“Concerted Redox” Catalysis in Living Radical Polymerization

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2016
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GENERAL INTRODUCTION

Background

Bimetallic Cooperative Catalysis

In the past few decades, transition metal catalysts have become one of the most efficient and powerful tools in organic and polymerization reactions due to their high activity, selectivity (stereo-, regio-, etc.), and extensibility on the basis of flexible and tunable design of the metal center or combined ligands.\textsuperscript{1-3} In some cases, the combination of another metal catalyst is efficient to improve the catalysis (i.e., activity, selectivity, etc.) or to open the door to new reaction through the corporation of two metal catalysts that have different roles therein. Thus, the concept of "bimetallic cooperative catalysis" is a research trend in the field of catalysis.\textsuperscript{4,5} Herein three types of "bimetallic cooperative catalysis" are explained along with the actual examples (Figure 1).

(a) Catalyst Activation (Cocatalyst)

(b) Substrate Activations

(c) Concerted Catalysis

Figure 1. Bimetallic cooperative catalysis: concepts and examples.
(a) **Activation of Main Catalyst.** In some reactions, a main catalyst (Cat\(^1\) in Figure 1a) is activated by another component (cocatalyst; Cat\(^2\)) to catalyze the reaction. A representative example is metal-catalyzed olefin polymerization or coordination polymerization with a group 4 metal catalysts (precatalyst; Cat\(^1\): Ti or Zr) in conjunction with methylaluminoxane \([-\text{Al(Me)}-\text{O}]-_n\) (MAO; Cat\(^2\)).\(^6,7\) MAO reacts with Cat\(^1\) to give *in situ* an active methylated catalyst carrying a vacant site, while transformed into a bulky counter anions for the active catalyst. Therefore, MAO is not only the catalyst activator but also the vital part of the cation–anion ion pairs of the active species, thus strongly affecting the polymerization.

(b) **Activation of Substrate.** In this case, one metal complex (Cat\(^1\) in Figure 1b) catalyzes the reaction, whereas another (Cat\(^2\)) activates the substrate to promote the reaction. Examples include the combination of an enolate-aluminium porphyrin (Cat\(^1\)) with a bulky organoaluminium (Cat\(^2\)) for high-speed living anionic polymerization of methyl methacrylate (MMA).\(^8\text{–}^{10}\) In this polymerization, the monomer is activated through coordination of the bulky organoaluminium (Cat\(^2\)) onto the carbonyl group to enhance the nucleophilic attack by Cat\(^1\), and at the same time unfavorable side reactions such as transmetallations can be suppressed due to its bulkiness. The two different aluminium complexes play their own roles orthogonally, i.e., initiation and activation, without interfering each other in the polymerization in this example.

(c) **Concerted Catalysis.** Here, one reaction is accomplished under two catalytic cycles with two metal catalysts (Figure 1c). Sonogashira coupling reaction is an example where a terminal alkyne reacts with an aryl or vinyl halide under a palladium (Pd)/copper (Cu) cooperated catalysis:\(^11,12\) Pd catalyzes activation of the aryl- and alkenyl halide (oxidative addition), whereas Cu catalyzes alkyne activation in the presence of an amine. The Pd-catalysis and the Cu-catalysis are in concert through the transmetallation step to form an alkylnyl-Pd complex, followed by the reductive elimination on Pd to give the product. Actually, the reaction could proceed with a Pd complex alone\(^13,14\) whereas the bimetallic catalysis allows milder reaction conditions.

This thesis deals with “concerted catalysis” in transition metal-catalyzed living radical polymerization (Mt-LRP) which is now an effective polymerization method to synthesize well-controlled polymers under metal catalysis. Mt-LRP may encompass atom transfer radical polymerizations (ATRP), where the catalysts are primarily copper complexes.
Given the fine reaction control, the versatility based on radical polymerizations, and other features, Mt-LRP is now widely employed in various fields: not only material science but also bioapplications and industry. However, the use of metals could be an issue in such applications, including the contamination of product and expensive processes. As will be discussed in this thesis, the concept of "bimetallic cooperative catalysis" is expected to enhance catalysis efficiency, leading to decreasing catalyst dose and more sustainable, safer, and environmentally friendly systems.

**Transition Metal-Catalyzed Living Radical Polymerization.** Mt-LRP is one of the most powerful precision radical polymerization methods that allow the synthesis of controlled polymers with well-defined primary structures and molecular weights.\(^{15-27}\) As illustrated in Figure 2, transition metal complexes catalyze the reversible activation of the carbon-halogen bond in an initiator (R–X; X = halogen) or the “dormant” polymer end (~~~C–X; ~~ = polymer chain) through the one electron redox reaction (Mt\(^n\) ↔ XMt\(^{n+1}\); Mt = metal) to give “active” radical species (~~~C•; C• = carbon centered radical) that propagates. The reversibility between dormant and active polymer ends, related to the efficiency of the one electron redox cycle driven by metal complexes, is crucial to suppress the radical concentration and, consequently, to suppress unfavorable side reactions such as bimolecular radical coupling and disproportionation. Therefore, the controllability depends on the transition metal catalysts.

![Figure 2. Transition metal-catalyzed living radical polymerization (Mt-LRP).](image-url)
Transition metals for Mt-LRP catalysts now cover a wide range in the periodic table of the elements, e.g., \(\text{Ru}^{28}\), \(\text{Fe}^{29,30}\), \(\text{Cu}^{31-33}\), \(\text{Ni}^{34,35}\), \(\text{Mo}^{36}\), \(\text{Mn}^{37,38}\), \(\text{Os}^{29}\), \(\text{Re}^{40,41}\), \(\text{Co}^{42}\), \(\text{Rh}^{43,44}\), \(\text{Pd}^{45}\), and \(\text{Ir}^{46}\). The monomers amenable for Mt-LRP include virtually all conjugated monomers for radical polymerizations such as methacrylates, styrenes, acrylates, and acrylamides.

The use of transition metal catalysts, on the other hand, has some specific issues in terms of industrial applications: (1) metal contamination of obtained polymers; (2) rising cost from precious metals; (3) deactivation of catalyst by polar groups. Especially for (1) and (2), a critical solution is to reduce the catalyst amount by efficiently facilitating the one electron redox cycle.

**Ruthenium (Ru)-Based Catalysis for Living Radical Polymerization.** Since the first report of ruthenium-catalyzed LRP of MMA with \(\text{RuCl}_2(\text{PPh}_3)_3\),\(^{28,47}\) various effective ruthenium catalysts have been developed mainly based on the ligand designs.\(^{18}\) Among them, ruthenium half-metalloccenes, such as pentamethyl cyclopentadienyl (Cp*)-ligated ruthenium complex \([\text{Ru(Cp*)}]\)\(^{48}\) and indenyl (Ind)-ligated ruthenium complex \([\text{Ru(Ind)}]\),\(^{49}\) are of a quite high catalytic activity (Figure 3), partly because of the lower redox potential resulting from the strong electron donation by Cp* or Ind ligands, meaning high activity for one electron redox reactions.\(^{50}\) They are often coordinatively saturated 18-electron (18e) complexes with phosphine ligands, and ligand dissociation is essential to give the coordinatively unsaturated 16e complexes that, in contrast to the 18e versions, can accept a halogen (X) from the dormant terminal (~~~C–X) to generate a growing radical. Therefore, the structure of phosphine ligands strongly affects the catalytic activity.

Actually, the use of a tetrameric Cp*-ligated Ru complex \([\text{Ru(Cp*)Cl}]_4\) as the catalyst precursor that accepts ligands (PR\(_3\)) by just mixing to give \(\text{Ru(Cp*)Cl(PPR}_3)_n\) \((n = 1, 2)\)\(^{51,52}\) dramatically accelerated the studies of combined ligands that are suitable for Cp*-ligated Ru allowing highly active catalysis.\(^{53}\) As a result, it turned out that the moderate steric bulkiness of phosphine ligands (e.g. the tri-metatolylphosphine \([\text{P}(m-\text{Tol})_3]\)) promote the catalysis due to the smooth ligand dissociation.\(^{53}\) As another example, it was reported that the asymmetric chelate ligands, bishosphine monoxides (BPMOs; \(\text{Ph}_2\text{P}–(\text{CH}_2)_n–\text{P(O)}\text{Ph}_2;\) \(n = 1,2\)) effectively facilitate the catalysis due to the chelating effect that can assist the dynamic ligand association/dissociation of the weakly coordinating phosphine oxide (PO) moiety.\(^{54}\) In addition, the ligand design is essential not only for facilitating the catalysis, but also for the development of the functionalized ruthenium
catalysts. For example, the phosphine ligand functionalized with the phenol group can give the water-soluble ruthenium catalysts that lead the aqueous highly fast living radical polymerizations.55

Besides ligand design, the design of additives (cocatalysts) is also important to promote the catalysis. In ruthenium-catalyzed LRP, metal alkoxides such as Al(Oi-Pr)3 and Ti(Oi-Pr)4,56 and alkyl amines53,57-59 are effective additives. The early studies suggest that Al(Oi-Pr)3 interacts with the ruthenium complex to stabilize the higher oxidation state RuIII, and thus to facilitate radical generation from a dormant species (~~~C–X; Scheme 1a). Alkyl amines were also coordinate to Ru complexes to form active forms [RuII(18e)–NHnR3-n; R: alkyl; n = 0,1,2] by the in situ ligand exchange with the phosphine ligands. This amine-coordinated 18e Ru can easily transform to the 16e form (RuII(18e)–NHnR3-n → RuII(16e) + NHnR3-n) due to the labile coordination of amines, and thereby promote the catalytic cycles (Scheme 1b).

![Scheme 1](image)

**Scheme 1.** Effects of Aluminium (a) and Amine Additives (b) in Ruthenium-Catalyzed Living Radical Polymerizations
Iron (Fe)-Based Catalysis for Living Radical Polymerization. As abundant, safer, environmentally friendly, and biocompatible catalysts, iron complexes may be more attractive than ruthenium and other transition metal counterparts.\textsuperscript{60,61} Since the first report for Mt-LRP with FeCl$_2$(PPh$_3$)$_2$,\textsuperscript{29} various iron-based catalysts have been reported (Figure 4).\textsuperscript{62}

For example, iron halides (FeX$_n$; $X = \text{Cl, Br}, n = 2, 3$) in conjunction with various organic ligands, including phosphines,\textsuperscript{29,30,63-67} amines,\textsuperscript{30,68-74} phosphine-amine chelates,\textsuperscript{75-77} and $N$-heterocyclic carbenes (NHC),\textsuperscript{78,79} are well studied in regard to their catalysis in radical polymerizations. Although some of these iron halides–based complexes are isolated prior to use, many catalysts are prepared \textit{in situ} by just mixing a precatalyst and ligand. In addition, onium salts such as $n$-Bu$_4$NBr can also be used for iron halide (FeBr$_2$)-catalyzed polymerization, in which am \textit{in situ} formed anionic complex [FeBr$_3^-\ n$-Bu$_4$N$^+$] is considered as the truly active catalyst.\textsuperscript{80,81} Interestingly, bulky and highly delocalized salts,
phosphazenium halides (PZN-X), showed a high catalytic activity for the polymerization of not only methyl methacrylate (MMA) but also PEG-functionalized methacrylate (PEGMA; PEG: poly(ethylene glycol)). The tolerance to the functional group (PEG) is probably due to the bulkiness of the counter cation (PZN+) which may protect the iron complex from the nucleophilic functional groups.

On the other hands, iron half-metallocenes are also studied. These complexes are quite active in living radical polymerizations of styrenes, acrylates, and acrylamides. In particular, Fe₅Cp₂(CO)₄ is applicable for not only conjugated monomers but vinyl acetate, although the polymerization was retarded at around 50% monomer conversion. These complexes can also be applied for the controlled polymerization of methacrylates in conjunction with phosphine ligands.

Recently, it was reported that iron oxides (FeO and Fe₃O₄) can be used as the effective catalysts in conjunction with phosphines or onium salts for MMA and styrene. The solid iron oxides were easily recovered from the polymerization solution with a magnet and, importantly, can be reused. As other types of catalysts, iron porphyrin complexes are attractive relative to bioinspiration. They show a high tolerance to functional groups and can be used in aqueous media where some organoiron catalysts may be poisoned.

In spite of these extensive studies, iron catalysts are, in general, inferior to ruthenium or copper complexes in regard to catalytic activity and monomer versatility and thus far from the practical applications yet. Especially, a serious problem is that iron-based catalysts are less robust over functional groups, rendering it difficult to apply iron catalysts to the polymerization of functional monomers, despite a few examples showing catalytic activity for highly polar monomers. Therefore, in author’s view, further efforts are waited for developing active and versatile iron catalysts.

Copper (Cu)-Based Catalysis for Living Radical Polymerization. Copper-catalyzed LRP (atom transfer radical polymerization: ATRP) has been studied well. The first report was presented by Matyjaszewski et al. with copper halides (CuX; X: Cl, Br) coupled with bipyridine (bipy) ligand. This catalysis led to well-controlled polymerizations of MMA, styrene (St), and acrylates, while quite high amounts of catalysts were required (often equivalent to an initiator). A solution for a lower catalyst load is based on the ligand design as with ruthenium catalysis. Some critical studies about the structural effects of ligands revealed that multidentate amines, such as N,N,N',N''-pentamethyldiethylenetriamine
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(PMDETA),\textsuperscript{96} tris(2-pyridylmethyl)amine (TPMA),\textsuperscript{99} and tris-[2-(dimethylamino)ethyl]amine (Me\textsubscript{6}TREN),\textsuperscript{100} gave high activity to the catalyst (Figure 5). In particular, Me\textsubscript{6}TREN, a tetradsentate nitrogen-based ligand, gives highly active catalyst in conjunction with CuBr, leading to fast and well-controlled polymerization of acrylates at a lower catalyst load (0.1 equivalent to the initiator; < 500 ppm for the monomer). Relative to these multidentate ligands, bipyridine is not so effective as described above. Recently, however, it turned out that, with CuBr, bipyridine derivatives bearing a highly electron-donating substituent, such as a methoxy (MeO-bipy) or a dimethylamino group (Me\textsubscript{2}N-bipy), led to much faster and better controlled polymerizations of MMA and MA.\textsuperscript{101}

![Figure 5. Representative nitrogen-based ligands for copper-catalyzed living radical polymerization.](image)

Toward more effective catalysis, “activator regenerated by electron transfer (ARGET)” systems have been developed, in which an oxidized copper halide (Cu\textsuperscript{II}X\textsubscript{2}) resulting from radical termination reactions (bimolecular radical coupling or disproportionation) is reduced to regenerate a less oxidized form (Cu\textsuperscript{I}X) by an excessively added reducing agent, such as tin(II) 2-ethylhexanoate (Sn(EH)\textsubscript{2}), glucose,\textsuperscript{102,103} ascorbic acid (AsAc),\textsuperscript{104} phenol,\textsuperscript{105} hydrazine,\textsuperscript{106} and nitrogen-containing monomers (Figure 6).\textsuperscript{107} Also, conventional radical sources such as azobisisobutyronitrile (AIBN) can be used for this concept, in which the free radicals therefrom act as a reducing agent (initiators for continuous activator regeneration: ICAR).\textsuperscript{106} Surprisingly, these systems allowed a well-controlled polymerization with only 5-50 ppm of a copper halide.
Zero-valent metals such as Cu\textsuperscript{0}, Fe\textsuperscript{0}, Mg\textsuperscript{0}, Zn\textsuperscript{0}, or Ag\textsuperscript{0} can also be used as reducing agents.\textsuperscript{109,110} In this system, zero-valent metals can act not only as a reducing agent but a supplemental activator (the dotted arrow in Scheme 2-a). Therefore, the system using zero-valent metals as reducing agents is called “supplemental activators and reducing agents (SARA)” ATRP. Interestingly, particularly when Cu\textsuperscript{0} is used as the reducing agent, as a result of the activator regeneration step (Cu\textsuperscript{II}X\textsubscript{2} \rightarrow Cu\textsuperscript{I}X), Cu\textsuperscript{0} is also transformed to Cu\textsuperscript{I}X, meaning the efficient generation of the activator (the bold arrows in Scheme 2-a).

**Figure 6.** Activator regeneration in copper-catalyzed living radical polymerization.

**Scheme 2.** Proposed Mechanisms for Living Radical Polymerizations in the Presence of Zerovalent Copper (Cu\textsuperscript{0}): (a) SARA-ATRP and (b) SET-LRP
Actually, Percec et al. proposed the different mechanism, called SET-LRP (single electron transfer living radical polymerization), for the polymerization in the presence of \( \text{Cu}^0 \), in which \( \text{Cu}^0 \) acts as the main activator for a dormant C-X terminal, and the generated \( \text{Cu}^1 \text{X} \) promptly disproportionates to \( \text{Cu}^0 \) and \( \text{Cu}^{11} \text{X}_2 \) (the bold arrows in Scheme 2-b).\(^{26,111}\) This continuous generation of both \( \text{Cu}^0 \) (activator) and \( \text{Cu}^{11} \text{X}_2 \) (deactivator) allows the highly fast and well-controlled polymerizations. Particularly when the polymerization is conducted in the presence of multidentate amine ligands such as Me\(_6\)TREN under highly polar solvents such as DMSO, the disproportionation is considered to take place frequently. Importantly, SET-LRP system can also be applied to the aqueous living radical polymerization, in which the polymerization proceeds very fast even at 0˚C with quite high controllability so as to allow the synthesis of multi-block copolymers.\(^{112,113}\)

As described above, the use of reducing agents, including zerovalent copper (\( \text{Cu}^0 \)), is the key in the development of copper-based catalysis for living radical polymerization. However, in the ruthenium or iron-mediated LRP, there are only few examples reported in this line.\(^{114,121}\)

In summary, the design of coupled ligands or cocatalysts is crucial for developing highly active catalysis that allows decreasing the usage of metal catalysts, which is one of the most important issues in Mt-LRP. In the design of cocatalysts, for example, one representative strategy is using reducing agents for the regeneration of active main catalysts in copper-catalyzed LRP, allowing the dramatic decrease in catalyst usage. For more sustainable system, the use of iron-based catalysis is attractive, but there are some problems for iron catalysis such as the low activity and robustness over polar functional groups.

As will be discussed later, in this thesis, the concept of "bimetallic cooperative catalysis" will be applied to Mt-LRP for achieving highly active and sustainable catalysis.
Objectives

In this thesis, the author presents the novel “bimetallic” catalysis for living radical polymerization in conjunction with “Ferrocene” and its derivatives as cocatalysts. Ferrocene (FeCp₂; Fc) is a coordinatively saturated (18-electron) organometallic compound where two cyclopentadienyl (Cp) ligands sandwich an iron (Fe II) atom. The history of ferrocene is old, and the discovery dates back until 1951, followed by the presumption of the sandwich structure in 1952, and the determination of the crystal structure in 1956.

Ferrocene now has great importance due to its unique features as follows (Figure 7).

- **Excellent Redox Property**: The one electron redox behavior (Fe II ↔ Fe III) of ferrocene is active and stable enough to be used as an internal standard for cyclic voltammetry (CV) analysis.
- **High Stability**: Ferrocene is highly stable even in aqueous or aerobic media, and easily handled.
- **Easy Derivatization**: Ferrocene is easily derivatized because of the aromaticity of two cyclopentadienyl rings. Now, various types of ferrocene derivatives are known including the commercialized product.

![Features and applications of ferrocene and its derivatives.](image)

**Figure 7.** Features and applications of ferrocene and its derivatives.
General Introduction

These features allowed the applications of ferrocene or its derivatives in various fields. For example, ferrocene derivatives bearing polymerizable groups such as a vinyl group (vinyl ferrocene; discussed in chapter 3 in this thesis) allowed the introduction of ferrocenyl groups into the polymers that show the redox-responsibility. In addition, ferrocene derivatives can also be applied to the conjugations with biomolecules, including amino acids, proteins, DNA, and RNA.

Ferrocene derivatives are very important also in organic reaction. For example, ferrocene derivatives bearing coordination sites (P, N, O, etc.) are widely used as the ligands for the metal catalysts in various types of organic reactions. In particular, ferrocene-based ligands are important in asymmetric synthesis, because easy derivatization of ferrocene enables the easy access to asymmetric ferrocene-based ligands. The application of ferrocene derivatives in organic synthesis is not limited to just the use as ligands. Recently, due to the highly active and stable one electron redox behavior, ferrocene derivatives have been used as one electron transfer catalyst in some organic reactions, in which ferrocene derivatives donate an electron to a substrate or reagent.

From these backgrounds, the author became interested in the use of ferrocene for Mt-LRP. Actually, however, as mentioned later in Chapter 1 and 4 of this thesis, ferrocene and its derivatives were found to be inactive for an activation of a dormant C-X terminal (\(\sim\sim C-X \rightarrow \sim\sim C^\cdot\)) probably because of its structural stability. Eventually, the author decided to use ferrocene as a cocatalyst in conjunction with a conventional ruthenium or iron-based catalysts (main catalysts). In this system, the author expected following two catalytic functions of ferrocene for promoting the one electron redox catalysis (Figure 8).

![Figure 8. Ferrocene-assisted metal-catalyzed living radical polymerization.](image-url)
“Concerted Redox” Catalysis for Living Radical Polymerization

- **Regeneration**: Ferrocene (Fc\textsuperscript{II}) reduces the higher oxidation state of the main catalyst (X-Mt\textsuperscript{n+1} in Figure 8) to regenerate the activator species (Mt\textsuperscript{n}) as well as ARGET ATRP system (X-Mt\textsuperscript{n+1} + Fe\textsuperscript{II} → Mt\textsuperscript{n} + X-Fc\textsuperscript{III}).

- **Halogen Capping**: The trivalent ferrocene (ferrocenium salt: X-Fc\textsuperscript{III}) is known to act as the one electron oxidant in organic synthesis. Therefore, X-Fc\textsuperscript{III} is expected to regenerate a dormant C-X terminal (~~~C• + X-Fc\textsuperscript{III} → ~~C–X + Fe\textsuperscript{II}).

If ferrocene really shows these catalytic functions, the one electron redox catalysis, driven only by one metal catalyst (Mt\textsuperscript{n}) in conventional systems, can be driven by two metal catalysts (Mt\textsuperscript{n} + Fe\textsuperscript{II}) in “concert”. Therefore this novel catalysis, coined “concerted redox catalysis”, is expected to overwhelm the conventional systems in terms of the catalytic activity and the polymerization control.

This thesis is composed of three segments, following these segments.

(1) *Ruthenium/Ferrocene Concerted Redox Catalysis*
(2) *Iron/Ferrocene Concerted Redox Catalysis: “All-Iron” Catalysis*
(3) *From “Living Radical Polymerization” to “Radical Coupling Chain Extension” via Concerted Redox*

The brief explanations for each part are given below.

**1 (1) Ruthenium/Ferrocene Concerted Redox Catalysis**

In the first segment, the author aimed to examine effects of ferrocene (FeCp\textsubscript{2}) in conjunction with ruthenium complexes as the main catalysts for living radical polymerization (Figure 9).

Firstly, the author combined FeCp\textsubscript{2} as the cocatalyst for a (Cp\textsuperscript{*})-ligated ruthenium complex [Ru(Cp\textsuperscript{*})Cl(PPh\textsubscript{3})\textsubscript{2}: Ru(Cp\textsuperscript{*})] and its cationic counterpart [Ru(Cp\textsuperscript{*})\textsuperscript{+}(CH\textsubscript{3}CN) (PPh\textsubscript{3})\textsubscript{2}PF\textsubscript{6}+: Ru(Cp\textsuperscript{*})\textsuperscript{+}] as the main catalyst in living radical polymerization of methyl methacrylate (MMA). The cocatalytic effects of FeCp\textsubscript{2} were examined by the polymerization with a tiny amount of ruthenium main catalyst or the synthesis of high molecular weight polymers. In addition, two model reactions were performed to verify the expected catalytic functions of FeCp\textsubscript{2}, the regeneration of the main catalyst (Ru\textsuperscript{II}) with FeCp\textsubscript{2} and the halogen capping reaction with the resultant ferrocenium ion ([Fe\textsuperscript{III}Cp\textsubscript{2}]\textsuperscript{+}Cl\textsuperscript{−}: Cl-Fc\textsuperscript{III}).
to the active radical species (\( \cdots \mathrm{C}^\bullet \rightarrow \cdots \mathrm{C}–\mathrm{Cl} \)).

In terms of the industrial applications, one serious problem for the ruthenium/ferrocene concerted redox catalysis is the difficulty in metal removal. Therefore, the author next developed the thermoresponsive polymer-supported catalyst consisting of a ruthenium (Ru) main catalyst and a ferrocene (Fc) cocatalyst to realize both high activity and efficient removal of metal residues. The polymer-supported catalyst was prepared by the radical copolymerization of vinylferrocene (VFc), phosphine-pendant monomer (SDP), and PEG-pendant methacrylate (PEGMA), followed by the introduction of ruthenium complexes through the phosphine ligation.

**Figure 9.** Ruthenium/ferrocene concerted redox catalysis for living radical polymerization.

(2) **Iron/Ferrocene Concerted Redox Catalysis: “All-Iron” Catalysis**

In the second segment, the author aimed to expand the concept of ferrocene-assisted concerted redox catalysis to iron-catalyzed living radical polymerization toward much more sustainable catalysis, named “all-iron” catalysis (Figure 10).

