

A Pentagonal Pyramidal Zirconium Imido Complex for Catalytic Hydroamination of Unactivated Alkenes

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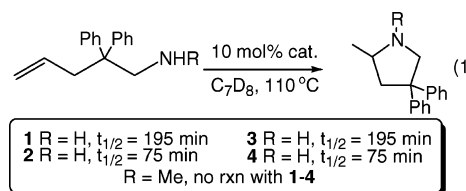
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Summary: The first, isolable group 4 imido complexes capable of promoting intramolecular olefin hydroamination for the preparation of N-containing heterocycles are presented. The structurally characterized 6-coordinate bis(amidate)-supported zirconium imido complex is a rare example of distorted-pentagonal-pyramidal geometry.

Selective formation of C–N bonds has many potential applications in the pharmaceutical and fine chemical industries. Although there are many synthetic routes to C–N bonds, the most efficient methodology is catalytic hydroamination: the formal addition of N–H to C–C unsaturation.¹ Many transition-metal complexes have been developed to promote this reaction, and in particular, group 4 metals have been successfully exploited for the catalytic hydroamination of alkynes.² This well-studied reaction is understood to involve an imido complex, which undergoes a cycloaddition reaction to form an azametallacyclobutene intermediate.^{2c,d,f,3} The analogous reaction with alkenes has met with less success using group 4 metals; however, cationic complexes have been shown to mediate this transformation with secondary aminoalkene substrates.⁴ These amido complexes likely employ a σ -bond insertion mechanism, analogous to the isoelectronic lanthanide catalysts pioneered by Marks and co-workers.^{1a,5} Interestingly, these cationic precatalysts cannot be used with primary amine substrates, which has been postulated to be due to the in situ formation of *catalytically inactive* imido complexes.^{4a} More recently, select neutral group 4 amido complexes have been shown to mediate the catalytic cyclohydroamination of primary aminoalkenes.^{6a,b} Substrate scope investigations with these systems suggest that imido complexes are the catalytically active species.⁶ However, despite

decades of research in the field of zirconium imido chemistry, there have been no previous reports of characterized group 4 imido complexes that mediate alkene hydroamination.⁷ Here we present the first bis(amidate)-supported group 4 imido complex, which is also the first isolable imido complex that is a competent precatalyst for alkene hydroamination.

Our research on the development of a new class of hydroamination catalysts has shown that bis(amidate)–bis(amido) complexes of Ti are efficient, modular systems for intra- and intermolecular alkyne and allene hydroamination.⁸ Here we show that, with elevated temperatures, these complexes are also active for catalytic cyclohydroamination of alkenes. Complexes **1** and **2** were tested with a commonly used aminoalkene substrate (eq 1),^{1a} and it was observed that the Zr complex **2** was much more



reactive than the analogous Ti complex **1**.⁹ While reported computational³ and substrate scope investigations support the intermediacy of an imido species, these reports do not obviate a σ -bond insertion mechanism.^{6a,b} To probe the reactivity of related imido species, the novel complexes **3** and **4** were synthesized from the bis(amido) precursors **1** and **2** (eq 2).

The synthesis of complexes **3** and **4** was accomplished in high yield in a single step. Isolation of 5-coordinate imido complexes was not successful, due to the electropositive nature of these compounds. Trapping of crystalline 16-electron,

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(1) (a) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673. (b) Muller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675. (c) Pohlki, F.; Doye, S. *Chem. Soc. Rev.* **2003**, *32*, 104. (d) Roesky, P. W.; Muller, T. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 2708. (e) Gribkov, D. V.; Hultsch, K. C.; Hampel, F. J. *Am. Chem. Soc.* **2006**, *128*, 3748. (f) Michael, F. E.; Cochran, B. M. *J. Am. Chem. Soc.* **2006**, *128*, 4246 and references therein.

(2) (a) McGrane, P. L.; Jensen, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1992**, *114*, 5459. (b) Baranger, A. M.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 2753. (c) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708. (d) Johnson, J. S.; Bergman, R. G. *J. Am. Chem. Soc.* **2001**, *123*, 2923. (e) Ackermann, L.; Bergman, R. G. *Org. Lett.* **2002**, *4*, 1475. (f) Pohlki, F.; Doye, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 2305. (g) Heutling, A.; Doye, S. *J. Org. Chem.* **2002**, *67*, 1961. (h) Tillack, A.; Castro, I. G.; Hartung, C. G.; Beller, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 2541. (i) Shi, Y.; Ciszewski, J. T.; Odom, A. L. *Organometallics* **2001**, *20*, 3967. (j) Ong, T.-G.; Yap, G. P. A.; Richeson, D. S. *Organometallics* **2002**, *21*, 2839. (k) Ackermann, L.; Bergman, R. G.; Loy, R. N. *J. Am. Chem. Soc.* **2003**, *125*, 11956 and references therein.

