Cooperative Heterobimetallic Catalysts in Coordination Insertion Polymerization

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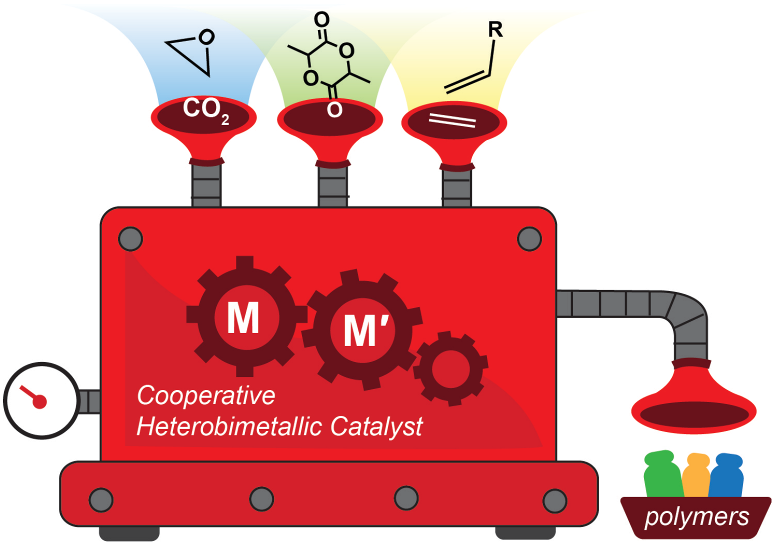

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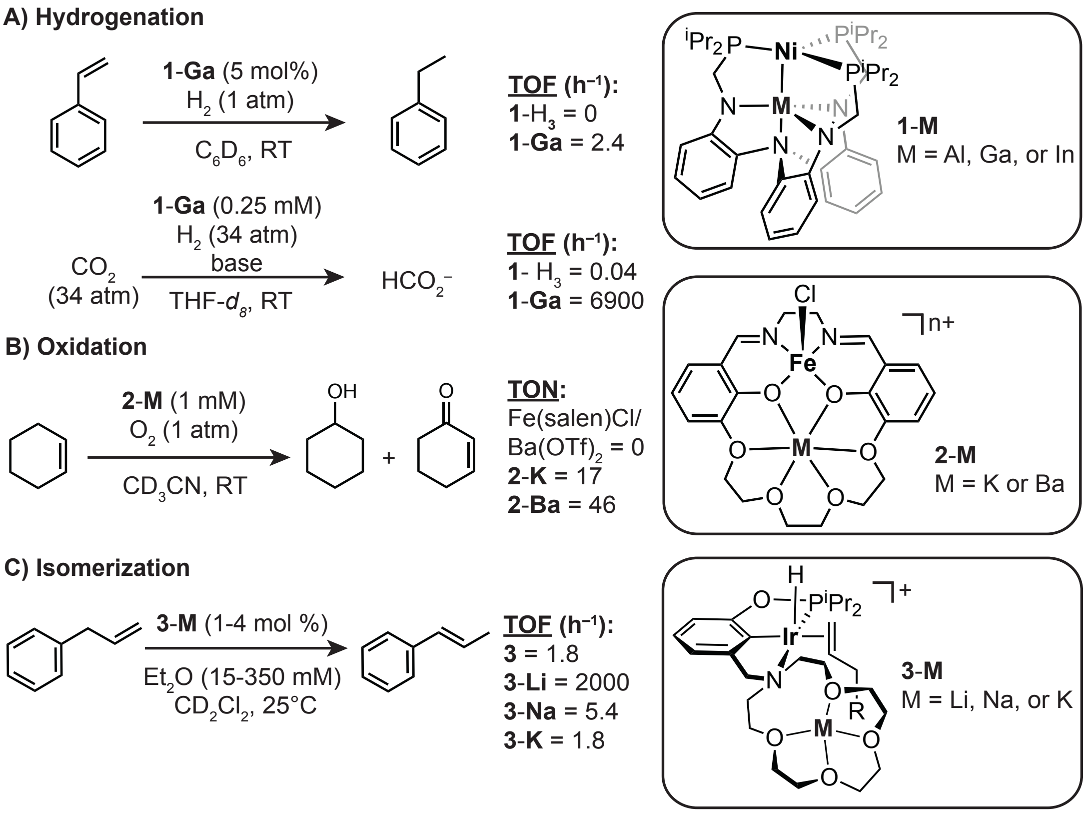
In this tutorial, we describe the applications of well-defined heterobimetallic complexes in coordination insertion polymerization catalysis. The presence of two different metals in a single catalyst platform imparts reactivity patterns that are distinct from those of their homobimetallic and monometallic counterparts. We will demonstrate that heterobimetallic complexes are a versatile and unique class of catalysts by providing representative examples from recent studies of carbon dioxide/epoxide, lactone, lactide, and olefin polymerization. We will focus on the various strategies employed to synthesize mixed metal species, methods to characterize their solid state and solution structures, and the mechanistic roles of the metal ions during polymerization. In many cases, the precise nature of heterobimetallic cooperativity is not well understood, which underscores the need for further research to enable the development of the next generation of advanced polymerization catalysts.

Keywords: heterobimetallic complexes; cooperativity; catalyst design;
homogenous catalysts; polymerization

Introduction

Biological enzymes often take advantage of multimetallic active sites to mediate chemically challenging reactions. Their distinct metal centers can participate in complementary tasks either simultaneously or sequentially. Cooperative catalysis in enzymes can manifest in various ways, such as in the selective binding of external substrates to the active site, stabilization of unusual transition states, or tuning of metal redox potentials. Some examples of multimetallic enzymes include cytochrome *c* oxidase,[1] phosphoglycerate mutase,[2] and nitric oxide reductase.[3] Synthetic chemists have long sought to emulate the extraordinary capabilities of biological enzymes by creating small-molecule mimics. For example, Collman and coworkers synthesized cytochrome *c* oxidase models comprising iron porphyrin and copper tris(amine) units that can promote the electrocatalytic reduction of O_2 to H_2O.[4] Lehnert and coworkers have demonstrated that non-heme diiron complexes that model nitric oxide reductases can convert NO directly to N_2O.[5] Studies of multimetallic protein mimics have allowed us to gain new insights into many fundamentally important molecular transformations.



