ACS Catalysis

Letter

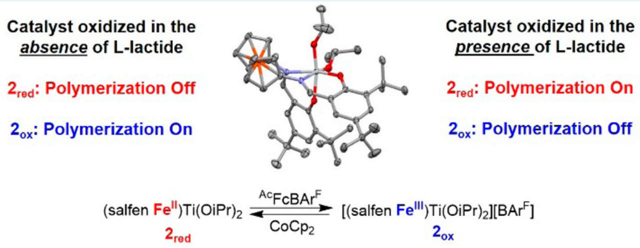
pubs.acs.org/acscatalysis

Effects of Ferrocenyl Proximity and Monomer Presence during Oxidation for the Redox-Switchable Polymerization of L-Lactide

Lauren A. Brown, Jennifer L. Rhinehart, and Brian K. Long*

Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996, United States

Supporting Information



ABSTRACT: A titanium(IV) salfen catalyst bearing a redox-active ferrocenyl center in close proximity to the active metal site was examined for the redox-switchable polymerization of L-lactide. The catalyst displayed an atypical β-cis geometry in both the solid- and solution-states, and placement of the redox-active moiety in close proximity to the active metal site was shown to provide an enhancement in catalytic "on—off—on" switching behavior when the redox events were performed in the presence of lactide monomer. More importantly, when comparing oxidized and reduced catalytic species, completely contrasting trends in polymerization behavior were observed, depending on whether the catalyst was oxidized in the absence or in the presence of lactide monomer. On the basis of NMR spectroscopic analysis, we propose that this unusual behavior is a result of a rapid switch in ligand coordination geometry that is facilitated by monomer coordination prior to any redox reactions. Additionally, when redox reactions were conducted in the absence of monomer, a trend in activity that contradicted those of all previously reported Ti-based redox-active catalysts was observed.

KEYWORDS: *L-lactide, redox-active, titanium, oxidation, reduction, polymerization, polyester*

Redox-switchable catalysis (RSC) offers a unique method by which the reactivity or selectivity of a catalytic process may be altered via modulations in the oxidation state of the active transition-metal site or its surrounding ligands.[1] This concept was first reported in 1995 by Wrighton and co-workers, who demonstrated that the reduced form of a diphosphinocobaltocene stabilized rhodium complex showed greater activity for the transfer hydrogenation of olefins than its oxidized analogue.[2] This difference in catalytic behavior was attributed to changes in the electron density at the active metal site as a function of ligand oxidation state and has since spawned a thriving area of research[1,3−5] that has expanded its impact even to several popular polymerization methodologies, such as ring-opening polymerizations and controlled radical polymerizations.[6−12]

To date, the majority of reported redox-switchable polymerizations (RSPs) have utilized single-site catalysts bearing redox-active ligands to achieve this "switch" in catalytic behavior, such as those containing ferrocenyl moieties.[7,9,11] However, a subset of reports have shown similar results can be observed when the active transition-metal site is itself oxidized or reduced, as has been reported for certain cerium- and iron-based catalysts.[10,12,13] A prominent example in which a redox-active ligand was used to facilitate RSP was reported by Gibson and co-workers in which a catalyst (**1**) bearing two ferrocenyl moieties located on the outer extremities of the ligand scaffold was used.[9] In that report, it was shown that the reduced form of catalyst **1** polymerized lactide at a significantly greater rate than its oxidized counterpart, an observation that was again attributed to changes in electron density at the active metal site. This observation in which the more electron-rich catalytic species displays an enhanced polymerization rate for the ring-opening polymerization of cyclic esters (as compared with their electron-deficient counterparts) is true for all early-transition-metal-based catalysts bearing salen-like ligands.[7,9,14] In contrast, initiators containing main group metals, such as aluminum[15−20] and indium,[11] typically exhibit the opposite behavior in which catalysts bearing electron-deficient ligands typically display the highest activity for the polymerization of lactide.

