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# *N,O*-Chelating Four-Membered Metallacyclic Titanium(IV) Complexes for Atom-Economic Catalytic Reactions

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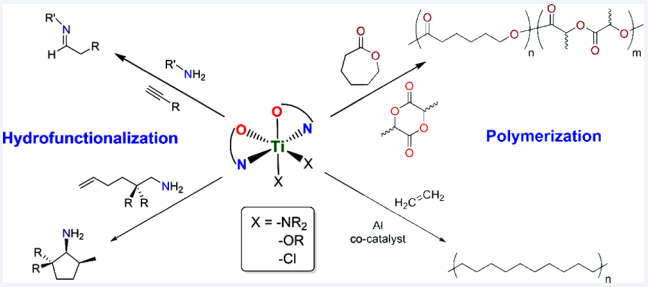
**CONSPECTUS:** Titanium, as the second most abundant transition metal in the earth's crust, lends itself as a sustainable and inexpensive resource in catalysis. Its nontoxicity and biocompatibility are also attractive features for handling and disposal. Titanium has excelled as a catalyst for a broad range of transformations, including ethylene and $\alpha$-olefin polymerizations. However, many reactions relevant to fine chemical synthesis have preferentially employed late transition metals, and reactive, inexpensive early transition metals have been largely overlooked. In addition to promising reactivity, titanium complexes feature more robust character compared with some other highly Lewis-acidic metals such as those found in the lanthanide series. Since the advent of modulating ligand scaffolds, titanium has found use in a growing variety of reactions as a versatile homogeneous catalyst. These catalytic transformations include hydrofunctionalization reactions (adding an element−hydrogen (E−H) bond across a C−C multiple bond), as well as the ring-opening polymerization of cyclic esters, all of which are atom-economic transformations.




Our investigations have focused on tight bite angle monoanionic *N,O*-chelating ligands, forming four-membered metallacycles. These ligand sets, including amidates, ureates, pyridonates, and sulfonamidates, have flexible binding modes offering a range of stable and reactive intermediates necessary for catalytic activity. Additionally, the simple form of these ligands leads to easily prepared proligands, along with facile tuning of steric and electronic factors. A sterically bulky titanium amidate complex has proven to be a leading catalyst for the selective formation of anti-Markovnikov addition products via intermolecular hydroamination of terminal alkynes, while sterically less demanding titanium pyridonates have opened the path to the selective formation of amine substituted cycloalkanes via the intramolecular hydroaminoalkylation of aminoalkenes over the competing hydroamination pathway. Sulfonamidates have boosted reactivity for hydrofunctionalization and polymerization reactions compared with amide ligands not bearing a sulfonyl group. *N,O*-Chelated titanium complexes have been used to synthesize ultrahigh molecular weight polyethylene and have been utilized in the challenging task of realizing equal incorporation of two different cyclic esters in a random ring-opening copolymerization. These discrete complexes have allowed for careful study of fundamental coordination chemistry and stoichiometric organometallic investigations. With inexpensive starting materials and modular ligands, titanium *N,O*-chelated complexes are well-suited to address the challenges of achieving greener chemical processes while accessing useful reaction manifolds for sustainable synthesis.

## 1. INTRODUCTION

Titanium is earth abundant, making it inexpensive, and its low-toxicity and biocompatibility make it attractive for application in chemical synthesis. Additionally, it has been shown to be a versatile catalyst for a broad spectrum of reactions including hydrofunctionalization reactions,[1,2] polymerization reactions,[3,4] aldol and allylic additions to ketones and aldehydes,[5,6] epoxidation of alkenes,[7] and carbonate formation with epoxides and $CO_2$.[8] Careful tuning of the electronic and steric properties of titanium complexes can be realized with monoanionic *N,O*-chelating ligands that form tight bite angle four-membered metallacycles, to give robust catalysts with comparable or complementary reactivity to more costly late transition metals. These *N,O*-chelating ligands, namely amidate, ureate, pyridonate, and sulfonamidate ligands, are assembled in a modular fashion, and they are simple to synthesize (Figure 1).

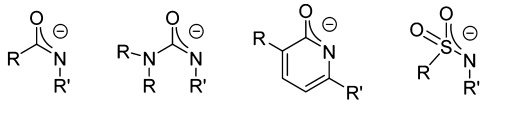



**Figure 1.** Deprotonated monoanionic *N,O*-chelating ligands.

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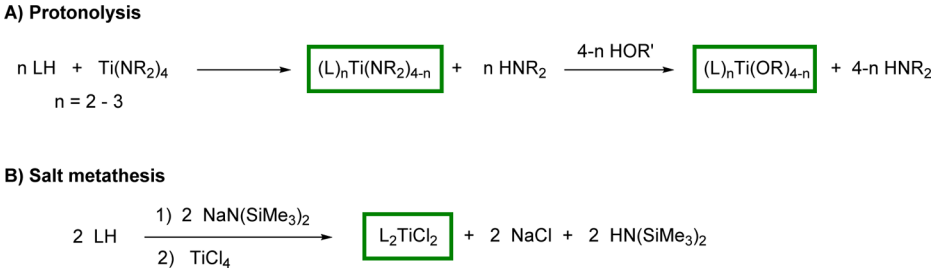
**Scheme 1. Protonolysis (A) and Salt Metathesis Route (B) for Titanium Complex Synthesis**




The range of catalysis that has been achieved with this class of *N,O*-chelated titanium complexes extends from hydroamination and hydroaminoalkylation to ring-opening polymerization (ROP) of cyclic esters and Ziegler−Natta-type polymerization of ethylene and $\alpha$-olefins. All of these reactions use catalytic amounts of titanium and are atom economical in their use of reagents, with the exception of aluminum cocatalysts for $\alpha$-olefin polymerization.

Synthesis of *N,O*-proligands in most cases is facile, while some are even commercially available. Amide proligands in particular are easily synthesized by the reaction of acid chlorides with primary amines, allowing for variation of both the substituent on the carbonyl carbon and that on the nitrogen.[9] Ureas demand a two-step, one-pot reaction to access proligands in high yields.[10] Pyridones, another highly versatile class of ligand, are either commercially available or can be synthesized from known literature methods.[11] Finally, sulfonamides are formed through the well-established amine protection protocols using sulfonyl groups.

