

**“Concerted Redox” Catalysis  
in Living Radical Polymerization**

**Kojiro Fujimura**

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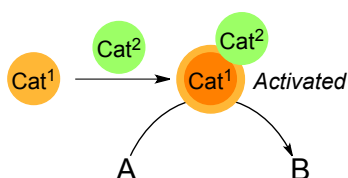
# GENERAL INTRODUCTION

## Background

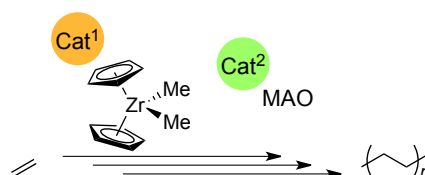
### Bimetallic Cooperative Catalysis

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.<sup>1-3</sup> 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.<sup>4,5</sup> Herein three types of "bimetallic cooperative catalysis" are explained along with the actual examples (Figure 1).

#### (a) Catalyst Activation (Cocatalyst)



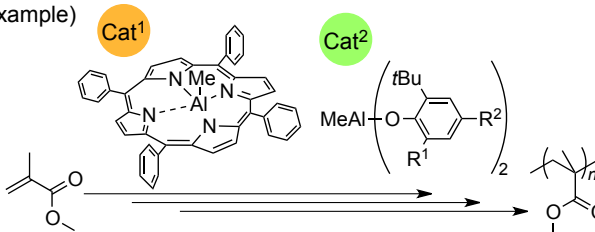
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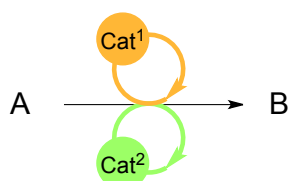
#### (b) Substrate Activations



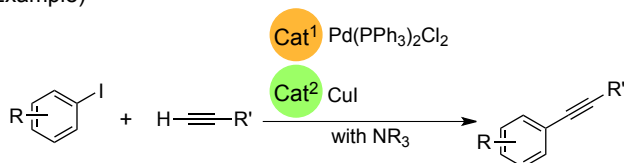
Example)



#### (c) Concerted Catalysis



Example)



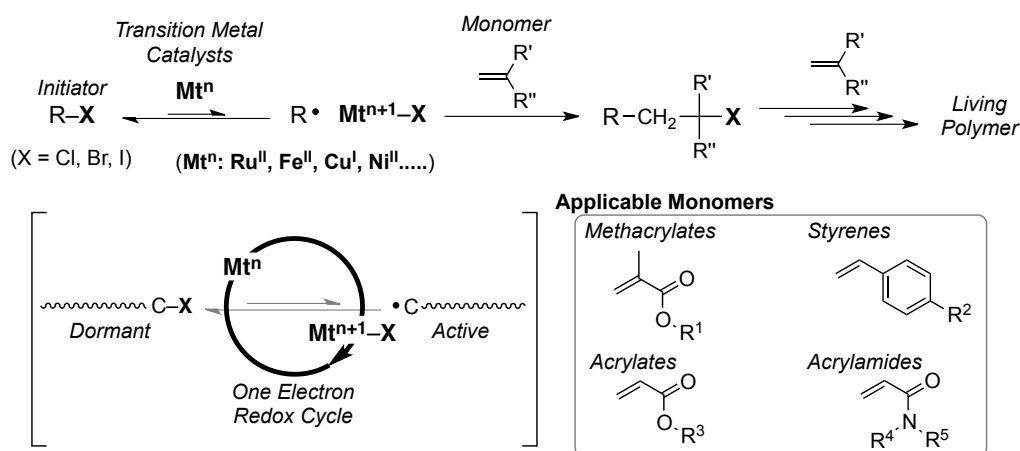
**Figure 1.** Bimetallic cooperative catalysis: concepts and examples.

- (a) **Activation of Main Catalyst.** In some reactions, a main catalyst ( $\text{Cat}^1$  in Figure 1a) is activated by another components (cocatalyst;  $\text{Cat}^2$ ) to catalyze the reaction. A representative example is metal-catalyzed olefin polymerization or coordination polymerization with a group 4 metal catalysts (precatalyst;  $\text{Cat}^1$ : Ti or Zr) in conjunction with methylaluminoxane  $[-\text{Al}(\text{Me})-\text{O}-]_n$  (MAO;  $\text{Cat}^2$ ).<sup>6,7</sup> MAO reacts with  $\text{Cat}^1$  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 ( $\text{Cat}^1$  in Figure 1b) catalyzes the reaction, whereas another ( $\text{Cat}^2$ ) activates the substrate to promote the reaction. Examples include the combination of an enolate-aluminium porphyrin ( $\text{Cat}^1$ ) with a bulky organoaluminium ( $\text{Cat}^2$ ) for high-speed living anionic polymerization of methyl methacrylate (MMA).<sup>8-10</sup> In this polymerization, the monomer is activated through coordination of the bulky organoaluminium ( $\text{Cat}^2$ ) onto the carbonyl group to enhance the nucleophilic attack by  $\text{Cat}^1$ , 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:<sup>11,12</sup> 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 alkynyl-Pd complex, followed by the reductive elimination on Pd to give the product. Actually, the reaction could proceed with a Pd complex alone<sup>13,14</sup> 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.<sup>15-27</sup> As illustrated in Figure 2, transition metal complexes catalyze the reversible activation of the carbon-halogen bond in an initiator ( $R-X$ ;  $X = \text{halogen}$ ) or the “dormant” polymer end ( $\sim\sim\sim C-X$ ;  $\sim\sim\sim = \text{polymer chain}$ ) through the one electron redox reaction ( $Mt^n \leftrightarrow XMt^{n+1}$ ;  $Mt = \text{metal}$ ) to give “active” radical species ( $\sim\sim\sim C\cdot$ ;  $C\cdot = \text{carbon centered radical}$ ) 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).

Transition metals for Mt-LRP catalysts now cover a wide range in the periodic table of the elements, e.g., Ru,<sup>28</sup> Fe,<sup>29,30</sup> Cu,<sup>31-33</sup> Ni,<sup>34,35</sup> Mo,<sup>36</sup> Mn,<sup>37,38</sup> Os,<sup>29</sup> Re,<sup>40,41</sup> Co,<sup>42</sup> Rh,<sup>43,44</sup> Pd,<sup>45</sup> and Ir;<sup>46</sup> the monomers amenable for Mt-LRP include virtually all conjugated monomers for radical polymerizations such as methacrylates, styrenes, acrylates, and acrylamides.

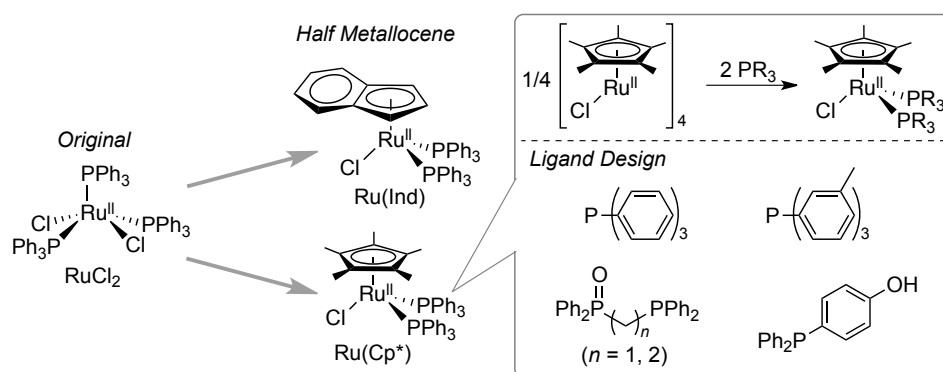
The use of transition metal catalysts, on the other hand, has some specific issues in terms of industrial applications: (1) metal contamination of obtained polymers; (2) rising cost from precious metals; (3) deactivation of catalyst by polar groups. Especially for (1) and (2), a critical solution is 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  $\text{RuCl}_2(\text{PPh}_3)_3$ ,<sup>28,47</sup> various effective ruthenium catalysts have been developed mainly based on the ligand designs.<sup>18</sup> Among them, ruthenium half-metallocenes, such as pentamethyl cyclopentadienyl ( $\text{Cp}^*$ )-ligated ruthenium complex  $[\text{Ru}(\text{Cp}^*)]^{48}$  and indenyl (Ind)-ligated ruthenium complex  $[\text{Ru}(\text{Ind})]$ ,<sup>49</sup> are of a quite high catalytic activity (Figure 3), partly because of the lower redox potential resulting from the strong electron donation by  $\text{Cp}^*$  or Ind ligands, meaning high activity for one electron redox reactions.<sup>50</sup> 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 ( $\sim\sim\text{C}-\text{X}$ ) to generate a growing radical. Therefore, the structure of phosphine ligands strongly affects the catalytic activity.

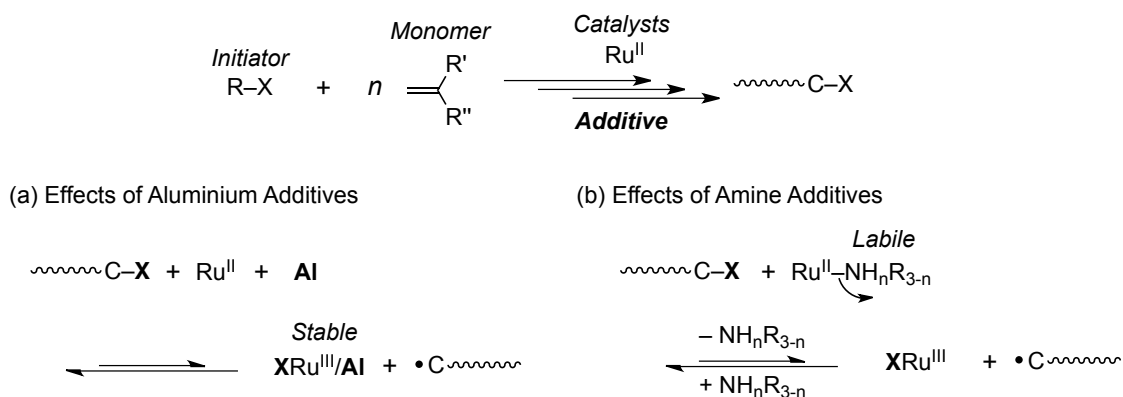
Actually, the use of a tetrameric  $\text{Cp}^*$ -ligated Ru complex  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$  as the catalyst precursor that accepts ligands ( $\text{PR}_3$ ) by just mixing to give  $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPR}_3)_n$  ( $n = 1, 2$ )<sup>51,52</sup> dramatically accelerated the studies of combined ligands that are suitable for  $\text{Cp}^*$ -ligated Ru allowing highly active catalysis.<sup>53</sup> As a result, it turned out that the moderate steric bulkiness of phosphine ligands (e.g. the tri-*meta*-tolylphosphine  $[\text{P}(m\text{-Tol})_3]$ ) promote the catalysis due to the smooth ligand dissociation.<sup>53</sup> As another example, it was reported that the asymmetric chelate ligands, bisphosphine monoxides (BPMOs;  $\text{Ph}_2\text{P}-(\text{CH}_2)_n-\text{P}(\text{O})\text{Ph}_2$ ;  $n = 1, 2$ ) 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.<sup>54</sup> 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.<sup>55</sup>

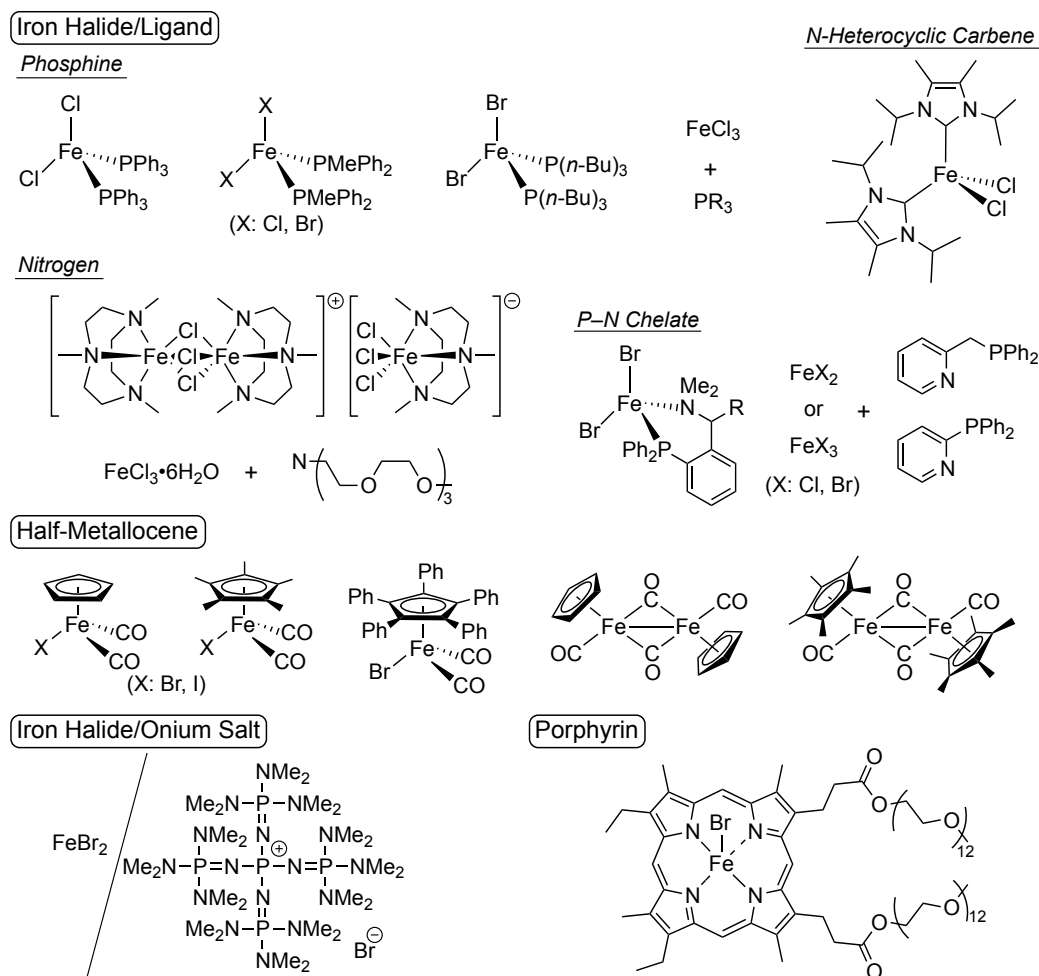
Besides ligand design, the design of additives (cocatalysts) is also important to promote the catalysis. In ruthenium-catalyzed LRP, metal alkoxides such as  $\text{Al}(\text{O}i\text{-Pr})_3$  and  $\text{Ti}(\text{O}i\text{-Pr})_4$ ,<sup>56</sup> and alkyl amines<sup>53,57-59</sup> are effective additives. The early studies suggest that  $\text{Al}(\text{O}i\text{-Pr})_3$  interacts with the ruthenium complex to stabilize the higher oxidation state  $\text{Ru}^{\text{III}}$ , and thus to facilitate radical generation from a dormant species ( $\sim\text{C-X}$ ; Scheme 1a). Alkyl amines were also coordinate to Ru complexes to form active forms  $[\text{Ru}^{\text{II}}(18\text{e})\text{-NH}_n\text{R}_{3-n}]$ ; 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 ( $\text{Ru}^{\text{II}}(18\text{e})\text{-NH}_n\text{R}_{3-n} \rightarrow \text{Ru}^{\text{II}}(16\text{e}) + \text{NH}_n\text{R}_{3-n}$ ) due to the labile coordination of amines, and thereby promote the catalytic cycles (Scheme 1b).



**Figure 3.** Catalyst development based on ligand designs in ruthenium-catalyzed living radical polymerization.



**Scheme 1.** Effects of Aluminium (a) and Amine Additives (b) in Ruthenium-Catalyzed Living Radical Polymerizations



**Figure 4.** Representative iron-based catalysts for living radical polymerization.

**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.<sup>60,61</sup> Since the first report for Mt-LRP with  $\text{FeCl}_2(\text{PPh}_3)_2$ ,<sup>29</sup> various iron-based catalysts have been reported (Figure 4).<sup>62</sup>

For example, iron halides ( $\text{FeX}_n$ ; X = Cl, Br,  $n = 2, 3$ ) in conjunction with various organic ligands, including phosphines,<sup>29,30,63-67</sup> amines,<sup>30,68-74</sup> phosphine-amine chelates,<sup>75-77</sup> and *N*-heterocyclic carbenes (NHC),<sup>78,79</sup> 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 *in situ* by just mixing a precatalyst and ligand. In addition, onium salts such as *n*-Bu<sub>4</sub>NBr can also be used for iron halide ( $\text{FeBr}_2$ )-catalyzed polymerization, in which an *in situ* formed anionic complex  $[\text{FeBr}_3^- \text{ } n\text{-Bu}_4\text{N}^+]$  is considered as the truly active catalyst.<sup>80,81</sup> Interestingly, bulky and highly delocalized salts,

phosphazanium 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)).<sup>82</sup> The tolerance to the functional group (PEG) is probably due to the bulkiness of the counter cation (PZN<sup>+</sup>) which may protect the iron complex from the nucleophilic functional groups.

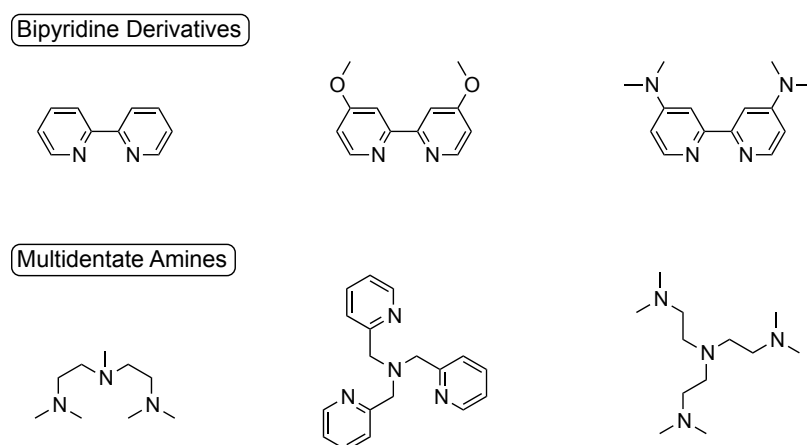
On the other hands, iron half-metallocenes are also studied. These complexes are quite active in living radical polymerizations of styrenes, acrylates, and acrylamides.<sup>83-85</sup> In particular, Fe<sub>2</sub>Cp<sub>2</sub>(CO)<sub>4</sub> is applicable for not only conjugated monomers but vinyl acetate, although the polymerization was retarded at around 50% monomer conversion.<sup>86</sup> These complexes can also be applied for the controlled polymerization of methacrylates in conjunction with phosphine ligands.<sup>87-89</sup>

Recently, it was reported that iron oxides (FeO and Fe<sub>3</sub>O<sub>4</sub>) can be used as the effective catalysts in conjunction with phosphines or onium salts for MMA and styrene.<sup>90,91</sup> 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.<sup>92-94</sup> 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.<sup>64,74,82,94</sup> 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.<sup>31,95</sup> 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<sup>96,97</sup> revealed that multidentate amines, such as *N,N,N',N'',N''*-pentamethyldiethylenetriamine

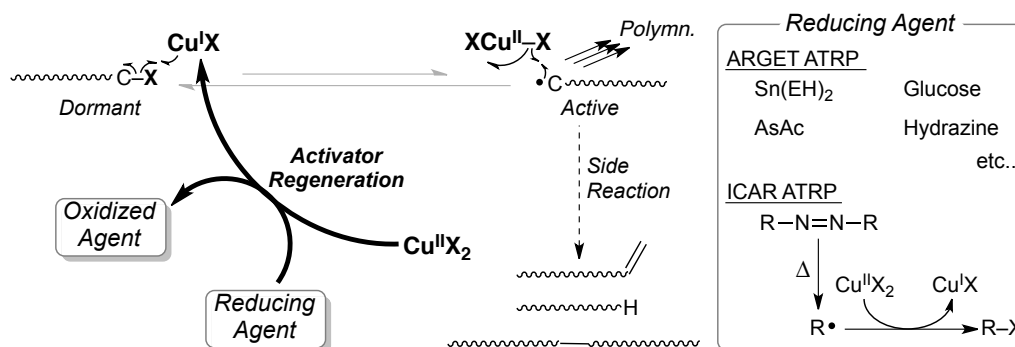
(PMDETA),<sup>98</sup> tris(2-pyridylmethyl)amine (TPMA),<sup>99</sup> and tris-[2-(dimethylamino)ethyl]amine (Me<sub>6</sub>TREN),<sup>100</sup> gave high activity to the catalyst (Figure 5). In particular, Me<sub>6</sub>TREN, a tetradentate nitrogen-based ligand, gives highly active catalyst in conjunction 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<sub>2</sub>N-bipy), led to much faster and better controlled polymerizations of MMA and MA.<sup>101</sup>



**Figure 5.** Representative nitrogen-based ligands for copper-catalyzed living radical polymerization.

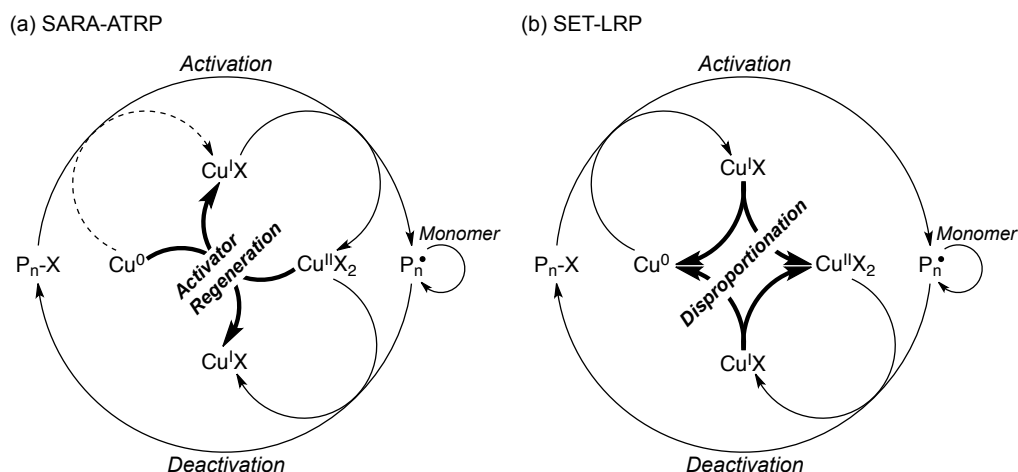
Toward more effective catalysis, “activator regenerated by electron transfer (ARGET)” systems have been developed, in which an oxidized copper halide ( $\text{Cu}^{\text{II}}\text{X}_2$ ) resulting from radical termination reactions (bimolecular radical coupling or disproportionation) is reduced to regenerate a less oxidized form ( $\text{Cu}^{\text{I}}\text{X}$ ) by an excessively added reducing agent, such as tin(II) 2-ethylhexanoate ( $\text{Sn}(\text{EH})_2$ ), glucose,<sup>102,103</sup> ascorbic acid (AsAc),<sup>104</sup> phenol,<sup>105</sup> hydrazine,<sup>106</sup> and nitrogen-containing monomers (Figure 6).<sup>107</sup> 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).<sup>106</sup> Surprisingly, these systems allowed a well-controlled polymerization with only 5-50 ppm of a copper halide.





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

Zero-valent metals such as  $\text{Cu}^0$ ,  $\text{Fe}^0$ ,  $\text{Mg}^0$ ,  $\text{Zn}^0$ ,<sup>108</sup> or  $\text{Ag}^0$  can also be used as reducing agents.<sup>109,110</sup> 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  $\text{Cu}^0$  is used as the reducing agent, as a result of the activator regeneration step ( $\text{Cu}^{\text{II}}\text{X}_2 \rightarrow \text{Cu}^{\text{I}}\text{X}$ ),  $\text{Cu}^0$  is also transformed to  $\text{Cu}^{\text{I}}\text{X}$ , meaning the efficient generation of the activator (the bold arrows in Scheme 2-a).



**Scheme 2.** Proposed Mechanisms for Living Radical Polymerizations in the Presence of Zerovalent Copper ( $\text{Cu}^0$ ): (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  $\text{Cu}^{\text{I}}\text{X}$  promptly disproportionates to  $\text{Cu}^0$  and  $\text{Cu}^{\text{II}}\text{X}_2$  (the bold arrows in Scheme 2-b).<sup>26,111</sup> This continuous generation of both  $\text{Cu}^0$  (activator) and  $\text{Cu}^{\text{II}}\text{X}_2$  (deactivator) allows the highly fast and well-controlled polymerizations. Particularly when the polymerization is conducted in the presence of multidentate amine ligands such as  $\text{Me}_6\text{TREN}$  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  $0^\circ\text{C}$  with quite high controllability so as to allow the synthesis of multi-block copolymers.<sup>112,113</sup>

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.<sup>114,121</sup>

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.

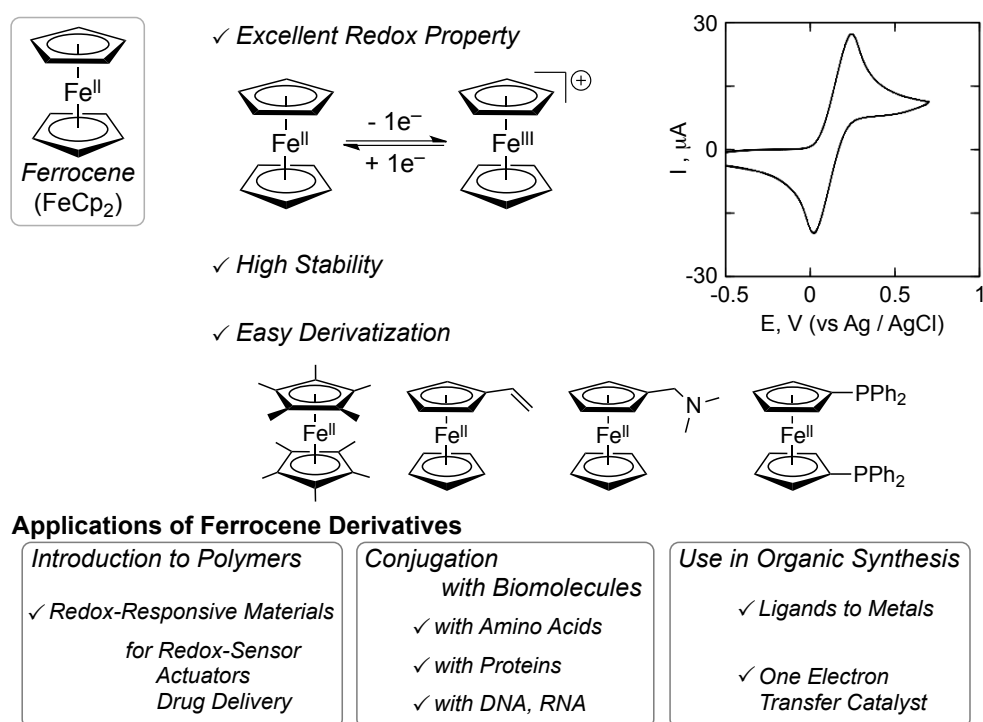
As will be discussed later, in this thesis, the concept of "bimetallic cooperative catalysis" will be applied to Mt-LRP for achieving highly active and sustainable catalysis.

## 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 ( $\text{FeCp}_2$ ; Fc) is a coordinatively saturated (18-electron) organometallic compound where two cyclopentadienyl (Cp) ligands sandwich an iron ( $\text{Fe}^{\text{II}}$ ) atom. The history of ferrocene is old,<sup>122</sup> and the discovery dates back until 1951,<sup>123</sup> followed by the presumption of the sandwich structure in 1952,<sup>124,125</sup> and the determination of the crystal structure in 1956.<sup>126</sup>

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

- **Excellent Redox Property:** The one electron redox behavior ( $\text{Fe}^{\text{II}} \leftrightarrow \text{Fe}^{\text{III}}$ ) of ferrocene is active and stable enough to be used as an internal standard for cyclic voltammetry (CV) analysis.<sup>127,128</sup>
- **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.

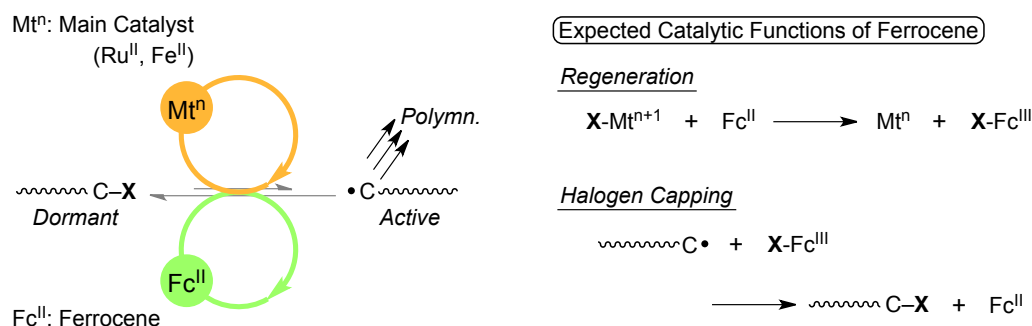


**Figure 7.** Features and applications of ferrocene and its derivatives.

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.<sup>129-131</sup> In addition, ferrocene derivatives can also be applied to the conjugations with biomolecules, including amino acids, proteins, DNA, and RNA.<sup>132,133</sup>

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.<sup>134</sup> In particular, ferrocene-based ligands are important in asymmetric synthesis, because easy derivatization of ferrocene enables the easy access to asymmetric ferrocene-based ligands.<sup>135,136</sup> 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.<sup>137,138</sup>

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 ( $\sim\sim\sim\text{C-X} \rightarrow \sim\sim\sim\text{C}\cdot$ ) 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.

- **Regeneration:** Ferrocene ( $\text{Fc}^{\text{II}}$ ) reduces the higher oxidation state of the main catalyst ( $\text{X-Mt}^{\text{n}+1}$  in Figure 8) to regenerate the activator species ( $\text{Mt}^{\text{n}}$ ) as well as ARGET ATRP system ( $\text{X-Mt}^{\text{n}+1} + \text{Fc}^{\text{II}} \rightarrow \text{Mt}^{\text{n}} + \text{X-Fc}^{\text{III}}$ ).
- **Halogen Capping:** The trivalent ferrocene (ferrocenium salt:  $\text{X-Fc}^{\text{III}}$ ) is known to act as the one electron oxidant in organic synthesis.<sup>137</sup> Therefore,  $\text{X-Fc}^{\text{III}}$  is expected to regenerate a dormant C-X terminal ( $\sim\sim\sim\text{C}\cdot + \text{X-Fc}^{\text{III}} \rightarrow \sim\sim\sim\text{C-X} + \text{Fc}^{\text{II}}$ ).

If ferrocene really shows these catalytic functions, the one electron redox catalysis, driven only by one metal catalyst ( $\text{Mt}^{\text{n}}$ ) in conventional systems, can be driven by two metal catalysts ( $\text{Mt}^{\text{n}} + \text{Fc}^{\text{II}}$ ) 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.

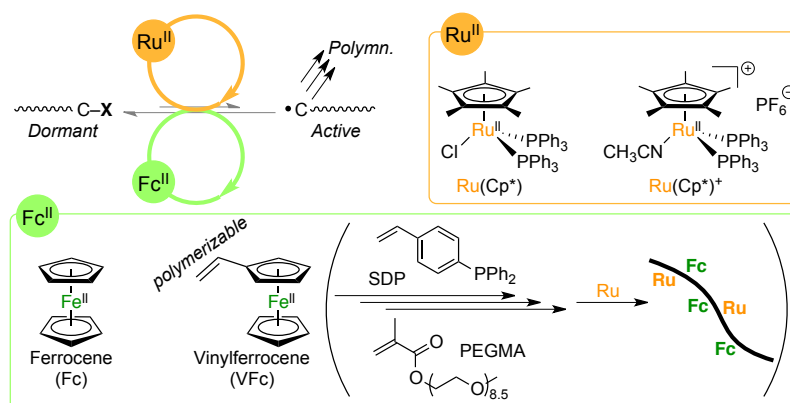
## **(1) Ruthenium/Ferrocene Concerted Redox Catalysis**

In the first segment, the author aimed to examine effects of ferrocene ( $\text{FeCp}_2$ ) in conjunction with ruthenium complexes as the main catalysts for living radical polymerization (Figure 9).

