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Redox-switchable atom transfer radical polymerization†

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Temporal control in atom transfer radical polymerization (ATRP) relies on modulating the oxidation state of a copper catalyst, as polymer chains are activated by L/Cu^{I} and deactivated by L/Cu^{II}. (Re)generation of L/Cu^{I} activator has been achieved by applying a multitude of external stimuli. However, switching the Cu catalyst off by oxidizing to L/Cu^{II} through external chemical stimuli has not yet been investigated. A redox switchable ATRP was developed in which an oxidizing agent was used to oxidize L/Cu^{I} activator to L/Cu^{II}, thus halting the polymerization. A ferrocenium salt or oxygen were used to switch off the Cu catalyst, whereas ascorbic acid was used to switch the catalyst on by (re)generating L/Cu^{I}. The redox switches efficiently modulated the oxidation state of the catalyst without sacrificing control over polymerization.

Catalysts activity can be efficiently tuned by external stimuli, altering their redox properties or steric environment. Redox-switchable catalysis can provide chemo-, regio- and stereochemical, as well as temporal control over reactions, thus being a fundamental tool in catalysis and supramolecular chemistry.[1–3] The most explored strategy consists of designing ligands that incorporate redox-active groups,[3] particularly ferrocenyl units.[4–7] Alternatively, the oxidation state of a catalyst center can be directly modulated to alter its activity.[1,8,9]

Controlled polymerization techniques have recently been advanced by applying external stimuli for triggering polymerization processes.[8,10,11] The use of external stimuli allows polymerizations to be controlled in a spatiotemporal manner, providing a great opportunity for synthesis of advanced polymers with pre-determined, tunable properties.

A great deal of research has been devoted to regulating various polymerization techniques by external control. Most widely studied stimuli include photochemistry,[12–19] electrochemistry,[20–22] mechanical,[23] chemical,[24,25] and redox control.[9,26–33] These stimuli reversibly affect the redox properties of the catalyst, thus allowing control over polymerization rate or mechanism.

Atom transfer radical polymerization (ATRP) has become a common technique to prepare well-defined polymers.[34–39] Recent advances in ATRP have focused on (re)generation of the activator form of the catalyst through external means. Using external stimuli for activator (re)generation elicits spatiotemporal control over ATRP processes.[11]

In Cu-catalyzed ATRP, temporal control depends on the concentration of L/Cu^{I} activator, as well as how fast it can be consumed or removed from the reaction media. In the absence of stimuli, L/Cu^{I} is mainly consumed by irreversible radical terminations. Each termination event causes the accumulation of two molecules of L/Cu^{II} deactivator. Subsequently, polymerization stops in the absence of activator regeneration. In this regard, the ATRP equilibrium and the ratio of [L/Cu^{II}]/[L/Cu^{I}] depend on the activity of the catalyst.[40] Therefore, for highly active catalytic systems, the large ATRP equilibrium constant results in a very low L/Cu^{I} concentration, and thus the reaction stops rapidly. Conversely, for less active systems, the presence of high concentration of activator species enables the polymerization to continue for longer, until all the catalyst is converted to L/Cu^{II}.[38]

The majority of ATRP reactions regulated by external stimuli relies on using the stimuli to switch the reaction on by reducing L/Cu^{II} to L/Cu^{I}.[11] However, oxidation of L/Cu^{I} to L/Cu^{II}, which would lead to on-demand switching of ATRP between on/off states, has not been widely studied. Electrochemically mediated ATRP uniquely enables both the reduction and oxidation of the Cu catalyst *via* alternate application of reducing and oxidizing currents or potentials.[20,41–43]

Indeed, the ATRP equilibrium—maintained *via* a redox process using a Cu catalyst—provides the possibility of on-demand switching of the polymerization by affecting the oxidation state of the catalyst. This behavior allows for efficient temporal control over chain growth to be attained in ATRP, which would not be accessible in other conventional or controlled radical polymerization techniques.

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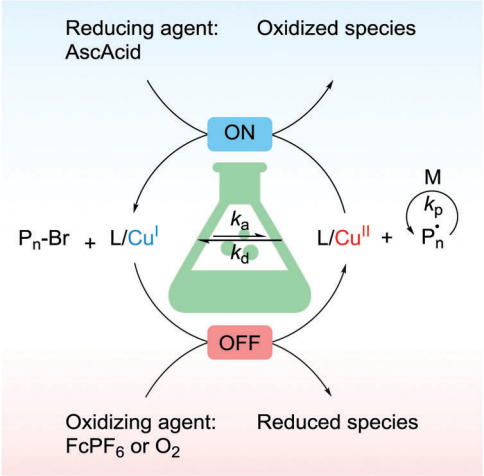

Scheme 1 Redox-switchable ATRP by using AscAcid as reducing agent and $FcPF_6$ or oxygen as oxidizing agents.

