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

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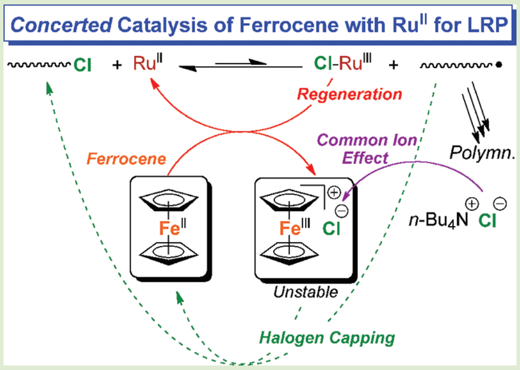
S *Supporting Information*

ABSTRACT: Ferrocene ($FeCp_2$), despite its high stability, was found, for the first time, to cocatalyze living radical polymerization in concert with a ruthenium main catalyst (Ru^{II}) that is directly responsible for generating growing radicals. $FeCp_2$ turned out to promote the following key reactions: regeneration of Ru^{II} through a reduction of XRu^{III} ($Fe^{II}Cp_2 + XRu^{III} \rightarrow Fe^{III}Cp_2^{+}X^{-} + Ru^{II}$; X: halogen); halogen-capping reaction, or regeneration of dormant species $\sim\sim\sim$C−X, by the resultant trivalent ferrocenium cation $Fe^{III}Cp_2^{+}$ ($\sim\sim\sim C\bullet + Fe^{III}Cp_2^{+}X^{-} \rightarrow \sim\sim\sim C{-}X + Fe^{II}Cp_2$). The cocatalysis was further improved by the addition of n-Bu_4NCl to allow a dramatic decrease in the initial Ru^{II} concentration without any loss of the high controllability. For example, in conjunction with $FeCp_2$/n-Bu_4NCl, only 50 ppm (for monomer) of Ru^{II} can catalyze living radical polymerization to give controlled polymers with high molecular weights and narrow molecular weight distributions ($M_n \sim 1.0 \times 10^5$; $M_w/M_n \sim 1.3$). Such a concerted catalysis with ferrocene would open the door to practical applications of living radical polymerization.



Metal-catalyzed living radical polymerization (LRP) is one of the useful tools to precisely prepare well-defined polymers.[1−8] The catalysis involves a reversible activation of a dormant carbon−halogen bond ($\sim\sim\sim$C−X; $\sim\sim\sim$: polymer chain; X: halogen) to give growing radical species, based on a one-electron redox of the catalyst ($Mt^{n} \leftrightarrow XMt^{n+1}$; 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 caused some specific issues: metal contamination of obtained polymers; deactivation of catalyst by polar groups; accumulation of oxidized forms by oxygen or unavoidable side reactions; and rising costs from precious metals.[3] An effective solution is to reduce the required amount of metal catalysts via promoting the catalytic cycle. Indeed, some methodologies have been developed for efficient catalysis for copper[5,8−12] and ruthenium[13−16] systems. Besides, an iron-based catalysis has recently attracted attention because of abundance, safety, and high biocompatibility. However, the current iron catalysis in LRP is still beyond satisfaction, as clearly indicated by few examples in precision polymer synthesis. Equally important, there seems little effective method for reducing the oxidized form (Ru^{III}) of ruthemium complexes into catalyticaly active, radical-generating reduced counterpart (Ru^{II}).[17]

Ferrocene ($FeCp_2$) is one of the most traditional organometallic complexes or metallocenes, and the robust η^6 ligation by two cyclopentadiene ligands with six electrons each is conductive to its high stability.[18] Therefore, $FeCp_2$ and the derivatives have rarely been employed as catalysts in polymerization and organic reactions. This is unexceptional in metal-catalyzed LRP: $FeCp_2$ 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 $FeCp_2$ is oxidized to the trivalent ferrocenium cation ($FeCp_2^{+}$).[19] For instance, $FeCp_2$ reacts with two equivalents of $FeCl_3$ as a strong oxidizing agent to give $FeCp_2^{+}FeCl_4^{-}$ and $FeCl_2$. In such $FeCp_2$-related redox reactions, the counteranion for the resulting cationic trivalent iron ($FeCp_2^{+}$) affects the stability of the salt: for example, $FeCp_2^{+}PF_6^{-}$ is stable enough to be isolated as a crystal, while $FeCp_2^{+}Cl^{-}$ is unstable and prone to decomposition.[20]