(3) Straub, B. F.; Bergman, R. G. *Angew. Chem., Int. Ed.* **2001**, *40*, 4632.

(4) (a) Gribkov, D. V.; Hultsch, K. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 5542. (b) Knight, P. D.; Munslow, I.; O'Shaughnessy, P. N.; Scott, P. *Chem. Commun.* **2004**, 894.

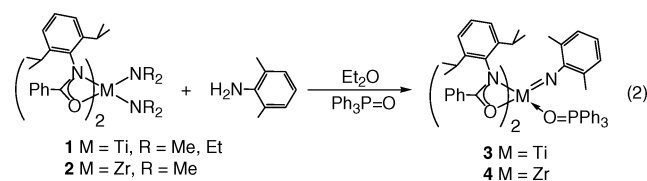
(5) (a) Gagne, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 4108. (b) See Figure 5 in the Supporting Information for the catalytic cycle.

(6) (a) Bexrud, J. A.; Beard, J. D.; Leitch, D. C.; Schafer, L. L. *Org. Lett.* **2005**, *7*, 1959. (b) Kim, H.; Lee, P. H.; Livinghouse, T. *Chem. Commun.* **2005**, 5205. (c) For the proposed catalytic cycle see Figure 4 in the Supporting Information.

(7) (a) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729. (b) Hoyt, H. M.; Michael, F. E.; Bergman, R. G. *J. Am. Chem. Soc.* **2004**, *126*, 1018. (c) Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731. (d) Cummins, C. C.; Schaller, C. P.; Duynes, G. D. V.; Wolczanski, P. T.; Chan, A. W. E.; Hoffmann, R. J. *Am. Chem. Soc.* **1991**, *113*, 2985. (e) Li, Y.; Shi, Y.; Odom, A. L. *J. Am. Chem. Soc.* **2004**, *126*, 1794. (f) Basuli, F.; Bailey, B. C.; Watson, L. A.; Tomaszewski, J.; Huffman, J. C.; Mindiola, D. J. *Organometallics* **2005**, *24*, 1886. (g) Mountford, P. *Chem. Commun.* **1997**, 2127. (h) Hazari, N.; Mountford, P. *Acc. Chem. Res.* **2005**, *38*, 839. (i) Kissounko, D. A.; Guzei, I. A.; Gellman, S. H.; Stahl, S. S. *Organometallics* **2005**, *24*, 5208. (j) Basuli, F.; Aneetha, H.; Huffman, J. C.; Mindiola, D. J. *J. Am. Chem. Soc.* **2005**, *127*, 17992. (k) Kissounko, D. A.; Epshteyn, A.; Fettingner, J. C.; Sita, L. R. *Organometallics* **2006**, *25*, 1076 and references therein.

(8) (a) Li, C.; Thomson, R. K.; Gillon, B.; Patrick, B. O.; Schafer, L. L. *Chem. Commun.* **2003**, 2462. (b) Zhang, Z.; Schafer, L. L. *Org. Lett.* **2003**, *5*, 4733. (c) Ayinla, R. O.; Schafer, L. L. *Inorg. Chim. Acta* **2006**, *359*, 3097.

(9) This trend has been seen previously with cationic group 4 catalysts.



6-coordinate imido complexes was possible upon addition of the electron donor triphenylphosphine oxide (TPPO). These complexes were characterized by ^1H , ^{13}C , and ^{31}P NMR spectroscopy as well as mass spectrometry and elemental analysis.^{10a} Complex **4** was also characterized by X-ray crystallography and found to be of distorted-pentagonal-pyramidal geometry, with the amidate and TPPO ligands bound pseudoequatorially and the imido moiety located in the axial position with a short $\text{M}=\text{N}$ bond length of 1.853 Å (Figure 1).^{10b} These structural features are consistent with a strongly donating imido moiety and the TPPO donor binding to an orthogonal orbital in the pseudoequatorial plane, along with the ionic amidate ligands.¹¹

Group 4 imido complexes have been widely studied over the past 20 years, resulting in stoichiometric reactions including C–H activation,^{7a–d} epoxide ring opening reactions,¹² and [2 + 2] cycloadditions to form azametallacyclic compounds.^{2c,7h} Catalytic advances include imine metathesis and hydroamination of alkynes^{2a,c,d,j,7e} and allenes,^{2k,8c} but interestingly, no group 4 imido complexes have been shown to promote the hydroamination of alkenes. Here, complexes **1** through **4** are all active for the cyclohydroamination reaction (eq 1), with the Zr imido complex once again being more reactive than the Ti analogue. Recent studies have suggested that proton also promotes these reactions in certain systems.¹³ In the presence of a bulky base (2,6-di-*tert*-butyl-4-methylpyridine) the catalytic activity of complexes **1–4** is unaffected, confirming metal-mediated reactivity.