Given that these oscillations in catalytic behavior are directly attributed to changes in electron density at the propagating metal center, it can be surmised that the proximity of the redox-active moiety may play a significant role in the differentiation of reduced and oxidized catalytic species; however, to date, there have been no direct investigations into the effects that redox-active site proximity (to the active metal site) has on the RSP of cyclic esters. Because of the straightforward accessibility and broad success of salen-based catalysts for the polymerization of cyclic esters, we chose to synthesize and study catalyst **2** in an effort to observe the effects associated with moving the redox moiety from the ligand's outer extremities to a location proximal to the active titanium site (Figure 1). Herein, we report the synthesis and catalytic behavior of catalyst **2** for the RSP of L-lactide.

Received: July 9, 2015
Revised: August 18, 2015
Published: September 14, 2015

ACS Publications

© 2015 American Chemical Society

DOI: 10.1021/acscatal.5b01434
ACS Catal. 2015, 5, 6057−6060

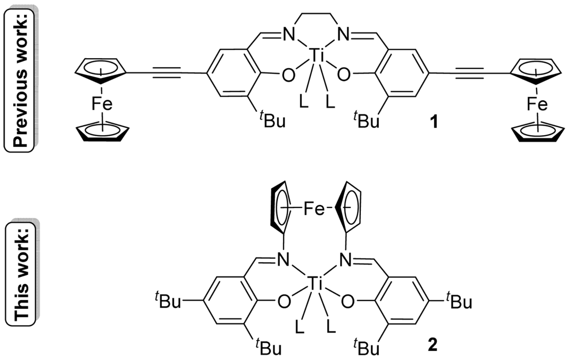
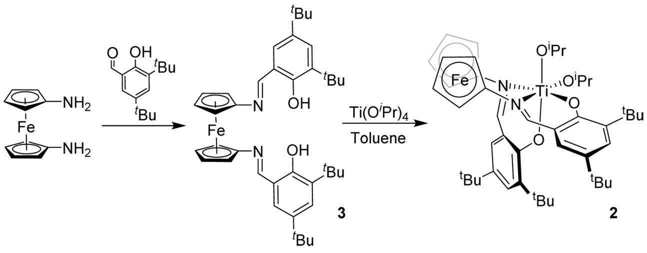


Figure 1. Comparison of catalysts bearing redox-active ferrocenyl moieties distal to the active metal site (**1**) and a ferrocenyl moiety proximal to the active metal center (**2**) (L = O^{i}Pr).

The H_2(salfen) pro-ligand **3** was synthesized as previously reported[21] and metalated using Ti(O^{i}Pr)$_4$ to yield catalyst **2** (Scheme 1). The metal complex was characterized using standard spectroscopic techniques and via solid-state, single-crystal X-ray diffraction in which suitable crystals were grown by slow evaporation of hexanes (Figure 2). As seen in Figure 2, catalyst **2** was found to adopt a distorted *β*-cis conformation in the solid state. ^{1}H NMR spectroscopy confirmed that the catalyst's *β*-cis conformation is present in the solution state, as well, in which the asymmetry of the catalyst's *β*-cis conformation causes each proton on the aryl, imine, and isopropoxide moieties to be magnetically inequivalent. This observation is unique in that similar Ti-based catalysts, such as complex **1**, are known to adopt a trans configuration in both the solid and solution states.[14,22−25]

Scheme 1. Synthesis of Redox-Active Catalyst 2



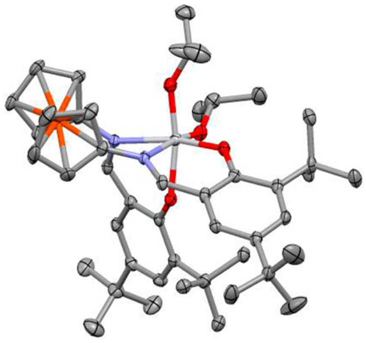
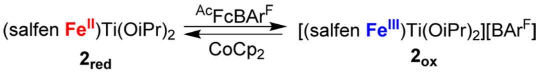


Figure 2. ORTEP representation of complex **2**. Thermal ellipsoids were drawn at 50% probability, and all hydrogen atoms were omitted for clarity.