These phenomena motivated us to employ $FeCp_2$ 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 regeneration of dormant C−X ends, which involves a reduction of XMt^{n+1} into Mt^{n} (the primary catalyst): $FeCp_2 + XMt^{n+1} \rightarrow FeCp_2^{+}X^{-} + Mt^{n}$. Furthermore, due to its relative instability, resultant $FeCp_2^{+}X^{-}$ may induce a direct halogen-capping reaction onto the growing radical species or another route to regenerate the dormant end: $\sim\sim\sim C\bullet + FeCp_2^{+}X^{-} \rightarrow \sim\sim\sim C{-}X + FeCp_2$. Evidently, organic halide anions, such as n-$Bu_4N^{+}X^{-}$, are incapable of promoting such a halogen-capping reaction to radical species. However, the nature of the halide anion in $FeCp_2^{+}X^{-}$ should be quite different from that in the onium salts, as speculated by the stability difference. Consequently, as shown in Scheme 1, a concerted

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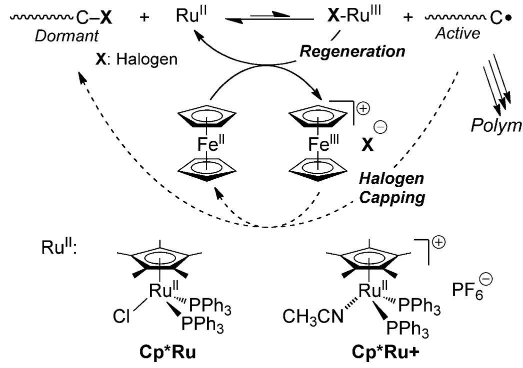
Scheme 1. Expected Cocatalysis of $FeCp_2$ in LRP and Ruthenium Catalysts in This Work



(co)catalysis of $FeCp_2$ and the main catalyst (e.g., ruthenium complex Ru^{II}) is expected. Herein, we report a novel catalysis via a concerted $FeCp_2$ cocatalysis for the ruthenium-catalyzed LRP.

A pentametylcyclopentatienyl rutheinum complex, Cp*-$RuCl(PPh_3)_2$ (**Cp*Ru**), is inherently active in metal-catalyzed LRP, as predicted by its lower redox potential and faster halogen exchange.[21] However, **Cp*Ru** usually needs a cocatalyst [e.g., $Al(O\textit{i}\text{-}Pr)_3$ or amine] that likely assists an in situ transformation of **Cp*Ru** into a coordinatively unsaturated, 16-electron form [e.g., $Cp^*RuCl(PPh_3)$] and a promotion of the halogen-capping reaction.[13,14,22] We, thus, selected **Cp*Ru** as a main catalyst to examine the cocatalysis of $FeCp_2$ in polymerization of methyl methacrylate (MMA) in conjunction with a chlorine initiator [H-$(MMA)_2$-Cl] in anisole at 100 °C: $[MMA]_0$ = 4.0 M, $[\text{H-(MMA)}_2\text{-Cl}]_0$ = 40 mM, $[\textbf{Cp*Ru}]_0$ = 4.0 mM, $[FeCp_2]_0$ = 40 mM. The addition of $FeCp_2$ obviously accelerated the polymerization (Figure 1A): Conversion in 49 h; 87% from 56% without $FeCp_2$. Obtained polymers were well-controlled and of narrow molecular weight distributions (MWDs; M_w/M_n < 1.2; Figure S1). Because $FeCp_2$ alone was totally inactive for MMA under otherwise the same conditions, these results indicate a concerted cocatalysis of $FeCp_2$ with the ruthenium primary catalyst.