Firstly, the author combined  $\text{FeCp}_2$  as the cocatalyst for a ( $\text{Cp}^*$ )-ligated ruthenium complex  $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2: \text{Ru}(\text{Cp}^*)]$  and its cationic counterpart  $[\text{Ru}(\text{Cp}^*)^+(\text{CH}_3\text{CN})(\text{PPh}_3)_2\text{PF}_6^-: \text{Ru}(\text{Cp}^*)^+]$  as the main catalyst in living radical polymerization of methyl methacrylate (MMA). The cocatalytic effects of  $\text{FeCp}_2$  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  $\text{FeCp}_2$ , the regeneration of the main catalyst ( $\text{Ru}^{\text{II}}$ ) with  $\text{FeCp}_2$  and the halogen capping reaction with the resultant ferrocenium ion ( $[\text{Fe}^{\text{III}}\text{Cp}_2]^+\text{Cl}^-: \text{Cl-Fc}^{\text{III}}$ ).

to the active radical species ( $\sim\sim\sim\text{C}\cdot \rightarrow \sim\sim\sim\text{C}-\text{Cl}$ ).

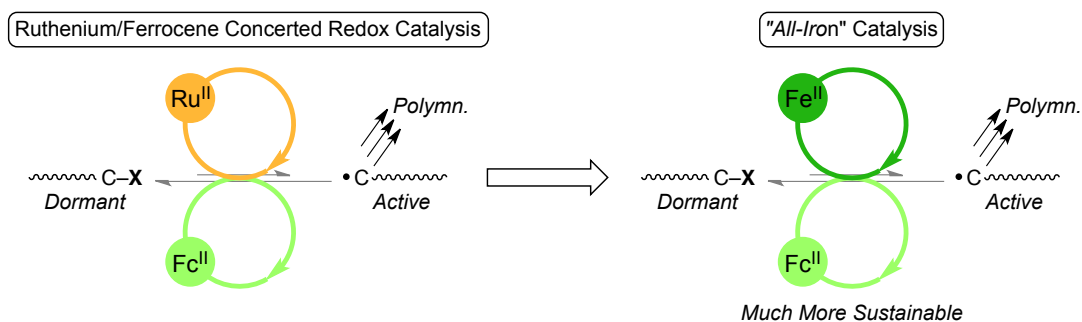
In terms of the industrial applications, one serious problem for the ruthenium/ferrocene concerted redox catalysis is the difficulty in metal removal. Therefore, the author next developed the thermoresponsive polymer-supported catalyst consisting of a ruthenium (Ru) main catalyst and a ferrocene (Fc) 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),<sup>139,140</sup> 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<sub>2</sub> with ammonium salt (*n*-Bu<sub>4</sub>NBr) was used as the main catalyst,<sup>80,81</sup> and the author examined the catalytic activity and the polymerization controllability from the polymerization of MMA. Next, ferrocene was used for a FeBr<sub>3</sub>-catalyzed polymerization, in which the FeBr<sub>3</sub> was firstly reduced by ferrocene to give FeBr<sub>2</sub>, the real activator species. The FeBr<sub>3</sub>/ferrocene catalyst system would be more ideal from a practical viewpoint, because the both complexes are air-stable and easily handled.

In addition, FeBr<sub>2</sub>/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.<sup>64</sup> 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.<sup>141,142</sup> As well as for living radical polymerization, the conventional catalyst systems for Kharasch addition were mainly made of ruthenium<sup>143,144</sup> and copper-based catalysts,<sup>145,146</sup> and there are little examples of active iron-based catalysis.<sup>147,148</sup> Therefore, all-iron catalysis, developed for living radical polymerizations, was applied to Kharasch addition reaction.

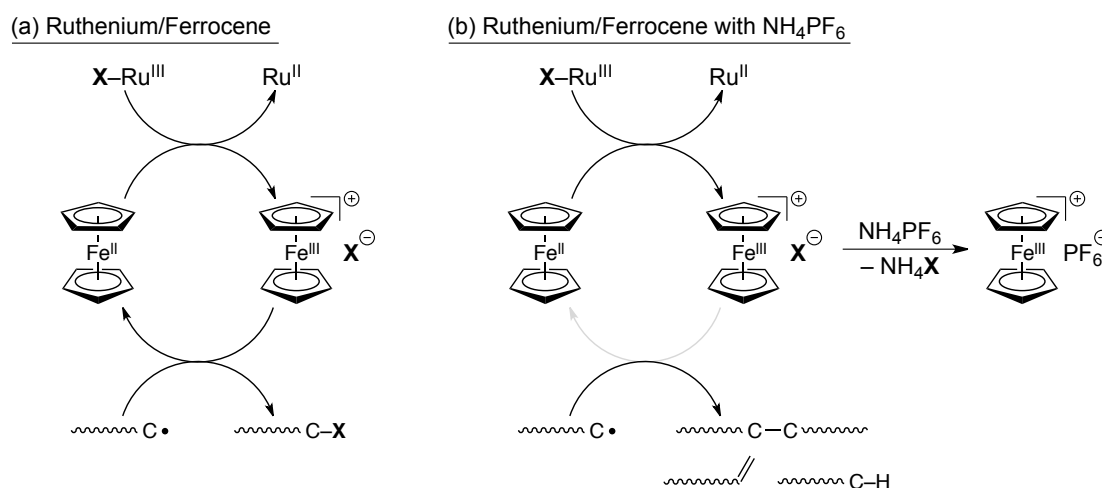
### **(3) From “Living Radical Polymerization” to “Radical Coupling Chain Extension” via Concerted Redox**

This segment dealt with the radical coupling reaction of ω-halogenated polystyrenes (PSt-X), prepared by Mt-LRP,<sup>149,150</sup> by ruthenium/ferrocene concerted redox catalysis in conjunction with NH<sub>4</sub>PF<sub>6</sub> 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<sup>II</sup>) and the halogen capping reaction with the resultant ferrocenium halide ([Fe<sup>III</sup>Cp<sub>2</sub>]<sup>+</sup>Cl<sup>-</sup>) to the active radical species (~~~C• → ~~~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<sub>4</sub>PF<sub>6</sub> is added as an additive, ferrocenium halide transforms into ferrocenium hexafluorophosphate ([Fe<sup>III</sup>Cp<sub>2</sub>]<sup>+</sup>PF<sub>6</sub><sup>-</sup>) through an anion exchange reaction ([Fe<sup>III</sup>Cp<sub>2</sub>]<sup>+</sup>Cl<sup>-</sup> + NH<sub>4</sub>PF<sub>6</sub> → [Fe<sup>III</sup>Cp<sub>2</sub>]<sup>+</sup>PF<sub>6</sub><sup>-</sup> + NH<sub>4</sub>Cl). Actually, [Fe<sup>III</sup>Cp<sub>2</sub>]<sup>+</sup>PF<sub>6</sub><sup>-</sup> is known as a highly stable complex salt, and not be able to act as the halogen capping agent.

Therefore, when  $\text{NH}_4\text{PF}_6$  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  $\text{NH}_4\text{PF}_6$ .

From these backgrounds, the author decided to apply this interesting catalyst system (ruthenium/ferrocene/ $\text{NH}_4\text{PF}_6$ ) for the quantitative radical coupling reaction of  $\omega$ -brominated polystyrenes prepared by Mt-LRP (R-PSt-Br; prepared with R-Br as an initiator), to give  $\alpha,\omega$ -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.

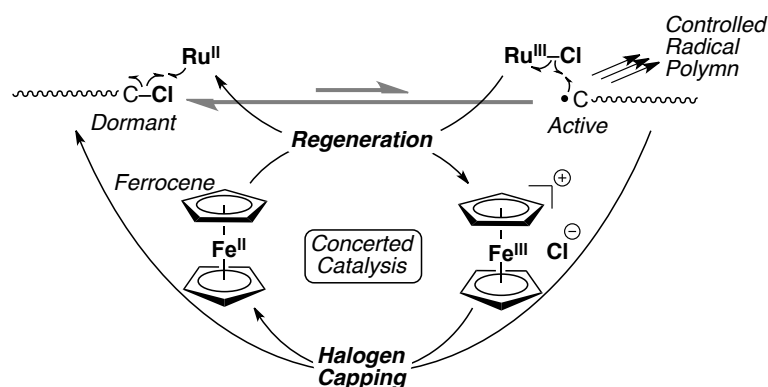


**Figure 11.** Changes in catalytic function of ferrocene triggered by the addition of  $\text{NH}_4\text{PF}_6$ : (a) catalytic functions of ferrocene in ruthenium/ferrocene concerted redox catalysis; (b) catalytic functions of ferrocene in ruthenium/ferrocene catalyst system in conjunction with  $\text{NH}_4\text{PF}_6$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



## 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/ $\text{NH}_4\text{PF}_6$  catalyst system for quantitative radical coupling reactions of  $\omega$ -halogenated polystyrenes as the extension of the ferrocene-assisted concerted redox catalysis toward the construction of unique polymer architectures.

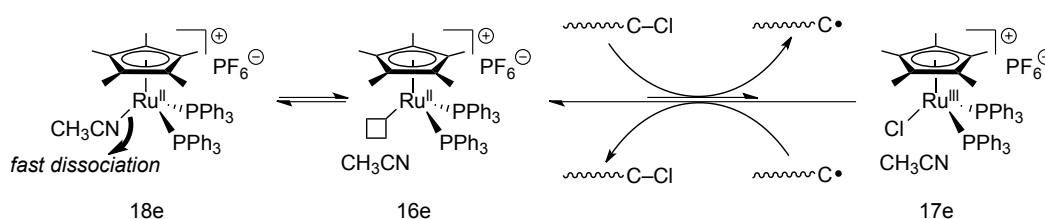


**Scheme 3.** Ruthenium/Ferrocene Concerted Redox Catalysis for Living Radical Polymerization

In Part 1, **Chapter 1** examines the effects of ferrocene ( $\text{FeCp}_2$ ) as a cocatalyst for ruthenium (Ru)-catalyzed living radical polymerization of MMA. When  $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$  was used as a main catalyst ( $[\text{Ru}]_0/[\text{initiator}]_0 = 1/10$ ), the polymerization proceeded to the higher monomer conversion ( $\sim 90\%$ ) by the addition of  $\text{FeCp}_2$  ( $[\text{Ru}]_0/[\text{FeCp}_2]_0 = 1/40$ ), while the polymerization retarded in the middle stage without  $\text{FeCp}_2$ . In addition, when the cationic  $\text{Ru}(\text{Cp}^*)$  complex  $[\text{Ru}(\text{Cp}^*)^+(\text{CH}_3\text{CN})(\text{PPh}_3)_2\text{PF}_6^-; \text{Ru}(\text{Cp}^*)^+]$  was used as the main catalyst in conjunction with  $\text{FeCp}_2$ , the polymerization was accelerated without any loss of controllability. The high catalytic activity of  $\text{Ru}(\text{Cp}^*)^+/\text{FeCp}_2$  catalyst system even allowed the synthesis of high molecular weight PMMA ( $M_n \sim 10^5$ ;  $M_w/M_n \sim 1.3$ ) with only 50 ppm of the Ru main catalyst. These positive effects of the addition of  $\text{FeCp}_2$  was turned out to come from the following two reactions by some model reactions (Scheme

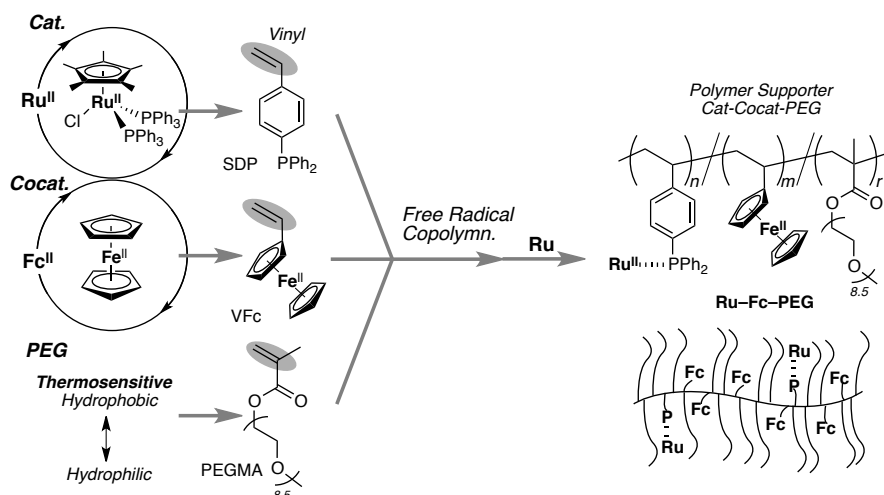
3): regeneration of  $\text{Ru}^{\text{II}}$  through a reduction of  $\text{XRu}^{\text{III}}$  ( $\text{Fe}^{\text{II}}\text{Cp}_2 + \text{XRu}^{\text{III}} \rightarrow \text{Fe}^{\text{III}}\text{Cp}_2^+\text{X}^- + \text{Ru}^{\text{II}}$ ; X: halogen); halogen-capping reaction, or regeneration of dormant species  $\sim\sim\sim\text{C}-\text{X}$ , by the resultant trivalent ferrocenium cation  $\text{Fe}^{\text{III}}\text{Cp}_2^+$  ( $\sim\sim\sim\text{C}\cdot + \text{Fe}^{\text{III}}\text{Cp}_2^+\text{X}^- \rightarrow \sim\sim\sim\text{C}-\text{X} + \text{Fe}^{\text{II}}\text{Cp}_2$ ).

In **Chapter 2**, the author presents the novel ruthenium catalyst  $\text{Ru}(\text{Cp}^*)^+$ . 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  $\text{Ru}(\text{Cp}^*)$  complex  $[\text{Ru}(\text{Cp}^*)^+; \text{Ru}(\text{Cp}^*)^+(\text{CH}_3\text{CN})(\text{PPh}_3)_2\text{PF}_6^-]$ . In living radical polymerizations of MMA with  $\text{Ru}(\text{Cp}^*)^+$  and the neutral counterpart  $\text{Ru}(\text{Cp}^*)$ , the author found that  $\text{Ru}(\text{Cp}^*)^+$  led to the faster polymerization rather than  $\text{Ru}(\text{Cp}^*)$  without any serious loss of controllability. In  $\text{Ru}(\text{Cp}^*)^+$ -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  $\text{CH}_3\text{CN}$  ligand (Scheme 4).



**Scheme 4.** Smooth Activation of a Dormant C-X Bond with  $\text{Ru}(\text{Cp}^*)^+$

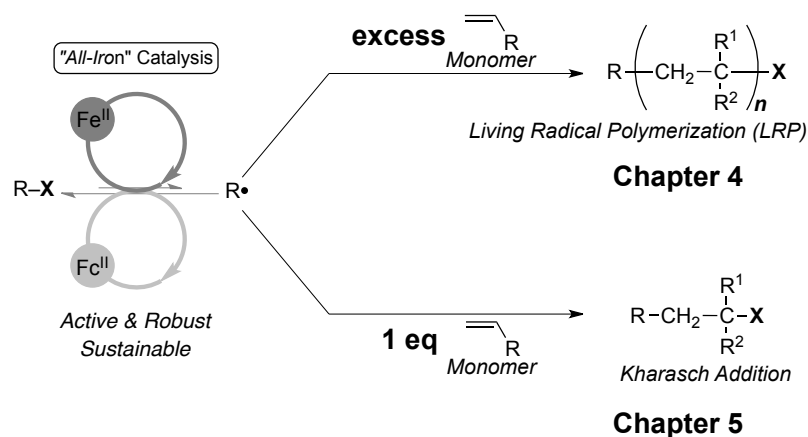
**Chapter 3** deals with a thermoresponsive polymer-supported catalyst consisting of a ruthenium main catalyst and a ferrocene cocatalyst was designed in order to realize both high activity and efficient removal of metal residues. The supported catalyst was easily prepared via random free radical copolymerization of vinylferrocene (VFc), phosphine-pendant monomer (SDP), and PEG-pendant methacrylate (PEGMA), followed by mixing with a Ru precursor ( $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$ ; 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  $\sim 99\%$ ).



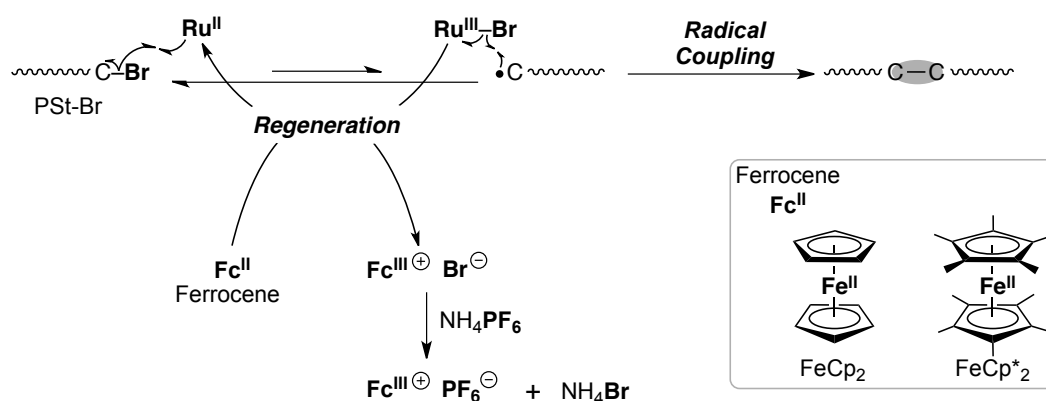
**Figure 12.** Design of a thermoresponsive polymer-supported catalyst consisting of a ruthenium main catalyst and a ferrocene cocatalyst for both high activity and efficient removal of metal residues.

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  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  as a main catalyst, the author found that decamethylferrocene ( $\text{FeCp}^*_2$ ), having lower redox potential than  $\text{FeCp}_2$ , successfully promoted the polymerization to give well-controlled PMMA ( $M_n \sim 10,000$ ;  $M_w/M_n \sim 1.1$ ), while  $\text{FeCp}_2$  showed no effects on the catalysis. Importantly, the “all-iron” catalysis allowed superior control of the polymerization to those without  $\text{FeCp}^*_2$  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 ( $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}/\text{FeCp}^*_2$ ) was applied to Kharasch addition reactions (Figure 13). In Kharasch addition reaction of bromotrichloromethane ( $\text{CCl}_3\text{Br}$ ) to MMA, “all-iron” catalysis was inferior to the reaction without  $\text{FeCp}^*_2$  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  $\text{CCl}_3\text{Br}$  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



**Figure 13.** Design of "all-iron" catalysis for living radical polymerization and Kharasch addition reaction.



**Scheme 5.** Radical Coupling Reaction of  $\omega$ -Brominated Polystyrenes (PSt-Br) with Ruthenium/Ferrocene/ $\text{NH}_4\text{PF}_6$  Catalyst System

olefin) of iron catalysts ( $\text{FeBr}_2$  and  $\text{FeCp}^*_2$ ), giving the mono adduct in high yield (> 70%).

In Part 3, **Chapter 6** presents the novel catalysis, composed of the ruthenium ( $\text{Ru}^{\text{II}}$ )/ferrocene ( $\text{Fc}^{\text{II}}$ ) concerted redox catalysis in conjunction with  $\text{NH}_4\text{PF}_6$  as an additive, for quantitative radical coupling reactions of  $\omega$ -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  $\text{Ru}^{\text{II}}$  active complex with  $\text{Fc}^{\text{II}}$  ( $\text{XRu}^{\text{III}} + \text{Fc}^{\text{II}} \rightarrow \text{Ru}^{\text{II}} + [\text{Fc}^{\text{III}}]^+\text{X}^-$ ); (b) scavenging halide anions ( $\text{X}^-$ ) with  $\text{NH}_4\text{PF}_6$  ( $[\text{Fc}^{\text{III}}]^+\text{X}^- + \text{NH}_4\text{PF}_6 \rightarrow [\text{Fc}^{\text{III}}]^+\text{PF}_6^- + \text{NH}_4\text{X}$ ). As a result of the radical coupling reaction of the  $\omega$ -brominated polystyrenes (PSt-Br;  $M_n \sim 2000$ ), the author found that  $\text{Ru}(\text{Cp}^*)/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  catalyst system gave the coupled PSt in high efficiency ( $\sim 93\%$ ) under the suspension media (reaction solvent: xylene/ $\text{H}_2\text{O}$ ), in which water associated with ruthenium catalyst to promote the

activation of a dormant C-X bond (radical generation). In addition, high solubility of  $\text{NH}_4\text{Br}$  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 ( $\text{Br}\sim\sim\sim\text{R}\sim\sim\sim\text{Br}$ ), giving the chain extended PSt ( $[\sim\sim\sim\text{R}\sim\sim\sim]_m$ ;  $m$  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  $\text{NH}_4\text{PF}_6$  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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## **PART I**

### **Ruthenium/Ferrocene Concerted Redox Catalysis**

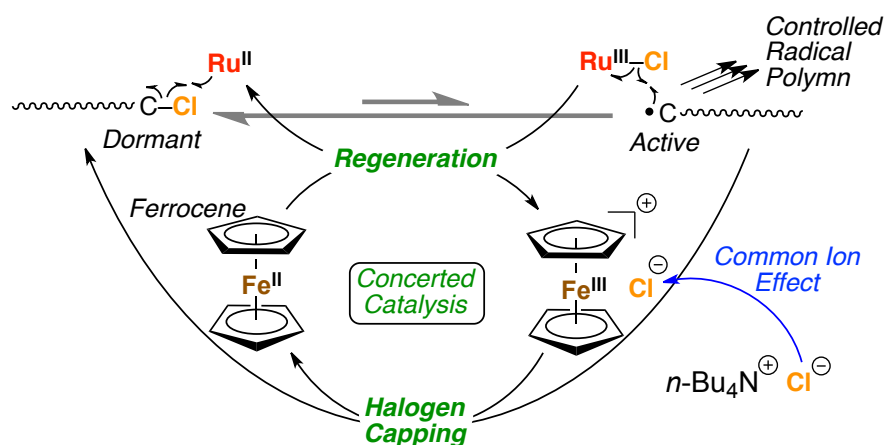


## Chapter 1

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

### Abstract

Ferrocene ( $\text{FeCp}_2$ ), despite its high stability, was found, for the first time, to co-catalyze living radical polymerization in concert with a ruthenium main catalyst ( $\text{Ru}^{\text{II}}$ ) that is directly responsible for generating growing radicals.  $\text{FeCp}_2$  turned out to promote the following key reactions: regeneration of  $\text{Ru}^{\text{II}}$  through a reduction of  $\text{XRu}^{\text{III}}$  ( $\text{Fe}^{\text{II}}\text{Cp}_2 + \text{XRu}^{\text{III}} \rightarrow \text{Fe}^{\text{III}}\text{Cp}_2^+\text{X}^- + \text{Ru}^{\text{II}}$ ; X: halogen); halogen-capping reaction, or regeneration of dormant species  $\sim\text{C-X}$ , by the resultant trivalent ferrocenium cation  $\text{Fe}^{\text{III}}\text{Cp}_2^+$  ( $\sim\text{C}\cdot + \text{Fe}^{\text{III}}\text{Cp}_2^+\text{X}^- \rightarrow \sim\text{C-X} + \text{Fe}^{\text{II}}\text{Cp}_2$ ). The cocatalysis was further improved by the addition of  $n\text{-Bu}_4\text{NCl}$  to allow a dramatic decrease in the initial  $\text{Ru}^{\text{II}}$  concentration without any loss of the high controllability. For example, in conjunction with  $\text{FeCp}_2/n\text{-Bu}_4\text{NCl}$ , only 50 ppm (for monomer) of  $\text{Ru}^{\text{II}}$  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.



## Introduction

Metal-catalyzed living radical polymerization (LRP) is one of the useful tools to precisely prepare well-defined polymers.<sup>1-8</sup> The catalysis involves a reversible activation of a dormant carbon–halogen bond ( $\sim\sim\sim\text{C-X}$ ;  $\sim\sim\sim$ : polymer chain; X: halogen) to give growing radical species, based on a one-electron redox of the catalyst ( $\text{Mt}^n \leftrightarrow \text{XMt}^{n+1}$ ; 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.

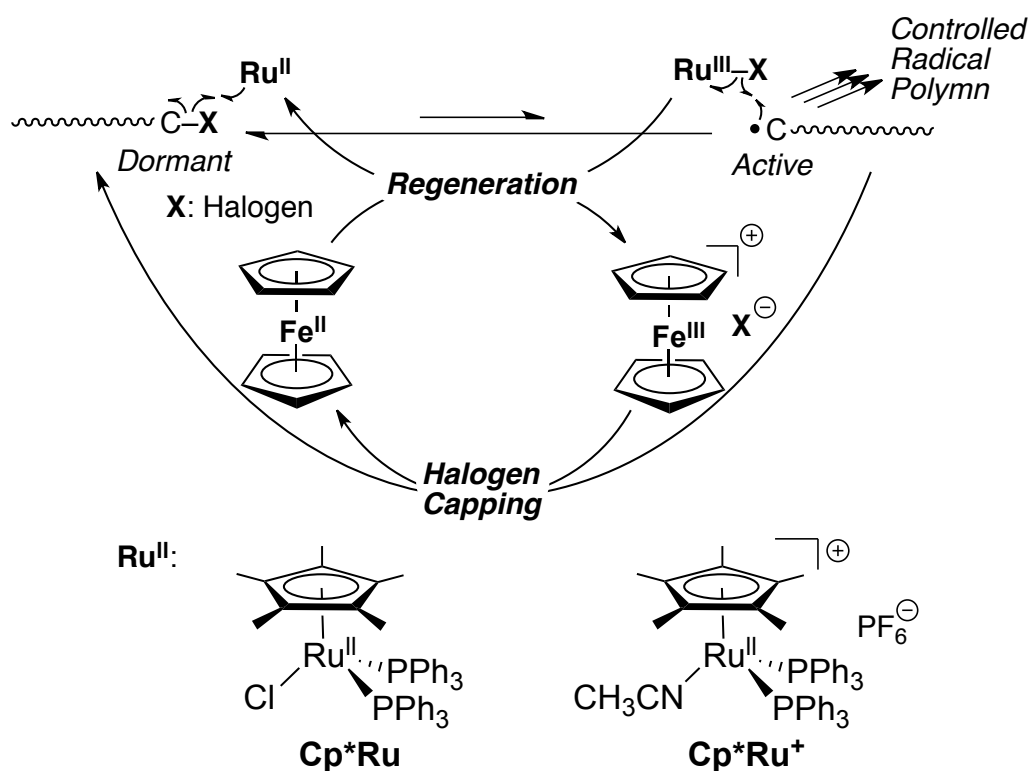
Though notably robust, versatile, and efficient, the usage of metal catalysts cause some specific issues: metal contamination of obtained polymers; deactivation of catalyst by polar groups; accumulation of oxidized forms by oxygen or unavoidable side reactions; rising cost from precious metals.<sup>3</sup> 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<sup>5,8-12</sup> and ruthenium<sup>13-16</sup> 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 ( $\text{Ru}^{\text{III}}$ ) of ruthenium complexes into catalytically active, radical-generating reduced counterpart ( $\text{Ru}^{\text{II}}$ ).<sup>17</sup>

Ferrocene ( $\text{FeCp}_2$ ) is one of the most traditional organometallic complexes or metallocenes, and the robust  $\eta^6$  ligation by two cyclopentadiene ligands with six electrons each is conducive to its high stability.<sup>18</sup> Therefore,  $\text{FeCp}_2$  and the derivatives have rarely been employed as catalysts in polymerization and organic reactions. This is unexceptional in metal-catalyzed LRP:  $\text{FeCp}_2$  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  $\text{FeCp}_2$  is oxidized to the trivalent ferrocenium cation ( $\text{FeCp}_2^+$ ).<sup>19</sup> For instance,  $\text{FeCp}_2$  reacts with two equivalents of  $\text{FeCl}_3$  as a strong oxidizing agent to give  $\text{FeCp}_2^+\text{FeCl}_4^-$  and  $\text{FeCl}_2$ . In such  $\text{FeCp}_2$ -related redox reactions, the counteranion for the resulting cationic trivalent iron ( $\text{FeCp}_2^+$ ) affects the stability of the salt: e.g.,  $\text{FeCp}_2^+\text{PF}_6^-$  is stable enough to be isolated as a crystal, while  $\text{FeCp}_2^+\text{Cl}^-$  is unstable and prone to decomposition.<sup>20</sup>

These phenomena motivated the author to employ  $\text{FeCp}_2$  as a *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  $\text{XMt}^{n+1}$  into  $\text{Mt}^n$  (the primary catalyst):  $\text{FeCp}_2 + \text{XMt}^{n+1} \rightarrow \text{FeCp}_2^+\text{X}^- + \text{Mt}^n$ . Furthermore, due to its relative unstability, resultant  $\text{FeCp}_2^+\text{X}^-$  may induce a direct halogen-capping reaction onto the growing radical species, or another route to re-generate the dormant end:  $\sim\sim\sim\text{C}^\bullet + \text{FeCp}_2^+\text{X}^- \rightarrow \sim\sim\sim\text{C-X} + \text{FeCp}_2$ . Evidently, organic halide anions, such as  $n\text{-Bu}_4\text{N}^+\text{X}^-$ , are incapable of promoting such a halogen-capping reaction to radical species. However, the nature of the halide anion in  $\text{FeCp}_2^+\text{X}^-$  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  $\text{FeCp}_2$  and the main catalyst (e.g., ruthenium complex  $\text{Ru}^{\text{II}}$ ) is expected. Herein, the author reports a novel catalysis via a concerted  $\text{FeCp}_2$  cocatalysis for the ruthenium-catalyzed LRP.



**Scheme 1.** Expected Cocatalysis of  $\text{FeCp}_2$  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)<sub>2</sub>-Cl initiator [H-(CH<sub>2</sub>CMeCO<sub>2</sub>Me)<sub>2</sub>-Cl]; an MMA dimer chloride] was prepared according to the literature.<sup>21)</sup> The ECPA initiator [ethyl 2-chloro-2-phenylacetate, Aldrich; >97%]<sup>22)</sup> was purified by distillation under reduced pressure before use. Cp\*RuCl(PPh<sub>3</sub>)<sub>2</sub> (Cp\*Ru: Aldrich), FeCp<sub>2</sub> (Aldrich; > 98%), [FeCp<sub>2</sub>][PF<sub>6</sub>] (Aldrich; > 97%), *n*-Bu<sub>4</sub>NCl (Tokyo Kasei; > 98%), NH<sub>4</sub>PF<sub>6</sub> (Aldrich; 99.99%), and 1,1'-Azobis(Cyclohexane-1-carbonitrile) (V-40) (Wako; > 95%) were used as received and handled in a glove box under a moisture- and oxygen-free argon atmosphere (H<sub>2</sub>O < 1 ppm, O<sub>2</sub> < 1 ppm). The cationic Cp\*-based ruthenium complex ([Cp\*Ru(CH<sub>3</sub>CN)(PPh<sub>3</sub>)<sub>2</sub>][PF<sub>6</sub>]: Cp\*Ru<sup>+</sup>) was prepared according to the literature.<sup>23)</sup> Tetralin (1,2,3,4-tetrahydronaphthalene) as an internal standard for <sup>1</sup>H NMR was dried over calcium chloride and distilled twice from calcium hydride before use. Anisole (Wako, dehydrated) and tetrahydrofuran (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)<sub>2</sub>-Cl/Cp\*Ru<sup>+</sup>/FeCp<sub>2</sub>/*n*-Bu<sub>4</sub>NCl is given below. In a 50 mL round-bottomed flask was placed Cp\*Ru<sup>+</sup> (5.7 mg, 0.006 mmol), FeCp<sub>2</sub> (44.6 mg, 0.24 mmol), *n*-Bu<sub>4</sub>NCl (66.7 mg, 0.24 mmol) under a glove box. Then, anisole (2.71 mL), tetralin (0.30 mL), MMA (2.57 mL, 24.0 mmol), and solutions of H-(MMA)<sub>2</sub>-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 <sup>1</sup>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.