Cyclic voltammetry (CV) experiments were performed in DCM with [*n*Bu$_4$N][PF$_6$] (0.2 M) as an electrolyte and scanned at a rate of 50 mV/s, which revealed that catalyst **2** had a redox half-wave potential ($E_{1/2}$) of −0.085 V versus Fc/Fc$^+$ (see Supporting Information). From this value, silver triflate and decamethylferrocene were initially chosen as suitable oxidizing and reducing agents, respectively; however, they were found to complicate our investigations, often requiring filtration to remove problematic Ag particulates after oxidation reactions. To avoid these issues, for all subsequent studies (Scheme 2), we utilized acetylferrocenium tetrakis(3,5-bis(trifluoromethyl)-phenyl) borate (^{Ac}FcBAr^F) and cobaltocene (CoCp$_2$) as redox agents, both of which have been successfully used in other RSC reports.[7]

Scheme 2. Redox-switch between catalysts $\mathbf{2}_{\mathrm{red}}$ and $\mathbf{2}_{\mathrm{ox}}$



$$\underset{\mathbf{2}_{\mathrm{red}}}{(\text{salfen Fe}^{\text{II}})\text{Ti(OiPr)}_2} \xrightleftharpoons[\text{CoCp}_2]{^{\text{Ac}}\text{FcBAr}^{\text{F}}} \underset{\mathbf{2}_{\mathrm{ox}}}{[(\text{salfen Fe}^{\text{III}})\text{Ti(OiPr)}_2][\text{BAr}^{\text{F}}]}$$

Polymerizations of L-lactide were performed at 90 °C in either benzene-d_6 or toluene and were monitored via variable temperature NMR. A plot of monomer conversion versus time is shown in Figure 3, in which the reduced catalyst $\mathbf{2}_{\mathrm{red}}$ demonstrates a dramatically slower rate of polymerization compared with that of oxidized catalyst $\mathbf{2}_{\mathrm{ox}}$ (note: catalyst $\mathbf{2}_{\mathrm{red}}$ was oxidized using ^{Ac}FcBAr^F prior to monomer addition), reaching only 2% conversion in 3.5 h, as compared with over 50% conversion when using catalyst $\mathbf{2}_{\mathrm{ox}}$ in that same amount of time. This indicated that the more electron-deficient catalyst $\mathbf{2}_{\mathrm{ox}}$ polymerized lactide at a much greater rate than the more electron-rich catalyst $\mathbf{2}_{\mathrm{red}}$, representing a completely opposite trend in catalytic activity as compared with catalyst **1**. Extended polymerization times up to 8 h show that catalyst $\mathbf{2}_{\mathrm{ox}}$ readily exceeds 90% conversion of monomer to polymer, whereas catalyst $\mathbf{2}_{\mathrm{red}}$ reaches only ∼10% conversion to polymer. The reactivity of catalyst $\mathbf{2}_{\mathrm{red}}$ is remarkably low when compared with similar Ti-based initiators, such as **1**, and although further studies must be conducted, we postulate that this contradictory trend in catalytic activity may be related to the unusual *β*-cis conformation adopted by $\mathbf{2}_{\mathrm{red}}$. It should also be noted that similarly low polymerization activities have been reported for related Ti-salen-based catalysts that are believed to also adopt a *β*-cis conformation.[14,22−25]