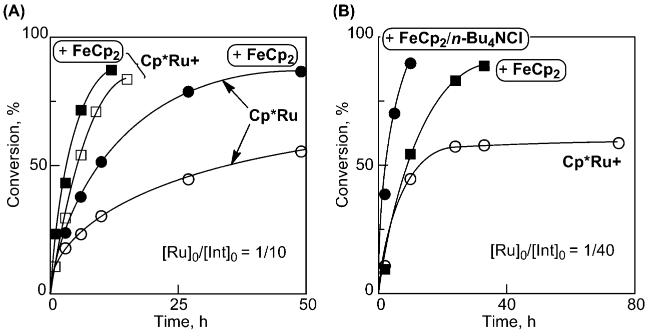


Figure 1. Effects of $FeCp_2$ on metal-catalyzed LRP of MMA with **Cp*Ru** or **Cp*Ru**$^+$ in anisole at 100 °C ($[MMA]_0/[\text{H-(MMA)}_2\text{-Cl}]_0$ = 4000/40 mM). (A) $[\textbf{Cp*Ru}]_0$ = 4.0 mM (○), $[\textbf{Cp*Ru}]_0/[FeCp_2]_0$ = 4.0/40 mM (●), $[\textbf{Cp*Ru}^+]_0$ = 4.0 mM (□), $[\textbf{Cp*Ru}^+]_0/[FeCp_2]_0$ = 4.0/40 mM (■); (B) $[\textbf{Cp*Ru}^+]_0$ = 1.0 mM (○), $[\textbf{Cp*Ru}^+]_0/[FeCp_2]_0$ = 1.0/40 mM (■), $[\textbf{Cp*Ru}^+]_0/[FeCp_2]_0/[n\text{-}Bu_4NCl]_0$ = 1.0/40/40 mM (●).

However, the polymerization with the **Cp*Ru**/$FeCp_2$ system was still not very fast, probably because ferrocene was incapable of generating coordinatively unsaturated ruthenium (Ru^{II}) species. Quite recently, we have found that a cationic ruthenium Cp* complex [$Cp^*Ru^+(CH_3CN)\text{-}(PPh_3)_2PF_6^-$: **Cp*Ru**$^+$] catalytically more active than **Cp*Ru** due to the smoother transformation into an unsaturated form via the spontaneous dissociation of the coordinated solvent (e.g., CH_3CN). Accordingly, a combination of **Cp*Ru+** with $FeCp_2$ led to a much faster polymerization (88% conversion in 12 h) with controllability retained (M_w/M_n < 1.1; Figure S2).

The cocatalytic effects of $FeCp_2$ were more remarkable at a lower initial dose of **Cp*Ru**$^+$ (1.0 mM, 1/40 equiv for the initiator; Figure 1B). The polymerization was retarded and leveled off without $FeCp_2$ (<60% conversion beyond 20 h), whereas with $FeCp_2$ smoothly reaching near completion and well controlled (89% conversion in 33 h; M_w/M_n = 1.13). Interestingly, the **Cp*Ru**$^+$/$FeCp_2$-catalyzed system was further accelerated upon addition of a chloride salt (n-Bu_4NCl, 40 mM), most likely via an additional promotion of the halogen-capping reaction by unstable $FeCp_2^+Cl^-$, in which n-Bu_4NCl 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" operated with the neutral **Cp*Ru** (Figure S3).

These positive effects of $FeCp_2$ also enabled the efficient synthesis of higher molecular weight polymers (1000 mer) at a high monomer concentration ($[MMA]_0$ = 6.0 M; $[\text{H-(MMA)}_2\text{-Cl}]_0$ = 6.0 mM). For this, an extremely small amount of **Cp*Ru**$^+$ (0.3 mM; 50 ppm for monomer) was injected along with $FeCp_2$ and n-Bu_4NCl ($[FeCp_2]_0$ = 12 mM; $[n\text{-}Bu_4NCl]_0$ = 0.5 mM). As shown in Figure 2, the observed M_ns 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.

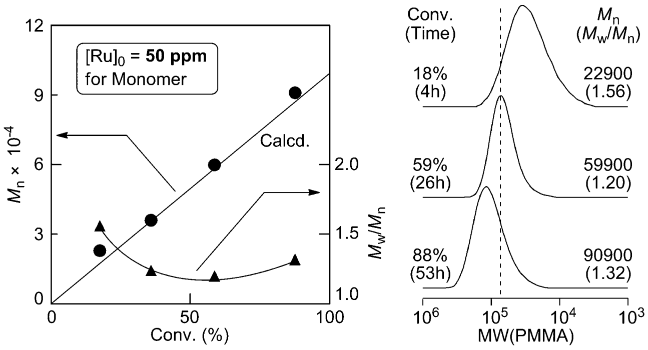


Figure 2. Syntheses of high MW poly(MMA)s with a low amount of ruthenium catalyst in conjunction with $FeCp_2$: $[MMA]_0/[\text{H-(MMA)}_2\text{-Cl}]_0/[\textbf{Cp*Ru}^+]_0/[FeCp_2]_0/[n\text{-}Bu_4NCl]_0$ = 6000/6.0/0.3/12/0.5 mM in anisole at 100 °C.