Scheme 1. Examples of heterobimetallic catalysts used in small molecule activation and other molecular transformations.

Inspired by nature, synthetic chemists have taken advantage of metal-metal cooperativity in chemical catalysis using heterobimetallic complexes.[6-8] Catalyst systems that feature two different metal centers are advantageous over those that have just one or even two of the same metals for several reasons. For example, heterobimetallic catalysts can be tuned simply by interchanging metals without having to modify the ligand framework. In some systems, both metal ions are directly involved in catalysis whereas in others, the primary metal is the site where catalysis occurs and the secondary metal modulates its reactivity. The many different M–M′ (where $M \neq M'$) combinations that are possible add a new dimension for catalyst design, which can complement traditional strategies that focus on making structural or electronic ligand variations. An advantage of heterobimetallics over homobimetallics is that when both metals have synergistic roles in catalysis, they can avoid deactivating each other (e.g. in homobimetallic systems, both metal ions can compete with one another during polymerization).

The versatility of heterobimetallic platforms is exemplified by several elegant examples of M–M′ cooperative catalysts. Lu and coworkers showed that Ni(0)-Ga(III) complexes supported by double-decker ligands can catalyze both olefin[9] and carbon dioxide hydrogenation[10] (Scheme 1A). It was found that the key to success was the ability of the Ga(III) metalloligands to stabilize anionic nickel-hydride intermediates that are capable of hydrogenating substrates. In another example, Yang and coworkers developed iron salen macrocycles that can bind K^+ and Ba^{2+} cations.[11] Their studies showed that iron-potassium and iron-barium complexes were capable of aerobic C–H bond oxidation, even though their metal redox potentials were significantly lower than those of mononuclear iron salen complexes with strongly electron withdrawing substituents (Scheme 1B). Yang's group attributed this unusual reactivity in part to the electrostatic effects of K^+ and Ba^{2+}, which can accelerate the rate-determining step of the reaction without shifting the redox potential of the catalyst to extreme values. Finally, Miller and coworkers have synthesized iridium pincer crown ether complexes that are capable of coordinating Li^+, Na^+, and K^+ ions (Scheme 1C).[12,13] They observed that the presence of Li$^+$ could enhance the rate of allylbenzene isomerization by up to 1000× compared to that using just the iridium catalyst alone.

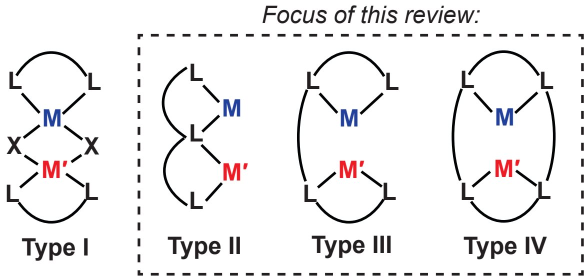
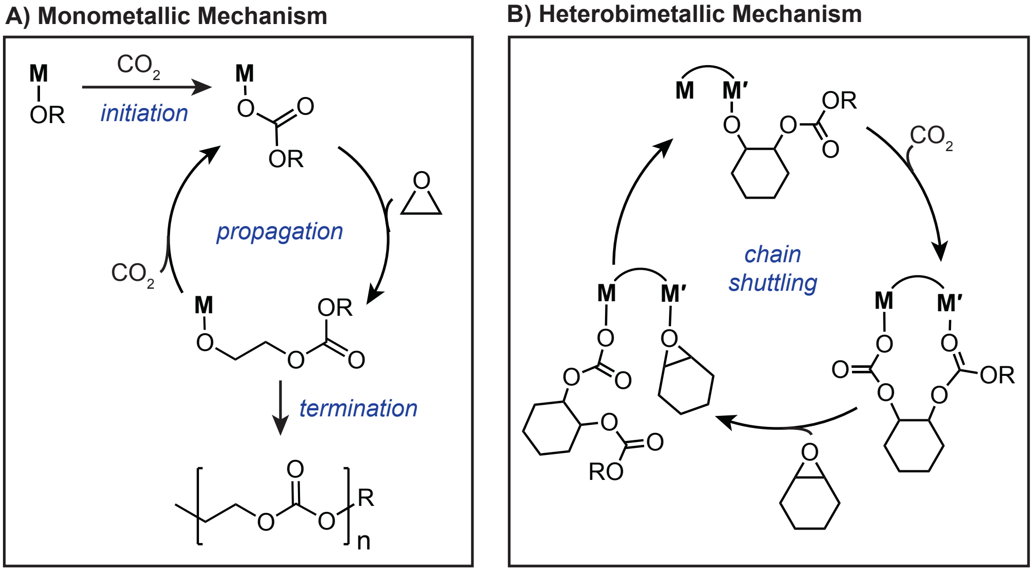


Chart 1. General heterobimetallic structure classifications. Abbreviations: M, M′ = different metal ions, L = ligand, X = bridging ligand or atom.

Heterobimetallic complexes have also been shown to be excellent coordination insertion polymerization catalysts.[14-17] A wide range of heterobimetallic motifs has been explored for this application (Chart 1). Type I complexes comprise two monometallic species that are bridged by one or more atoms (e.g. oxo or halides) or external ligands. Because there are no covalent linkages connecting the M and M′ units, the dinuclear structure is prone to dissociate in coordinating solvents, particularly at low concentrations when the bimetallic species is not entropically favored.[18] In contrast, heterobimetallic compounds that are supported by dinucleating ligands have greater structural integrity. Type II complexes have short M–M′ bond distances due to the bridging of both metal centers by a single donor group, whereas Type III and IV complexes have M–M′ bond distances that are dependent on the length and flexibility of their linkers. In this tutorial, we will focus primarily on the Type II–IV heterobimetallics in coordination insertion polymerization catalysis. Studies of Type I heterobimetallics[19] and homobimetallics[20,21] have been described in other excellent reviews. This article will discuss only select examples to illustrate the various applications of heterobimetallic catalysts, rather than provide a comprehensive review of the current literature. We will focus on the methods employed to prepare heterobimetallic compounds, techniques used to determine their structures and compositions, and the mechanistic roles of M and M′ during the polymerization process. Finally, we will summarize the challenges of research in this field and offer advice on how to avoid some common pitfalls.