## 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),  $\text{FeCp}_2$  (22.3 mg, 0.120 mmol),  $\text{NH}_4\text{PF}_6$  (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

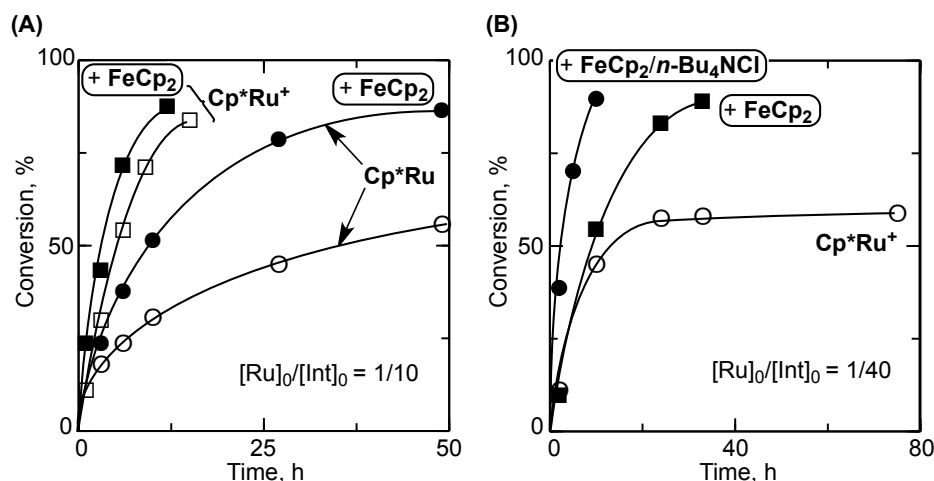
The  $M_n$ ,  $M_w/M_n$ , and MWD curves of the polymers were determined by size-exclusion chromatography at 40 °C in THF as an eluent on three polystyrene–gel columns (Shodex LF-404; exclusion limit =  $2 \times 10^6$ ; particle size = 6  $\mu\text{m}$ ; pore size = 3000 Å; 0.46 cm i.d.  $\times$  25 cm; flow rate, 0.3 mL  $\text{min}^{-1}$ ) 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;  $M_n$  = 630 – 1 200 000;  $M_w/M_n$  = 1.02–1.30) as well as the monomer.

## Results and Discussion

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

A pentamethylcyclopentadienyl ruthenium complex,  $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$  ( $\text{Cp}^*\text{Ru}$ ), is inherently active in metal-catalyzed LRP, as predicted by its lower redox potential and faster halogen exchange.<sup>24</sup> However,  $\text{Cp}^*\text{Ru}$  usually needs a cocatalyst [e.g.,  $\text{Al}(\text{O}i\text{-Pr})_3$  or amine] that likely assists an *in-situ* transformation of  $\text{Cp}^*\text{Ru}$  into a coordinatively unsaturated, 16-electron form [e.g.,  $\text{Cp}^*\text{RuCl}(\text{PPh}_3)$ ] and/or a promotion of the halogen-capping reaction.<sup>13,14,25</sup> The author, thus, selected  $\text{Cp}^*\text{Ru}$  as a main catalyst to examine the cocatalysis of  $\text{FeCp}_2$  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  $\text{FeCp}_2$  obviously

accelerated the polymerization (Figure 1A): Conversion in 49 h; 87% from 56% without  $\text{FeCp}_2$ . Obtained polymers were well controlled and of narrow molecular weight distributions (MWDs) ( $M_w/M_n < 1.2$ ). Because  $\text{FeCp}_2$  alone was totally inactive for MMA under otherwise the same conditions, these results indicate a concerted co-catalysis of  $\text{FeCp}_2$  with the ruthenium primary catalyst.

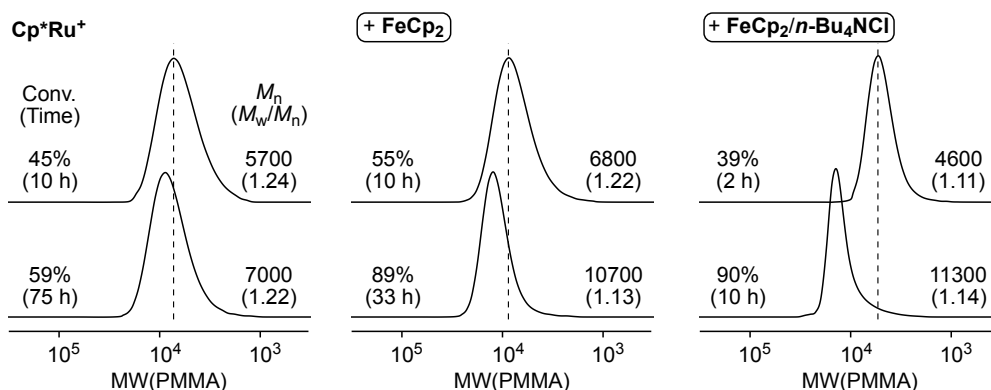


**Figure 1.** Effects of  $\text{FeCp}_2$  on ruthenium-catalyzed LRP of MMA with  $\text{Cp}^*\text{Ru}$  or  $\text{Cp}^*\text{Ru}^+$  in anisole at  $100^\circ\text{C}$  ( $[\text{MMA}]_0/[\text{H}-(\text{MMA})_2-\text{Cl}]_0 = 4000/40 \text{ mM}$ ). (A)  $[\text{Cp}^*\text{Ru}]_0 = 4.0 \text{ mM}$  ( $\circ$ ),  $[\text{Cp}^*\text{Ru}]_0/[\text{FeCp}_2]_0 = 4.0/40 \text{ mM}$  ( $\bullet$ ),  $[\text{Cp}^*\text{Ru}^+]_0 = 4.0 \text{ mM}$  ( $\square$ ),  $[\text{Cp}^*\text{Ru}^+]_0/[\text{FeCp}_2]_0 = 4.0/40 \text{ mM}$  ( $\blacksquare$ ); (B)  $[\text{Cp}^*\text{Ru}^+]_0 = 1.0 \text{ mM}$  ( $\circ$ ),  $[\text{Cp}^*\text{Ru}^+]_0/[\text{FeCp}_2]_0 = 1.0/40 \text{ mM}$  ( $\blacksquare$ ),  $[\text{Cp}^*\text{Ru}^+]_0/[\text{FeCp}_2]_0/[n\text{-Bu}_4\text{NCl}]_0 = 1.0/40/40 \text{ mM}$  ( $\bullet$ ).

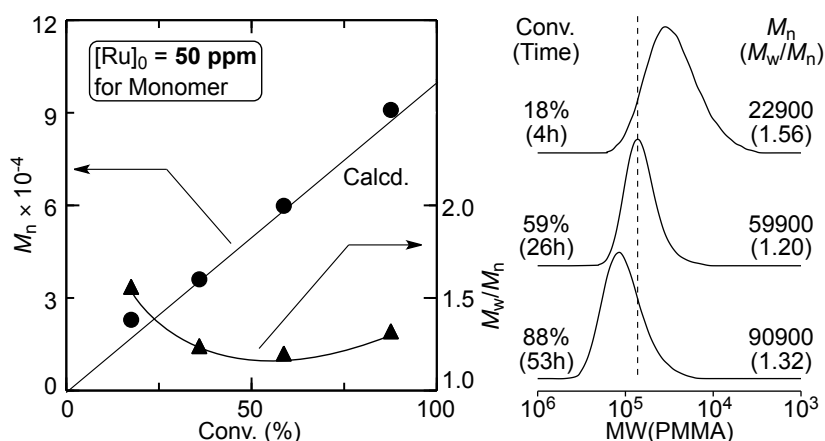
However, the polymerization with the  $\text{Cp}^*\text{Ru}/\text{FeCp}_2$  system was still not very fast, probably because ferrocene was incapable of generating coordinatively unsaturated ruthenium ( $\text{Ru}^{\text{II}}$ ) species. Actually, as described in chapter 2 of this thesis, the author has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

The cocatalytic effects of  $\text{FeCp}_2$  were more remarkable at a lower initial dose of  $\text{Cp}^*\text{Ru}^+$  (1.0 mM, 1/40 eq for the initiator; Figure 1B and Figure 2). The polymerization

was retarded and leveled off without  $\text{FeCp}_2$  (< 60% conversion beyond 20 h), whereas with  $\text{FeCp}_2$  smoothly reaching near completion and well controlled (89% conversion in 33 h;  $M_w/M_n = 1.13$ ). Interestingly, the  $\text{Cp}^*\text{Ru}^+/\text{FeCp}_2$ -catalyzed system was further accelerated upon addition of a chloride salt ( $n\text{-Bu}_4\text{NCl}$ , 40 mM), most likely via an additional promotion of the halogen-capping reaction by unstable  $\text{FeCp}_2^+\text{Cl}^-$ , in which  $n\text{-Bu}_4\text{NCl}$  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  $\text{Cp}^*\text{Ru}$ .



**Figure 2.** SEC curves of PMMAs obtained via ruthenium-catalyzed LRP with  $\text{Cp}^*\text{Ru}^+$  in conjunction with  $\text{FeCp}_2$  and  $n\text{-Bu}_4\text{NCl}$ . See Figure 1 (B) for condition.



**Figure 3.** Syntheses of high MW poly(MMA)s with low amount of ruthenium catalyst in conjunction with  $\text{FeCp}_2$ :  $[\text{MMA}]_0/[\text{H}-(\text{MMA})_2\text{-Cl}]_0/[\text{Cp}^*\text{Ru}^+]_0/[\text{FeCp}_2]_0/[n\text{-Bu}_4\text{NCl}]_0 = 6000/6.0/0.3/12/0.5$  mM in anisole at  $100^\circ\text{C}$ .

## 2. Highly Active Catalysis: Synthesis of higher Molecular Weight Polymers with A Small Amount of Ru Catalysts

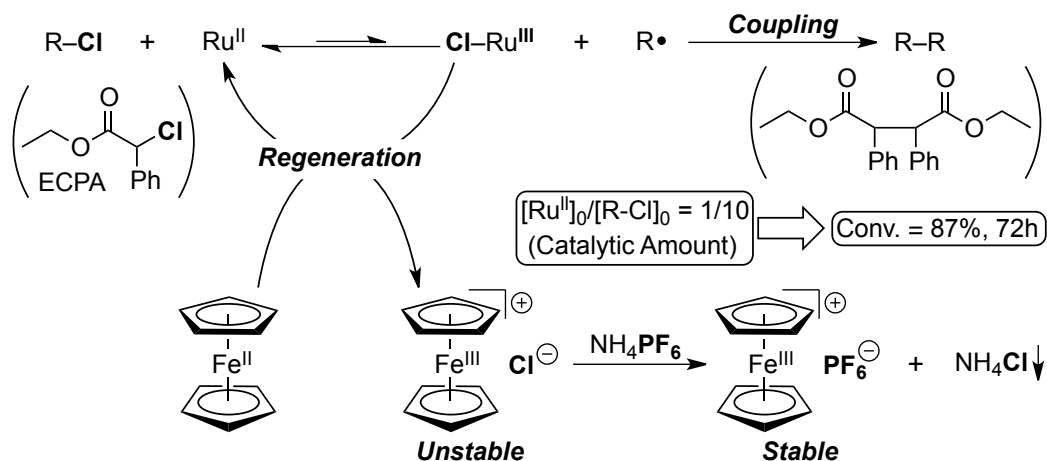
These positive effects of  $\text{FeCp}_2$  also enabled the efficient synthesis of higher molecular weight polymers (1000 mer) at a high monomer concentration ( $[\text{MMA}]_0 = 6.0 \text{ M}$ ;  $[\text{H}-(\text{MMA})_2-\text{Cl}]_0 = 6.0 \text{ mM}$ ). For this, an extremely small amount of  $\text{Cp}^*\text{Ru}^+$  (0.3 mM; 50 ppm for monomer) was injected along with  $\text{FeCp}_2$  and  $n\text{-Bu}_4\text{NCl}$  ( $[\text{FeCp}_2]_0 = 12 \text{ mM}$ ;  $[n\text{-Bu}_4\text{NCl}]_0 = 0.5 \text{ mM}$ ). 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 $\text{FeCp}_2$

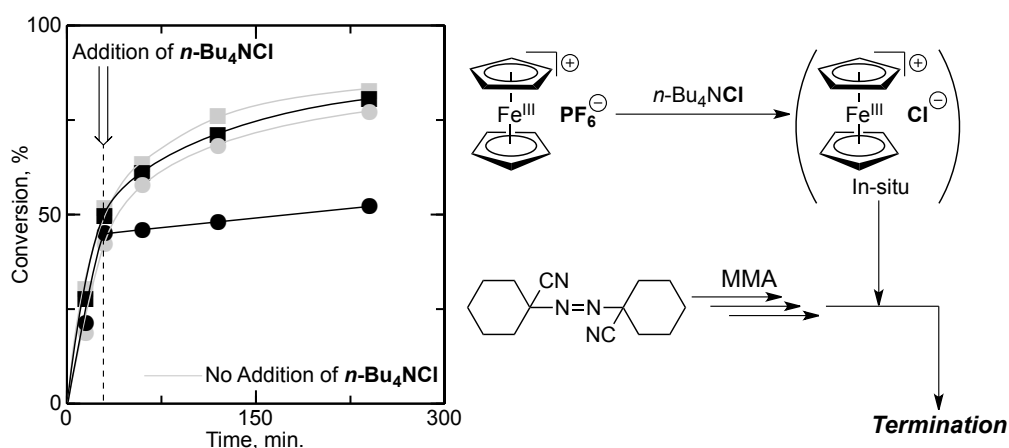
The redox-promoting function of  $\text{FeCp}_2$  as a reducing agent was verified by a radical coupling reaction of a model dormant end  $[\text{R}-\text{Cl}]$ : ethyl 2-chloro-2-phenylacetate (ECPA)] catalyzed with the  $\text{Cp}^*\text{Ru}^+/\text{FeCp}_2$  pair (without  $n\text{-Bu}_4\text{NCl}$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

Another expected contribution of  $\text{FeCp}_2$  to LRP is the promotion of the halogen-capping of radical species via in situ generated  $\text{FeCp}_2^+\text{Cl}^-$ :  $\sim\text{C}\cdot + \text{FeCp}_2^+\text{Cl}^- \rightarrow \sim\text{C}-\text{Cl} + \text{FeCp}_2$ . 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  $\text{FeCp}_2^+\text{PF}_6^-$ , and, at 40-50% monomer conversion, an equimolar amount of  $n\text{-Bu}_4\text{NCl}$  was added in situ to transform  $\text{FeCp}_2^+\text{PF}_6^-$  into  $\text{FeCp}_2^+\text{Cl}^-$ . The polymerization was terminated, where the

$\text{FeCp}_2^+\text{Cl}^-$  effectively capped the free radicals into inactive covalent terminals. On the other hand, the polymerization with V-40 in the *absence* of  $\text{FeCp}_2^+\text{PF}_6^-$  was not disturbed by addition of  $n\text{-Bu}_4\text{NCl}$ . From these results,  $\text{FeCp}_2^+\text{Cl}^-$  (in situ generated in LRP) promotes the radical capping reaction via the reduction of itself.



**Figure 4.** Coupling reaction of ECPA with  $\text{Cp}^*\text{Ru}^+$  in conjunction with  $\text{FeCp}_2/\text{NH}_4\text{PF}_6$  in toluene- $d_8$ /THF (2/1 v/v) at 100 °C:  $[\text{ECPA}]_0/[\text{Cp}^*\text{Ru}^+]_0/[\text{FeCp}_2]_0/[\text{NH}_4\text{PF}_6]_0 = 40/4.0/40/40$  mM.



**Figure 5.** Effects of a combination of  $\text{FeCp}_2^+\text{PF}_6^-$  and  $n\text{-Bu}_4\text{NCl}$  on free radical polymerization of MMA with 1,1'-Azobis(cyclohexane-1-carbonitrile) (V-40): (●): polymerization in the presence of  $\text{FeCp}_2^+\text{PF}_6^-$ , (■): polymerization in the absence of  $\text{FeCp}_2^+\text{PF}_6^-$ ; (black line): addition of  $n\text{-Bu}_4\text{NCl}$  in 30 min, (gray line): no addition of  $n\text{-Bu}_4\text{NCl}$ :  $[\text{MMA}]_0 = 2.0$  M,  $[\text{V-40}]_0 = 20$  mM,  $[\text{FeCp}_2^+\text{PF}_6^-]_0 = 40$  mM. An equivalent of  $n\text{-Bu}_4\text{NCl}$  was added for  $\text{FeCp}_2^+\text{PF}_6^-$ .

## 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  $\text{Ru}^{\text{II}}$  but also halogen-capping reaction for growing radical species along with its own redox cycle ( $\text{Fe}^{\text{II}} \leftrightarrow \text{Fe}^{\text{III}}$ ). 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  $\text{FeCp}_2^+\text{Cl}^-$  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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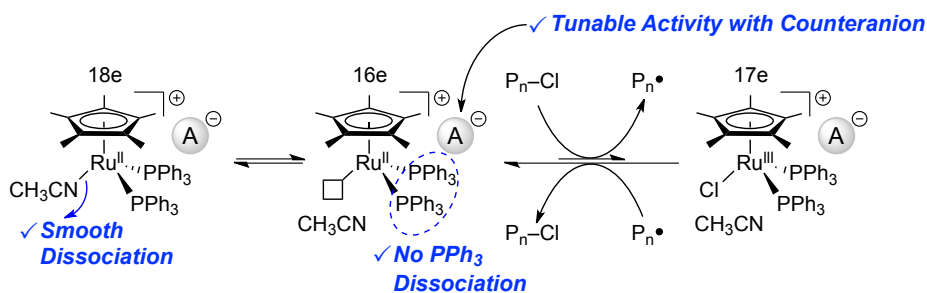


## Chapter 2

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

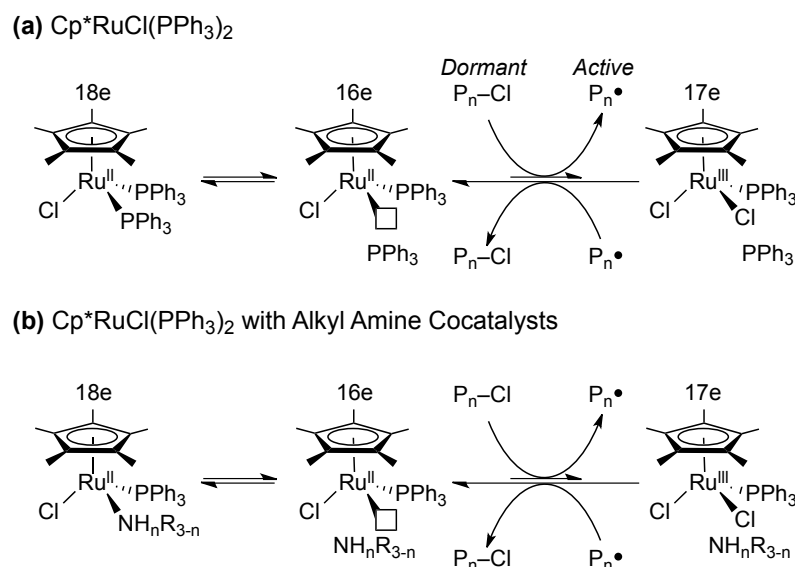
### Abstract

The Author presents the cationic Cp\*-ruthenium complexes  $[\text{Cp}^*\text{Ru}(\text{CH}_3\text{CN})(\text{PPh}_3)_2\text{A}]^+$   $\text{A}^-$ ;  $\text{A}^-$ : the counter anion; abbreviated to  $\text{Cp}^*\text{Ru}^+\text{A}^-$ ] 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 (conversion  $> 80\%$  in 15 h). The catalytic feature was clearly different from the neutral counterpart  $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$ :  $\text{Cp}^*\text{Ru}$ ] resulting in retarded polymerization. Interestingly, the catalytic activity was strongly influenced by the counter anions. For example, the  $\text{PF}_6^-$ -based complex did not afford catalysis for controlled polymerization of methyl acrylate (MA), but  $\text{SbF}_6^-$ -based  $[\text{Cp}^*\text{Ru}(\text{CH}_3\text{CN})(\text{PPh}_3)_2\text{SbF}_6]^+$   $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$ ] 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.,  $\text{CH}_3\text{CN}$ ) is likely to be eliminated to give 16e complex instead of the neutral phosphine ligand (e.g.,  $\text{PPh}_3$ ). 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  $\text{PPh}_3$ .



## 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.<sup>1-7</sup> In Mt-LRP, a carbon-halogen bond at a polymer end ( $\sim\text{C-X}$ ;  $\sim\sim$ : polymer chain; X: halogen) is reversibly activated by transition metal catalysts through the one electron redox ( $\text{Mt}^n \leftrightarrow \text{XMt}^{n+1}$ ; Mt: metal) to allow dynamic dormant-active equilibrium leading to suppression of “irreversible” side reactions (coupling, disproportionation, etc.).

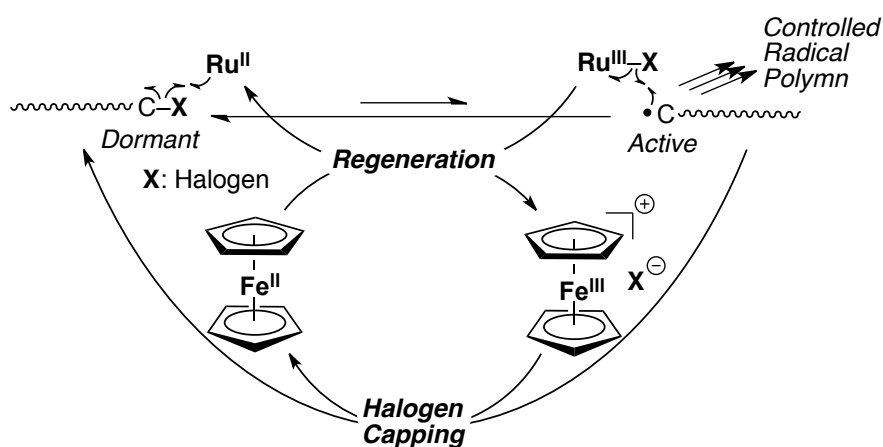


**Figure 1.** The mechanism of transition metal-catalyzed living radical polymerization with  $\text{Cp}^*\text{Ru}$ -based catalysis: (a)  $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ ; (b)  $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ /alkyl amine cocatalysts.

Among available metals for Mt-LRP such as ruthenium (Ru),<sup>8</sup> copper (Cu),<sup>9-11</sup> iron (Fe),<sup>12-14</sup> nickel (Ni),<sup>15,16</sup> Ru complexes are known as one of the most active catalysts as designable organometallic complexes. For example, the pentamethylcyclopentadienyl ( $\text{Cp}^*$ )-ligated ruthenium complexes  $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$ :  $\text{Cp}^*\text{Ru}$  are widely used for LRP of various monomers including methacrylates, acrylates, and styrenes.<sup>17</sup> However,  $\text{Cp}^*\text{Ru}$  usually needs cocatalysts to promote polymerization, because  $\text{Cp}^*\text{Ru}$  alone does not have the sufficient activity<sup>18</sup> 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,<sup>19</sup> 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).

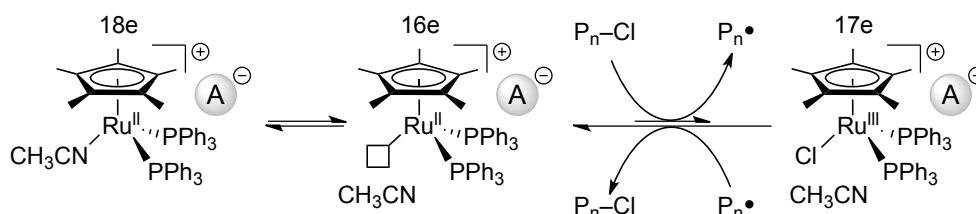
In addition, as described in chapter 1 of this thesis, Ferrocene is also able to act as a cocatalyst for  $Cp^*Ru$  and it is speculated that it could contribute to halogen-capping reaction of growing radical species to regenerate a dormant end as well as reduction of accumulated higher oxidized ruthenium complex (Figure 2: Mechanism of Ferrocene).<sup>20</sup> 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.



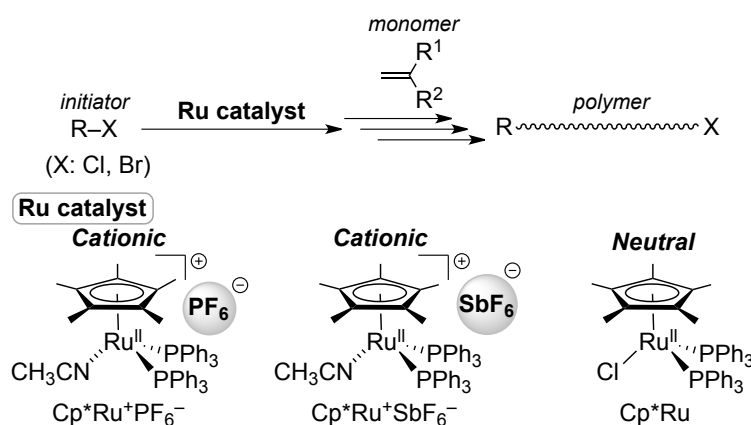
**Figure 2.** Ferrocene-assisted concerted redox catalysis for metal-catalyzed living radical polymerization.

In this chapter, therefore, the author is describing interesting catalysis of cationic  $Cp^*Ru$  complex [e.g.,  $[Cp^*Ru(CH_3CN)(PPh_3)_2]^+PF_6^-$ ] 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

dissociation of coordinating solvent (e.g., CH<sub>3</sub>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<sup>\*</sup>Ru<sup>+</sup>A<sup>-</sup> could be tuned through the selection of the counter anion (A<sup>-</sup>), as demonstrated in organic reactions with similar cationic metal complexes.<sup>22,23</sup> 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<sup>\*</sup>Ru complex as the catalyst for living radical polymerization.



**Scheme 1.** Transition Metal-Catalyzed Living Radical Polymerization with “Cationic” and “Neutral” Cp<sup>\*</sup>Ru Complexes.

## 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 ( $\text{CH}_2=\text{CMeCO}_2-(\text{CH}_2\text{CH}_2\text{O})_n$ ; Me = CH<sub>3</sub>; *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)<sub>2</sub>-X; X = Cl,<sup>24</sup> Br<sup>25</sup>) were prepared according to the literature. The ECPA initiator (ethyl 2-chloro-2-phenylacetate)<sup>26</sup> (Aldrich; purity > 97%) and the H-EMA-Br initiator ((CH<sub>3</sub>)<sub>2</sub>C(CO<sub>2</sub>Et)Br) (TCI; > 98%) were purified by distillation under reduced pressure before use. The cationic Cp\*Ru complexes, Cp\*Ru<sup>+</sup>PF<sub>6</sub><sup>-</sup> and Cp\*Ru<sup>+</sup>SbF<sub>6</sub><sup>-</sup>, were prepared according to the literature<sup>21</sup> by using AgPF<sub>6</sub> and AgSbF<sub>6</sub> as cationizing agents. The ruthenium tetramer [Cp\*RuCl]<sub>4</sub> was prepared according to the literature.<sup>27,28</sup> Cp\*RuCl(PPh<sub>3</sub>)<sub>2</sub> (Aldrich), Cp\*Ru(CH<sub>3</sub>CN)<sub>3</sub>PF<sub>6</sub> (Aldrich; purity 98%), AgPF<sub>6</sub> (Aldrich; purity 99.99%), AgSbF<sub>6</sub> (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 (H<sub>2</sub>O < 1 ppm, O<sub>2</sub> < 1 ppm). *n*-Octane (internal standard for gas chromatography), and 1,2,3,4-tetrahydronaphthalene (tetralin; internal standard for <sup>1</sup>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. Acetonitrile (CH<sub>3</sub>CN), anisole, tetrahydrofane (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)<sub>2</sub>-Cl/Cp\*Ru<sup>+</sup>PF<sub>6</sub><sup>-</sup> was as follows. In a 50 mL round-bottomed flask was placed Cp\*Ru<sup>+</sup>PF<sub>6</sub><sup>-</sup> (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)<sub>2</sub>-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 <sup>1</sup>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<sub>3</sub>CN)<sub>3</sub>PF<sub>6</sub> (8.1 mg, 0.016 mmol) and bipy (2.5 mg, 0.016 mmol) under a grove box. Then, CH<sub>3</sub>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<sub>3</sub>CN. Next, THF (1.84 mL), *n*-octane (0.20 mL), MMA (1.71 mL, 16.0 mmol), and a solution of H-(MMA)<sub>2</sub>-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]<sub>4</sub> (4.3 mg, 0.004 mmol) and bipy (2.5 mg, 0.016 mmol) under a grove 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)<sub>2</sub>-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.

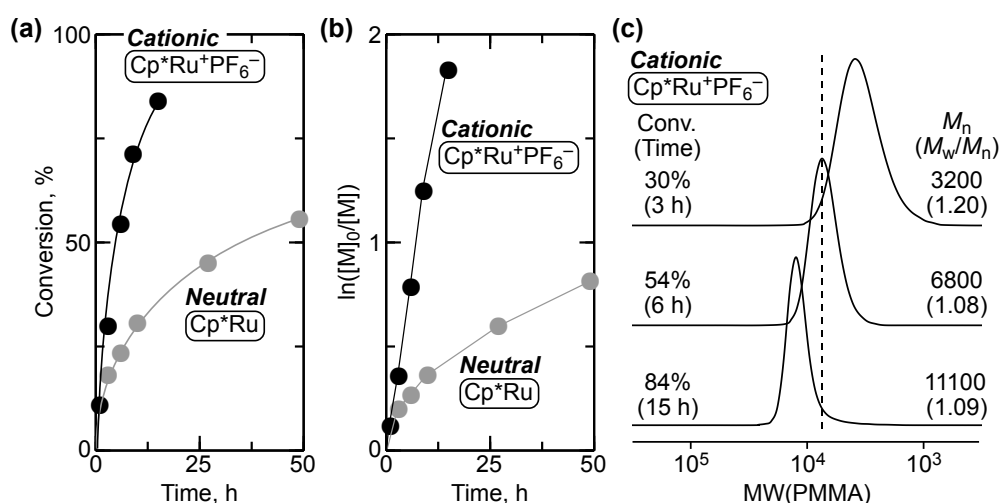
### **Model Reaction: Radical Coupling of ECPA**

A typical procedure for radical coupling reaction with ECPA/Cp\*<sup>+</sup>Ru<sup>+</sup>PF<sub>6</sub><sup>-</sup> was as follows. A solution of Cp\*<sup>+</sup>Ru<sup>+</sup>PF<sub>6</sub><sup>-</sup> (28.4 mg, 0.030 mmol) and ECPA (0.196 mL of 612.0 mM, 0.120 mmol) in toluene-*d*<sub>8</sub> 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 <sup>1</sup>H and <sup>31</sup>P 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*<sub>n</sub> and *M*<sub>w</sub>/*M*<sub>n</sub> 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<sup>6</sup>; particle size = 6 μm; pore size = 3000 Å; 0.46 cm i.d. × 25 cm; flow rate, 0.3 mL min<sup>-1</sup>) 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*<sub>n</sub> = 620–1200000; *M*<sub>w</sub>/*M*<sub>n</sub> = 1.06–1.22) or 13 standard poly(St) samples (Polymer Laboratories; *M*<sub>n</sub> = 500–3840000; *M*<sub>w</sub>/*M*<sub>n</sub> = 1.01–1.14) as well as the monomer. For poly(PEGMA), *M*<sub>n</sub> and *M*<sub>w</sub>/*M*<sub>n</sub> 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 × 10<sup>6</sup>; particle size = 5000 Å; 0.8 cm i.d. × 30 cm; flow rate, 1.0 mL min<sup>-1</sup>) 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*<sub>n</sub> = 630–1200000; *M*<sub>w</sub>/*M*<sub>n</sub> = 1.02–1.30) as well as the monomer. <sup>1</sup>H and <sup>31</sup>P NMR spectra were measured at room temperature on a JEOL JNM-ECA500

spectrometer operating at 500.16 and 202.47 MHz, respectively. For the  $^{31}\text{P}$  NMR analysis, a capillary of  $(\text{C}_2\text{H}_5\text{O})_2\text{POH}$  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  $^1\text{H}$  NMR and MALDI-TOF-MS were fractionated by preparative SEC (column: Shodex K-5002F).