In this paper, a chemically controlled ATRP was developed in which the activity of the Cu catalyst was switched *via* redox processes (Scheme 1). As in activators regenerated by electron transfer (ARGET) ATRP, ascorbic acid (AscAcid) was used as a reducing agent to (re)generate the L/Cu^I activator and switch the reaction on.[44] Ferrocenium hexafluorophosphate ($FcPF_6$) or oxygen were used as oxidizing agents to oxidize L/Cu^I to L/Cu^{II}, and therefore turn the reaction off.

ARGET ATRP of methyl acrylate (MA) was conducted in *N*,*N*-dimethylformamide (DMF) using $CuBr_2$/Me_6TREN as a catalyst (Me_6TREN: tris[2-(dimethylamino)ethyl]amine). AscAcid was added initially to start the polymerization. Monomer conversion reached 56% in 6 h, with the rate of the polymerization decreasing over time (Fig. 1). Size exclusion chromatography (SEC) analysis showed the final polymer with a low dispersity ($Đ$ = 1.10), and molecular weight (MW) matching theoretical value ($M_{n,th}$ = 9850, M_n = 10 100). The activator L/Cu^I was switched off by oxidizing to L/Cu^{II} using $FcPF_6$ as an oxidizing agent. ARGET ATRP of MA was conducted under similar initial conditions, with ~30% monomer conversion reached within 1 h. Afterward, $FcPF_6$ (10 mol% with respect to Cu) was added. Kinetic results showed a significant decrease in the rate of the reaction, which continued to only ~39% monomer conversion, and then stopped (Fig. 1). Indeed, it was previously determined that the standard reduction potential of $CuBr_2$/Me_6TREN in DMF is $E^0_{[(L/Cu^{II})/(L/Cu^I)]} = -0.32$ V *vs.* saturated calomel electrode (SCE),[45] whereas $E^0_{(Fc^+/Fc)} = 0.48$ V *vs.* SCE was measured for the redox couple of ferrocenium/ferrocene in DMF.[46] Therefore, ferrocenium is a suitable oxidant for the Cu catalyst. In addition, AscAcid is oxidized by reacting with both L/Cu^{II} and $FcPF_6$.[47] However, the small increase in monomer conversion suggested that residual AscAcid further regenerated the L/Cu^I activator, which continued the polymerization. Importantly, SEC analysis showed a polymer with a monomodal, symmetric MW distribution ($M_{n,th}$ = 6950, M_n = 7050 and $Đ$ = 1.12). Interestingly, when the amount of $FcPF_6$ was increased to 50 mol% with respect to Cu, the reaction was instantaneously and completely stopped. In this case, the $FcPF_6$ salt oxidized all the L/Cu^I and residual AscAcid, so that no monomer conversion was observed.

Vis-NIR spectroscopy of the Cu catalyst confirmed its successive reduction and oxidation upon sequential addition of AscAcid and $FcPF_6$ (Fig. 2). A decrease in the absorption peak of L/Cu^{II} at ~960 nm was observed upon addition of AscAcid, indicating reduction to L/Cu^I. $FcPF_6$ was later added to the solution, and the absorption spectra increased to the initial state. These observations proved that L/Cu^{II} could be successfully reduced to L/Cu^I by addition of AscAcid and oxidized back to L/Cu^{II} in the presence of $FcPF_6$.

Having confirmed the efficiency of AscAcid and $FcPF_6$ in switching the redox properties of Cu species, and hence controlling the reaction, temporal control was attempted using these chemical redox switches. AscAcid started the ARGET ATRP of MA with 27% monomer conversion obtained in 1 h. Afterward, $FcPF_6$ (25 mol% with respect to Cu) was added to stop the reaction (Fig. 3). Negligible monomer conversion was observed during the 5 h period after the addition of $FcPF_6$, and the reaction stopped (30% conversion at 6 h). A second batch of AscAcid ([AscAcid] = [L/Cu]) was added to switch the reaction on

