Mechanism of Insertion of Carbodiimides into the Zr−C Bonds of Zirconaaziridines. Formation of α-Amino Amidines

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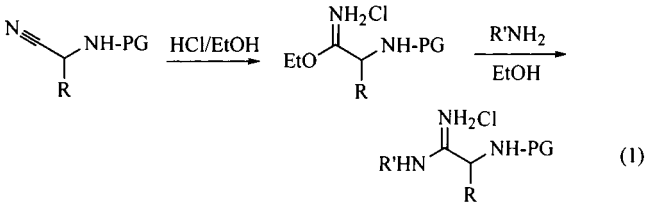
Treatment of zirconaaziridines Cp_2Zr-η^2-[$N(R^1)CH(R^2)$](THF) with carbodiimides results in the insertion of the carbodiimide into the Zr−C bonds. The insertion of bis(trimethylsilyl)-carbodiimide is reversible, which becomes significant at high THF concentrations. Kinetic data indicate that the THF ligand must dissociate prior to carbodiimide insertion. Protic cleavage of the organic fragment from zirconium results in formation of α-amino amidines.

Introduction

Zirconocene η^2-imine complexes, also known as zirconaaziridines, are the synthetic equivalents of α-amino carbanions (Scheme 1).[1−3] Previous investigations have shown that heterocumulenes such as isocyanates, and to some extent CO_2, insert into the Zr−C bond of zirconaaziridines;[2] likewise, cyclic carbonates insert into zirconaaziridines, yielding α-amino acid esters after treatment with methanol.[2,3] These studies have led to the current investigation of carbodiimide[4] insertion, which should yield the analogous α-amino amidines (Scheme 1).[5]

α-Amino amidines can be found in the antitumor antibiotic bleomycin[6] and in the iminopeptide antibiotic bottromycin[7] and are intermediates in the biosynthesis of purines.[8] Furthermore, amino amidines have recently attracted interest as NO synthase inhibitors.[9] Despite the potential pharmaceutical applications and utility in peptide modification,[10] few syntheses of α-substituted α-amino amidines or iminopeptides have been developed.[11,12] Most use the method of Mengelberg, which utilizes *N*′-protected α-amino iminoethers as intermediates (eq 1).



(1)

Herein we report that carbodiimides insert into the Zr−C bond of zirconaaziridines, leading to α-amino amidines **5** after protic cleavage (Scheme 2).

Results

Synthesis of α-Amino Amidines. Bis(trimethylsilyl)carbodiimide inserts rapidly and quantitatively into the Zr−C bonds of zirconaaziridines in aromatic solvents. Addition of HCl/Et_2O results in precipitation of the hydrochlorides of desilylated α-aminoamidines, **5** (R^1 = Ph, H; R^2 = Ar, Bn, Pr), in good yield (Table 1).

Similarly, 1,3-di-*p*-tolyl carbodiimide inserts into zirconaaziridine **1c** to give **4c** in ca. 80% yield.[13] Although no products derived from Zr−N insertion have been

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(1) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486−4494. (b) Grossman, R. B.; Davis, W. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 2321−2322. (c) Coles, N.; Harris, M. C. J.; Whitby, R. J.; Blagg, J. *Organometallics* **1994**, *13*, 190−199.

(2) Gately, D. A.; Norton, J. R.; Goodson, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 986. (b) Gately, D. A. Norton, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 3479.

(3) Tunge, J. A.; Gately, D. A.; Norton, J. R. *J. Am. Chem. Soc.* **1999**, *121*, 4520−4521.

(4) Williams, A.; Ibrahim, I. T. *Chem. Rev.* **1981**, *81*, 589. (b) Mikolajczyk, M.; Kielbasinski, P. *Tetrahedron* **1981**, *37*, 233.

(5) For syntheses and pharmaceutical uses of amidines see: (a) Patai, S. *The Chemistry of Amidines and Imidates*; John Wiley and Sons: New York, 1975. (b) Patai, S. *The Chemistry of Amidines and Imidates, Vol 2*.; John Wiley and Sons: New York, 1991.

(6) Umezawa, H.; Takita, T.; Sugiura, Y.; Otsuka, M.; Kobayashi, S.; Ohno, M. *Tetrahedron* **1984**, *40*, 501−509.

(7) Schipper, D.; Gist-Brocades, V.; Delft, N. *J. Antibiot.* **1983**, *36*, 1076−1077. (b) Yamada, T.; Takashima, K.; Miyazawa, T.; Kuwata, S.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 878−883. (c) Yamada, T.; Miyazawa, T.; Kuwata, S.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1827−1830. (d) Yamada, T.; Suegane, K.; Kuwata, S.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1088−1093.

(8) Korshin, E. E.; Soboleva, G. I.; Levin, Y. A.; Zakharova, L. G.; Litvinov, I. A.; (b) Naumov, V. A.; Podval'nyi, E. A.; Efremov, Y. Y. *Zh. Org. Khim.* **1992**, *28*, 1242−1256. (c) Goto, T.; Isobe, M.; Covielle, D. A.; Kishi, Y.; Inoue, S. *Tetrahedron* **1973**, *29*, 2035−2039.

(9) Patents include: (a) G.D. Searle & Co. PCT Int. Appl. WO99/46240, 1999. (b) Merck & Co., Inc. Patent 5,629,322, 1997. (c) G.D. Searle & Co. 9635677, 1996. WO95/11232; Fisons Co., Patent WO95/05363, 1995. (d) G.D. Searle & Co. Patent WO95/11014, 1995.

(10) Sauve, G.; Rao, V. S.; Lajoie, G.; Belleau, B. *Can. J. Chem.* **1985**, *63*, 3089.

(11) Barluenga, J.; Aznar, F.; Liz, R. *J. Chem. Soc., Chem. Comm.* **1981**, 1181. (b) Barluenga, J.; Aznar, F.; Liz, R. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1093. (c) Mengelberg, M. *Chem. Ber.* **1960**, 2230.

(12) For references related to glycine amidines see: (a) Korshin, E. E.; Soboleva, G. I.; Levin, Y. A.; Podval'nyi, E. A.; Efremov, Y. Y. *Zh. Org. Khim.* **1993**, *29*, 577−587. (b) Korshin, E. E.; Eliseenkova, R. M.; Zyablikova, L. G.; Zakharov, L. G.; Akhmadullin, A. G.; Nusinovich, V. D.; Levin, Y. A. *Russ. Chem. Bull.* **1993**, *42*, 1071−1077. (c) Ueda, T.; Okamoto, Y.; Tsuji, T.; Muraoka, M. *Chem. Pharm. Bull.* **1968**, *26*, 2355−2361.