With proligands in hand, the synthesis of titanium complexes is also a facile procedure. All of the aforementioned ligands can be installed on the titanium metal center using protonolysis with the inexpensive and commercially available homoleptic $Ti(NMe_2)_4$. The liberated dimethylamine can be removed *in vacuo* along with solvent, leaving behind crude product that is often quite pure, though recrystallization is typically required to obtain material that passes combustion analysis. Formation of mixed *N,O*-chelated alkoxide complexes can then be achieved by adding an appropriate number of equivalents of alcohol to the (dimethylamido)titanium complex, liberating dimethylamine and generating the titanium alkoxide product. Notably, the direct synthesis from $Ti(O^iPr)_4$ and proligand leads to multiple species in the reaction mixture, necessitating this two-step approach (Scheme 1A).[12]

Salt metathesis can be employed to access metal chloride complexes; however variable results are often obtained, presumably due to the formation of ate complexes. The most reliable approach developed is deprotonation of the proligand by $NaN(SiMe_3)_2$ (NaHMDS), followed by addition of half an equivalent of $TiCl_4$ to generate the bis(amidate)dichloride complex (Scheme 1B).[10] Alternatively, a protonolysis route using 2 equiv of proligand and $Ti(NMe_2)_2Cl_2$ is a very reliable preparative method.[10]

It is well-known that tight bite angle *N,O*-chelating ligands can have a number of coordination modes (Figure 2). While the $\kappa^2$-binding mode is commonly observed, these ligands are hemilabile and are capable of monodentate coordination through either heteroatom. When sterically congested, $\kappa^1$-(*O*) binding can be favored over chelation resulting in an alkoxy-imine type ligand motif.[13] Lastly, a bridging motif can be accessed across two metal centers.[14] In addition to relief of steric crowding at the metal center, these types of structures are invoked in a variety of *N,O*-chelating coordination chemistry mechanisms, allowing access of substrates to the reactive metal center.

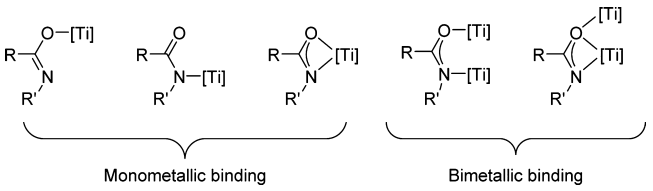


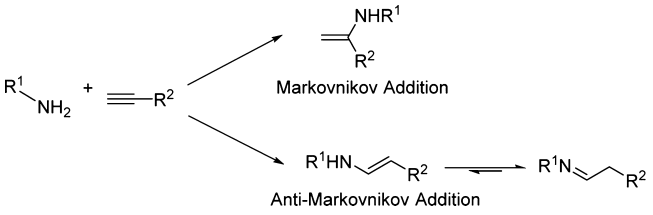

**Figure 2.** Binding modes of *N,O*-chelating ligands, exemplified by amidates.

## 2. CATALYTIC HYDROFUNCTIONALIZATION REACTIONS OF Ti *N,O*-CHELATED COMPLEXES

### 2.1. Hydroamination

The most prolific use of titanium *N,O*-chelates, especially amidates, is in the field of hydroamination: a C−N bond forming hydrofunctionalization reaction involving the addition of an amine across a C−C multiple bond (Scheme 2).[1] This transformation is attractive because it is 100% atom-economic and directly functionalizes C−C unsaturations. Hydroamination of alkynes leads to enamines, which are in equilibrium with their imine isomers. Imines are synthetically useful reactive intermediates that can then undergo further reactivity in sequence or in one-pot reactions.

**Scheme 2. Hydroamination of Terminal Alkynes with Primary Amines**




This reaction was initially explored in the early and mid-20th century with heterogeneous metal oxides and salts under forcing conditions for the amination of olefins.[15] Over the next few decades, main group and late transition metal catalysts improved functional group tolerance with less harsh conditions and managed to achieve some regioselectivity favoring the Markovnikov addition products.[16] Recently, large strides toward greater control of regioselectivity and access to the anti-Markovnikov products have been made. For alkenes, the intramolecular hydroamination reaction has also seen progress; however, a broadly useful homogeneous catalyst for inter-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molecular alkene hydroamination under mild conditions remains a challenge to this day.

The first example of intermolecular alkyne hydroamination catalyzed by titanium was published by Doye in 1999, using dimethyltitanocene.[17] The active species in this work has been proposed to be a mono-Cp imido complex,[18] formed from amine in solution displacing a cyclopentadienyl ring. This prompted further exploration of non-Cp ligand sets and led to the first report of an *N*,*O*-chelated titanium complex used as a catalyst for hydroamination, from Bergman in 2002 (Figure 3,

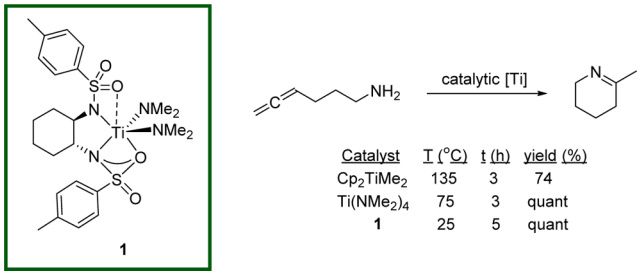



**Figure 3.** Selected results for titanium catalyzed intramolecular hydroamination of an aminoallene.

complex **1**).[19] The reactivity for intramolecular alkyne and allene hydroamination was explored using a previously reported titanium complex bearing a diamide chelating ligand with N-tosyl groups, resulting in the possibility of sulfonamidate *N*,*O*-binding.[20] For the intramolecular hydroamination of allenes, **1** is a reactive catalyst at room temperature. This contrasts with $Ti(NMe_2)_4$, which requires slightly elevated temperatures (75 °C), and dimethyltitanocene, which requires even more heating (135 °C) to efficiently catalyze the reaction (Figure 3).[19]

In 2003, Schafer first published titanium amidate complexes for hydroamination, reporting improved reactivity over homoleptic variants for both intra- and intermolecular alkyne hydroamination.[9] Shortly thereafter, Schafer reported an improved bis(amidate)titanium complex, which is one of the most robust, regioselective, and active homogeneous catalysts for intermolecular alkyne hydroamination.[21] This catalyst, complex **2**, as seen in Figure 4, imparts full anti-Markovnikov