**Figure 10.** Development of “all-iron” (iron/ferrocene concerted redox) catalysis.
In this study, FeBr$_2$ with ammonium salt ($n$-Bu$_4$NBr) was used as the main catalyst, and the author examined the catalytic activity and the polymerization controllability from the polymerization of MMA. Next, ferrocene was used for a FeBr$_3$-catalyzed polymerization, in which the FeBr$_3$ was firstly reduced by ferrocene to give FeBr$_2$, the real activator species. The FeBr$_3$/ferrocene catalyst system would be more ideal from a practical viewpoint, because the both complexes are air-stable and easily handled.

In addition, FeBr$_2$/ferrocene catalysis was applied to various types of monomers in order to examine the monomer versatility. As already mentioned, the conventional iron catalyst systems, basically combined with organic ligands, are normally less robust to functional groups, probably because the polar groups interact with iron center to incur the irreversible release of the ligands. However, all-iron catalysis is free from any organic ligands, and expected to show high robustness to functional groups.

In this segment, the author also aimed to apply all-iron catalysis to Kharasch addition reaction, which is the radical addition reaction of organohalogen compounds to olefins. As well as for living radical polymerization, the conventional catalyst systems for Kharasch addition were mainly made of ruthenium and copper-based catalysts, and there are little examples of active iron-based catalysis. Therefore, all-iron catalysis, developed for living radical polymerizations, was applied to Kharasch addition reaction.

(3) From “Living Radical Polymerization” to “Radical Coupling Chain Extension” via Concerted Redox

This segment dealt with the radical coupling reaction of ω-halogenated polystyrenes (PSt-X), prepared by Mt-LRP, by ruthenium/ferrocene concerted redox catalysis in conjunction with NH$_4$PF$_6$ as an additive.

As already mentioned, the expected catalytic functions of ferrocene in ruthenium/ferrocene concerted redox catalysis are the regeneration of the main catalyst (Ru$^{II}$) and the halogen capping reaction with the resultant ferrocenium halide ([Fe$^{III}$Cp$_2$]$^{+}$Cl$^{-}$) to the active radical species (~~~C• $\rightarrow$ ~~~C–Cl; Figure 11-a). Here, because ferrocenium halide is an ionic complex, an additional onium salt should strongly affect the catalytic function. For example, if NH$_4$PF$_6$ is added as an additive, ferrocenium halide transforms into ferrocenium hexafluorophosphate ([Fe$^{III}$Cp$_2$]$^{+}$PF$_6$) through an anion exchange reaction ([Fe$^{III}$Cp$_2$]$^{+}$Cl$^{-}$ + NH$_4$PF$_6$ $\rightarrow$ [Fe$^{III}$Cp$_2$]$^{+}$PF$_6$ $^{-}$ + NH$_4$Cl). Actually, [Fe$^{III}$Cp$_2$]$^{+}$PF$_6$ is known as a highly stable complex salt, and not be able to act as the halogen capping agent.
Therefore, when NH$_4$PF$_6$ is combined with ruthenium/ferrocene concerted redox catalysis, radical termination reactions (bimolecular radical coupling or disproportionation) may be promoted, while these reactions are suppressed with the ruthenium/ferrocene concerted redox catalysis itself (Figure 11-b). It is interesting that the catalytic functions of ruthenium/ferrocene concerted redox catalysis are significantly changed triggered by just adding a simple onium salt NH$_4$PF$_6$.

From these backgrounds, the author decided to apply this interesting catalyst system (ruthenium/ferrocene/NH$_4$PF$_6$) for the quantitative radical coupling reaction of ω-brominated polystyrenes prepared by Mt-LRP (R-PSt-Br; prepared with R-Br as an initiator), to give α,ω-telechelic polymers (R-PSt-PSt-R). This study is important in terms of the application of ruthenium/ferrocene concerted redox catalysis toward the construction of unique polymer architectures.

![Diagram](image-url)

**Figure 11.** Changes in catalytic function of ferrocene triggered by the addition of NH$_4$PF$_6$: (a) catalytic functions of ferrocene in ruthenium/ferrocene concerted redox catalysis; (b) catalytic functions of ferrocene in ruthenium/ferrocene catalyst system in conjunction with NH$_4$PF$_6$. 
Outline of This Study

This thesis consists of three parts including 6 chapters: Part I (Chapter 1-3) deals with the development of the ruthenium/ferrocene concerted redox for highly active and well-controlled catalysis for living radical polymerizations. Part II (Chapter 4-5) focuses on the extension of the ferrocene-assisted catalysis to iron-catalyzed living radical polymerization and related radical addition reaction (Kharasch addition reaction) in order to develop the sustainable “all-iron” catalysis. In addition, Part III (Chapter 6) presents the ruthenium/ferrocene/NH₄PF₆ catalyst system for quantitative radical coupling reactions of ω-halogenated polystyrenes as the extension of the ferrocene-assisted concerted redox catalysis toward the construction of unique polymer architectures.

Scheme 3. Ruthenium/Ferrocene Concerted Redox Catalysis for Living Radical Polymerization

In Part 1, Chapter 1 examines the effects of ferrocene (FeCp₂) as a cocatalyst for ruthenium (Ru)-catalyzed living radical polymerization of MMA. When Ru(Cp*) complex [Ru(Cp*)Cl(PPh₃)₂] was used as a main catalyst ([Ru]₀/[initiator]₀ = 1/10), the polymerization proceeded to the higher monomer conversion (~ 90%) by the addition of FeCp₂ ([Ru]₀/[FeCp₂]₀ = 1/40), while the polymerization retarded in the middle stage without FeCp₂. In addition, when the cationic Ru(Cp*) complex [Ru(Cp*)⁺(CH₃CN) (PPh₃)₂PF₆⁻ : Ru(Cp*)⁺⁻] was used as the main catalyst in conjunction with FeCp₂, the polymerization was accelerated without any loss of controllability. The high catalytic activity of Ru(Cp*)⁺⁻/FeCp₂ catalyst system even allowed the synthesis of high molecular weight PMMA (Mₙ ~ 10⁵; M_w/Mₙ ~ 1.3) with only 50 ppm of the Ru main catalyst. These positive effects of the addition of FeCp₂ was turned out to come from the following two reactions by some model reactions (Scheme
3): regeneration of Ru$^{II}$ through a reduction of XRu$^{III}$ (Fe$^{II}$Cp$_2$ + XRu$^{III}$ → Fe$^{III}$Cp$_2^+$X$^- + $ Ru$^{II}$; X: halogen); halogen-capping reaction, or regeneration of dormant species ~~~C–X, by the resultant trivalent ferrocenium cation Fe$^{III}$Cp$_2^+$ (~~~C• + Fe$^{III}$Cp$_2^+$X$^- → ~~~C–X + Fe$^{II}$Cp$_2$).

In Chapter 2, the author presents the novel ruthenium catalyst Ru(Cp*)$^+$. As shown in Scheme 3, in ruthenium/ferrocene concerted redox catalysis, ferrocene does not contribute to the activation of a dormant C-X terminal. Therefore, in order to improve the catalytic activity of ruthenium/ferrocene concerted redox catalysis, it is needed to develop much more active ruthenium catalyst that effectively activates a dormant C-X terminal. From these objectives, the author designed the cationic Ru(Cp*) complex [Ru(Cp*)$^+$; Ru(Cp*)$^+$](CH$_3$CN)(PPh$_3$)$_2$PF$_6$]. In living radical polymerizations of MMA with Ru(Cp*)$^+$ and the neutral counterpart Ru(Cp*), the author found that Ru(Cp*)$^+$ led to the faster polymerization rather than Ru(Cp*) without any serious loss of controllability. In Ru(Cp*)$^+$-catalyzed LRP, the 16e complex that can accept halogen from a dormant C-X terminal is smoothly generated by the fast dissociation of the weakly coordinated CH$_3$CN ligand (Scheme 4).

![Scheme 4. Smooth Activation of a Dormant C-X Bond with Ru(Cp*)$^+$](image):

Chapter 3 deals with a thermoresponsive polymer-supported catalyst consisting of a ruthenium main catalyst and a ferrocene cocatalyst was designed in order to realize both high activity and efficient removal of metal residues. The supported catalyst was easily prepared via random free radical copolymerization of vinylferrocene (VFc), phosphine-pendant monomer (SDP), and PEG-pendant methacrylate (PEGMA), followed by mixing with a Ru precursor ([Ru(Cp*)Cl]$_4$; Figure 12). The supported catalyst was preferably soluble in water at room temperature but moved to the toluene phase at high temperature for polymerization. Therefore, the supported catalyst showed high catalytic activity for living radical polymerization of MMA in toluene to give controlled PMMAs, and the metal residues in PMMA can almost be quantitatively removed via water washing of the resulting polymerization solution (removal efficiency ~ 99%).
In Part 2, Chapter 4 describes the extension of ferrocene-assisted concerted redox catalysis for iron catalyzed living radical polymerization in order to develop more sustainable catalysis. In the living radical polymerization of MMA with FeBr₂/n-Bu₄NBr as a main catalyst, the author found that decamethylferrocene (FeCp*₂), having lower redox potential than FeCp₂, successfully promoted the polymerization to give well-controlled PMMA (\(M_n \sim 10,000; M_w/M_n \sim 1.1\)), while FeCp₂ showed no effects on the catalysis. Importantly, the “all-iron” catalysis allowed superior control of the polymerization to those without FeCp*₂ to give high halogen functionalities of obtained polymers. In addition, the higher activity was achieved without relying on ligands, and the catalysis was more robust over polar groups, such as poly(ethylene glycol) (PEGMA), hydroxyl (HEMA), and carboxyl (MAA), which can be differentiated from conventional iron catalysts.

In Chapter 5, “all-iron” catalysis (FeBr₂/n-Bu₄NBr/FeCp*₂) was applied to Kharasch addition reactions (Figure 13). In Kharasch addition reaction of bromotrichloromethane (CCl₃Br) to MMA, “all-iron” catalysis was inferior to the reaction without FeCp*₂ in terms of both the reaction rate and yield of the mono adduct. In addition, “all-iron” catalysis was applied to other types of olefins, including styrene (St), acrylate, and 1-alkene, and the desirable mono adduct was obtained in relatively high yield in every case. Especially in the Kharasch addition of CCl₃Br to St, the reaction proceeded smoothly to give the mono adduct almost quantitatively (\(\sim 96\%\) yield). This highly active “all-iron” catalysis allowed the efficient Kharasch addition reaction with a tiny amount (around 1 mol\% for
olefin) of iron catalysts (FeBr₂ and FeCp*₂), giving the mono adduct in high yield (> 70%).

In Part 3, Chapter 6 presents the novel catalysis, composed of the ruthenium (RuⅡ)/ferrocene (FcⅡ) concerted redox catalysis in conjunction with NH₄PF₆ as an additive, for quantitative radical coupling reactions of ω-brominated polystyrenes prepared by Mt-LRP. The reaction scheme is shown in Scheme 5, in which the following two steps are crucial for promoting the reaction: (a) the regeneration of RuⅡ active complex with FcⅡ (XRuⅢ + FeⅡ → RuⅡ + [FcⅢ]⁺X⁻); (b) scavenging halide anions (X⁻) with NH₄PF₆ ([FcⅢ]⁺X⁻ + NH₄PF₆ → [FcⅢ]⁺PF₆⁻ + NH₄X). As a result of the radical coupling reaction of the ω-brominated polystyrenes (PSt-Br; M„ ~ 2000), the author found that Ru(Cp*)/FeCp*₂/NH₄PF₆ catalyst system gave the coupled PSt in high efficiency (~ 93%) under the suspension media (reaction solvent: xylene/H₂O), in which water associated with ruthenium catalyst to promote the
activation of a dormant C-X bond (radical generation). In addition, high solubility of NH$_4$Br in water would also promote the radical coupling reaction. In this chapter, the author also studied the radical coupling reaction of the $\alpha,\omega$-dibrominated PST (Br~~~R~~~Br), giving the chain extended PST ($\text{[~~~R~~~]}_m$: $m$ was roughly estimated to $m = 5.7$).

In summary, this thesis presents the novel catalysis, ferrocene-assisted concerted redox catalysis, for living radical polymerizations or related radical reactions. This catalysis contributed well to overcome the challenges of metal-catalyzed living radical polymerization or Kharasch addition reaction, such as lowering the catalyst usage, quantitative catalyst removal, and the development of highly active and robust iron-based catalysis. In addition, ruthenium/ferrocene concerted redox catalysis was also applied to the quantitative radical coupling reactions in conjunction with NH$_4$PF$_6$ as an additive. The author hopes that this thesis study leads to further developments of highly active, robust, and sustainable catalysis for living radical polymerizations.
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General Introduction


General Introduction

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PART I

Ruthenium/Ferrocene Concerted Redox Catalysis
Chapter 1

Ferrocene Cocatalysis in Ruthenium-Catalyzed Living Radical Polymerization: Concerted Redox for Highly Active Catalysis

Abstract

Ferrocene (FeCp₂), despite its high stability, was found, for the first time, to co-catalyze living radical polymerization in concert with a ruthenium main catalyst (Ru II) that is directly responsible for generating growing radicals. FeCp₂ turned out to promote the following key reactions: regeneration of Ru II through a reduction of XRu III (Fe II Cp₂ + XRu III → Fe III Cp₂⁻X⁻ + Ru II; X: halogen); halogen-capping reaction, or regeneration of dormant species ~~~C–X, by the resultant trivalent ferrocenium cation Fe III Cp₂⁺ (~~~C• + Fe III Cp₂⁻X⁻ → ~~~C–X + Fe II Cp₂). The cocatalysis was further improved by the addition of n-Bu₄NCl to allow a dramatic decrease in the initial Ru II concentration without any loss of the high controllability. For example, in conjunction with FeCp₂/n-Bu₄NCl, only 50 ppm (for monomer) of Ru II can catalyze living radical polymerization to give controlled polymers with high molecular weights and narrow molecular weight distributions ($M_n \sim 1.0 \times 10^5$; $M_w/M_n \sim 1.3$). Such a concerted catalysis with ferrocene would open the door to practical applications of living radical polymerization.
Chapter 1

Introduction

Metal-catalyzed living radical polymerization (LRP) is one of the useful tools to precisely prepare well-defined polymers.\textsuperscript{1-8} The catalysis involves a reversible activation of a dormant carbon–halogen bond (\abbreviated{~~~}C–X; \abbreviated{~~~}: polymer chain; X: halogen) to give growing radical species, based on a one-electron redox of the catalyst (Mt\textsuperscript{n}↔XMt\textsuperscript{n+1}; Mt: metal). The reversibility is critical in suppressing an instant elevation of radical concentration, consequently reducing unfavorable side reactions such as bimolecular radical coupling and disproportionation.

Though notably robust, versatile, and efficient, the usage of metal catalysts cause some specific issues: metal contamination of obtained polymers; deactivation of catalyst by polar groups; accumulation of oxidized forms by oxygen or unavoidable side reactions; rising cost from precious metals.\textsuperscript{3} An effective solution is to reduce the required amount of metal catalysts via promoting the catalytic cycle. Indeed, some methodologies have been developed for efficient catalysis for copper\textsuperscript{5,8-12} and ruthenium\textsuperscript{13-16} systems. Besides, an iron-based catalysis has recently attracted attention because of its abundance, safety, and high biocompatibility. However, the current iron catalysis in LRP is still beyond satisfaction, as clearly indicated by few examples in precision polymer synthesis. Equally important, there seems little effective method for reducing the oxidized form (Ru\textsuperscript{III}) of ruthenium complexes into catalytically active, radical-generating reduced counterpart (Ru\textsuperscript{II}).\textsuperscript{17}

Ferrocene (FeCp\textsubscript{2}) is one of the most traditional organometallic complexes or metallocenes, and the robust \textit{η}\textsubscript{6} ligation by two cyclopentadiene ligands with six electrons each is conductive to its high stability.\textsuperscript{18} Therefore, FeCp\textsubscript{2} and the derivatives have rarely been employed as catalysts in polymerization and organic reactions. This is unexceptional in metal-catalyzed LRP: FeCp\textsubscript{2} is too stable to activate a carbon–halogen bond into a carbon radical. However, it affords a one-electron redox and behaves as an electron reservoir, where FeCp\textsubscript{2} is oxidized to the trivalent ferrocenium cation (FeCp\textsubscript{2}\textsuperscript{+}).\textsuperscript{19} For instance, FeCp\textsubscript{2} reacts with two equivalents of FeCl\textsubscript{3} as a strong oxidizing agent to give FeCp\textsubscript{2}\textsuperscript{+}FeCl\textsubscript{4} and FeCl\textsubscript{2}. In such FeCp\textsubscript{2}-related redox reactions, the counteranion for the resulting cationic trivalent iron (FeCp\textsubscript{2}\textsuperscript{+}) affects the stability of the salt: e.g., FeCp\textsubscript{2}\textsuperscript{+}PF\textsubscript{6} is stable enough to be isolated as a crystal, while FeCp\textsubscript{2}\textsuperscript{+}Cl\textsuperscript{-} is unstable and prone to decomposition.\textsuperscript{20}

These phenomena motivated the author to employ FeCp\textsubscript{2} as a \textit{cocatalyst} for metal-catalyzed LRP because it might contribute to an enhancement of the catalytic cycle via a promotion of deactivation process, or re-generation of dormant C–X ends, which involves a
reduction of $XM_{n+1}$ into $M_n$ (the primary catalyst): $FeCp_2 + XM_{n+1} \rightarrow FeCp_2^+X^- + M_n$. Furthermore, due to its relative unstability, resultant $FeCp_2^+X^-$ may induce a direct halogen-capping reaction onto the growing radical species, or another route to re-generate the dormant end: $\sim\sim C^\bullet + FeCp_2^+X^- \rightarrow \sim\sim C-X + FeCp_2$. Evidently, organic halide anions, such as $n$-Bu$_4$N$^+X^-$, are incapable of promoting such a halogen-capping reaction to radical species. However, the nature of the halide anion in $FeCp_2^+X^-$ should be quite different from that in the onium salts, as speculated by the stability difference. Consequently, as shown in Scheme 1, a concerted (co)catalysis of $FeCp_2$ and the main catalyst (e.g., ruthenium complex Ru$^{II}$) is expected. Herein, the author reports a novel catalysis via a concerted $FeCp_2$ cocatalysis for the ruthenium-catalyzed LRP.

Scheme 1. Expected Cocatalysis of $FeCp_2$ in LRP and Ruthenium Catalysts in This Work
Experimental Section

Materials

MMA (Tokyo Kasei; > 99%) was dried overnight over calcium chloride, and purified by double distillation from calcium hydride before use. The H–(MMA)$_2$–Cl initiator [H–(CH$_2$CMeCO$_2$Me)$_2$–Cl]; an MMA dimer chloride] was prepared according to the literature.$^{21}$ The ECPA initiator [ethyl 2-chloro-2-phenylacetate, Aldrich; >97%]$^{22)}$ was purified by distillation under reduced pressure before use. Cp*RuCl(PPh$_3$)$_2$ (Cp*Ru: Aldrich), FeCp$_2$ (Aldrich; > 98%), [FeCp$_2$][PF$_6$] (Aldrich; > 97%), n-Bu$_4$NCl (Tokyo Kasei; > 98%), NH$_4$PF$_6$ (Aldrich; 99.99%), and 1,1’-Azobis(Cyclohexane-1-carbonitrile) (V-40) (Wako; > 95%) were used as received and handled in a grove box under a moisture- and oxygen-free argon atmosphere (H$_2$O < 1 ppm, O$_2$ < 1 ppm). The cationic Cp*-based ruthenium complex ([Cp*Ru(CH$_3$CN)(PPh$_3$)$_2$][PF$_6$]: Cp*Ru$^+$) was prepared according to the literature.$^{23}$ Tetralin (1,2,3,4-tetrahydronaphthalene) as an internal standard for $^1$H NMR was dried over calcium chloride and distilled twice from calcium hydride before use. Anisole (Wako, dehydrated) and tetrahydrofrane (THF) (Wako, dehydrated) were bubbled with argon for more than 15 min before use.

Polymerization Procedure

All polymerizations were carried out under dry argon in backed and sealed glass tubes. A typical example for MMA polymerization with the H–(MMA)$_2$–Cl/Cp*Ru$^+$/FeCp$_2$/n-Bu$_4$NCl is given below. In a 50 mL round-bottomed flask was placed Cp*Ru$^+$ (5.7 mg, 0.006 mmol), FeCp$_2$ (44.6 mg, 0.24 mmol), n-Bu$_4$NCl (66.7 mg, 0.24 mmol) under a grove box. Then, anisole (2.71 mL), tetralin (0.30 mL), MMA (2.57 mL, 24.0 mmol), and solutions of H–(MMA)$_2$–Cl (0.43 mL of 560.1 mM in toluene were added sequentially in this order at room temperature under dry argon. The total volume of the reaction mixture was thus 6.0 mL. Immediately after mixing, aliquots (0.50–1.0 mL each) of the solution were injected into backed glass tubes, which were then sealed and placed in an oil bath kept at 100 °C. In predetermined intervals, the polymerization was terminated by cooling the reaction mixtures to –78 °C. Monomer conversion was determined from the concentration of residual monomer measured by $^1$H NMR from the integrated peak area of the olefinic protons of the monomer with tetralin as an internal standard. The quenched solutions were evaporated to dryness to give the products, which were subsequently dried overnight under vacuum at room temperature.
**Ferrocene Cocatalysis in Ruthenium-Catalyzed Living Radical Polymerization**

### Coupling Reaction of ECPA

A typical example of radical coupling reaction with \( \text{Cp}^*\text{Ru}^+ / \text{FeCp}_2 / \text{NH}_4\text{PF}_6 \) is given below. Solutions of \( \text{Cp}^*\text{Ru}^+ \) (11.3 mg, 0.012 mmol), FeCp\(_2\) (22.3 mg, 0.120 mmol), NH\(_4\)PF\(_6\) (19.6 mg, 0.120 mmol), and ECPA (0.196 mL of 612.0 mM, 0.120 mmol) in toluene-\(d_8\)/THF (1/2, v/v) were mixed in a glass tube under moisture- and oxygen-free argon atmosphere at 0 °C. The mixture was sealed in an NMR tube and then placed in an oil bath kept at 100 °C. In predetermined intervals, the reaction was terminated by cooling the reaction mixtures to −78 °C, and \( ^1\text{H} \) NMR spectra were recorded on a JEOL JNM-ECA500 spectrometer in toluene-\(d_8\) at 25 °C, operating at 500.16 MHz. Coupling ratios were determined from the peak intensity of the signal of the chlorine compound and that of the produced coupling compound with toluene as a standard.

### Measurements

The \( M_n, M_w/M_n \), and MWD curves of the polymers were determined by size-exclusion chromatography at 40 °C in THF as an eluent on three polystyrene–gel columns (Shodex LF-404; exclusion limit = 2 \( \times \) 10\(^6\); particle size = 6 \( \mu \)m; pore size = 300 Å; 0.46 cm i.d. \( \times \) 25 cm; flow rate, 0.3 mL min\(^{-1}\)) connected to a DU-H2000 pump, a RI-74 reflective-index detector, and a UV-41 ultraviolet detector (all from Shodex). The columns were calibrated against 13 standard poly(MMA) samples (Polymer Laboratories; \( M_n = 630 – 1200 000; M_w/M_n = 1.02–1.30 \)) as well as the monomer.

### Results and Discussion

#### 1. Effects of Ferrocene on Ruthenium-Catalyzed LRP of MMA

A pentametylcyclopentatienyln ruthenium complex, \( \text{Cp}^*\text{RuCl(PPh}_3\text{)}_2 \) (\( \text{Cp}^*\text{Ru} \)), is inherently active in metal-catalyzed LRP, as predicted by its lower redox potential and faster halogen exchange.\(^{24}\) However, \( \text{Cp}^*\text{Ru} \) usually needs a cocatalyst [e.g., Al(O\(i\)-Pr\(_3\)) or amine] that likely assists an \textit{in-situ} transformation of \( \text{Cp}^*\text{Ru} \) into a coordinatively unsaturated, 16-electron form [e.g., \( \text{Cp}^*\text{RuCl(PPh}_3\text{)} \)] and/or a promotion of the halogen-capping reaction.\(^{13,14,25}\) The author, thus, selected \( \text{Cp}^*\text{Ru} \) as a main catalyst to examine the cocatalysis of FeCp\(_2\) in polymerization of methyl methacrylate (MMA) in conjunction with a chlorine initiator \( [\text{H}-(\text{MMA})_2-\text{Cl}] \) in anisole at 100 °C: \( [\text{MMA}]_0 = 4.0 \text{ M, } [\text{H}-(\text{MMA})_2-\text{Cl}]_0 = 40 \text{ mM, } [\text{Cp}^*\text{Ru}]_0 = 4.0 \text{ mM, } [\text{FeCp}_2]_0 = 40 \text{ mM. The addition of FeCp}_2 \) obviously
Chapter 1

accelerated the polymerization (Figure 1A): Conversion in 49 h; 87% from 56% without FeCp₂. Obtained polymers were well controlled and of narrow molecular weight distributions (MWDs) \( M_w/M_n < 1.2 \). Because FeCp₂ alone was totally inactive for MMA under otherwise the same conditions, these results indicate a concerted co-catalysis of FeCp₂ with the ruthenium primary catalyst.