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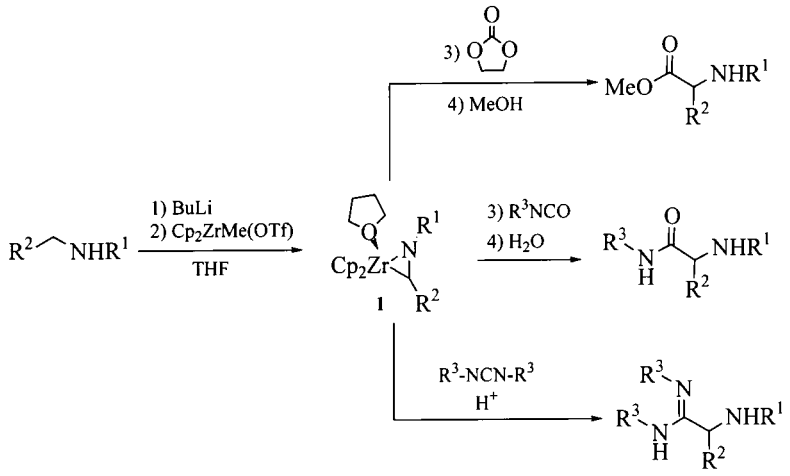
Scheme 1



Scheme 2

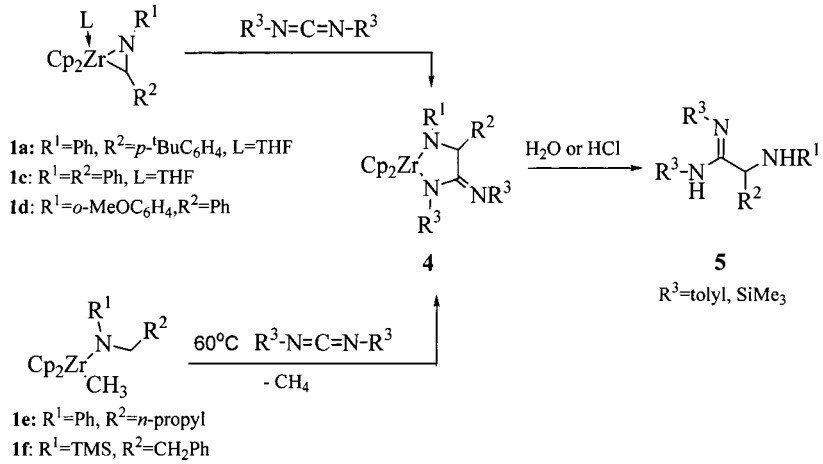


Table 1. Isolated Yields of α-Amino Amidines[a]

α-amino amidine	R^1	R^2	R^3	yield (%)
5a[b]	Ph	*p*-^{t}BuC$_5$H$_4$	H	91
5b	Ph	*p*-^{t}BuC$_5$H$_4$	*p*-tolyl	53
5c	Ph	Ph	*p*-tolyl	35
5d	*o*-anisyl	Ph	*p*-tolyl	59
5e[b,c]	Ph	*n*-Pr	H	74
5f[b,c]	H	CH_2Ph	H	85

[a] Prepared from a 1:1 mix of carbodiimide and zirconaaziridine in C_6H_6 and cleaved with H_2O (**5b**−**d**) or HCl. [b] Isolated as the HCl salts. [c] Zirconaaziridines were generated in situ by the thermolysis of $Cp_2Zr[N(R^1)CH_2(R^2)]Me$.

isolated, competitive Zr−N insertion is the likely reason for lowered yield of **4c**. Such a side reaction was observed with isocyanate insertion and suppressed by the use of *o*-anisyl substituents on nitrogen (e.g., **1d**).[2] Indeed, treatment of **1d** with di-*p*-tolyl carbodiimide gives metallacycle **4d** in >95% yield by ^{1}H NMR. Treatment of the *p*-tolyl-substituted metallacycles **4** with H_2O liberates the amino amidines **5**, which can be purified by chromatography (Table 1). In addition to isolable zirconaaziridines **1a**−**d**, zirconaaziridines generated in situ from $Cp_2ZrMe(OTf)$ and lithium amides (**1e**,**f**) are efficiently trapped by carbodiimides. These results suggest that a wide variety of α-amino amidines should be accessible by our method.

(13) NMR yields were determined by integration vs hexamethylcyclotrisiloxane internal standard.

Mechanism of Carbodiimide Insertion into Zr−C Bonds. Insertion of carbodiimides into main group[14] and early M−C[15] bonds is an important method for the preparation of metal amidinate olefin polymerization catalysts.[14−17] While much is known about the mechanisms of insertion of olefins, acetylenes, and CO into early transition metal−carbon bonds,[18] far less is known about the mechanism of insertion of heterocumulenes.[19] Braunstein has suggested that "precoordination of heterocumulenes [is] necessary" prior to insertion into Zr−C bonds.[20] The proposal of an intermediate complex

(14) Coles, M. P.; Swenson, D. C.; Jordan, R. F.; Young Jr.; V. G. *Organometallics* **1998**, *17*, 4042−4048. (b) Coles, M. P.; Swenson, D. C.; Jordan, R. F. *Organometallics* **1997**, *16*, 5183−5194. (c) Chang, C.; Hsiung, C.; Su, H,; Srinivas, B.; Chiang, M. Y.; Lee, G.; Wang, Y. *Organometallics* **1998**, *17*, 1595−1601.

(15) Jayaratne, K. C.; Sita, L. R. *J. Am. Chem. Soc.* **2000**, *122*, 958−959. (b) Koterwas, L. A.; Fetinger, J. C.; Sita, L. R. *Organometallics* **1999**, *18*, 4183. (c) Sita, L. R.; Babcock, J. R. *Organometallics* **1998**, *17*, 5228−5230.

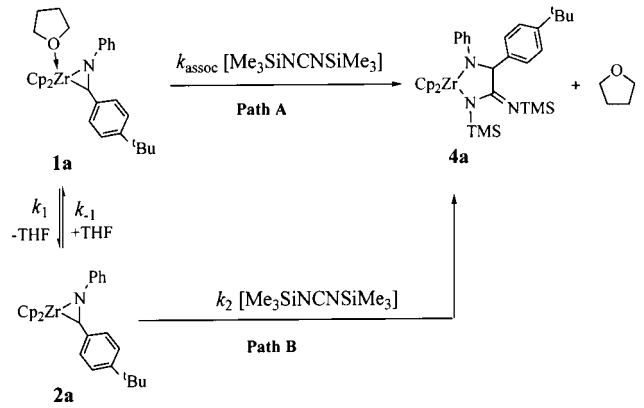
(16) Volkis, V.; Shmulinson, M.; Averbuj, C.; Lisovskii, A,; Edelmann, F. T.; Eisen, M. S. *Organometallics* **1998**, *17*, 3155−3157. (b) Averbuj, C.; Tish, E.; Eisen, M. S. *J. Am. Chem. Soc.* **1998**, *120*, 8640−8646.

(17) Patents include: (a) Jordan, R. F.; Coles, M. P. Patent 5,973,-088, 1999. (b) Jordan, R. F.; Coles, M. P. Patent 5,777,120, 1998. (c) Schlund, R.; Lux, M.; Edelmann, F.; Reissmann, U.; Rhode, W. BASF Patent 5,707,913, 1998. (d) Flores, J. C.; Rausch, M. D. Patent 5,502,-128, 1996.

