An improved method for the synthesis of zirconium (CCC-*N*-heterocyclic carbene) pincer complexes and applications in hydroamination†

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Upon heating $Zr(NMe_2)_4$, 1,3-bis(*N*-butyl-imidazolium)benzene diiodide and toluene analytically pure Zr pincer complex was obtained, which was found to be an intramolecular hydroamination catalyst.

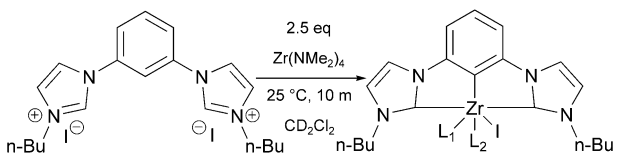
Recently, stable carbenes have been isolated and characterized,[1,2] and *N*-heterocyclic carbene (NHC) ligands have become ubiquitous in the field of catalysis.[3] Singlet carbenes are stronger σ-donors and dissociate less readily than phosphines thus generating more robust catalysts.[4] This explosion of reports has led to interest in non-NHC carbenes and their use as ligands also.[5] Pincer ligand complexes are a large and important class of organometallic complexes.[6] Currently several groups have been developing NHC variants of the pincer complexes. Pyridylene,[7] xylylene,[8] and 2,6-lutidinyl[9] bridged bis-NHC ligands have been developed by others. We have been developing the phenylene bridged versions (CCC-NHC ligands) of these complexes (Scheme 1).[10] NHC pincer complexes have shown catalytic activity toward various transformations such as the polymerization of alkenes,[11] transfer hydrogenation,[12] and the Heck,[13] Suzuki,[13] and Sonogashira[13] cross coupling reactions. We have recently reported the catalytic hydroamination/cyclization of unactivated secondary aminoalkenes with late transition metal CCC-NHC pincer complexes.[14,15] Recently several groups have demonstrated that neutral and cationic early transition metal amido complexes are catalytically active.[16,17]

Our previous methodology (Scheme 1) exploited the basicity and electrophilicity of $Zr(NMe_2)_4$ to activate the three C–H bonds of ligand precursor **1** for coordination to the Zr metal.[10b] Although this method rapidly produced the desired complex, it employed an excess of $Zr(NMe_2)_4$, produced a mixture of coordination spheres at Zr (**2a** and **2b**) and did not lead to ready separation of the Zr pincer product from the excess reagent.

The use of a stoichiometric amount of the Zr reagent was highly desired. Subliming $Zr(NMe_2)_4$ prior to use, employing higher boiling solvents and longer reaction times provided the desired complex in high yield and purity. Combining the bis(imidazolium) salt **1**, $Zr(NMe_2)_4$ (1.1 eq), toluene and heating in a sealed vessel produced a homogeneous reaction mixture (Scheme 2). Metallation was found to proceed efficiently and quantitatively as observed by ^1H NMR spectroscopy. Metallation was incomplete at 150 min, but longer reaction times were found to be satisfactory. Upon scaling up the reaction an additional advantage was found. At the completion of the reaction the desired complex **3** precipitated upon cooling in analytically pure form (1.8 g, 67%) as shiny yellow crystals. The only by-product of reaction was the volatile and soluble Me_2HN. The slight excess of $Zr(NMe_2)_4$ remained in solution.

^1H and ^{13}C NMR spectroscopic analysis of the precipitated yellow crystals confirmed that pure CCC-NHC pincer **3** was synthesized.‡ X-Ray quality crystals of **3** were selected from the precipitate. An ORTEP® view of complex **3** is presented in Fig. 1. In the solid state zirconium adopts a distorted octahedral geometry. The Zr–C(carbene) distances, 2.367(3) and 2.362(3) Å, are similar to previous reports of pincer NHC complexes of Zr,[10b,18] and shorter than non-chelated NHC–Zr distances (2.43–2.46 Å).[19] The Zr–C12(aryl) distance is 2.310(3) Å, slightly shorter than the complex **2b**, which contained an equatorial amido group. The axial Zr–I1 distance, which is *trans* to NMe_2, is 3.0038(4) Å, demonstrating a stronger *trans* influence for the amido group compared to the aryl group,[20] since the equatorial Zr–iodide distance, *trans* to Ar, is 2.8431(4) Å. The Zr–N (amido) distance is 1.986(3) Å. The crystal shows evidence of a slight axial/equatorial disorder that was modeled at a 94 : 6 occupancy. Additional data are listed Fig. 1 and the supporting information.†

The CCC-NHC zirconium pincer complex **3** was assayed for hydroamination activity against 2,2-diphenyl-4-pentenamine **4**. The results of these experiments are summarized in Table 1. All of the catalytic reactions were conducted in deuterated solvent, and the reaction progress was monitored by ^1H NMR spectroscopy. At 80 °C the CCC-NHC pincer zirconium complex **3** did



1 **2a** : $L_1, L_2 = NMe_2$
2b : $L_1 = NMe_2$, $L_2 = I$

Scheme 1 Original synthesis with excess reagent.