However, the polymerization with the Cp*Ru/FeCp₂ system was still not very fast, probably because ferrocene was incapable of generating coordinatively unsaturated ruthenium (RuII) species. Actually, as described in chapter 2 of this thesis, the author has found that a cationic ruthenium Cp* complex \([\text{Cp*Ru}^+\text{CH}_3\text{CN}(\text{PPh}_3)_2\text{PF}_6]: \text{Cp*Ru}^+\] catalytically more active than Cp*Ru due to the smoother transformation into an unsaturated form via the spontaneous dissociation of the coordinated solvent (e.g., CH₃CN).²⁶ Accordingly, a combination of Cp*Ru⁺ with FeCp₂ led to a much faster polymerization (88% conversion in 12 h) with controllability retained \( M_w/M_n < 1.1 \).

The cocatalytic effects of FeCp₂ were more remarkable at a lower initial dose of Cp*Ru⁺ (1.0 mM, 1/40 eq for the initiator; Figure 1B and Figure 2). The polymerization

\[ \text{Figure 1. Effects of FeCp}_2 \text{ on ruthenium-catalyzed LRP of MMA with Cp*Ru or Cp*Ru}^+ \text{ in anisole at 100°C ([MMA]₀/[H(–(MMA)₂–Cl]₀ = 4000/40 mM). (A) [Cp*Ru]₀ = 4.0 mM (○), [Cp*Ru]₀/[FeCp}_2 \text{]₀ = 4.0/40 mM (●), [Cp*Ru}^+ \text{]₀ = 4.0 mM (□), [Cp*Ru}^+ \text{]₀/[FeCp}_2 \text{]₀ = 4.0/40 mM (■); (B) [Cp*Ru}^+ \text{]₀ = 1.0 mM (○), [Cp*Ru}^+ \text{]₀/[FeCp}_2 \text{]₀ = 1.0/40 mM (■), [Cp*Ru}^+ \text{]₀/[n-Bu}_4\text{NCl]₀ = 1.0/40/40 mM (●).} \]
was retarded and leveled off without FeCp₂ (< 60% conversion beyond 20 h), whereas with FeCp₂ smoothly reaching near completion and well controlled (89% conversion in 33 h; $M_w/M_n = 1.13$). Interestingly, the Cp*Ru⁺/FeCp₂-catalyzed system was further accelerated upon addition of a chloride salt ($n$-Bu₄NCl, 40 mM), most likely via an additional promotion of the halogen-capping reaction by unstable FeCp₂⁺Cl⁻, in which $n$-Bu₄NCl serves as a halogen donor for a growing radical. Despite the low catalyst concentration, the polymerization was controlled and faster than the salt-free system (90% conversion in 10 h; $M_w/M_n = 1.14$). A similar "salt-effect" also operated with the neutral Cp*Ru.

Figure 2. SEC curves of PMMAs obtained via ruthenium-catalyzed LRP with Cp*Ru⁺ in conjunction with FeCp₂ and $n$-Bu₄NCl. See Figure 1 (B) for condition.

Figure 3. Syntheses of high MW poly(MMA)s with low amount of ruthenium catalyst in conjunction with FeCp₂: $[\text{MMA}]_0/[\text{H}-(\text{MMA})_2-\text{Cl}]_0/[\text{Cp*Ru}^+]_0/[\text{FeCp}_2]_0/[n$-Bu₄NCl]₀ = 6000/6.0/0.3/12/0.5 mM in anisole at 100°C.
2. Highly Active Catalysis: Synthesis of higher Molecular Weight Polymers with A Small Amount of Ru Catalysts

These positive effects of FeCp$_2$ also enabled the efficient synthesis of higher molecular weight polymers (1000 mer) at a high monomer concentration ([MMA]$_0$ = 6.0 M; [H–(MMA)$_2$–Cl]$_0$= 6.0 mM). For this, an extremely small amount of Cp*Ru$^+$ (0.3 mM; 50 ppm for monomer) was injected along with FeCp$_2$ and n-Bu$_4$NCl ([FeCp$_2$]$_0$ = 12 mM; [n-Bu$_4$NCl]$_0$ = 0.5 mM). As shown in Figure 3, the observed $M_n$s agreed well with the calculated values, while MWD remained relatively narrow. The fine reaction control at the high molecular weight range demonstrates an efficient redox cycle coupled with a high turnover frequency.

3. Model Reactions and Proposed Effects of FeCp$_2$

The redox-promoting function of FeCp$_2$ as a reducing agent was verified by a radical coupling reaction of a model dormant end [R–Cl: ethyl 2-chloro-2-phenylacetate (ECPA)] catalyzed with the Cp*Ru$^+$/FeCp$_2$ pair (without n-Bu$_4$NCl; Figure 4). The reaction was carried out in the presence of a chlorine-free ammonium salt (NH$_4$PF$_6$) to exclude the secondary role of FeCp$_2$ as an indirect chloride donor via FeCp$_2$–Cl$^–$, which forms in situ as the reduction proceeds: FeCp$_2$ + ClRu$_{III}$ → FeCp$_2$–Cl$^–$ + Ru$_{II}$. The added NH$_4$PF$_6$ instead transforms the chloride irreversibly into a more stable form FeCp$_2$–PF$_6$$. Despite a low catalyst dose ([Cp*Ru$^+$]/[ECPA]$_0$ = 1/10), the coupling product (R–R) was obtained in high yield (87% in 72 h). Without FeCp$_2$, the reaction was retarded (<13%), indicative of the accumulation of ClRu$_{III}$. These results support cocatalysis of FeCp$_2$ via the reduction of ClRu$_{III}$ into Ru$_{II}$. Additionally, this catalytic performance suggests an in situ catalysis transformation (a one-pot cascade reaction) to be triggered just by addition of NH$_4$PF$_6$; for example, from the FeCp$_2$-cocatalyzed LRP into a coupling reaction of the obtained polymer chains. This will be further discussed later in chapter 6 of this thesis.$^{27}$

Another expected contribution of FeCp$_2$ to LRP is the promotion of the halogen-capping of radical species via in situ generated FeCp$_2$–Cl$: \sim\simtext{C}^\bullet + \text{FeCp}_2^+\text{Cl}^- \rightarrow \sim\simtext{C}^\text{Cl}^- + \text{FeCp}_2$. This was confirmed in conventional free radical polymerization (Figure 5): MMA was first polymerized with an azo initiator [1,1'-azobis(cyclohexane-1- carbonitrile) (V-40); 10 h half-life decomposition temperature 88 °C] in the presence of FeCp$_2$–PF$_6$–, and, at 40-50% monomer conversion, an equimolar amount of n-Bu$_4$NCl was added in situ to transform FeCp$_2$+$^+$PF$_6$– into FeCp$_2$+$^+$Cl$^-$. The polymerization was terminated, where the
FeCp₂⁺Cl⁻ effectively capped the free radicals into inactive covalent terminals. On the other hand, the polymerization with V-40 in the absence of FeCp₂⁺PF₆⁻ was not disturbed by addition of n-Bu₄NCl. From these results, FeCp₂⁺Cl⁻ (in situ generated in LRP) promotes the radical capping reaction via the reduction of itself.

**Figure 4.** Coupling reaction of ECPA with Cp*Ru⁺ in conjunction with FeCp₂/NH₄PF₆ in toluene-d₈/THF (2/1 v/v) at 100 °C: [ECPA]₀/[Cp*Ru⁺]₀/[FeCp₂]₀/[NH₄PF₆]₀ = 40/4.0/40/40 mM.

**Figure 5.** Effects of a combination of FeCp₂⁺PF₆⁻ and n-Bu₄NCl on free radical polymerization of MMA with 1,1’-Azobis(cyclohexane-1-carbonitrile) (V-40): (●): polymerization in the presence of FeCp₂⁺PF₆⁻, (■): polymerization in the absence of FeCp₂⁺PF₆⁻; (black line): addition of n-Bu₄NCl in 30 min, (gray line): no addition of n-Bu₄NCl: [MMA]₀ = 2.0 M, [V-40]₀ = 20 mM, [FeCp₂⁺PF₆⁻]₀ = 40 mM. An equivalent of n-Bu₄NCl was added for FeCp₂⁺PF₆⁻.
Conclusions

In conclusion, the author has demonstrated the concerted catalysis of ferrocene for metal-catalyzed LRP. In addition to positive effects on LRP such as acceleration, the catalysis is unique and of interest. Coupled with ruthenium complex, ferrocene contributes to not only the regeneration of Ru^{II} but also halogen-capping reaction for growing radical species along with its own redox cycle (Fe^{II}⇌Fe^{III}). Thus, the redox catalytic cycle in LRP was efficiently rotated to allow a decrease in the dose of the main catalyst without serious loss of control. The additional experiments (i.e., a coupling reaction of R–X and in situ formation of FeCp_{2}^{+}Cl^{-} in free radical polymerization) supported these contributions. Such a concerted catalysis with ferrocene would open the door to practical applications of living radical polymerization.

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Chapter 2

Cationic Cp*-Ruthenium Catalysts for Metal-Catalyzed Living Radical Polymerization: Highly Active Catalysis with Smooth Activation Process

Abstract

The Author presents the cationic Cp*-ruthenium complexes \([\text{Cp}*\text{Ru(CH}_3\text{CN})\text{(PPh}_3\text{)}_2\text{A; A}^\text{–}]:\) the counter anion; abbreviated to \(\text{Cp}*\text{Ru}^\text{+}\text{A}^\text{–}\) as the active catalyst for metal-catalyzed living radical polymerization (Mt-LRP) that can activate a dormant carbon-halogen bond smoothly by itself, in order to develop the highly active catalysis in conjunction with ferrocene as an cocatalyst as shown in chapter 1 of this thesis. The cationic complex in conjunction with a halogen initiator led to controlled polymerization of methyl methacrylate (MMA) giving well-controlled PMMAs with narrow molecular weight distribution \((M_w/M_n < 1.10)\) at appropriate polymerization rate \((\text{conversion} > 80\% \text{ in } 15 \text{ h})\). The catalytic feature was clearly different from the neutral counterpart \([\text{Cp}*\text{RuCl(PPh}_3\text{)}_2\text{: Cp}*\text{Ru}]\) resulting in retarded polymerization. Interestingly, the catalytic activity was strongly influenced by the counter anions. For example, the PF\(_6\)-based complex did not afford catalysis for controlled polymerization of methyl acrylate (MA), but SbF\(_6\)-based \([\text{Cp}*\text{Ru(CH}_3\text{CN})(\text{PPh}_3)_2\text{SbF}_6\text{: Cp}*\text{Ru}^\text{+}\text{SbF}_6^\text{–}]\) allowed control of the polymerization. In addition, model reaction analysis revealed the unique transformation of cationic complex through activation process for carbon-halogen bond: weakly coordinated solvent (e.g., CH\(_3\)CN) is likely to be eliminated to give 16e complex instead of the neutral phosphine ligand (e.g., PPh\(_3\)). Indeed, bipyridine (bipy) was available as the neutral ligand for the cationic complex unlike the neutral counterpart, although it could coordinate on ruthenium more strongly than PPh\(_3\).
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Introduction

In the past decades, transition metal-catalyzed living radical polymerization (Mt-LRP) has been established as the useful method for preparing well-controlled polymers with defined primary structures and desired architectures.1-7 In Mt-LRP, a carbon-halogen bond at a polymer end (~~~C-X; ~~~: polymer chain; X: halogen) is reversibly activated by transition metal catalysts through the one electron redox (Mt^n ↔ XMt^{n+1}; Mt: metal) to allow dynamic dormant-active equilibrium leading to suppression of “irreversible” side reactions (coupling, disproportionation, etc.).

Figure 1. The mechanism of transition metal-catalyzed living radical polymerization with Cp*Ru-based catalysis: (a) Cp*RuCl(PPh3)_2; (b) Cp*RuCl(PPh3)_2/alkyl amine cocatalysts.

Among available metals for Mt-LRP such as ruthenium (Ru),8 copper (Cu),9-11 iron (Fe),12-14 nickel (Ni),15,16 Ru complexes are known as one of the most active catalysts as designable organometallic complexes. For example, the pentamethylocyclopentadienyl (Cp*)-ligated ruthenium complexes [Cp*RuCl(PPh3)_2] [Cp*Ru] are widely used for LRP of various monomers including methacrylates, acrylates, and styrenes.17 However, Cp*Ru usually needs cocatalysts to promote polymerization, because Cp*Ru alone does not have the sufficient activity18 partly due to slow transformation from coordinatively saturated complex
of 18e to unsaturated of 16e to accept the halogen (X) from a dormant end (Figure 1a). Alkyl amine is helpful as a cocatalyst to accelerate controlled polymerization, and herein the amine cocatalyst would coordinate onto Ru center to give amine-coordinating complex, which is easily transformed into the 16e-complex due to the labile coordination of amines (Figure 1b).

In addition, as described in chapter 1 of this thesis, Ferrocene is also able to act as a cocatalyst for Cp*Ru and it is speculated that it could contribute to halogen-capping reaction of growing radical species to regenerate a dormant end as well as reduction of accumulated higher oxidized ruthenium complex (Figure 2: Mechanism of Ferrocene). Ferrocene is helpful for decrease in catalyst does, which is favorable for industrial applications, through promotion of catalysis. One problem in further improvements of this catalysis, however, is that ferrocene cannot assist the activation of a dormant C-X bond as shown in Figure 2. Therefore, it should be needed to develop the highly active Ru catalyst that can activate a dormant C-X bond smoothly by itself.

![Figure 2. Ferrocene-assisted concerted redox catalysis for metal-catalyzed living radical polymerization.](image)

In this chapter, therefore, the author is describing interesting catalysis of cationic Cp*Ru complex [e.g., [Cp*Ru(CH3CN)(PPh3)2]PF6] that can be obtained via the elimination of Cl– ligand from the neutral counterpart (Cp*Ru)21 for Mt-LRP. The cationic complex carrying poor nucleophilic anion can be smoothly transformed to 16e-complex along with
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dissociation of coordinating solvent (e.g., CH$_3$CN) without that of triphenylphosphine. The feature might be suitable for smoother activation of C-X bonds without any cocatalysts (Figure 3). In addition, the catalytic activity of Cp*Ru$^{+}$A$^-$ could be tuned through the selection of the counter anion (A$^-$), as demonstrated in organic reactions with similar cationic metal complexes. Thus, effects of counter anion on catalysis of Mt-LRP was studied as well as comparisons with the neutral complex (Scheme 1). Furthermore, possibility of new design with stronger coordinating ligand is also described, which is derived from that the catalysis proceeds without elimination of the neutral ligand.

![Figure 3. Cationic Cp*Ru complex as the catalyst for living radical polymerization.](image)

![Scheme 1. Transition Metal-Catalyzed Living Radical Polymerization with “Cationic” and “Neutral” Cp*Ru Complexes.](image)
**Experimental Section**

**Materials**

MMA, MA, St (all from TCI; purity > 99%), and n-BA (Nacalai; purity > 99%) were dried overnight over calcium chloride and purified by double distillation from calcium hydride before use. PEGMA (CH₃=CMeCO₂-(CH₂CH₂O)ₙ; Me = CH₃; n = 8.5 on average) (Aldrich) was purified by passing through an inhibitor-removal column (Aldrich) and was subsequently degassed by three times vacuum-argon bubbling cycles before use. The MMA-dimeric initiators (H-(MMA)₂-X; X = Cl, Br) were prepared according to the literature. The ECPA initiator (ethyl 2-chloro-2-phenylacetate) (Aldrich; purity > 97%) and the H-EMA-Br initiator ((CH₃)₂C(CO₂Et)Br) (TCI; > 98%) were purified by distillation under reduced pressure before use. The cationic Cp*Ru complexes, Cp*Ru⁺PF₆⁻ and Cp*Ru‘SbF₆, were prepared according to the literature by using AgPF₆ and AgSbF₆ as cationizing agents. The ruthenium tetramer [Cp*RuCl]₄ was prepared according to the literature. Cp*RuCl(PPh₃)₂ (Aldrich), Cp*Ru(CH₃CN)₃PF₆ (Aldrich; purity 98%), AgPF₆ (Aldrich; purity 99.99%), AgSbF₆ (Aldrich; purity 98%), and 2,2'-bipyridyl (Ald; purity >99%) were used as received and handled in a glove box (M. Braun Labmaster 130) under a moisture- and oxygen-free argon atmosphere (H₂O < 1 ppm, O₂ < 1 ppm). n-Octane (internal standard for gas chromatography), and 1,2,3,4-tetrahydrousnaphthalene (tetralin; internal standard for ¹H NMR) were dried over calcium chloride and distilled twice from calcium hydride before use. Toluene (Kishida Kagaku, Osaka, Japan; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, SG Water USA, Nashua, NH; Glass Counter) and bubbled with dry nitrogen for more than 15 min immediately before use. Acetonitrile (CH₃CN), anisole, tetrahydrofrane (THF), ethanol (all from Wako, dehydrated), and water (wako) were bubbled with dry nitrogen for more than 15 min before use.

**Polymerization Procedure**

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock or in sealed glass vials. A typical procedure for MMA polymerization with H-(MMA)₂-Cl/Cp*Ru⁺PF₆⁻ was as follows. In a 50 mL round-bottomed flask was placed Cp*Ru⁺PF₆⁻ (15.2 mg, 0.016 mmol) under a glove box. Then, anisole (1.84 mL), n-octane (0.20 mL), MMA (1.71 mL, 16.0 mmol), and a solution of H-(MMA)₂-Cl (0.25 mL of 638.1 mM in toluene, 0.16 mmol) were added sequentially in this
order at room temperature under dry argon; the total volume was 4.00 mL. Immediately after mixing, aliquots (0.50–1.0 mL each) of the solution were injected into backed glass tubes, which were then sealed and placed in an oil bath kept at 100 °C. In predetermined intervals, the polymerization was terminated by cooling the reaction mixtures to −78 °C in dry ice-methanol. Monomer conversion was determined from the concentration of residual monomer measured by gas chromatography with $n$-octane as an internal standard. The quenched solutions were evaporated to dryness to give the products, which were subsequently dried overnight under vacuum at room temperature. For St and MA, the same procedures described above were applied. For the polymerization of PEGMA, the same procedures as described above were applied, except that monomer conversion was determined by $^1$H NMR spectroscopy from the integrated peak area of the olefinic protons of the monomer with tetralin as an internal standard.

**Polymerization of MMA with Bipy-Ligated “Cationic” Cp*Ru Complex**

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock or in sealed glass vials. In a 50 mL round-bottomed flask were placed Cp*Ru(CH$_3$CN)$_3$PF$_6$ (8.1 mg, 0.016 mmol) and bipy (2.5 mg, 0.016 mmol) under a glove box. Then, CH$_3$CN (0.5 mL) was added at room temperature under dry argon. The solution was stirred at room temperature for 1 h for introduction of bipy into the cationic Cp*Ru complex, followed by the evaporation into dryness in order to remove CH$_3$CN. Next, THF (1.84 mL), $n$-octane (0.20 mL), MMA (1.71 mL, 16.0 mmol), and a solution of H-(MMA)$_2$-Cl (0.25 mL of 638.1 mM in toluene, 0.16 mmol) were added sequentially in this order at room temperature under dry argon; the total volume was 4.00 mL. The prepared solution was used for polymerization with similar method described above.

**Polymerization of MMA with Bipy-Ligated “Neutral” Cp*Ru Complex**

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock or in sealed glass vials. In a 50 mL round-bottomed flask were placed [Cp*RuCl]$_4$ (4.3 mg, 0.004 mmol) and bipy (2.5 mg, 0.016 mmol) under a glove box. Then, toluene (1.0 mL) was added at room temperature under dry argon. The flask was placed in an oil bath kept at 80 °C and the solution was stirred for 12 h for introduction of bipy into the neutral Cp*Ru complex, followed by the evaporation into
dryness in order to remove toluene. Next, THF (1.84 mL), n-octane (0.20 mL), MMA (1.71 mL, 16.0 mmol), and a solution of H-(MMA)_2-Cl (0.25 mL of 638.1 mM in toluene, 0.16 mmol) were added sequentially in this order at room temperature under dry argon; the total volume was 4.00 mL. The prepared solution was used for polymerization with similar method described above.

**Model Reaction: Radical Coupling of ECPA**

A typical procedure for radical coupling reaction with ECPA/Cp*RuPF₆⁻ was as follows. A solution of Cp*RuPF₆⁻ (28.4 mg, 0.030 mmol) and ECPA (0.196 mL of 612.0 mM, 0.120 mmol) in toluene-d₈ were mixed in a glass tube under moisture- and oxygen-free argon atmosphere at 0 °C. The mixture was sealed in an NMR tube and then placed in an oil bath kept at 80 °C. In predetermined intervals, the reaction was terminated by cooling the reaction mixtures to –78 °C in dry ice-methanol, and ¹H and ³¹P NMR spectra were recorded on a JEOL JNM-ECA500 spectrometer at room temperature, operating at 500.16 MHz. Coupling ratios were determined from the peak intensity of the signal of the chlorine compound and that of the produced coupling compound with toluene as a standard.

**Measurements**

For poly(MMA), poly(St), and poly(MA), \( M_n \) and \( M_w/M_n \) were measured by size exclusion chromatography at 40 °C in THF as an eluent on three polystyrene-gel columns (Shodex LF-404; exclusion limit = 2 × 10⁶; particle size = 6 µm; pore size = 3000 Å; 0.46 cm i.d. × 25 cm; flow rate, 0.3 mL min⁻¹) connected to a DU-H2000 pump, a RI-74 reflective-index detector, and a UV-41 ultraviolet detector (all from Shodex). The columns were calibrated against 13 standard poly(MMA) samples (Polymer Laboratories; \( M_n = 620–1200000; M_w/M_n = 1.06–1.22 \)) or 13 standard poly(St) samples (Polymer Laboratories; \( M_n = 500–3840000; M_w/M_n = 1.01–1.14 \)) as well as the monomer. For poly(PEGMA), \( M_n \) 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-805 L; exclusion limit = 4 × 10⁶; particle size = 5000 Å; 0.8 cm i.d. × 30 cm; flow rate, 1.0 mL min⁻¹) connected to a PU-2080 pump, 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; \( M_n = 630–1200000; M_w/M_n = 1.02–1.30 \)) as well as the monomer. ¹H and ³¹P 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 analysis, a capillary of $(C_2H_5O)_2$POH solution (50 mM in toluene-$d_8$) was used as an internal chemical shift standard (12 ppm for the phosphite). MALDI-TOF-MS analysis was performed on a Shimadzu AXIMA-CFR instrument equipped with 1.2 m linear flight tubes and a 337 nm nitrogen laser with dithranol (1,8,9-anthracenetriol) as an ionizing matrix and sodium trifluoroacetate as a cationizing agent. Polymer samples for $^1$H NMR and MALDI-TOF-MS were fractionated by preparative SEC (column: Shodex K-5002F).

![Figure 4](image-url)

**Figure 4.** The polymerization of MMA with the cationic Cp*Ru complex (Cp*Ru$^{+}$PF$_6^{-}$) and the neutral counterpart (Cp*Ru) ([MMA]$_0$/[H-(MMA)$_2$-Cl]$_0$/[Ru]$_0$ = 4000/40/4.0 mM in anisole at 100 °C): (a) plots of conversion vs time; (b) plots of ln([M]$_0$/[M]) vs time; (c) SEC curves of PMMAs obtained with Cp*Ru$^{+}$PF$_6^{-}$.

### Results and Discussion

#### 1. Catalytic Activity of Cationic Ruthenium Complex

The author first employed the cationic Cp*Ru complex carrying PF$_6^{-}$ (Cp*Ru$^{+}$PF$_6^{-}$) for polymerization of methyl methacrylate (MMA) in conjunction with a chlorine initiator [H–(MMA)$_2$–Cl] and compared the catalytic activity with that of the neutral counterpart (Cp*Ru) under the same condition (i.e., cocatalyst free). As shown in Figure 4a, a clear difference was observed between the two catalysts in terms of polymerization rate: the cationic complex allowed a faster polymerization and finally reached than the neutral resulting retarded polymerization. The ln([M]$_0$/[M]) value was linearly increased as the
conversion, indicating the concentration of radical species was fairly kept during the polymerization (Figure 4b). Molecular weights of obtained polymers were well controlled and its distribution is quite narrow (Figure 4c: $M_n = 11100$, $M_w/M_n = 1.09$ in 84% conversion). The activity of the cationic complex even without cocatalyst would be likely due to easy transformation into coordinatively unsaturated 16-electron complex.

2. Applicable Monomers

The author then examined other monomers to see the monomer versatility of Cp*Ru$^+$PF$_6^−$. As shown in Figure 5, Cp*Ru$^+$PF$_6^−$ was capable to catalyze the controlled polymerization of functional methacrylate (PEGMA: the methacrylate bearing the PEG pendant chain) to give narrow molecular weight distribution even at high conversion ($M_n = 30200$, $M_w/M_n = 1.24$ at 91% conversion). Notably, the polymerization of PEGMA can be controlled even in aqueous media at lower temperature [in EtOH/H$_2$O (75/25, v/v) at 40 °C]; (for St) [St]/[H-(MMA)$_2$-Cl]/[Ru]$_0$ = 4000/40/4.0 mM in anisole at 100 °C; (for MA) [MA]/[H-EMA-Br]/[Ru]$_0$ = 4000/40/4.0 mM in toluene at 80 °C.