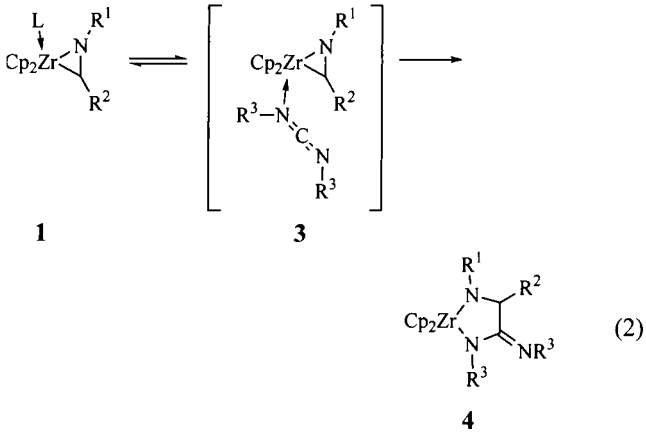
(18) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*, 1st ed.; University Science Books: Mill Valley, CA, 1987.

(19) Gambarotta, S.; Strologo, S.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *Inorg. Chem.* **1985**, *24*, 654.

Scheme 3



3 raises the issue of whether ligand dissociation from **1** is required before such an electrophile can insert into the Zr−C bond of zirconaaziridines (eq 2). To this end we have investigated the mechanism of such insertions by carbodiimides.



(2)

Treatment of an orange toluene solution of **1a** with 1 equiv of bis(trimethylsilyl)carbodiimide (NCN) results in quantitative formation of the dark purple complex **4a**. The obvious mechanisms are A and B. (A) The five-membered metallacycle **4a** may be formed through an associative mechanism in which **1a** reacts directly with carbodiimide (Scheme 3). (B) If heterocumulene coordination is required before insertion, a coordinatively unsaturated intermediate such as **2a** may be necessary (Scheme 3).

In principle, associative (path A) and dissociative (path B) mechanisms can be distinguished by the dependence of the reaction rate on [THF]. The rate of associative insertion should be insensitive to [THF], whereas the kinetics of a dissociative mechanism should exhibit an inverse relation between the rate and [THF].

To determine whether carbodiimide insertion occurs through an associative or dissociative mechanism, the rates of insertion were measured with various THF concentrations at 265 K. The disappearance of **1a**, followed in the presence of >10-fold excess of NCN to ensure pseudo-first-order conditions, gave the apparent rate constants, k_{app}, at individual THF concentrations. Varying [THF] from 0.54 to 1.34 M showed an inverse relationship between k_{app} and [THF]. Within this concentration range plots of $1/k_{app}$ vs [THF] were linear (Figure 1), suggesting that dissociation of THF is required prior to insertion.

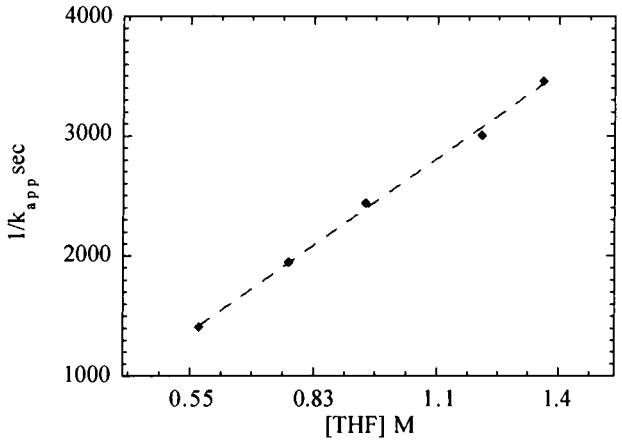


Figure 1. Plot of $1/k_{app}$ vs [THF] for the reaction of 0.035 M **1a** with 0.41 M NCN in solutions containing 0.54−1.34 M [THF] at 265 K.

A dissociative mechanism such as path B in Scheme 3 can be described by two sets of simplifying kinetic assumptions.[21] The rate law in eq 3 is obtained if we assume rapid equilibration of **1a** and **2a** followed by rate-determining insertion of carbodiimide. If we assume instead that **2a** is highly reactive and thus does not accumulate as the reaction progresses, the rate law given is the steady-state one in eq 4. If $k_1, k_{-1}[\mathrm{THF}] \gg k_2$

$$-\frac{\mathrm{d}[\mathbf{1}]}{\mathrm{d}t} = \frac{K_1 k_2 [\mathrm{NCN}]([\mathbf{1}] + [\mathbf{2}])}{[\mathrm{THF}] + K_1} \qquad (3)$$

where $K_1 = k_1/k_{-1}$. If $(k_{-1}[\mathrm{THF}] + k_2[\mathrm{NCN}]) \gg k_1$

$$-\frac{\mathrm{d}[\mathbf{1}]}{\mathrm{d}t} = \frac{k_1 k_2 [\mathrm{NCN}][\mathbf{1}]}{k_{-1}[\mathrm{THF}] + k_2[\mathrm{NCN}]} \qquad (4)$$

The two mechanisms can be distinguished by the dependence of the reaction rates on carbodiimide concentration. Equation 4 predicts that at high [NCN] (k_2[NCN] ≫ k_{-1}[THF]) the rate of insertion will approach saturation (rate constant k_1); however, preequilibrium kinetics (eq 3) should not exhibit this behavior. At the carbodiimide concentrations investigated (0.41−1.4 M) the reaction is first order in [NCN], consistent with either rate law and set of assumptions.

Kinetics and Equilibrium of THF Dissociation from Zirconaaziridine 1a. To determine whether eq 3 or eq 4 is correct, we studied the kinetics and equilibrium of THF dissociation from **1a**. Previously we had studied the kinetics of THF dissociation from **1c**.[2a] Using a similar procedure, ^{1}H NMR spectra of **1a** were collected in a 1.0 M THF solution. These spectra show separate resonances for free and coordinated THF below 273 K; at 230 K the THF resonances are no longer broadened by exchange. No evidence for **2a** is observed

(20) Braunstein, P.; Nobel, D. *Chem. Rev.* **1989**, *89*, 1927.

(21) Espenson, J. H *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: New York, 1995; pp 77−90.

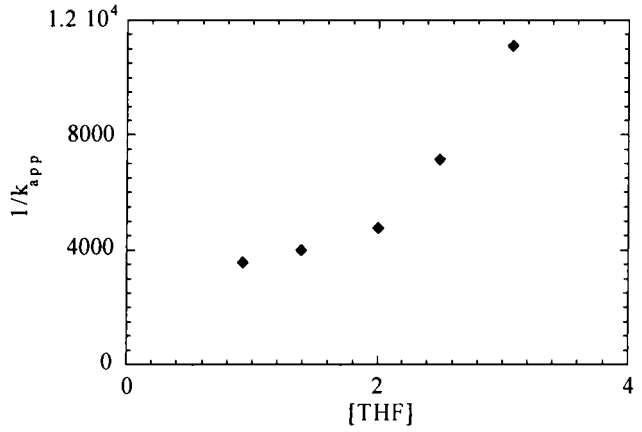


Figure 2. Plot of $1/k_{app}$ vs [THF] for the reaction of 0.037 M **1a** with 0.41 M NCN in solutions containing 0.79−3.08 M [THF] at 265 K.