Some amido systems that have been developed for alkyne hydroamination show a significant induction period, during which the catalytically active imido species is postulated to form.^{2d} However, preliminary kinetic investigations directly comparing complexes **2** and **4**, with constant catalyst concentrations, confirmed that the reaction is first order in substrate (Figure 2), consistent with a protonolysis event being rate limiting. This is in contrast to reports of hydroamination catalysts using group 3 and lanthanide metal complexes, which are known to proceed through a σ -bond insertion mechanism. For those systems careful kinetic investigations have shown a zero-order dependence upon substrate, consistent with the intramolecular olefin insertion step being rate-limiting.^{1a} Furthermore, in our case there is no observable induction period for either precatalyst (Figure 2).^{10c}

A comparison of the half-lives for the bis(amido) and imido complexes (**2** vs **4**) showed no appreciable difference between the two complexes for two separate runs at 5% and 10% catalyst loading, implying that both precatalysts share a common catalytically active species. The reaction was determined to be

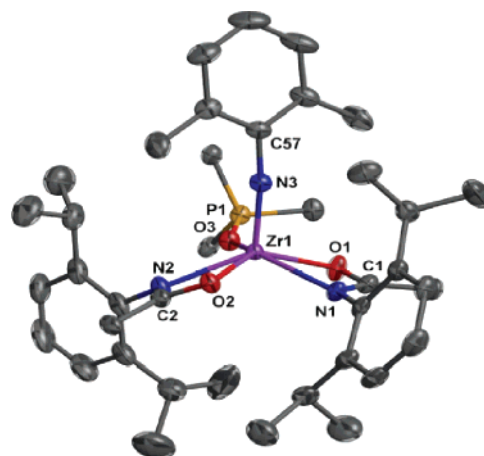


Figure 1. Solid-state structure of **4** with 6-coordinate, distorted-pentagonal-pyramidal geometry. Non ipso phenyl carbons have been removed for clarity. Selected bond distances (Å) and angles (deg): $\text{Zr}(1)\text{--N}(3) = 1.8531(18)$, $\text{Zr}(1)\text{--N}(1) = 2.3124(18)$, $\text{Zr}(1)\text{--O}(1) = 2.2034(15)$, $\text{Zr}(1)\text{--O}(3) = 2.2086(14)$; $\text{C}(57)\text{--N}(3)\text{--Zr}(1) = 173.54(16)$, $\text{N}(3)\text{--Zr}(1)\text{--O}(3) = 100.07(7)$, $\text{O}(1)\text{--Zr}(1)\text{--O}(3) = 78.14(6)$, $\text{N}(1)\text{--Zr}(1)\text{--N}(2) = 121.90(7)$.

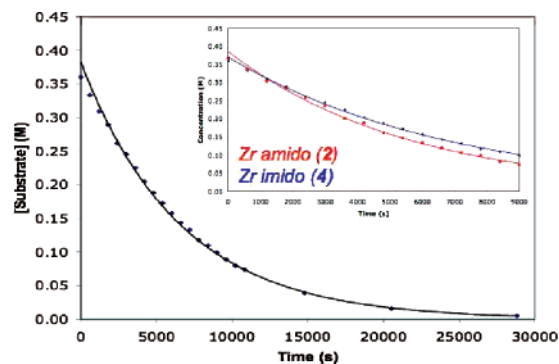


Figure 2. Plot of first-order substrate consumption by **4** and comparison between Zr amido (**2**) and imido (**4**) complexes (inset).

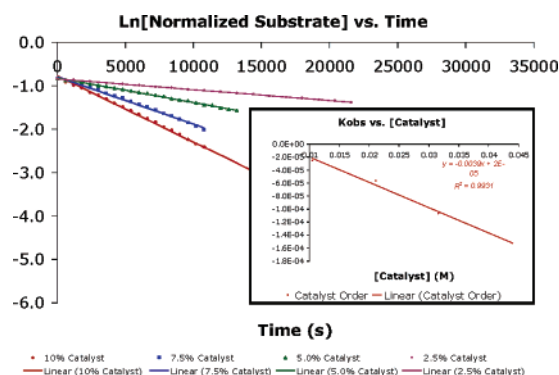


Figure 3. Plot of first-order catalyst dependence for cyclohydroamination with complex **4**.

first order in catalyst, consistent with a single-site catalyst (Figure 3).^{10d}