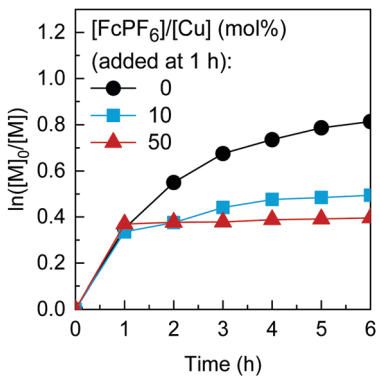

Fig. 1 Redox control in ATRP by using AscAcid and $FcPF_6$ as redox agents. Reaction conditions: [MA]/[EBiB]/[$CuBr_2$]/[Me_6TREN]/[AscAcid] = 200/1/0.04/0.04/0.04 in 50 vol% DMF at 25 °C. AscAcid added initially. $FcPF_6$ (10 or 50 mol% with respect to Cu) added at 1 h.

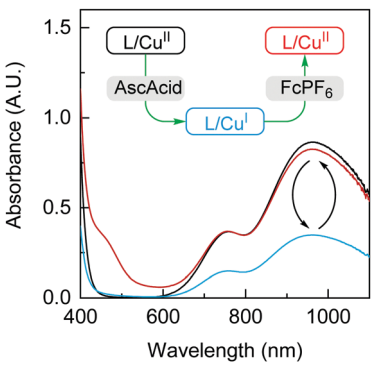

Fig. 2 Evolution of the Vis-NIR spectra of Cu catalyst after sequential addition of AscAcid and $FcPF_6$. [$CuBr_2$/Me_6TREN] = [AscAcid] = [$FcPF_6$] = 2.22 mM in DMF. $FcPF_6$ was added 30 min after addition of AscAcid.

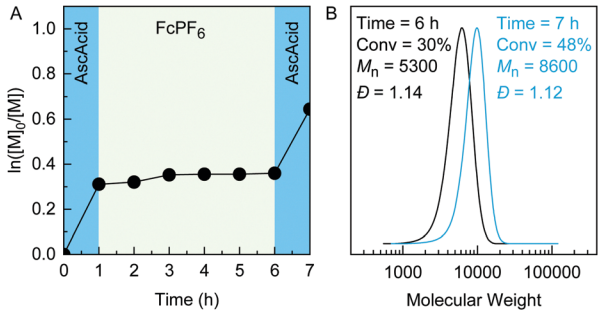

Fig. 3 (A) Temporal control of ATRP using AscAcid and $FcPF_6$ as redox switches. (B) SEC traces after addition of $FcPF_6$ and AscAcid. Reaction conditions: [MA]/[EBiB]/[$CuBr_2$]/[Me_6TREN]/[AscAcid] = 200/1/0.04/0.04/0.04 in 50 vol% DMF at 25 °C. AscAcid added at 0 and 6 h. $FcPF_6$ (25 mol% with respect to Cu) added at 1 h.

by regenerating L/Cu^I. Monomer conversion reached 48% within 1 h, confirming the preservation of chain-end functionality in the presence of chemical switches. Importantly, SEC analysis of the polymer showed monomodal, symmetric MW distributions upon successive addition of redox switches. SEC traces showed a clear shift toward higher MWs after the addition of the second batch of AscAcid, indicating a well-controlled process.

Oxygen was a simple alternative to $FcPF_6$ as an oxidizing agent for L/Cu^I, efficiently turning the ATRP catalyst off. An ARGET ATRP of MA was conducted under similar conditions using AscAcid, with 37% monomer conversion reached in 1 h (Fig. 4). Then, the polymerization solution was bubbled with air for 1 min. No monomer conversion was observed after exposure to oxygen, indicating complete oxidation of all activator and AscAcid. Consequently, the polymerization was successfully switched off. The standard reduction potential of oxygen in DMF was estimated as $E^{\theta}_{(O_2/H_2O)} = 1.08$ V *vs.* SCE, therefore oxygen is a stronger oxidizing agent compared to $FcPF_6$.[48] Importantly, the reaction was restarted upon the addition of a second batch of AscAcid ([AscAcid] = [L/Cu]) after 6 h. Monomer conversion reached 63% within the following hour. SEC analysis of the polymer revealed a symmetric, mono-modal MW distribution after the addition of AscAcid. These results indicated that a well-controlled polymerization was achieved in the presence of AscAcid and oxygen as redox switches. The chain-end functionality was preserved throughout the reaction enabling further chain growth in a controlled manner.