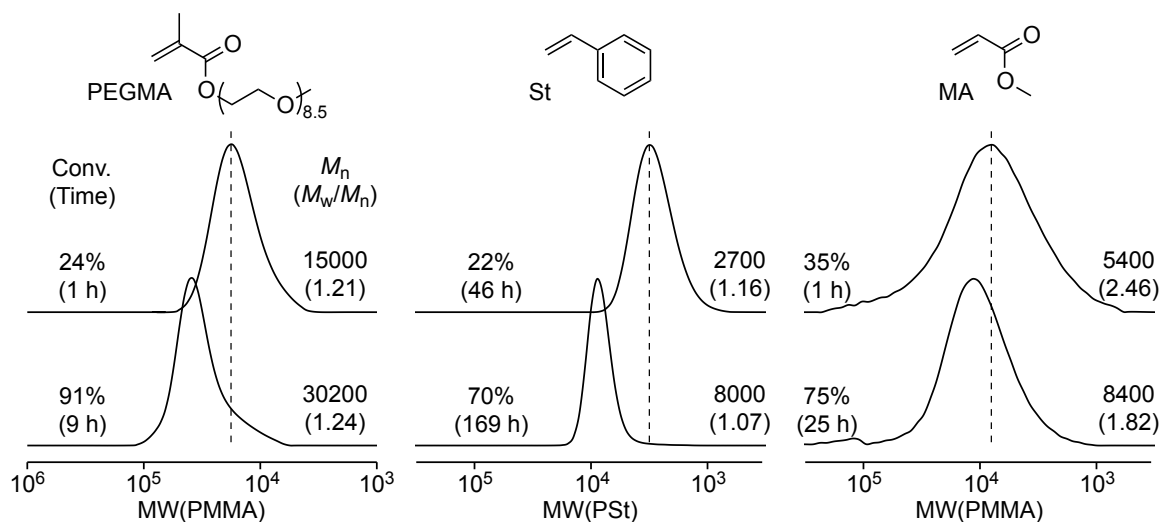
**Figure 4.** The polymerization of MMA with the cationic  $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$  and the neutral counterpart ( $\text{Cp}^*\text{Ru}$ ) ( $[\text{MMA}]_0/[\text{H}-(\text{MMA})_2\text{-Cl}]_0/[\text{Ru}]_0 = 4000/40/4.0$  mM in anisole at  $100^\circ\text{C}$ ): (a) plots of conversion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

## Results and Discussion

### 1. Catalytic Activity of Cationic Ruthenium Complex

The author first employed the cationic  $\text{Cp}^*\text{Ru}$  complex carrying  $\text{PF}_6^-$  ( $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$ ) for polymerization of methyl methacrylate (MMA) in conjunction with a chlorine initiator  $[\text{H}-(\text{MMA})_2\text{-Cl}]$  and compared the catalytic activity with that of the neutral counterpart ( $\text{Cp}^*\text{Ru}$ ) 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  $\ln([\text{M}]_0/[\text{M}])$  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 16e-complex.



**Figure 5.**  $Cp^*Ru^+PF_6^-$ -catalyzed living radical polymerization of PEGMA, St, and MA: (for PEGMA)  $[PEGMA]_0/[H-(MMA)_2-Cl]_0/[Ru]_0 = 500/5.0/2.0$  mM in EtOH/H<sub>2</sub>O (75/25, v/v) at 40 °C; (for St)  $[St]_0/[H-(MMA)_2-Cl]_0/[Ru]_0 = 4000/40/4.0$  mM in anisole at 100 °C; (for MA)  $[MA]_0/[H-EMA-Br]_0/[Ru]_0 = 4000/40/4.0$  mM in toluene at 80 °C.

## 2. Applicable Monomers

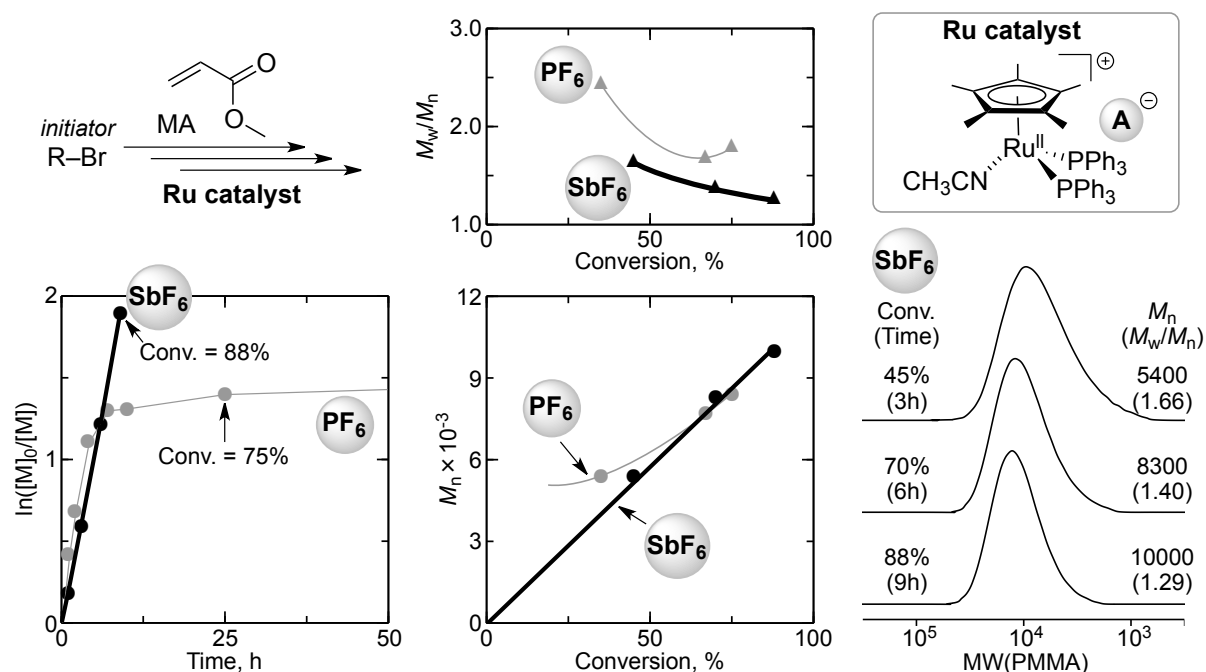
The author then examined other monomers to see the monomer versatility of  $Cp^*Ru^+PF_6^-$ . As shown in Figure 5,  $Cp^*Ru^+PF_6^-$  was capable to catalyze the controlled polymerization of functional methacrylate (PEGMA: the methacrylate bearing the PEG pendant chain) to give narrow molecular weight 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<sub>2</sub>O (75/25, v/v) at 40 °C], implying high tolerance to functional groups (-OH) similar to previously reported  $Cp^*Ru$  based complex.<sup>29,30</sup>

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

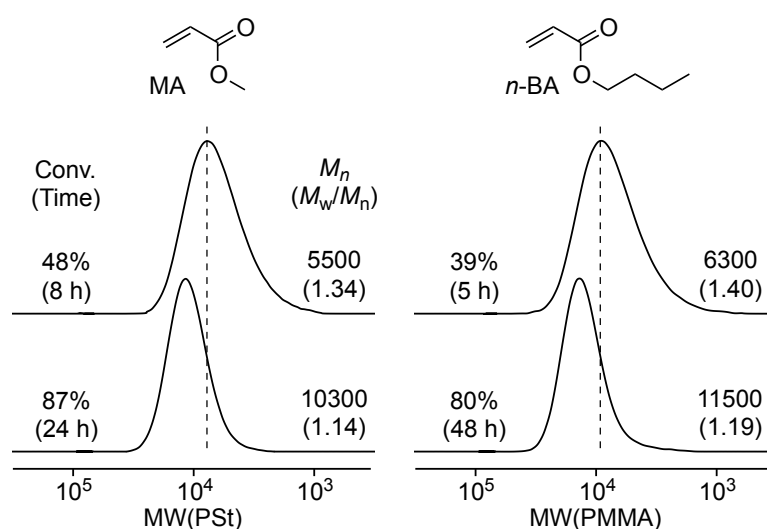
An existence of the counter anion is characteristic of cationic metal complex, and indeed some examples are known that the counter anion of cationic catalyst could affect the catalysis,<sup>22,23</sup> as described in Introduction. For the use as polymerization catalyst, modification of the counter anion is interesting toward tune of catalytic activity according to reactivity of monomers. Thus, the counter anion ( $\text{PF}_6^-$ ) in  $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$  was replaced with  $\text{SbF}_6^-$ , which is also typical counter anion of lower nucleophilicity, to prepare another type of cationic complex,  $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$ . The complex was employed as the catalyst for polymerization of MA, which was not so precisely controlled with the original  $\text{PF}_6^-$ -based cationic complex.



**Figure 6.** Effects of counteranions on living radical polymerization of MA with cationic  $\text{Cp}^*\text{Ru}$  complexes ( $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$  vs  $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$ ):  $[\text{MA}]_0/[\text{H-EMA-Br}]_0/[\text{Ru}]_0 = 4000/40/4.0$  mM in toluene at  $80^\circ\text{C}$ .

**Table 1.**  $Cp^*Ru^+SbF_6^-$ -catalyzed living radical polymerizations of acrylate monomers<sup>a</sup>

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

<sup>a</sup> $[Monomer]_0/[Initiator]_0 = 4000/40$  mM in toluene at 80 °C.**Figure 7.** Living radical polymerizations of MA and *n*-BA with  $Cp^*Ru^+SbF_6^-$  in conjunction with H-(MMA)<sub>2</sub>-Br as the initiator:  $[Monomer]_0/[H-(MMA)_2-Br]_0/[Ru]_0 = 4000/40/4.0$  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  $[H-(MMA)_2-Br]$ <sup>25</sup> than H-EMA-Br allowed narrower molecular

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).

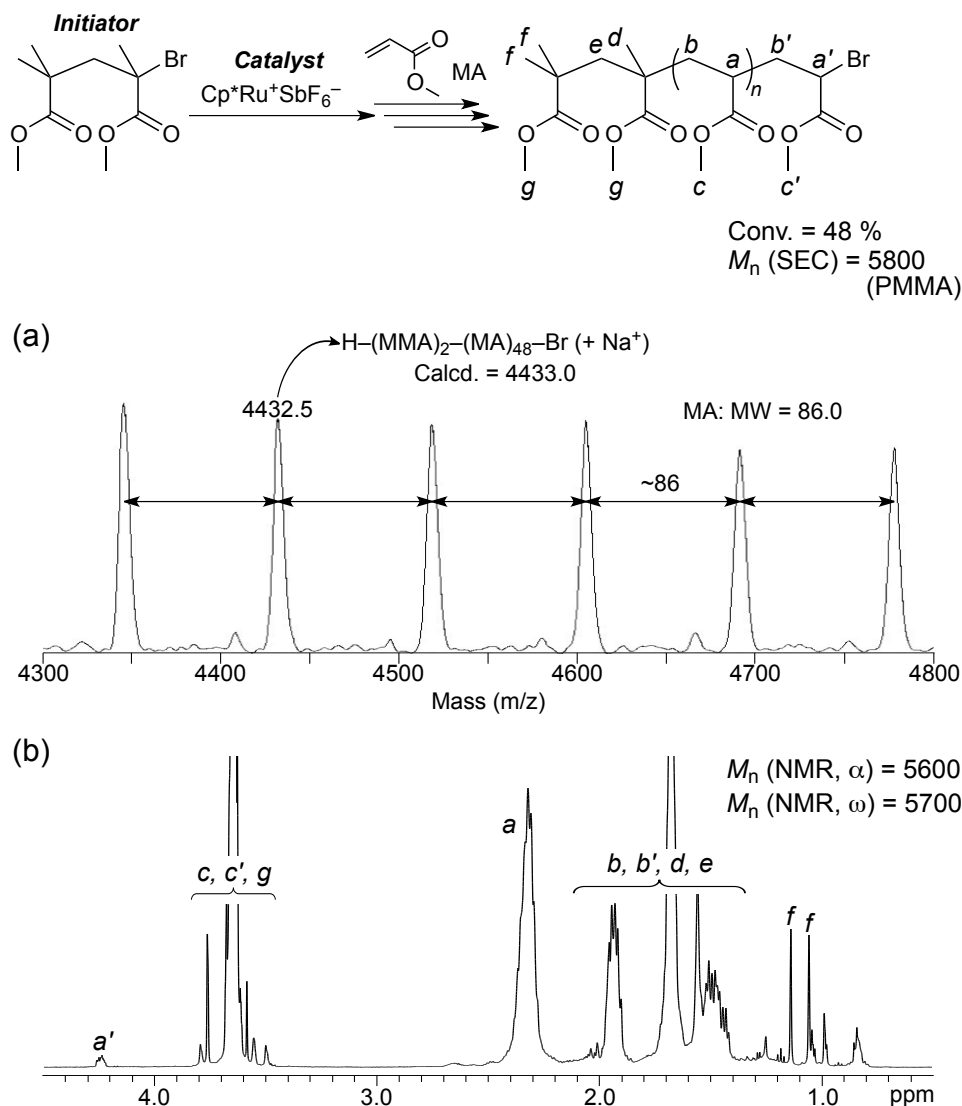
The terminal structure of PMA was analyzed with MALDI-TOF-MS and  $^1\text{H}$  NMR. The sample was prepared with  $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$  in conjunction with  $\text{H}-(\text{MMA})_2\text{-Br}$ : conversion = 48% for 100 mer condition;  $M_n = 5800$ ,  $M_w/M_n = 1.30$ . As seen in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

$^1\text{H}$  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,  $M_n(\text{NMR}, \alpha)$  and  $M_n(\text{NMR}, \omega)$  were calculated:  $M_n(\text{NMR}, \alpha) = 5600$  and  $M_n(\text{NMR}, \omega) = 5700$ . 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:  $M_n(\text{NMR}, \alpha) = 10300$  and  $M_n(\text{NMR}, \omega) = 11100$  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<sup>a</sup>

| Entry | Conv. (%) | $M_n(\text{SEC})^b$ | $M_w/M_n^b$ | $M_n(\text{NMR}, \alpha)^c$ | $M_n(\text{NMR}, \omega)^d$ | $f_n(\omega)^e$ |
|-------|-----------|---------------------|-------------|-----------------------------|-----------------------------|-----------------|
| 1     | 48        | 5800                | 1.30        | 5600                        | 5700                        | 0.98            |
| 2     | 68        | 7700                | 1.22        | 7500                        | 7700                        | 0.97            |
| 3     | 87        | 10500               | 1.14        | 10300                       | 11100                       | 0.93            |

<sup>a</sup> $[\text{MA}]_0/[\text{H}-(\text{MMA})_2\text{-Br}]_0/[\text{Ru}]_0 = 4000/40/4.0$  mM in toluene at 80 °C. <sup>b</sup>Polymers were fractionated by preparative SEC. <sup>c</sup> $M_n(\text{NMR}, \alpha) = \text{MW}(\text{initiator moiety}) + \text{MW}(\text{MA}) \times \text{DP}_n(\text{NMR}, \alpha)$  with  $\text{DP}_n(\text{NMR}, \alpha)$  obtained from  $^1\text{H}$  NMR peak intensity ratio; 3a/*f* (see Figure 8b). <sup>d</sup> $M_n(\text{NMR}, \omega) = \text{MW}(\text{initiator moiety}) + \text{MW}(\text{MA}) \times \text{DP}_n(\text{NMR}, \omega)$  with  $\text{DP}_n(\text{NMR}, \omega)$  obtained from  $^1\text{H}$  NMR peak intensity ratio; a/*a'* (see Figure 8b). <sup>e</sup> $f_n(\omega) = M_n(\text{NMR}, \alpha) / M_n(\text{NMR}, \omega)$ .

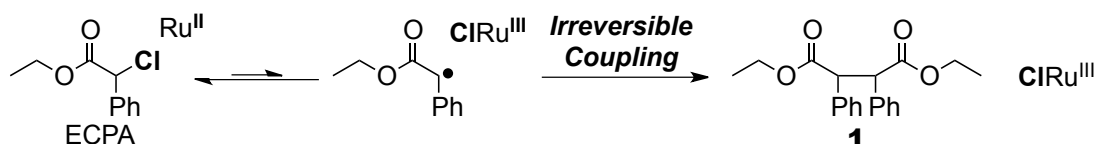


**Figure 8.** Structural analysis with (a) MALDI-TOF-MS spectrum and (b)  $^1H$  NMR (in  $CDCl_3$ ) spectrum for PMA obtained with  $Cp^*Ru^+SbF_6^-$  in conjunction with  $H-(MMA)_2-Br$  as an initiator:  $[MA]_0/[H-(MMA)_2-Br]_0/[Ru]_0 = 4000/40/4.0$  mM in toluene at 80 °C.

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.<sup>31</sup> 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

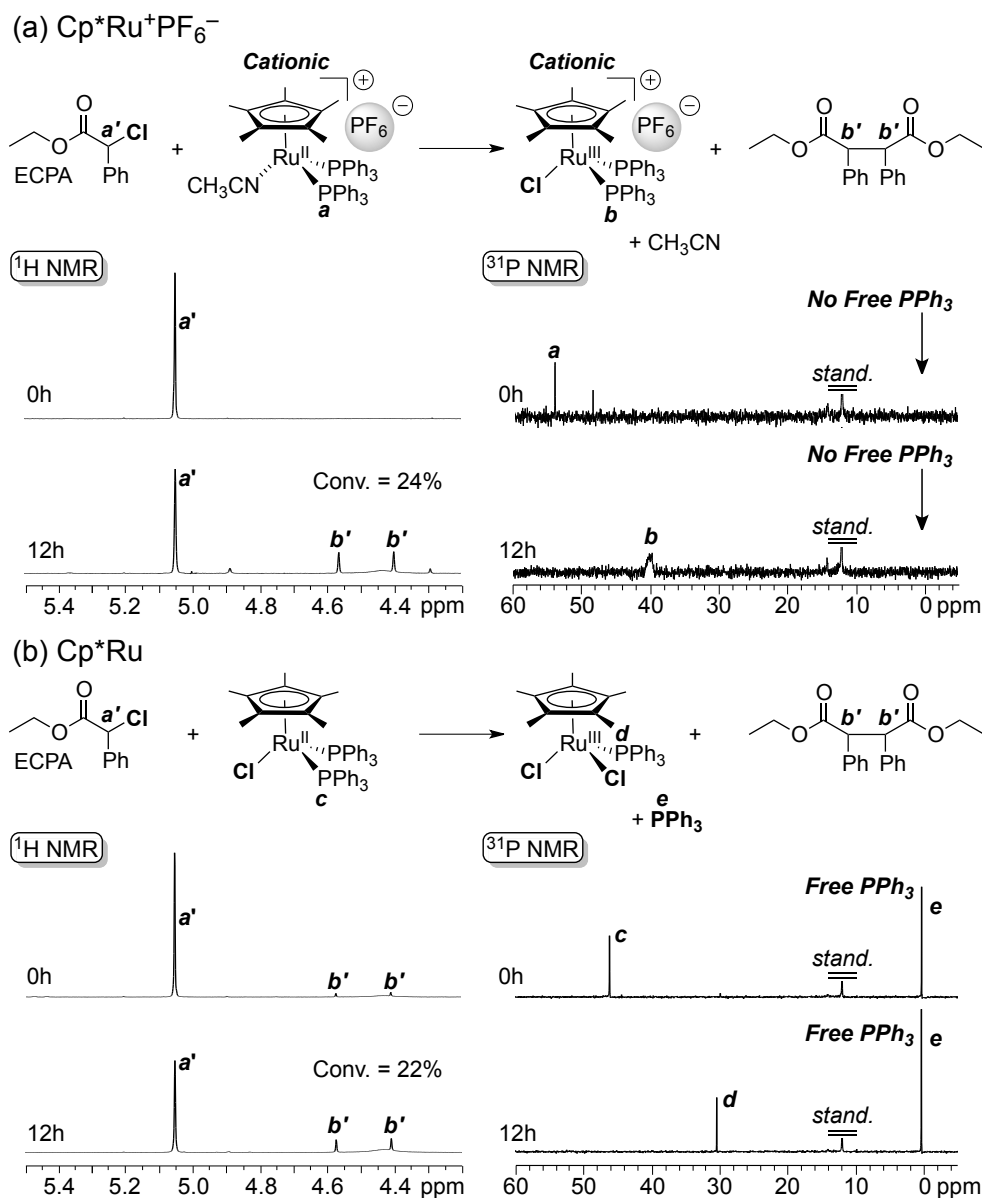
For the detailed discussion on the catalytic mechanism with cationic ruthenium complexes, the structural transformation through an activation of a carbon–halogen bond was examined. Therefore, a model reaction of halogen initiator was performed with  $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$  in the absence 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  $\text{Ru}^{\text{III}}$  complex (Scheme 2). The reaction was performed in toluene- $d_8$  at 80 °C, and directly traced by  $^1\text{H}$  and  $^{31}\text{P}$  NMR analysis.



**Scheme 2.** Irreversible Radical Coupling Reaction of ECPA with Divalent Ru Complexes ( $\text{Ru}^{\text{II}}$ ) for Accumulation of Trivalent Ru Complexes ( $\text{ClRu}^{\text{III}}$ )

The conversion of ECPA reached 24% in 12 h (Figure 9a). Since the feed ratio of Ru to ECPA ( $[\text{Ru}]_0/[\text{ECPA}]_0$ ) is 0.25, the conversion value is reasonable assuming the halogen molecule is stoichiometrically converted into other molecules under catalysis by the ruthenium complex.  $^1\text{H}$  NMR spectrum of the resultant solution supported generation of coupled product (**1**; 23% yield) and most probably generation of trivalent complex ( $\text{XRu}^{\text{III}}$ ) would be accompanied through the bimolecular coupling radical reaction. In  $^{31}\text{P}$  NMR spectrum, the peak *a* corresponding to phosphine on the divalent complex ( $\text{Ru}^{\text{II}}$ ) was vanished in 12 h, and instead a new peak *b* was observed: this would be from the generated  $\text{XRu}^{\text{III}}$ . Most importantly, no peak from "free"  $\text{PPh}_3$  was found in the spectra around 0 ppm, which was clearly different from the reaction with the neutral counterpart  $\text{Cp}^*\text{Ru}$  giving the peak from free  $\text{PPh}_3$  ligands (Figure 9b). These results would indicate that  $\text{XRu}^{\text{III}}$  was generated without the dissociation of phosphine ligands through the catalysis with  $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$ . Supposedly, the weakly coordinating solvent molecule (i.e.,  $\text{CH}_3\text{CN}$ ) 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  $\text{Cp}^*\text{Ru}$ , two phosphine ligands likely remain on the ruthenium center.





**Figure 9.**  $^1H$  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.<sup>32</sup> 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  $\text{PPh}_3$ . Herein bipyridine (bipy) was selected because bipy is widely used for both neutral and cationic  $\text{Cp}^*$ -based Ru complexes in organic reactions.<sup>33,34</sup>

Thus the cationic  $\text{Cp}^*\text{Ru}$  complexes bearing bipy ligand was prepared as well as the neutral version for comparison of catalytic activity. Each ruthenium complex precursor [ $\text{Cp}^*\text{Ru}(\text{CH}_3\text{CN})_3\text{PF}_6$  for cationic<sup>34</sup> and [ $\text{Cp}^*\text{RuCl}_4$  for neutral<sup>19,33</sup>] 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).

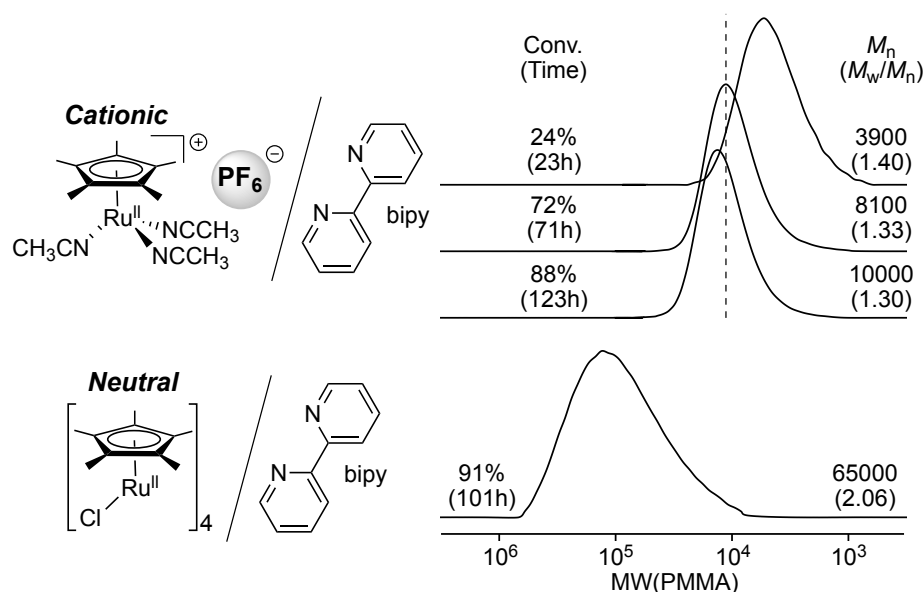
The polymerization with the cationic  $\text{Cp}^*\text{Ru}$  complex was relatively slow but the conversion finally reached almost 90% (88% in 123 h). The obtained PMMAs showed unimodal MWDs and molecular weight of the final product was fairly controlled ( $M_n = 10000$ ,  $M_w/M_n = 1.30$ ). On the 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  $\text{Cp}^*\text{Ru}$  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  $\text{Cp}^*\text{Ru}(\text{CH}_3\text{CN})_3\text{PF}_6$  as the precursor<sup>35</sup> is advantageous to test various ligands toward more active catalysts.

## Conclusions

In this chapter, the author studied the cationic  $\text{Cp}^*\text{Ru}$  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,  $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$  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  $\text{Cp}^*\text{Ru}$  resulted in the slow and retarded polymerization under the same reaction condition. Secondly, the catalytic activity of the cationic  $\text{Cp}^*\text{Ru}$  complexes can be tuned by the combined counter anions. In polymerization of MA,  $\text{Cp}^*\text{Ru}^+\text{PF}_6^-$  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  $\text{Cp}^*\text{Ru}^+\text{SbF}_6^-$  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.



**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)  $[Cp^*Ru(CH_3CN)_3PF_6]_0/[bipy]_0 = 1/1$  in  $CH_3CN$  at r.t. for 1h; (preparation of the “neutral” complex)  $[[Cp^*RuCl]_4]_0/[bipy]_0 = 1/4$  in toluene at 80 °C for 12 h.

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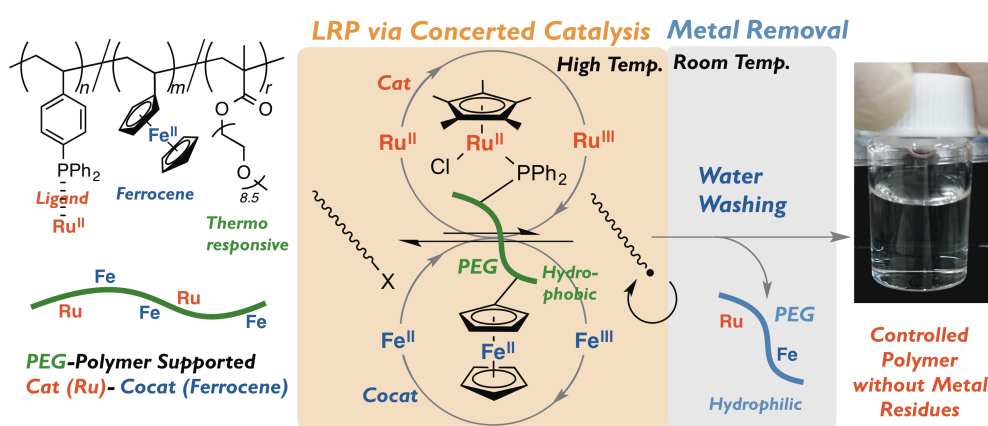


## Chapter 3

### 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 ( $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$ ). 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

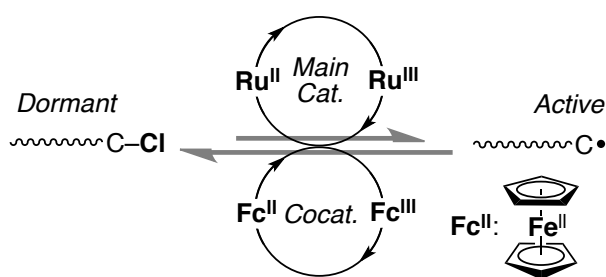
A transition metal catalyst is now one of the most powerful tools in synthesis of polymers as well as organic molecules because of its high activity and selectivity as well as its extensibility, while the difficulty in removal of metal residues is a serious problem for industrial applications. One classical idea for this problem is using polymer-supported insoluble metal catalysts, such as polystyrene (PSt)-supported catalysts.<sup>1,2</sup> Despite its practical advantage, however, insolubility often incurs loss of reaction efficiency and selectivity. The design of thermoresponsive 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.<sup>3-5</sup> 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 ( $\sim\sim\sim\text{C-X} \leftrightarrow \sim\sim\sim\text{C}\cdot$ ;  $\sim\sim\sim$ : polymer chain, X: halogen) through the one electron redox reaction of the transition metal catalyst ( $\text{Mt}^n \leftrightarrow \text{XMt}^{n+1}$ ).<sup>6-12</sup> 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.,  $\text{XMt}^{n+1}$ ), 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<sup>13-15</sup> or the reducing agent<sup>16-19</sup> is efficient to promote the catalysis for living radical polymerization.

In this context, the author has recently reported that a combination of ferrocene ( $\text{FeCp}_2$ ; Fc) allows promotion of the catalysis of ruthenium-catalyzed living radical polymerization<sup>20</sup>. Ferrocene is incapable of catalyzing living radical polymerization itself but could assist the ruthenium-based catalysis through two contributions from some mechanistic studies: (1) reduction of the trivalent ruthenium complex;  $\text{XRu}^{\text{III}} + \text{Fc}^{\text{II}} \rightarrow \text{Ru}^{\text{II}} + \text{XFc}^{\text{III}}$ , (2) halogen-capping for growing radical species by the resulting  $\text{XFc}^{\text{III}}$ ;  $\sim\sim\sim\text{C}\cdot + \text{XFc}^{\text{III}} \rightarrow \sim\sim\sim\text{C-X} + \text{Fc}^{\text{II}}$ . The author coined the ferrocene-combined system as the

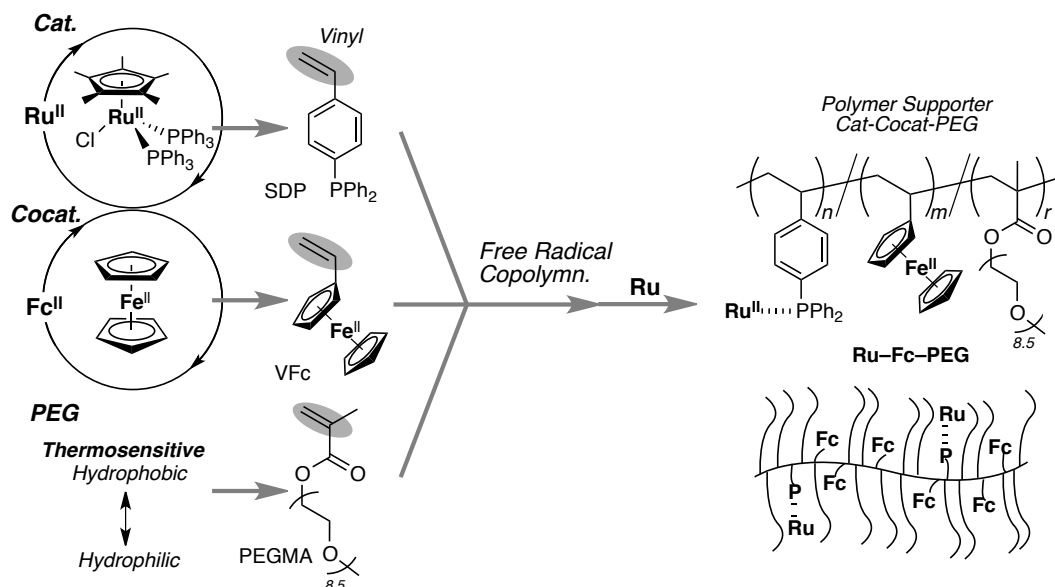


“ferrocene-concerted redox catalysis” (Figure 1), and indeed it allowed the synthesis of high molecular weight PMMA with a narrow molecular weight distribution ( $M_n \sim 1.0 \times 10^5$ ;  $M_w/M_n \sim 1.3$ ) even under really catalytic conditions with only 50 ppm (for a monomer) of the Ru main catalysts. However, toward practical applications of this system, the author has to remove the ferrocene residue as well as ruthenium from obtained polymers.



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

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.<sup>21,22</sup> 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 through ligation;<sup>23,24</sup> methacrylate carrying a PEG chain (PEGMA) to provide a thermoresponsive feature to the supporter. The ternary random copolymer (PPh<sub>3</sub>-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.



**Figure 2.** Design of the thermoresponsive polymer supporter for ferrocene-concerted redox catalysis in ruthenium-catalyzed living radical polymerization.