![Figure 5](image-url)

**Figure 5.** Cp*Ru$^+$PF$_6^−$-catalyzed living radical polymerization of PEGMA, St, and MA: (for PEGMA) [PEGMA]/[H-(MMA)$_2$-Cl]/[Ru]$_0$ = 500/5.0/2.0 mM in EtOH/H$_2$O (75/25, v/v) at 40 °C; (for St) [St]/[H-(MMA)$_2$-Cl]/[Ru]$_0$ = 4000/40/4.0 mM in anisole at 100 °C; (for MA) [MA]/[H-EMA-Br]/[Ru]$_0$ = 4000/40/4.0 mM in toluene at 80 °C.

The cationic complex also allowed controlled polymerization of styrene (St), although the polymerization was quite slow (conversion = 70% in 169 h, $M_n = 8000$, $M_w/M_n =$
1.07). On the other hand, for the polymerization of methyl acrylate (MA), the degree of polymerization control was not so high resulting in broader molecular weight distributions ($M_n = 8400$, $M_w/M_n = 1.82$ at 75% conversion). This result of poorer control for MA polymerization encouraged the author to modify the counter anion of the cationic complex as follows.

3. Effects of Counter Anions on Catalysis

An existence of the counter anion is characteristic of cationic metal complex, and indeed some examples are known that the counter anion of cationic catalyst could affect the catalysis,\textsuperscript{22,23} as described in Introduction. For the use as polymerization catalyst, modification of the counter anion is interesting toward tune of catalytic activity according to reactivity of monomers. Thus, the counter anion (PF\textsubscript{6}–) in Cp*Ru\textsuperscript{+}PF\textsubscript{6}– was replaced with SbF\textsubscript{6}–, which is also typical counter anion of lower nucleophilicity, to prepare another type of cationic complex, Cp*Ru\textsuperscript{+}SbF\textsubscript{6}–. The complex was employed as the catalyst for polymerization of MA, which was not so precisely controlled with the original PF\textsubscript{6}–-based cationic complex.

Figure 6. Effects of counteranions on living radical polymerization of MA with cationic Cp*Ru complexes (Cp*Ru\textsuperscript{+}PF\textsubscript{6}– vs Cp*Ru\textsuperscript{+}SbF\textsubscript{6}–): [$\text{MA}]_0/[$H-EMA-Br]_0/[Ru]_0 = 4000/40/4.0$ mM in toluene at 80 °C.
The polymerization smoothly proceeded where the conversion reached around 90% conversion within 10 h. The molecular weights of the obtained polymers were linearly increased with monomer conversion and the molecular weight distributions were apparently narrower ($M_w/M_n = 1.29$ at 88% conversion) than with Cp*Ru$^+$PF$_6^-$ (Figure 6). Furthermore, the polymerization conditions were studied toward more effective controlled polymerization (Table 1). Double catalyst dose [[Ru]$_0$/[MA]$_0 = 1/500; 1/1000 (original)] allowed an improvement in polymerization control to give narrower molecular weight distributions of obtained PMAs (Table 1, Entry 2: $M_w/M_n = 1.21$). Using more active initiator, MMA-dimeric initiator [H–(MMA)$_2$–Br]$^{25}$ than H–EMA–Br allowed narrower molecular

### Table 1. Cp*Ru$^+$SbF$_6^-$-catalyzed living radical polymerizations of acrylate monomers$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Monomer (M)</th>
<th>Initiator</th>
<th>[Ru]$_0$/[M]$_0$</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>$M_n$</th>
<th>$M_w/M_n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MA</td>
<td>H-EMA-Br</td>
<td>1/1000</td>
<td>9</td>
<td>88</td>
<td>10000</td>
<td>1.29</td>
</tr>
<tr>
<td>2</td>
<td>MA</td>
<td>H-EMA-Br</td>
<td>1/500</td>
<td>9</td>
<td>90</td>
<td>10500</td>
<td>1.21</td>
</tr>
<tr>
<td>3</td>
<td>MA</td>
<td>H-(MMA)$_2$-Br</td>
<td>1/1000</td>
<td>24</td>
<td>87</td>
<td>10300</td>
<td>1.15</td>
</tr>
<tr>
<td>4</td>
<td>n-BA</td>
<td>H-(MMA)$_2$-Br</td>
<td>1/1000</td>
<td>48</td>
<td>80</td>
<td>11500</td>
<td>1.19</td>
</tr>
</tbody>
</table>

$^a$[Monomer]$_0$/[Initiator]$_0 = 4000/40$ mM in toluene at 80 $^\circ$C.

**Figure 7.** Living radical polymerizations of MA and n-BA with Cp*Ru$^+$SbF$_6^-$ in conjunction with H-(MMA)$_2$-Br as the initiator: [Monomer]$_0$/[H-(MMA)$_2$-Br]$_0$/[Ru]$_0 = 4000/40/4.0$ mM in toluene at 80 $^\circ$C.
weight distributions (Table 1, Entry 3: $M_w/M_n = 1.15$; SEC curves are shown in Figure 7a). Another type of acrylate, $n$-butyl acrylate ($n$-BA), was also applicable as the monomer to give controlled polymers (Table 1, Entry 4: $M_w/M_n = 1.19$; SEC curves are shown in Figure 7b).

The terminal structure of PMA was analyzed with MALDI-TOF-MS and $^1$H NMR. The sample was prepared with $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$ in conjunction with H-(MMA)$_2$-Br: conversion = 48% for 100 mer condition; $M_n = 5800$, $M_w/M_n = 1.30$. As seen in the MALDI-TOF-MS spectrum (Figure 8a), a single series of peaks were observed and the peak interval was almost same as the MA mass ($MW = 86.0$), and each peak mass is identical to that for the expected living polymer [H-(MMA)$_2$-(MA)$_n$-Br + Na$^+$]. The result could indicate that the polymerization quantitatively initiated from H-(MMA)$_2$-Br and no side reactions occurred during polymerization, such as coupling and chain transfer reaction.

$^1$H NMR spectrum also supported the generation of controlled PMA (Figure 8b). In addition to the large peaks derived from the main-chain protons ($a$, $b$, and $c$), some minor ones from the end groups at $\alpha$- and $\omega$-end were observed ($f$ from $\alpha$-end, $a'$ from $\omega$-end). From integration ratios of the terminal peaks and main chain ones, $M_n$(NMR, $\alpha$) and $M_n$(NMR, $\omega$) were calculated: $M_n$(NMR, $\alpha$) = 5600 and $M_n$(NMR, $\omega$) = 5700. The good agreement between the two values could imply that all polymer chains almost carry bromine at $\omega$-terminals. Notably, the good agreement of both values are kept even at the higher conversion [Table 2: $M_n$(NMR, $\alpha$) = 10300 and $M_n$(NMR, $\omega$) = 11100 at 87% conversion]. These results denote that the polymerization with $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$ proceeded under living nature without any unfavorable side reactions, such as coupling and disproportionation between radical species.

### Table 2. End functionality analysis for PMA obtained with $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$-catalyzed living radical polymerization

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conv. (%)</th>
<th>$M_d$(SEC)$^b$</th>
<th>$M_w/M_n$</th>
<th>$M_n$(NMR, $\alpha$)$^c$</th>
<th>$M_n$(NMR, $\omega$)$^d$</th>
<th>$f_d(\omega)^e$</th>
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<tr>
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<td>10500</td>
<td>1.14</td>
<td>10300</td>
<td>11100</td>
<td>0.93</td>
</tr>
</tbody>
</table>

$^a$[MA]$_0$/[H-(MMA)$_2$-Br]$_0$/[Ru]$_0$ = 4000/40/4.0 mM in toluene at 80 °C. $^b$Polymers were fractionated by preparative SEC. $^cM_n$(NMR, $\alpha$) = MW(initiator moiety) + MW(MA) × DP$_n$(NMR, $\alpha$) with DP$_n$(NMR, $\alpha$) obtained from $^1$H NMR peak intensity ratio; $3a/f$ (see Figure 8b). $^dM_n$(NMR, $\omega$) = MW(initiator moiety) + MW(MA) × DP$_n$(NMR, $\omega$) with DP$_n$(NMR, $\omega$) obtained from $^1$H NMR peak intensity ratio; $a/a'$ (see Figure 8b). $^e f_d(\omega) = M_d$(NMR, $\alpha$)/$M_d$(NMR, $\omega$).
Thus Cp*Ru-SbF$_6$– showed much superior catalysis to Cp*Ru-PF$_6$– for polymerization of MA, although the difference between two complexes is just the structure of counter anions (SbF$_6$– vs PF$_6$–). The higher activity is probably due to the lower nucleophilicity of SbF$_6$– than PF$_6$–, and indeed similar result was reported by Verpoort: BF$_4$–-based cationic ruthenium-alkylidene complex showed higher catalytic activity for the controlled radical suspension polymerization than TfO– or TsO–-based counterpart. These results are indicating the possibility that we could tune the catalytic activity by the structure of the counter anion, as well as ligand designs.
4. Model reaction for catalytic mechanism

For the detailed discussion on the catalytic mechanism with cationic ruthenium complexes, the structural transformation through an activation of a carbon–halogen bond was examined. Therefore, a model reaction of halogen initiator was performed with Cp*Ru^+PF_6^- in the absence of monomers. Herein ethyl 2-chloro-2-phenylacetate (ECPA) was employed as the initiator because the secondary carbon–halogen bond is active enough to easily give the bimolecular coupled product along with accumulate Ru^{III} complex (Scheme 2). The reaction was performed in toluene-d_8 at 80 °C, and directly traced by ^1H and ^31P NMR analysis.

The conversion of ECPA reached 24% in 12 h (Figure 9a). Since the feed ratio of Ru to ECPA ([Ru]/[ECPA]) is 0.25, the conversion value is reasonable assuming the halogen molecule is stoichiometrically converted into other molecules under catalysis by the ruthenium complex. ^1H NMR spectrum of the resultant solution supported generation of coupled product (1; 23% yield) and most probably generation of trivalent complex (XRu^{III}) would be accompanied through the bimolecular coupling radical reaction. In ^31P NMR spectrum, the peak a corresponding to phosphine on the divalent complex (Ru^{II}) was vanished in 12 h, and instead a new peak b was observed: this would be from the generated XRu^{III}. Most importantly, no peak from "free" PPh_3 was found in the spectra around 0 ppm, which was clearly different from the reaction with the neutral counterpart Cp*Ru giving the peak from free PPh_3 ligands (Figure 9b). These results would indicate that XRu^{III} was generated without the dissociation of phosphine ligands through the catalysis with Cp*Ru^+PF_6^-.

Supposedly, the weakly coordinating solvent molecule (i.e., CH_3CN) is released from the coordinatively saturated cationic complex (18e) to give the unsaturated 16e form, which can activate C-X bond to give carbon-centered radical species. Thus, unlike the reaction with the neutral complex Cp*Ru, two phosphine ligands likely remain on the ruthenium center.
Figure 9. \(^1\)H and \(^{31}\)P NMR spectra (in toluene-\(d_8\)) to trace the radical coupling reaction of ECPA with (a) Cp\(^*\)Ru\(^+\)PF\(_6^-\) or (b) Cp\(^*\)Ru: [ECPA]_0/[Ru]_0 = 40/10 mM in toluene-\(d_8\) at 80 °C.

5. Cationic Ru(Cp\(^*\)) complex bearing chelating ligand.

It is reported that multidentate ligands of strong coordination are not suitable for conventional Cp\(^*\)Ru catalysts, because dissociation of ligand is required to receive halogen from growing terminal for the activation process.\(^ {32} \) However, in the case with Cp\(^*\)Ru\(^+\)PF\(_6^-\), the weakly coordinating solvent molecule (i.e., \(CH_3CN\)) is dissociated on behalf of phosphine
ligands, as demonstrated in the model reaction. The unique structural transformation of the
cationic Ru complex motivated the author to introduce chelate ligand instead of PPh$_3$. Herein bipyridine (bipy) was selected because bipy is widely used for both neutral and
cationic Cp*-based Ru complexes in organic reactions.$^{33,34}$

Thus the cationic Cp*Ru complexes bearing bipy ligand was prepared as well as the
neutral version for comparison of catalytic activity. Each ruthenium complex precursor
[Cp*Ru(CH$_3$CN)$_3$PF$_6$ for cationic$^{34}$ and [Cp*RuCl]$_4$ for neutral$^{19,33}$] was mixed with bipy
under suitable condition (see Experimental Section) and the resultant complex was directly
used for the polymerization of MMA in conjunction with a chlorine initiator in THF at 80 °C
(Figure 10).

The polymerization with the cationic Cp*Ru complex was relatively slow but the
conversion finally reached almost 90% (88% in 123 h). The obtained PMMAs showed
unimodal MWDs and molecular weight of the final product was fairly controlled ($M_n = 10000,
M_w/M_n = 1.30$). On the other hand, the neutral counterpart resulted in uncontrolled
polymerization to give broader MWDs ($M_n = 65000$, $M_w/M_n = 2.06$ at 91% conversion)
probably due to that the dissociation of bipy was not so smooth.

The catalysis of the cationic Cp*Ru complexes without dissociation of ligand would
allow coordination of various types of ligands, which is preferable in terms of expansion of
the variation in catalyst design. Furthermore the aging preparation with Cp*Ru(CH$_3$CN)$_3$
PF$_6$ as the precursor$^{35}$ is advantageous to test various ligands toward more active catalysts.

Conclusions

In this chapter, the author studied the cationic Cp*Ru complexes as the catalysts for
Mt-LRP to find some specific features. Firstly, such cationic complexes have the superior
catalytic activity to the neutral counterpart. For example, Cp*Ru$^+$PF$_6^-$ led to the fast and
controlled polymerization of MMA in which the monomer conversion reached over 80%
within 15 h, and the molecular weight of the obtained polymers and its distribution were well
controlled ($M_w/M_n < 1.10$), while Cp*Ru resulted in the slow and retarded polymerization
under the same reaction condition. Secondly, the catalytic activity of the cationic Cp*Ru
complexes can be tuned by the combined counter anions. In polymerization of MA,
Cp*Ru$^+$PF$_6^-$ gave the ill controlled polymerization in which the molecular weight distribution
of the obtained polymer was relatively broad ($M_w/M_n \sim 1.8$), while Cp*Ru$^+$SbF$_6^-$ resulted in
the well controlled polymerization to give the PMA whose molecular weight and its
distribution were well controlled ($M_n = 10000$, $M_w/M_n = 1.29$), and high halogen end
functionality was obtained even at the higher monomer conversion ($f_n(\omega) = 0.93$ at 87% conversion). Thirdly, the phosphine ligand dissociation is not required for the activation of a
dormant C-X bond with the cationic Cp*Ru, whereas it is indispensable with the neutral
counterpart Cp*Ru. Thanks to the mechanism, chelate ligand (e.g., bipy) can be combined
as the ligand for controlled polymerization of MMA. These futures are indicating cationic
Cp*Ru complexes are flexibly “tunable” as catalysts with design of counter anion and ligand.

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**Figure 10.** “Bipy-ligated” cationic and neutral Cp*Ru complexes for living radical
polymerization of MMA ([MMA]$_0$/[H-(MMA)$_2$-Cl]$_0$/[Ru]$_0$ = 4000/40/4.0 mM in THF at
80 °C): (preparation of the “cationic” complex) $[\text{Cp}^*\text{Ru}(\text{CH}_3\text{CN})_3\text{PF}_6]_0/\text{bipy}]_0 = 1/1$ in
CH$_3$CN at r.t. for 1h; (preparation of the “neutral” complex) $[[\text{Cp}^*\text{RuCl}_4]_0/\text{bipy}]_0 = 1/4$ in
toluene at 80 °C for 12 h.
References

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Chapter 3

Thermoresponsive Polymer Supporter for Concerted Redox Catalysis of Ferrocene with Ruthenium Catalyst: High Activity and Efficient Removal of Metal Residues

Abstract

A thermoresponsive polymer-supported catalyst consisting of a ruthenium (Ru) main catalyst and a ferrocene (Fc) cocatalyst was designed to realize both high activity and efficient removal of metal residues. The supported catalyst/cocatalyst was easily prepared via ternary random free radical copolymerization of vinylferrocene (VFc), phosphine-pendant monomer (SDP), and PEG-pendant methacrylate (PEGMA), followed by mixing with a Ru precursor ([Ru(Cp*)Cl]4). The thermoresponsive feature was confirmed by visual appearance with a water/toluene binary solvent: it was preferably soluble in water at room temperature but moved to the toluene phase at high temperature for polymerization. The supported catalyst/cocatalyst showed high catalytic activity for living radical polymerization of MMA in toluene to give controlled PMMAs with narrow molecular weight distributions and a high halogen end functionality (e.g., \(M_w/M_n = 1.16\) and 96 % Cl-end of PMMA obtained at 89 % conversion in 24h). The metal residues in PMMA can almost be quantitatively removed via water washing of the resulting polymerization solution [Residual Ru: 5.7 ppm (99.8% removal), residual Fe: 89 ppm (98.5% removal), characterized by ICP-AES analysis].
Introduction

A transition metal catalyst is now one of the most powerful tools in synthesis of polymers as well as organic molecules because of its high activity and selectivity as well as its extensibility, while the difficulty in removal of metal residues is a serious problem for industrial applications. One classical idea for this problem is using polymer-supported insoluble metal catalysts, such as polystyrene (PSt)-supported catalysts.\textsuperscript{1,2} Despite its practical advantage, however, insolubility often incurs loss of reaction efficiency and selectivity. The design of the more responsive properties in catalysts would be one solution to dissolve the dilemma, and for this purpose poly(ethylene glycol) (PEG) has received attention as the supporter for metal catalysts due to the fact that the chemical structure of the ether bond is less sensitive to metal catalysis despite the high solubility in various solvents.\textsuperscript{3-5} The PEG-bound metal catalyst is hydrophilic at ambient temperature but lipophilic at higher temperature, which allows homogeneous catalysis in organic solvents (at higher temperature) and removal after the reaction just through water washing at ambient temperature.

Transition metal-catalyzed living radical polymerization (Mt-LRP) is one of the most widely used among precision polymerization methods, where the carbon-halogen bond as the dormant species is reversibly activated into the carbon-centered radical species (\textasciitilde\textasciitilde C–X \leftrightarrow \textasciitilde\textasciitilde C•; \textasciitilde\textasciitilde: polymer chain, X: halogen) through the one electron redox reaction of the transition metal catalyst (Mt\textsuperscript{n} \leftrightarrow XMt\textsuperscript{n+1}).\textsuperscript{6-12} Herein, there is a limit to efficiency in catalyzing the both reactions (i.e., activation and deactivation) with only one metal complex. Besides, a tiny level of side reactions (coupling and disproportionation), which are unavoidable at a later stage in living radical polymerization, incurs accumulation of the high oxidation state complex (i.e., XMt\textsuperscript{n+1}), and thus the reduction to a lower state is required to keep the equilibrium balance. Thus, as already demonstrated in some systems, a concomitant use of the cocatalyst\textsuperscript{13-15} or the reducing agent\textsuperscript{16-19} is efficient to promote the catalysis for living radical polymerization.

In this context, the author has recently reported that a combination of ferrocene (FeCp\textsubscript{2}; Fc) allows promotion of the catalysis of ruthenium-catalyzed living radical polymerization\textsuperscript{20}. Ferrocene is incapable of catalyzing living radical polymerization itself but could assist the ruthenium-based catalysis through two contributions from some mechanical studies: (1) reduction of the trivalent ruthenium complex; XRu\textsuperscript{III} + Fc\textsuperscript{II} \rightarrow Ru\textsuperscript{II} + XFc\textsuperscript{III}, (2) halogen-capping for growing radical species by the resulting XFc\textsuperscript{III}; \textasciitilde\textasciitilde C• + XFc\textsuperscript{III} \rightarrow \textasciitilde\textasciitilde C–X + Fc\textsuperscript{II}. The author coined the ferrocene-combined system as the
“ferrocene-concerted redox catalysis” (Figure 1), and indeed it allowed the synthesis of high molecular weight PMMA with a narrow molecular weight distribution ($M_n \sim 1.0 \times 10^5$; $M_w/M_n \sim 1.3$) even under really catalytic conditions with only 50 ppm (for a monomer) of the Ru main catalysts. However, toward practical applications of this system, the author has to remove the ferrocene residue as well as ruthenium from obtained polymers.

One possibility to develop the ferrocene-concerted system is derivatization of the ferrocene cocatalyst. For instance, vinyl ferrocene (VFc) would be suitable for the design of polymer-supported ferrocene, since it can be easily polymerized via free radical propagation.\textsuperscript{21,22} A combination of suitable comonomers with VFc would allow further functionalization of the polymer to be a useful supporter, and herein the author designed two comonomers: a phosphine-bearing styrene derivative (diphenylphosphino styrene) to support the main ruthenium catalyst though ligation;\textsuperscript{23,24} methacrylate carrying a PEG chain (PEGMA) to provide a thermoresponsive feature to the supporter. The ternary random copolymer (PPh$_3$–Fc–PEG) was treated with ruthenium precursor for complexation of the ruthenium catalyst (Figure 2). The obtained polymer catalyst (Ru–Fc–PEG) was then used for living radical polymerization of methyl methacrylate (MMA) to evaluate its catalytic activity and removal efficiency by washing with water. As a result, the author found that the supported ruthenium and ferrocene can catalyze well-controlled living radical polymerization to give PMMA with a narrow molecular weight distribution and a high end-functionality. In addition, the metal residues were almost quantitatively removed with the PEG-based supporter by just washing the polymerization solution with water.

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{figure1.png}
\caption{Ferrocene-concerted redox catalysis in ruthenium catalyzed living radical polymerization.}
\end{figure}
**Experimental Section**

**Materials**

MMA (TCI; purity: >99%) was dried overnight over calcium chloride and purified by distillation from calcium hydride before use. PEGMA (CH$_2$=CMeCO$_2$(CH$_2$CH$_2$O)$_n$; Me = CH$_3$; $n$ = 8.5 on average) (Aldrich) was purified by passing through an inhibitor-removal column (Aldrich) and was subsequently degassed by the three-time vacuum-argon bubbling cycle before use. Diphenylphosphinostyrene (SDP; kindly supplied by Hokko Chemical; purity: >99.9%), vinyl ferrocene (Wako; purity: >95%) and 2,2'-azobisisobutyronitrile (AIBN; TCI; purity: >98%) were degassed by reduced pressure and purged by argon before use. The H-(MMA)$_2$-Cl initiator for LRP (H-(CH$_2$CMeCO$_2$Me)$_2$-Cl; an MMA dimer chloride) was prepared according to the literature.$^{25}$ Ru(Cp*)Cl(PPh$_3$)$_2$ (Aldrich), Ferrocene (FeCp$_2$; Aldrich; purity >98%), and Triphenylphosphine (PPh$_3$; Aldrich; purity: 99%) were used as received. A ruthenium precursor complex (chloro(pentamethylcyclopentadienyl) ruthenium(II) tetramer: [Ru(Cp*)Cl]$_4$) was prepared according to the literature.$^{26,27}$ Ru(Cp*)Cl(PPh$_3$)$_2$, FeCp$_2$, PPh$_3$, and [Ru(Cp*)Cl]$_4$ were handled in a glove box under a moisture- and oxygen-free argon atmosphere (H$_2$O < 1 ppm, O$_2$ < 1 ppm). Tetralin (1,2,3,4-tetrahydronaphthalene; Kisida Chemical; purity: >98%) as an internal standard for $^1$H
NMR was dried over calcium chloride and distilled from calcium hydride before use. Toluene as a solvent of the polymerization was purified by passing through a purification column. (Solvent Dispensing System; glass counter; HANSEN&CO., Ltd). For a solubility test of the polymer, water (Wako; distilled) was bubbled with dry nitrogen for more than 15 min immediately before use. Hexane (Wako; dehydrated) for polymer precipitation was used as received.

**Synthesis of PPh₃–Fc–PEG**

The polymer supporter (PPh₃–Fc–PEG) was synthesized under argon. In a 50 mL round-bottomed flask were placed SDP (34.6 mg, 0.12 mmol), VFc (424 mg, 2.0 mmol), and AIBN (26.3 mg, 0.16 mmol). Toluene (4.1 mL), tetralin (internal standard: 0.4 mL), and PEGMA (3.5 mL, 8.0 mmol) were added sequentially in this order at room temperature under dry argon. Immediately after mixing, the flask with the reaction solution was placed in an oil bath at 60 °C, and stirred for 48 h. After SDP, VFc, and PEGMA were completely consumed (confirmed by ¹H NMR with the peak from tetralin), the reaction solution was cooled to room temperature. The mixture was evaporated, and then the crude product was purified by precipitation from the dichloromethane solution into hexane three times. The orange colored sticky product, PPh₃–Fc–PEG, was dried under reduced pressure (3.51 g, yield: 82.4%; $M_n = 57200$, $M_w/M_n = 4.25$, SEC in DMF, PMMA calibration). The ¹H and ³¹P NMR spectra of PPh₃–Fc–PEG are shown in Figure 3 and Figure 6A respectively. The mole concentrations of the phosphine ligand ([PPh₃]) and ferrocene ([Fc]) per polymer weight were determined to be 0.028 mmol/g ([PPh₃]) and 0.47 mmol/g ([Fc]) respectively from the ¹H NMR spectrum.