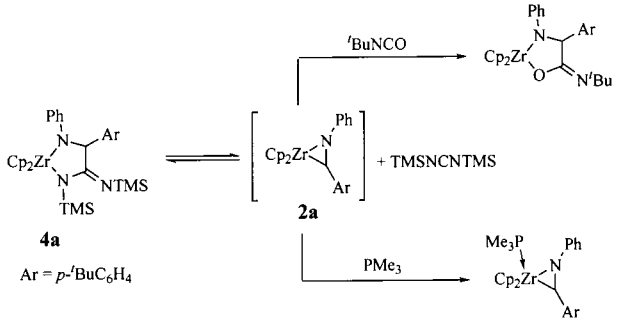
in these spectra or in others collected at low temperature in the absence of added THF. Thus the equilibrium between THF-coordinated zirconaaziridine **1a** and ligand-free zirconaaziridine **2a** favors the former. Line-broadening data for the two separate α-proton resonances of the coordinated THF ligand were collected over a 250−270 K temperature range.[22] Eyring analysis gives $\Delta H^{\ddagger} = 16.1(6)$ kcal/mol and $\Delta S^{\ddagger} = 11(2)$ eu, suggesting that THF exchange occurs through a dissociative mechanism. Confirming this hypothesis, the line broadening was found to be independent of [THF$_{free}$]. Therefore, the line broadening is a direct measure of the rate of THF dissociation, k_1; for **1a**, k_1 at 265 K is 79 s^{-1}. Since the equilibrium between **1a** and **2a** lies far to the left (k_{-1}[THF] ≫ k_1), and k_1 is >4 orders of magnitude larger than the apparent rates of carbodiimide insertion, **1a** must be rapidly equilibrating with small concentrations of **2a** on the time scale of insertion, so k_1,k_{-1}[THF] ≫ k_2[NCN] and eqs 3 and 4 are indistinguishable.

Reversibility of Carbodiimide Insertion. At THF concentrations over 2 M significant, reproducible, curvature is observed in the $1/k_{app}$ vs [THF] plots (Figure 2). This prompted investigation of the effect of high [THF] on the reaction kinetics. When complex **1a** was treated with bis(trimethylsilyl)carbodiimide in 12 M THF-d_8, the reaction went to only 15% of completion, suggesting that carbodiimide insertion is reversible. Confirming this hypothesis, treatment of toluene solutions of pure **4a** with PMe_3 or *tert*-BuNCO resulted in carbodiimide extrusion and formation of new zirconium products expected from **2a** (Scheme 4).[2]

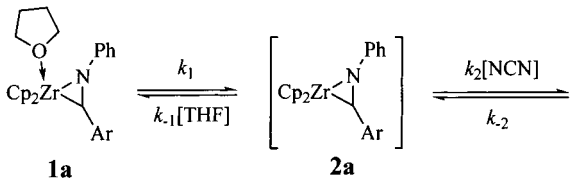
To investigate the thermodynamics of carbodiimide insertion, a solution prepared from 0.04 M **1a** and 0.06 M NCN in 11 M THF was allowed to equilibrate at 273 K overnight and the ^{1}H NMR spectrum recorded. Integration of the solution species relative to an internal standard gave $K_{eq} = 150$ at 273 K. Monitoring the equilibrium between **1a** + NCN and **4a** + THF (eq 5) as a function of temperature resulted in a linear van't Hoff plot, giving $\Delta H° = -4.3(2)$ kcal/mol and $\Delta S° = -5.8(5)$ eu. Importantly, these data show that

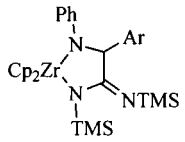
(22) Sandstrom, J. *Dynamic NMR Spectroscopy*; Academic Press: New York, 1982.

Scheme 4



lower temperatures favor insertion of carbodiimide to give **4a**.





4a (5)

$$\text{Ar} = p\text{-}^t\text{BuC}_6\text{H}_4 \qquad K_1 = \frac{k_1}{k_{-1}} \qquad K_2 = \frac{k_2}{k_{-2}} \qquad K_{eq} = K_1K_2 = \frac{[\mathbf{4a}][\text{THF}]}{[\mathbf{1a}][\text{NCN}]}$$

The thermodynamics of carbodiimide insertion reveal that while the reaction goes to >98% completion during the well-behaved kinetics obtained at low [THF] (Figure 1), reversibility of carbodiimide insertion becomes significant at higher THF concentrations. For example, at 3.0 M THF, under the conditions used to generate the curve in Figure 2 ($K_{eq} = 150$), the insertion proceeds to only 95% completion. The curvature originally observed at high [THF] resulted from treating the high [THF] kinetics as irreversible rather than as an approach to equilibrium. The equilibrium kinetic situation is pictured in eq 5, and the rate law for approach to equilibrium is given in eq 6. Fitting the data in Figure 2 as an approach to equilibrium using a floating endpoint exponential[21] results in the corrected curve shown in Figure 3. The improved linear fit of the corrected data indicates that carbodiimide extrusion, k_{-2}, is significant at high [THF].

$$-\frac{\mathrm{d}[\Delta\mathbf{1}]}{\mathrm{d}t} = \frac{k_1k_2[\text{NCN}] + k_{-1}k_{-2}[\text{THF}]}{k_{-1}[\text{THF}] + k_2[\text{NCN}]}[\Delta\mathbf{1}] \quad (6)$$

Analysis of Carbodiimide Insertion Data. The investigation of THF dissociation has already shown that $k_{-1} \gg k_2$, so eq 6 can be simplified to give the k_{obs} in eq 7. From eq 7 it is apparent that plots of k_{obs} vs 1/[THF] should be linear with a slope of K_1k_2[NCN] ($K_1 = k_1/k_{-1}$) and an intercept of k_{-2}. These plots are indeed linear and give $K_1k_2 = 1.00(2) \times 10^{-3}$ s^{-1} at 265 K and $K_1k_2 = 2.03(5) \times 10^{-3}$ s^{-1} at 273 K. Using the observed K_1k_2 and the value of k_1, we can determine that $k_{-1}/k_2 = 7.9 \times 10^4$ at 265 K and 7.6×10^4 at 273 K, so intermediate **2a** is trapped much more rapidly by THF