Epoxide and Carbon Dioxide Copolymerization

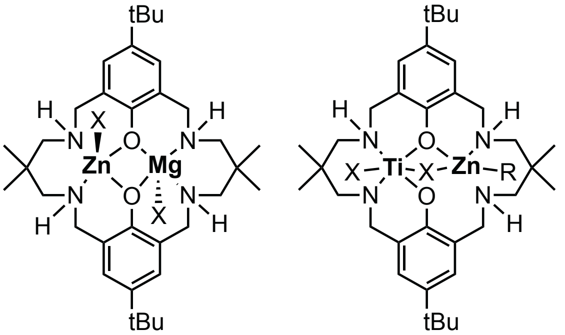
The alternating copolymerization of epoxide and carbon dioxide (CO_2) is an appealing strategy for the preparation of polycarbonates because CO_2 is an inexpensive and abundant C_1 feedstock.[18,22,23] Since Inoue's discovery of heterogeneous $ZnEt_2/H_2O$ mixture for the copolymerization of propylene oxide and CO_2 in 1969,[24] many homogenous systems have now been developed, such as those using Zn(II)(*β*-diiminate),[25] Co(III)(salen),[26] or Cr(III)(salen)[27] (salen = *N*,*N′*-bis(salicylidene)-1,2-diaminoalkane). It is believed that the general mechanism for epoxide and CO_2 copolymerization involve initiation by nucleophilic attack of a Lewis acid-activated epoxide to generate a metal alkoxide complex (Scheme 2A). This species can insert CO_2 to give a metal-carbonate intermediate that can undergo chain propagation through repetitive sequences of epoxide ring opening and CO_2 insertion reactions. Chain termination occurs by chain transfer with water or alcohol. The disadvantages of some catalysts are that they can homopolymerize epoxides, decarboxylate to give ether polymer linkages, or form cyclic carbonates through backbiting. Furthermore, achieving both high activity and stereoselectivity during the polymerization process can also be challenging.



Scheme 2. Mechanisms for epoxide/CO_2 copolymerization by A) monometallic and B) heterobimetallic catalysts.

To overcome the deficiencies of conventional catalysts, studies have focused on using bimetallic systems instead.[28-31] One of the most impressive demonstrations of heterobimetallic cooperativity in epoxide and CO_2 copolymerization is work by Williams and coworkers.[32-34] Motivated by reports that mixed-metal materials (e.g. Zn/Co or Zn/Fe) are excellent heterogeneous catalysts, Williams' group synthesized homogeneous zinc-magnesium complexes containing symmetric diphenolate tetraamine macrocycles (**4**, Chart 2). In their initial work, the investigators found that mixing the macrocyclic ligand with $ZnEt_2$, followed by treatment with Mg(acetate)$_2$, provided a mixture of **4**, Zn_2, and Mg_2 species that could not be separated.[32] However, in a subsequent study,[33] the heterobimetallic ZnMg complex was isolated in pure form by using a two step procedure. The monozinc species was prepared first by reacting the macrocycle with $ZnEt_2$ and was then treated with $MgBr_2$ in pyridine/THF at -78˚C. The use of coordinating solvents and low temperature was found to be conducive to achieving high yields of **4**. Interestingly, mass spectrometric analysis showed that when an equimolar mixture of pure homobimetallic Zn_2 and Mg_2 complexes was heated at

80°C for 24 h, no metal exchange to **4** was observed. However, upon further heating for an additional 24 h, about 25% of the heterobimetallic species was detected by ^{1}H NMR spectroscopy. These experiments suggest that the heterobimetallic species are thermodynamically favored over their homobimetallic analogues. However, redistribution of the metals is slow once the dinuclear complexes are formed (i.e. this process if kinetically slow).



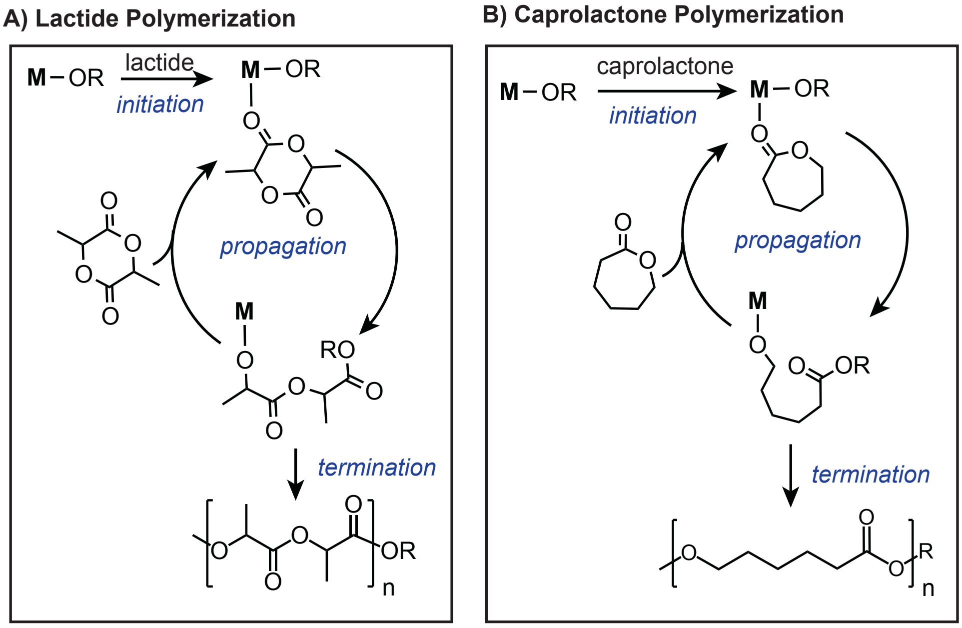
4
(X = OAc, or Br)

5
(X = OiPr, R = Et or Ph)

Chart 2. Examples of heterobimetallic catalysts for epoxide/CO_2 copolymerization. The X-ray structure of **5** (X = OiPr) shows that the Zn center is four-coordinate in the solid state (Ref. 34).