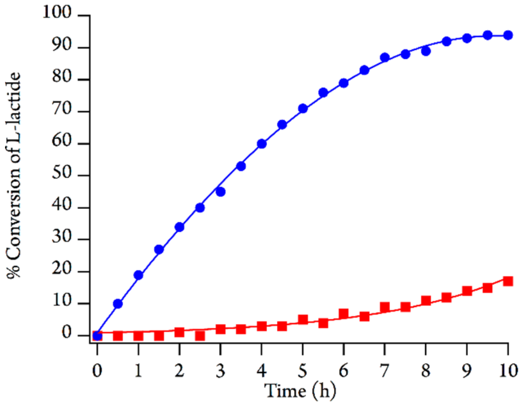


Figure 3. Plot of polymerization conversion versus time for the polymerization of L-lactide (100 equiv, 1 M) in C_6D_6 at 90 °C using catalyst $\mathbf{2}_{\mathrm{red}}$ (red squares) or $\mathbf{2}_{\mathrm{ox}}$ (blue circles) (note: the oxidation of catalyst $\mathbf{2}_{\mathrm{red}} \rightarrow \mathbf{2}_{\mathrm{ox}}$ was performed prior to monomer addition).

To examine the redox-switching ability of catalyst **2**, polymerizations were conducted in which the catalyst oxidation state was modulated in situ via addition of ^{Ac}FcBAr^{F} and CoCp$_2$ respectively (Figure 4). In this experiment, reduced catalyst $\mathbf{2}_{\mathrm{red}}$ was added to 100 equiv of monomer and heated to 90 °C. ^{1}H NMR analysis showed virtually no monomer conversion to polymer after 3 h (time period A, Figure 4), as was predicted by the results in Figure 3. However, upon addition of ^{Ac}FcBAr^{F} to oxidize the ferrocenyl moiety, the polymerization rate increased quickly, as predicted, yet subsided after reaching only ∼4−6% conversion (time period B, Figure 4). Even more remarkably, when the oxidized catalyst was rereduced using CoCp$_2$, the catalyst began to polymerize L-lactide at an even greater rate (time period C, Figure 4). This unexpected behavior is in complete contrast to the polymerization behavior previously observed in Figure 3 for catalyst $\mathbf{2}_{\mathrm{red}}$. Furthermore, subsequent oxidation of this catalyst showed that virtually all polymerization activity was arrested (time period D, Figure 4) and, after rereduction, once again proceeded at a high relative rate (time period E, Figure 4).

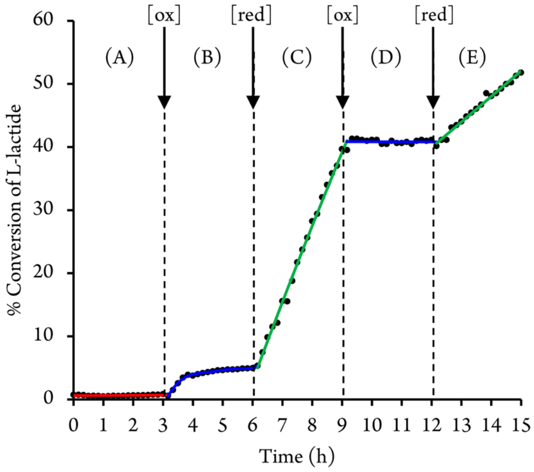


Figure 4. Plot of conversion versus time for the polymerization of L-lactide (100 equiv, 1 M) in C_6D_6 at 90 °C with in situ redox-switching, starting with catalyst **2**. Times at which oxidant ([ox] = ^{Ac}FcBAr^{F}, 1 equiv) or reductant ([red] = CoCp$_2$, 1 equiv) were added are denoted at the top, and time-periods between additions are labeled as A, B, C, D, and E.

Although the results obtained in time-periods C, D, and E demonstrate that placing the redox-active ferrocenyl moiety in close proximity to the active metal site ($\mathbf{2}_{\mathrm{red}}$) yields an enhanced "on−off−on" switch in catalytic activity when compared with catalyst **1**, its unexpected behavior in time periods B and C required further investigation. After careful analysis and multiple reproductions of the kinetic experiments found in Figure 3 and in situ switching experiments shown in Figure 4, we hypothesized that the rates of polymerization may actually be dependent upon the chemical species present during the oxidation and reduction reactions. Specifically, we noted that for the initial lactide polymerizations represented in Figure 3, catalyst $\mathbf{2}_{\mathrm{red}}$ was oxidized using ^{Ac}FcBAr^{F} (in the absence of monomer) and then added to a monomer containing solution to observe its rate of polymerization. In contrast, the catalyst oxidation and reduction reactions for the in situ switching trials (Figure 4) were performed in the presence of excess lactide.