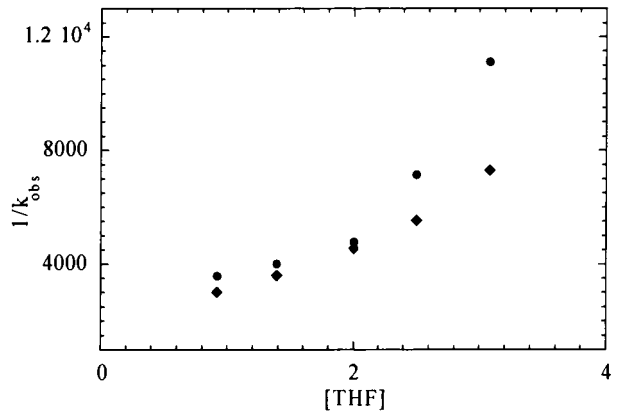


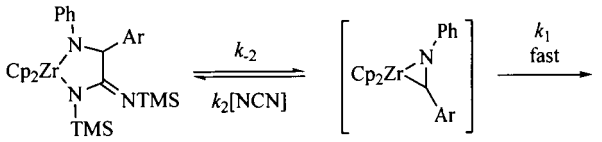
Figure 3. (●) Data in Figure 2 ($r^2 = 0.86$). (◆) Corrected data obtained by exponential fits of kinetic traces using floating infinity point ($r^2 = 0.98$).[21]

than by carbodiimide. The values of k_{-2} cannot be determined directly from the intercepts (which are too close to zero to be determined with precision), but dividing K_1k_2 by K_{eq} gives k_{-2} as 5.3×10^{-6} s^{-1} at 265 K and 1.4×10^{-5} s^{-1} at 273 K.

$$-\frac{d[\Delta\mathbf{1}]}{dt} = \frac{k_1k_2[NCN] + k_{-1}k_{-2}[THF]}{k_{-1}[THF]}[\Delta\mathbf{1}]$$

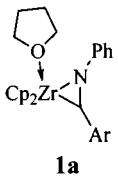
$$k_{obs} = \frac{k_1k_2[NCN]}{k_{-1}[THF]} + k_{-2} \quad (7)$$

Kinetics of Carbodiimide Extrusion from Complex 4a. Treatment of **4a** with 11 M THF in the absence of free NCN (k_2[NCN] ≪ k_{-2}) results in complete conversion to **1a** (eq 8). The disappearance of the 509 nm visible absorbance of complex **4a** shows good first-order behavior. At 298 K the rate of carbodiimide extrusion to form **1a** is 3.1×10^{-4} s^{-1} at 11 M THF and 3.3×10^{-4} s^{-1} at 6.7 M THF. This result suggests that the reaction is zero order in [THF], so k_{-2} is rate limiting and the observed rate of disappearance of **4a** is equal to k_{-2}. The temperature dependence of k_{-2} shows good Eyring behavior, giving $\Delta H^{\ddagger} = 20.0(3)$ kcal/mol and $\Delta S^{\ddagger} = -7(1)$ eu.[23] Extrapolation of these data to 265 K gives $k_{-2} = 5.6(4) \times 10^{-6}$ s^{-1}, in good agreement with that calculated above from the kinetics of carbodiimide insertion.



Ar= *p*-^{t}BuC$_6$H$_4$

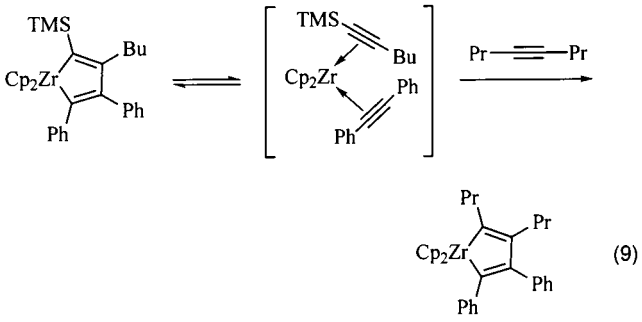
4a **2a**



(8)

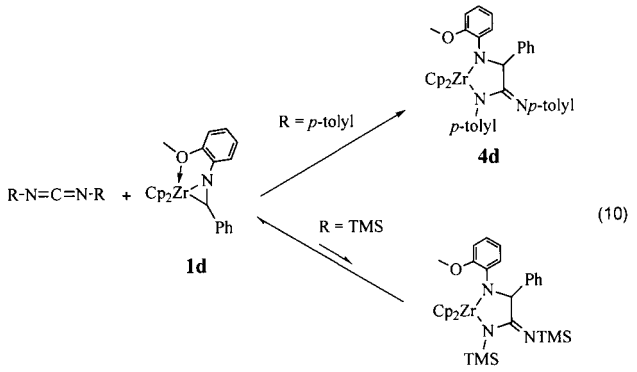
1a

The process of carbodiimide extrusion is formally the activation of the β-C−C bond of **4a**. Cleavage of the equivalent bond in five-membered zirconacarbocycles is well known[24] and has been exploited synthetically by Takahashi.[25] The activation energies of alkyne extrusion are highly dependent on the size of the alkyne substituents; trimethylsilylacetylenes are easily substituted by various unsaturated compounds (eq 9).



(9)

To test whether TMS substituents promote carbodiimide loss from **4**, we have compared the equilibria for bis(trimethylsilyl)carbodiimide and di-*p*-tolyl carbodiimide insertions into zirconaaziridine **1d**. While di-*p*-tolyl carbodiimide inserts quantitatively, the insertion of bis(trimethylsilyl)carbodiimide is less than 5% at equilibrium (eq 10), indicating the steric effect noted by Takahashi may apply to carbodiimide insertion also.



(10)

Conclusions. We have investigated the formation of amino amidines from zirconaaziridines and carbodiimides. A variety of α-amino amidines can be produced by simply varying the reactant amine and the carbodiimide. The rate of insertion of carbodiimides into the Zr−C bonds of zirconaaziridines is inversely proportional to [THF], so the insertion of carbodiimides occurs after dissociation of THF from **1**. At high [THF] the reversibility of bis(trimethylsilyl))carbodiimide insertion becomes apparent, but the insertion of di-*p*-tolyl carbodiimide appears unaffected. The thermolysis of the amino amidine metallacyle **4a** can be used to generate the ligand-free zirconaaziridine **2a**, which can react with other electrophiles. Braunstein's suggestion[20] that co-

(23) For an elementary step in which **4a** forms **2a** and free carbodiimide, the entropy of activation would be expected to be positive. The observed negative entropy of activation suggests that a coordination complex such as **3** (eq 2) may be the direct product of k_{-2}, although dissociative reactions can have negative entropies of activation.

(24) McDade, C.; Bercaw, J. E. *J. Organomet. Chem.* **1985**, *279*, 281−315. (b) Erker, G.; Dorf, U.; Rheingold, A. L. *Organometallics* **1988**, *7*, 138−143. (c) Grubbs, R. H.; Miyashita, A. *J. Am. Chem. Soc.* **1978**, *100*, 1300−1303.

(25) Takahashi, T.; Xi, C.; Xi, Z.; Kageyama, M.; Fischer, R.; Nakajima, K.; Negishi, E. *J. Org. Chem.* **1998**, *63*, 6802−6806. (b) Takahashi, T.; Kotora, M.; Hara, R.; Xi, Z. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2591−2603, and references therein.

ordination of heterocumulenes is a prerequisite for insertion is supported by the fact that THF must dissociate before carbodiimide insertion.