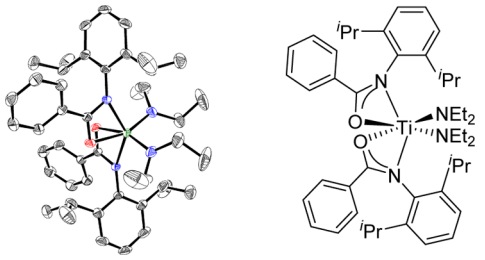
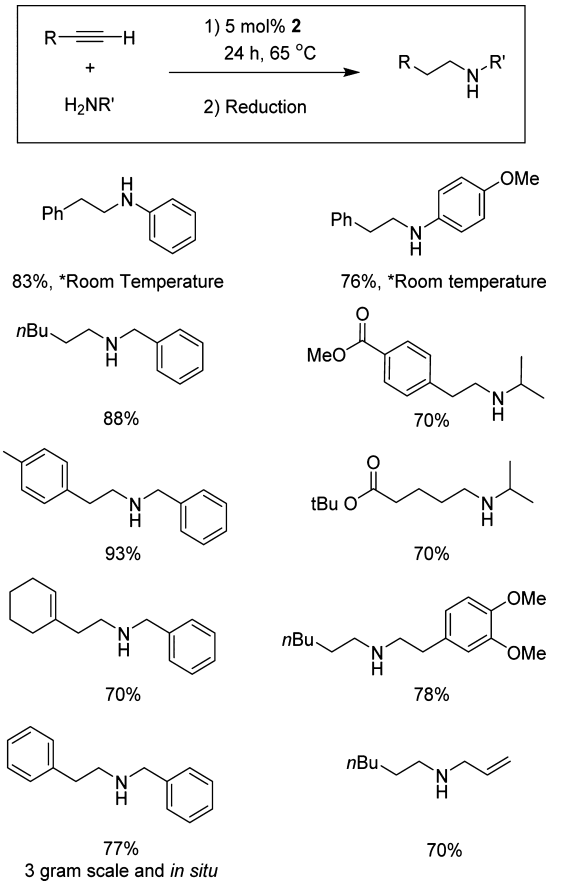



**Figure 4.** Solid state structure and depiction of **2**.

regioselectivity using challenging alkyl amines at modest reaction temperatures (65 °C) and room temperature reactivity with aniline substrates.[22] Sufficient bulk on the nitrogen substituent was found to be necessary to achieve this reactivity when multiple ligands were screened.[21]

A number of challenging terminal alkyne substrates with alkyl and select aryl amines are catalyzed by **2** at moderate temperatures with great regioselectivity, exemplified by the range of products shown in Chart 1. Importantly, **2** has been shown to be nearly as proficient when generated *in situ* using

**Chart 1. Selected Products of Intermolecular Hydroamination of Terminal Alkynes with Isolated Yields**




benchtop syringe techniques with commercially available $Ti(NMe_2)_4$ and 2 equiv of amide. This methodology has additionally proven to work well on larger, multigram scale reactions. A number of functional groups are tolerated with this catalyst, including ethers and protected alcohols, esters, and allyl amines.[22]

The functional group tolerance of complex **2** in the atom-economic hydroamination reaction makes **2** well suited for *in situ* generation of reactive imine intermediates that can be used in complex chemical syntheses. This has been put to use in the preparation of bioactive heterocycles using tandem or sequential reactions to modify the imine product. These reactions include aldehyde formation by hydrolysis or preparation of $\alpha$-aminonitriles using TMSCN,[23] which can then be converted to diamines, $\alpha$-amino amides, $\alpha$-amino acids, $\alpha$-amino esters, and $\beta$-amino alcohols (Figure 5A).[22,24] Hydrohydrazination followed by Fischer-indole synthesis can yield variably substituted indoles (Figure 5B),[22] while hydroamination followed by a Pictet−Spengler reaction yields tetrahydroisoquinolines (Figure 5C).[25] Asymmetric transfer hydrogenation of cyclic imine product gives the enantioselective synthesis of morpholines (Figure 5D).[26] A combination of terminal alkyne hydroamination with allyl amine, followed by TMSCN addition and diastereoselective intramolecular alkene hydroamination using a zirconium ureate catalyst yields a variety of substituted piperazines (Figure 5E).[26]

Alkyne hydroamination proceeds through a catalytically active imido species, which is generated upon loss of two secondary amine equivalents with the addition of a primary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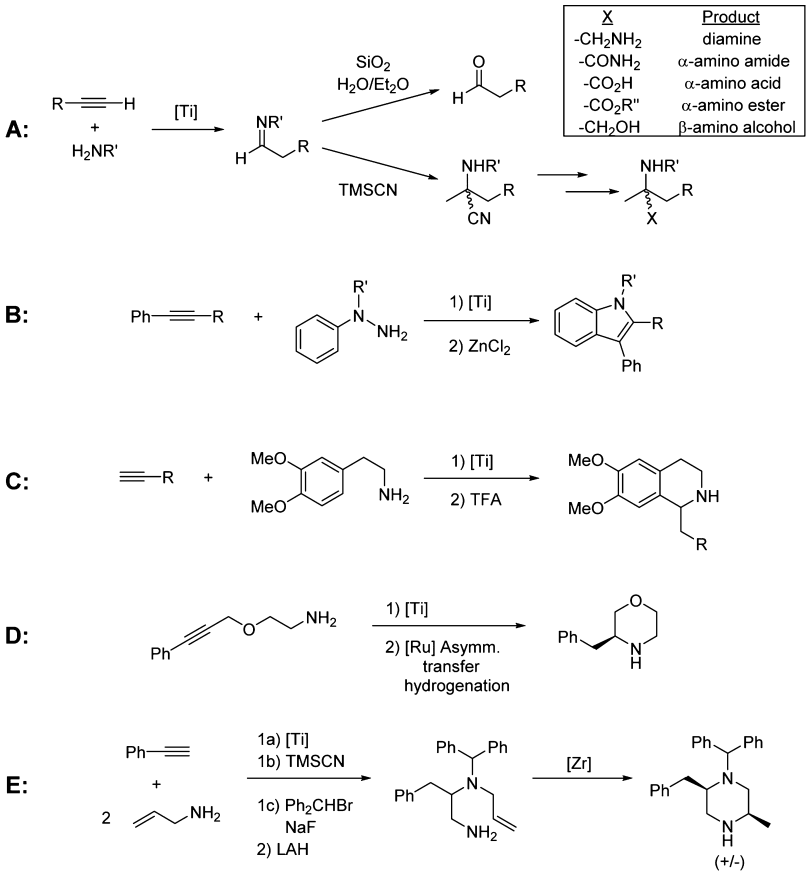


**Figure 5.** Tandem and sequential reactions with alkyne hydroamination using titanium catalyst **2** ([Ti] = **2**).

amine.[19,25,27] A concerted cycloaddition step with the C−C unsaturation follows, which upon two protonation events from an incoming amine regenerates the imido catalyst and liberates the enamine/imine product (Figure 6). An important implication of this mechanism is that the substrate scope is limited to primary amines, which are necessary to form the active imido species.