## Experimental Section

### Materials

MMA (TCI; purity: >99%) was dried overnight over calcium chloride and purified by distillation from calcium hydride before use. PEGMA ( $\text{CH}_2=\text{CMeCO}_2(\text{CH}_2\text{CH}_2\text{O})_n$ ; Me =  $\text{CH}_3$ ;  $n = 8.5$  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)<sub>2</sub>-Cl initiator for LRP ( $\text{H}-(\text{CH}_2\text{CMeCO}_2\text{Me})_2\text{-Cl}$ ; an MMA dimer chloride) was prepared according to the literature.<sup>25</sup>  $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$  (Aldrich), Ferrocene ( $\text{FeCp}_2$ ; Aldrich; purity >98%), and Triphenylphosphine ( $\text{PPh}_3$ ; Aldrich; purity: 99%) were used as received. A ruthenium precursor complex (chloro(pentamethylcyclopentadienyl) ruthenium(II) tetramer:  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$ ) was prepared according to the literature.<sup>26,27</sup>  $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ ,  $\text{FeCp}_2$ ,  $\text{PPh}_3$ , and  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$  were handled in a glove box under a moisture- and oxygen-free argon atmosphere ( $\text{H}_2\text{O} < 1$  ppm,  $\text{O}_2 < 1$  ppm). Tetralin (1,2,3,4-tetrahydronaphthalene; Kisida Chemical; purity: >98%) as an internal standard for  $^1\text{H}$

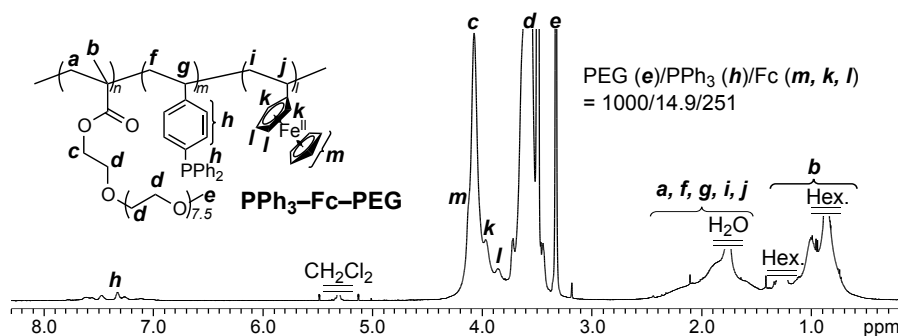
NMR was dried over calcium chloride and distilled from calcium hydride before use. Toluene as a solvent of the polymerization was purified by passing through a purification column. (Solvent Dispensing System; glass counter; HANSEN&CO., Ltd). For a solubility test of the polymer, water (Wako; distilled) 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 PPh<sub>3</sub>-Fc-PEG**

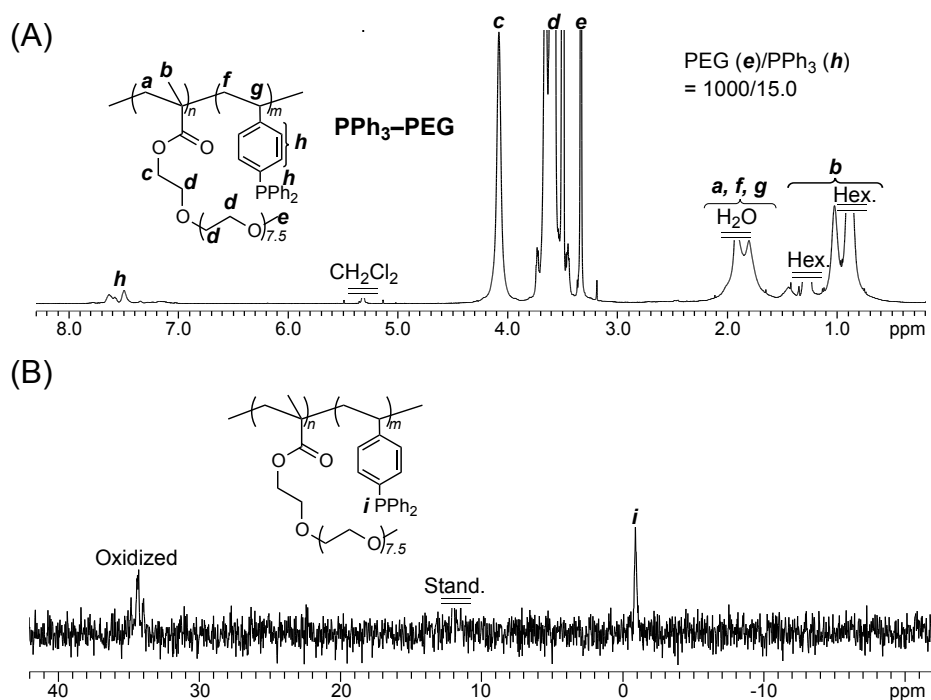
The polymer supporter (PPh<sub>3</sub>-Fc-PEG) was synthesized under argon. In a 50 mL round-bottomed flask were placed SDP (34.6 mg, 0.12 mmol), VFc (424 mg, 2.0 mmol), and AIBN (26.3 mg, 0.16 mmol). Toluene (4.1 mL), tetralin (internal standard: 0.4 mL), and PEGMA (3.5 mL, 8.0 mmol) were added sequentially 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 <sup>1</sup>H 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, PPh<sub>3</sub>-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 <sup>1</sup>H and <sup>31</sup>P NMR spectra of PPh<sub>3</sub>-Fc-PEG are shown in Figure 3 and Figure 6A respectively. The mole concentrations of the phosphine ligand ([PPh<sub>3</sub>]) and ferrocene ([Fc]) per polymer weight were determined to be 0.028 mmol/g ([PPh<sub>3</sub>]) and 0.47 mmol/g ([Fc]) respectively from the <sup>1</sup>H NMR spectrum.

### **Synthesis of PPh<sub>3</sub>-PEG**

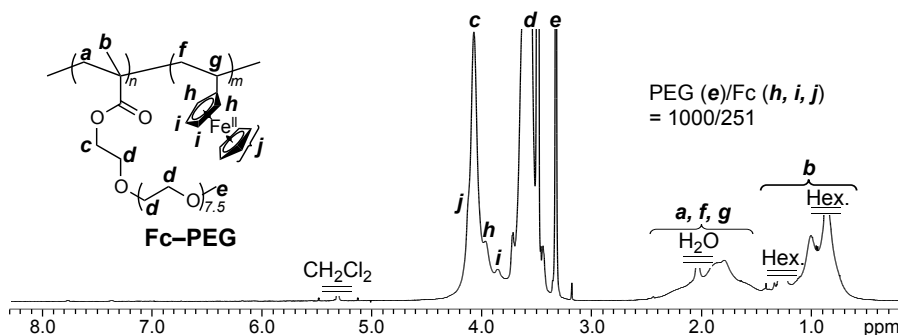
The ferrocene-free supporter (PPh<sub>3</sub>-PEG) was synthesized via free radical polymerization similar to the above procedure without using VFc: SDP (17.3 mg, 0.06 mmol), AIBN (13.1 mg, 0.08 mmol), PEGMA (1.8 mL, 4.0 mmol), tetralin (0.4 mL), and toluene (5.8 mL). After the re-precipitation procedure, PPh<sub>3</sub>-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 <sup>1</sup>H and <sup>31</sup>P NMR spectra of PPh<sub>3</sub>-PEG are shown in Figure 4. The mole concentration of the phosphine ligand ([PPh<sub>3</sub>]) per polymer weight was determined to be 0.031 mmol/g from the <sup>1</sup>H NMR spectrum.



**Figure 3.**  $^1\text{H}$  NMR spectrum of  $\text{PPh}_3\text{-Fc-PEG}$  in  $\text{CD}_2\text{Cl}_2$  at room temperature.



**Figure 4.** (A)  $^1\text{H}$  (in  $\text{CD}_2\text{Cl}_2$ ), and (B)  $^{31}\text{P}$  NMR (in  $\text{CDCl}_3$ ) spectrum of  $\text{PPh}_3\text{-PEG}$  at room temperature.



**Figure 5.**  $^1\text{H}$  NMR spectrum of  $\text{Fc-PEG}$  in  $\text{CD}_2\text{Cl}_2$  at room temperature.

### Synthesis of Fc-PEG

The phosphine-free supporter (Fc-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, PPh<sub>3</sub>-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 <sup>1</sup>H NMR spectrum of Fc-PEG is shown in Figure 5. The concentration of ferrocene ([Fc]) per polymer weight was determined to be 0.47 mmol/g from the <sup>1</sup>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)<sub>2</sub>-Cl/Ru-Fc-PEG is given below. [Ru(Cp\*)Cl]<sub>4</sub> (1.7 mg, 0.002 mmol), a  $400 \times 10^{-3}$  g/mL toluene solution of PPh<sub>3</sub>-Fc-PEG (1.7 mL, 0.019 mmol of the PPh<sub>3</sub> 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)<sub>2</sub>-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 <sup>1</sup>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<sup>-1</sup>) 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;  $M_n = 620\text{--}1\,200\,000$ ;  $M_w/M_n = 1.06\text{--}1.22$ ) as well as the monomer. For  $\text{PPh}_3\text{--Fc--PEG}$ ,  $\text{PPh}_3\text{--PEG}$ , and  $\text{Fc--PEG}$ ,  $M_n$  and  $M_w/M_n$  were measured by size exclusion chromatography at  $40\text{ }^\circ\text{C}$  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 =  $5000\text{ \AA}$ ;  $0.8\text{ cm i.d.} \times 30\text{ cm}$ ; flow rate,  $1.0\text{ mL min}^{-1}$ ) 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;  $M_n = 630\text{--}1\,200\,000$ ;  $M_w/M_n = 1.02\text{--}1.30$ ) as well as the monomer.  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectra were recorded in  $\text{CD}_2\text{Cl}_2$  and  $\text{CDCl}_3$  at room temperature on a JEOL JNM-ECA500 spectrometer, operating at 500.16 MHz and 202.47 MHz, respectively. For the  $^{31}\text{P}$  NMR analysis, a capillary of the  $(\text{C}_2\text{H}_5\text{O})_2\text{POH}$  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

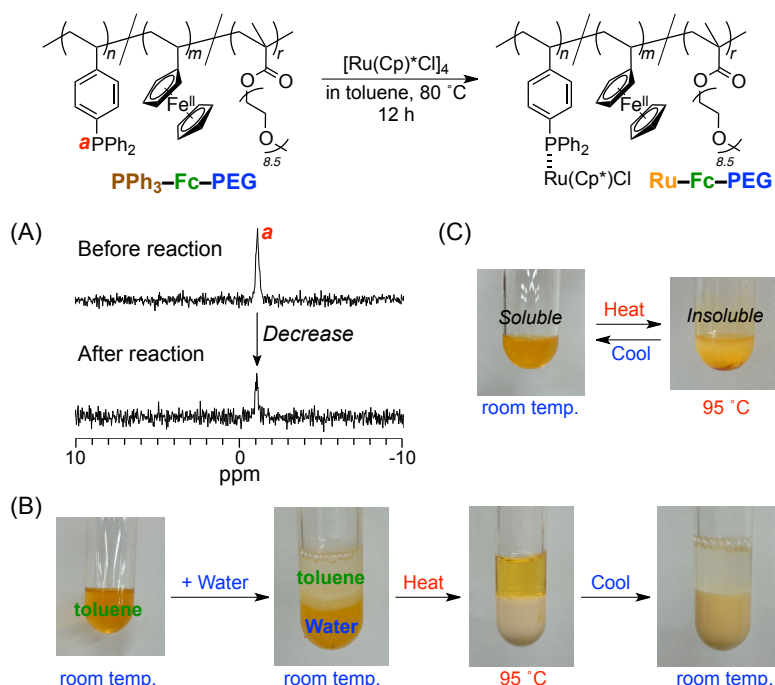
### 1. Synthesis of $\text{PPh}_3\text{--Fc--PEG}$

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

### 2. Ru–Fc–PEG: thermoresponsive polymer catalyst

A tetrameric  $\text{Cp}^*\text{-ligated}$  ruthenium complex  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$  can accept phosphine based ligands ( $\text{PR}_3$ ) by just mixing to give coordinatively saturated (18e) or unsaturated (16e) complexes ( $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PR}_3)_n$ ;  $n = 1, 2$ ), which are well known to be useful for living radical

polymerization.<sup>15</sup> A mixture solution of  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$  and  $\text{PPh}_3\text{-Fc-PEG}$  in toluene ( $[\text{Ru}]_0/[\text{PPh}_3 \text{ in } \text{PPh}_3\text{-Fc-PEG}]_0 = 1/2.4$ ; a little excess  $\text{PPh}_3$  was mixed to perfectly promote complexation) was stirred at  $80^\circ\text{C}$  for 12 h. From the  $^{31}\text{P}$  NMR spectra, the signal at  $-1$  ppm originating from the  $\text{PPh}_3$  pendant on the polymer was clearly decreased upon mixing with  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$  (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  $\text{PPh}_3$  on the polymer supporter, which was also reported with other polymer-supported Ru catalysts.<sup>23,24,28</sup>



**Figure 6.** Synthesis of Ru-Fc-PEG ( $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4/[\text{PPh}_3 \text{ in polymer}]_0 = 0.25/2.4$  mM in toluene at  $80^\circ\text{C}$ ) and its thermoresponsive solubility: (A)  $^{31}\text{P}$  NMR spectra (in  $\text{CDCl}_3$ ) for Ru introduction reaction (upper: before reaction ( $\text{PPh}_3\text{-Fc-PEG}$ ); lower: after reaction ( $\text{Ru-Fc-PEG}$ )); (B) thermoresponsive phase transfer behavior of Ru-Fc-PEG in a toluene/water biphasic solution; (C) thermoresponsive solubility of Ru-Fc-PEG in water.

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

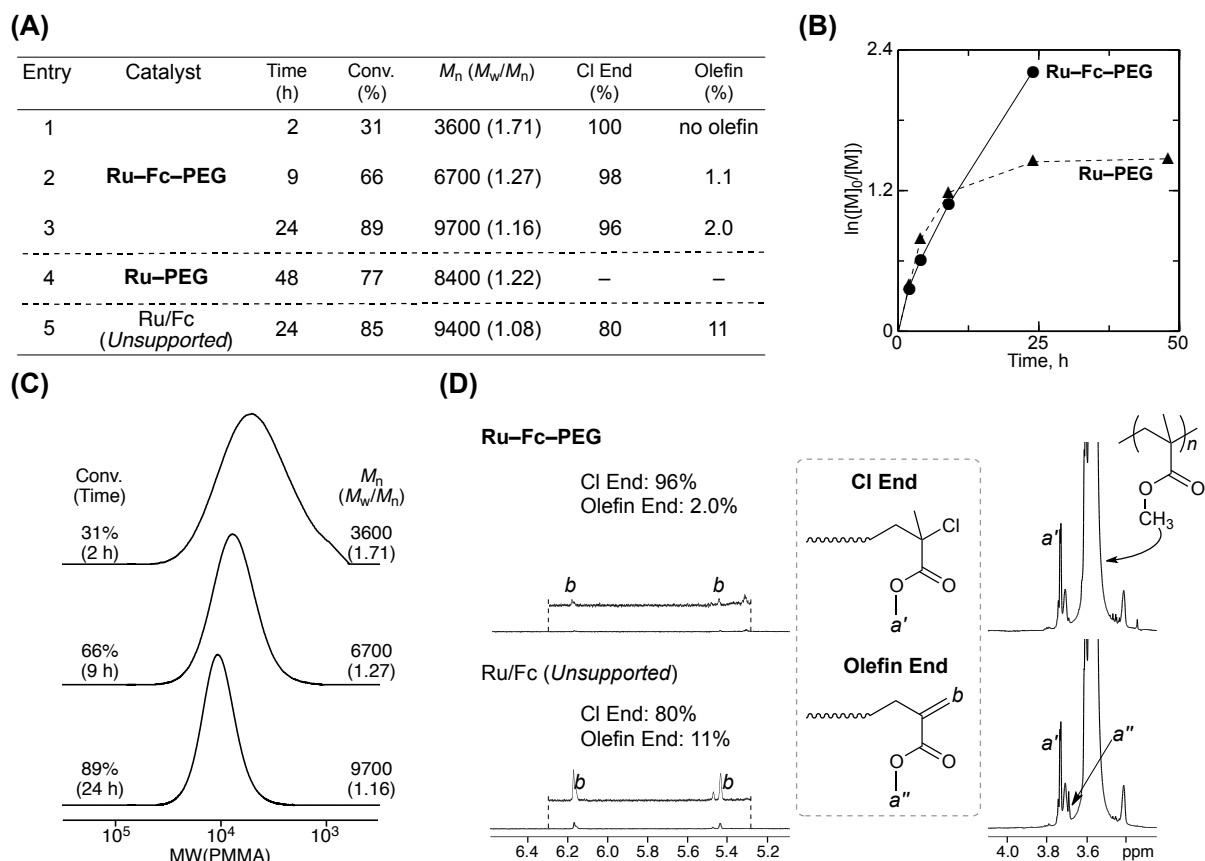
lower phase (water: Figure 6B), indicating the preference of the polymer for water rather than hydrophobic solvent at room temperature. Once the bilayer was heated up to 95 °C that is higher than reported LCST of the PEGMA homopolymer ( $\sim 90^\circ\text{C}$ ),<sup>29</sup> the color moved to the upper 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  $[\text{H}-(\text{MMA})_2-\text{Cl}]$  in toluene at 100 °C:  $[\text{MMA}]_0 = 4.0 \text{ M}$ ,  $[\text{H}-(\text{MMA})_2-\text{Cl}]_0 = 40 \text{ mM}$ ,  $[\text{Ru}]_0 = 1.0 \text{ mM}$ ,  $[\text{FeCp}_2 (\text{Fc}) \text{ in polymer}]_0 = 40 \text{ mM}$  (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.<sup>23,24</sup>

By comparison, the unsupported catalyst was also examined under the same conditions. The ruthenium catalyst was prepared by mixing  $[\text{Ru}(\text{Cp}^*)\text{Cl}]_4$  with  $\text{PPh}_3$  at the same ratio as with  $\text{PPh}_3\text{-Fc-PEG}$  ( $[\text{Ru}]_0/[\text{PPh}_3]_0 = 1/2.4$ ). It was, then, employed in conjunction with  $\text{FeCp}_2$  for the MMA polymerization.

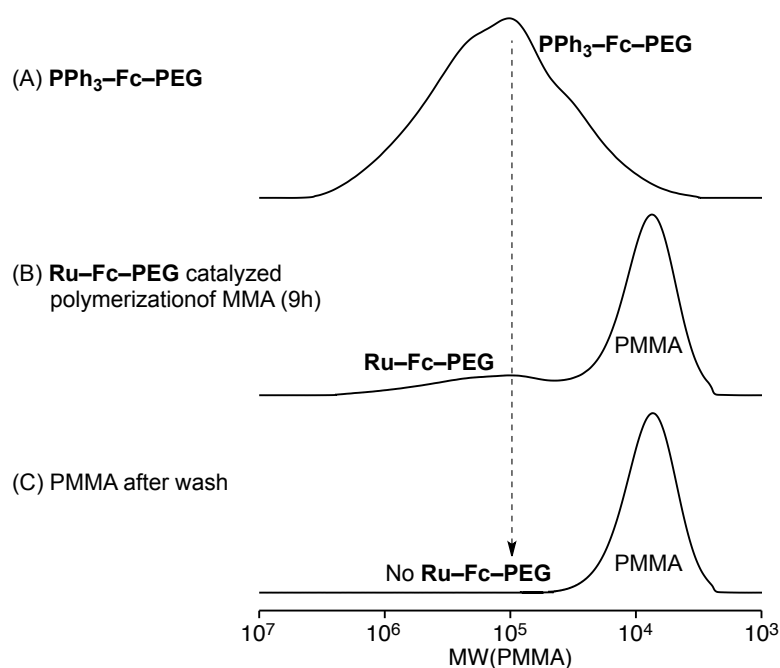




**Figure 7.** Ru-Fc-PEG catalyzed living radical polymerization of MMA and comparison with Ru-PEG and unsupported systems (Ru/Fc) ( $[MMA]_0/[H-(MMA)_2-Cl]_0/[Ru]_0/[Fc]_0 = 4000/40/1.0/40$  mM in toluene at 100 °C): A) fundamental data of polymerizations; B) kinetic plots of  $\ln([M]_0/[M])$  vs time; C) SEC curves of PMMAs obtained with Ru-Fc-PEG; D)  $^1H$  NMR spectra (in  $CDCl_3$ ) of PMMAs obtained with Ru-Fc-PEG (upper) and Ru/Fc unsupported systems (lower).

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,  $^1H$  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



**Figure 8.** Removal of the Ru-Fc-PEG polymer catalyst from the obtained PMMA by washing with water: SEC curves of PPh<sub>3</sub>-Fc-PEG (A), the solution of Ru-Fc-PEG catalyzed polymerization of MMA for 9 h (see Figure 7A, entry 2; B), and the obtained PMMA after washing with water (C).

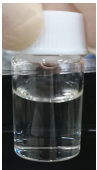
radical species by XFc<sup>III</sup> and/or XRu<sup>III</sup> on the supporter. It is interesting that the polymer-support showed a positive effect in addition to the expected function as described below.

#### 4. Catalyst removability

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.<sup>30,31</sup>

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.

|                            | (A)                                                                                | (B)                                                                                | (C)                                                                                 | (D)                                                                                  |
|----------------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| Catalyst                   | Ru-Fc-PEG                                                                          | Ru-PEG + Fc                                                                        | Ru + Fc-PEG                                                                         | Ru + Fc                                                                              |
| Washed PMMA                |  |  |  |  |
| Residual Ru (Removability) | 5.7 ppm<br>(99.8%)                                                                 | 29 ppm<br>(89.9%)                                                                  | 100 ppm<br>(63.9%)                                                                  | 200 ppm<br>(29.6%)                                                                   |
| Residual Fe (Removability) | 89 ppm<br>(98.5%)                                                                  | 2600 ppm<br>(59.0%)                                                                | 280 ppm<br>(95.4%)                                                                  | 2700 ppm<br>(56.9%)                                                                  |

**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.

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- (29) Lutz, J.-F. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, 46, 3459-3470.
- (30) The removability of ruthenium ( $Ru_{\text{remov}}$ ) was calculated as  $Ru_{\text{remov}} = 1 - (\text{Residual Ru from ICP-AES}) / (\text{Weight of the initially added Ru in 1g of PMMA; } Ru_{\text{init}})$ , where  $Ru_{\text{init}}$  was calculated as  $Ru_{\text{init}} = (101.07 \text{ g/mol}) \cdot (\text{Ru feed on polymerization, mM}) / (100.12 \text{ g/mol}) \cdot (\text{MMA feed on polymerization, mM}) \cdot (\text{Monomer Conversion})$ .
- (31) The removability of iron ( $Fe_{\text{remov}}$ ) was calculated as  $Fe_{\text{remov}} = 1 - (\text{Residual Fe from ICP-AES}) / (\text{Weight of the initially added Fe in 1g of PMMA; } Fe_{\text{init}})$ , where  $Fe_{\text{init}}$  was calculated as  $Fe_{\text{init}} = (55.845 \text{ g/mol}) \cdot (\text{Fe feed on polymerization, mM}) / (100.12 \text{ g/mol}) \cdot (\text{MMA feed on polymerization, mM}) \cdot (\text{Monomer Conversion})$ .



## **PART II**

### **Iron/Ferrocene Concerted Redox Catalysis: “All-Iron” Catalysis**





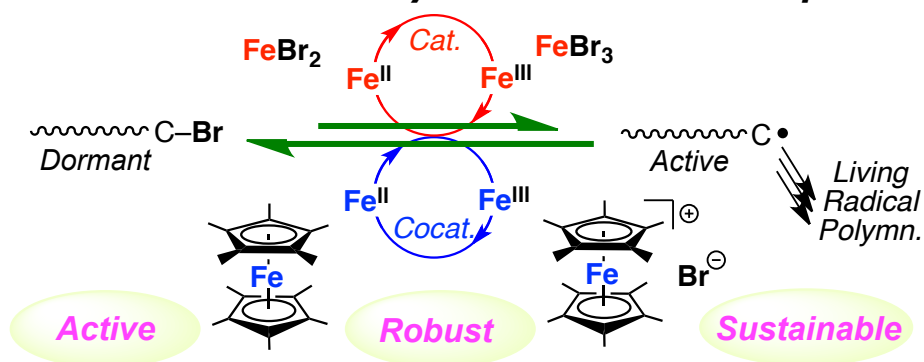
## Chapter 4

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

### Abstract

Decamethylferrocene ( $\text{FeCp}^*_2$ ) was found to be an effective cocatalyst for metal-catalyzed living radical polymerization with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  as the main catalyst. For polymerization of methyl methacrylate (MMA) with a bromine-type initiator, the conversion was limited in the absence of  $\text{FeCp}^*_2$ , whereas the polymerization was apparently promoted up to higher conversion ( $\sim 90\%$ ) upon combination with  $\text{FeCp}^*_2$ . 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  $\text{FeCp}^*_2$  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  $\text{FeCp}^*_2$ -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.

### Concerted Redox Catalysis with Two Iron Complexes



## Introduction

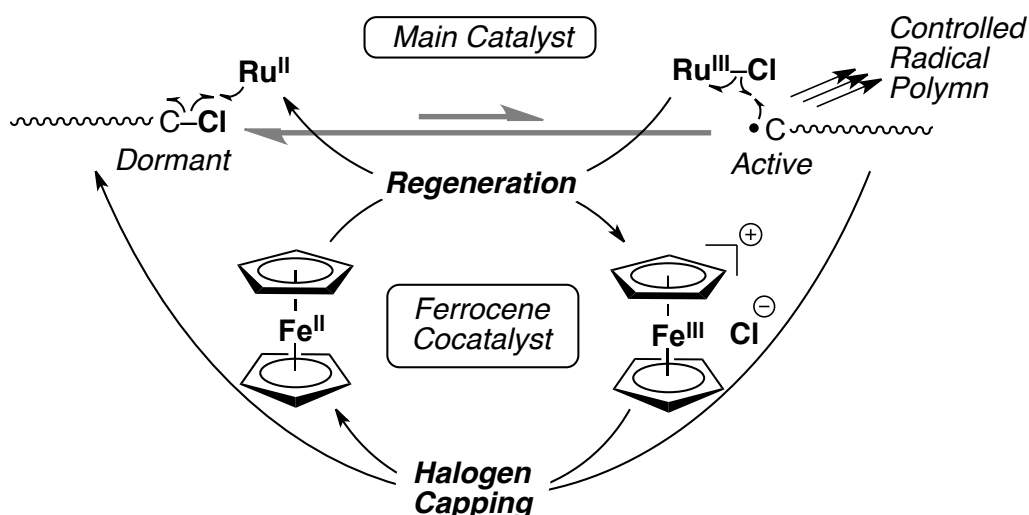
Metal-catalyzed living radical polymerization (Mt-LRP)<sup>1-8</sup> has become the most powerful tool to synthesize controlled polymers with well-defined primary structures (e.g., molecular weight, its distribution, and terminal structures) and to construct desired architectures (e.g., block, graft, and star). In Mt-LRP, transition metal complexes catalyze the reversible activation of a carbon-halogen bond at the growing end ( $\sim\text{C-X}$ ;  $\sim\sim$  = polymer chain, X = halogen) through the one-electron-redox reaction ( $\text{Mt}^n \leftrightarrow \text{XMt}^{n+1}$ ; Mt = metal) to allow suppression of irreversible side reactions. The polymerization controllability is dependent on the reversibility between dormant ( $\sim\sim\text{C-X}$ ) and active species ( $\sim\sim\text{C}^\bullet$ ), 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,<sup>9</sup> copper,<sup>10</sup> iron,<sup>11</sup> nickel,<sup>12,13</sup> and other late transition metals. Among these metals, ruthenium complexes are known as active catalysts<sup>1-3</sup> as well as copper derivatives, and versatile ligand designs have allowed modulation of the catalysis depending on requirements for polymerization.<sup>14-28</sup> 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  $\text{FeCl}_2(\text{PPh}_3)_2$ ,<sup>11</sup> some types of iron catalysts have been developed with various ligands, such as phosphines, amines, imines, carbenes, cyclopentadiene, etc.<sup>29-69</sup> 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.<sup>42,65,67</sup>

Ferrocene ( $\text{FeCp}_2$ ), where two cyclopentadienyl (Cp) ligands sandwich an iron ( $\text{Fe}^{\text{II}}$ ) atom,<sup>70,71</sup> is known as a typical iron complex showing redox property ( $\text{Fe}^{\text{II}} \leftrightarrow \text{Fe}^{\text{III}}$ ) 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.<sup>72</sup> 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  $\text{Ru}^{\text{II}}$  complex through reduction of oxidized ruthenium ( $\text{XRu}^{\text{III}}$ ) but also halogen-capping reaction for growing radical species by ferrocenium halide ion ( $\text{Fe}^{\text{III}}\text{Cp}_2\text{X}^-$ ) that is accordingly given from  $\text{FeCp}_2$  through the reduction of  $\text{XRu}^{\text{III}}$ . The author has thus

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 ( $\text{FeCp}^*_2$ ) was effective as the cocatalyst in conjunction with iron halide and ammonium salt (i.e.,  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$ ) 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 ( $\text{CH}_2=\text{CMeCO}_2(\text{CH}_2\text{CH}_2\text{O})_n$ ; Me =  $\text{CH}_3$ ;  $n = 8.5$  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)<sub>2</sub>-Br) was prepared according to the literature.<sup>73</sup> The EBPA initiator (ethyl-2-bromo-2-phenylacetate) (Aldrich; purity 97%) was purified by distillation under reduced pressure before use. Iron(II) bromide (FeBr<sub>2</sub>) (Aldrich; purity >98%), iron(III) bromide (FeBr<sub>3</sub>) (Aldrich; purity 98%), ferrocene (FeCp<sub>2</sub>) (Aldrich; purity >98%), decamethylferrocene (FeCp\*<sub>2</sub>) (Aldrich; purity 97%), tetrabutylammonium bromide (*n*-Bu<sub>4</sub>NBr) (TCI; purity >99%), and tetrabutylammonium hexafluorophosphate (*n*-Bu<sub>4</sub>NPF<sub>6</sub>) (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<sub>2</sub>O <1 ppm; O<sub>2</sub> <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 <sup>1</sup>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)<sub>2</sub>-Br/FeBr<sub>2</sub>/*n*-Bu<sub>4</sub>NBr/FeCp\*<sub>2</sub> was as follows. In a 50 mL round-bottomed flask were placed FeBr<sub>2</sub> (8.7 mg, 0.040 mmol), *n*-Bu<sub>4</sub>NBr (12.9 mg, 0.040 mmol), and FeCp\*<sub>2</sub> (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)<sub>2</sub>-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 <sup>1</sup>H NMR spectroscopy from the integrated peak area of olefinic protons of monomer with tetralin as an internal standard.

## 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  $\mu\text{m}$ ; pore size = 3000 Å; 0.46 cm i.d.  $\times$  25 cm; flow rate, 0.3 mL min<sup>-1</sup>) 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 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.  $\times$  30 cm; flow rate, 1.0 mL min<sup>-1</sup>) 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;  $M_n$  = 630–1 200 000;  $M_w/M_n$  = 1.02–1.30) as well as the monomer. <sup>1</sup>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\*<sub>2</sub> is described. FeCp\*<sub>2</sub> (13.1 mg, 0.040 mmol) and a solution of *n*-Bu<sub>4</sub>NPF<sub>6</sub> (supporting electrolyte) in ClCH<sub>2</sub>CH<sub>2</sub>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 Vs<sup>-1</sup> 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<sup>+</sup> electrode (reference electrode) from BAS Inc.

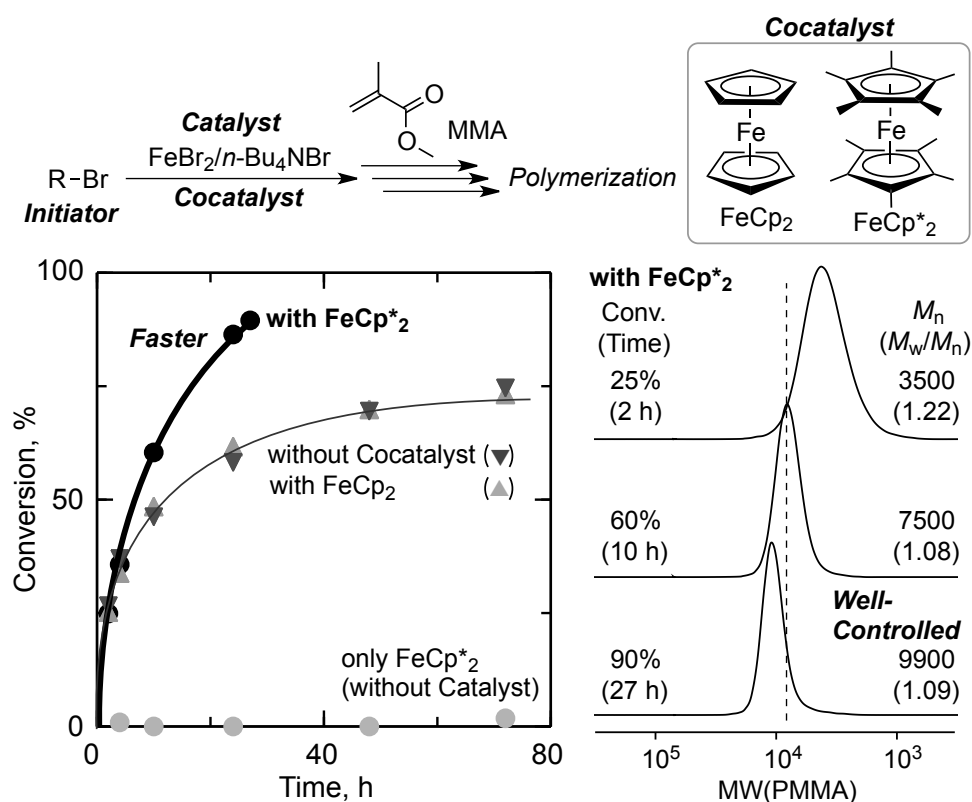
## Results and Discussion

### 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<sub>2</sub> with ammonium salt (*n*-Bu<sub>4</sub>NBr)<sup>38,45,60</sup> 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<sup>III</sup>) 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;<sup>38</sup> the combined ammonium salt might contribute to ferrocene cocatalysis through stabilization of ferrocenium ion ( $\text{Fe}^{\text{III}}$ ) as a halogen anion supplier, as speculated in ruthenium/ferrocene-concerted system.<sup>72</sup> Thus,  $\text{FeCp}_2$  was combined with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  for polymerization of MMA in conjunction with  $\text{H-(MMA)}_2\text{-Br}$  as an initiator (in THF at 60 °C: Figure 1).