Excitingly, the heterobimetallic **4** significantly outperformed structurally similar homobimetallic Mg_2 and Zn_2 complexes in polymerization.[33] For example, complex **4** was about 5× more active than using a 1:1 molar ratio of Mg_2/Zn_2 and 2× more active than Mg_2 in cyclohexene oxide and CO_2 copolymerization. The homobimetallic Zn_2 and monometallic Zn complexes were inactive. The polymers obtained using **4** showed >99% of carbonate linkages (rather than ether) and have narrow molecular weight distributions, which is indicative of controlled polymerization. A bimetallic "chain shuttling" mechanism was proposed (Scheme 2B),[35] in which the growing polymer chain shuttles between the two metals with each insertion. The activity enhancement is believed to originate from the two metals having separate functions: the Lewis acidic zinc ion enhances epoxide coordination while the labile magnesium accelerates carbonate attack.

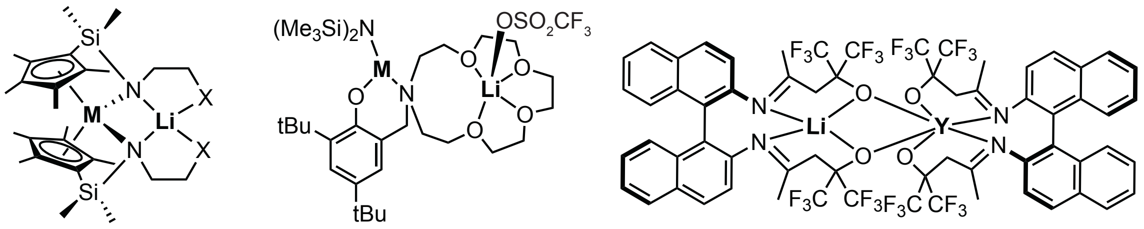
Williams' group also extended their heterobimetallic studies to titanium/zinc complex **5** (Chart 2) for epoxide and CO_2 copolymerization.[34] The mixed metal compound was prepared successfully by sequential metallation of diphenol tetraamine macrocycles with $Ti(OiPr)_4$, followed by the addition of $ZnEt_2$. In addition to characterization by elemental analysis and MALDI-TOF, compound **5** was shown to be a single species in solution by DOSY NMR, which showed that all of the resonances have the same diffusion coefficient. When tested in cyclohexene oxide and CO_2 copolymerization, the heterobimetallic **5** exhibited moderate activity, whereas the monometallic titanium and zinc analogues were inactive. Although **5** appears to be less active than the Ti diphenolate and Ti bis(salophen) complexes that require co-catalysts, it can initiate polymerization without any external additives.



Scheme 3. Mechanisms for the coordination insertion polymerization of A) lactide and B) caprolactone.

Lactide and Caprolactone Polymerization

Polyesters such as polylactides and polylactones are popular commodity plastics because of their attractive material properties.[36-38] For single-use or short shelf-life applications, polyesters are advantages over polyolefins because they can be readily degraded in the environment and thus, do not accumulate in landfills and natural habitats. The low toxicity of polyesters allows them to be integrated into many biomedical applications, such as in drug delivery, surgical sutures, and implantable contraceptives. Furthermore, monomers such as ε-caprolactones and lactides are relatively low cost and can be derived from biorenewable resources. Although polyesters can be synthesized using polycondensation, cationic polymerization, or anionic polymerization, coordination insertion polymerization using metal catalysts is advantageous because it enables the preparation of narrowly dispersed high molecular weight polymers.[39-44] The coordination insertion mechanism is proposed to involve binding of a monomer to the Lewis acidic metal, which renders the carbonyl group more susceptible to nucleophilic addition (Scheme 3). Subsequent attack by an alkoxide then leads to polymer chain growth and propagation. Polymer termination occurs upon hydrolysis or alcoholysis of the propagating species. The current challenges in coordination insertion polymerization of cyclic esters are achieving high activity and selectivity. Some undesired side reactions that commonly occur are transesterification, formation of cyclic oligomers, and back reaction to monomers. Furthermore, for functionalized ε-caprolactone and lactide monomers, stereoselectivity is important because polymer tacticity (the relative arrangement of adjacent chiral centers in the macromolecule) determines the material's crystallinity and thermal and mechanical properties.[45]



6a, M = Y, X = OMe
6b, M = Y, X = NMe$_2$
6c, M = Lu, X = OMe

7a, M = Ge
7b, M = Sn

8

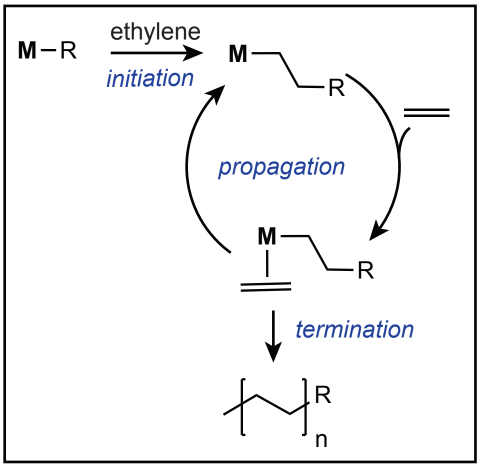
Chart 3. Examples of heterobimetallic complexes for lactide and lactone polymerization.