An amidate-supported titanium imido complex has been isolated and rigorously characterized (Figure 7).[25] Notably, the isolated titanium imido complex is catalytically active and

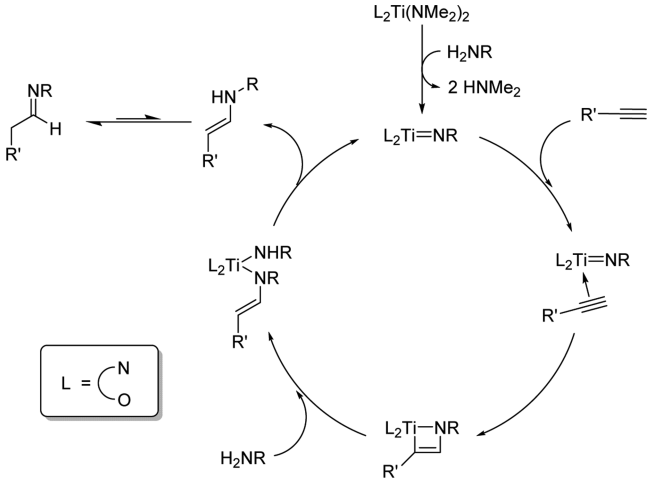


**Figure 6.** Catalytic cycle for intermolecular hydroamination of alkynes with **2**.

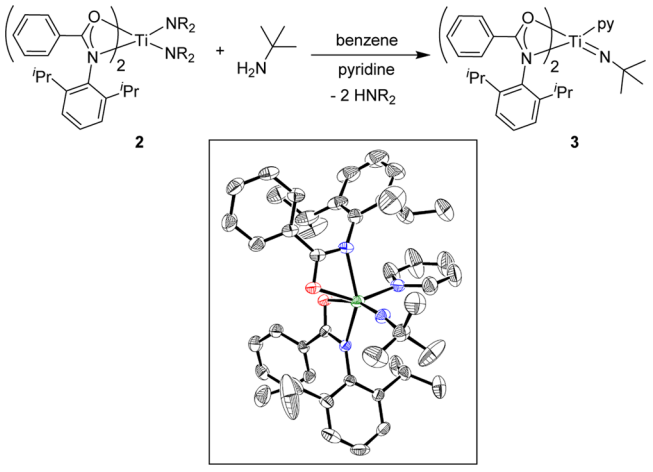


**Figure 7.** Synthesis of titanium imido complex **3** from **2**, along with the solid state structure.

displays similar rates of catalytic reactivity, further supporting the proposal that imido species are the active catalysts for this reaction.[28]

Schafer also reported **2** as an active catalyst for the intermolecular hydroamination of allenes (Scheme 3).[29] The intermolecular reaction poses a more significant challenge than intramolecular aminoallene hydroamination both entropically and due to multiple isomeric outcomes. With **2**, a number of aryl and alkyl substituted amines are tolerated to selectively give the Markovnikov branched enamine product, which can be isolated as the isomerized imine or reduced to a secondary



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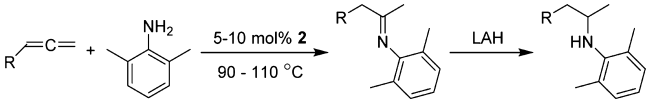
**Scheme 3. Branched Product of Intermolecular Allene Hydroamination with 2**




amine. The functional group tolerance of **2** was extended to include reactivity with selective oxygen-substituted allenes.[30]

A natural progression from alkyne and allene hydroamination was to test the viability of these complexes for intramolecular alkene hydroamination. In 2005, Schafer reported $Ti(NMe_2)_4$ as a catalyst for intramolecular hydroamination of aminoalkenes, setting the stage for further exploration of group 4 metals for this application.[31] A year later, complex **2** and its zirconium analogue were reported for this reaction.[28] These experiments revealed that zirconium *N,O*-chelates are more competent for alkene hydroamination than their titanium congeners, presumably due to enhanced steric accessibility about the metal center. However, the related *N,N*-chelating system of aminopyridonates, when installed on titanium, has shown great promise delivering room temperature reactivity for intramolecular aminoalkene hydroamination.[32]

The most competent titanium amidate complexes to date for the cyclization of aminoalkenes were reported by Zi.[33] These chiral bis(amidate) complexes, prepared alongside their zirconium analogues, can effect nearly full conversion of aminoalkenes; however, the titanium congeners require twice as much time as the zirconium-mediated reactions (48 vs 24 h for >90% conversion). These chiral ligand sets on titanium did, however, influence the enantioselectivity, achieving ee's ranging from 46 to 68%, with the leading example shown in Figure 8.[34]

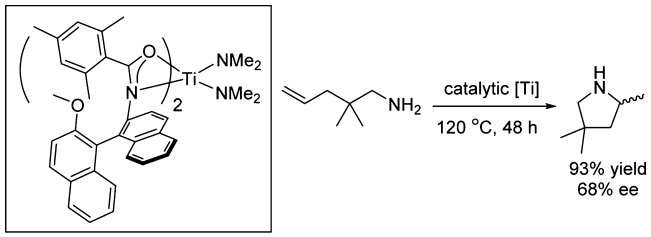



**Figure 8.** Chiral bis(amidate)titanium catalyst for hydroamination of 1-amino-2,2-dimethylpent-4-ene.

These are the most promising enantioselective catalysts for intramolecular alkene hydroamination using a Ti catalyst. In contrast, a variety of Zr complexes are known to yield products with ee's up to 98%.[35−37]

## 2.2. Hydroaminoalkylation

Hydroaminoalkylation (HAA) or the $\alpha$-alkylation of amines is a recently developed area of catalysis featuring a C−H activation adjacent to an amine functionality, and the addition of this C−H bond across an alkene (Figure 9).[2] This reaction was originally observed for group 5 metals;[38,39] however, a hydroaminoalkylation product was identified as a titanium-mediated hydroamination byproduct in 2008.[40] Subsequently, the reaction has been explored using titanium for both inter- and intramolecular reactivity. Hydroaminoalkylation is proposed to proceed by activating a C−H bond to yield a metallaziridine species, as shown in Figure 9.

Such titanaziridine intermediates have been isolated, such as complex **4** reported by Schafer in 2009 (Figure 10).[14]

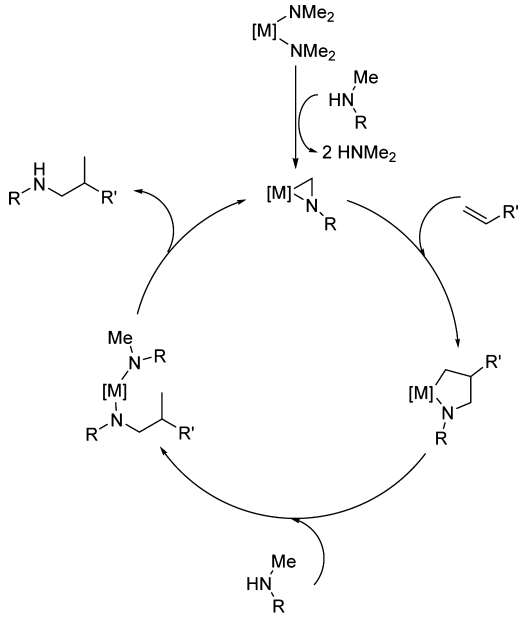



**Figure 9.** General hydroaminoalkylation catalytic cycle.

Intriguingly, the titanaziridine functionality bridges two metal centers. The solid state molecular structure of **4** reveals two additional bridging ligands, an amidate and imido ligand. Supported by this result, a bridging titanaziridine is proposed to be a key intermediate for the hydroaminoalkylation reaction of primary aminoalkenes with *N,O*-chelated titanium complexes. Gratifyingly, complex **4** was found to be catalytically active, though with a limited substrate scope.[14]

