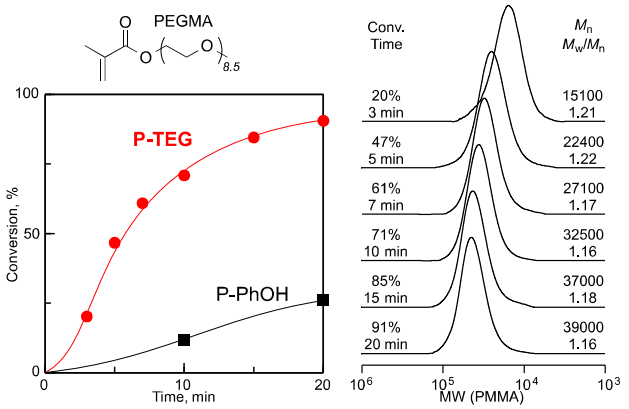

Figure 3. Effects of Ligand on aqueous polymerizations of PEGMA with H-$(MMA)_2$-Cl/$[Cp^*Ru(\mu_3\text{-Cl})]_4$/Ligand in H_2O at 40 ˚C: $[PEGMA]_0$ = 500 mM; $[H\text{-}(MMA)_2\text{-Cl}]_0$ = 5.0 mM; $[[Cp^*Ru(\mu_3\text{-Cl})]_4]_0$ = 0.5 mM; $[Ligand]_0$ = 4.0 mM.

Decrease in catalyst dose

Most of practical applications with hydrophilic polymers, little metal residue is highly required, especially for bioapplications. Use of catalyst insoluble in water might be useful in terms of removal of metal residue, but in this case controllability would be sacrificed. One simple but feasible idea is utilizing very lower amount of catalyst for homogeneous polymerization, though it may be not perfect panacea. The very active catalysis with the **P-TEG** catalyst encouraged us to decrease the catalytic amount for the polymerization.

In above polymerization, one-tenth amount of catalyst was used for the initiator ($[cat]_0/[init]_0$ = 1/10). Lower catalyst amount of 1/50 and 1/100 were tested for the polymerization (Figure 4). Consequently, polymerizations proceeded even with such lower amount of catalyst without serious loss of polymerization rate, and polymerizations were basically controlled, though the MWDs of obtained polymers were broader. As shown in photographs of polymerization solutions, the polymerization solution of 1/100 was almost colorless indicating very low amount of ruthenium catalyst. Unfortunately, further decrease in catalyst (i.e., 1/200) resulted in much broader MWDs of obtained polymers.

HEMA polymerization at low temperature in aqueous media

HEMA is also an important water-soluble methacrylate monomer, and the polymer has been used for functional materials such as soft contact lens. High catalytic activity of **P-TEG** ligated ruthenium catalyst for aqueous polymerization of PEGMA encouraged us to apply it for HEMA polymerization. Since it has been reported that HEMA polymerization in neat water incurs cross-linking reaction to give insoluble gel[42], we used water-ethanol mixed solvent (1/1 v/v%) (Figure 5).

Consequently, HEMA was also polymerized with the **P-TEG** ligated ruthenium complex to reach high conversion (>80%) and SEC curves of obtained polymer showed narrow MWDs (M_w/M_n ~1.2). The mixed solvent with ethanol allowed polymerization at 0 ˚C without freezing and the polymerization smoothly proceeded even at 0 ˚C to give higher conversion (~90%), though the polymerization got slower. Thus, catalytic activity of the **P-TEG** ligated ruthenium complex was