Experimental Section

Materials. All air-sensitive compounds were prepared and handled under a N_2 atmosphere using standard Schlenk and inert-atmosphere box techniques. Hexanes, benzene, THF, and toluene were distilled under nitrogen from sodium benzophenone ketyl. Cp_2ZrCl_2, generously donated by Boulder Scientific, was converted to $Cp_2ZrMe(OTf)$ as previously described.[1,2] $Cp_2Zr[\eta^2$-N(Ph)CHPh]·THF,[2] $Cp_2Zr[\eta^2$-N(*o*-anisyl)CHPh],[2] and $Cp_2Zr(TMSNCH_2CH_2Ph)CH_3$[3] were prepared as previously described. ^{1}H NMR were recorded at 300 MHz, and ^{13}C NMR were recorded at 75 MHz unless otherwise noted. NMR solution concentrations were determined from integration vs a hexamethylcyclotrisiloxane standard. All kinetics were monitored for $>3t_{1/2}$, and temperatures were measured using a MeOH standard.[26] Chromatography was done on a Chromatotron (Harrison Research Inc.) with silica gel (Merck, TLC grade 7749) as the adsorbent.

***N*-Phenyl-4-*tert*-butylbenzylamine.** Aniline (1.1 mL, 12 mmol) and ca. 1 g $MgSO_4$ were added to a C_6H_6 (30 mL) solution of 4-*tert*-butylbenzaldehyde (2 mL, 12 mmol). After stirring for 3 h the mixture was filtered. EtOH (5 mL) was added to the filtrate, which was then treated with $NaBH_4$ (1 g, 26 mmol). The mixture was stirred for 30 min, at which point 1 M HCl was added *slowly* until there was no visible reaction. The mixture was made basic with $NaHCO_3$, and the aqueous layer extracted 2 × 5 mL C_6H_6. The combined organic layers were dried ($MgSO_4$) and removed, leaving a white solid. Yield: 2.44 g, 85%. ^{1}H NMR ($CDCl_3$): δ 7.26 (d, 2H), 7.21 (d, 2H), 7.08 (t, 2H), 6.62 (t, 1H), 6.54 (d, 1H), 4.18 (s, 2H), 3.95 (br s, 1H), 1.22 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 150.2, 148.2, 136.3, 129.2, 127.4, 125.5, 117.5, 112.8, 48.0, 34.5, 31.4. HRMS for ($C_{17}H_{22}N$) [M + H] calcd 240.1752, found 240.1740.

$Cp_2Zr(\eta^2$-PhNC(H)$C_6H_4C(CH_3)_3$)THF (1a). An Et_2O (10 mL) solution of *N*-phenyl-4-*tert*-butylbenzylamine (940 mg, 3.9 mmol) was cooled to −10 °C and treated with BuLi (2.45 mL, 3.9 mmol). After this solution was stirred for 10 min, it was added to a THF (20 mL) solution of $Cp_2ZrMe(OTf)$ (1.50 g, 3.9 mmol) at −60 °C. The solution, which immediately turned bright yellow, was stirred at this temperature for 30 min, warmed slowly to room temperature, and stirred for 4 h to produce an orange solution. The solvent was removed in vacuo, leaving an orange solid, which was treated with C_6H_6 (25 mL). The solution was filtered to remove the LiOTf, which was washed with an additional 10 mL of C_6H_6. The solvent was removed to leave an orange solid, which was dried under vacuum. Yield: 1.71 g (82%), 95% pure by ^{1}H NMR. The solid was recrystallized from a solution of 6 mL of THF and 35 mL of hexanes, which gave 1.06 g (62% recovery). ^{1}H NMR (C_6D_6): δ 7.53 (d, 2H), 7.26 (t, 3H), 6.83 (m, 3H), 5.60 (s, 5H), 5.47 (s, 5H), 3.77 (br s, 1H), 3.35 (br s, 4H), 1.41 (s, 9H), 1.22 (br s, 4H). ^{13}C NMR (C_6D_6): δ 129.3, 125.4, 118.9, 116.6, 109.5, 107.8, br s 73, 34.5, 32.1, 25.7. The α-THF protons and the zirconaaziridine methine are broadened considerably by exchange. Anal. Calcd for ($C_{31}H_{37}NOZr$): C, 70.14; H, 7.03; N, 2.64. Found: C, 67.36; H, 6.79; N, 2.54 (not reanalyzed in view of the straightforward relationship to known zirconaaziridines).[1−3]

$Cp_2Zr(PhNCH_2CH_2CH_2CH_3)CH_3$ (1e). To a solution of *N*-phenyl butylamine (2.6 mmol) in 7 mL of Et_2O at 0 °C was added 1.6 mL of 1.6 M BuLi/hexane solution. This was stirred for 10 min, then added to a solution of 1.03 g of $Cp_2ZrMeOTf$ (2.6 mmol) in 25 mL of THF at −50 °C. After stirring for 1 h, the solution was warmed to room temperature and the solvent removed. A 15 mL sample of hexanes was added and the solid filtered. The lithium triflate was further washed with 2 × 5 mL of hexanes. Removal of the hexanes produced an orange solid, which was dried under vacuum. Yield: 910 mg (91%). ^{1}H NMR (C_6D_6): δ 7.21 (t, 1H), 6.92 (t, 2H), 6.67 (d, 2H), 5.67 (s, 10H), 3.10 (m, 2H), 1.32 (m, 2H) 1.16 (s, 2H), 0.81 (t, J = 7.2 Hz, 3H) 0.29 (s, 3H). ^{13}C NMR (C_6D_6): δ 158.3, 128.6, 123.4, 120.6, 110.3, 51.8, 32.2, 23.5, 20.9, 14.3. Anal. Calcd ($C_{21}H_{27}NZr$): C, 65.57; H, 7.07; N, 3.64. Found: C, 65.23; H, 6.82; N, 3.13.

$Cp_2Zr(TMSNCH_2CH_2Ph)CH_3$ (1f). To a solution of 0.33 mL (2.6 mmol) of phenethylamine in 10 mL of Et_2O at 0 °C was added 1.6 mL of 1.6 M BuLi/hexane solution. After 10 min this was followed by 0.33 mL of TMSCl. This mixture was stirred for 10 min before addition of 1.6 mL of 1.6 M BuLi. The resulting mixture was stirred 10 min, then added to a solution of 1.0 g of $Cp_2ZrMeOTf$ (2.6 mmol) in 25 mL of THF at −50 °C. After stirring for 1 h, the solution was warmed to room temperature, and the solvent removed. A 15 mL portion of hexanes was added and the solid filtered. The solid was further washed with 2 × 5 mL of hexanes. Removal of the hexanes produced a white solid, which was dried under vacuum. Yield: 860 mg (78%). ^{1}H NMR (C_6D_6): δ 7.21 (m, 5H), 5.75 (s, 10H), 2.75 (m, 2H), 2.41 (m, 2H), 0.35 (s, 3H), 0.19 (s, 9H). ^{13}C NMR (C_6D_6): δ 139.8, 129.1, 128.3, 126.3, 110.9, 46.1, 42.7, 24.9, 3.5.