**Synthesis of PPh₃–PEG**

The ferrocene-free supporter (PPh₃–PEG) was synthesized via free radical polymerization similar to the above procedure without using VFc: SDP (17.3 mg, 0.06 mmol), AIBN (13.1 mg, 0.08 mmol), PEGMA (1.8 mL, 4.0 mmol), tetralin (0.4 mL), and toluene (5.8 mL). After the re-precipitation procedure, PPh₃–PEG was obtained as the colorless oil (1.51 g, yield: 78.7%; SEC in DMF: $M_n = 55100$, $M_w/M_n = 3.97$). The ¹H and ³¹P NMR spectra of PPh₃–PEG are shown in Figure 4. The mole concentration of the phosphine ligand ([PPh₃]) per polymer weight was determined to be 0.031 mmol/g from the ¹H NMR spectrum.
Figure 3. $^1$H NMR spectrum of PPh₃–Fc–PEG in CD₂Cl₂ at room temperature.

Figure 4. (A) $^1$H (in CD₂Cl₂), and (B) $^{31}$P NMR (in CDCl₃) spectrum of PPh₃–PEG at room temperature.

Figure 5. $^1$H NMR spectrum of Fc–PEG in CD₂Cl₂ at room temperature.
Synthesis of Fe–PEG

The phosphine-free supporter (Fe–PEG) was synthesized via free radical polymerization similar to the above procedure without using SDP: VFc (424 mg, 2.0 mmol), PEGMA (3.5 mL, 8.0 mmol), AIBN (26.3 mg, 0.16 mmol), tetralin (0.4 mL), and toluene (4.1 mL). After the re-precipitation procedure, PPh₃–PEG was obtained as the orange colored oil (3.16 g, yield: 74.8%; SEC in DMF: $M_n = 60600$, $M_w/M_n = 4.49$). The $^1$H NMR spectrum of Fe–PEG is shown in Figure 5. The concentration of ferrocene ([Fc]) per polymer weight was determined to be 0.47 mmol/g from the $^1$H NMR spectrum.

Procedures for Living Radical Polymerization

The polymerization was carried out by syringe technique under dry argon in backed glass tubes equipped with a three-way stopcock. A typical procedure for MMA polymerization with H–(MMA)$_2$–Cl/Ru–Fc–PEG is given below. [Ru(Cp*)Cl]$_4$ (1.7 mg, 0.002 mmol), a $400 \times 10^{-3}$ g/mL toluene solution of PPh$_3$–Fc–PEG (1.7 mL, 0.019 mmol of the PPh$_3$ ligand and 0.32 mmol of the ferrocene cocatalyst), and toluene (0.98 mL) were added into a schlenk tube. The mixture was placed in an oil bath at 80 °C for 12 h to give Ru–Fc–PEG. Into the in situ formed Ru–Fc–PEG solution, tetralin (0.3 mL), MMA (2.57 mL, 24 mmol), and a $540 \times 10^{-3}$ M toluene solution of H-(MMA)$_2$–Cl (0.45 mL, 0.24 mmol) were added at room temperature under argon (total volume: 6.0 mL). Six aliquots (1.0 mL each) of the mother solution were distributed into the backed glass tubes that were subsequently sealed and placed in an oil bath at 100 °C. After predetermined periods, the reaction was terminated by cooling the solutions to −78 °C. The conversion of MMA was determined from the concentration of the residual monomer measured by $^1$H NMR from the integrated peak area of the olefinic protons of the monomer with tetralin as an internal standard. The terminated reaction solutions were diluted with toluene, washed with water three times, and evaporated to dryness to give the polymers, which were subsequently dried overnight under vacuum at room temperature.

Measurement

$M_n$ and $M_w/M_n$ of PMMA were measured by size exclusion chromatography at 40 °C in THF as an eluent on three polystyrene-gel columns (Shodex LF-404; exclusion limit = $2 \times 10^6$; particle size = 6 µm; pore size = 3000 Å; 0.46 cm i.d. × 25 cm; flow rate, 0.3 mL min$^{-1}$) connected to a DU-H2000 pump, a RI-74 refractive-index detector and a UV-41 ultraviolet
detector (all from Shodex). The columns were calibrated against 13 standard poly(MMA) samples (Polymer Laboratories; $M_n = 620–1\,200\,000$; $M_w/M_n = 1.06–1.22$) as well as the monomer. For PPh$_3$–Fc–PEG, PPh$_3$–PEG, and Fc–PEG, $M_n$ 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-805 L; exclusion limit = $4 \times 10^6$; particle size = 5000 Å; 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.

$^1$H and $^{31}$P NMR spectra were recorded in CD$_2$Cl$_2$ and CDCl$_3$ at room temperature on a JEOL JNM-ECA500 spectrometer, operating at 500.16 MHz and 202.47 MHz, respectively. For the $^{31}$P NMR analysis, a capillary of the (C$_2$H$_5$O)$_2$POH solution (50 mM in toluene-$d_8$) was used as an internal chemical shift standard (12 ppm for the phosphite). The residual ruthenium and iron amounts in the obtained PMMA were determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES: IRIS Intrepid II XDL Radial; Thermo Fisher Scientific).

Results and Discussion

1. Synthesis of PPh$_3$–Fc–PEG

The author synthesized the ligand polymer (PPh$_3$–Fc–PEG) by free radical copolymerization of SDP, VFc, and PEGMA in conjunction with AIBN as the radical initiator in toluene at 60 °C ([SDP]$_0$/[VFc]$_0$/[PEGMA]$_0$/[AIBN]$_0$ = 15/250/1000/20 mM: the feed ratio of SDP and VFc was set according to the previous report about Ru/ferrocene concerted redox catalysis).$^{20}$ Three monomers were all consumed quantitatively in 48 h to give PPh$_3$–Fc–PEG ($M_n = 57200$), and the ratio of PPh$_3$ (from SDP), FeCp$_2$ (from VFc), and the PEG chain (from PEGMA) in the obtained polymer was determined to be [PPh$_3$]/[FeCp$_2$]/[PEG chain] = 14.9/251/1000 from the $^1$H NMR spectrum (Figure 3), which was well fitted to the monomer feed ratio.

2. Ru–Fe–PEG: thermoresponsive polymer catalyst

A tetrameric Cp*-ligated ruthenium complex [Ru(Cp*)Cl]$_4$ can accept phosphine based ligands (PR$_3$) by just mixing to give coordinatively saturated (18e) or unsaturated (16e) complexes (Ru(Cp*)Cl(PR$_3$)$_n$; $n = 1, 2$), which are well known to be useful for living radical
polymerization. A mixture solution of $[\text{Ru(Cp}^\ast\text{)}\text{Cl}_4]$ and PPh$_3$–Fc–PEG in toluene ([Ru]$_0$/[PPh$_3$ in PPh$_3$–Fc–PEG]$_0$ = 1/2.4; a little excess PPh$_3$ was mixed to perfectly promote complexation) was stirred at 80 °C for 12 h. From the $^{31}$P NMR spectra, the signal at −1 ppm originating from the PPh$_3$ pendant on the polymer was clearly decreased upon mixing with $[\text{Ru(Cp}^\ast\text{)}\text{Cl}_4]$ (Figure 6A), implying Ru introduction to the polymer by phosphine ligation. The new signal originating from Ru ligation was not observed because of the low mobility of ligating PPh$_3$ on the polymer supporter, which was also reported with other polymer-supported Ru catalysts.

The obtained Ru–Fc–PEG was soluble in toluene at room temperature to give yellowish-orange colored homogeneous solution. When the same volume of water was added to prepare a bilayer solution, the color was transferred from the upper (toluene) to the

![Figure 6](image_url)

Figure 6. Synthesis of Ru–Fc–PEG ($[[\text{Ru(Cp}^\ast\text{)}\text{Cl}_4]]/[\text{PPh}_3\text{ in polymer}])_0 = 0.25/2.4$ mM in toluene at 80 °C) and its thermoresponsive solubility: (A) $^{31}$P NMR spectra (in CDCl$_3$) for Ru introduction reaction (upper: before reaction (PPh$_3$–Fc–PEG); lower: after reaction (Ru–Fc–PEG)); (B) thermoresponsive phase transfer behavior of Ru–Fc–PEG in a toluene/water biphasic solution; (C) thermoresponsive solubility of Ru–Fc–PEG in water.
lower phase (water: Figure 6B), indicating the preference of the polymer for water rather than hydrophobic solvent at room temperature. Once the bilayer was heated up to 95°C that is higher than reported LCST of the PEGMA homopolymer (~ 90°C), the color moved to the upper phase, whereas the color was back to the lower phase upon cooling to room temperature. These results indicate that the supported Ru/Fc, Ru–Fc–PEG showed thermo-responsibility fitted to both catalysis and removal for polymerization of hydrophobic monomers, i.e., it prefers the hydrophobic solvent at higher temperature for polymerization, whereas favors water at room temperature for the workup process. As another demonstration for thermo-responsibility of Ru–Fc–PEG, the polymer gave a transparent solution in water at room temperature but it became cloudy at around 90 °C (Figure 6C). Rather unsurprisingly, such thermoresponsive behaviors were not observed with the corresponding unsupported complexes.

3. Living radical polymerization via polymer-supported metal catalysts

The polymer-supported binary metal catalysts (Ru–Fc–PEG) were then applied to living radical polymerization of MMA in conjunction with a chlorine initiator [H–(MMA)$_2$–Cl] in toluene at 100 °C: [MMA]$_0$ = 4.0 M, [H–(MMA)$_2$–Cl]$_0$ = 40 mM, [Ru]$_0$ = 1.0 mM, [FeCp$_2$ (Fc) in polymer]$_0$ = 40 mM (Figure 7A, Entry 1-3). The polymerization proceeded smoothly to reach around 90% conversion in 24 h and showed an almost linear first-order kinetic plot (Figure 7B), indicating that the catalytic activity was almost retained during polymerization. On the other hand, similar polymer supported catalysts bearing only the ruthenium catalyst (Ru–PEG) resulted in slower and retarded polymerization. Thus, an acceleration effect in conjunction with ferrocene is also demonstrated even on the polymer supporter. The resultant polymerization solution with Ru–Fc–PEG was washed with water at room temperature to remove polymer catalysts (Figure 8), followed by SEC analyses. The molecular weights of the obtained PMMAs were well fitted to the calculated values and a narrow molecular weight distribution was observed (Figure 7C). The MWD was relatively broad at the earlier stage, which is similar to polymerization with star polymer-supported ruthenium catalysts. By comparison, the unsupported catalyst was also examined under the same conditions. The ruthenium catalyst was prepared by mixing [Ru(Cp*)Cl]$_4$ with PPh$_3$ at the same ratio as with PPh$_3$–Fc–PEG ([Ru]$_0$/[PPh$_3$]$_0$ = 1/2.4). It was, then, employed in conjunction with FeCp$_2$ for the MMA polymerization.
The polymerization smoothly occurred to give narrow MWDs, as the author reported before ($M_n = 9400, M_w/M_n = 1.08$, conv. = 85% in 24 h: Figure 7A Entry 5), and a little significant advantage of Ru–Fc–PEG was observed over the unsupported system.

However, $^1$H NMR analyses of the terminal structure showed a difference between the two systems. For the Ru–Fc–PEG catalyzed polymerization, quite high Cl–end functionalities were observed during polymerization, and the high functionality was maintained even at the later polymerization stage (96% of Cl-end in 89% conversion: Figure 7D). On the other hand, with the unsupported binary catalyst, 20% of the Cl–end was lost at 85% conversion. Some neighboring effects may work in halogen capping for propagating...
radical species by $XFc^{III}$ and/or $XRu^{III}$ on the supporter. It is interesting that the polymer-support showed a positive effect in addition to the expected function as described below.

4. Catalyst removable

The toluene solution of the obtained PMMA (Conv. = 92% in 48 h; $M_n = 10700$, $M_w/M_n = 1.17$) with Ru–Fc–PEG was washed with water at room temperature three times to remove the polymer catalyst. After the washing process, the THF solution of PMMA (2 wt%) was colorless (Figure 9A), indicating the removal of metal residues. For quantitative analysis, the metal residues (Ru, Fe) in the PMMA sample were determined with the inductively coupled plasma-atomic emission spectrometry (ICP-AES) analysis. The weight ratio of ruthenium (Ru) and iron (Fe) was 5.7 ppm and 89 ppm respectively, meaning that 99.8% (Ru) and 98.5% (Fe) were removed for the initially added metal catalysts.$^{30,31}$

To observe the effects of the polymer support on the removability of the two metal
complexes, similar binary catalyst systems without either ruthenium or ferrocene on the chains (Ru–PEG + Fc, or Ru + Fc–PEG) were also used for the polymerization of MMA as well as the both-unsupported (Ru + Fc: see above), and resultant PMMAs were measured with ICP-AES to evaluate the weight ratio of Ru and Fe. Both catalyst systems allowed the controlled polymerizations (Ru–PEG + Fc system: conv. = 88% in 48 h: $M_n = 10500, M_w/M_n = 1.20$; Ru + Fc–PEG system: conv. = 91% in 48 h: $M_n = 11100, M_w/M_n = 1.18$). However, solutions of these obtained PMMA samples after water-washing treatment obviously changed to yellow. Rather naturally, the weight ratio of the unsupported metal was higher, indicating the difficulty in removal without the polymer support.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Washed PMMA</th>
<th>Residual Ru (Removability)</th>
<th>Residual Fe (Removability)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru–Fc–PEG</td>
<td><img src="image1.png" alt="Image" /></td>
<td>5.7 ppm (99.8%)</td>
<td>89 ppm (98.5%)</td>
</tr>
<tr>
<td>Ru–PEG + Fc</td>
<td><img src="image2.png" alt="Image" /></td>
<td>29 ppm (89.9%)</td>
<td>2600 ppm (59.0%)</td>
</tr>
<tr>
<td>Ru + Fc–PEG</td>
<td><img src="image3.png" alt="Image" /></td>
<td>100 ppm (63.9%)</td>
<td>280 ppm (95.4%)</td>
</tr>
<tr>
<td>Ru + Fc</td>
<td><img src="image4.png" alt="Image" /></td>
<td>200 ppm (29.6%)</td>
<td>2700 ppm (56.9%)</td>
</tr>
</tbody>
</table>

Figure 9. Removal of metal catalysts from PMMA obtained with Ru–Fc–PEG (A), Ru–PEG + Fc (B), Ru + Fc–PEG (C), and Ru + Fc (D): photographs of THF solutions of the washed PMMA (2 wt%) and residual amounts of Ru and Fe from ICP-AES analysis.

Conclusions

To achieve the efficient removal of metal residues for ruthenium-ferrocene concerted catalysis in living radical polymerization, the binary metal catalysts were embedded on the thermoresponsive polymer-supporter. Thus the obtained PEG-based polymer, Ru–Fc–PEG, showed a thermoresponsive feature, i.e., hydrophilic at room temperature but hydrophobic at higher temperature as well as high activity in metal-catalyzed living radical polymerization. Importantly, the halogen functionality of the polymer terminal was quite higher even at the
later polymerization stage, likely due to concerted catalysis on the condensed polymer backbone. The water washing process of the obtained polymer allowed almost quantitative removal of the metal residues (~ 99%), which was supported by ICP-AES analyses.

For industrial processes, compatibility of high activity in the polymerization and easy purification of the product free from metal residues is required. In this context, the design of concerted catalysis on a thermoresponsive polymer supporter is promising for practical applications with metal-catalyzed living radical polymerization.

References

(30) The removability of ruthenium (Ru_{remov}) was calculated as Ru_{remov} = 1–(Residual Ru from ICP–AES)/(Weight of the initially added Ru in 1g of PMMA; Ru_{init}), where Ru_{init} was calculated as Ru_{init} = (101.07 g/mol)•(Ru feed on polymerization, mM)/(100.12 g/mol)•(MMA feed on polymerization, mM)•(Monomer Conversion).
(31) The removability of iron (Fe_{remov}) was calculated as Fe_{remov} = 1–(Residual Fe from ICP–AES)/(Weight of the initially added Fe in 1g of PMMA; Fe_{init}), where Fe_{init} was calculated as Fe_{init} = (55.845 g/mol)•(Fe feed on polymerization, mM)/(100.12 g/mol)•(MMA feed on polymerization, mM)•(Monomer Conversion).
PART II

Iron/Ferrocene Concerted Redox Catalysis:
“All-Iron” Catalysis
Chapter 4

Concerted Redox Catalysis for Iron-Catalyzed Living Radical Polymerization: “All-Iron” Catalysis for Active, Robust, and Sustainable System

Abstract

Decamethylferrocene (FeCp*₂) was found to be an effective cocatalyst for metal-catalyzed living radical polymerization with FeBr₂/n-Bu₄NBr as the main catalyst. For polymerization of methyl methacrylate (MMA) with a bromine-type initiator, the conversion was limited in the absence of FeCp*₂, whereas the polymerization was apparently promoted up to higher conversion (~90%) upon combination with FeCp*₂. Despite the acceleration, molecular weights and its distributions (MWDs) were fairly controlled ($M_w/M_n < 1.1$, Conversion = 90%). The “concerted” catalysis with the two iron complexes allowed superior control of the polymerization to those without FeCp*₂ to give high halogen functionalities of obtained polymers. Importantly, the two iron complexes can perform the catalysis helping each other, independently of electron-support from ligands (e.g., phosphine). Therefore, ligand dissociation by polar groups, i.e., “catalyst poison”, does not matter in the FeCp*₂-concerted system, leading to control over (co)polymerizations with functional monomers with polar pendant groups, such as poly(ethylene glycol) (PEGMA), hydroxyl (HEMA), and carboxyl (MAA). The robust catalysis with the sustainable and safe metal, iron, would be promising toward actual applications with metal-catalyzed living radical polymerization.
**Introduction**

Metal-catalyzed living radical polymerization (Mt-LRP)\(^{1-8}\) has become the most powerful tool to synthesize controlled polymers with well-defined primary structures (e.g., molecular weight, its distribution, and terminal structures) and to construct desired architectures (e.g., block, graft, and star). In Mt-LRP, transition metal complexes catalyze the reversible activation of a carbon-halogen bond at the growing end (~C-X; X = halogen) through the one-electron-redox reaction (Mt\(^n\) ↔ XMt\(^{n+1}\); Mt = metal) to allow suppression of irreversible side reactions. The polymerization controllability is dependent on the reversibility between dormant (~C-X) and active species (~C •), which are related to the efficiency of the catalytic cycle driven by metal complexes. Since the first report in 1995, Mt-LRP has been achieved with ruthenium,\(^9\) copper,\(^10\) iron,\(^11\) nickel,\(^12,13\) and other late transition metals. Among these metals, ruthenium complexes are known as active catalysts\(^1-3\) as well as copper derivatives, and versatile ligand designs have allowed modulation of the catalysis depending on requirements for polymerization.\(^14-28\) However, ruthenium is relatively expensive and therefore unfavorable in terms of practical applications.

In terms of practical utility, an iron-catalyzed system is favored because of its abundance, safety, and inherent biocompatibility. Since the first report with FeCl\(_2\)(PPh\(_3\))\(_2,\)\(^11\) some types of iron catalysts have been developed with various ligands, such as phosphines, amines, imines, carbenes, cyclopentadiene, etc.\(^29-69\) However, these iron catalysts are still far from the actual usage because they cannot be widely used due to insufficient activity and, more seriously, less robustness over polar functional groups. Indeed, there are a few examples showing catalytic activity for highly polar monomers.\(^42,65,67\)

Ferrocene (FeCp\(_2\)), where two cyclopentadienyl (Cp) ligands sandwich an iron (Fe\(^{II}\)) atom,\(^70,71\) is known as a typical iron complex showing redox property (Fe\(^{II}\) ↔ Fe\(^{III}\)) but incapable of catalyzing living radical polymerization as a main catalyst likely due to the too stable form on the basis of the coordinatively saturated (18-electron). However, the author has recently found that ferrocene can work as a cocatalyst to promote ruthenium-catalyzed living radical polymerization.\(^72\) Thanks to the ferrocene cocatalysis, the polymerization was accelerated, keeping the controllability even under mild conditions with a tiny amount of ruthenium catalyst. Some model reactions indicated that ferrocene contributes to not only regeneration of Ru\(^{II}\) complex through reduction of oxidized ruthenium (XRu\(^{III}\)) but also halogen-capping reaction for growing radical species by ferrocenium halide ion (Fe\(^{III}\)Cp\(_2\)X\(^-\)) that is accordingly given from FeCp\(_2\) through the reduction of XRU\(^{III}\). The author has thus
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termed the system relying on ferrocene cocatalyst as “concerted redox catalysis” (Scheme 1).

In this work, the author expanded the concept of ferrocene-concerted catalysis with ruthenium-catalyzed system to that with iron-based to approach “all-iron” active system. As shown below, decamethylferrocene (FeCp*) was effective as the cocatalyst in conjunction with iron halide and ammonium salt (i.e., FeBr₂/n-Bu₄NBr) to show high catalytic activity. More importantly, the catalytic system was robust over polar groups, and thus polymerizations were controlled even with functional monomers, whose polymerizations were difficult to be controlled with conventional iron-based systems.

Scheme 1. Concerted Redox Catalysis with Ferrocene in Living Radical Polymerization

Experimental Section

Materials

MMA, and MA (both from TCI; purity >99%) were dried overnight over calcium chloride and purified by double distillation from calcium hydride before use. 2-Hydroxyethyl methacrylate (HEMA) (Aldrich; purity >99%), and methacrylic acid (MAA) (TCI; purity >99%) were distilled under reduced pressure before use. PEGMA (CH₂=CMeCO₂(CH₂CH₂O)₅; Me = CH₃; n = 8.5 on average) (Aldrich) was purified by passing through an inhibitor-removal column (Aldrich) and was subsequently degassed by three times vacuum-argon bubbling cycles before use. The MMA-dimeric initiators
(H-(MMA)$_2$-Br) was prepared according to the literature.$^{73}$ The EBPA initiator (ethyl-2-bromo-2-phenylacetate) (Aldrich; purity 97%) was purified by distillation under reduced pressure before use. Iron(II) bromide (FeBr$_2$) (Aldrich; purity >98%), iron(III) bromide (FeBr$_3$) (Aldrich; purity 98%), ferrocene (FeCp$_2$) (Aldrich; purity >98%), decamethylferrocene (FeCp$^{*2}$) (Aldrich; purity 97%), tetrabutylammonium bromide ($n$-Bu$_4$NBr) (TCI; purity >99%), and tetrabutylammonium hexafluorophosphate ($n$-Bu$_4$NPF$_6$) (Aldrich; purity >98%) were used as received and handled in a glovebox (M. Braun Labmaster 130) under a moisture- and oxygen-free argon atmosphere (H$_2$O < 1 ppm; O$_2$ < 1 ppm). Tetrahydrofuran (THF) (Wako, super-dehydrated, stabilizer free), ethanol (EtOH) (Wako, super-dehydrated), and anisole (Wako) were bubbled with argon for more than 15 min before use. $n$-Octane (internal standard for gas chromatography) and 1,2,3,4-tetrahydronaphthalene (tetralin; internal standard for $^1$H NMR) were dried over calcium chloride and distilled twice from calcium hydride.

**Polymerization Procedure**

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock or in sealed glass vials. A typical procedure for MMA polymerization with H-(MMA)$_2$-Br/FeBr$_2$/n-Bu$_4$NBr/FeCp$^{*2}$ was as follows. In a 50 mL round-bottomed flask were placed FeBr$_2$ (8.7 mg, 0.040 mmol), n-Bu$_4$NBr (12.9 mg, 0.040 mmol), and FeCp$^{*2}$ (52.2 mg, 0.16 mmol) under a glovebox. Then, THF (1.73 mL), $n$-octane (0.20 mL), MMA (1.71 mL, 16 mmol), and a solution of H-(MMA)$_2$-Br (0.16 mL of 440 mM in toluene, 0.16 mmol) were added sequentially in this order at room temperature under dry argon; the total volume was 4.00 mL. Immediately after mixing, aliquots (0.50–1.0 mL each) of the solution were injected into backed glass tubes, which were then sealed and placed in an oil bath kept at 60 °C. In predetermined intervals, the polymerization was terminated by cooling the reaction mixture to −78 °C in dry ice-methanol. Monomer conversion was determined from the concentration of residual monomer measured by gas chromatography with $n$-octane as an internal standard. For MA, the same procedures as described above were applied. For PEGMA, HEMA, and MAA, the same procedures as described above were applied, except that monomer conversion was determined by $^1$H NMR spectroscopy from the integrated peak area of olefinic protons of monomer with tetralin as an internal standard.
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Measurements

For (co)polymers consisting of MMA and MA, $M_n$ and $M_w/M_n$ were measured by size exclusion chromatography at 40 °C in THF as an eluent on three polystyrene-gel columns (Shodex LF-404; exclusion limit = $2 \times 10^6$; particle size = 6 µm; pore size = 3000 Å; 0.46 cm i.d. × 25 cm; flow rate, 0.3 mL min$^{-1}$) connected to a DU-H2000 pump, a RI-74 refractive-index detector, and a UV-41 ultraviolet detector (all from Shodex). The columns were calibrated against 13 standard poly(MMA) samples (Polymer Laboratories; $M_n = 620–1200000$; $M_w/M_n = 1.06–1.22$) as well as the monomer. For polar (co)polymers including polar units such as HEMA, MAA, and PEGMA, $M_n$ 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-805 L; exclusion limit = $4 \times 10^6$; particle size = 5000 Å; 0.8 cm i.d. × 30 cm; flow rate, 1.0 mL min$^{-1}$) connected to a PU-2080 pump, 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; $M_n = 630–1200000$; $M_w/M_n = 1.02–1.30$) as well as the monomer. $^1$H NMR spectra were measured at room temperature on a JEOL JNM-ECA500 spectrometer operating at 500.16 MHz.