In 2012, Doye extended the application of titanium to intermolecular hydroaminoalkylation, utilizing sulfonamidate complexes.[41] This sulfonamidate ligand is unique in having two nitrogen substituents, allowing for two *N,O*-chelating interactions, bridging two metal centers. Both 1 and 2 equiv of sulfonamidate ligand were utilized to form dimeric complexes; however, only the complex with 1 equiv of ligand per two metal centers, **5**, was shown to be a viable intermolecular HAA catalyst (Scheme 4). With 5 mol % of this catalyst, yields up to 77% with 97:3 branched/linear amine product were obtained in the hydroamination of aryl and alkyl secondary amines with terminal alkenes. These results are a significant improvement over homoleptic titanium complexes where $Ti(NMe_2)_4$ yielded less than 2% product for the above reaction under identical conditions.[41] Notably, **5** is also competent as a catalyst for the intramolecular hydroamination of some aminoalkenes.[41]

For intramolecular hydroaminoalkylation, a major limitation is the selective formation of the desired hydroaminoalkylation product over the hydroamination product. Early attempts at reactivity with aminoalkenes resulted in mixtures of both products.[40] To overcome this selectivity problem, early efforts focused on substrate control for selective intramolecular hydroaminoalkylation reactivity. For example, substrates that favor the formation of six-membered rings by hydroaminoalkylation over the less favorable seven-membered rings by hydroamination yield the hydroaminoalkylation product preferentially. However, with evidence suggesting that titanium hydroaminoalkylation catalysts access bridged titanaziridine species, ligands that promote the formation of bridging imido species were anticipated to access catalyst-controlled selectivity (Figure 11).



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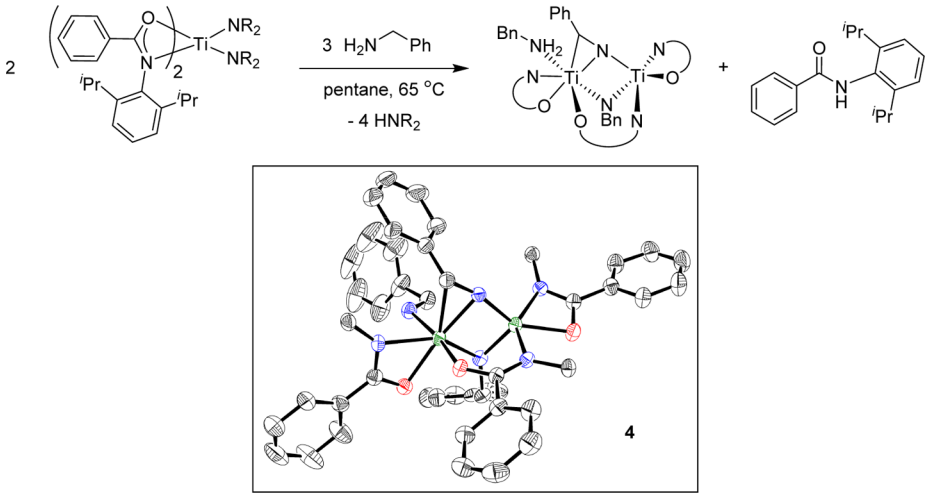
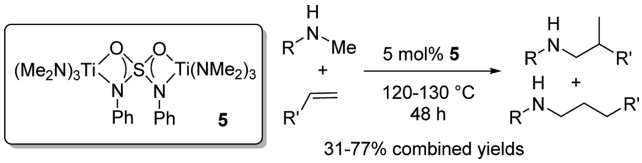



**Figure 10.** Synthesis and solid state structure of bridging titanaziridine complex **4** (dipp groups removed for clarity).

**Scheme 4. Intermolecular Hydroaminoalkylation with a Titanium Sulfonamidate Complex, 5**




The first report of catalyst-controlled selectivity for intramolecular hydroaminoalkylation over hydroamination was reported by Schafer in 2013 (Figure 12).[42] Bis(3-phenyl-2-pyridonate)bis(dimethylamido)titanium, **6**, was able to selectively catalyze the intramolecular reaction with over 90% preference for the challenging five-membered hydroaminoalkylation product over the six-membered hydroamination product. It is hypothesized that the hydroaminoalkylation selective catalysis results from the preferred formation of dimeric species due to the 3-substituted pyridonate ligand. Such dimeric species

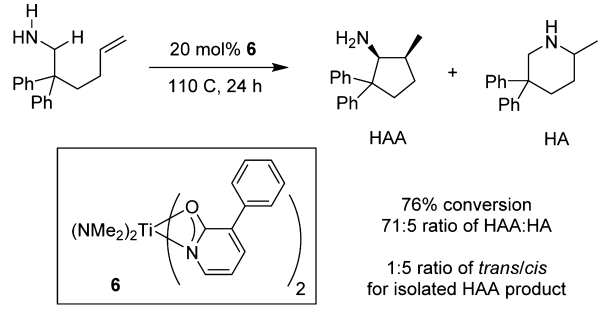



**Figure 12.** Preferential hydroaminoalkylation over hydroamination of aminohexene.

are postulated to facilitate the formation of the requisite bridging metallaziridine as in **4**.

For intermolecular reactivity, titanium complexes can only catalyze hydroamination reactions with primary amines, due to the necessary Ti-imido intermediate. Thus, acknowledging that the [2 + 2] cycloaddition mechanism of hydroamination