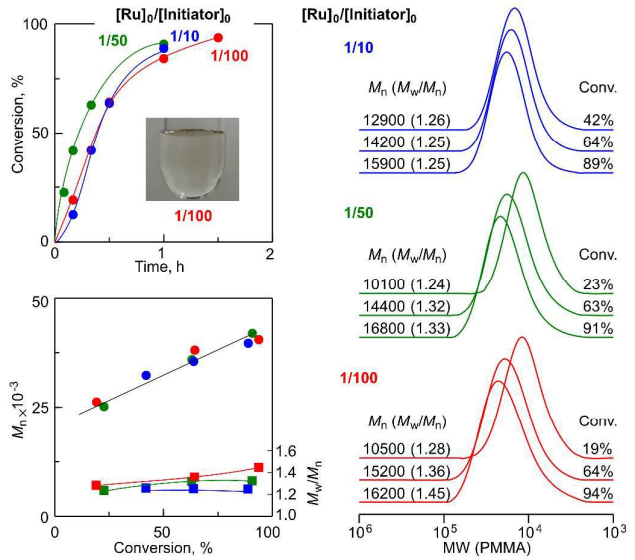

Figure 4. Decrease in catalyst dose on aqueous polymerizations of PEGMA with H-$(MMA)_2$-Cl/$[Cp^*Ru(\mu_3\text{-Cl})]_4$/P-TEG in H_2O at 40 ˚C: $[PEGMA]_0$ = 500 mM; $[H\text{-}(MMA)_2\text{-Cl}]_0$ = 20 mM; $[[Cp^*Ru(\mu_3\text{-Cl})]_4]_0$ = 0.5, 0.1 or 0.05 mM; $[P\text{-TEG}]_0$ = 4.0, 0.8 or 0.4 mM.

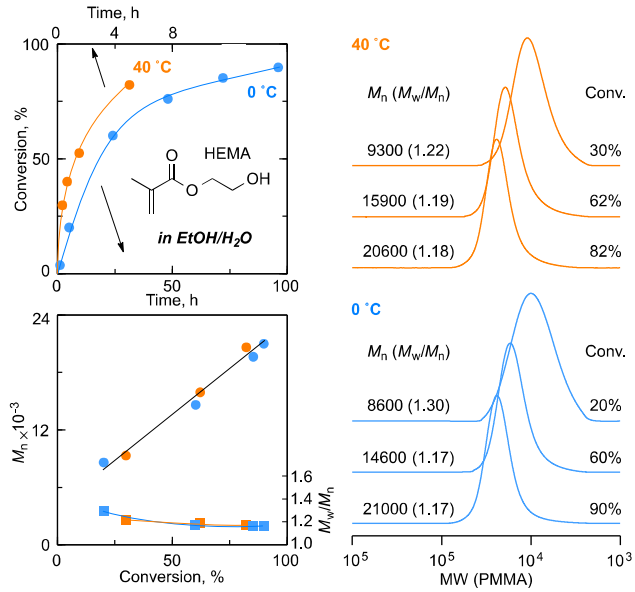

Figure 5. Effects of temperature on HEMA polymerizations with H-$(MMA)_2$-Cl/$[Cp^*Ru(\mu_3\text{-Cl})]_4$ in EtOH/H_2O (1/1, v/v) at 40 ˚C or 0 ˚C: $[HEMA]_0$ = 2.0 M; $[H\text{-}(MMA)_2\text{-Cl}]_0$ = 20 mM; $[[Cp^*Ru(\mu_3\text{-Cl})]_4]_0$ = 0.5 mM; $[\textbf{P-TEG}]_0$ = 4.0 mM.

sufficiently high to catalyze aqueous polymerization even at lower temperature. This would be a great advantage for bio-conjugation application using temperature-sensitive biomolecules.

Aqueous block copolymerization with PEG

Block copolymerization is a very important application with living polymerization techniques because it would involve various possibilities. The results on controlled propagation in water with the **P-TEG** ligated ruthenium complex motivated us to prepare block copolymers in water by using hydrophilic macroinitiator. Herein, polyethylene glycol (PEG)-based initiator (PEG–Cl: M_n = 4500, M_w/M_n = 1.04) was selected as the macroinitiator because PEG is one of most important water-soluble polymers due to the high biocompatible features. Herein we used an ammonium salt-based methacrylate carrying cationic pendant side chain (MeDMA) as well as HMEA as the monomer for the second block segment.

In both of the polymerizations, the monomers were smoothly consumed and finally the conversion reached around 90% in 4 hours. SEC curves of the obtained polymers clearly shifted to higher molecular weight increase in the monomer conversion almost keeping the unimodal distributions. However, in the case of polymerization of MeDMA, small shoulder peaks was clearly detected at lower molecular weight region, although the ratio to the main peak was gradually decreased as the polymerization proceeded. The molecular weight distributions curves were obtained by aqueous SEC equipped with columns suitable for analyses of cationic polymers in water, which was different from that for analyses of HEMA-based block copolymers with DMF eluent. This may affect the SEC analyses, resulting in clear bimodal molecular weight distribution curves. It may be necessary to improve the condition of aqueous SEC analyses,[43] but it is likely concluded that the propagations in the two block copolymerizations in water are fairly controlled.