Cyclic voltammograms were recorded by using ALS model 600D from BAS Inc. The sample preparation for FeCp*$_2$ is described. FeCp*$_2$ (13.1 mg, 0.040 mmol) and a solution of n-Bu$_4$NPF$_6$ (supporting electrolyte) in ClCH$_2$CH$_2$Cl solution (100 mM, 8 mL) were added sequentially in a baked glass tube equipped with a three-way stopcock under argon. Measurements were carried out at 0.1 V s$^{-1}$ under argon. A three-electrode cell was used which was equipped with a PTE platinum electrode (working electrode), a platinum wire electrode (counter electrode), and an RE-7 nonaqueous Ag/Ag$^+$ electrode (reference electrode) from BAS Inc.

Results and Discussion

1. Effects of Ferrocene Derivatives on Iron-Catalyzed LRP of MMA

Toward “all-iron” system on the basis of ferrocene cocatalyst, the author focused on FeBr$_2$ with ammonium salt (n-Bu$_4$NBr) as the main catalyst. The selection was due to the following reasons: retardation behavior of the polymerization rate likely due to accumulation of the higher oxidation state complex (Fe$^{III}$) as the polymerization progresses is rather convenient to see effects of ferrocene cocatalysis; the ligand-independent catalysis is
promising for polymerizations of polar monomers because ligand dissociation could not matter there; the combined ammonium salt might contribute to ferrocene cocatalysis through stabilization of ferrocenium ion ($\text{Fe}^{III}$) as a halogen anion supplier, as speculated in ruthenium/ferrocene-concerted system. Thus, $\text{FeCp}_2$ was combined with $\text{FeBr}_2/n-\text{Bu}_4\text{NBr}$ for polymerization of MMA in conjunction with $\text{H-}(\text{MMA})_2\text{-Br}$ as an initiator (in THF at 60 °C: Figure 1).

Contrary to our expectation, no effects of the combination with $\text{FeCp}_2$ were observed on polymerization behaviors such as polymerization rate, molecular weights, and its distributions. However, when $\text{FeCp}_2$ was replaced with the derivative, decamethylferrocene ($\text{FeCp}^*_2$: Cp* = pentamethyl Cp), the polymerization was obviously accelerated up to higher conversion (90% in 27 h). Despite such acceleration, molecular weights were precisely controlled to give narrow molecular weight distributions ($M_w/M_n = 1.09$ for 90% conversion).

**Figure 1.** Effects of ferrocene cocatalyst ($\text{FeCp}_2$ vs $\text{FeCp}^*_2$) on iron-catalyzed living radical polymerization of MMA with $\text{FeBr}_2/n-\text{Bu}_4\text{NBr}$: $[\text{MMA}]_0/[\text{H-}(\text{MMA})_2\text{-Br}]_0/[\text{FeBr}_2]_0 /[n-\text{Bu}_4\text{NBr}]_0/[\text{ferrocene}]_0 = 4000/40/10/10/40$ mM in THF at 60 °C: $\text{FeCp}^*_2$ (black ●); $\text{FeCp}_2$ (▲); without ferrocene cocatalyst (▼); only $\text{FeCp}^*_2$ instead of $\text{FeBr}_2/n-\text{Bu}_4\text{NBr}$ (gray ●).
Note that the use of only FeCp*₂ as the catalyst resulted in no polymerization, indicating FeCp*₂ itself is incapable to catalyze the polymerization.

As shown above, the decamethylferrocene successfully promoted the living radical polymerization with FeBr₂/n-Bu₄NBr as the cocatalyst, whereas the normal ferrocene showed no effects on the catalysis. It was conceivable that the clear difference in the catalysis is related to relationship of the redox potential between main catalyst and cocatalyst. Thus, cyclic voltammetry (CV) was measured to compare redox potential among FeBr₂ (with n-Bu₄NBr), FeCp₂, and FeCp*₂ in the presence of n-Bu₄NPF₆ as the supporting electrolyte. The redox potential of FeCp*₂ was apparently lower than FeCp₂, as predicted by the structure: the electron density of the iron center is richer due to the electron donation by decamethyl substituents. Interestingly, the redox curve of FeBr₂ was observed between the two ferrocenes: the redox potential of FeCp*₂ was lower than that of FeBr₂, whereas FeCp₂ of no effect showed higher redox potential (Figure 2). Thus, lower redox potential than the main catalyst (i.e., FeBr₂) is probably one of requisites as the cocatalysis for the concerted catalysis.

Figure 2. Cyclic voltammograms of FeBr₂/n-Bu₄NBr and ferrocene cocatalysts (FeCp₂ and FeCp*₂) with n-Bu₄NPF₆ as supporting electrolyte: [iron complex]₀/[n-Bu₄NPF₆]₀ = 5.0/100 mM in ClCH₂CH₂Cl at 25 °C.
2. End Functionality Analysis

To evaluate the nature of living polymerization with the FeCp*2-assisted catalysis, we examined the terminal structure of obtained PMMA by 1H NMR spectroscopy. Figure 3 shows the 1H NMR spectrum of the polymer, which was obtained at 65% conversion when ethyl 2-bromo-2-phenylacetate (EBPA) was employed as the initiator to verify the α-end functionality.

![Figure 3](image)

**Figure 3.** 1H NMR spectrum (in CDCl₃) of PMMA obtained with EBPA/FeBr₂/n-Bu₄NBr/FeCp*₂ in THF at 60 °C; [MMA]/[EBPA]/[FeBr₂]/[n-Bu₄NBr]/[FeCp*₂]₀ = 4000/40/10/10/40 mM.

![Figure 4](image)

**Figure 4.** Effects of FeCp*₂ on ω-end functionalities [Fₙ(ω)ₜ] of obtained PMMAs: [MMA]/[EBPA]/[FeBr₂]/[n-Bu₄NBr]/[FeCp*₂]₀ = 4000/40/10/10/40 or 0 mM in THF at 60 °C.
In addition to the characteristic signals of the main chain (a–c), some minor signals were detected from the end groups. The terminal-related peaks are identified as shown in Figure 3: d and e from the α-end: a’, b’, and c’ from the ω-end. On the assumption that all chains carry the end group, \( M_n \) (NMR) can be calculated from integration ratios of the minor peaks from either α- or ω-end to main ones \([M_n \text{ (NMR, } \alpha)]\) and \([M_n \text{ (NMR, } \omega)]\). Thus, the end functionalities can be estimated from the ratio of \( M_n \) (SEC) to \( M_n \) (NMR): \( F_n(\alpha) = 1.05 \) and \( F_n(\omega) = 0.93 \). These results suggest that the polymer chains were almost quantitatively generated from the initiator and little unfavorable side reactions giving irregular terminals (i.e., coupling and disproportionation between radical species) occurred during the polymerization.

In addition, the ω-end functionalities \([F_n(\omega)]\) at different conversions were examined and compared with those obtained in the absence of FeCp*2. Figure 4 show plots of \( F_n(\omega) \) against conversion for the two systems. A trend was seen that \( F_n(\omega) \) is gradually decreased as the conversion in both cases, but \( F_n(\omega) \) with the combination of FeCp*2 was clearly higher than in the absence of FeCp*2. The difference between the two systems was remarkable especially at the latter polymerization stage: \( F_n(\omega) \) with FeCp*2 = 0.84 at 80% conversion; \( F_n(\omega) \) without FeCp*2 = 0.61 at 73%. The higher end-group functionality would be due to more effective halogen capping reaction, as speculated in the ruthenium-catalyzed system72 (discussed later).

3. High Catalytic Activity: Monomer Addition and Synthesis of Higher Molecular Weight Polymer

To ensure the high catalytic activity and controllability of the concerted catalysis with FeCp*2, a monomer addition experiment was tested for the polymerization of MMA. When the conversion reached 90% (27 h), a fresh feed of MMA was added to the polymerization solution without additional injection of catalyst/cocatalyst. As shown in Figure 5, although the polymerization rate was decreased, MMA was consumed even in the second polymerization, giving an additional 80% (total 170%). The molecular weights of the obtained polymers were linearly increased to the conversion even in the second stage keeping the narrow molecular weight distributions, although a small peak probably due to dead chains was detected.

The high activity of the catalysis encouraged the author to synthesize the higher molecular weight PMMAs. The monomer/initiator ratio was thus set to be 1000 targeting 100000 of \( M_n \) at 100% conversion (Figure 6: \([\text{MMA}]_0/[\text{H-(MMA)}_2\text{-Br}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0\).
Figure 5. Monomer addition experiments in the polymerization of MMA with FeCp*₂:

\[ [\text{MMA}]_0/[\text{MMA}]_{\text{add}}/[\text{H-(MMA)}_2\text{-Br}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*\text{Br}]_0 = 4000/4000/40/10/10/40 \text{ mM in THF at 60 °C}. \]

Figure 6. Synthesis of higher molecular weight PMMAs with FeCp*₂: [MMA]₀/[H-(MMA)_2-Br]₀/[FeBr₂]₀/[n-Bu₄NBr]₀/[FeCp*₂]₀ = 5000/5.0/5.0/5.0/20 mM in THF at 60 °C.
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\[ [\text{FeCp}^*]_0 = 5000/5.0/5.0/5.0/20 \text{ mM}. \]  The conversion reached over 80% in 120 h, and molecular weights of obtained polymers almost agreed with the theoretical values keeping the narrow molecular weight distributions \((M_w/M_n < 1.2)\). Thus, the two experiments support that catalytic activity of the concerted catalysis with FeCp*2 was certainly high in comparisons with conventional iron catalysts.

4. Polymerization with Catalytic Amount of FeCp*2

Given that the plausible cocatalysis by FeCp*2 contributing to both “regeneration of catalyst” and “halogen capping reaction” as shown in Scheme 1, FeCp*2 would be capable of working “catalytically”. Thus, polymerization with lower amount of FeCp*2 was tested to see effects on polymerization results (Figure 7).

![Figure 7](image_url)

**Figure 7.** Effects of the amount of FeCp*2 on the polymerization of MMA with FeBr2/n-Bu4NBr in THF at 60 °C: \([\text{MMA}]_0/[\text{H-(MMA)}_2-\text{Br}]_0/[\text{FeBr}_2]_0/[n-\text{Bu}_4\text{NBr}]_0 = 4000/40/10/10 \text{ mM}; [\text{FeCp}^*]_0 = 40, 2.5, \text{ or } 0 \text{ mM}.\)

Even when the amount of FeCp*2 was decreased from 40 to 2.5 mM for the main catalyst (FeBr2/n-Bu4NBr, 10 mM each), the polymerization was apparently faster than the case without FeCp*2 to give controlled molecular weight and narrow molecular weight distribution (conversion = 90% in 48 h, \(M_n = 9900, M_w/M_n = 1.10\), though the polymerization decelerated especially at latter polymerization stage. Other concentrations of FeCp*2 such
as 10 and 20 mM also gave similar polymerization results in terms of the rate and molecular weights of obtained polymers. The weak dependence of reaction rate on the amount of FeCp*₂ would indicate that FeCp*₂ is regenerated after reduction of Fe(III) catalyst to contribute to promotion of catalysis. One plausible explanation is that the higher oxidized ferrocene (FeCp*₂Br) that would be generated through reduction of Fe(III) catalyst could undergo halogen capping reaction for growing radical species to regenerate FeCp*₂, as speculated with the combination of Ru(II) and FeCp₂ (see Scheme 1).

5. Polymerization with FeBr₃ as the Starting Main Catalyst

FeCp*₂ as a reductant for higher oxidation state iron (Fe^{III}) to be reduced to one-electron lower (Fe^{II}) in the concerted catalysis would allow use of FeBr₃ as the starting catalyst instead of FeBr₂. The system using FeBr₃ and FeCp*₂ would be more ideal from a practical viewpoint, since the both complexes are stable and easily handled.

Thus, FeBr₃ was employed as the starting catalyst for the MMA polymerization in conjunction with ammonium salt (n-Bu₄NBr) and an initiator (H-(MMA)₂-Br: Figure 8). Without FeCp*₂, no polymerization occurred, whereas a combination with FeCp*₂ induced monomer consumption to yield polymer. This result would indicate that FeCp*₂ reduced FeBr₃ into FeBr₂ capabale of activating the C-Br bond.

However, the polymerization was very slow (49% in 72 h). In this system, FeBr₃ could exist in complex salt [n-Bu₄N][Br-FeBr₃⁻] in the presence of n-Bu₄NBr⁴⁵ and anion exchange with the ferrocenium halide salt [FeCp*₂][Br⁻], which is generated as a result of the reduction of FeBr₃, may give more stable salt, [FeCp*₂][Br-FeBr₃], along with [n-Bu₄N][Br⁻].⁷⁶ The slow polymerization is probably due to the in-situ formation of the stable complex salt,⁷⁵ resulting in freeze of the dynamic transformation. Thus, both catalysts (FeBr₃ and [FeCp*₂][Br⁻]) were gradually trapped into this stable complex salt, leading to loss of the catalytic activity. When FeBr₂ is used as the starting catalyst, the transformation into the stable salt is probably negligible because the amount of FeBr₃ is lower.

To solve the problem of slow polymerization, n-Bu₄NPF₆ was used as the ammonium salt instead of n-Bu₄NBr. As a result, polymerization was accelerated without any serious loss of the precision control (82% MMA conversion in 50 h; $Mₙ = 9500$; $Mₘ/Mₙ = 1.13$). The use of hexafluorophosphate salt would generate the corresponding ferrocenium ion ([FeCp*₂][PF₆]),⁷⁴,⁷⁷ which may be a little more reactive than [FeCp*₂][Br-FeBr₃], leading to dynamic equilibrium between dormant and active species.
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6. Polymerization Mechanism

From some experiments, the author presents the plausible mechanism as follows (Scheme 2). First, the main iron catalyst (FeBr₂) activates the terminal carbon-halogen bond (C-X) with one electron oxidation (FeBr₂ → FeBr₃) to give carbon-centered radical species for initiation/propagation, while FeCp*₂ cannot activate it as the main catalyst. Subsequently, the resulting FeBr₃ reacts with the growing radical species on propagation with monomers to give the dormant species, but part of the FeBr₃ complex would be reduced to FeBr₂ by FeCp*₂ to promote the dynamic equilibrium between the two species. Such reduction by FeCp*₂ would be plausible because FeBr₃ can work as the starting catalyst in conjunction with FeCp*₂. In addition, the cocatalysis effect was observed even with catalytic amount of FeCp*₂, indicating FeCp*₂ is regenerated from [FeCp*₂][Br]⁻, which can be formed via the reduction of FeBr₃. One possibility is the reaction of the ferrocenium ion with radical species to give dormant species and FeCp*₂, which was also proposed in Ru/FeCp₂-concerted catalysis. The halogen-capping reaction can be supported by the high ω-end functionality of obtained polymers.
Scheme 2. Plausible Mechanism for Ferrocene-Concerted Living Radical Polymerization

Figure 9. Living radical (co)-polymerization with FeBr$_2$/n-Bu$_4$NBr/FeCp*$_2$ for various monomers in THF: (A) [PEGMA]$_0$/[H-(MMA)$_2$-Br]$_0$/[FeBr$_2$]$_0$ = 500/5.0/5.0 mM at 60 °C; (B) [HEMA]$_0$/[H-(MMA)$_2$-Br]$_0$/[FeBr$_2$]$_0$ = 2000/40/10 mM at 60 °C; (C) [MMA]$_0$/[HEMA]$_0$/[H-(MMA)$_2$-Br]$_0$/[FeBr$_2$]$_0$ = 1000/1000/20/5.0 mM at 60 °C; (D) [MMA]$_0$/[MAA]$_0$/[H-(MMA)$_2$-Br]$_0$/[FeBr$_2$]$_0$ = 3800/200/40/10 mM at 60 °C; (E) [MA]$_0$/[H-(MMA)$_2$-Br]$_0$/[FeBr$_2$]$_0$ = 6000/60/15 mM at 80 °C; (F) [MMA]$_0$/[MA]$_0$/[H-(MMA)$_2$-Br]$_0$/[FeBr$_2$]$_0$ = 2000/2000/40/10 mM at 60 °C; [FeBr$_2$]$_0$/[n-Bu$_4$NBr]$_0$/[FeCp*$_2$]$_0$ = 1/1/4.
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Highly Robust Catalysis over Polar Monomers and Solvents

For conventional iron catalysts in living radical polymerization, selection of ligand, such as phosphine ligand in FeBr$_2$(PR$_3$)$_2$, was crucial toward higher catalytic activity.$^{36,37,42}$ However, when functional polar monomers are employed, the polar groups interact with the iron center to incur irreversible dissociation of the ligands resulting in “catalyst poison”. Thus, most of iron catalysts were generally less active unless special decollation is conducted.$^{42}$ On the other hand, the FeCp*$_2$-cocatalyzed system was active enough without relying on any organic ligands for the catalysis. This feature motivated the author to study applicable monomers with the concerted catalysis, especially functional polar ones.

As shown in Figure 9, functional methacrylate monomers carrying polar side chains, such as PEG (PEGMA), hydroxy (HEMA) and carboxylic acid (MAA), can be polymerized under conditions of homopolymerization or copolymerization. Though relatively slow polymerization occurred in some systems, SEC curves of obtained polymers shifted to higher molecular weight according to the monomer conversions, keeping the monodisperse curves. It is noteworthy that MAA can be copolymerized with the iron-catalyzed system.$^{78}$ Additionally, the system can survive even in the presence of ethanol (Figure 10: polymerization of PEGMA; 67% conversion in 48 h, $M_n = 30900$, $M_w/M_n = 1.36$). Such robustness over polar compounds (i.e., monomer and solvent) of the iron-catalyzed system is apparently superior to conventional with iron catalysts$^{31-69}$, and the contributing factor would be that turnover frequency can be enhanced without relying on ligands.

Figure 10. Living radical polymerization of PEGMA with FeBr$_2$/n-Bu$_4$NBr in conjunction with FeCp*$_2$: $[\text{PEGMA}]_0/[\text{H-(MMA)}_2\text{-Br}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0/[\text{FeCp*}_2]_0 = 500/5.0/5.0/5.0/20$ mM in THF or THF/EtOH (50/50 v/v) at 60 °C.
The system was also available for polymerization with acrylate monomer (methyl acrylate: MA), though the polymerization was slower than that of MMA [(E) and (F) in Figure 9].

Conclusions

This chapter presented the “concerted redox catalysis” using decamethylferrocene (FeCp*₂) for iron (Fe)-catalyzed living radical polymerization with FeBr₂/n-Bu₄NBr as the main catalyst. The concerted “all-iron” system induced the superior catalysis to give controlled molecular weights and narrow molecular weight distributions even under condition for high molecular weight polymers, and notably the end functionality was kept to be higher than the case without FeCp*₂. Importantly, the higher activity was achieved without relying on ligands, and the catalysis was more robust over polar groups, which can be differentiated from conventional iron catalysts. Although rooms for improvement in the catalysis are left, the concerted catalysis consisting of sustainable metal, iron, would open the door to practical applications of metal-catalyzed living radical polymerization.

References

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(78) Higher loading of MAA resulted in uncontrolled polymerization. The carboxylic acid chains probably coordinate on iron center strongly to change the character.
Chapter 5

“All-Iron” Catalysis as Active and Versatile Iron-Based Catalysis for Kharasch Addition Reaction

Abstract

In this paper, the concerted redox catalysis with FeBr$_2$/n-Bu$_4$NBr (main catalyst) and FeCp*$_2$ (cocatalyst), “all-iron” catalysis, which showed high activity and controllability in metal-catalyzed living radical polymerization (Mt-LRP), was successfully applied to the related single addition reaction called Kharasch addition reaction with bromotrichloromethane (CCl$_3$Br) to various olefins, methyl methacrylate (MMA), styrene (St), methyl acrylate (MA), and 1-Hexene. In the reaction with MMA, “all-iron” catalysis allowed the fast and efficient reaction, in which MMA was quantitatively consumed (> 99% olefin conversion) in 1 h to give the desirable mono adduct in around 90% yield, while the reaction without FeCp*$_2$ led to the slow and retarded reaction. This highly efficient catalysis also allowed the reaction with St, MA, and 1-Hexene to give the mono adduct in relatively high yield. Especially in the reaction with St, the desirable mono adduct was obtained almost quantitatively (96% yield). Importantly, by using “all-iron” catalysis, we successfully decreased the usage of the iron catalysts (FeBr$_2$ and FeCp*$_2$) to lower than 1mol% for olefins.

\[
\begin{align*}
\text{R–Br} & \quad \text{Fe}^{II}\text{Br}_2 \\
\text{R} & \quad \text{Fe}^{III}\text{Br}_3 \\
\text{R} & \quad \text{Fe}^{II}\text{Cp}^*_2 \\
\text{[Fe}^{III}\text{Cp}^*_2]^{+}[\text{Br}]^- & \quad \text{R•} \\
\text{R•} & \quad \text{R'} \\
\text{R} & \quad \text{R'}
\end{align*}
\]
Introduction

Radical species are neutral and so highly tolerant to various functional groups such as hydroxyl (–OH), amino (–NR₂), and carboxyl (–COOH). Therefore, radical reactions, which proceed through radical intermediates, are powerful methodologies for constructing unique small molecules or polymers containing functional moieties.

One of the most effective radical reactions is Kharasch addition reaction, which is the radical addition reaction of organohalogen compounds (e.g. polyhalogen compounds, haloesters, etc.) to olefins in conjunction with free radical initiators, light,¹⁻³ or transition metal complexes such as ruthenium (Ru) and copper (Cu) as catalysts.⁴,⁵ Especially, a transition metal-catalyzed systems are quite attractive and well studied because the desirable adduct can be obtained in high yield.⁶ The transition metal-catalyzed Kharasch addition reaction proceeds through the one-electron redox reaction of the transition metal catalyst according to the following mechanism (Scheme 1): (a) the activation of a carbon-halogen bond of a organohalogen compound (R–X → R•) with one-electron oxidation of transition metal catalyst (Mtⁿ → XMtⁿ⁺¹; Mt: transition metal); (b) the addition of the obtained carbon-centered radicals to olefins; (c) the halogen capping reaction for the resultant radical species by the higher oxidation state metal (XMtⁿ⁺¹ → Mtⁿ). Therefore, it is crucial to develop highly redox active metal catalysts both for accelerating the reaction and improving the yield of the mono adduct.

In ruthenium-catalyzed systems, since the first report with RuCl₂(PPh₃)₃,⁷ the critical design of combined ligands gave birth to various types of highly active ruthenium catalysts, such as halfsandwich types,⁸⁻¹¹ alkylidene types,¹²⁻¹⁴ and polynuclear types.¹⁵⁻¹⁸ In addition, the use of reducing agents, such as magnesium¹⁹ or free radical initiators (AIBN),²⁰ as additives further improved the catalysis to lower the catalyst usage (0.01 mol% for olefins), in which the higher oxidation state complexes (Ru³⁺), easily accumulated because of the unfavorable side reactions such as bimolecular radical couplings or disproportionations, were reduced to regenerate the lower oxidation state complex (Ru²⁺). Actually, this concept was well studied also in copper catalyzed systems.²¹,²²

Other than ruthenium and copper catalysts, iron (Fe) catalysts have also been studied due to its abundance, safety, and biocompatibility. However, iron catalysts are unfortunately inferior to ruthenium and copper catalysts in terms of the catalytic activity and versatility. Therefore, in iron-catalyzed Kharasch addition reactions, generally higher amounts of iron catalysts (5-10 mol% for olefins) are needed.²³ Actually, there are some interesting
iron-based catalyst systems that showed the efficient Kharasch addition reactions with lower amount of iron catalysts (< 2.0 mol%).\textsuperscript{24-30} These systems, however, are applicable mainly for Kharasch addition reactions to 1-alkenes, and some trials for conjugated olefins, such as styrene, butadiene, and acrylonitrile, resulted in the lower yields of the desirable mono adducts.\textsuperscript{24-26}

![Scheme 1. Transition Metal-Catalyzed Kharasch Addition Reaction](image)

Transition metal-catalyzed living radical polymerization (Mt-LRP)\textsuperscript{31-38} is one of the most useful precision polymerization method, and proceeds under the similar mechanism with Kharasch addition reactions, in which a carbon-halogen bond of the organohalogen compound (initiator) is activated by transition metal catalysts (Ru, Cu, Fe, etc...) to give the active radical species, followed by the addition reaction with \textit{“large excess”} of olefins (monomer) resulting in the chain propagations (Scheme 2). Here, the active radical species are reversibly transformed to a halogen-capped form (dormant species: $\sim$C–X; $\sim$: polymer chain) by higher oxidation state catalysts (XMt\textsuperscript{n+1}). This dormant-active equilibrium controlled by the transition metal catalysts is crucial to lower the concentration of the radical active species, resulting in the suppression of the unfavorable side reactions to give the well-controlled polymers.