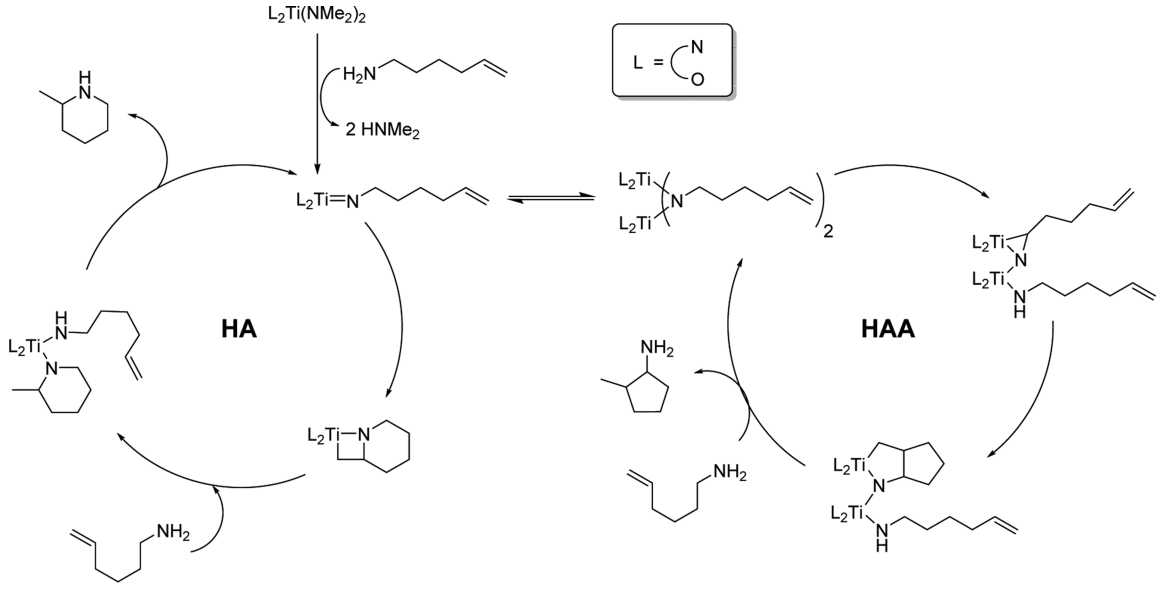



**Figure 11.** Competing titanium-mediated hydroamination and hydroaminoalkylation catalytic cycles with primary aminoalkene substrates.



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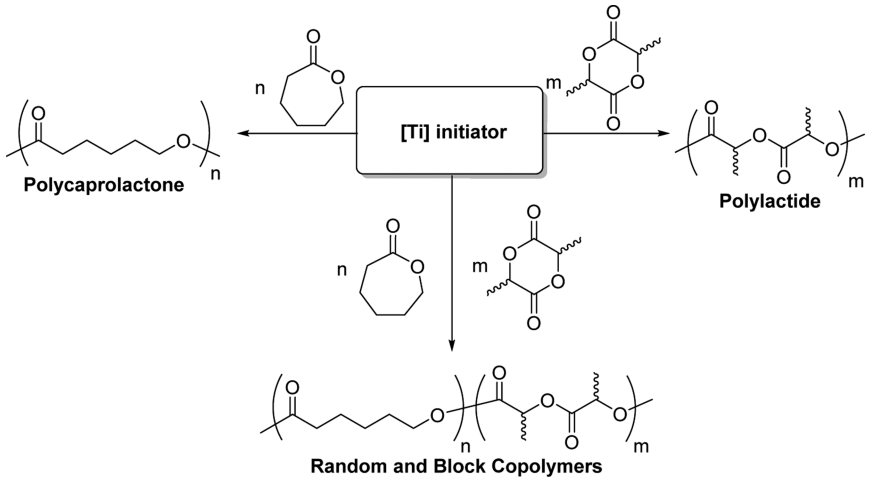
**Scheme 5. Ring-Opening Polymerization of ε-Caprolactone and *rac*-Lactide**




demands a terminal imido species, intermolecular hydroaminoalkylation reactions with Ti catalysts can be promoted with secondary amine substrates.[41] Interestingly, to date, titanium catalyzed intramolecular hydroaminoalkylation reactions do not proceed with secondary amines.[42]

## 3. POLYMERIZATIONS

### 3.1. Catalytic Ring-Opening Polymerization (ROP) of Cyclic Esters

Polyesters, generated by ROP of cyclic esters, are desirable materials due to their biodegradability.[43,44] The monomers that have been investigated for ROP by titanium *N,O*-chelated complexes are lactide and ε-caprolactone (Scheme 5). Lactide is biorenewable, derived from plant sources like corn and sugar cane, making it an attractive feedstock.[45] Lactide has two stereocenters and when used as a racemic mixture can result in the formation of polymers with variable tacticity and crystallinity; therefore, control of meso and racemic linkages can lead to varying material properties.[45] Properties of polymers change greatly when two monomer types are copolymerized and can vary further depending on block copolymerization or the more challenging random copolymerization.[12]

Titanium is a useful metal for ROP starting with $CpTiCl_2(OR)$ being reported for this transformation in 1993.[46] The development of new initiators now includes a wide variety of ancillary ligand-supported complexes.[3] The first examples of four-membered metallacyclic *N,O*-chelated titanium complexes used for ROP were sulfonamidates. Zi reported ethanoanthracene-based ligands bound to titanium through two sulfonamidate arms in 2010 (Figure 13A).[47] Polymerization studies with *rac*-lactide gave polylactide in quantitative yield at 70 °C over 24 h, making it the most active four-membered metallacyclic titanium *N,O*-chelate so far reported for the homopolymerization of *rac*-lactide. A high isotactic bias with over 70% probability of meso-linkages was measured for this system.[47]

Mountford also reported a sulfonamidate titanium complex for the ROP of cyclic esters.[48,49] A set of related polydentate ligands were tested with variations in neutral donor positions and carbon substituents on the sulfur of the sulfonamidate ligand (one complex shown in Figure 13B). With *rac*-lactide, the titanium sulfonamidates were poor initiators, leading to incomplete polymerizations. The sulfonamidate substituent was found to have minimal effects; however, the least bulky substituents produced the most active initiators. For polymerization of ε-caprolactone, all titanium initiators eventually yielded high conversions over varying time durations, again favoring less bulky ligands.[48,49]

The first use of titanium amidate and pyridonate complexes as initiators for ROP of cyclic esters was reported by Schafer in 2013.[12] Titanium bis(amidate) and bis(pyridonate) complexes were prepared for the homopolymerization of *rac*-lactide and ε-caprolactone, along with random copolymers of the two. This was the first report of well-defined titanium-alkoxides bearing these *N,O*-chelating ligands. The structurally characterized pseudo-octahedral bis(*N,O*-chelate)bis(alkoxide) complexes **7** and **8** (Figure 14) are representative examples.

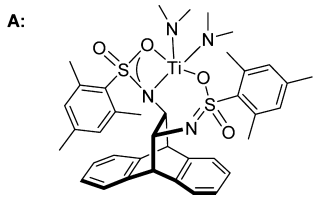
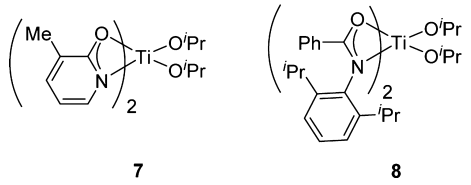



**Figure 13.** Titanium sulfonamidates from (A) Zi and (B) Mountford.



**7** **8**

**Figure 14.** Bis(pyridonate) and bis(amidate) alkoxide titanium catalysts.

For the homopolymerization of cyclic esters, good yields were obtained. Bis(amidate) titanium initiators led to the overall highest molecular weight polylactide. The homopolymerization of ε-caprolactone showed the opposite trend with these titanium initiators; the 6-methyl-2-pyridonate ligated species led to molecular weights nearly twice as high as the others.