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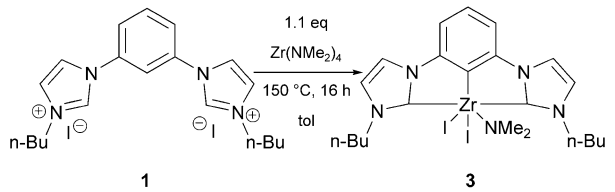
[b] *Department of Chemistry and Biochemistry, Mississippi College, Clinton, Mississippi, 39058, USA. E-mail: valente@mc.edu; Fax: 601 925-3933; Tel: 601 925-3424*

† Electronic supplementary information (ESI) available: Synthetic procedures, spectroscopic data and X-ray crystal structure details of **3** are included, along with details of the hydroamination procedure. CCDC reference number 684720. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b805174g



Scheme 2 Improved metallation procedure for triple C–H activation.

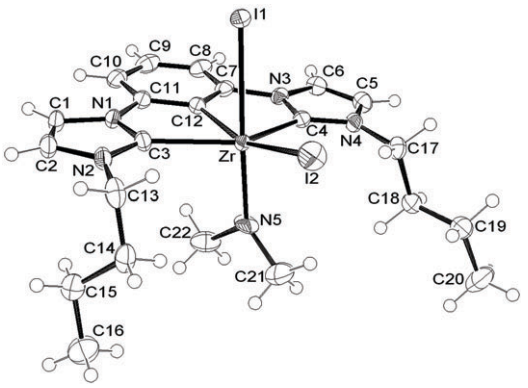
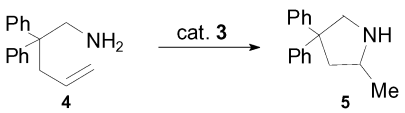


Fig. 1 ORTEP® representation of the molecular structure of **3** (major isomer illustrated, 94%). Selected geometric data: Zr–C12, 2.310(3) Å; Zr–C3, 2.367(3) Å, Zr–C4, 2.362(3) Å; Zr–I1, 3.0038 Å; Zr–I2, 2.8431(4) Å; Zr–N5, 1.986(3) Å; C12–Zr–C3, 68.20(11)°; C12–Zr–C4, 68.28(11)°; C12–Zr–I1, 79.88(7)°; C12–Zr–I2, 162.66(7)°; C12–Zr–N5, 107.11(12)°; C3–Zr–C4, 136.40(11)°; I1–Zr–I2, 83.278(11)°; N5–Zr–I1, 172.86(10)°.§

Table 1 Optimization of hydroamination conditions



4 5

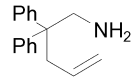
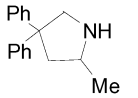
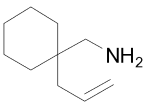
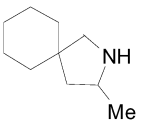
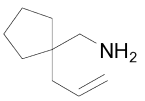
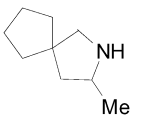
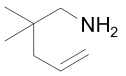
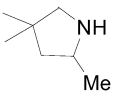
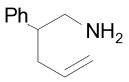
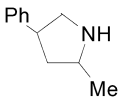
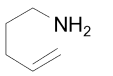
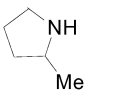
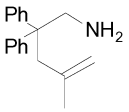
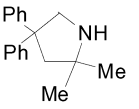
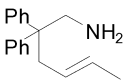
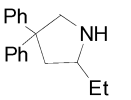
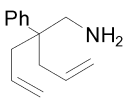
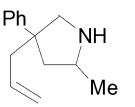
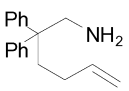
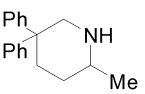
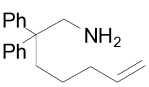
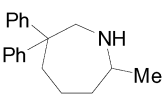
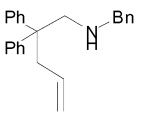
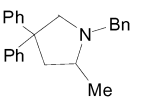
Entry	mol% **3**	Temp. °C	Time	Conv (%)[a]
1	5	80	18 h	0[b]
2	5	100	3 h	>98
3	5	120	100 min	>98
4	5	160	50 min	>98
5	2.5	160	2 h	>98
6	1	160	7.5 h	97

[a] All conversions were determined by ^{1}H NMR. [b] Solvent = C_6D_6. All others: solvent = C_7D_8.

not show any catalytic activity (Table 1, entry 1). Changing the solvent to toluene and increasing the temperature from 80° to 100 °C (entry 2) revealed excellent catalytic activity with 2,2-diphenyl-4-pentenamine **4** quantitatively converted into the corresponding pyrrolidine **5** after 100 min. Conducting the reaction in a sealed NMR tube and increasing the temperature to 120 °C (entry 3) and 160 °C (entry 4) yielded the cyclized pyrrolidine **5** in quantitative yield more rapidly (100 min and 50 min). The catalyst loading could be reduced to 2.5 and 1 mol% (entry 5 and 6) with success.