The redox-promoting function of $FeCp_2$ as a reducing agent was verified by a radical coupling reaction of a model dormant end [R–Cl: ethyl 2-chloro-2-phenylacetate (ECPA)] catalyzed with the **Cp*Ru**$^+$/$FeCp_2$ pair (without n-Bu_4NCl; Figure 3). The reaction was carried out in the presence of a chlorine-free ammonium salt (NH_4PF_6) to exclude the secondary role of $FeCp_2$ as an indirect chloride donor via $FeCp_2^+Cl^-$, which forms in situ as the reduction proceeds: $FeCp_2 + ClRu^{III} \rightarrow FeCp_2^+Cl^- + Ru^{II}$. The added NH_4PF_6 instead transforms the

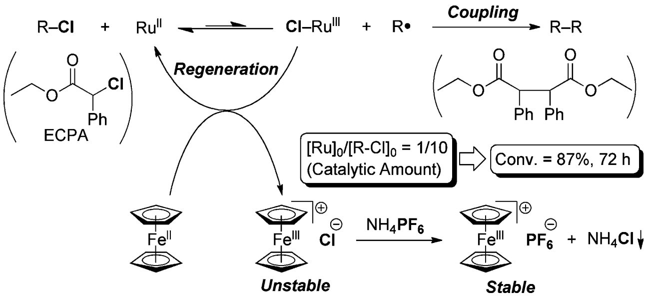


Figure 3. Coupling reaction of ECPA with **Cp*Ru$^+$** in conjunction with FeCp$_2$/NH$_4$PF$_6$ in toluene-d_8/THF (2/1 v/v) at 100 °C. [ECPA]$_0$/[**Cp*Ru$^+$**]$_0$/[FeCp$_2$]$_0$/[NH$_4$PF$_6$]$_0$ = 40/4.0/40/40 mM.

chloride irreversibly into a more stable form FeCp$_2{}^+$PF$_6$. Despite a low catalyst dose ([**Cp*Ru$^+$**]$_0$/[ECPA]$_0$ = 1/10), the coupling product (R−R) was obtained in high yield (87% in 72 h; Figures S4 and S5). Without FeCp$_2$, the reaction was retarded (<13%), indicative of the accumulation of ClRu^{III}. These results support cocatalysis of FeCp$_2$ via the reduction of ClRu^{III} into Ru^{II}. Additionally, this catalytic performance suggests an in situ catalysis transformation (a one-pot cascade reaction) to be triggered just by addition of NH$_4$PF$_6$; for example, from the FeCp$_2$-cocatalyzed LRP into a coupling reaction of the obtained polymer chains. This is now under investigation.

Another expected contribution of FeCp$_2$ to LRP is the promotion of the halogen-capping of radical species via in situ generated FeCp$_2{}^+$Cl$^-$: ∼∼∼C• + FeCp$_2{}^+$Cl$^-$ → ∼∼∼C−Cl + FeCp$_2$. This was confirmed in conventional free radical polymerization (Figure S6): MMA was first polymerized with an azo initiator [1,1′-azobis(cyclohexane-1-carbonitrile) (V-40); 10 h half-life decomposition temperature 88 °C] in the presence of FeCp$_2{}^+$PF$_6{}^-$, and, at 40−50% monomer conversion, an equimolar amount of n-Bu$_4$NCl was added in situ to transform FeCp$_2{}^+$PF$_6{}^-$ into FeCp$_2{}^+$Cl$^-$. The polymerization was terminated, where the FeCp$_2{}^+$Cl$^-$ effectively capped the free radicals into inactive covalent terminals. On the other hand, the polymerization with V-40 in the *absence* of FeCp$_2{}^+$PF$_6{}^-$ was not disturbed by addition of n-Bu$_4$NCl. From these results, FeCp$_2{}^+$Cl$^-$ (in situ generated in LRP) promotes the radical capping reaction via the reduction of itself.

In conclusion, we have demonstrated the concerted catalysis of ferrocene for metal-catalyzed LRP. In addition to positive effects on LRP such as acceleration, the catalysis is unique and of interest. Coupled with ruthenium complex, ferrocene contributes to not only the regeneration of Ru^{II} but also the halogen-capping reaction for growing radical species along with its own redox cycle (Fe^{II} ↔ Fe^{III}). Thus, the redox catalytic cycle in LRP was efficiently rotated to allow a decrease in the dose of the main catalyst without serious loss of control. The additional experiments (i.e., a coupling reaction of R-X and in situ formation of FeCp$_2{}^+$Cl$^-$ in free radical polymerization) likely support these contributions, although they are not perfect as the evidence yet. We are now studying a relation of redox potential between the main catalyst and ferrocene to clarify more detailed mechanism. Thus, our next interest is directed to a combination of FeCp$_2$ with an iron-based catalyst toward more practical LRP systems that are faster, more efficient, robust, have higher functionality, and are tolerant with a minute use of metal catalysts.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and results (SEC curves, ^{1}H NMR, and time−conversion curves) for polymerization and coupling reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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