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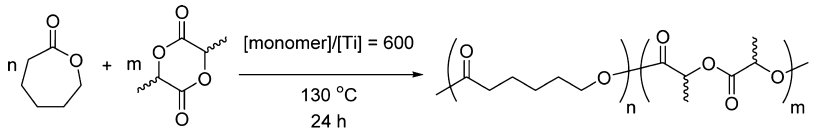
**Table 1. Copolymerization of ε-Caprolactone and *rac*-Lactide[a]**




| catalyst | yield (%) | $M_n$ (g/mol) | $M_w/M_n$ | % CL/% LA | $L_{CL}/L_{LL}$ |
|---|---|---|---|---|---|
| 7 | 83 | 19070 | 1.29 | 52/48 | 1.9/2.9 |
| 8 | 68 | 19190 | 1.37 | 64/36 | 3.1/2.4 |

[a] $M_n$ = number average MW; $M_w$ = weight average MW, $L_{CL}/L_{LL}$ = average chain length ratio.

With successful homopolymerization reactions and distinguishable trends in the influence on reactivity by the *N*,*O*-chelating ligands, the more challenging copolymerization of these two monomers was investigated. Initiators often have a bias toward one monomer over the other, leading to unequal incorporation or block copolymers, therefore it was an exciting result to find that the bis(pyridonate) titanium complexes led to random copolymer formation with nearly equal incorporation of monomers (Table 1). Bis(amidate) titanium complexes had less success in copolymerizing the two monomers.

This work was extended in 2015, expanding on titanium pyridonate complexes with differently substituted ligands along with varied stoichiometry of ligand to metal by synthesizing bis- and tris(pyridonate) complexes.[50] Here block copolymers were accessed by stepwise monomer addition.

The reactivity trends for sulfonamidate, amidate, and pyridonate supported titanium complexes show that the ligand significantly affects polymerization. Titanium sulfonamidate complexes were able to display reasonable progress toward synthesizing isotactic polylactide, and titanium pyridonate complexes were critical for producing random copolymers. Sulfonamidate complexes were also more active initiators than related amido complexes not bearing sulfonyl groups. These results display that *N*,*O*-chelating ligands warrant further investigation to improve the activity of titanium initiators and to promote stereocontrol and monomer selectivity in the formation of copolymers with variable and tunable mechanical properties.

### 3.2. α-Olefin Polymerization

α-Olefin polymerization reactions, especially the synthesis of polyethylene, have long been known to be initiated by group 4 transition metals.[4] The breakthrough work of Ziegler and Natta led to group 4 catalysts, in the presence of cocatalysts, such as MAO (methylalumoxane), and these catalysts have prolific use in the plastics industry.[51,52] As the field progressed, simple homoleptic metal initiators gave way to predominantly metallocene initiators.[53] Recently, however, other ligand motifs have been explored, including *N*,*O*-chelates and related *N*,*N*-chelating ligands such as amidinates.[54,55] *N*,*O*-Chelates forming larger metallacycles, such as phenoxyimines, have been explored extensively,[56] while four-membered metallacyclic *N*,*O*-chelating ligands, such as amidates, have only just begun to be investigated as supporting scaffolds for α-olefin polymerizations.[57−60]

In 2001, Arnold reported the first titanium amidate complexes to be synthesized, which were screened for ethylene polymerization (Figure 15, complex **9**).[57] These tethered bis(amidate) ligated complexes were found to offer low activity for polyethylene synthesis, whether bearing dimethylamido or chloro ligands.

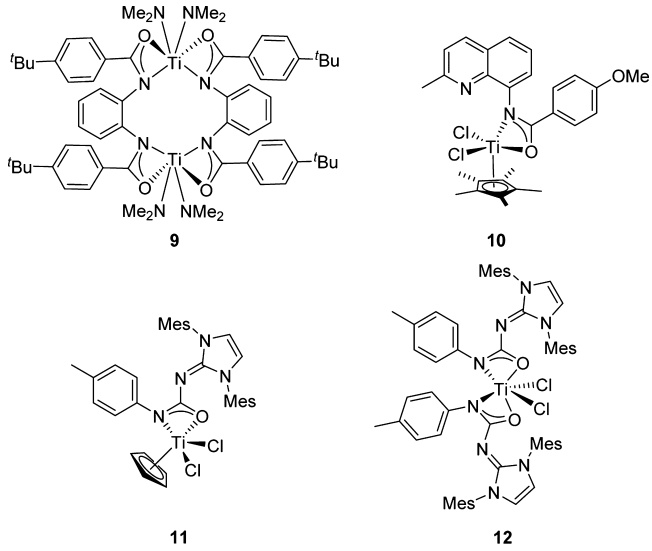



**Figure 15.** Catalysts for ethylene and α-olefin polymerization.

In 2010, Sun revisited titanium *N*,*O*-chelated complexes for this application by synthesizing a series of half-sandwich cyclopentadienyl−amidate titanium dichloride complexes.[58] Steric effects of the ligands were probed by using either cyclopentadienyl (Cp) or pentamethylcyclopentadienyl (Cp*) ligands, and electronic effects of the amidate ligand were varied by incorporation of various electron-donating and withdrawing substituents (Figure 15, complex **10**). With MAO as a cocatalyst, these complexes were tested for ethylene polymerization with 10 atm of ethylene at 30 °C. The Cp*-bound complexes were found to have higher catalytic activities. Notably, this system displayed tunable electronic effects, as the incorporation of electron-donating substituents on the amidate ligand resulted in increased catalytic activity. Therefore, **10** led to the highest activity of 2170 kg(polyethylene)/[mol(titanium)·h]. However, the Cp-bound analogues promoted polymer chain lengths ten times that of the Cp*-bound complexes (180−437 kg/mol for Cp vs 20−31 kg/mol for Cp*), supporting the conclusion that Cp* decreases the chain propagation rate, increasing the possibility of chain transfer and lowering average molecular weights. Complex **10** was also tested for the copolymerization of ethylene with 1-hexene or 1-octene, leading to polymer with approximately 15 mol % incorporation of longer chain α-olefin in either case.[58]

This class of complexes was further elaborated by Lavoie in 2013 with two titanium ureate catalysts.[59] Similar to Sun's work, one complex (**11**) is a half-sandwich cyclopentadienyl−ureate titanium dichloride, while the second (**12**) is a bis(ureate) titanium dichloride, using the same ureate ligand in both cases. An interesting ureate ligand was utilized, forming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an imine functionality on the noncoordinating nitrogen of the ureate by incorporating an N-heterocyclic carbene. Unlike earlier work, these reactions were conducted under only 1 atm of ethylene at room temperature. Perhaps due to these conditions, polyethylene was obtained with considerably lower activities, achieving 360 kg(polymer)/[mol(catalyst)·h].