Preparation of $Cp_2Zr[N(TMS)C(N\text{-}TMS)CH(4\text{-}^tBuC_6H_4)N(C_6H_5)]$ (4a) in Situ. A C_6D_6 (0.7 mL) solution of zirconaaziridine **1a** (30 mg, 56 μmol) was treated with bis(trimethylsilyl)carbodiimide (15 μL, 67 μmol), and the solution changed from orange to dark purple. Yield: >95% yield by ^{1}H NMR. ^{1}H NMR (C_6D_6): δ 7.45 (d, 2H), 7.21 (m, 4H), 6.90 (t, 1H), 6.59 (d, 2H), 6.00 (s, 1H), 5.89 (s, 5H), 5.84 (s, 5H), 1.16 (s, 9H), 0.45 (s, 9H), 0.28 (s, 9H). ^{13}C (C_6D_6): δ 171.1, 157.4, 150.1, 140.2, 129.4, 125.0, 120.9, 120.5, 114.3, 80.2, 34.4, 31.4, 3.2, 2.3. HRMS for ($C_{34}H_{48}N_3Si_2Zr$): [M + H] calcd 644.2434, found 644.2451.

Preparation of $Cp_2Zr[N(TMS)C(N\text{-}TMS)CH(CH_2Ph)N(TMS)]$ (4f) in Situ. A C_7D_8 (0.7 mL) solution of $Cp_2Zr(Me)N(TMS)CH_2CH_2Ph$[3] (30 mg, 70 μmol) was treated with bis(trimethylsilyl)carbodiimide (18 μL, 86 μmol) and heated at 60 °C for 75 min, resulting in a bright orange solution. Yield: >95% yield by ^{1}H NMR. ^{1}H NMR (C_6D_6): δ 7.27 (d, 2H), 7.19 (t, 2H), 7.07 (m, 1H), 6.14 (s, 5H), 6.08 (s, 5H), 3.97 (dd, J = 10.1, 2.1 Hz, 1H), 3.37 (dd, J = 12.8, 10.3 Hz, 1H), 2.94 (dd, J = 12.8, 2.1 Hz, 1H), 0.34 (s, 9H), 0.11 (s, 9H), −0.08 (s, 9H). ^{13}C (C_7D_8): δ 168.9, 140.0, 130.6, 128.4, 126.5, 115.0, 114.7, 79.5, 47.3, 3.5, 2.9, 2.1.

Preparation of $Cp_2Zr[N(TMS)C(N\text{-}TMS)CH(n\text{-}propyl)N(Ph)]$ (4e) in Situ. A C_7D_8 (0.7 mL) solution of $Cp_2Zr(Me)N(Ph)CH_2CH_2CH_2CH_3$[3] (30 mg, 78 μmol) was treated with bis(trimethylsilyl)carbodiimide (18 μL, 86 μmmol) and heated at 60 °C for 75 min, resulting in a dark purple solution. Yield: >95% yield by ^{1}H NMR. ^{1}H NMR (C_7D_8): δ 7.11 (m, 2H), 6.77 (m, 1H), 6.33 (m, 2H), 6.13 (s, 5H), 5.86 (s, 5H), 4.61 (dd, J = 9.5, 4.0 Hz, 1H), 2.10 (m, 1H), 1.87 (m, 1H), 1.39 (m, 1H), 1.22 (m, 1H), 0.81 (dd, J = 9.7, 7.3 Hz, 3H), 0.37 (s, 9H), 0.30 (s, 9H). ^{13}C (C_7D_8): δ 173.6, 156.6, 129.04, 119.6, 119.2, 114.6, 114.4, 78.0, 39.3, 20.8, 14.7, 3.3, 2.7.

α-Amino Amidines 5. Amino amidines **5a**−**c** were prone to decomposition; over the period of months gummy yellow solids were formed. The product of decomposition is not yet known. Remaining amino amidines in these mixtures could be recovered by titurating in hexane.

$H_2NC(NH)CH(4\text{-}^tBuC_6H_4)NH(C_6H_5)$·HCl (5a). A toluene (5 mL) solution of **1a** (250 mg, 0.47 mmol) was treated with 1,3-bis(trimethylsilyl)carbodiimide (95 μL, 0.52 mmol). After 15 min, 1 M HCl/Et_2O (4 mL) was added and immediately filtered. The precipitate was washed with Et_2O (4 mL). Yield: 135 mg (91%). IR (Nujol): ν(NH) 3500−2500, ν(C=N) 1684, ν(C=C) 1601 cm^{-1}. ^{1}H NMR (D_2O): δ 7.45 (d, 2H), 7.32 (d, 2H), 7.14 (t, 2H), 5.11 (s, 1H), 1.17 (s, 9H) ^{13}C NMR (D_2O): δ 153.8, 146.2, 132.8, 130.0, 127.7, 126.9, 119.9, 118.8, 113.8,

(26) Van Geet, A. L. *Anal. Chem.* **1970**, *42*, 679−680.

59.9, 34.4, 30.7. HRMS for ($C_{18}H_{24}N_3$): calcd 282.1970, found 282.1975.

4-Me-C_6H_4(H)NC(N-4-Me-C_6H_4)CH(4-^{t}Bu-C_6H_4)NH-(C_6H_5) (5b). A toluene (5 mL) solution of **1a** (150 mg, 0.28 mmol) was treated with 1,3-di-*p*-tolylcarbodiimide (63 mg, 0.28 mmol). After 30 min, 0.5 mL of H_2O was added, stirred 15 min, and dried over $MgSO_4$. The mixture was filtered and the solvent removed. The residue was taken up in CH_2Cl_2 and spotted on a chromatotron plate. Eluting with 5:1 pentane/EtOAc gave a white solid. Yield: 68.3 mg (53%). IR (Nujol): ν(NH) 3328, 3241, ν(C═N) 1633, ν(C═C) 1605 cm^{-1}. ^{1}H NMR ($(CD_3)_2SO$): δ. 8.40 (s, 1H), 7.62 (br d, 2H), 7.42 (d, 2H), 7.32 (d, 2H), 7.12 (t, 2H), 7.03 (t, 4H), 6.67−6.54 (m, 5H), 6.13 (d, J = 8.0 Hz, 1H), 5.20 (d, J = 8.0 Hz), 2.23 (s, 3H), 2.22 (s, 3H). ^{13}C NMR ($(CD_3)_2SO$): δ 154.9, 151.2, 147.8, 147.7, 139.0, 137.3, 131.5, 131.4, 130.1, 129.8, 129.6, 128.2, 126.2, 121.5, 120.0, 118.5, 114.0, 57.1, 35.1, 32.0, 21.2. HRMS for ($C_{32}H_{36}N_3$): [M + H] calcd 462.2909, found 462.2890.