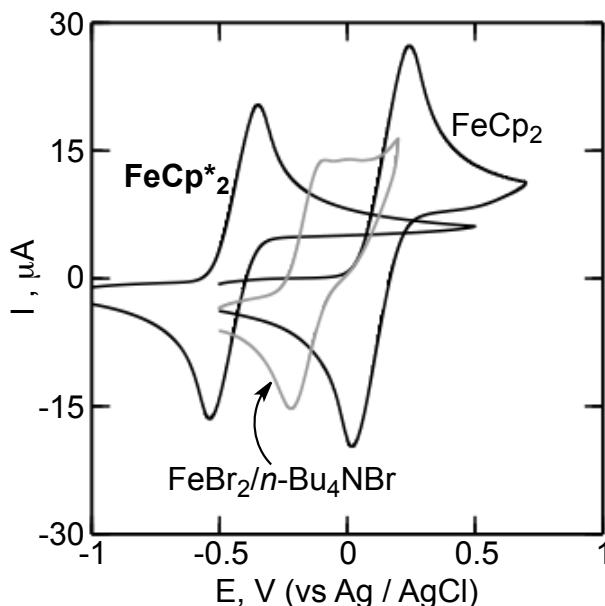
Contrary to our expectation, no effects of the combination with  $\text{FeCp}_2$  were observed on polymerization behaviors such as polymerization rate, molecular weights, and its distributions. However, when  $\text{FeCp}_2$  was replaced with the derivative, decamethylferrocene ( $\text{FeCp}^*_2$ :  $\text{Cp}^*$  = 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  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$ :  $[\text{MMA}]_0/[\text{H-(MMA)}_2\text{-Br}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0/[\text{ferrocene}]_0 = 4000/40/10/10/40$  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  $\text{FeCp}^*_2$  as the catalyst resulted in no polymerization, indicating  $\text{FeCp}^*_2$  itself is incapable to catalyze the polymerization.

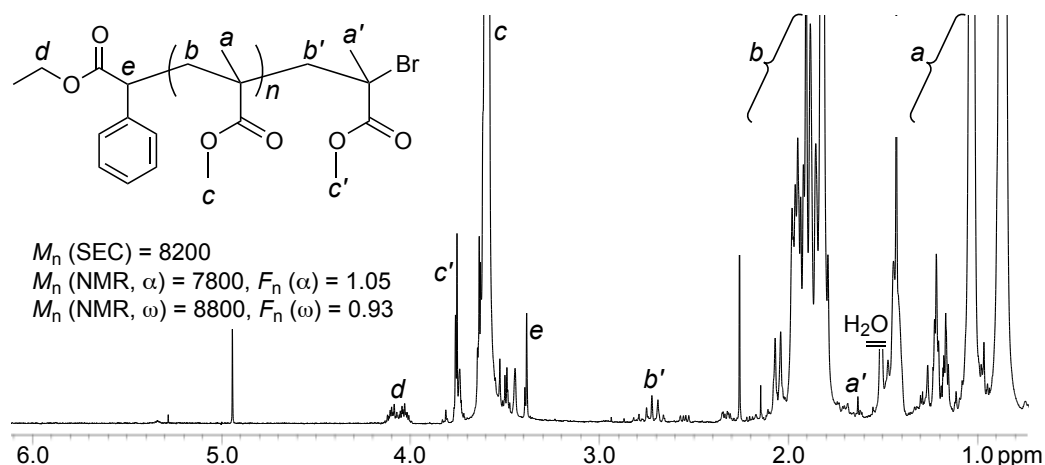
As shown above, the decamethylferrocene successfully promoted the living radical polymerization with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  as the cocatalyst, whereas the normal ferrocene showed no effects on the catalysis. It was conceivable that the clear difference in the catalysis is related to relationship of the redox potential between main catalyst and cocatalyst. Thus, cyclic voltammetry (CV) was measured to compare redox potential among  $\text{FeBr}_2$  (with  $n\text{-Bu}_4\text{NBr}$ ),  $\text{FeCp}_2$ , and  $\text{FeCp}^*_2$  in the presence of  $n\text{-Bu}_4\text{NPF}_6$  as the supporting electrolyte. The redox potential of  $\text{FeCp}^*_2$  was apparently lower than  $\text{FeCp}_2$ , as predicted by the structure: the electron density of the iron center is richer due to the electron donation by decamethyl substituents.<sup>74</sup> Interestingly, the redox curve of  $\text{FeBr}_2$  was observed between the two ferrocenes: the redox potential of  $\text{FeCp}^*_2$  was lower than that of  $\text{FeBr}_2$ , whereas  $\text{FeCp}_2$  of no effect showed higher redox potential (Figure 2). Thus, lower redox potential than the main catalyst (i.e.,  $\text{FeBr}_2$ ) is probably one of requisites as the cocatalysis for the concerted catalysis.



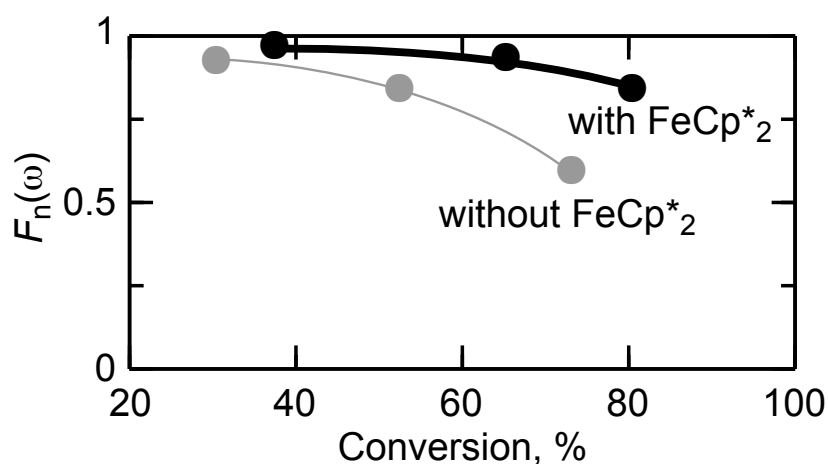
**Figure 2.** Cyclic voltammograms of  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  and ferrocene cocatalysts ( $\text{FeCp}_2$  and  $\text{FeCp}^*_2$ ) with  $n\text{-Bu}_4\text{NPF}_6$  as supporting electrolyte:  $[\text{iron complex}]_0/[\text{n-Bu}_4\text{NPF}_6]_0 = 5.0/100$  mM in  $\text{ClCH}_2\text{CH}_2\text{Cl}$  at 25 °C.

## 2. End Functionality Analysis

To evaluate the nature of living polymerization with the  $\text{FeCp}^*_2$ -assisted catalysis, we examined the terminal structure of obtained PMMA by  $^1\text{H}$  NMR spectroscopy. Figure 3 shows the  $^1\text{H}$  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  $\alpha$ -end functionality.



**Figure 3.**  $^1\text{H}$  NMR spectrum (in  $\text{CDCl}_3$ ) of PMMA obtained with EBPA/ $\text{FeBr}_2$ / $n\text{-Bu}_4\text{NBr}$ / $\text{FeCp}^*_2$  in THF at 60 °C;  $[\text{MMA}]_0/[\text{EBPA}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 4000/40/10/10/40$  mM.



**Figure 4.** Effects of  $\text{FeCp}^*_2$  on  $\omega$ -end functionalities  $[F_n(\omega)]$ s of obtained PMMAs:  $[\text{MMA}]_0/[\text{EBPA}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 4000/40/10/10/40$  or 0 mM in THF at 60 °C.



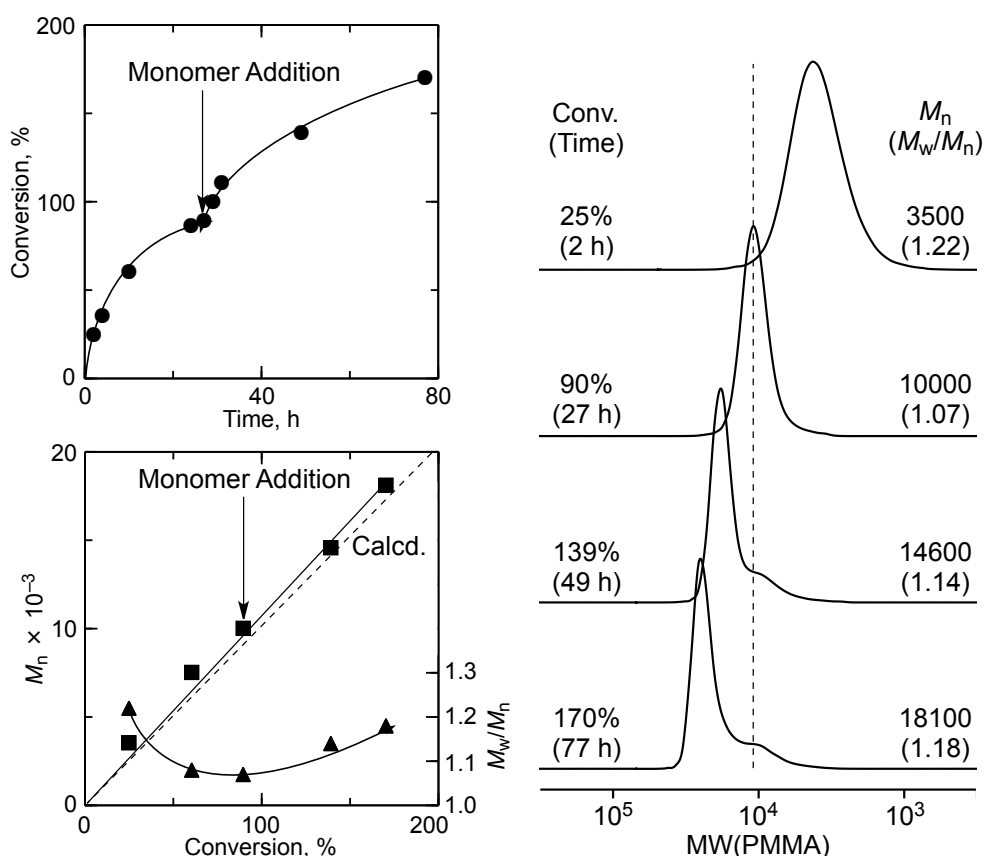
In addition to the characteristic signals of the main chain (*a-c*), some minor signals were detected from the end groups. The terminal-related peaks are identified as shown in Figure 3: *d* and *e* from the  $\alpha$ -end: *a'*, *b'*, and *c'* from the  $\omega$ -end. On the assumption that all chains carry the end group,  $M_n$  (NMR) can be calculated from integration ratios of the minor peaks from either  $\alpha$ - or  $\omega$ -end to main ones [ $M_n$  (NMR,  $\alpha$ ) and  $M_n$  (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  $\omega$ -end functionalities [ $F_n(\omega)$ s] at different conversions were examined and compared with those obtained in the absence of FeCp\*<sub>2</sub>. 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\*<sub>2</sub> was clearly higher than in the absence of FeCp\*<sub>2</sub>. The difference between the two systems was remarkable especially at the latter polymerization stage:  $F_n(\omega)$  with FeCp\*<sub>2</sub> = 0.84 at 80% conversion;  $F_n(\omega)$  without FeCp\*<sub>2</sub> = 0.61 at 73%. The higher end-group functionality would be due to more effective halogen capping reaction, as speculated in the ruthenium-catalyzed system<sup>72</sup> (discussed later).

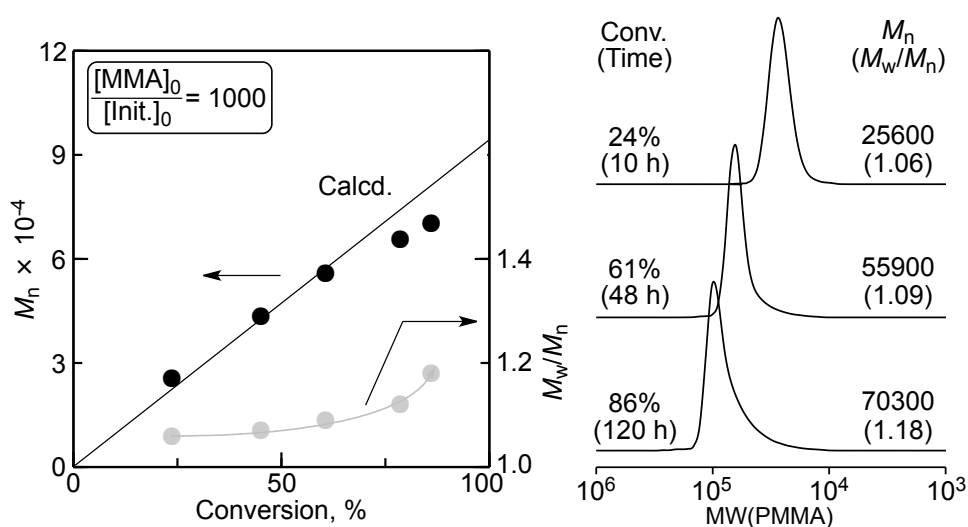
### 3. High Catalytic Activity: Monomer Addition and Synthesis of Higher Molecular Weight Polymer

To ensure the high catalytic activity and controllability of the concerted catalysis with FeCp\*<sub>2</sub>, 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:  $[MMA]_0/[H-(MMA)_2-Br]_0/[FeBr_2]_0/[n-Bu_4NBr]_0$



**Figure 5.** Monomer addition experiments in the polymerization of MMA with  $\text{FeCp}^*_2$ :  $[\text{MMA}]_0/[\text{MMA}]_{\text{add}}/[\text{H}-(\text{MMA})_2\text{-Br}]_0/[\text{FeBr}_2]_0/[\text{n-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 4000/4000/40/10/10/40$  mM in THF at 60 °C.

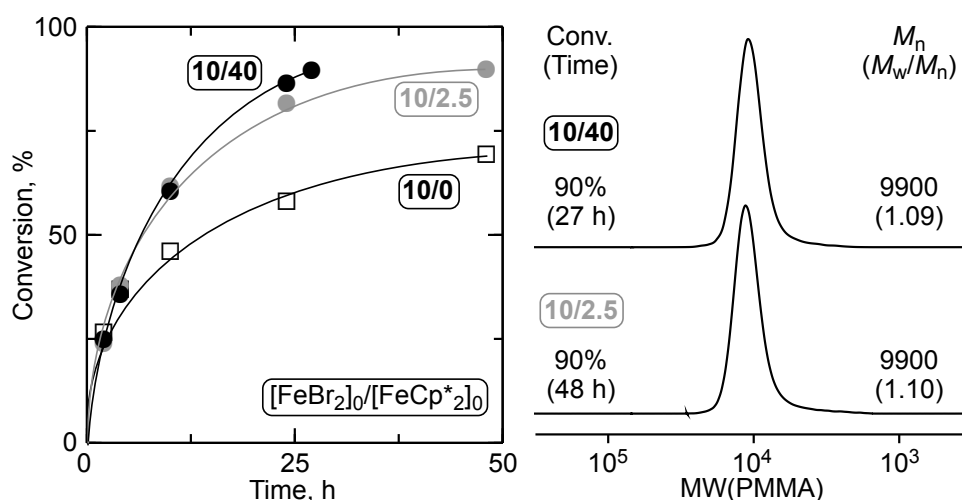


**Figure 6.** Synthesis of higher molecular weight PMMAs with  $\text{FeCp}^*_2$ :  $[\text{MMA}]_0/[\text{H}-(\text{MMA})_2\text{-Br}]_0/[\text{FeBr}_2]_0/[\text{n-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 5000/5.0/5.0/5.0/20$  mM in THF at 60 °C.

$[\text{FeCp}^*_2]_0 = 5000/5.0/5.0/5.0/20 \text{ mM}$ ). 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  $\text{FeCp}^*_2$  was certainly high in comparisons with conventional iron catalysts.

#### 4. Polymerization with Catalytic Amount of $\text{FeCp}^*_2$

Given that the plausible cocatalysis by  $\text{FeCp}^*_2$  contributing to both “regeneration of catalyst” and “halogen capping reaction” as shown in Scheme 1,  $\text{FeCp}^*_2$  would be capable of working “catalytically”. Thus, polymerization with lower amount of  $\text{FeCp}^*_2$  was tested to see effects on polymerization results (Figure 7).



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

Even when the amount of  $\text{FeCp}^*_2$  was decreased from 40 to 2.5 mM for the main catalyst ( $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$ , 10 mM each), the polymerization was apparently faster than the case without  $\text{FeCp}^*_2$  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  $\text{FeCp}^*_2$  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  $\text{FeCp}^*_2$  would indicate that  $\text{FeCp}^*_2$  is regenerated after reduction of  $\text{Fe(III)}$  catalyst to contribute to promotion of catalysis. One plausible explanation is that the higher oxidized ferrocene ( $\text{FeCp}^*_2\text{Br}$ ) that would be generated through reduction of  $\text{Fe(III)}$  catalyst could undergo halogen capping reaction for growing radical species to regenerate  $\text{FeCp}^*_2$ , as speculated with the combination of  $\text{Ru(II)}$  and  $\text{FeCp}_2$  (see Scheme 1).

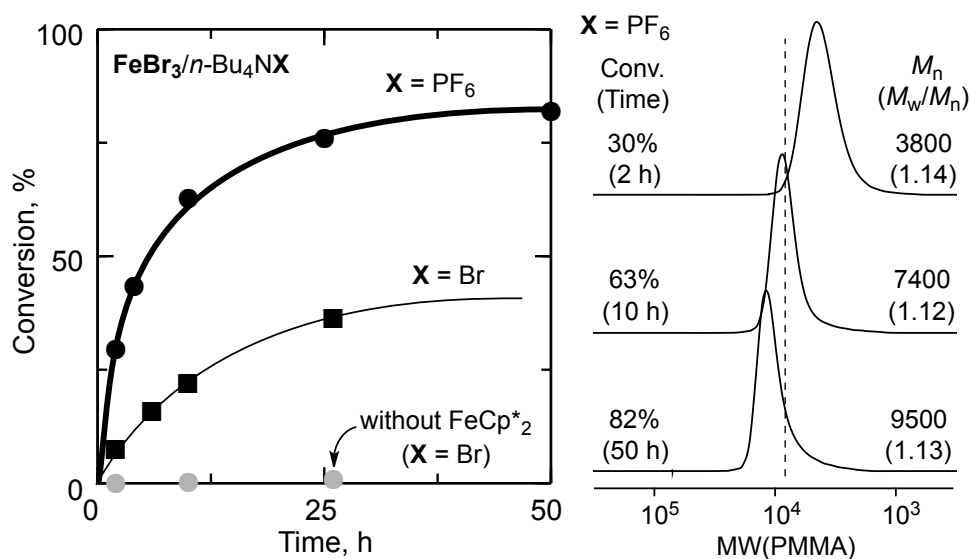
## 5. Polymerization with $\text{FeBr}_3$ as the Starting Main Catalyst

$\text{FeCp}^*_2$  as a reductant for higher oxidation state iron ( $\text{Fe}^{\text{III}}$ ) to be reduced to one-electron lower ( $\text{Fe}^{\text{II}}$ ) in the concerted catalysis would allow use of  $\text{FeBr}_3$  as the starting catalyst instead of  $\text{FeBr}_2$ . The system using  $\text{FeBr}_3$  and  $\text{FeCp}^*_2$  would be more ideal from a practical viewpoint, since the both complexes are stable and easily handled.

Thus,  $\text{FeBr}_3$  was employed as the starting catalyst for the MMA polymerization in conjunction with ammonium salt ( $n\text{-Bu}_4\text{NBr}$ ) and an initiator ( $\text{H-(MMA)}_2\text{-Br}$ ; Figure 8). Without  $\text{FeCp}^*_2$ , no polymerization occurred, whereas a combination with  $\text{FeCp}^*_2$  induced monomer consumption to yield polymer. This result would indicate that  $\text{FeCp}^*_2$  reduced  $\text{FeBr}_3$  into  $\text{FeBr}_2$  capable of activating the C-Br bond.

However, the polymerization was very slow (49% in 72 h). In this system,  $\text{FeBr}_3$  could exist in complex salt  $[n\text{-Bu}_4\text{N}]^+[\text{Br-FeBr}_3]^-$  in the presence of  $n\text{-Bu}_4\text{NBr}$ <sup>45</sup> and anion exchange with the ferrocenium halide salt  $[\text{FeCp}^*_2]^+[\text{Br}]^-$ , which is generated as a result of the reduction of  $\text{FeBr}_3$ , may give more stable salt,  $[\text{FeCp}^*_2]^+[\text{Br-FeBr}_3]^-$ , along with  $[n\text{-Bu}_4\text{N}]^+[\text{Br}]^-$ .<sup>76</sup> The slow polymerization is probably due to the in-situ formation of the stable complex salt,<sup>75</sup> resulting in freeze of the dynamic transformation. Thus, both catalysts ( $\text{FeBr}_3$  and  $[\text{FeCp}^*_2]^+[\text{Br}]^-$ ) were gradually trapped into this stable complex salt, leading to loss of the catalytic activity. When  $\text{FeBr}_2$  is used as the starting catalyst, the transformation into the stable salt is probably negligible because the amount of  $\text{FeBr}_3$  is lower.

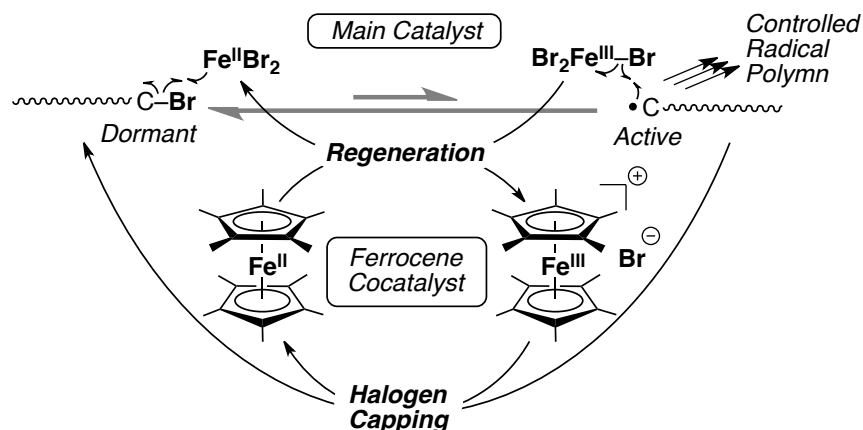
To solve the problem of slow polymerization,  $n\text{-Bu}_4\text{NPF}_6$  was used as the ammonium salt instead of  $n\text{-Bu}_4\text{NBr}$ . As a result, polymerization was accelerated without any serious loss of the precision control (82% MMA conversion in 50 h;  $M_n = 9500$ ;  $M_w/M_n = 1.13$ ). The use of hexafluorophosphate salt would generate the corresponding ferrocenium ion ( $[\text{FeCp}^*_2]^+[\text{PF}_6]^-$ ),<sup>74,77</sup> which may be a little more reactive than  $[\text{FeCp}^*_2]^+[\text{Br-FeBr}_3]^-$ , leading to dynamic equilibrium between dormant and active species.



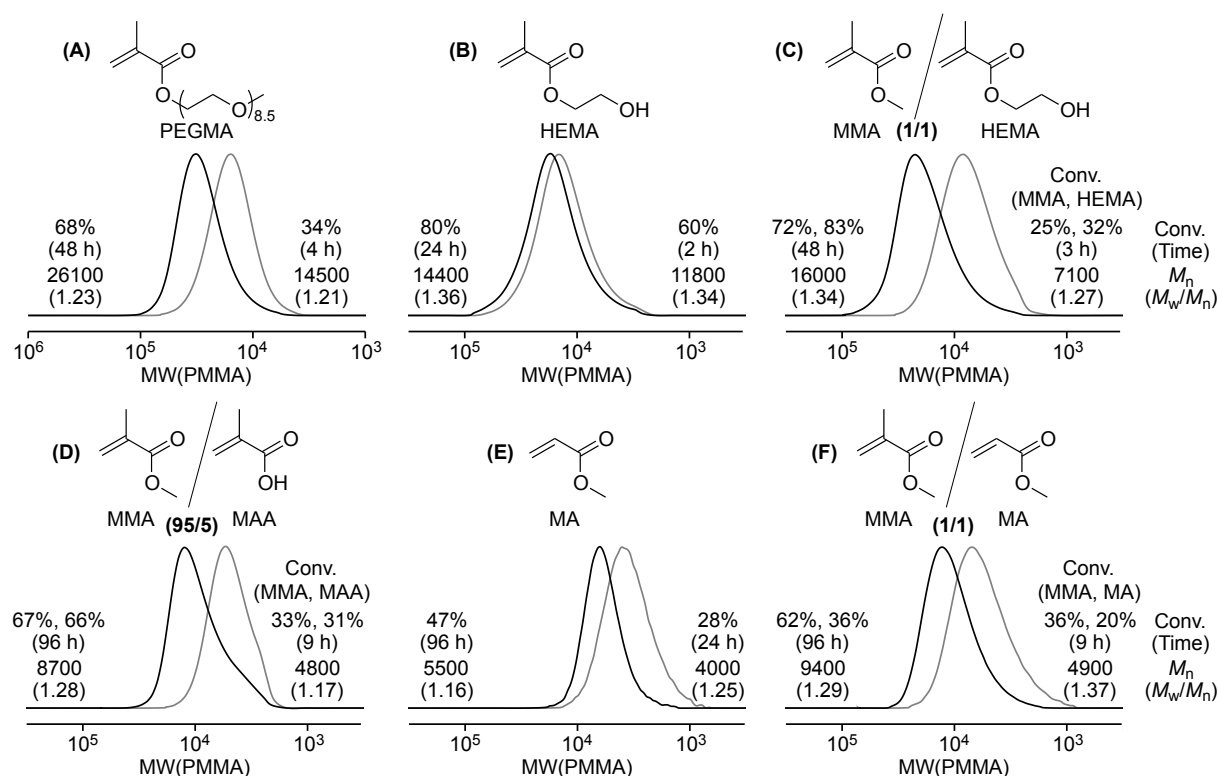
**Figure 8.** Ferrocene-concerted iron-catalyzed living radical polymerization of MMA with  $FeBr_3$  as the starting catalyst:  $[MMA]_0/[H-(MMA)_2-Br]_0/[FeBr_3]_0/[n-Bu_4NX]_0/[FeCp^*_2]_0 = 2000/20/10/10/40$  mM in THF at 80 °C:  $n-Bu_4NPF_6$  (●);  $n-Bu_4NBr$  (■);  $n-Bu_4NBr$  without  $FeCp^*_2$  (●).

## 6. Polymerization Mechanism

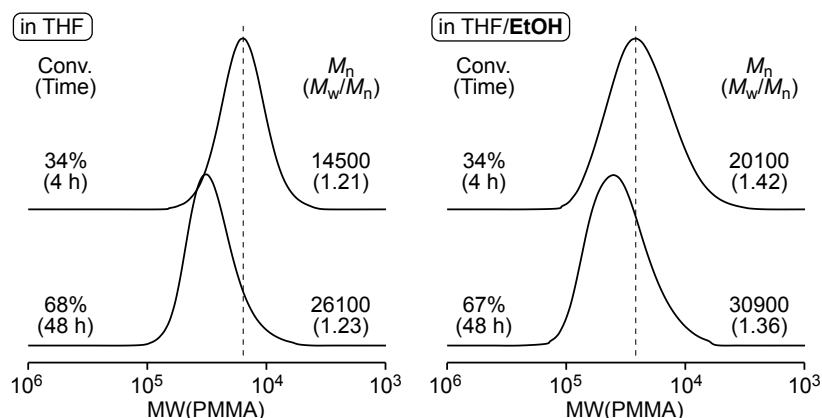
From some experiments, the author presents the plausible mechanism as follows (Scheme 2). First, the main iron catalyst ( $FeBr_2$ ) activates the terminal carbon-halogen bond (C-X) with one electron oxidation ( $FeBr_2 \rightarrow FeBr_3$ ) to give carbon-centered radical species for initiation/propagation, while  $FeCp^*_2$  cannot activate it as the main catalyst. Subsequently, the resulting  $FeBr_3$  reacts with the growing radical species on propagation with monomers to give the dormant species, but part of the  $FeBr_3$  complex would be reduced to  $FeBr_2$  by  $FeCp^*_2$  to promote the dynamic equilibrium between the two species. Such reduction by  $FeCp^*_2$  would be plausible because  $FeBr_3$  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  $FeBr_3$ . 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/ $FeCp_2$ -concerted catalysis.<sup>72</sup> The halogen-capping reaction can be supported by the high  $\omega$ -end functionality of obtained polymers.



**Scheme 2.** Plausible Mechanism for Ferrocene-Concerted Living Radical Polymerization



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



**Figure 10.** Living radical polymerization of PEGMA with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  in conjunction with  $\text{FeCp}^*_2$ :  $[\text{PEGMA}]_0/[\text{H-(MMA)}_2\text{-Br}]_0/[\text{FeBr}_2]_0/[n\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 500/5.0/5.0/5.0/20$  mM in THF or THF/EtOH (50/50 v/v) at 60 °C.

## 7. Highly Robust Catalysis over Polar Monomers and Solvents

For conventional iron catalysts in living radical polymerization, selection of ligand, such as phosphine ligand in  $\text{FeBr}_2(\text{PR}_3)_2$ , was crucial toward higher catalytic activity.<sup>36,37,42</sup> 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.<sup>42</sup> On the other hand, the  $\text{FeCp}^*_2$ -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.<sup>78</sup> 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<sup>31-69</sup>, and the contributing factor would be that turnover frequency can be enhanced without relying on ligands.

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 ( $\text{FeCp}^*_2$ ) for iron (Fe)-catalyzed living radical polymerization with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  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  $\text{FeCp}^*_2$ . 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.

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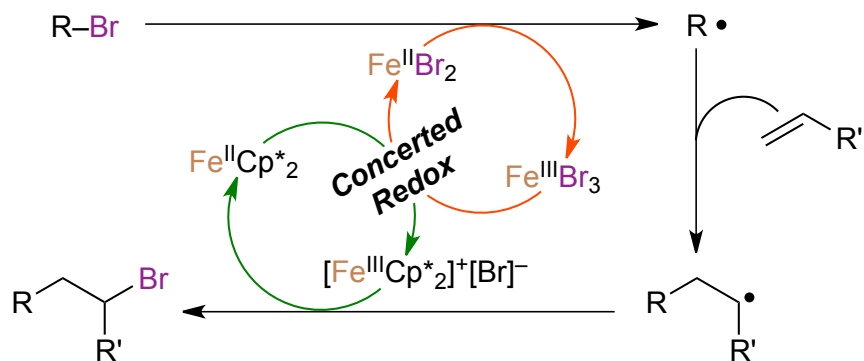


## Chapter 5

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

#### Abstract

In this paper, the concerted redox catalysis with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  (main catalyst) and  $\text{FeCp}^*_2$  (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 ( $\text{CCl}_3\text{Br}$ ) 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  $\text{FeCp}^*_2$  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 ( $\text{FeBr}_2$  and  $\text{FeCp}^*_2$ ) to lower than 1mol% for olefins.