The robustness of this polymerization system was further confirmed by switching the polymerization for multiple times using AscAcid and oxygen as redox switches (Fig. 5 and Fig. S4, ESI†). The polymerization was proceeded in the presence of AscAcid, which regenerated the activator. Introducing oxygen stopped the reaction through oxidation of the catalyst. The polymerization was well-controlled upon successive additions of AscAcid and oxygen. It is worth mentioning that in these experiments the amount of oxidizing agents was always relatively low, so as to allow an effective re-starting of the process by adding AscAcid and to limit the contamination of the system.

The reduction and oxidation of the Cu catalyst by AscAcid and oxygen was also confirmed by Vis-NIR spectroscopy. The absorption peak of L/Cu^{II} at ~960 nm decreased upon addition of AscAcid indicating reduction to L/Cu^I. The solution was bubbled with air and the absorption peak partially increased, suggesting re-oxidation to L/Cu^{II} (Fig. S5, ESI†). Interestingly, further addition of AscAcid resulted in a reduction to L/Cu^I. These results supported that the Cu catalyst can be reversibly toggled between L/Cu^I and L/Cu^{II} states using redox switches, for multiple times.

In summary, the activity of the Cu catalyst in ATRP was effectively switched on and off using chemical redox switches. AscAcid acted as a reducing agent that turned the reaction on by (re)generating the L/Cu^I activator. An oxidizing agent, such as the $FcPF_6$ salt or oxygen, switched off the Cu catalyst by oxidizing it to L/Cu^{II}, thus stopping the reaction. These species efficiently altered the oxidation state of the Cu catalyst enabling perfect temporal control over the polymerization. Importantly, chain-end functionality was preserved in the presence of oxidizing agents, as further addition of AscAcid restarted the polymerization in a controlled manner.

Future work will focus on investigating temporal control in ATRP regulated by external stimuli to improve the mechanistic understanding of these techniques and broaden their scope.

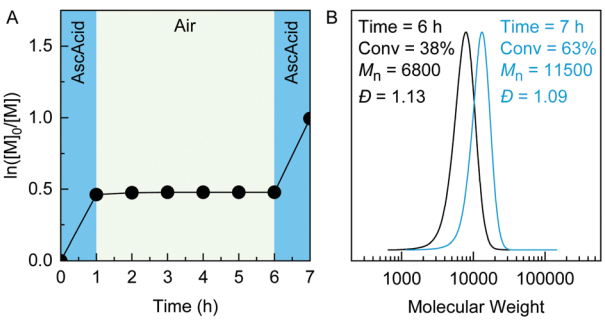

Fig. 4 (A) Temporal control of ATRP using AscAcid and oxygen as redox switches. (B) SEC traces after bubbling with air and addition of AscAcid. Reaction conditions: [MA]/[EBiB]/[$CuBr_2$]/[Me_6TREN]/[AscAcid] = 200/1/0.04/0.04/0.04 in 50 vol% DMF at 25 °C. AscAcid added at 0 and 6 h. Air bubbled for 1 min at 1 h. Nitrogen bubbled for 2 min at 6 h.

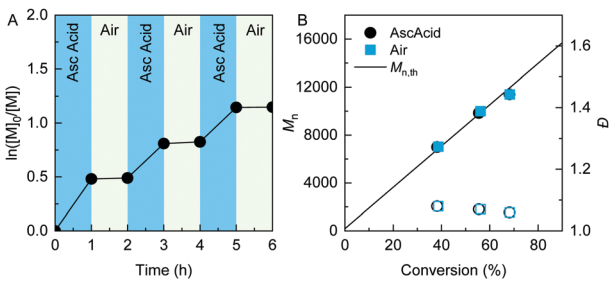

Fig. 5 (A) Kinetics of temporal control using AscAcid and oxygen as redox agents. (B) Number-average molecular weight (M_n, solid points) and dispersity ($Đ$, open points) as a function of monomer conversion. Reaction conditions: [MA]/[EBiB]/[$CuBr_2$]/[Me_6TREN]/[AscAcid] = 200/1/0.04/0.04/0.04 in 50 vol% DMF at 25 °C. AscAcid added at 0, 2 and 4 h. Air bubbled for 1 min at 1, 3, and 5 h. Nitrogen bubbled for 2 min at 2 and 4 h.

In addition to the chemical stimuli presented in here, new advanced techniques comprised of orthogonal multi-stimuli will be developed to precisely modulate the ATRP catalyst.

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Conflicts of interest

There are no conflicts to declare.

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