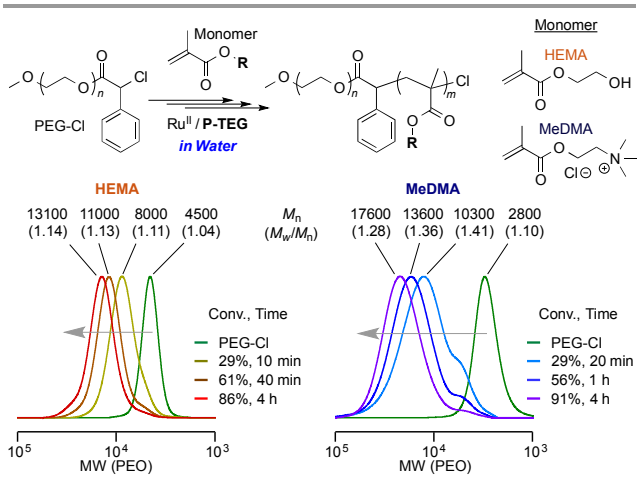

Figure 6. Aqueous block polymerizations of HEMA or EtOH with PEG-Cl (M_n ~ 5000) in water/ethanol (9/1, v/v) at 40 ˚C: $[HEMA]_0$ = 2000 mM, $[PEG\text{-}Cl]_0$ = 20 mM, $[[Cp^*Ru(\mu_3\text{-}Cl)]_4]_0$ = 0.5 mM, $[\textbf{P-TEG}]_0$ = 4.0 mM; $[MeDMA]_0$ = 1000 mM, $[PEG\text{-}Cl]_0$ = 20 mM, $[[Cp^*Ru(\mu_3\text{-}Cl)]_4]_0$ = 0.5 mM, $[\textbf{P-TEG}]_0$ = 4.0 mM.

Conclusions

In this paper, we newly designed a TEG-decorated phosphine ligand (**P-TEG**) for ruthenium-catalyzed living radical polymerization in water. The two phosphine ligated complex [Cp*RuCl(**P-TEG**)$_2$] showed high activity for aqueous controlled radical polymerization of PEGMA in conjunction with a chlorine-based initiator without any cocatalysts. The high activity allowed reduction in catalyst dose and controlled catalysis for HEMA polymerization even at low temperature as well as aqueous block copolymerizations of hydrophilic monomers. We believe that the catalytic system with the **P-TEG** ligated ruthenium complex is highly suitable for precise preparation of water-soluble polymers further leading to development in terms material- and bio-applications.

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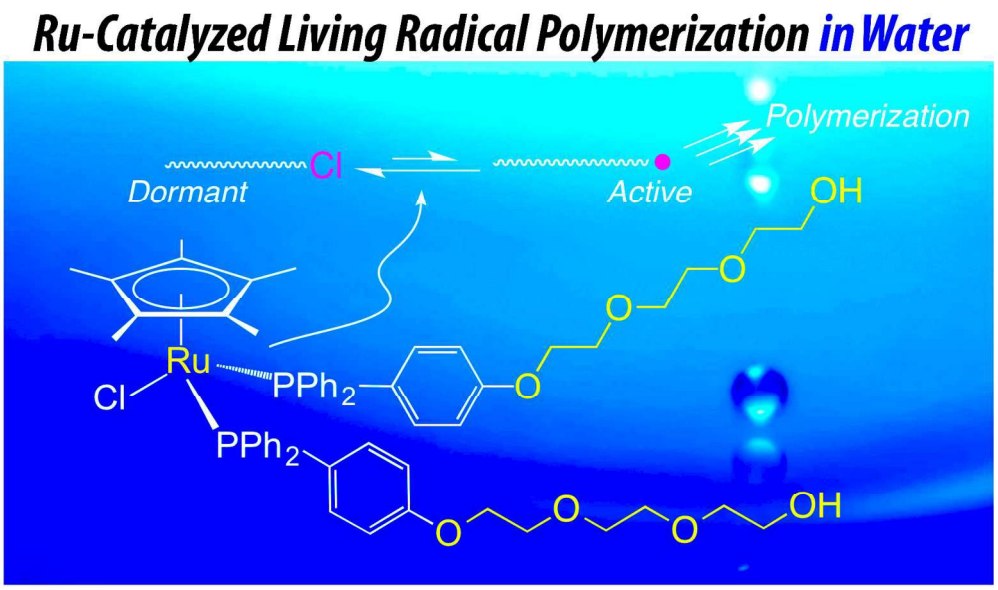
References