## Introduction

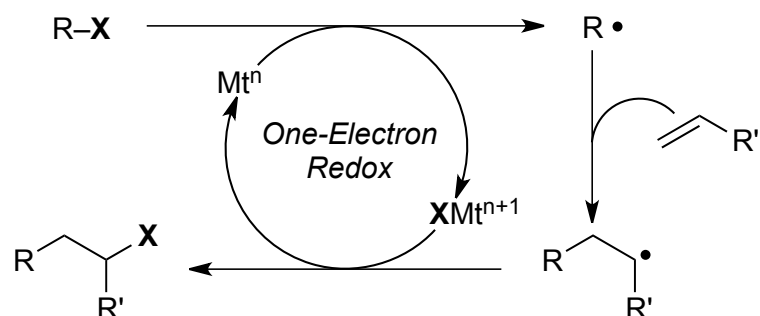
Radical species are neutral and so highly tolerant to various functional groups such as hydroxyl ( $-\text{OH}$ ), amino ( $-\text{NR}_2$ ), and carboxyl ( $-\text{COOH}$ ). Therefore, radical reactions, which proceed through radical intermediates, are powerful methodologies for constructing unique small 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,<sup>1-3</sup> or transition metal complexes such as ruthenium (Ru) and copper (Cu) as catalysts.<sup>4,5</sup> Especially, a transition metal-catalyzed systems are quite attractive and well studied because the desirable adduct can be obtained in high yield.<sup>6</sup> 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 ( $\text{R-X} \rightarrow \text{R}\cdot$ ) with one-electron oxidation of transition metal catalyst ( $\text{Mt}^n \rightarrow \text{XMt}^{n+1}$ ; 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 ( $\text{XMt}^{n+1} \rightarrow \text{Mt}^n$ ). 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  $\text{RuCl}_2(\text{PPh}_3)_3$ ,<sup>7</sup> the critical design of combined ligands gave birth to various types of highly active ruthenium catalysts, such as halfsandwich types,<sup>8-11</sup> alkylidene types,<sup>12-14</sup> and polynuclear types.<sup>15-18</sup> In addition, the use of reducing agents, such as magnesium<sup>19</sup> or free radical initiators (AIBN),<sup>20</sup> as additives further improved the catalysis to lower the catalyst usage (0.01 mol% for olefins), in which the higher oxidation state complexes ( $\text{Ru}^{\text{III}}$ ), easily accumulated because of the unfavorable side reactions such as bimolecular radical couplings or disproportionations, were reduced to regenerate the lower oxidation state complex ( $\text{Ru}^{\text{II}}$ ). Actually, this concept was well studied also in copper catalyzed systems.<sup>21,22</sup>

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.<sup>23</sup> Actually, there are some interesting

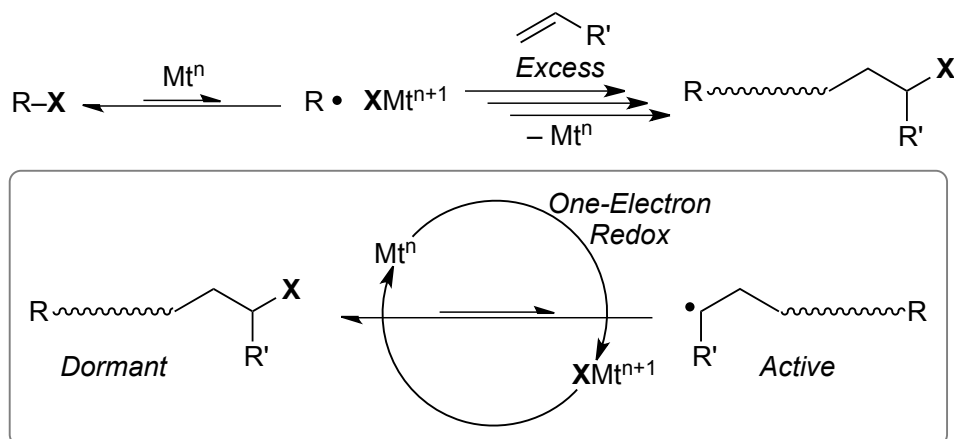
iron-based catalyst systems that showed the efficient Kharasch addition reactions with lower amount of iron catalysts ( $< 2.0 \text{ mol}\%$ ).<sup>24-30</sup> These systems, however, are applicable mainly for Kharasch addition reactions to 1-alkenes, and some trials for conjugated olefins, such as styrene, butadiene, and acrylonitrile, resulted in the lower yields of the desirable mono adducts.<sup>24-26</sup>



**Scheme 1.** Transition Metal-Catalyzed Kharasch Addition Reaction

Transition metal-catalyzed living radical polymerization (Mt-LRP)<sup>31-38</sup> 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 “*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:  $\sim\text{C-X}$ ;  $\sim\sim$ : polymer chain) by higher oxidation state catalysts ( $\text{XMt}^{n+1}$ ). 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 ( $\text{FeCp}_2$ ; Fc), which is highly redox active metal complexes<sup>39</sup> 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.<sup>40</sup> 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



**Scheme 2.** Transition Metal-Catalyzed Living Radical Polymerization (Mt-LRP)

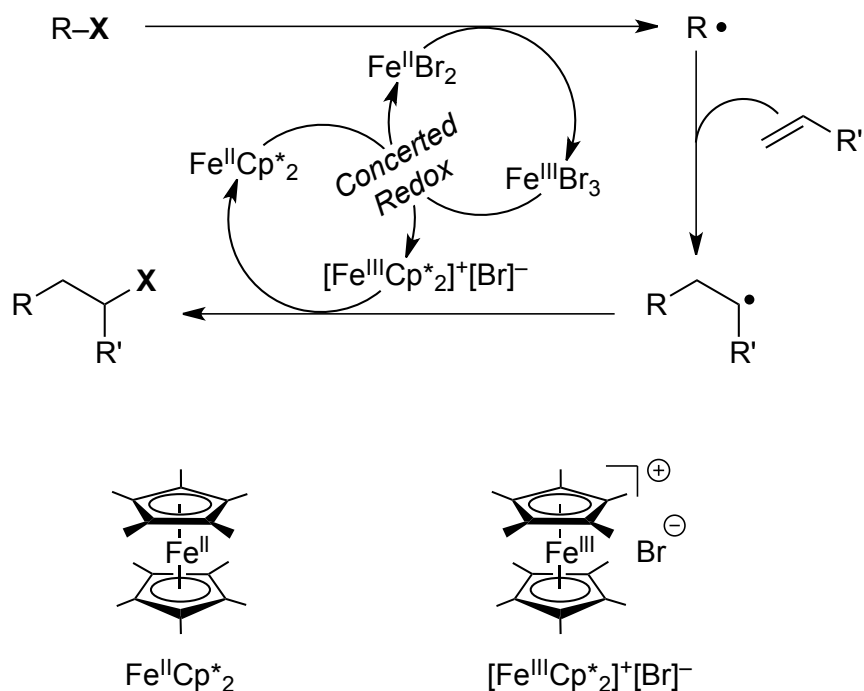
oxidation state ruthenium catalyst ( $\text{XRu}^{\text{III}}$ ) to regenerate the lower oxidation state form ( $\text{Ru}^{\text{II}}$ );  $\text{XRu}^{\text{III}} + \text{Fc}^{\text{II}} \rightarrow \text{Ru}^{\text{II}} + \text{XFc}^{\text{III}}$ , (b) halogen-capping for growing radical species by  $\text{XFc}^{\text{III}}$ ;  $\sim\text{C}\cdot + \text{XFc}^{\text{III}} \rightarrow \sim\text{C-X} + \text{Fc}^{\text{II}}$ . 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<sup>41</sup> in conjunction with  $\text{FeBr}_2$  combined with an onium salt ( $n\text{-Bu}_4\text{NBr}$ ) as the main catalyst<sup>42,43</sup> in order to develop the highly sustainable catalysis.<sup>44</sup> As a result, it was found that the use of decamethylferrocene ( $\text{FeCp}^*_2$ ;  $\text{Fc}^*$ ), the ferrocene derivative that has the lower redox potential than  $\text{Fc}$ , 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 ( $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}/\text{FeCp}^*_2$ ) 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 ( $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}/\text{FeCp}^*_2$ ) 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.



**Scheme 3.**  $\text{FeBr}_2/\text{FeCp}^*_2$  Concerted Redox Catalysis (“All-Iron” Catalysis) for Kharasch Addition Reaction

## 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 ( $\text{CCl}_3\text{Br}$ ) was bubbled with argon for more than 15 min before use. Iron(II) bromide ( $\text{FeBr}_2$ ) (Aldrich; purity >98%), ferrocene ( $\text{FeCp}_2$ ) (Aldrich; purity >98%), decamethylferrocene ( $\text{FeCp}^*_2$ ) (Aldrich; purity 97%), and tetrabutylammonium bromide ( $n\text{-Bu}_4\text{NBr}$ ) (TCI; purity >99%) were used as received and handled in a glovebox (M. Braun Labmaster 130) under a moisture- and oxygen-free argon atmosphere ( $\text{H}_2\text{O}$  <1 ppm;  $\text{O}_2$  <1 ppm). Tetrahydrofrane (THF) (Wako, super-dehydrated, stabilizer free) was bubbled with argon for more than 15

min before use. *n*-Octane (internal standard for  $^1\text{H}$  NMR traces for the reaction with MMA) and 1,2,3,4-tetrahydronaphthalene (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  $\text{CCl}_3\text{Br}$  to St with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr/FeCp}^*_2$  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  $\text{CCl}_3\text{Br}$  (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  $\text{CCl}_3\text{Br}$ ) was added into a Schlenk tube with  $\text{FeBr}_2$  (6.5 mg, 0.03 mmol), *n*- $\text{Bu}_4\text{NBr}$  (9.7 mg, 0.03 mmol), and  $\text{FeCp}^*_2$  (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 ( $\text{Mg}_{0.7}\text{Al}_{0.3}\text{O}_{1.15}$ ); 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

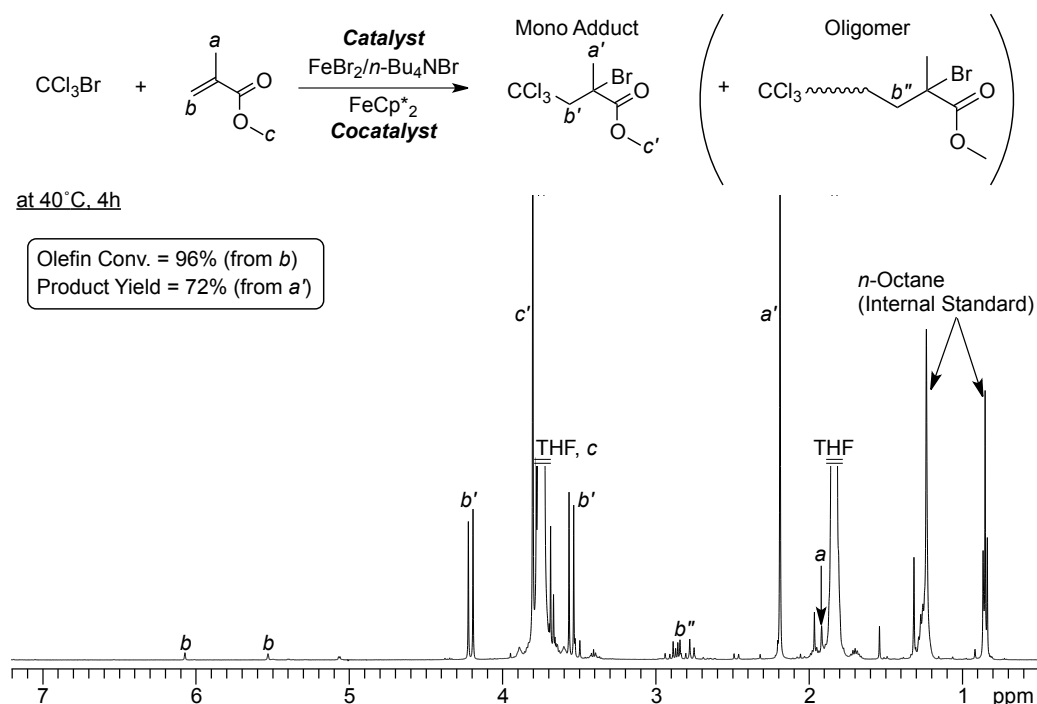
In the previous report about the “all-iron” catalysis for living radical polymerization,<sup>44</sup> the author mainly dealt with the polymerization of methacrylate monomers and it worked well to give well-controlled polymers. Therefore, the Kharasch addition reaction of bromotrichloromethane ( $\text{CCl}_3\text{Br}$ ) to methyl methacrylate (MMA) was firstly performed in order to evaluate the catalytic activity. When  $\text{FeBr}_2$  and *n*- $\text{Bu}_4\text{NBr}$  were used as the main catalyst in conjunction with  $\text{FeCp}^*_2$  as the cocatalyst ( $[\text{MMA}]_0/[\text{CCl}_3\text{Br}]_0/$

$[\text{FeBr}_2]_0/[\textit{n}\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 1400/2000/10/10/40$  mM in THF at 40 °C), MMA was consumed smoothly to reach 96% conversion in 4 h (Table 1, Entry1). From the  $^1\text{H}$  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  $\text{CCl}_3\text{Br}$  to MMA with “all-iron” catalysis<sup>a</sup>

| Entry | $[\text{FeBr}_2]_0/[\textit{n}\text{-Bu}_4\text{NBr}]_0$<br>(mM) | Cocat. <sup>b</sup> | Temp. (°C) | Time (h) | Conv. (%) <sup>c</sup> | Yield (%) <sup>c</sup> |
|-------|------------------------------------------------------------------|---------------------|------------|----------|------------------------|------------------------|
| 1     | 10/10                                                            | $\text{FeCp}^*_2$   | 40         | 4        | 96                     | 72                     |
| 2     | 10/10                                                            | —                   | 40         | 4        | 32                     | 18                     |
| 3     | 10/10                                                            | $\text{FeCp}_2$     | 40         | 4        | 35                     | 22                     |
| 4     | 10/10                                                            | $\text{FeCp}^*_2$   | 60         | 1        | 97                     | 75                     |
| 5     | 40/40                                                            | $\text{FeCp}^*_2$   | 40         | 1        | >99                    | 89                     |

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



**Figure 1.**  $^1\text{H}$  NMR spectrum (in  $\text{CDCl}_3$  at r.t.) for the reaction solution of the Kharasch addition of  $\text{CCl}_3\text{Br}$  to MMA catalyzed by “all-iron” catalysis ( $\text{FeBr}_2/\textit{n}\text{-Bu}_4\text{NBr}/\text{FeCp}^*_2$ ;  $[\text{MMA}]_0/[\text{CCl}_3\text{Br}]_0/[\text{FeBr}_2]_0/[\textit{n}\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 1400/2000/10/10/40$  mM in THF at 40 °C; reaction time: 4 h).

If the same reaction was conducted without  $\text{FeCp}^*_2$  (only  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$ ), the reaction slowed down and retarded in the early stage (Entry 2), implying the crucial effects of  $\text{FeCp}^*_2$  for promoting the catalysis. In addition, the use of  $\text{FeCp}_2$  as the cocatalyst, in place of  $\text{FeCp}^*_2$ , gave no effects (Entry 3) because  $\text{FeCp}_2$  has the higher redox potential than the main catalyst ( $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$ ) and so cannot act as the reducing agent.

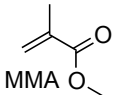
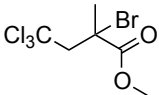
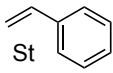
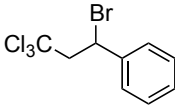
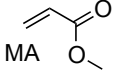
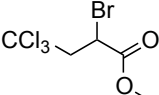
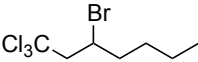
Next, the reaction with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}/\text{FeCp}^*_2$  was examined in higher temperature ( $60\text{ }^\circ\text{C}$ ), resulting in the faster reaction in which the olefin conversion reached 97% in 1 h without the loss of the product yield (Entry 4). Finally, the reaction was performed with a higher amount of the catalyst ( $[\text{FeBr}_2]_0/[\text{n-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 10/10/40\text{ mM}$  in THF at  $40\text{ }^\circ\text{C}$ ). 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

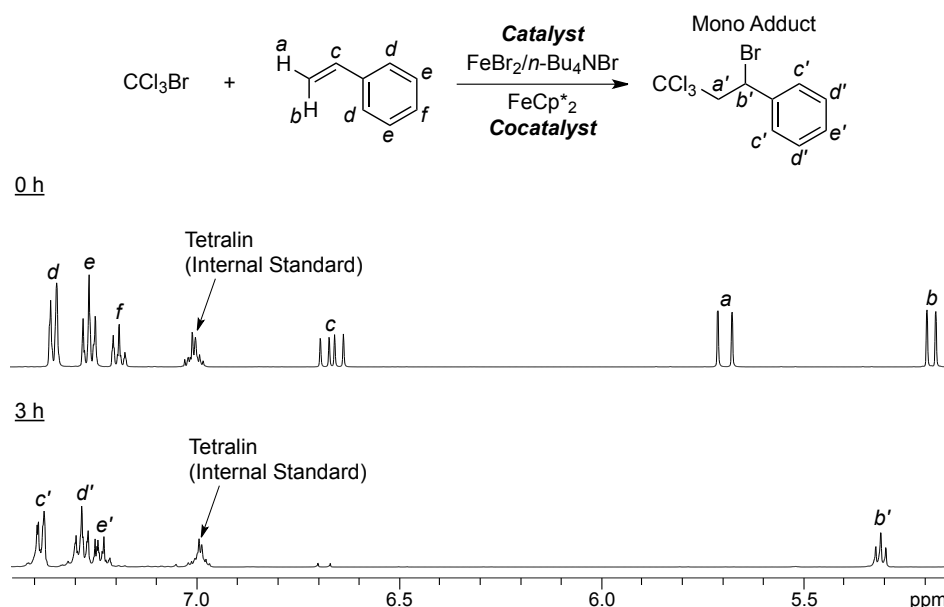
Next, “all-iron” was applied catalysis to Kharasch addition reactions with other olefins in conjunction with  $\text{CCl}_3\text{Br}$  as the halogenated compound (Table 2). Firstly, the Kharasch addition reaction with styrene (St) was performed under the same condition with that with MMA ( $[\text{Olefin}]_0/[\text{CCl}_3\text{Br}]_0/[\text{FeBr}_2]_0/[\text{n-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 1400/2000/10/10/40\text{ mM}$  in THF at  $60\text{ }^\circ\text{C}$ ). From  $^1\text{H}$  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 ( $k_p$ ),<sup>45</sup> 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,<sup>45</sup> 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 CCl<sub>3</sub>Br to various olefins with “all-iron” catalysis<sup>a</sup>

| Entry | Olefin                                                                            | Mono Adduct                                                                        | Temp. (°C) | Time (h) | Conv. (%) <sup>b</sup> | Yield (%) <sup>b</sup> |
|-------|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------|----------|------------------------|------------------------|
| 1     |  |   | 60         | 1        | 97                     | 75                     |
| 2     |  |   | 60         | 3        | >99                    | 96                     |
| 3     |  |   | 60         | 24       | 90                     | 62                     |
| 4     |  |  | 60         | 24       | 91                     | 83                     |

<sup>a</sup>[Olefin]<sub>0</sub>/[CCl<sub>3</sub>Br]<sub>0</sub>/[FeBr<sub>2</sub>]<sub>0</sub>/[*n*-Bu<sub>4</sub>NBr]<sub>0</sub>/[FeCp\*<sub>2</sub>]<sub>0</sub> = 1400/2000/10/10/40 mM in THF. <sup>b</sup>Determined by <sup>1</sup>H NMR with *n*-octane (for Entry 1) and tetralin (for Entry 2-4) as internal standards.



**Figure 2.** <sup>1</sup>H NMR traces (in CDCl<sub>3</sub> at r.t.) for the Kharasch addition reaction of CCl<sub>3</sub>Br to St catalyzed by “all-iron” catalysis (FeBr<sub>2</sub>/*n*-Bu<sub>4</sub>NBr/FeCp\*<sub>2</sub>): [St]<sub>0</sub>/[CCl<sub>3</sub>Br]<sub>0</sub>/[FeBr<sub>2</sub>]<sub>0</sub>/[*n*-Bu<sub>4</sub>NBr]<sub>0</sub>/[FeCp\*<sub>2</sub>]<sub>0</sub> = 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  $\text{CCl}_3\text{Br}$  to St ( $[\text{St}]_0/[\text{CCl}_3\text{Br}]_0 = 1400/2000$  mM in THF at  $60^\circ\text{C}$ ). Firstly, the reaction was performed with half amounts of iron catalysts with keeping the same feed ratio of  $\text{FeBr}_2$  and  $\text{FeCp}^*_2$ : from  $[\text{FeBr}_2]_0/[\textit{n}\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 10/10/40$  mM (amounts of Fe ( $\text{FeBr}_2$  and  $\text{FeCp}^*_2$ ): 3.6 mol% to St; Table 3, Entry 1) to  $[\text{FeBr}_2]_0/[\textit{n}\text{-Bu}_4\text{NBr}]_0/[\text{FeCp}^*_2]_0 = 5.0/5.0/20$  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  $\text{FeCp}^*_2$  was reduced with the fixed amount of the main catalyst ( $\text{FeBr}_2/\textit{n}\text{-Bu}_4\text{NBr}$ : 5.0 mM; Entry 2-4). The lower the amount of  $\text{FeCp}^*_2$ , the lower the product yield. However, 70% yield was observed even with 5.0 mM of  $\text{FeCp}^*_2$  (amounts of Fe: 0.7 mol%). Finally, the reaction with the lower amount of the main catalyst ( $[\text{FeBr}_2]_0/[\textit{n}\text{-Bu}_4\text{NBr}]_0 = 2.5/2.5$  mM) was examined in conjunction with 10 mM of  $\text{FeCp}^*_2$  (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  $\text{FeBr}_2$  (Entry 3). Therefore, it was found that the amount of the main catalyst affects the reaction efficiency more strongly than that of  $\text{FeCp}^*_2$ .

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

**Table 3.** Lowering the catalyst amounts in Kharasch addition reactions of  $\text{CCl}_3\text{Br}$  to St with “all-iron” catalysis

| Entry | $[\text{FeBr}_2]_0$ (mM) <sup>b</sup> | $[\text{FeCp}^*_2]_0$ (mM) | Fe (mol%) <sup>c</sup> | Time (h) | Conv. (%) <sup>d</sup> | Yield (%) <sup>d</sup> |
|-------|---------------------------------------|----------------------------|------------------------|----------|------------------------|------------------------|
| 1     | 10                                    | 40                         | 3.6                    | 3        | >99                    | 96                     |
| 2     | 5                                     | 20                         | 1.8                    | 24       | 98                     | 83                     |
| 3     | 5                                     | 10                         | 1.1                    | 24       | 93                     | 82                     |
| 4     | 5                                     | 5                          | 0.7                    | 24       | 85                     | 70                     |
| 5     | 2.5                                   | 10                         | 0.9                    | 24       | 70                     | 59                     |

<sup>a</sup> $[\text{St}]_0/[\text{CCl}_3\text{Br}]_0 = 1400/2000$  mM in THF at  $60^\circ\text{C}$ . <sup>b</sup>Equimolar amounts of *n*-Bu<sub>4</sub>NBr was combined.

<sup>c</sup> $([\text{FeBr}_2]_0 + [\text{FeCp}^*_2]_0) \cdot 100/[\text{St}]_0$  <sup>d</sup>Determined by <sup>1</sup>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 MMA, the use of  $\text{FeCp}^*_2$  as the cocatalyst in conjunction with  $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$  as the main catalyst allowed the fast and efficient reaction in which MMA was almost clearly consumed in 1 h to give the desirable mono adduct in around 90% yield. In addition, “all-iron” catalysis ( $\text{FeBr}_2/n\text{-Bu}_4\text{NBr}$ ) 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  $\text{FeCp}^*_2$ ) to lower than 1 mol% for olefins.

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## **PART III**

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

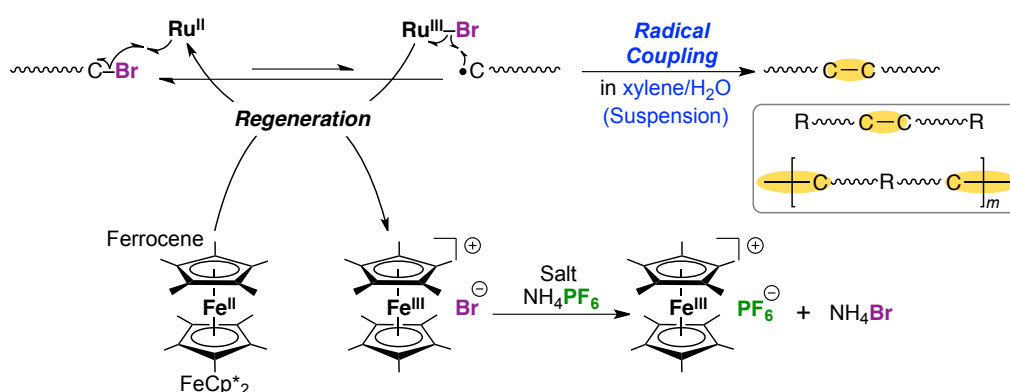


## Chapter 6

# 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  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2$  catalyst pair ( $\text{Cp}^*\text{Ru}$ :  $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ ) in conjunction with  $\text{NH}_4\text{PF}_6$  as an additive. In this catalyst system, following two key steps were crucial for promoting the reaction: (a) effective regeneration of  $\text{Ru}^{\text{II}}$  complex by  $\text{FeCp}^*_2$  through a reduction of  $\text{XRu}^{\text{III}}$ , generated as a result of the radical coupling ( $\text{XRu}^{\text{III}} + \text{Fe}^{\text{II}}\text{Cp}^*_2 \rightarrow \text{Ru}^{\text{II}} + [\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{X}^-$ ; X: halogen); (b) formation of the stable ferrocenium salt ( $[\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{PF}_6^-$ ) by the anion exchange reaction between  $[\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{X}^-$  and  $\text{NH}_4\text{PF}_6$  ( $[\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{X}^- + \text{NH}_4\text{PF}_6 \rightarrow [\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{PF}_6^- + \text{NH}_4\text{X}$ ). The  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  catalyst system was firstly used for the radical coupling reaction of  $\omega$ -brominated polystyrenes ( $\text{PSt-Br}$ ), 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  $x_c = 0.93$ ). Next, the catalysis was applied to the radical coupling reaction of the  $\alpha,\omega$ -dibrominated PSt ( $\text{Br}\sim\sim\text{R}\sim\sim\text{Br}$ ) to give chain extended PSt ( $M_p(\text{extended}) = 14200$ ,  $M_p(\text{prepolymer}) = 2500$ ).



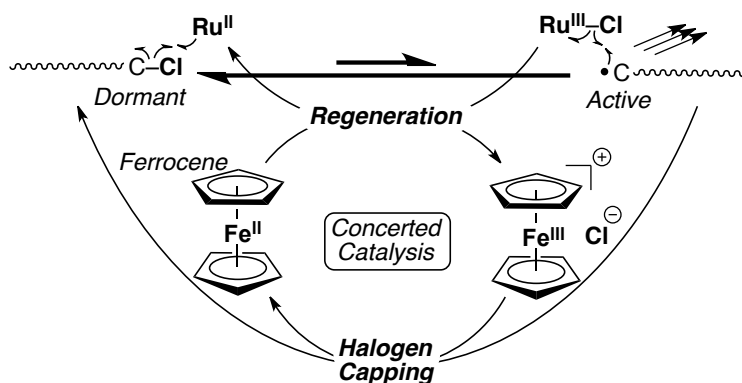
## Introduction

Ferrocene ( $\text{FeCp}_2$ ;  $\text{Fc}$ ) or the derivatives are well-known organometallic complexes,<sup>1,2</sup> where the central iron is sandwiched between two cyclopentadienyl anion ( $\text{Cp}$ ) rings. The noteworthy property is the one-electron redox behavior ( $\text{Fe}^{\text{II}} \leftrightarrow \text{Fe}^{\text{III}}$ ),<sup>3</sup> and the most general utility is an internal standard for cyclic voltammetry (CV) analysis.<sup>4</sup> Another characteristic application is use as a chiral ligand: the aromaticity of  $\text{Cp}$  ring allows introduction of bearing coordination sites (P, N, O, etc.)<sup>5-7</sup> 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.<sup>8</sup>

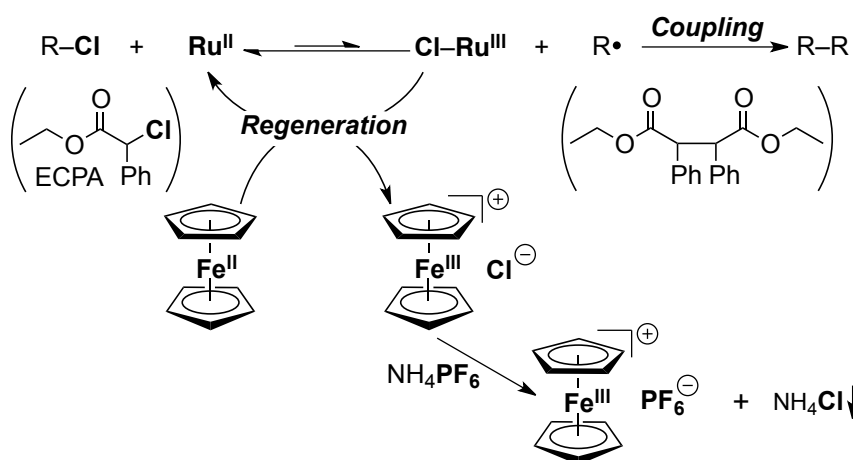
The author has recently reported that ferrocene can act as an effective cocatalyst for ruthenium-catalyzed living radical polymerization.<sup>9</sup> In metal-catalyzed living radical polymerization (Mt-LRP) or ATRP, a carbon-halogen bond at a dormant end is reversibly activated to a radical species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

In the “ferrocene-concerted catalysis”, ferrocenium ion ( $\text{XFc}^{\text{III}}$ ), which is generated via reduction reaction of higher oxidized metal by ferrocene ( $\text{Fc}^{\text{II}}$ ), is ionic species ( $[\text{Fc}^{\text{III}}]^+\text{X}^-$ ) 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,<sup>9</sup> the author demonstrated the radical coupling reaction of a model dormant end [ $\text{R-Cl}$ : ethyl 2-chloro-2-phenylacetate (ECPA)] catalyzed by Ru/ferrocene catalyst in conjunction with  $\text{NH}_4\text{PF}_6$  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  $\sim 90\%$ ), although the radical coupling reaction is the unfavorable side reaction in LRP and effectively inhibited when using only Ru/ferrocene (without  $\text{NH}_4\text{PF}_6$ ) as shown in Figure 1. This dramatic difference in catalysis by just adding  $\text{NH}_4\text{PF}_6$  is probably because ferrocenium halide ( $[\text{Fc}^{\text{III}}]^+\text{X}^-$ ) reacts with  $\text{NH}_4\text{PF}_6$  to give ferrocenium hexafluorophosphate ( $[\text{Fc}^{\text{III}}]^+\text{PF}_6^-$ : highly stable and unable to act as halogen capping agent) and  $\text{NH}_4\text{X}$ . It is important that halide anions ( $\text{X}^-$ ) are scavenged as  $\text{NH}_4\text{X}$  and released from the reaction solution ( $\text{NH}_4\text{X}$  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  $\text{NH}_4\text{PF}_6$ .<sup>9</sup>

As the extension of this unique catalysis with Ru/ferrocene/ $\text{NH}_4\text{PF}_6$ , this chapter presents the radical coupling reaction of polystyrene (PSt) prepared by Mt-LRP of styrene, having halogen at  $\omega$ -chain end ( $\sim\text{C-X}$ ;  $\sim$ : polystyrene, X: halogen). The radical coupling reaction is highly useful method for preparing  $\alpha,\omega$ -telechelic polymers ( $F_n\sim\sim F_n$ ;  $F_n$ : functional group) that have functional groups derived from the initiator for Mt-LRP ( $F_n\text{-X}$ ), and actually some research groups have already studied in this line by using copper (Cu) catalysts.<sup>20-23</sup> 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/ $\text{NH}_4\text{PF}_6$  catalyst system allowed the almost quantitative radical coupling reactions under the xylene/ $\text{H}_2\text{O}$  mixed solvent (suspension system). Obtained coupling products had two initiator moieties at  $\alpha$ - and  $\omega$ -chain ends, supported by  $^1\text{H}$  NMR analysis. In addition, this catalysis was successfully applied to the chain extension reaction of  $\alpha,\omega$ -halogenated PSt ( $\text{X}\sim\sim F_n'\sim\sim\text{X}$ ; prepared by Mt-LRP of St in conjunction with the difunctional initiator,  $\text{X-F}_n'\text{-X}$ ), giving high molecular weight PSt having initiator moieties ( $F_n'$ ) periodically ( $[\sim\sim F_n'\sim\sim]_n$ ).