In recent years, some exciting advances have been achieved in the development of heterobimetallic catalysts for the coordination insertion of cyclic esters. Okuda and coworkers introduced an amido-cyclopentadienyl ligand system to assemble a class of heterobimetallic Y-Li (**6a-6b**) and Lu-Li (**6c**) complexes (Chart 3).[46,47] The researchers attempted to synthesize half-sandwich complexes from the reaction of YCl_3 or $LuCl_3$ with lithium amido-cyclopentadienyl anion but isolated heterobimetallic yttrium-lithium and lutetium-lithium bis(ligand) complexes instead, respectively. Removal of Li^+ from the products by treatment with 12-crown-4 was not successful, which suggests that binding of lithium ions to the pendant nitrogen/or oxygen donors is quite strong. These air- and water-sensitive compounds were found to be active catalysts for both ε-caprolactone and lactide polymerization. The polymers formed by the Y-Li or Lu-Li complexes generally have molecular weights $M_n > 10{,}000$ and polydispersity $M_w/M_n < 2.0$. ^{1}H NMR spectroscopic analysis of the polylactides isolated indicated that the catalysts have no preference for either D- or L-monomer during polymerization. Although it was not possible to obtain the corresponding mononuclear yttrium or lutetium complexes for reactivity comparison with **6**, Okuda's group showed that polymerizations performed using the monometallic $Y(N(SiMe_3)_2)_3$ catalyst provided polymers with M_w/M_n > 2.0, which suggests that **6** catalyzes more controlled polymerizations than $Y(N(SiMe_3)_2)_3$.

Heterobimetallic cooperativity in lactide polymerization was also explored by Sarazin and coworkers.[48] They reported that group 4 complexes could be prepared cleanly from the protonolysis of aminophenol ligands with $M(N(SiMe_3)_2)_2$ (M = Ge, Sn, or Pb). The germanium and tin complexes that feature aza-15-crown-5 side arms were capable of binding $Li(SO_3CF_3)$ to yield the corresponding Ge-Li (**7a**) and Sn-Li (**7b**) heterobimetallics (Chart 3). Metallation attempts starting from the lithiated ligand, followed by the addition of $Ge(N(SiMe_3)_2)_2$ or $Sn(N(SiMe_3)_2)_2$ did not furnish **7a** and **7b**, respectively. The addition of $Na(SO_3CF_3)$ or $[Na(OEt_2)_4][NH_2(B(C_6F_5)_3)_2]$ instead of $Li(SO_3CF_3)$ to the monometallic germanium or tin compounds also failed to yield the desired heterobimetallic species. The identities of the pure mixed-metal complexes were confirmed in the solid state by X-ray crystallography and in solution by heteronuclear NMR spectroscopy (^{119}Sn, ^{29}Si, and/or ^{7}Li). Notably, the lithium ion in **7a** and **7b** has no direct interactions with the neighboring germanium or tin center. When the heterobimetallics were tested in lactide polymerization, **7a** was about 2× more active and **7b** was about 4× less active than their parent monometallic complexes. The authors proposed that the reaction rate acceleration using **7a** was due to the presence of the Lewis acidic lithium cation, which was able to activate incoming monomers for ring opening polymerization. However, this hypothesis has not yet been established experimentally. In the case of **7b**, its lower catalyst activity was attributed to rapid catalyst decomposition under the reaction conditions employed.

In a separate study, Sarazin, Carpentier and coworkers used (*R*)-enantiopure Binap-based hydroxy-imine ligands to assemble yttrium-lithium heterobimetallics (**8**, Chart 3).[49] The researchers found that the one pot reaction of the protonated ligand, $Y(N(SiMe_3)_2)_3$, and $LiN(SiMe_3)_2$ in a 2:1:1 ratio afforded **8** in quantitative yield.

Interestingly, the 1:1 reaction of the Binap-based ligand with $Y(N(SiMe_3)_2)_3$ did not provide the mononuclear yttrium complex. The heterobimetallic **8** was characterized by NMR spectroscopy (^{1}H, ^{19}F, and ^{7}Li), X-ray crystallography, and elemental analysis. Its solid-state structure shows that both yttrium and lithium ions are six-coordinate and that the Y–Li bond distance is too long to have any direct metal-metal interactions. Studies by DOSY NMR spectroscopy and diffusion molecular weight analysis suggest that **8** exists as a heterobimetallic species in THF solvent. This complex was demonstrated to be highly active in lactide ring opening polymerization. Remarkably, **8** generated polylactide with 99% heterotacticity (stereoregular sequences of -*RRSS*- blocks) from *racemic* lactide (*RR* + *SS* monomers) and 80% syndiotacticity (stereoregular sequences of -*RS*-) from *meso* lactide (*RS* monomers). In comparison, a mononuclear indium catalyst ligated by the same Binap-based ligand gave polymers with lower heteroselectivity and molecular weight. However, because the lithium ion in **8** is an essential structural component of the heterobimetallic motif, direct reactivity comparisons with its monometallic analogues are difficult to make since their metal centers have different geometries and donor sets. Kinetic studies by NMR spectroscopy indicate that **8** polymerizes D-lactide at the same rate as L-lactide, which is consistent with the high heteroselectivity observed.



Scheme 4. Mechanism for the coordination insertion polymerization of ethylene. Chain walking to give branched polymers can also occur (not depicted).

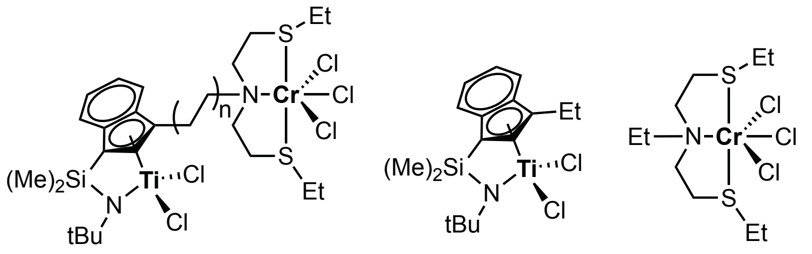
Olefin Polymerization

Polyolefins make up greater than 40% of the 300+ million tons of plastics that are manufactured worldwide each year.[50] Because of their tremendous importance in our society, research in olefin polymerization continues to be a major focus in many industrial[51,52] and academic laboratories.[53-55] One of the most efficient methods to synthesize polyolefins is through coordination insertion polymerization using transition metal catalysts. In such processes, polymerization is initiated when an olefin inserts into a metal–alkyl/aryl bond to generate a new metal–alkyl species (Scheme 4). Subsequent olefin binding and insertion then leads to polymer chain growth. Chain termination proceeds through chain transfer, which can involve either *β*-hydride elimination or *β*-hydride transfer. Although an extensive assortment of metal complexes is capable of catalyzing olefin polymerization, new technological innovations are still needed. For example, it is difficult to access monodispersed linear low-density polyethylene directly from ethylene (without the need for α-olefin comonomers)[56] and polar polyolefins with high molecular weight and random functional group distribution.[57,58] The discovery of high performance catalysts that can simplify the synthesis of common polyolefins or provide practical routes to novel polyolefins would be a major advance in materials science.