From the series of hydroaminations with **4**, the optimized condition of 5 mol% catalyst loading in toluene-d_8 under reflux was selected to study the scope and limitation of catalyst **3** (Table 2). It was found that a broad range of unactivated alkenyl amines underwent cyclization in near quantitative yield with a range of rates similar to previously reported group 4 catalysts.[16,21] As illustrated in Table 2 entries 1-4,

Table 2 Substrate survey of hydroamination catalytic activity[a]

Entry	Amine	Heterocycle	Time	Conv (%)[a]
1			50 min	>98%
2			3 h	>98%
3			18 h	92%
4			38 h	88%
5			11 h	18%
6			41 h	—[c]
7			8 h	>98%
8			39 h	—[c]
9			1 h	>98%[d]
10			2 h	90%
11			49 h	—[c]
12			29 h	—[c]

[a] 5 mol% of **3**, Toluene-d_8, 160 °C. [b] Conversion determined by ^{1}H NMR spectroscopy. [c] No reaction. [d] Diastereomeric ratio: ~1 : 1.

disubstituted amines illustrate a *gem*-dialkyl effect leading to high yields of the cyclized product.[22] Spiro-pyrrolidine products were successfully obtained (entries 2–3).

The "*gem*-dialkyl effect" became more apparent when monophenyl-substituted alkenyl amine (entry 5) and unsubstituted substrate (entry 6) were observed to react slowly or not at all.[22] A 1,1-disubstituted alkenes (entry 7) and an internal alkene (entry 8) were found to have very different reactivity. The internal olefin did not undergo cyclization. Most importantly, the 1,1-disubstituted alkene was cyclized to form a pyrrolidine containing a quaternary center (Table 2, entry 7) adding to the few known examples of generating these *via* hydroamination.[23] The di-allyl substituted starting material underwent rapid cyclization (entry 9) yielding a functionalized pyrrolidine, but without diastereoselectivity. Importantly, the formation of piperidines was successful (entry 10). However, a seven-membered ring was not generated even with extended reaction time (entry 11). Secondary amines were not cyclized by **3** (entry 12). CCC-NHC pincer zirconium complex **3** successfully catalyzed the hydroamination of unactivated primary alkene to generate pyrrolidine and piperidine products in high yields.

In conclusion, we report herein an efficient method for preparing analytically pure and on large-scale Zr CCC-NHC pincer complex **3**. Complex **3** has been shown to have excellent catalytic activity in the hydroamination/cyclization of unactivated alkenyl–amine yielding pyrrolidines and piperidines.

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Notes and references

‡ 2-(1,3-*Bis*(*N*-*butyl-imidazol*-2-*ylidene*)*phenylene*)(*dimethylamido*)*bis*(*iodo*) *zirconium* (*IV*), **3**. 1,3-*Bis*(1-butylimidazol-3-yl) benzene diiodide **1** (2.17 g, 3.75 mmol), $Zr(NMe_2)_4$ (1.10 g, 4.12 mmol) and toluene (150 mL) were combined in sealable reaction tube. The resulting mixture was stirred for 15 h in a 160 °C oil bath. The reaction was cooled to room temperature during which time a solid precipitated. It was collected and dried yielding lemon-colored crystals (1.77 g, 67%). An X-ray quality crystal was selected from this sample: H NMR (CD_2Cl_2) δ 7.51 (s, 2H), 7.30 (t, J = 8 Hz, 1H), 7.11 (s, 2H), 7.09 (d, J = 8 Hz, 2H), 4.44 (br s, 2H), 4.32 (br s, 2H), 2.95 (s, 6H), 1.95 (br s, 2H), 1.90 (br s, 2H), 1.47 (sxt, J = 7.5 Hz, 4H), 1.00 ppm (t, J = 7.5 Hz, 6H); $^{13}C\{^1H\}$ (125 MHz, CD_2Cl_2): δ 193.7, 164.8, 146.9, 129.2, 121.8, 115.7, 110.6, 52.2, 42.4, 34.1, 20.3, 14.2 ppm. Anal. calcd For $C_{22}H_{31}I_2N_5Zr$: C, 37.19; H, 4.40; N, 9.86. found: C, 37.19; H, 4.17; N, 9.79.

§ *Crystal Data* for $C_{22}H_{31}I_2N_5Zr$, **3**; M = 710.56, monoclinic, $P2(1)/n$, a = 10.1754(2) Å, b = 23.4958(4) Å, c = 10.8780(2) Å, α = 90°, β = 98.495(2)°, γ = 90°, U = 2572.17(8) Å^3, Z = 4, T = 153(2) K, d_{calcd} = 1.835 Mg m^{-3}, $F(000)$ = 1376, μ(Mo–Kα) = 2.846 mm^{-1}, λ(Mo–Kα) = 0.71073 Å, 7719 unique reflections measured, R_1 = 0.0363 ($I > 2.00\sigma(I)$), w$R(F^2)$ = 0.0941 (all data). The axial–equatorial disorder was modeled at 0.94 I(ax) : 0.06 I(eq). Even after correction for absorption, it was not possible to model a small contribution from a NMe2(eq) group with the usual larger difference peaks near I(eq). NMe_2(ax) was given occupancy 1.0.

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