## 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  $n\text{-Bu}_3\text{N}$  (TCI; purity > 98%) as an additive for Ru-catalyzed living radical polymerization were degassed by reduced pressure before use.  $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$  ( $\text{Cp}^*\text{Ru}$ ) (Aldrich), ferrocene ( $\text{FeCp}_2$ ) (Aldrich; purity > 98%), decamethylferrocene ( $\text{FeCp}^*_2$ ) (Aldrich; purity 97%),  $\text{NH}_4\text{PF}_6$  (Aldrich; purity 99.99%), and  $n\text{-Bu}_4\text{NPF}_6$  (Aldrich; purity > 98%) were used as received and handled in a glove box (M. Braun Labmaster 130) under a moisture- and oxygen-free argon atmosphere ( $\text{H}_2\text{O} < 1$  ppm,  $\text{O}_2 < 1$  ppm).  $n$ -Octane (internal standard for gas chromatography) and 1,2,3,4-tetrahydronaphthalene (tetralin; internal standard for  $^1\text{H}$  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  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  was as follows. In a 50 mL round-bottomed flask were placed  $\text{Cp}^*\text{Ru}$  (9.6 mg, 0.012 mmol),  $\text{FeCp}^*_2$  (39.3 mg, 0.12 mmol), and  $\text{NH}_4\text{PF}_6$  (19.6 mg, 0.12 mmol) under a grove 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  $^1\text{H}$  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  $\text{Cp}^*\text{Ru}$  (25.5 mg, 0.032 mmol) under a grove box. Then, toluene (2.42 mL), *n*-octane (0.40 mL), *n*- $\text{Bu}_3\text{N}$  (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<sub>3</sub>N), xylene (4.00 mL) was added, and PSt-Br, Cp\*Ru, and *n*-Bu<sub>3</sub>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<sub>3</sub>N/FeCp\*<sub>2</sub>/NH<sub>4</sub>PF<sub>6</sub> in xylene/H<sub>2</sub>O mixed solvent was as follows. In a 50 mL round-bottomed flask were placed Cp\*Ru (19.1 mg, 0.024 mmol), FeCp\*<sub>2</sub> (78.3 mg, 0.24 mmol), and NH<sub>4</sub>PF<sub>6</sub> (39.1 mg, 0.24 mmol) under a glove 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<sub>3</sub>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<sub>3</sub>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<sub>3</sub>N), xylene (4.00 mL) was added, and PSt-Br, Cp\*Ru, and *n*-Bu<sub>3</sub>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  $\text{Cp}^*\text{Ru}/n\text{-Bu}_3\text{N}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  in xylene/ $\text{H}_2\text{O}$  mixed solvent was as follows. In a 50 mL round-bottomed flask with  $\text{Cp}^*\text{Ru}$  (19.1 mg, 0.024 mmol),  $\text{FeCp}^*_2$  (78.3 mg, 0.24 mmol), and  $\text{NH}_4\text{PF}_6$  (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  $\text{Cp}^*\text{Ru}$ , and 0.24 mmol of  $n\text{-Bu}_3\text{N}$ ) 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.

## **Measurements**

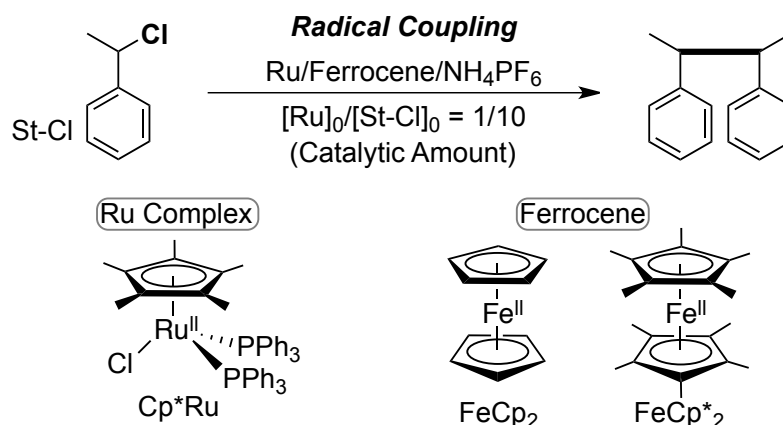
For PSt,  $M_n$  and  $M_w/M_n$  were measured by size exclusion chromatography at 40 °C in THF as an eluent on three polystyrene-gel columns (Shodex LF-404; exclusion limit =  $2 \times 10^6$ ; particle size = 6  $\mu\text{m}$ ; pore size = 3000 Å; 0.46 cm i.d.  $\times$  25 cm; flow rate, 0.3 mL  $\text{min}^{-1}$ ) 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 PSt samples (Polymer Laboratories;  $M_n$  = 500–3840000;  $M_w/M_n$  = 1.01–1.14) as well as the monomer.  $^1\text{H}$  spectra were measured at room temperature on a JEOL JNM-ECA500 spectrometer operating at 500.16 MHz. For  $^1\text{H}$  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  $\text{NH}_4\text{PF}_6$  was studied for optimizing the catalyst system (Scheme 1).

Firstly, the reaction was performed with the  $\text{Cp}^*$ -ligated ruthenium complex  $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2: \text{Cp}^*\text{Ru}]^{24}$  in conjunction with  $\text{FeCp}_2$  and  $\text{NH}_4\text{PF}_6$  in toluene at 100 °C



**Scheme 1.** Radical Coupling Reaction of (1-Chloroethyl)benzene (St-Cl)

**Table 1.** Radical coupling reaction of St-Cl with ruthenium/ferrocene catalysts in conjunction with ammonium salts<sup>a</sup>

| Entry | Ruthenium              | Ferrocene         | Salt                     | Conv. (%) <sup>b</sup> | Yield (%) <sup>b</sup> |
|-------|------------------------|-------------------|--------------------------|------------------------|------------------------|
| 1     | $\text{Cp}^*\text{Ru}$ | $\text{FeCp}_2$   | $\text{NH}_4\text{PF}_6$ | 6                      | —                      |
| 2     | $\text{Cp}^*\text{Ru}$ | $\text{FeCp}^*_2$ | $\text{NH}_4\text{PF}_6$ | 70                     | 66                     |
| 3     | $\text{Cp}^*\text{Ru}$ | —                 | —                        | 4                      | —                      |
| 4     | $\text{Cp}^*\text{Ru}$ | $\text{FeCp}^*_2$ | —                        | 5                      | —                      |
| 5     | —                      | $\text{FeCp}^*_2$ | $\text{NH}_4\text{PF}_6$ | 3                      | —                      |

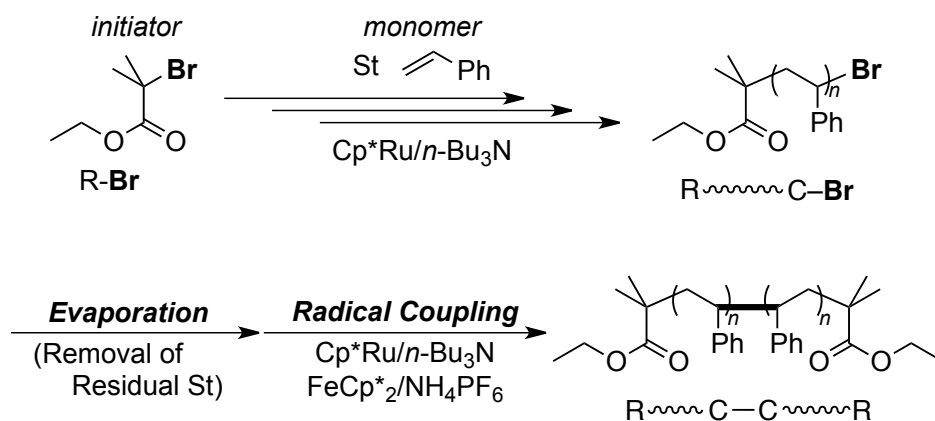
<sup>a</sup> $[\text{St-Cl}]_0/[\text{ruthenium}]_0/[\text{ferrocene}]_0/[\text{salt}]_0 = 40/4.0/40/40$  mM in toluene at 100 °C; reaction time: 48 h. <sup>b</sup>Determined by  $^1\text{H}$  NMR.

(Table 1, Entry 1). 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,  $\text{FeCp}^*_2$ , more reducing ferrocene derivative having lower redox potential than  $\text{FeCp}_2$ ,<sup>6,19</sup> was used in place of  $\text{FeCp}_2$ , giving the efficient reaction (Entry 2; conversion = 70%, yield = 66%).

Controlled experiments<sup>3-5</sup> strongly suggested that three components of the catalysis ( $\text{Cp}^*\text{Ru}$ ,  $\text{FeCp}^*_2$ , and  $\text{NH}_4\text{PF}_6$ ) are all needed for driving radical coupling reactions. Especially, it is important that the use of the ammonium salt ( $\text{NH}_4\text{PF}_6$ ), the halide scavenger, is crucial, supporting the catalytic mechanism shown in Figure 2.

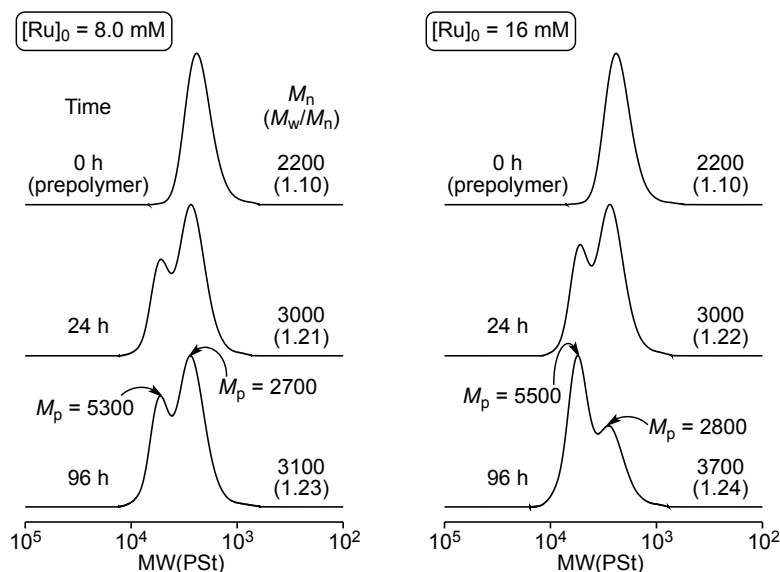
## 2. Radical Coupling Reactions of PSt-Br

From the results of model reactions (Table 1),  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  catalyst system was chosen for the radical coupling reactions of  $\omega$ -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  $\text{Cp}^*\text{Ru}$  and  $n\text{-Bu}_3\text{N}$  (additive)<sup>25,26</sup> as the catalyst (in toluene at 100 °C:  $[\text{St}]_0 = 4.0 \text{ M}$ ,  $[\text{H-EMA-Br}]_0 = 40 \text{ mM}$ ,  $[\text{Cp}^*\text{Ru}]_0 = 4.0 \text{ mM}$ ,  $[n\text{-Bu}_3\text{N}]_0 = 40 \text{ mM}$ ). 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 ( $\text{Cp}^*\text{Ru}$  and  $n\text{-Bu}_3\text{N}$  were remained).  $\text{FeCp}^*_2$  and  $\text{NH}_4\text{PF}_6$  were then added, and the radical coupling reaction was performed in toluene at 100 °C.



**Scheme 2.** Synthesis and Radical Coupling Reaction of PSt-Br

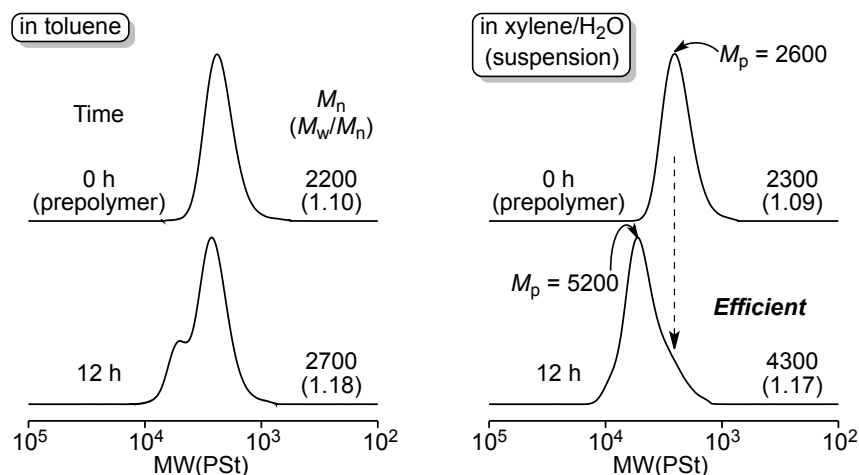
The reaction was performed in a concentrated condition to enhance the radical coupling ( $[\text{PSt-Br}]_0 = 80 \text{ mM}$ ,  $[\text{Cp}^*\text{Ru}]_0 = 8.0 \text{ mM}$ ,  $[n\text{-Bu}_3\text{N}]_0 = [\text{FeCp}^*_2]_0 = [\text{NH}_4\text{PF}_6]_0 = 80 \text{ mM}$ ). From SEC traces (Figure 3), a bimodal distribution was observed that was composed of the coupled PSt along with the residual PSt (reaction time = 96 h):  $M_p(\text{coupled PSt}) = 5300$ ,  $M_p(\text{residual PSt}) = 2700$  ( $M_p$ : 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 ( $[\text{Cp}^*\text{Ru}]_0 = 16 \text{ mM}$ ) 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.



**Figure 3.** SEC traces for the radical coupling reactions of PSt-Br with  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  in toluene at 100 °C:  $[\text{PSt-Br}]_0/[\text{Cp}^*\text{Ru}]_0/[n\text{-Bu}_3\text{N}]_0/[\text{FeCp}^*_2]_0/[\text{NH}_4\text{PF}_6]_0 = 80/8.0$  (left) or 16 (right)/ 80/80/80 mM.

### 3. Radical Coupling Reactions in Xylene/ $\text{H}_2\text{O}$ 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,  $\text{RuCl}_2$ -based catalyst  $[\text{RuCl}_2(\text{PPh}_3)_3]$  allowed much faster polymerization of methyl methacrylate (MMA) in toluene/ $\text{H}_2\text{O}$  mixtures (suspension system) than in toluene to give polymers with controlled molecular weights and its distributions.<sup>27</sup> In addition,  $\text{Cp}^*\text{Ru}$ -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).<sup>28</sup> 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/ $\text{H}_2\text{O}$  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 prepolymers (PSt-Br) after 12 h, although the residual polymers are slightly remained.



**Figure 4.** Remarkable acceleration of radical coupling reaction of PSt-Br by using suspension system: [PSt-Br]<sub>0</sub>/[Cp\*Ru]<sub>0</sub>/[*n*-Bu<sub>3</sub>N]<sub>0</sub>/[FeCp\*<sub>2</sub>]<sub>0</sub>/[NH<sub>4</sub>PF<sub>6</sub>]<sub>0</sub> = 80/16/80/80/80 mM in toluene at 100 °C (left) or in xylene/H<sub>2</sub>O (organic phase/water = 1/1 v/v) at 90 °C (right). The concentrations were based on the volume of the organic layer in suspension system.

**Table 2.** Radical coupling reaction of PSt-Br with Cp\*Ru/FeCp\*<sub>2</sub> catalysts in conjunction with ammonium salts<sup>a</sup>

| Entry | Solvent                              | Temp. (°C) | Ferrocene          | Salt                                       | Time (h) | $M_{n,0}^c$ | $M_{n,c}^d$ | $x_c^e$ |
|-------|--------------------------------------|------------|--------------------|--------------------------------------------|----------|-------------|-------------|---------|
| 1     | Toluene                              | 100        | FeCp* <sub>2</sub> | NH <sub>4</sub> PF <sub>6</sub>            | 96       | 2200        | 3700        | 0.81    |
| 2     | Xylene/H <sub>2</sub> O <sup>b</sup> | 90         | FeCp* <sub>2</sub> | NH <sub>4</sub> PF <sub>6</sub>            | 12       | 2300        | 4300        | 0.93    |
| 3     | Xylene/H <sub>2</sub> O <sup>b</sup> | 90         | —                  | NH <sub>4</sub> PF <sub>6</sub>            | 48       | 2300        | 2600        | 0.23    |
| 4     | Xylene/H <sub>2</sub> O <sup>b</sup> | 90         | FeCp* <sub>2</sub> | —                                          | 48       | 2200        | 2900        | 0.48    |
| 5     | Xylene/H <sub>2</sub> O <sup>b</sup> | 90         | FeCp* <sub>2</sub> | <i>n</i> -Bu <sub>4</sub> NPF <sub>6</sub> | 48       | 2300        | 3600        | 0.72    |

<sup>a</sup>[PSt-Br]<sub>0</sub>/[Cp\*Ru]<sub>0</sub>/[*n*-Bu<sub>3</sub>N]<sub>0</sub>/[FeCp\*<sub>2</sub>]<sub>0</sub>/[Salt]<sub>0</sub> = 80/16/80/80/80 mM in toluene or xylene/H<sub>2</sub>O (suspension; the concentrations were based on the volume of the organic layer). <sup>b</sup>Organic phase/water = 1/1 v/v. <sup>c</sup> $M_{n,0}$ :  $M_n$  of prepolymers. <sup>d</sup> $M_{n,c}$ :  $M_n$  of resulting polymers. <sup>e</sup> $x_c$ : coupling efficiency;  $x_c = 2(1 - M_{n,0}/M_{n,c})$ .

According to the previous report from Matyjaszewski et al.,<sup>23</sup> 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<sub>2</sub>O was performed without FeCp\*<sub>2</sub>, resulting the quite low coupling efficiency ( $x_c = 0.23$ ) even after 48 h (Entry 3). This result indicates that FeCp\*<sub>2</sub> is crucial for the “catalytic” (about Ru) radical coupling reaction. In addition, the catalysis without NH<sub>4</sub>PF<sub>6</sub> (Cp\*Ru/FeCp\*<sub>2</sub>) also led an inefficient reaction ( $x_c = 0.48$ ), indicating the importance of scavenging halogen (Br) by NH<sub>4</sub>PF<sub>6</sub> (Entry 4). Another controlled experiment was performed with Cp\*Ru/FeCp\*<sub>2</sub> in conjunction with *n*-Bu<sub>4</sub>NPF<sub>6</sub>, resulting the lower coupling efficiency ( $x_c = 0.72$ ) in 48 h (Entry 5) probably because *n*-Bu<sub>4</sub>NBr is soluble to organic phase and Br cannot be efficiently scavenged.

#### 4. <sup>1</sup>H NMR Analysis

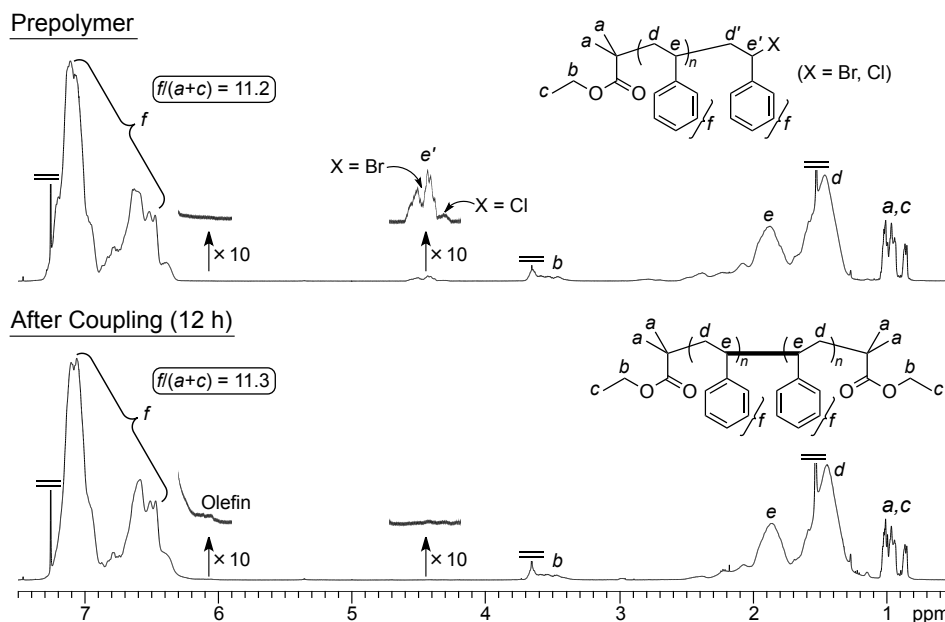
<sup>1</sup>H NMR spectra for the prepolymer (PSt-Br) and the coupled PSt (obtained by the suspension radical coupling reaction: 12 h) are shown in Figure 5. In the spectrum of the prepolymer, in addition to the characteristic signals of the main chain (*d–f*), some minor signals from chain ends were 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.<sup>29,30</sup> 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<sup>31</sup> reaction that causes small amounts of residual prepolymers in Figure 3.<sup>21</sup>

#### 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.<sup>32</sup> As shown in Figure 6, the suspension system allowed the efficient reaction to give chain extended PSt that have much higher  $M_p$



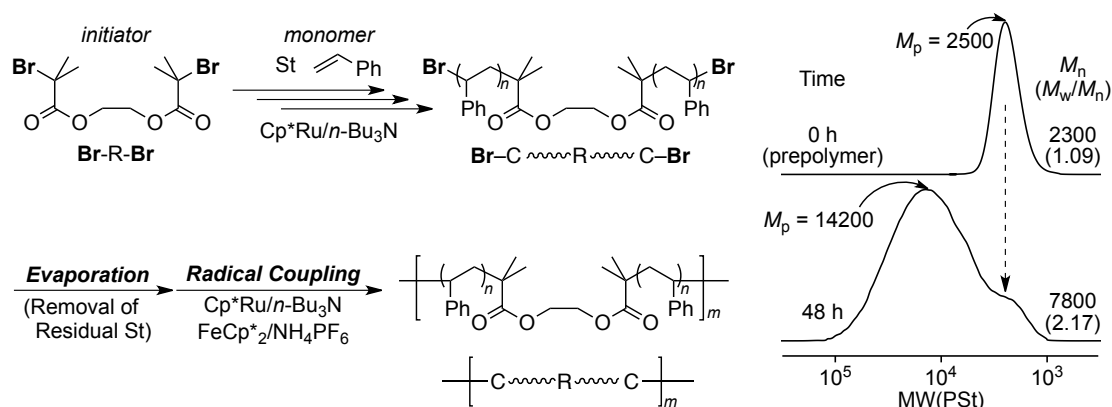


**Figure 5.**  $^1\text{H}$  NMR (500 MHz,  $30^\circ\text{C}$ ) analysis for the suspension radical coupling reaction of PSt-Br with  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  (see Figure 4 for the reaction condition):  $[\text{polymer}] = 30 \text{ mg/mL}$  in  $\text{CDCl}_3$ .

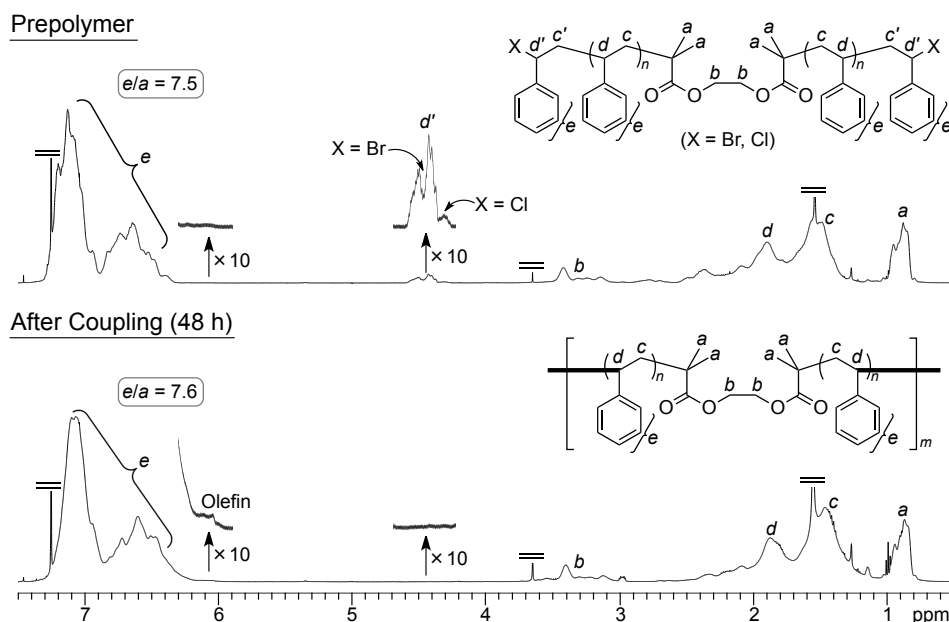
than prepolymers:  $M_p(\text{extended PSt}) = 14200$ ,  $M_p(\text{prepolymer}) = 2500$ . The averaged number of extended PSt units ( $m$ ) was roughly estimated to 5.7 from the ratio of the peak top molecular weight ( $m = M_p(\text{extended PSt})/M_p(\text{prepolymer})$ ).

$^1\text{H}$  NMR spectra for the prepolymer and the extended PSt (reaction time = 48 h) were shown in Figure 7. From the spectrum of the 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 moieties ( $a$ ) was almost same with that of the prepolymer (the prepolymer:  $e/a = 7.5$ , the coupled PSt:  $e/a = 7.6$ ) despite the clear increase of  $M_n(\text{SEC})$  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:  $[\text{Br-PSt-Br}]_0/[\text{Cp}^*\text{Ru}]/[n\text{-Bu}_3\text{N}]_0/[\text{FeCp}^*_2]_0/[\text{FeCp}^*_2]_0/[\text{NH}_4\text{PF}_6]_0 = 40/16/80/80/80$  mM in xylene/ $\text{H}_2\text{O}$  (organic phase/water = 1/1 v/v) at  $90^\circ\text{C}$ . The concentrations were based on the volume of the organic layer.



**Figure 7.**  $^1\text{H}$  NMR (500 MHz,  $30^\circ\text{C}$ ) analysis for the suspension radical coupling reaction of Br-PSt-Br with  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  (see Figure 6 for the reaction condition):  $[\text{polymer}] = 30$  mg/mL in  $\text{CDCl}_3$ .

## Conclusions

Efficient radical coupling reactions of end-halogenated polystyrenes were performed by using catalytic amount of Ru main catalysts ( $\text{Cp}^*\text{Ru}$ ) in conjunction with  $\text{FeCp}^*_2$  and  $\text{NH}_4\text{PF}_6$ , in which the following two steps are crucial for promoting the reaction: (a) the regeneration of  $\text{Ru}^{\text{II}}$  active complex with  $\text{FeCp}^*_2$  ( $\text{XRu}^{\text{III}} + \text{FeCp}^*_2 \rightarrow \text{Ru}^{\text{II}} + [\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{X}^-$ ); (b) scavenging halide anions ( $\text{X}^-$ ) with  $\text{NH}_4\text{PF}_6$  ( $[\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{X}^- + \text{NH}_4\text{PF}_6 \rightarrow [\text{Fe}^{\text{III}}\text{Cp}^*_2]^+\text{PF}_6^- + \text{NH}_4\text{X}$ ). In the radical coupling reaction of  $\omega$ -brominated polystyrene (PSt-Br), the author found that the suspension reaction (reaction solvent: xylene/ $\text{H}_2\text{O}$ ) 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  $\text{Cp}^*\text{Ru}/\text{FeCp}^*_2/\text{NH}_4\text{PF}_6$  was also used for the  $\alpha,\omega$ -dibrominated PSt ( $\text{Br}\sim\sim\text{R}\sim\sim\text{Br}$ ), giving the chain extended PSt having initiator moieties (R) periodically ( $[\sim\sim\text{R}\sim\sim]_m$ :  $m$  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

*ACS Macro Lett.* **2012**, *1*, 321–323.

### 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

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### 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

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## Part II

### Chapter 4

“Ferrocene Cocatalysis for Iron-Catalyzed Living Radical Polymerization: Active, Robust, and Sustainable System under Concerted Catalysis by Two Iron Complexes”

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### **Chapter 5**

“Efficient Kharasch Addition Reaction with  $\text{FeBr}_2/\text{FeCp}^*_2$  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**

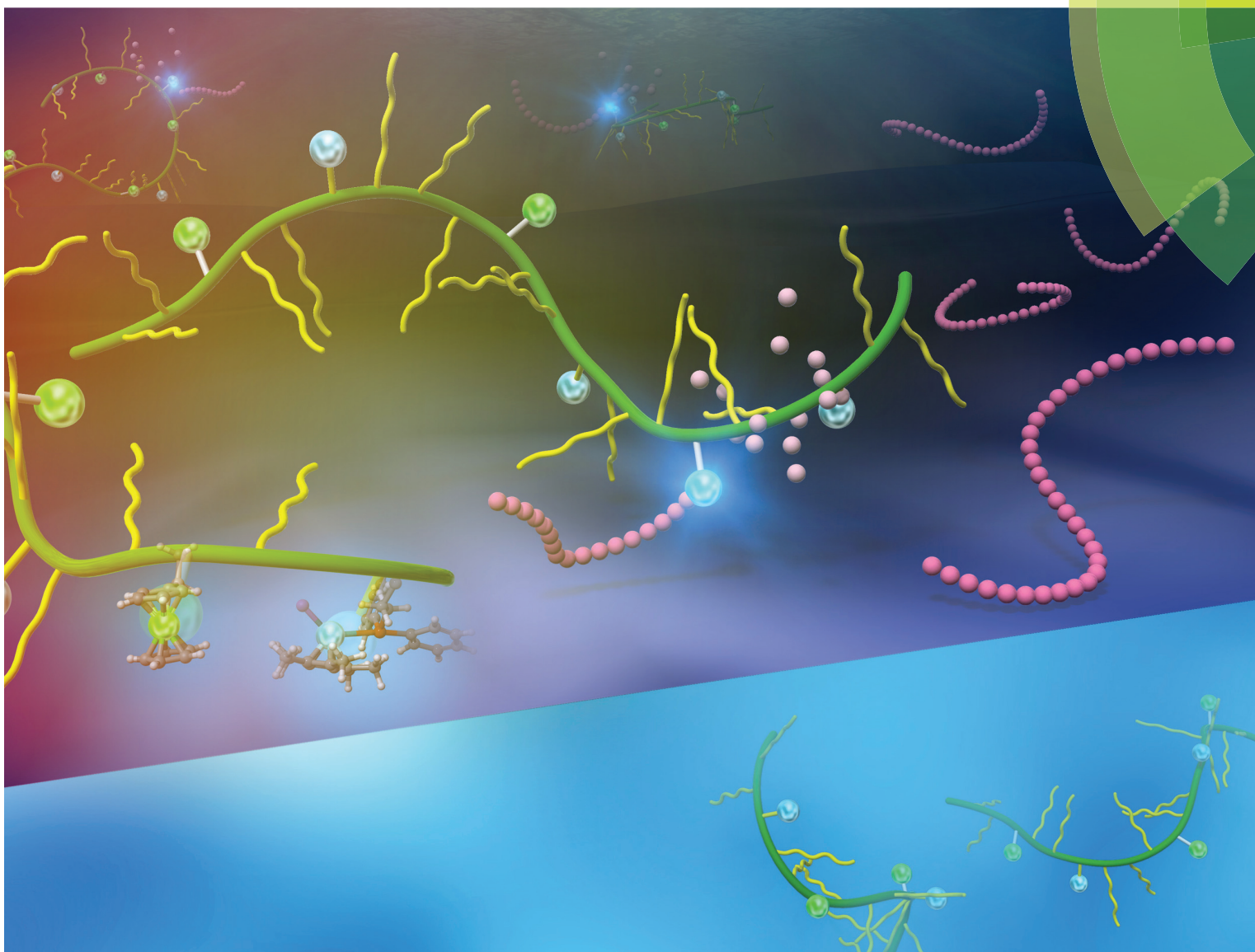
“Ferrocene Cocatalysis in Ruthenium-Catalyzed Radical Coupling Chain Extension: Catalytic Reaction through Catalyst Regeneration and Halogen Removal”

Kojiro Fujimura, Makoto Ouchi, and Mitsuo Sawamoto

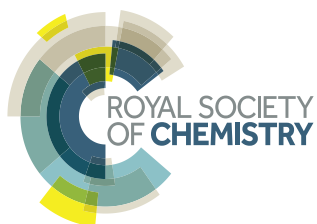
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## PAPER

Makoto Ouchi, Mitsuo Sawamoto *et al.*

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*Kojiro Fujimura*

*Department of Polymer Chemistry  
Graduate School of Engineering  
Kyoto University*