Researchers have explored many creative strategies to improve the performance of existing olefin polymerization catalysts, such as by using structural constraints,[59-61] hemilabile ancillary donors,[62,63] or hydrogen[64] and fluorine bonding.[65,66] There is growing interest in the application of heterobimetallic complexes as olefin polymerization catalysts because of their unique multi-functionality.

Ethylene Trimerization/Polymerization Tandem Catalysts: Delferro, Marks, and coworkers have developed titanium-chromium platforms to achieve more efficient tandem catalysis.[56,67] Their heterobimetallic complexes were synthesized in a stepwise fashion, by first reacting $Ti(NMe_2)_4$ with asymmetrically functionalized indene ligands to yield chelated half-sandwich titanium complexes. These compounds were then - treated with $SiMe_3Cl$, followed by $CrCl_3(THF)_3$ to generate the corresponding titanium-chromium species (Chart 4). A series of heterobimetallics was prepared, in which each complex has a different linker length connecting the titanium to the chromium center (**9a**-**9c**, n = 0, 1, 3, respectively). The mixed metal compounds were characterized by elemental analysis, ^{1}H NMR spectroscopy (peaks were broad due to paramagnetism), and MALDI-TOF mass spectrometry.

The motivation behind Delferro/Marks' titanium-chromium catalyst design was to take advantage of the close proximity of an olefin polymerization catalyst (Ti) with an ethylene trimerization catalyst (Cr) to synthesize linear low-density polyethylene using ethylene as the sole monomer feed.[56,67] It was proposed that the 1-hexene formed by the chromium center could be delivered to the adjacent titanium center to be incorporated in a subsequent ethylene/1-hexene enchainment process. The investigators observed that the Ti-Cr complexes showed increasing catalyst activity and polymer molecular weight according to the trend **9a** > **9b** > **9c**. Catalyst **9a** provided polymers with higher density of butyl branches (~26 per 1000 carbons) compared to that by **9b** (~18 branches) and **9c** (~7 branches) (Figure 1). Ethylene polymerization using a 1:1 mixture of mono-titanium **10** and mono-chromium **11** in a conventional tandem catalysis reaction gave polyethylene with only ~7 branches per 1000 carbons. Interestingly, the branching density of the polymer obtained using heterobimetallic **9a** was independent of polymerization time, whereas the tandem catalysts **10**+**11** provided polymers with greater branching density at longer reaction times. These data strongly suggest that having short Ti–Cr bond distances improve the shuttling of the 1-hexene monomers generated from chromium to titanium and enable synergistic interactions between the metal centers.



9a, n = 0
9b, n = 1
9c, n = 3

10

11

Chart 4. Structures of the heterobimetallic titanium-chromium (**9a-9c**) and monometallic **10** and **11** complexes studied in ethylene trimerization/polymerization.

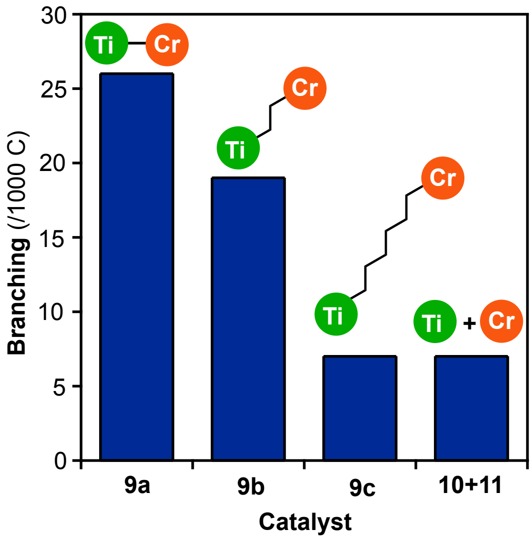
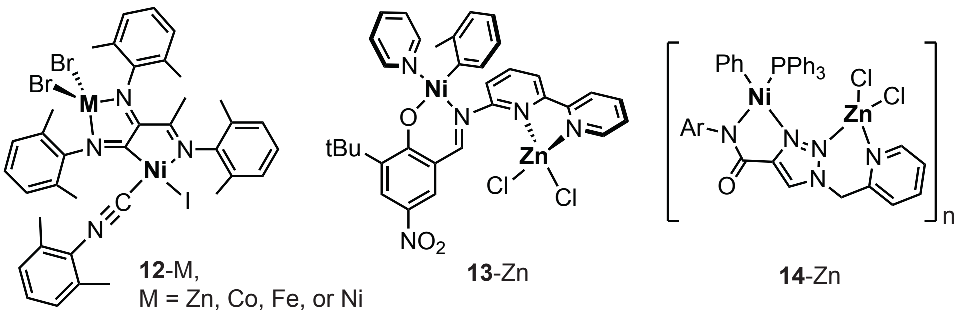


Figure 1. Comparison of the branching density observed in polyethylene produced by catalysts **9a-9c**, and **10+11** under identical reaction conditions.

Etheylene Homopolymerization Catalysts: Several research groups have investigated the use of secondary metal ions to modulate the reactivity of late transition metal ethylene polymerization catalysts (Chart 5). In 2005, Nagashima and coworkers synthesized azanickellacyclopentene complexes (**12**) that have free diimino groups that are capable of binding secondary metal ions.[68] The researchers observed that the addition of $ZnBr_2$, $CoBr_2$, $FeBr_2$, or $NiBr_2$ to **12** led to moderate olefin polymerization rate enhancement, which was attributed to rigidification of the ligand backbone. Reactions of ethylene with **12**-Fe and **12**-Ni provided polymers with bimodal distributions, suggesting that both metal centers in the bimetallic catalysts are capable of polymerization.