1 M. Kato, M. Kamigaito, M. Sawamoto and T. Higashimuras, *Macromolecules*, 1995, **28**, 1721–1723.
2 M. Kamigaito, T. Ando and M. Sawamoto, *Chem. Rev.*, 2001, **101**, 3689–3746.
3 M. Ouchi, T. Terashima and M. Sawamoto, *Acc. Chem. Res.*, 2008, **41**, 1120–1132.
4 M. Ouchi, T. Terashima and M. Sawamoto, *Chem. Rev.*, 2009, **109**, 4963–5050.
5 J. Wang and K. Matyjaszewski, *J. Am. Chem. Soc.*, 1995, **117**, 5614–5615.
6 K. Matyjaszewski and J. Xia, *Chem. Rev.*, 2001, **101**, 2921–2990.
7 N. V Tsarevsky and K. Matyjaszewski, *Chem. Rev.*, 2007, **107**, 2270–2299.
8 K. Matyjaszewski and N. V. Tsarevsky, *J. Am. Chem. Soc.*, 2014, **136**, 6513–6533.
9 B. M. Rosen and V. Percec, *Chem. Rev.*, 2009, **109**, 5069–5119.
10 C. J. Hawker, A. W. Bosman and E. Harth, *Chem. Rev.*, 2001, **101**, 3661–3688.
11 J. Nicolas, Y. Guillaneuf, C. Lefay, D. Bertin, D. Gigmes and B. Charleux, *Prog. Polym. Sci.*, 2013, **38**, 63–235.
12 G. Moad, E. Rizzardo and S. H. Thang, *Polymer*, 2008, **49**, 1079–1131.
13 G. Moad, E. Rizzardo and S. H. Thang, *Aust. J. Chem.*, 2012, **65**, 985–1076.
14 S. Yamago, *Chem. Rev.*, 2009, **109**, 5051–5068.
15 A. Debuigne, R. Poli, C. Jérôme, R. Jérôme and C. Detrembleur, *Prog. Polym. Sci.*, 2009, **34**, 211–239.
16 M. Ouchi, H. Yoda, T. Terashima and M. Sawamoto, *Polym. J.*, 2012, **44**, 51–58.
17 W. He, L. Zhang, J. Miao, Z. Cheng and X. Zhu, *Macromol. Rapid Commun.*, 2012, **33**, 1067–1073.
18 A. Simakova, M. Mackenzie, S. E. Averick, S. Park and K. Matyjaszewski, *Angew. Chem., Int. Ed.*, 2013, **52**, 12148–12151.
19 K. Yamashita, K. Yamamoto and J. Kadokawa, *Polymer*, 2013, **54**, 1775–1778.