The author has previously reported that ferrocene (FeCp\textsubscript{2}; Fc), which is highly redox active metal complexes\textsuperscript{39} but not be able to catalyze living radical polymerization in itself because of the structural stability, can act as the effective cocatalyst for Mt-LRP in conjunction with ruthenium complexes as the main catalyst.\textsuperscript{40} From model reaction analysis, It was found that ferrocene plays following two important roles for promoting the one-electron redox catalysis with the ruthenium main catalyst: (a) the reduction of the highly
oxidation state ruthenium catalyst (XRu\textsuperscript{III}) to regenerate the lower oxidation state form (Ru\textsuperscript{II});
XRu\textsuperscript{III} + Fe\textsuperscript{II} → Ru\textsuperscript{II} + XFe\textsuperscript{III}, (b) halogen-capping for growing radical species by XFe\textsuperscript{III};
\sim \sim \sim C + XFe\textsuperscript{III} → \sim \sim \sim C-X + Fe\textsuperscript{II}. In this system, the one electron redox catalysis is promoted not only by the ruthenium main catalyst but also by ferrocene, so the author coined it as “ferrocene-assisted concerted redox catalysis”. This novel catalysis is quite efficient to allow the polymerization even with a tiny amount of ruthenium catalyst (50 ppm for olefin monomers) to give well-controlled polymers.

As one interesting extension of this catalysis, the author next reported the use of ferrocene-assisted concerted redox catalysis iron-catalyzed living radical polymerization\textsuperscript{41} in conjunction with FeBr\textsubscript{2} combined with an onium salt (n-Bu\textsubscript{4}NBr) as the main catalyst\textsuperscript{42,43} in order to develop the highly sustainable catalysis.\textsuperscript{44} As a result, it was found that the use of decamethylferrocene (FeCp*\textsubscript{2}; Fe*), the ferrocene derivative that has the lower redox potential than Fe, as the cocatalyst resulted in the highly active iron-based catalysis (“all-iron” catalysis) that allows the synthesis of well-controlled polymers with controlled molecular weights, narrow molecular weight distributions, and well-defined end structures. Importantly, “all-iron” catalysis (FeBr\textsubscript{2}/n-Bu\textsubscript{4}NBr/FeCp*\textsubscript{2}) was also able to be applied to the living radical (co)polymerization of the functional methacrylates with polar functional groups. Such an active and robust iron-based catalysis was quite attractive in terms of the practical applications of iron-based catalysis for living radical polymerizations.

From these backgrounds, this chapter presents the application of “all-iron” catalysis (FeBr\textsubscript{2}/n-Bu\textsubscript{4}NBr/FeCp*\textsubscript{2}) for Kharasch addition reaction (Scheme 3). In this study, It is
expected that the “ferrocene-assisted concerted redox catalysis” effectively facilitates the one electron redox catalysis to give the desirable mono adducts in higher yield even in the reaction with conjugated olefins, and this highly efficient catalysis allows the significant decrease of the catalyst usage.

Experimental Section

Materials

MMA, St, MA (all from TCI; purity > 99%), and 1-Hexene (TCI; purity > 95%) were dried overnight over calcium chloride and purified by double distillation from calcium hydride before use. The halogenated compound, bromotrichloromethane (CCl₃Br) was bubbled with argon for more than 15 min before use. Iron(II) bromide (FeBr₂) (Aldrich; purity >98%), ferrocene (FeCp₂) (Aldrich; purity >98%), decamethylferrocene (FeCp*₂) (Aldrich; purity 97%), and tetrabutylammonium bromide (n-Bu₄NBr) (TCI; purity >99%) were used as received and handled in a glovebox (M. Braun Labmaster 130) under a moisture- and oxygen-free argon atmosphere (H₂O <1 ppm; O₂ <1 ppm). Tetrahydrofuran (THF) (Wako, super-dehydrated, stabilizer free) was bubbled with argon for more than 15 min before use.
min before use.  *n*-Octane (internal standard for \(^1\text{H}\) NMR traces for the reaction with MMA) and 1,2,3,4-tetrahydrousnaphthalene (tetralin; internal standard for \(^1\text{H}\) NMR traces for the reaction with St, MA, and 1-Hexene) were dried over calcium chloride and distilled twice from calcium hydride before use.

**Procedures for Kharasch Addition Reaction.**

All reactions were performed by the syringe technique under argon in a baked glass tubes equipped with a three-way stopcock. A typical procedure for the Kharasch addition reaction of CCl\(_3\)Br to St with FeBr\(_2/n\)-Bu\(_4\)NBr/FeCp\(^*\)\(_2\) is given below. Into a Schlenk tube, THF (2.37 mL), tetralin (internal standard: 0.2 mL), St (0.64 mL, 5.6 mmol), and CCl\(_3\)Br (0.79 mL, 8.0 mmol) were added sequentially in this order at room temperature under dry argon. Then, 3 mL of the prepared solution (including 4.2 mmol of St and 6.0 mmol of CCl\(_3\)Br) was added into a Schlenk tube with FeBr\(_2\) (6.5 mg, 0.03 mmol), *n*-Bu\(_4\)NBr (9.7 mg, 0.03 mmol), and FeCp\(^*\)\(_2\) (39.2 mg, 0.12 mmol) at room temperature under dry argon. Immediately after mixing, the Schlenk tube was placed in an oil bath kept at 60 °C. In predetermined intervals, aliquots were removed by syringes under dry argon, and then cooled to -78 °C in dry ice-methanol to quench the reaction. The quenched reaction solutions were diluted with THF and rigorously shaken with an absorbent [KYOWAAD-2000G-7 (Mg\(_{0.7}\)Al\(_{0.3}\)O\(_{1.15}\)); Kyowa Chemical Industry Co., Ltd.] to remove the iron-bromide residues before \(^1\text{H}\) NMR analyses. The conversion of St and the yield of the mono adduct were determined by the \(^1\text{H}\) NMR spectrum, recorded at room temperature on a JEOL JNM-ECA500 spectrometer operating at 500.16 MHz, from the peak intensity of the signal of St and that of the produced mono adduct with tetralin as an internal standard.

**Results and Discussion**

1. **Effects of Ferrocene on Ruthenium-Catalyzed LRP of MMA**

In the previous report about the “all-iron” catalysis for living radical polymerization,\(^{44}\) the author mainly dealt with the polymerization of methacrylate monomers and it worked well to give well-controlled polymers. Therefore, the Kharasch addition reaction of bromotrichloromethane (CCl\(_3\)Br) to methyl methacrylate (MMA) was firstly performed in order to evaluate the catalytic activity. When FeBr\(_2\) and *n*-Bu\(_4\)NBr were used as the main catalyst in conjunction with FeCp\(^*\)\(_2\) as the cocatalyst ([MMA]\(_0\)/[CCl\(_3\)Br]\(_0\)/
[FeBr$_2$/[n-Bu$_4$NBr]/[FeCp*$_2$]$_0$ = 1400/2000/10/10/40 mM in THF at 40 °C), MMA was consumed smoothly to reach 96% conversion in 4 h (Table 1, Entry1). From the $^1$H NMR spectrum of the reaction solution (Figure 1), the characteristic peaks of the desirable mono adduct ($a'$, $b'$, and $c'$) were observed and the product yield was calculated to 72% (based on the initial charge of the olefins), while the minor peaks coming from the oligomers (such as $b''$) were also detected.

### Table 1. Kharasch addition reactions of CCl$_3$Br to MMA with “all-iron” catalysis

<table>
<thead>
<tr>
<th>Entry</th>
<th>[FeBr$_2$/[n-Bu$_4$NBr]$_0$ (mM)</th>
<th>Cocat.$^b$</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>Conv. (%)$^c$</th>
<th>Yield (%)$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/10 FeCp*$_2$</td>
<td>40</td>
<td>4</td>
<td>96</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10/10</td>
<td>–</td>
<td>40</td>
<td>4</td>
<td>32</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>10/10 FeCp$_2$</td>
<td>40</td>
<td>4</td>
<td>35</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>10/10 FeCp*$_2$</td>
<td>60</td>
<td>1</td>
<td>97</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>40/40 FeCp*$_2$</td>
<td>40</td>
<td>1</td>
<td>&gt;99</td>
<td>89</td>
<td></td>
</tr>
</tbody>
</table>

$^a$[MMA]$_0$/[CCl$_3$Br]$_0$ = 1400/2000 mM in THF. $^b$[Cocat.]$_0$ = 40 mM. $^c$Determined by $^1$H NMR with n-octane as an internal standards.

Figure 1. $^1$H NMR spectrum (in CDCl$_3$ at r.t.) for the reaction solution of the Kharasch addition of CCl$_3$Br to MMA catalyzed by “all-iron” catalysis (FeBr$_2$/n-Bu$_4$NBr/FeCp*$_2$; [MMA]$_0$/[CCl$_3$Br]$_0$/[FeBr$_2$]$_0$/[n-Bu$_4$NBr]$_0$/[FeCp*$_2$]$_0$ = 1400/2000/10/10/40 mM in THF at 40 °C; reaction time: 4 h).
If the same reaction was conducted without FeCp*₂ (only FeBr₂/n-Bu₄NBr), the reaction slowed down and retarded in the early stage (Entry 2), implying the crucial effects of FeCp*₂ for promoting the catalysis. In addition, the use of FeCp₂ as the cocatalyst, in place of FeCp*₂, gave no effects (Entry 3) because FeCp₂ has the higher redox potential than the main catalyst (FeBr₂/n-Bu₄NBr) and so cannot act as the reducing agent.

Next, the reaction with FeBr₂/n-Bu₄NBr/FeCp*₂ was examined in higher temperature (60 °C), resulting in the faster reaction in which the olefin conversion reached 97% in 1 h without the loss of the product yield (Entry 4). Finally, the reaction was performed with a higher amount of the catalyst ([FeBr₂]₀/[n-Bu₄NBr]₀/[FeCp*₂]₀ = 10/10/40 mM in THF at 40 °C). As a result, the complete consumption of MMA was observed in 1 h to give the desirable mono adducts in around 90% yield (Entry 5).

2. Kharasch Addition Reactions to Other Olefins

Next, “all-iron” was applied catalysis to Kharasch addition reactions with other olefins in conjunction with CCl₃Br as the halogenated compound (Table 2). Firstly, the Kharasch addition reaction with styrene (St) was performed under the same condition with that with MMA ([Olefin]₀/[CCl₃Br]₀/[FeBr₂]₀/[n-Bu₄NBr]₀/[FeCp*₂]₀ = 1400/2000/10/10/40 mM in THF at 60 °C). From ¹H NMR traces (Figure 2), the characteristic peaks coming from olefinic protons of St (a, b, and c) were almost completely vanished in 3 h, and the new peak coming from the desirable mono adduct (b’) was observed. Interestingly, the yield of mono adducts, calculated from the integrated peak areas of the initially fed St and the generated mono adduct standardized by the peak area of the internal standard (tetralin), was quite high (96%; Table 2, Entry 2), partly because of the lower propagation rate coefficient \(k_p\), meaning that the oligomerization reaction can be more easily avoided than MMA.

Next, the author performed the Kharasch addition reaction with methyl acrylate (MA). In terms of its higher \(k_p\) value rather than that of MMA or St, it became difficult to avoid the oligomerizations, but the desirable mono adduct was obtained in 60% yield in 24 h (Entry 3). Finally, the reaction with 1-hexene was examined under the same condition. The reaction proceeded a bit slower (olefin conversion: 91% in 24 h), but the product yield was relatively higher (83% yield; Entry 4). As described above, it turned out that “all-iron” catalysis can be applied various types of olefins to give the desirable mono adducts in relatively high yield (60 ~ 100%).
Table 2. Kharasch addition reactions of CCl₃Br to various olefins with “all-iron” catalysis

<table>
<thead>
<tr>
<th>Entry</th>
<th>Olefin</th>
<th>Mono Adduct</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MMA</td>
<td>C₃Cl₃Br₂O</td>
<td>60</td>
<td>1</td>
<td>97</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>St</td>
<td>C₃Cl₃BrO₂</td>
<td>60</td>
<td>3</td>
<td>&gt;99</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>MA</td>
<td>C₃Cl₃BrO₂</td>
<td>60</td>
<td>24</td>
<td>90</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>1-Hexene</td>
<td>C₃Cl₃Br</td>
<td>60</td>
<td>24</td>
<td>91</td>
<td>83</td>
</tr>
</tbody>
</table>

“[Olefin]₀/[CCl₃Br]₀/[FeBr₂]₀/[n-Bu₄NBr]₀/[FeCp*₂]₀ = 1400/2000/10/10/40 mM in THF.”

“Determined by ¹H NMR with n-octane (for Entry 1) and tetralin (for Entry 2-4) as internal standards.”

Figure 2. ¹H NMR traces (in CDCl₃ at r.t.) for the Kharasch addition reaction of CCl₃Br to St catalyzed by “all-iron” catalysis (FeBr₂/n-Bu₄NBr/FeCp*₂): [St]₀/[CCl₃Br]₀/[FeBr₂]₀/[n-Bu₄NBr]₀/[FeCp*₂]₀ = 1400/2000/10/10/40 mM in THF at 60 °C.
3. Lowering Catalyst Usage

The high catalytic activity of “all-iron” catalysis encouraged the author to try lowering the catalyst amounts in Kharasch addition reaction of CCl$_3$Br to St ([St]$_0$/[CCl$_3$Br]$_0$ = 1400/2000 mM in THF at 60 °C). Firstly, the reaction was performed with half amounts of iron catalysts with keeping the same feed ratio of FeBr$_2$ and FeCp*$_2$: from [FeBr$_2$]$_0$/[n-Bu$_4$NBr]$_0$/[FeCp*$_2$]$_0$ = 10/10/40 mM (amounts of Fe (FeBr$_2$ and FeCp*$_2$): 3.6 mol% to St; Table 3, Entry 1) to [FeBr$_2$]$_0$/[n-Bu$_4$NBr]$_0$/[FeCp*$_2$]$_0$ = 5.0/5.0/20 mM (amounts of Fe: 1.8 mol%; Entry 2). As a result, the reaction slowed down and the yield of the mono adduct becomes a bit lower. Next, the amount of FeCp*$_2$ was reduced with the fixed amount of the main catalyst (FeBr$_2$/n-Bu$_4$NBr: 5.0 mM; Entry 2-4). The lower the amount of FeCp*$_2$, the lower the product yield. However, 70% yield was observed even with 5.0 mM of FeCp*$_2$ (amounts of Fe: 0.7 mol%). Finally, the reaction with the lower amount of the main catalyst ([FeBr$_2$]$_0$/[n-Bu$_4$NBr]$_0$ = 2.5/2.5 mM) was examined in conjunction with 10 mM of FeCp*$_2$ (amounts of Fe: 0.9 mol%) in order to study the effects of the amount of the main catalyst (Entry 5). Unfortunately, the product yield became lower by more than 20% compared with the reaction with 5.0 mM of FeBr$_2$ (Entry 3). Therefore, it was found that the amount of the main catalyst affects the reaction efficiency more strongly than that of FeCp*$_2$.

As above, the usage of the iron catalysts (FeBr$_2$ and FeCp*$_2$) was lowered to around 1 mol% (for St) to give the relatively high product yield (> 70%). Especially, the usage of FeBr$_2$ (main catalyst) was cut to 0.36 mol%, which is the significant result compared with previously reported effective iron-based catalyst systems.$^{24-30}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>[FeBr$_2$]$_0$ (mM)$^b$</th>
<th>[FeCp*$_2$]$_0$ (mM)</th>
<th>Fe (mol%)$^c$</th>
<th>Time (h)</th>
<th>Conv. (%)$^d$</th>
<th>Yield (%)$^d$</th>
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<tr>
<td>1</td>
<td>10</td>
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<td>0.9</td>
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<td>70</td>
<td>59</td>
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</table>

$^a$[St]$_0$/[CCl$_3$Br]$_0$ = 1400/2000 mM in THF at 60°C. $^b$Equimolar amounts of n-Bu$_4$NBr was combined. $^c$([FeBr$_2$]$_0$ + [FeCp*$_2$]$_0$)•100/[St]$_0$ $^d$Determined by $^1$H NMR with tetralin as an internal standard.
Conclusions

In conclusion, this chapter presented the application of “all-iron” catalysis for Kharasch addition reactions for the development of the highly active and versatile iron-based system. In the Kharasch addition reaction of \( \text{CCl}_3\text{Br} \) to \( \text{MMA} \), the use of \( \text{FeCp}^*\text{Br}_2 \) as the cocatalyst in conjunction with \( \text{FeBr}_2/\text{Bu}_4\text{NBr} \) as the main catalyst allowed the fast and efficient reaction in which \( \text{MMA} \) was almost clearly consumed in 1 h to give the desirable mono adduct in around 90% yield. In addition, “all-iron” catalysis (\( \text{FeBr}_2/\text{Bu}_4\text{NBr} \)) was also successfully applied to the reaction with St, MA, 1-Hexene as the olefins. Especially, in the reaction with St, the mono adduct was obtained in quite high yield (96% in 3 h). Finally, the highly active catalysis with “all-iron” system allowed the dramatic decrease in the usage of the iron catalysts (\( \text{FeBr}_2 \) and \( \text{FeCp}^*\text{Br}_2 \)) to lower than 1 mol% for olefins.

References

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PART III

From “Living Radical Polymerization” to “Radical Coupling Chain Extension” via Concerted Redox
Chapter 6

Ferrocene Cocatalysis in Ruthenium-Catalyzed Radical Coupling Chain Extension: Catalytic Reaction through Catalyst Regeneration and Halogen Removal

Abstract

In this study, Ru/ferrocene concerted redox catalysis, highly efficient for metal-catalyzed living radical polymerization, was applied to efficient radical coupling reactions by using Cp*Ru/FeCp*₂ catalyst pair (Cp*Ru: Cp*RuCl(PPh₃)₂) in conjunction with NH₄PF₆ as an additive. In this catalyst system, following two key steps were crucial for promoting the reaction: (a) effective regeneration of Ru II complex by FeCp*₂ through a reduction of XRu III, generated as a result of the radical coupling (XRu III + Fe II Cp*₂ → Ru II + [Fe III Cp*₂] X⁻; X: halogen); (b) formation of the stable ferrocenium salt ([Fe III Cp*₂]PF₆⁻) by the anion exchange reaction between [Fe III Cp*₂] X⁻ and NH₄PF₆ ([Fe III Cp*₂] X⁻ + NH₄PF₆ → [Fe III Cp*₂]PF₆⁻ + NH₄X). The Cp*Ru/FeCp*₂/NH₄PF₆ catalyst system was firstly used for the radical coupling reaction of ω-brominated polystyrenes (PSt-Br), in which the author found that the use of water as solvent (suspension) can facilitate the reaction to give desirable coupling products almost quantitatively (coupling efficiency xₖ = 0.93). Next, the catalysis was applied to the radical coupling reaction of the α,ω-dibrominated PSt (Br~~~R~~~Br) to give chain extended PSt (Mₚ(extended) = 14200, Mₚ(prepolymer) = 2500).
Introduction

Ferrocene (FeCp$_2$; Fc) or the derivatives are well-known organometallic complexes,$^{1,2}$ where the central iron is sandwiched between two cyclopentadienyl anion (Cp) rings. The noteworthy property is the one-electron redox behavior (Fe$^{II} \leftrightarrow$ Fe$^{III}$),$^3$ and the most general utility is an internal standard for cyclic voltammetry (CV) analysis.$^4$ Another characteristic application is use as a chiral ligand: the aromaticity of Cp ring allows introduction of bearing coordination sites (P, N, O, etc.)$^5$-$^7$ and the sandwich structure is useful to construct chiral environment in reaction as the ligand for another metal. On the other hand, examples of reactions with ferrocene as a metal catalyst are limited likely due to the high stability.$^8$

The author has recently reported that ferrocene can act as an effective cocatalyst for ruthenium-catalyzed living radical polymerization.$^9$ In metal-catalyzed living radical polymerization (Mt-LRP) or ATRP, a carbon-halogen bond at a dormant end is reversibly activated to a radical species ($\sim$C-X $\leftrightarrow$ $\sim$C•; $\sim$: polymer chain, X: halogen) through one electron redox of the transition metal catalyst (Mt$^n$ $\leftrightarrow$ Mt$^{n+1}$).$^{10-16}$ From model reaction analyses, ferrocene could contribute to the catalysis with the following roles: (a) reduction of higher oxidation state complex to lower complex; XRu$^{III}$ + Fe$^{II}$ $\rightarrow$ Ru$^{II}$ + XFc$^{III}$ (for ruthenium main catalyst), (b) halogen-capping for growing radical species to regenerate dormant C–X bonds; $\sim$C• + XFc$^{III}$ $\rightarrow$ $\sim$C-X + Fe$^{II}$ (Figure 1). The concerted redox catalysis allows the dramatic decrease of the loading amount of Ru main catalysts and the precise synthesis of the high molecular weight polymer (DP~1000). Furthermore, the ferrocene-concerted redox catalysis can be applied to iron-catalyzed LRP with FeBr$_2$/n-Bu$_4$NBr as the main catalyst,$^{17,18}$ in conjunction with decamethylferrocene (FcP*$_2$: Cp* = pentamethyl Cp) of lower redox potential instead of ferrocene.$^{19}$ The “all-iron” system showed high activity for various methacrylate monomers including functional monomers with polar pendant groups (e.g., –OH, –PEG, –COOH).

In the “ferrocene-concerted catalysis”, ferrocenium ion (XFc$^{III}$), which is generated via reduction reaction of higher oxidized metal by ferrocene (Fc$^{II}$), is ionic species ([Fe$^{III}$]$^+$X$^-$) as well as one-electron oxidizing agent. The ionic feature allows a change in the catalytic mechanism by addition of appropriate salts. For example, in Ru/ferrocene concerted system,$^9$ the author demonstrated the radical coupling reaction of a model dormant end [R-Cl: ethyl 2-chloro-2-phenylacetate (ECPA)] catalyzed by Ru/ferrocene catalyst in conjunction with NH$_4$PF$_6$ as the model reaction to verify the cocatalytic function of ferrocene as a
reducing agent (Figure 2). As a result, the reaction proceeded almost quantitatively (Conversion ~ 90%), although the radical coupling reaction is the unfavorable side reaction in LRP and effectively inhibited when using only Ru/ferrocene (without NH₄PF₆) as shown in Figure 1. This dramatic difference in catalysis by just adding NH₄PF₆ is probably because ferrocenium halide ([Fe^{III}]X) reacts with NH₄PF₆ to give ferrocenium hexafluorophosphate ([Fe^{III}]PF₆⁻: highly stable and unable to act as halogen capping agent) and NH₄X. It is important that halide anions (X⁻) are scavenged as NH₄X and released from the reaction solution (NH₄X is insoluble to nonpolar organic solvents).

**Figure 1.** Ferrocene-assisted concerted redox catalysis in ruthenium-catalyzed living radical polymerization.

**Figure 2.** Catalytic radical coupling reaction of ethyl 2-chloro-2-phenylacetate (ECPA) with Ru catalyst in conjunction with ferrocene and NH₄PF₆.⁹
As the extension of this unique catalysis with Ru/ferrocene/NH$_4$PF$_6$, this chapter presents the radical coupling reaction of polystyrene (PSt) prepared by Mt-LRP of styrene, having halogen at ω-chain end (~~~C-X; ~~~: polystyrene, X: halogen). The radical coupling reaction is highly useful method for preparing α,ω-telechelic polymers (F$_n$~~~F$_n$; F$_n$: functional group) that have functional groups derived from the initiator for Mt-LRP (F$_n$-X), and actually some research groups have already studied in this line by using copper (Cu) catalysts.$^{20-23}$ In this study, the author examined the reaction conditions that is suitable for efficient radical coupling of PSt-X, such as the catalyst selection (ferrocene derivatives and ammonium salts), catalyst amounts, reaction solvents, and so on. As a result, it was found that Ru/ferrocene/NH$_4$PF$_6$ catalyst system allowed the almost quantitative radical coupling reactions under the xylene/H$_2$O mixed solvent (suspension system). Obtained coupling products had two initiator moieties at α- and ω-chain ends, supported by $^1$H NMR analysis. In addition, this catalysis was successfully applied to the chain extension reaction of α,ω-halogenated PSt (X~~~F$_n$~~~X; prepared by Mt-LRP of St in conjunction with the difunctional initiator, X-F$_n'$-X), giving high molecular weight PSt having initiator moieties (F$_n'$) periodically ([~~~F$_n'$~~~]$_n$).