In 2016, Tonks and coworkers prepared Ni(II) phenoxyimine complexes (**13**) bearing pendant bipyridyl donors (Chart 5).[69] It was found that the direct mixing of $ZnCl_2$ with **13** led to decomposition, presumably due to scavenging of the coordinated pyridine ligands. Instead, addition of Zn^{2+} to **13** was achieved by slow diffusion of a THF solution of $ZnCl_2$ into a cold toluene solution of the nickel complex. Tonks' group observed that the heterobimetallic **13**-Zn complexes were more active ethylene polymerization catalysts than their parent mononickel complex **13**. The heterobimetallic catalysts, however, gave polymers with broad polydispersities (M_w/M_n = ~4–11). It was hypothesized that the zinc ion in **13**-Zn could dissociate during polymerization to yield at least two different catalytically active nickel species.



12-M,
M = Zn, Co, Fe, or Ni

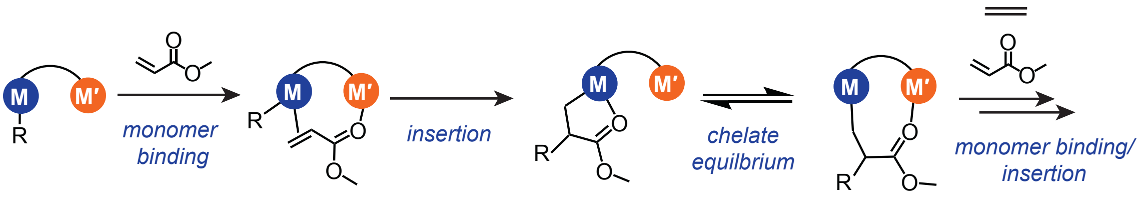
13-Zn

14-Zn

Chart 5. Structures of heterobimetallic catalysts tested in olefin polymerization.

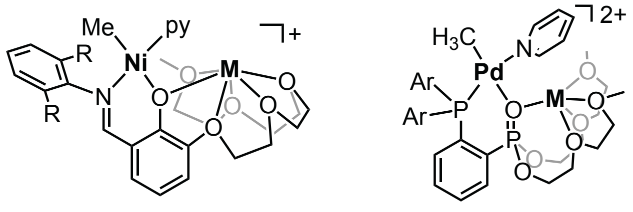
Our research group also investigated the effects of zinc ions on the polymerization activity of homogenous nickel catalysts. To diversify the ligand structures used to prepare active olefin polymerization catalysts, we developed a 4-carboxamidate-1,2-3-triazole platform that could be metallated with nickel.[70,71] We found that the introduction of a picolyl donor group to the nickel construct was necessary to increase its association with external zinc salts (**14**-Zn, Chart 5). Although our NMR spectroscopic studies demonstrated that the parent nickel complex **14** binds to Zn^{2+} in $CDCl_3$, we could not establish the exact structure or composition of the resulting nickel-zinc adduct. Upon activation by treatment with $Ni(COD)_2$ (COD = 1,5-cyclooctadiene), this undefined **14**-Zn species was found to be active for ethylene polymerization. However, time-dependent polymerization studies showed that the catalyst activity increased with increasing reaction time. Furthermore, gel permeation chromatography (GPC) analysis of the products revealed that the polymers were multimodal and their relative molecular weight distributions varied as a function of time. These data clearly indicated that the **14**-Zn heterometallic formed multiple active species during polymerization. We postulate that our current carboxamidatetriazole platform is incapable of supporting discrete heterobimetallic species in solution, which suggests that further ligand modifications are needed to access well-defined single site catalysts.

Expanding the Capabilities of Olefin Polymerization Catalysts: The tremendous potentials of heterobimetallic catalysts in olefin polymerization provide many unexplored avenues for further research. For example, we envision that a wide array of different polyolefin microstructures could be obtained by judicious pairing of a secondary metal salt with a Ni or Pd catalyst. Because the electrophilicity, charge, size, and chemical properties of metals can differ significantly, this strategy offers a simple way to customize catalysts to different user preferences. Furthermore, we hypothesize that it might be possible to overcome the tendency of polar groups to form chelated metallacycles in ethylene and polar vinyl olefin copolymerization by exploiting outer sphere Lewis acid interactions (Scheme 5).[72,73] Excitingly, there is some literature precedence that multi-nuclear catalysts can access reactivity patterns that are different than those of mononuclear catalysts.[74,75]



Scheme 5. Proposed pathway for ethylene and methyl acrylate copolymerization by heterobimetallic catalysts. The insertion step can occur through either a 1,2– (shown above) or 2,1–insertion pathway.

As proof of concept, our lab first investigated the effects of alkali ions (Li^+, Na^+ and K^+) on the polymerization activity of nickel phenoxyimine catalysts.[76-78] To reinforce a short nickel–alkali bond distance, we installed polyethylene glycol (PEG) chains to the nickel complex as binding arms for secondary metals. We determined by metal titration studies that the nickel phenoxyimine-PEG complexes could form both 1:1 and 2:1 nickel-alkali species in solution. Our data suggest that the match between the PEG chain length and the cation size determines their relative metal binding affinities. Complex **15a** (R= iPr), which has a tetra(ethylene glycol) unit, formed exclusively 1:1 nickel-sodium species. Several of our heterobimetallic structures were determined by X-ray crystallography, including the nickel-sodium and nickel-potassium complexes. We demonstrated that the addition of 1.1 equiv. of $NaBAr^F_4$ ($BAr^F_4{}^-$ = tetrakis(3,5-bis(trifluoromethyl)phenyl)borate anion) to **15a** led to a ~77× increase in catalyst activity as well as branching in comparison to polymerizations using **15a** without salt additives. Since the presence of Na^+ enhances both the electrophilicity and steric bulk of the nickel center, it is difficult to determine how each of these factors contributed to the observed reactivity. We also prepared bulky catalyst variants with R = phenyl (**15b**) and 3,5-bis(trifluoromethyl)phenyl (**15c**) *N*-substituents. When combined with either Na^+ or K^+ ions, these catalysts displayed up to ~30× greater activity for ethylene polymerization compared to that of a control catalyst lacking secondary alkali ions. Unfortunately, our heterobimetallic catalysts were significantly inhibited in the presence of polar olefins such as vinyl acetate, allyl acetate, and propyl vinyl ether, which is a known limitation for nickel phenoxyimine catalyst systems.