To support our hypothesis, polymerization trials were conducted in which the Ti-based catalyst $\mathbf{2}_{\mathrm{red}}$ was oxidized in the presence of excess L-lactide, thereby mimicking an environment similar to what would be encountered in actual redox-switching experiments (such as those shown in Figure 4). Those results (Figure 5) indicated that when catalyst $\mathbf{2}_{\mathrm{red}}$ is oxidized in the presence of excess L-lactide in solution, there is a rapid conversion of monomer to polymer, reaching ∼4−6% conversion but then becoming virtually inactive in reactions extending up to and beyond 10 h. This result was extremely encouraging because all of our in situ switching experiments have shown similar behaviors in which monomer conversion essentially stops after ∼4−6% lactide conversion is reached. Subsequently, when this oxidized species is rereduced using CoCp$_2$, once again in the presence of excess monomer, the reduced species shows dramatically increased polymerization activity, reaching over 80% conversion in only 5 h for NMR scale polymerizations (Figure 5, green triangles). Larger scale polymerizations were also performed using catalyst $\mathbf{2}_{\mathrm{red}}$, which was rereduced in the presence of monomer; those results are shown in Table 1. From these results, it is clear that the activity of the oxidized and reduced analogs of this Ti-based catalyst differs

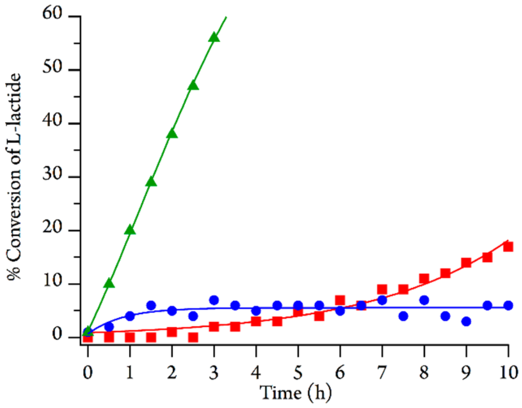


Figure 5. Plot of conversion versus time for the polymerization of L-lactide (100 equiv, 1 M) in C_6D_6 at 90 °C using catalyst $\mathbf{2}_{\mathrm{red}}$ (red squares), oxidized catalyst $\mathbf{2}_{\mathrm{ox}}$ (blue circles), and rereduced catalyst $\mathbf{2}_{\mathrm{red}}$ (green triangles) (note: oxidation of catalyst $\mathbf{2}_{\mathrm{red}} \rightarrow \mathbf{2}_{\mathrm{ox}}$ and its rereduction from $\mathbf{2}_{\mathrm{ox}} \rightarrow \mathbf{2}_{\mathrm{red}}$ were performed in the presence of lactide monomer).

Table 1. Polymerization Data for Catalyst $\mathbf{2}_{\mathrm{red}}$ after Rereduction in the Presence of Monomer[a]

entry	time (h)	L-lactide: $\mathbf{2}_{\mathrm{red}}$[a]	conv[b] (%)	M_n[c] (g/mol)	M_n[d] (theor)	M_w/M_n[c]
1	6	100:1	55	6 900	4 000	1.11
2	12	100:1	71	7 800	5 100	1.15
3	18	100:1	85	12 100	6 100	1.28
4	24	100:1	84	11 500	6 100	1.20
5	24	50:1	89	7 600	3 200	1.69
6	24	200:1	69	13 300	9 900	1.20

[a] Polymerization conditions: catalyst $\mathbf{2}_{\mathrm{red}}$ was obtained after subsequent oxidation (^{Ac}FcBAr^{F}) and rereduction (CoCp$_2$) in the presence of L-lactide, [monomer] = 1.0 mmol, 2 mL of toluene, 90 °C. [b] Conversion was determined using ^{1}H NMR at 70 °C. [c] Determined using gel permeation chromatography at 40 °C in THF and are reported relative to polystyrene standards. [d] Theoretical M_n's were calculated on the basis of conversion and assuming dual propagating chains.

radically, depending on whether the redox events occur in the presence or absence of L-lactide monomer.