Finally, if an imido complex is the catalytically active species, then no reaction would be expected for the secondary aminoalkene substrate ($\text{R} = \text{Me}$ in eq 1), as the requisite imido species cannot form. It should be noted that cationic group 4 complexes, which have been proposed to promote this reaction by a σ -bond insertion mechanism, are known to mediate the cyclohydroamination of such secondary amine substrates.⁴ In our case, no reaction was observed for the secondary amine substrate shown in eq 1 ($\text{R} = \text{Me}$). Neither complex **2** nor

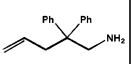
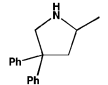
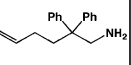
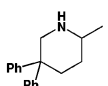
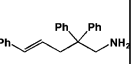
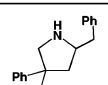
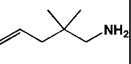
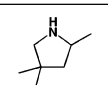
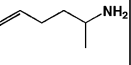
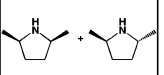
(10) (a) See the Supporting Information for details. (b) For full crystallographic details, see the Supporting Information. (c) See the Supporting Information for kinetic details. (d) For a kinetic plot see Figure 22 in the Supporting Information.

(11) Thomson, R. K.; Zahariev, F. E.; Zhang, Z.; Patrick, B. O.; Wang, Y. A.; Schafer, L. L. *Inorg. Chem.* **2005**, *44*, 8680.

(12) Blum, S. A.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **2003**, *125*, 14276.

(13) Anderson, L. L.; Arnold, J.; Bergman, R. G. *J. Am. Chem. Soc.* **2005**, *127*, 14542.

Table 1. Catalytic Cyclohydroamination Results^e

Entry	Amino-alkene	Product	Catalyst 1 ^a % (h)	Catalyst 4 ^a % (h)
1			90 ^a (10)	98 ^a (4)
2			17 ^a (48)	82(24) ^a
3			N/R(96)	38 ^a (96) 48 ^{b,d} (192)
4			12 ^b (48) 25 ^b (120)	73 ^b (120) 87 ^{b,d} (96)
5			N/R(144)	72 ^{b,d} (96) 'syn': 'anti' 1:11.3 ^c

^a Isolated yield. ^b Yield determined by ¹H NMR (internal standard 1,3,5-trimethoxybenzene). ^c Ratio determined by ¹H NMR. ^d 10% catalyst. ^e Unless otherwise stated, 5 mol % of catalyst was utilized and reaction times were unoptimized.

complex **4**, even with prolonged reaction times (up to 4 days) and elevated reaction temperatures (up to 140 °C), showed any trace of product formation. Thus, both kinetic investigations and substrate scope experiments support the intermediacy of an imido complex.¹⁴

Preliminary substrate scope investigations were performed (Table 1) to directly compare the bis(amido) complex **1** with the imido complex **4** as precatalysts for heterocycle formation. All results demonstrate the improved reactivity obtained with Zr catalysts vs Ti catalysts, in contrast to alkyne hydroamination.^{7a} In addition to pyrrolidine products (entry 1), substituted piperidine compounds can also be isolated (entry 2). Complex **4**

(14) We cannot rule out the conversion of an imido species to a catalytically active bis(amido) species that can subsequently catalyze hydroamination via a σ -bond insertion process.

was capable of cyclizing a substrate with an internal alkene, albeit slowly (entry 3). The more volatile substrate in entry 4 demonstrates the importance of size on the *gem*-dialkyl effect. Finally, good diastereoselectivity was observed for the cyclohydroamination in entry 5 with precatalyst **4**. This selectivity is consistent with a chairlike transition state in which there is a preference for the α -methyl substituent being in the equatorial position.

While the aforementioned lack of reactivity for the secondary amine substrate may be considered to be due to steric bulk, comparison to the bulky primary amine substrate in entry 5 (which also lacks reactivity-enhancing geminal substituents) suggests that the Zr precatalyst **4** can accommodate steric bulk at the reactive site. Furthermore, it should be noted that substantially more congested cationic Ti complexes are known to mediate the cyclohydroamination of secondary aminoalkenes.^{4a}

In conclusion, we have presented the first amidate-supported Zr imido complex (**4**) that exhibits a unique pentagonal-pyramidal geometry in the solid state. This is also the first neutral group 4 imido complex that is a precatalyst for intramolecular alkene hydroamination. Preliminary kinetic experiments and substrate scope investigations support an imido-based cycloaddition mechanism for this reactivity, and current efforts are focused on the full elucidation of the mechanism for this reaction. This mechanistic insight will serve to guide the rational design of new complexes displaying enhanced reactivity and selectivity.

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Supporting Information Available: Text, figures, and tables giving experimental procedures and characterization data for new compounds and a CIF file giving X-ray crystallographic data for **4**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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