Alternative Preparation of 5b Directly from Amine. A toluene (5 mL) solution of *N*-phenyl-4-*tert*-butylbenzylamine (310 mg, 1.3 mmol) was cooled to −10 °C and treated with BuLi (0.82 mL, 1.3 mmol). After this solution was stirred for 10 min, it was added to a toluene (10 mL) solution of Cp_2ZrMe-(OTf) (500 mg, 1.3 mmol) at −60 °C and stirred 20 min; di-*p*-tolylcarbodiimide (300 mg, 1.3 mmol) was added and the resulting solution warmed to room temperature. After 2 h, 1 mL of H_2O was added and the solution stirred 1/2 h and dried over $MgSO_4$. The mixture was filtered, and the solvent removed under vacuum, leaving a white solid, which was washed with 3 mL of Et_2O. Yield: 216 mg (36%).

4-Me-C_6H_4(H)NC(N-4-Me-C_6H_4)CH(C_6H_5)NH(C_6H_5) (5c). A C_6H_6 (5 mL) solution of $Cp_2Zr[\eta^2$-N(Ph)CHPh]·THF (250 mg, 0.53 mmol) was treated with 1,3-di-*p*-tolylcarbodiimide (118 mg, 0.53 mmol). After 30 min, 1 mL of H_2O was added and the solution stirred 1/2 h and dried over $MgSO_4$. The mixture was filtered and the solvent removed. The residue was taken up in CH_2Cl_2 and placed on a chromatotron plate. Eluting with 20:1 hexane/EtOAc gave a white solid. Yield: 74 mg (35%). IR (Nujol): ν(NH) 3347, ν(C═N) 1638, ν(C═C) 1601 cm^{-1}. ^{1}H NMR ($(CD_3)_2CO$): δ 8.31 (br s, 1H), 7.70 (br s, 2H), 7.32 (s, 5H), 7.17 (t, 2H), 7.05−6.95 (br m, 4H), 6.79 (d, 2H), 6.71 (t, 1H) 6.52 (br d, 2H) 5.36 (br s, 1H), 5.22 (d, 1H, J = 4.02 Hz), 2.23 (s, 6H). ^{13}C NMR ($(CD_3)_2CO$): δ 154.4, 147.8, 140.0, 131.6, 131.5, 129.5, 129.2, 129.0, 128.5, 121.6, 119.8, 119.0, 118.8, 113.9, 59.2, 20.3. HRMS for ($C_{28}H_{28}N_3$): [M + H] calcd 406.2283, found 406.2281.

4-Me-C_6H_4(H)NC(N-4-Me-C_6H_4)CH(C_6H_5)NH(2-MeO−C_6H_4) (5d). A C_6H_6 (5 mL) solution of $Cp_2Zr[\eta^2$-N(*o*-anisyl)-CHPh] (324 mg, 0.75 mmol) was treated with di-*p*-tolylcarbodiimide (167 mg, 0.75 mmol). After 30 min, 1 mL of H_2O was added, stirred 1/2 h, and dried over $MgSO_4$. The mixture was filtered and the solvent removed. The residue was taken up in CH_2Cl_2 and spotted on chromatotron. Eluting with 30:1 hexane/EtOAc gave a white solid. Yield: 192 mg (59%). ^{1}H NMR ($CDCl_3$): δ 8.29 (s, 1H), 7.75 (d, 2H), 7.15 (m, 3H), 6.95 (m, 5H), 6.87 (m, 3H), 6.73 (m, 3H), 6.48 (d, 1H), 5.33 (s, 1H), 4.68 (s, 1H), 3.73 (s, 3H), 2.11 (s, 3H), 2.05 (s, 3H). ^{13}C ($CDCl_3$): δ 154.15, 147.42, 147.19, 140.03, 137.72, 137.20, 132.35, 131.32, 129.60, 129.45, 129.21, 128.70, 128.45, 121.94, 121.80, 119.96, 119.55, 112.31, 109.81, 60.32, 56.67, 21.12. Anal. Calcd for ($C_{29}H_{29}N_3O$): C, 79.97; H, 6.71; N, 9.65. Found: C, 79.83; H, 6.67; N, 10.00.

H_2NC(NH)CH(*n*-propyl)NH(C_6H_5)·HCl (5e). A toluene (5 mL) solution of *N*-butyl aniline (320 μL, 2.0 mmol) at −10 °C was treated with BuLi (2 mL, 2.0 mmol). This was stirred 5 min, then added to a toluene (5 mL) solution of $Cp_2ZrMeOTf$ (770 mg, 2.0 mmol) at −60 °C. The resulting orange mixture was stirred at −10 °C for 30 min. Bis(trimethylsilyl)carbodiimide (420μL, 2.0 mmol) was then added and the solution heated to 60 °C for 75 min, turning dark purple. This mixture was filtered, then added to 10 mL of 1 M HCl/Et_2O. The resulting precipitate was immediately collected and washed with 5 × 1 mL of CH_3CN. The remaining white solid was dried under vacuum. Yield: 337 mg, 74%. IR (Nujol): ν(NH) 3800−2200, ν(C═N) 1691. ^{1}H NMR (D_2O): δ 7.17 (t, 2H), 6.75 (t, 1H), 6.57 (d, 2H) 4.04 (t, 1H), 1.78 (q, 2H), 1.39 (sp, 2H) 0.82 (t, 3H). ^{13}C NMR (D_2O): δ 173.07, 146.38, 130.05, 119.46, 113.42, 55.60, 35.72, 18.85, 13.07. HRMS for ($C_{11}H_{18}N_3$): calcd 192.1501, found 192.1494.

H_2NC(NH)CH(CH_2Ph)NH_2·HCl (5f). A toluene (4 mL) solution of $Cp_2Zr(Me)[N(TMS)CH_2CH_2Ph]$[3] (325 mg, 0.76 mmol) at −10 °C was treated with bis(trimethylsilyl)carbodiimide (162 mg, 0.87 mmol) and heated to 60 °C for 100 min, turning orange. It was filtered, then added to 10 mL of 1 M HCl/Et_2O. The resulting precipitate was immediately collected and washed with 5 × 1 mL of CH_3CN. The remaining solid was recrystallized from ethanol, giving white needles. Yield: 129 mg (85%). IR (Nujol): ν(NH) 3534, 3500−2443, ν(C═N) 1697 cm^{-1}. ^{1}H NMR (D_2O): δ 7.39−7.18 (m, 5H), 4.35 (dd, J = 8.8, 6.9 Hz, 1H), 3.28 (dd, J = 14.0, 6.9, 1H), 3.15 (dd, J = 13.9, 8.9, 1H). ^{13}C NMR (D_2O): δ 165.5, 132.7, 129.7, 128.8, 53.5, 37.0. HRMS for ($C_9H_{14}N_3$): calcd 164.1188, found 164.1183.

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Supporting Information Available: Kinetic data, plots of these data, kinetic derivations, and selected NMR spectra are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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