Although further investigations are required to elucidate the source of this behavior, careful analysis of in situ polymerization ^{1}H NMR spectra revealed that the rereduced catalyst (Figure 5, green triangles) and the unperturbed catalyst $\mathbf{2}_{\mathbf{red}}$ (Figure 5, red squares) were structurally distinct from one another, as was evidenced by a change in aromatic and imine ^{1}H signals (see Supporting Information). Likewise, CV experiments conducted in the presence of monomer showed that catalyst $\mathbf{2}_{\mathbf{ox}}$ exhibited a −0.087 V shift in reduction potential when the catalyst was heated in the presence of monomer (see Supporting Information). On the basis of these results, we propose that the observed change in catalytic behavior may be attributed to a switch in catalyst geometry from its original β-cis conformation, which shows four aromatic ^{1}H signals and two imine ^{1}H signals to either an α-cis or trans geometry, both of which display only two aromatic signals and one imine ^{1}H NMR signal. We believe this geometry change is promoted in the presence of monomer during the in situ oxidation reaction, and although both the α-cis or trans geometries are plausible, the large number of previously reported catalysts adopting a trans configuration make it the most likely form.[14,22−25]

In summary, we have synthesized a new redox-active, Ti-based salfen catalyst and investigated its behavior for the RSP of L-lactide. Initial polymerizations in which catalyst $\mathbf{2}_{\mathbf{red}}$ was oxidized in the absence of monomer showed that the oxidized catalyst $\mathbf{2}_{\mathbf{ox}}$ proceeded at a significantly faster rate than its reduced analogue $\mathbf{2}_{\mathbf{red}}$, which contradicts all other reported group 4 catalysts for RSP. In contrast, when the oxidation and reduction reactions were carried out in the presence of monomer, polymerization activity was completely reversed in which the reduced species polymerized L-lactide at a much greater rate than the oxidized version.

Although the catalytic ring-opening polymerization behavior of catalysts $\mathbf{2}_{\mathbf{red}}$ and $\mathbf{2}_{\mathbf{ox}}$ has proven to be quite complex, requiring further investigations to elucidate the source or sources of this behavior, our results demonstrate that positioning the redox-active ferrocenyl moiety in close proximity to the active transition-metal site ($\mathbf{2}_{\mathbf{red}}$) produced an enhanced "on−off−on" switch (Figure 4, time periods C, D, and E) in polymerization activity when compared with catalyst **1**. Second, and more importantly, we have demonstrated that the activity of catalysts $\mathbf{2}_{\mathbf{red}}$ and $\mathbf{2}_{\mathbf{ox}}$ are not only dependent on the redox state of the ligand but are also dependent on the chemical species present during their in situ oxidation and reduction reactions. The source of this unusual behavior must be investigated further; however, these results serve as direct evidence that monomer presence and redox-active moiety placement within the ligand scaffold must be considered during redox-switching studies.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b01434.

Detailed synthetic procedures, NMR spectroscopy, X-ray crystallography, and electrochemistry (PDF)
Crystallographic data (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: Long@utk.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors wish to acknowledge the Army Research Office (Contract No. W911NF-1-0127) for their financial support of this work. The authors would also like to thank Preeti Chandrachud for her help with X-ray crystallographic analysis of compound **2**.