Most recently, Schafer disclosed a series of bis(amidate) titanium complexes for ethylene polymerization.[60] Reactive chloride ligands resulted in the more active catalysts, though a series of bis(amido)bis(amidate) titanium complexes were also tested. At 50−80 °C under 350 psi of ethylene, complexes **13**−**16** (Figure 16) reached activities of 5700 kg(polymer)/[mol(catalyst)·h] over 30 min and over 10000 kg(polymer)/[mol(catalyst)·h] in a 10 min reaction (Table 2). In addition to the highest activities seen for four-membered metallocyclic titanium complexes with *N*,*O*-chelates, the polymeric product is notable for its high average molecular weights. These catalysts produced polyethylene up to 4300 kg/mol with somewhat broad dispersities but could still achieve 3600 kg/mol while maintaining a dispersity of 1.3. These large average molecular weights put the polymer in the range of ultrahigh molecular weight polyethylene (UHMWPE), an attractive material for a number of applications.[61] Attempts at copolymerization of ethylene and larger $\alpha$-olefins were unsuccessful for these complexes.

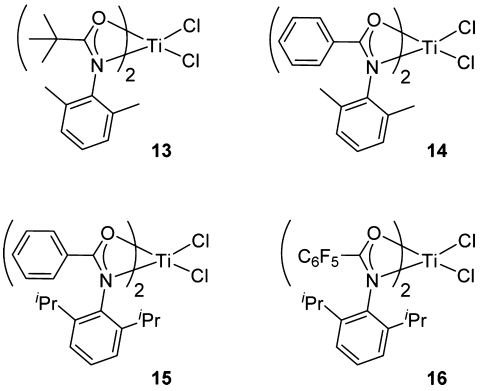
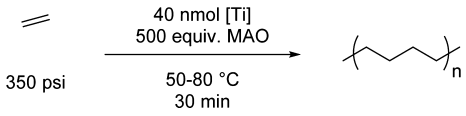



**Figure 16.** Bis(amidate)titanium dichloride complexes for ethylene polymerization.

**Table 2. Ethylene Polymerization Results of Catalysts 13−16**




| catalyst | $T$ (°C) | $A^a$ | $M_n$ (kg/mol) | $M_w/M_n$ |
|---|---|---|---|---|
| **13** | 50 | 1150 | 4300 | 1.5 |
| **13** | 80 | 2350 | 4000 | 1.6 |
| **14** | 50 | 3350 | 4200 | 1.9 |
| **14** | 80 | 1250 | 3700 | 3.3 |
| **15**[b] | 50 | 10350 | 3900 | 2.1 |
| **15** | 80 | 2300 | 3200 | 2.3 |
| **16** | 50 | 2950 | 3000 | 1.3 |
| **16** | 80 | 5750 | 3600 | 1.3 |

[a]Activity in kg(polymer)/[mol(catalyst)·h]. [b]10 min reaction.

Titanium continues to be the prominent metal for ethylene and $\alpha$-olefin polymerizations, and these results demonstrate that amidate and ureate ligands are also a promising class of ligands as research reaches beyond Cp-based ligand frameworks. Additionally, new results show possible applications in more niche areas of high molecular weight polyethylene. The exploration of these ligands is only beginning in comparison to the plethora of other frameworks utilized for ethylene polymerization.

## 4. CONCLUSION AND OUTLOOK

Tight bite angle *N*,*O*-chelates are growing to be a popular ligand for metals across the periodic table.[62−66] This Account demonstrates that the asymmetric binding and coordinatively flexible environment of titanium *N*,*O*-chelates allows for impressive and unique reactivities to be accessed with these complexes. Though activity can be lower than similar highly Lewis acidic metals, such as lanthanide metals, the benefit of the more robust and functional group tolerant titanium complexes can be advantageous. Additionally, the different classes of *N*,*O*-chelating ligands (amidates, ureates, pyridonates, and sulfonamidates) offer unique characteristics with complementary reactivity, allowing for their application in a growing variety of reactions. In the catalytic synthesis of substituted amines, electrophilic *N*,*O*-chelated titanium complexes have been shown to be useful for hydroamination and hydroaminoalkylation. The steric bulk of amidate ligands leads to the favored formation of terminal-imido intermediates and extensive reactivity and selectivity in hydroamination reactions. In contrast, the less sterically demanding pyridonate ligands offer access to binuclear species, which favors intramolecular hydroaminoalkylation over hydroamination. Notably, the incorporation of steric bulk at specific positions on the pyridonate framework is an area of ongoing investigation. In contrast, polymerizations can be mediated by a range of *N*,*O*-chelated titanium complexes. Interestingly, random copolymer synthesis by ROP and also Zeigler−Natta-type polymerizations to give high molecular weight polyethylene can be achieved using both titanium pyridonates and amidates. From these examples, it can be seen that this developing family of complexes helps to ensure that titanium is a desirable metal for homogeneous catalysis, not only for its associated cost and low environmental impact, but for its unique catalytic reactivity in C−N, C−O, and C−C bond forming reactions. Furthermore, study of these discrete complexes is offering continual insight into reactivity and mechanistic details, guiding future catalyst development opportunities.

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### Notes

The authors declare no competing financial interest.

### Biographies

**Scott Ryken** obtained his Bachelor of Science degree, with college honors, in 2010 from the University of Washington in Seattle, majoring in chemistry. He is currently pursuing his doctoral degree at the University of British Columbia in Vancouver. His research under the supervision of Prof. Schafer has been focused on the exploration of novel *N*,*O*-chelated and aryloxide titanium complexes for catalytic hydrofunctionalization reactions.

**Laurel Schafer** completed her undergraduate and graduate degrees in Canada at the University of Guelph (1993) and the University of



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Victoria (1999), respectively. Upon completion of her doctoral work, she joined the laboratories of Prof. T. Don Tilley at the University of California—Berkeley as an NSERC Postdoctoral Fellow. In 2001, she joined the faculty at the University of British Columbia, where she is now a Full Professor. She was named a Sloan Fellow in 2007 and a Humboldt Fellow in 2009, and in 2011, she was named a Canada Research Chair in Catalyst Development (Tier 2). Her research program investigates the synthesis, structure, and reactivity of *N,O*-chelated complexes of early transition metals and lanthanides, specifically focused towards the catalytic synthesis of nitrogen-containing molecules. Her research has led to the development of a new family of catalysts for hydroaminoalkylation and hydroamination reactions.

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