20 S. Coca, C. B. Jasieczek, K. L. Beers and K. Matyjaszewski, *J. Polym. Sci. Part A Polym. Chem.*, 1998, **36**, 1417–1424.
21 E. J. Ashford, V. Naldi, R. O'Dell, N. C. Billingham and S. P. Armes, *Chem. Commun.*, 1999, 1285–1286.
22 X.-S. Wang, R. a Jackson and S. P. Armes, *Macromolecules*, 2000, **33**, 255–257.
23 X. S. Wang and S. P. Armes, *Macromolecules*, 2000, **33**, 6640–6647.
24 E. J. Lobb, I. Ma, N. C. Billingham, S. P. Armes and A. L. Lewis, *J. Am. Chem. Soc.*, 2001, **123**, 7913–7914.
25 J. K. Oh, F. Perineau, B. Charleux and K. Matyjaszewski, *J. Polym. Sci. Part A Polym. Chem.*, 2009, **47**, 1771–1781.
26 N. Bortolamei, A. a. Isse, A. J. D. Magenau, A. Gennaro and K. Matyjaszewski, *Angew. Chem., Int. Ed.*, 2011, **50**, 11391–11394.
27 D. Konkolewicz, A. J. D. Magenau, S. E. Averick, A. Simakova, H. He and K. Matyjaszewski, *Macromolecules*, 2012, **45**, 4461–4468.
28 A. Simakova, S. E. Averick, D. Konkolewicz and K. Matyjaszewski, *Macromolecules*, 2012, **45**, 6371–6379.
29 Q. Zhang, P. Wilson, Z. Li, R. McHale, J. Godfrey, A. Anastasaki, C. Waldron and D. M. Haddleton, *J. Am. Chem. Soc.*, 2013, **135**, 7355–7363.
30 Q. Zhang, Z. Li, P. Wilson and D. M. Haddleton, *Chem. Commun.*, 2013, **49**, 6608–6610.
31 C. M. R. Abreu, a C. Serra, a V Popov, K. Matyjaszewski, T. Guliashvili and J. F. J. Coelho, *Polym. Chem.*, 2013, **4**, 5629–5636.
32 C. Waldron, Q. Zhang, Z. Li, V. Nikolaou, G. Nurumbetov, J. Godfrey, R. McHale, G. Yilmaz, R. K. Randev, M. Girault, K. McEwan, D. M. Haddleton, M. Droesbeke, A. J. Haddleton, P. Wilson, A. Simula, J. Collins, D. J. Lloyd, J. a. Burns, C. Summers, C. Houben, A. Anastasaki, M. Li, C. R. Becer, J. K. Kiviaho and N. Risangud, *Polym. Chem.*, 2014, **5**, 57–61.
33 D. Konkolewicz, P. Krys, J. R. Góis, P. V. Mendonça, M. Zhong, Y. Wang, A. Gennaro, A. a Isse, M. Fantin and K. Matyjaszewski, *Macromolecules*, 2014, **47**, 560–570.
34 F. Alsubaie, A. Anastasaki, P. Wilson and D. M. Haddleton, *Polym. Chem.*, 2015, **6**, 406–417.
35 S. R. Samanta, V. Nikolaou, S. Keller, M. J. Monteiro, D. a. Wilson, D. M. Haddleton and V. Percec, *Polym. Chem.*, 2015, **6**, 2084–2097.
36 M. Zhang, M. F. Cunningham and R. a. Hutchinson, *Polym. Chem.*, 2015, **6**, 6509–6518.
37 Q. Zhang, M. Li, C. Zhu, G. Nurumbetov, Z. Li, P. Wilson, K. Kempe and D. M. Haddleton, *J. Am. Chem. Soc.*, 2015, **137**, 9344–9353.
38 F. Alsubaie, A. Anastasaki, V. Nikolaou, A. Simula, G. Nurumbetov, P. Wilson, K. Kempe and D. M. Haddleton, *Macromolecules*, 2015, **48**, 6421–6432.
39 P. J. Fagan, M. D. Ward and J. C. Calabrese, *J. Am. Chem. Soc.*, 1989, **111**, 1698–1719.
40 P. J. Fagan, W. S. Mahoney, J. C. Calabrese and I. D. Williams, *Organometallics*, 1990, **9**, 1843–1852.
41 T. Ando, M. Kamigaito and M. Sawamoto, *Macromoleculars*, 1998, **2**, 6708–6711.
42 K. L. Robinson, M. a. Khan, M. V. De Paz Báñez, X. S. Wang and S. P. Armes, *Macromolecules*, 2001, **34**, 3155–3158.
43 Indeed, measured value of M_n for PEG–Cl (M_n = 2800) was much lower than ideal, although it was calculated under PEG-based calibration. In such aqueous SEC, hydrophobic moities in hydrophilic polymers likely affect elution behaviors even though they are minor components.



158x93mm (300 x 300 DPI)