■ REFERENCES

(1) Allgeier, A. M.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 894−908.
(2) Lorkovic, I. M.; Duff, R. R.; Wrighton, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 3617−3618.
(3) Sussner, M.; Plenio, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 6885−6888.
(4) Tennyson, A. G.; Lynch, V. M.; Bielawski, C. W. *J. Am. Chem. Soc.* **2010**, *132*, 9420−9429.
(5) Ringenberg, M. R.; Nilges, M. J.; Rauchfuss, T. B.; Wilson, S. R. *Organometallics* **2010**, *29*, 1956−1965.
(6) Magenau, A. J. D.; Strandwitz, N. C.; Gennaro, A.; Matyjaszewski, K. *Science* **2011**, *332*, 81−84.
(7) Wang, X. K.; Thevenon, A.; Brosmer, J. L.; Yu, I. S.; Khan, S. I.; Mehrkhodavandi, P.; Diaconescu, P. L. *J. Am. Chem. Soc.* **2014**, *136*, 11264−11267.
(8) Broderick, E. M.; Diaconescu, P. L. *Inorg. Chem.* **2009**, *48*, 4701−4706.
(9) Gregson, C. K. A.; Gibson, V. C.; Long, N. J.; Marshall, E. L.; Oxford, P. J.; White, A. J. P. *J. Am. Chem. Soc.* **2006**, *128*, 7410−7411.
(10) Biernesser, A. B.; Li, B.; Byers, J. A. *J. Am. Chem. Soc.* **2013**, *135*, 16553−16560.
(11) Broderick, E. M.; Guo, N.; Vogel, C. S.; Xu, C. L.; Sutter, J.; Miller, J. T.; Meyer, K.; Mehrkhodavandi, P.; Diaconescu, P. L. *J. Am. Chem. Soc.* **2011**, *133*, 9278−9281.
(12) Sauer, A.; Buffet, J. C.; Spaniol, T. P.; Nagae, H.; Mashima, K.; Okuda, J. *ChemCatChem* **2013**, *5*, 1088−1091.
(13) Broderick, E. M.; Guo, N.; Wu, T. P.; Vogel, C. S.; Xu, C. L.; Sutter, J.; Miller, J. T.; Meyer, K.; Cantat, T.; Diaconescu, P. L. *Chem. Commun.* **2011**, *47*, 9897−9899.
(14) Gregson, C. K. A.; Blackmore, I. J.; Gibson, V. C.; Long, N. J.; Marshall, E. L.; White, A. J. P. *Dalton Trans.* **2006**, 3134−3140.
(15) Hormnirun, P.; Marshall, E. L.; Gibson, V. C.; Pugh, R. I.; White, A. J. P. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 15343−15348.
(16) Cameron, P. A.; Jhurry, D.; Gibson, V. C.; White, A. J. P.; Williams, D. J.; Williams, S. *Macromol. Rapid Commun.* **1999**, *20*, 616−618.
(17) Alcazar-Roman, L. M.; O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *Dalton Trans.* **2003**, 3082−3087.
(18) Qian, F.; Liu, K. Y.; Ma, H. Y. *Dalton Trans.* **2010**, *39*, 8071−8083.
(19) Pang, X.; Du, H. Z.; Chen, X. S.; Wang, X. H.; Jing, X. B. *Chem. - Eur. J.* **2008**, *14*, 3126−3136.
(20) Gong, S. G.; Ma, H. Y. *Dalton Trans.* **2008**, 3345−3357.
(21) Shafir, A.; Fiedler, D.; Arnold, J. *J. Chem. Soc. Dalton* **2002**, 555−560.
(22) Gibson, V. C.; Gregson, C. K. A.; Halliwell, C. M.; Long, N. J.; Oxford, P. J.; White, A. J. P.; Williams, D. J. *J. Organomet. Chem.* **2005**, *690*, 6271−6283.
(23) Chen, H. Y.; White, P. S.; Gagne, M. R. *Organometallics* **1998**, *17*, 5358−5366.
(24) Clarkson, G. J.; Gibson, V. C.; Goh, P. K. Y.; Hammond, M. L.; Knight, P. D.; Scott, P.; Smit, T. M.; White, A. J. P.; Williams, D. J. *Dalton Trans.* **2006**, 5484−5491.
(25) Sauer, A.; Kapelski, A.; Fliedel, C.; Dagorne, S.; Kol, M.; Okuda, J. *Dalton Trans.* **2013**, *42*, 9007−9023.