15a-M, R = iPr, M = Na or K
15b-M, R = Ph, M = Na or K
15c-M, R = 3,5-$(CF_3)_2$Ph, M = Na or K

16-M, Ar = 2-MeOPh
M = Li, Na, or K

Chart 6. Examples of heterobimetallic complexes for Lewis-acid promoted olefin copolymerization.

Our early success using a Lewis acid/secondary metal activation strategy motivated us to explore whether this approach could be implemented in other related catalyst systems. We were particularly interested in the Drent-type complexes because they are among the most efficient catalysts for ethylene and polar olefin copolymerization.[79] The Pd phosphine-phosphonate catalysts reported by Jordan and coworkers provided a convenient platform for us to make further synthetic modifications.[80] Specifically, we were able to incorporate two PEG chains into the phosphate group to provide a second metal binding site for alkali ions.[81] Using the method of continuous variation, we demonstrated that the 1:1 palladium:alkali (Li^+, Na^+, or K^+) complex is the optimal stoichiometry in solution. The identity of the palladium-sodium complex was confirmed by X-ray crystallography. Consistent with our previous studies, addition of alkali salts to **16** generated single-site catalysts (**16**-M) that are more active for ethylene polymerization than **16** itself. The palladium-alkali catalysts also showed improved activity for ethylene and alkyl acrylate copolymerization compared to their parent monopalladium catalysts, although their effect on polymer branching and molecular weight was surprisingly modest. These heterobimetallic systems displayed long catalyst lifetimes at 100°C and were able to operate at temperatures as high as

140°C. Studies are currently underway to understand the reasons for their greater catalyst activity and thermal stability.

Challenges and Future Outlook

Although many successful examples of heterobimetallic catalysts have now been reported, constructing synthetic systems that take advantage of metal–metal cooperativity is still a formidable goal. First, the preparation of well-defined heterobimetallic compounds is not always a trivial task. Metallation of symmetric dinucleating ligands can lead to a mixture of homobimetallic and heterobimetallic species that are difficult to separate.[32] Furthermore, a ligand having two identical sets of donor groups might not be able to support a specific M–M′ combination due to the different coordination preferences of the individual metals. Although asymmetric dinucleating ligands can solve the metal selectivity problem by having two distinct sets of donors that accommodate two different metal ions, they are typically more time consuming to synthesize than symmetric ligands. In many cases, ligand synthesis is the rate-limiting step of the catalyst development process.

Second, once the desired heterobimetallic complexes have been prepared, rigorous physical characterization work must be performed to establish their identities and structures. Determining the X-ray crystal structures of the heterobimetallic complexes provide useful information about their atom connectivity in the solid state. However, it is also necessary to employ methods to determine their speciation in solution, such as by mass spectrometry (e.g. ESI, MALDI-TOF),[32,67] NMR spectroscopy (e.g. 1-D, DOSY),[32,48,49] or metal binding studies (e.g. titration, Job Plot).[76,81] It is important to assess whether the heterobimetallic species equilibrate in solution to form homobimetallics or self-assemble into higher nuclearity species (i.e. greater than 2).

Finally, a third challenge in heterobimetallic catalyst development is identifying the factors that contribute to the cooperative effect. One of the most compelling evidence for M–M′ cooperativity comes from reactivity studies. If a heterobimetallic catalyst displays reactivity that is different than that of their homobimetallic or monometallic analogues, then a case could be made for synergistic heterobimetallic interactions. A potential problem, however, is that synthesizing suitable homobimetallic or monometallic complexes for reactivity comparisons is not always possible. Even if a heterobimetallic effect is supported by experimental data, investigating the specific roles of M and M′ in catalysis can be exceedingly difficult. To obtain a complete mechanistic picture, we need to acquire information about the structures of key catalyst intermediates and gain insights into the thermodynamics and kinetics of the elementary steps in the polymerization process. This mechanistic work is particularly challenging if the intermediates of interest cannot be trapped or observed by current physical characterization techniques.

Despite the challenges delineated above, synthetic chemists are well equipped to overcome some of these common obstacles. When designing new heterobimetallic catalysts, there are now many known structural motifs to model after. The best design will depend on catalyst criteria such as M–M′ bond distance, structural flexibility, coordinative unsaturation, and thermal stability. In our experience, the most effective method to prepare heterobimetallic complexes is to metallate dinucleating ligands in a stepwise fashion (adding M first followed by M′ or vise versa) rather than in a one-pot reaction (adding both M and M′ at the same time). It is important to use a combination of physical characterization methods to verify the identity of the heterobimetallic complex in both the solid state and solution. As we had demonstrated in our studies of the nickel carboxamidatetriazole complexes described above,[70,71] understanding catalyst speciation in operando is critical to the catalyst design process.

To study mechanism, a variety of modern spectroscopic tools are available. For some catalysts, it might be possible to generate reaction intermediates at low temperature[82] or trap them by rapid freeze quench techniques for further characterization.[83] In addition to using conventional methods (e.g. NMR spectroscopy) to probe these intermediates, synchrotron-based techniques (e.g. X-ray absorption spectroscopy, nuclear resonance vibrational spectroscopy, etc.) could offer complementary information.[84,85] To answer mechanistic questions that might not be accessible experimentally, computational studies could also be very powerful.[86,87] As indicated by our survey of recent literature, interest in heterobimetallic systems is growing in the catalysis community. We anticipate that further research in this area will lead to new conceptual breakthroughs in polymerization catalysis and provide access to novel and sustainable materials that could enhance the quality of everyday life.

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