**Experimental Section**

**Materials**

St (from TCI; purity > 99%) was dried overnight over calcium chloride and purified by double distillation from calcium hydride before use. (1-chloroethyl)benzene (St-Cl) (TCI; purity > 97%) and the H-EMA-Br initiator (ethyl 2-bromoisobutyrate) (TCI; purity > 98%) were purified by distillation under reduced pressure before use. The difunctional bromine initiator EBBiB (ethylene bis(2-bromoisobutyrate)) (Aldrich; purity 97%) and $n$-Bu$_3$N (TCI; purity > 98%) as an additive for Ru-catalyzed living radical polymerization were degassed by reduced pressure before use. Cp*RuCl(PPh$_3$)$_2$ (Cp*Ru) (Aldrich), ferrocene (FeCp$_2$) (Aldrich; purity > 98%), decamethylferrocene (FeCp*$_2$) (Aldrich; purity 97%), NH$_4$PF$_6$ (Aldrich; purity 99.99%), and $n$-Bu$_4$NPF$_6$ (Aldrich; purity > 98%) were used as received and handled in a grove box (M. Braun Labmaster 130) under a moisture- and oxygen-free argon atmosphere (H$_2$O < 1 ppm, O$_2$ < 1 ppm). $n$-Octane (internal standard for gas chromatography) and 1,2,3,4-tetrahydronaphthalene (tetralin; internal standard for $^1$H NMR) were dried over calcium chloride and distilled twice from calcium hydride before use.
Toluene (Kishida Kagaku, Osaka, Japan; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, SG Water USA, Nashua, NH; Glass Counter) and bubbled with dry nitrogen for more than 15 min immediately before use. Xylene (Wako, dehydrated) and water (Wako) were bubbled with dry nitrogen for more than 15 min before use.

**Radical Coupling Reactions of St-Cl**

Reactions were carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock. A typical procedure for the radical coupling reaction of St-Cl with Cp*Ru/FeCp*₂/NH₄PF₆ was as follows. In a 50 mL round-bottomed flask were placed Cp*Ru (9.6 mg, 0.012 mmol), FeCp*₂ (39.3 mg, 0.12 mmol), and NH₄PF₆ (19.6 mg, 0.12 mmol) under a glove box. Then, toluene (2.66 mL), tetralin (0.15 mL), and St-Cl (0.19 mL of 637.9 mM in toluene, 0.12 mmol) were added sequentially in this order at room temperature under dry argon; the total volume was 3.00 mL. Immediately after mixing, the flask was placed in an oil bath kept at 100 °C. In predetermined intervals, the reaction mixtures were terminated by cooling to −78 °C in dry ice-methanol to terminate the reaction. The conversion of St-Cl and the yield of the coupling product were determined by ¹H NMR spectroscopy from the peak intensity of the signal of the chlorine compound and that of the produced coupling compound with tetralin as an internal standard.

**Synthesis of PSt-Br**

The synthesis of PSt-Br prepolymer was carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock via Ru-catalyzed living radical polymerization. In a 50 mL round-bottomed flask was placed Cp*Ru (25.5 mg, 0.032 mmol) under a glove box. Then, toluene (2.42 mL), n-octane (0.40 mL), n-Bu₃N (0.80 mL of 400 mM in toluene, 0.32 mmol), St (3.67 mL, 32.0 mmol), and H-EMA-Br (0.72 mL of 446.5 mM in toluene, 0.32 mmol) were added sequentially in this order at room temperature under dry argon; the total volume was 8.00 mL. Immediately after mixing, the flask was placed in an oil bath kept at 100 °C. After the polymerization had reached around 20% conversion in 8 h (conversion: determined from the concentration of residual monomer measured by gas chromatography with n-octane as an internal standard), the solution was evaporated at 25 °C to remove St residue, toluene, and n-octane. Into the flask with the resulting polymer (PSt-Br: $M_n$ and $M_w/M_n$ can be found in results and discussion) and
non-volatile agents (Cp*Ru and n-Bu$_3$N), xylene (4.00 mL) was added, and PST-Br, Cp*Ru, and n-Bu$_3$N were homogeneously solubilized at room temperature. This prepolymer solution was used to the radical coupling reaction without purification.

**Radical Coupling Reactions of PST-Br**

Reactions were carried out by the syringe technique under dry argon in baked glass tubes equipped with three-way stopcock. A typical procedure for the coupling reaction with Cp*Ru/n-Bu$_3$N/FeCp*_2/NH$_4$PF$_6$ in xylene/H$_2$O mixed solvent was as follows. In a 50 mL round-bottomed flask were placed Cp*Ru (19.1 mg, 0.024 mmol), FeCp*$_2$ (78.3 mg, 0.24 mmol), and NH$_4$PF$_6$ (39.1 mg, 0.24 mmol) under a grove box. Then, the prepolymer solution prepared above (3.00 mL, 0.24 mmol of PST-Br, 0.024 mmol of Cp*Ru, and 0.24 mmol of n-Bu$_3$N) and water (3.00 mL) were added sequentially in this order at room temperature under dry argon; the total volume was 6.00 mL. Immediately after mixing, the flask was placed in an oil bath kept at 90 °C. In predetermined intervals, the reaction mixtures were terminated by cooling to −78 °C in dry ice-methanol to terminate the reaction. The organic phase of the quenched solutions was evaporated to dryness to give the products, which were subsequently dried overnight under vacuum at room temperature.

**Synthesis of Br-PST-Br**

Br-PST-Br was prepared in analogy to PST-Br using EBBiB instead of H-EMA-Br. In a 50 mL round-bottomed flask with Cp*Ru (25.5 mg, 0.032 mmol), toluene (2.80 mL), n-octane (0.40 mL), n-Bu$_3$N (0.80 mL of 400 mM in toluene, 0.32 mmol), St (3.67 mL, 32.0 mmol), and EBBiB (0.33 mL of 487.8 mM in toluene, 0.16 mmol) were added sequentially in this order at room temperature under dry argon; the total volume was 8.00 mL. Immediately after mixing, the flask was placed in an oil bath kept at 100 °C. After the polymerization had reached around 10% conversion in 3 h (conversion: determined from the concentration of residual monomer measured by gas chromatography with n-octane as an internal standard), the solution was evaporated at 25 °C to remove St residue, toluene, and n-octane. Into the flask with the resulting polymer (Br-PST-Br: $M_n$ and $M_w/M_n$ can be found in results and discussion) and non-volatile agents (Cp*Ru and n-Bu$_3$N), xylene (4.00 mL) was added, and PST-Br, Cp*Ru, and n-Bu$_3$N were homogeneously solubilized at room temperature. This prepolymer solution was used to the radical coupling reaction without purification.
Synthesis of Chain Extended PST via Radical Coupling Reactions of Br-PSt-Br

The chain extended PST was synthesized by the radical coupling reaction of Br-PSt-Br performed in analogy to the radical coupling reaction of PST-Br. A typical procedure for the coupling reaction with Cp*Ru/n-Bu3N/FeCp*2/NH4PF6 in xylene/H2O mixed solvent was as follows. In a 50 mL round-bottomed flask with Cp*Ru (19.1 mg, 0.024 mmol), FeCp*2 (78.3 mg, 0.24 mmol), and NH4PF6 (39.1 mg, 0.24 mmol), the prepolymer solution prepared above (3.00 mL, 0.12 mmol of Br-PSt-Br, 0.024 mmol of Cp*Ru, and 0.24 mmol of n-Bu3N) and water (3.00 mL) were added sequentially in this order at room temperature under dry argon; the total volume was 6.00 mL. Immediately after mixing, the flask was placed in an oil bath kept at 90 °C. In predetermined intervals, the reaction mixtures were terminated by cooling to –78 °C in dry ice-methanol to terminate the reaction. The organic phase of the quenched solutions was evaporated to dryness to give the products, which were subsequently dried overnight under vacuum at room temperature.

Measurements

For PST, Mn and Mw/Mn were measured by size exclusion chromatography at 40 °C in THF as an eluent on three polystyrene-gel columns (Shodex LF-404; exclusion limit = 2 × 10^6; particle size = 6 μm; pore size = 3000 Å; 0.46 cm i.d. × 25 cm; flow rate, 0.3 mL min⁻¹) connected to a DU-H2000 pump, a RI-74 reflective-index detector, and a UV-41 ultraviolet detector (all from Shodex). The columns were calibrated against 13 standard PST samples (Polymer Laboratories; Mn = 500–3840000; Mw/Mn = 1.01–1.14) as well as the monomer. 1H spectra were measured at room temperature on a JEOL JNM-ECA500 spectrometer operating at 500.16 MHz. For 1H NMR analysis, polymer samples were fractionated by preparative SEC (column: Shodex K-5002F).

Results and Discussion

1. Model Reaction: Radical Coupling Reaction with St-Cl

The radical coupling reaction of (1-chloroethyl)benzene (St-Cl: the model compound of the dormant end of PST-X) with a Ru catalyst in conjunction with ferrocene and NH4PF6 was studied for optimizing the catalyst system (Scheme 1).

Firstly, the reaction was performed with the Cp*-ligated ruthenium complex [Cp*RuCl(PPh3)2: Cp*Ru]2⁺ in conjunction with FeCp2 and NH4PF6 in toluene at 100 °C.
However, the reaction proceeded very slowly (conversion = 6% in 48 h) because the C-Cl bond of St-Cl is stable and the concentration of radical species becomes low. In order to accelerate the reaction, FeCp*\textsubscript{2}, more reducing ferrocene derivative having lower redox potential than FeCp\textsubscript{2},\textsuperscript{6,19} was used in place of FeCp\textsubscript{2}, giving the efficient reaction (Entry 2; conversion = 70%, yield = 66%).

Controlled experiments\textsuperscript{3-5} strongly suggested that three components of the catalysis (Cp*Ru, FeCp*\textsubscript{2}, and NH\textsubscript{4}PF\textsubscript{6}) are all needed for driving radical coupling reactions. Especially, it is important that the use of the ammonium salt (NH\textsubscript{4}PF\textsubscript{6}), the halide scavenger, is crucial, supporting the catalytic mechanism shown in Figure 2.

(Table 1, Entry 1). The data in Table 1 also show that the use of FeCp*\textsubscript{2}, more reducing ferrocene derivative, is necessary for radical coupling reactions. The use of FeCp\textsubscript{2} alone (Entry 4) did not give the desired product, whereas FeCp*\textsubscript{2} alone (Entry 5) did not give the desired product either, indicating that the use of both Cp*Ru and FeCp*\textsubscript{2} is crucial for the reaction.
2. Radical Coupling Reactions of PSt-Br

From the results of model reactions (Table 1), Cp*Ru/FeCp*₂/NH₄PF₆ catalyst system was chosen for the radical coupling reactions of ω-brominated polystyrene (PSt-Br). The reaction scheme is shown in Scheme 2. Firstly, PSt-Br was prepared by Mt-LRP using the bromine initiator (H-EMA-Br) in conjunction with Cp*Ru and n-Bu₃N (additive)²⁵,²⁶ as the catalyst (in toluene at 100 °C; [St]₀ = 4.0 M, [H-EMA-Br]₀ = 40 mM, [Cp*Ru]₀ = 4.0 mM, [n-Bu₃N]₀ = 40 mM). After stopping the polymerization (at 8 h) by cooling the reaction mixture to room temperature, the solution was evaporated in vacuo to remove toluene and the residual monomer (Cp*Ru and n-Bu₃N were remained). FeCp*₂ and NH₄PF₆ were then added, and the radical coupling reaction was performed in toluene at 100 °C.

The reaction was performed in a concentrated condition to enhance the radical coupling ([PSt-Br]₀ = 80 mM, [Cp*Ru]₀ = 8.0 mM, [n-Bu₃N]₀ = [FeCp*₂]₀ = [NH₄PF₆]₀ = 80 mM). From SEC traces (Figure 3), a bimodal distribution was observed that was composed of the coupled PSt along with the residual PSt (reaction time = 96 h): Mₚ(coupled PSt) = 5300, Mₚ(residual PSt) = 2700 (Mₚ: peak top molecular weight). A large amount of the residual PSt peak means the insufficient coupling efficiency. Therefore, the author next performed the coupling reaction with a larger amount of Ru catalysts ([Cp*Ru]₀ = 16 mM) in order to generate radical species in higher concentrations, resulting a larger amount of the coupled PSt peak from SEC curve (reaction time = 96 h) that means a better coupling efficiency. However, even with such a large amount of Ru catalysts, the residual PSt peak was remained.
Chapter 6

3. Radical Coupling Reactions in Xylene/H₂O Suspension System

In ruthenium-catalyzed LRP, it is previously reported that the use of water as a solvent can efficiently promote the catalytic cycle to give fast and well-controlled polymerizations. For example, RuCl₂-based catalyst [RuCl₂(PPh₃)₃] allowed much faster polymerization of methyl methacrylate (MMA) in toluene/H₂O mixtures (suspension system) than in toluene to give polymers with controlled molecular weights and its distributions.²⁷ In addition, Cp*Ru-based complexes were able to catalyze the aqueous living radical polymerizations that allows the fast and quantitative polymerizations in water at a low temperature (40 °C) with a low ruthenium dose (< 200 ppm relative to monomer).²⁸ One effect of water is the coordination to the Ru complexes that facilitates the activation of a dormant carbon-halogen (C-X) bond to give radical species effectively. This positive effect of water is quite attractive for the enhancement of radical coupling reactions. Therefore, the radical coupling of PSt-Br was conducted in xylene/H₂O mixed solvent (Figure 4; organic phase/water = 1/1 v/v). As a result, the reaction proceeded very fast to give polymers that show a monomodal distribution (SEC traces) whose peak top molecular weight is twice as high as that of prepolymer (PSt-Br) after 12 h, although the residual polymers are slightly remained.

Figure 3. SEC traces for the radical coupling reactions of PSt-Br with Cp*Ru/FeCp*₂/NH₄PF₆ in toluene at 100 °C: [PSt-Br]₀/[Cp*Ru]₀/[n-Bu₃N]₀/[FeCp*₂]₀/[NH₄PF₆]₀ = 80/8.0 (left) or 16 (right)/ 80/80/80 mM.
According to the previous report from Matyjaszewski et al.,\textsuperscript{23} in the radical coupling reaction of PSt-Br, the coupling efficiency ($x_c$) can be obtained as $x_c = 2(1-M_{n,0}/M_{n,c})$ ($M_{n,0}$: the number average molecular weight ($M_n$) of prepolymer (PSt-Br), $M_{n,c}$: $M_n$ of the resulting polymer). From this equation, in the suspension radical coupling reaction, the efficiency can be estimated to $x_c = 0.93$ (Table 2, Entry 2), while the efficiency in the reaction in toluene was $x_c = 0.81$ (Entry 1).
Next, as the controlled experiment, the radical coupling reaction in xylene/H$_2$O was performed without FeCp$_2^*$, resulting the quite low coupling efficiency ($x_c = 0.23$) even after 48 h (Entry 3). This result indicates that FeCp$_2^*$ is crucial for the “catalytic” (about Ru) radical coupling reaction. In addition, the catalysis without NH$_4$PF$_6$ (Cp*Ru/FeCp$_2^*$) also led an inefficient reaction ($x_c = 0.48$), indicating the importance of scavenging halogen (Br) by NH$_4$PF$_6$ (Entry 4). Another controlled experiment was performed with Cp*Ru/FeCp$_2^*$ in conjunction with n-Bu$_4$NPF$_6$, resulting the lower coupling efficiency ($x_c = 0.72$) in 48 h (Entry 5) probably because n-Bu$_4$NBr is soluble to organic phase and Br cannot be efficiently scavenged.

4. $^1$H NMR Analysis

$^1$H NMR spectra for the prepolymer (PSt-Br) and the coupled PSt (obtained by the suspension radical coupling reaction: 12 h) are shown in Figure 5. In the spectrum of the prepolymer, in addition to the characteristic signals of the main chain (d–f), some minor signals from chain ends were observed: $a$–$c$ from the $\alpha$-end; $e'$ from the $\omega$-halogenated end. The signal $e'$ includes not only $\omega$-brominated ends but also a small amount of $\omega$-chlorinated ends that results from the halogen exchange reaction with Cp*Ru.$^{29,30}$ From the ratio between the peaks of the $\alpha$-end ($a, c$) and the $\omega$-halogenated end ($e'$), the end halogen functionality was calculated to 95%. In addition, the integration ratio of the peaks the aromatic protons ($f$) to the $\alpha$-end ($a, c$) was calculated to $f/(a + c) = 11.2$.

From the spectrum of the coupled PSt, the peak from the $\omega$-halogenated end ($e'$) disappeared. Additionally, the integration ratio of the peaks the aromatic protons ($f$) to the $\alpha$-end ($a, c$) did not change: $f/(a + c) = 11.3$. These results suggest a formation of the coupled polymers that have two initiator moieties. Note that the new peak from the olefinic proton at 6.05 to 6.2 ppm was observed after the reaction, implying the disproportionation$^{31}$ reaction that causes small amounts of residual prepolymer in Figure 3.$^{21}$

5. Chain Extended PSt by Radical Coupling Reactions of Br-PSt-Br

The author next prepared the $\alpha, \omega$-dibrominated PSt (Br~~~R~~~Br) by Ru-catalyzed LRP of St with the difunctional initiator [Br-R-Br: ethylene bis(2-bromoisobutyrate) (EBBiB)], and was used as the prepolymer for the radical coupling reaction to give chain extended PSt having initiator moieties periodically.$^{32}$ As shown in Figure 6, the suspension system allowed the efficient reaction to give chain extended PSt that have much higher $M_p$.
Figure 5. $^1$H NMR (500 MHz, 30 °C) analysis for the suspension radical coupling reaction of PST-Br with Cp*Ru/FeCp*$_2$/NH$_4$PF$_6$ (see Figure 4 for the reaction condition): [polymer] = 30 mg/mL in CDCl$_3$.

To calculate $M_n(\text{extended PST})$ to $M_p(\text{prepolymer})$, the end halogen functionality was calculated to 95% from the ratio of the peak of the halogenated chain end ($d'$) to that of the initiator moiety ($a$), indicating the formation of the $\alpha,\omega$-dihalogenated PST that carries one initiator moiety in the middle of the chain.

From the spectrum of the extended PST, the peak from halogenated chain ends was not found. In addition, the integration ratio of the aromatic protons of the main chain ($e$) to the methyl protons of the initiator moiety ($a$) was almost same with that of the prepolymer ($e/a = 7.5$, the coupled PST: $e/a = 7.6$) despite the clear increase of $M_n$(SEC) shown in Figure 6, indicating that PST chains carrying one initiator unit were connected by the radical coupling reaction. As well as the radical coupling reaction of PST-Br (Figure 5), the peak from the olefin chain ends was found because of the disproportionation reaction.
Figure 6. Radical coupling reaction of Br-PSt-Br for the chain extended PSt: [Br-PSt-Br]₀/[Cp*Ru]₀/[n-Bu₃N]₀/[FeCp*₂]₀/[FeCp*₂]₀/[NH₄PF₆]₀ = 40/16/80/80/80 mM in xylene/H₂O (organic phase/water = 1/1 v/v) at 90 °C. The concentrations were based on the volume of the organic layer.

Figure 7. ¹H NMR (500 MHz, 30 °C) analysis for the suspension radical coupling reaction of Br-PSt-Br with Cp*Ru/FeCp*₂/NH₄PF₆ (see Figure 6 for the reaction condition): [polymer] = 30 mg/mL in CDCl₃.
Conclusions

Efficient radical coupling reactions of end-halogenated polystyrenes were performed by using catalytic amount of Ru main catalysts (Cp*Ru) in conjunction with FeCp*₂ and NH₄PF₆, in which the following two steps are crucial for promoting the reaction: (a) the regeneration of Ru²⁺ active complex with FeCp*₂ (XRu³⁺ + FeCp*₂ → Ru²⁺ + [Fe³⁺Cp*₂]⁺X⁻); (b) scavenging halide anions (X⁻) with NH₄PF₆ ([Fe³⁺Cp*₂]⁺X⁻ + NH₄PF₆ → [Fe³⁺Cp*₂]⁺PF₆⁻ + NH₄X). In the radical coupling reaction of ω-brominated polystyrene (PSt-Br), the author found that the suspension reaction (reaction solvent: xylene/H₂O) gave the coupled PSt in high efficiency (x_c = 0.93) due to the water assisted effective radical generation. In addition, the suspension radical coupling reaction with Cp*Ru/FeCp*₂/NH₄PF₆ was also used for the α,ω-dibrominated PSt (Br~~~R~~~Br), giving the chain extended PSt having initiator moieties (R) periodically ([~~~R~~~]ₘ: m was roughly estimated to m = 5.7 from SEC analysis).

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LIST OF PUBLICATIONS

Part I

Chapter 1
“Ferrocene Cocatalysis in Metal-Catalyzed Living Radical Polymerization: Concerted Redox for Highly Active Catalysis”
Kojiro Fujimura, Makoto Ouchi, and Mitsuo Sawamoto

Chapter 2
“Cationic Cp*-Ruthenium Catalysts for Metal-Catalyzed Living Radical Polymerization: Cocatalyst-Independent Catalysis Tuned by Counter Anions”
Kojiro Fujimura, Makoto Ouchi, Junya Tsujita, and Mitsuo Sawamoto
Macromolecules, submitted.

Chapter 3
“A Thermoresponsive Polymer Supporter for Concerted Catalysis of Ferrocene with A Ruthenium Catalyst in Living Radical Polymerization: High Activity and Efficient Removal of Metal Residues”
Kojiro Fujimura, Makoto Ouchi, and Mitsuo Sawamoto
Polym. Chem. 2015, 6, 7821-7826.
(Selected for the Inside Front Cover)

Part II

Chapter 4
“Ferrocene Cocatalysis for Iron-Catalyzed Living Radical Polymerization: Active, Robust, and Sustainable System under Concerted Catalysis by Two Iron Complexes”
Kojiro Fujimura, Makoto Ouchi, and Mitsuo Sawamoto
(Selected for the Front Cover)
Chapter 5

“Efficient Kharasch Addition Reaction with FeBr$_2$/FeCp*$_2$ Concerted Redox Catalysis as An Active and Versatile Iron-Based Catalysis”
Kojiro Fujimura, Makoto Ouchi, and Mitsuo Sawamoto
to be submitted.

Part III

Chapter 6

“Ferrocene Cocatalysis in Ruthenium-Catalyzed Radical Coupling Chain Extension: Catalytic Reaction through Catalyst Regeneration and Halogen Removal”
Kojiro Fujimura, Makoto Ouchi, and Mitsuo Sawamoto
to be submitted.
Makoto Ouchi, Mitsuo Sawamoto et al.

A thermoresponsive polymer supporter for concerted catalysis of ferrocene with a ruthenium catalyst in living radical polymerization: high activity and efficient removal of metal residues
ACKNOWLEDGMENTS

This thesis presents the study that the author carried out from 2010 to 2016 at the Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University under the direction of Professor Mitsuo Sawamoto and Associate Professor Makoto Ouchi.

First of all, the author would like to express his sincere gratitude to Professor Mitsuo Sawamoto for his continuous guidance and encouragement throughout the course of this work and to Associate Professor Makoto Ouchi and Assistant Professor Takaya Terashima for their helpful and convincing suggestions, and stimulating discussions.

The author acknowledges his appreciation to Professor Michinori Suginome and Professor Yoshiki Chujo for careful reviewing of this thesis and fruitful comment.

The author wishes to express his special thanks to all members of Sawamoto Laboratory for useful suggestion and their friendship during the course of research. Especially, his sincere thanks go to Mr. Junya Tsujita (Asahi Kasei Corporation) for his discussion and kind guidance in experimental technique in the early phase of this research, Dr. Shohei Ida (Assistant Professor, the University of Shiga Prefecture), Dr. Kazuhiro Nakatani (Mitsubishi Chemical Co., Ltd.), Dr. Sang-Ho Lee (Postdoctoral Researcher, the University of California), Dr. Yusuke Hibi (Postdoctoral Researcher, Tokyo Institute of Technology), and Dr. Yuta Koda (Postdoctoral Researcher, Kyoto University) for their stimulating suggestion and encouragement, and Mr. Takahiro Arima (Kuraray, Co., Ltd.), Mr. Yusuke Ogura, Mr. Sho Kitagawa (Sumitomo Chemical Co., Ltd.), Mr. Takanori Sugita (Daicel Corporation), and Mr. Keita Nishizawa for their deep kindness and friendship. The author is also obliged to Mrs. Miro Takayama for her kind assistance during the author’s school life.

The author acknowledges Dr. Takeshi Niitani (Nippon Soda Co., Ltd.) for the measurements of Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES) in Chapter 3.
ACKNOWLEDGMENTS

The author also wishes to thank to Professor Yoshio Okamoto (Nagoya University and Harbin Engineering University), Professor Yoshitsugu Hirokawa (the University of Shiga Prefecture), Professor Masao Tanihara (Nara Institute of Science and Technology), Professor Sadahito Aoshima (Osaka University), Professor Eiji Yashima (Nagoya University), Professor Masami Kamigaito (Nagoya University), and to all “ORION” members of their laboratory, especially to Mr. Ryohei Saitoh, Mr. Tomoya Yoshizaki, Mr. Mineto Uchiyama, and Mr. Takamasa Soejima for their meaningful discussion and kind encouragement.

Importantly, the author is most grateful to Assistant Professor Jeremiah A. Johnson (Massachusetts Institute of Technology, U. S. A.) for his hosting, kind support, and valuable suggestion during the author’s unforgettable and brilliant stay in Boston (April to June 2014). The author also expresses his thanks to Graduate School of Engineering, Kyoto University for the financial support during his stay in Boston (Madume Research encouragement Award).

Furthermore, the author is grateful to the Japan Society for the Promotion of Sciences (JSPS) for JSPS Research Fellowship for Young Scientists from April 2013 to March 2016.

Finally, the author wishes to express his deepest appreciation to his parents, Masahiko Fujimura and Keiko Fujimura, his brother Soichiro Fujimura, his brother’s wife Kana Fujimura, and his family members for their constant care and affectionate encouragement which are indispensable in his research life.

March, 2016

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