Use of Steric Hindrance and a Metallacyclobutene Resting State to Develop Robust and Kinetically Characterizable Zirconium-Based Imine Metathesis Catalysts

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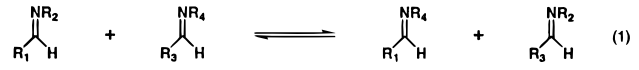
Olefin metathesis has found many exciting applications in organic and polymer chemistry as a method for the formation of new carbon−carbon double bonds.[1,2] Analogous metal-catalyzed methods for selectively metathesizing double bonds to nitrogen (e.g., imines, diazenes) also offer substantial promise as synthetic tools. However, such reactions have been virtually unexplored until now.[3−5] In addition, as recently noted by Mountford,[4] there is a clear need to subject such systems to "mechanistic scrutiny" before drawing conclusions as to the role played by the metal center. We now report the successful generation of robust catalysts for imine metathesis (eq 1). Our system employs well-



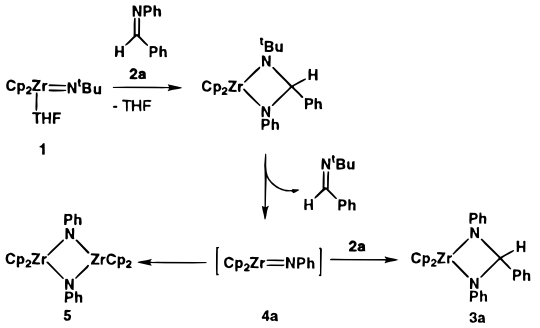
(1)

characterized zirconium imido complexes and metallacyclobutenes as catalyst precursors. Through a detailed kinetic analysis, we have identified diazametallacycles as key intermediates and established the role they play in the overall mechanism.

Previously reported[6,7] work from our laboratory demonstrated that treatment of *N*-*tert*-butylimidozirconocene complex **1** with 2 equiv of benzaldehyde *N*-phenylimine (**2a**) results in a stoichiometric exchange of imine N substituents accompanied by the formation of diazametallacycle **3a** (Scheme 1). However, attempts to utilize this reaction to develop a catalytic imine metathesis process were frustrated by the irreversible formation of the catalytically inactive dimer **5**.

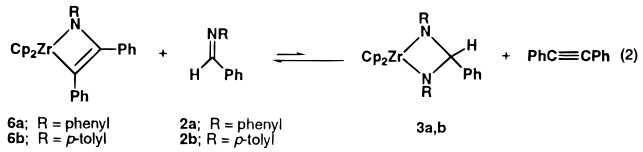
We have explored two approaches to obtaining catalysts not prone toward irreversible dimerization. In the first we increased the steric bulk around the zirconium metal center by replacing one of the Cp ligands of complex **1** with a Cp* (pentamethylcyclopentadienyl) ligand.[8] Crystals of Cp*CpZr=N^{t}Bu(THF) (**7**) have been obtained and fully characterized by X-ray diffraction. When 5 mol % of **7** was used as the catalyst precursor for the metathesis of PhCH=NPh and *p*-TolCH=*N*-*p*-Tol in C_6D_6 at 105 °C, a slow but constant ($t_{1/2} \approx 170$ m; TON = 1.77 h^{-1}) rate was observed. The Cp*-substituted catalyst was still active after 20

Scheme 1



d (long after the first charge of imines had come to equilibrium; estimated 847 turnovers), which was demonstrated by adding more imine starting materials to the system and observing the reinitiation of metathesis. Additionally, there was no spectroscopic evidence for any imido complex dimer formation.[10,11]

Given the expected second-order dependence of the rate of dimerization of transient imido complex **4** on its concentration, we guessed that the bis-cyclopentadienyl catalyst lifetime might be increased by the addition of a ligand that would minimize the concentration of the free imido complex. This proved to be successful as well. When 5 mol % of diphenylacetylene was added to 5 mol % of **1** and larger equimolar amounts of PhCH=NPh and *p*-TolCH=*N*-*p*-Tol in C_6D_6, an equilibrium mixture (1:1:1:1) of the two starting imines and the two metathesized product imines was obtained after heating for 6 h at 105 °C. Analysis of the reaction mixture by ^{1}H NMR spectroscopy under working metathesis conditions revealed metallacyclobutene complexes **6a** and **6b** as the predominant (>90%) Zr-containing species. Once again no dimeric species were observed in the reaction mixture, even after heating for 4 d at 105 °C. The catalyst was still active at this time (total turnovers ca. 410). The reaction rate ($t_{1/2} \approx 70$ m; TON = 4.3 h^{-1}) was slowed by about a factor of 9 compared to that of the reaction with no added diphenylacetylene, as one would expect in the presence of a more thermodynamically stable resting state. Independent determination of equilibrium constants for the interconversions of **3** and **6** in the presence of excess imines and diphenylacetylene (eq 2) gave $K_{eq} = 1.8 \times 10^{-3}$ at 75 °C for



6a/**3a**; for **6b** and **3b** $K_{eq} = 1.2 \times 10^{-3}$ at 105 °C.[12]

For kinetic experiments, azametallacyclobutene **6b** was employed as the catalyst precursor due to its stability under the reaction conditions.[13] The imines PhCH=*N*-*p*-Tol and *p*-F−C_6H_4CH=*N*-*p*-F−C_6H_4 were chosen as starting materials because the CH resonances for these compounds and their

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(2) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−56.
(3) (a) Cantrell, G. K.; Meyer, T. Y. *J. Am. Chem. Soc.* **1998**, *120*, 8035−42. (b) Cantrell, G. K.; Meyer, T. Y. *Organometallics* **1997**, *16*, 5381−3. (c) Cantrell, G. K.; Meyer, T. Y. *Chem. Commun.* **1997**, 1551−2.
(4) McInnes, J. M.; Mountford, P. *Chem. Commun.* **1998**, 1669−70.
(5) Tóth, G.; Pintér, I.; Messmer, A. *Tetrahedron Lett.* **1974**, 735−8.
(6) Meyer, K. E.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1995**, *117*, 974−85.
(7) Meyer, K. E.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1994**, *116*, 2669−70.
(8) Reaction of the known[9] complex Cp*CpZrMe$_2$ with 1 equiv of Me$_3$NH$^+$Cl$^-$ in THF gave Cp*CpZr(Me)Cl. Treatment of Cp*CpZr(Me)Cl with LiNH^{t}Bu in THF afforded Cp*CpZr(Me)NH^{t}Bu. Thermolysis of Cp*CpZr(Me)NH^{t}Bu in THF gave complex **7.** Characterization data for all new compounds are given in the Supporting Information. Experimental details will be published in a full paper.
(9) Wolczanski, P. T.; Bercaw, J. E. *Organometallics* **1982**, *1*, 793−9.
(10) Complexes **1**, **6a**, and **7** did not catalyze the metathesis of *N*-aryl and *N*-alkyl imines (e.g., *p*-TolCH=*N*-*p*-Tol and PhCH=NMe) at reaction temperatures up to 150 °C. Complexes **1** and **7** did catalyze the metathesis of *N*-alkyl imines (e.g., PhCH=NMe and p-TolCH=*N*-*n*-Pr), but only at temperatures exceeding 135 °C.; the mechanisms of these reactions are currently under investigation.
(11) Since trace amounts of acid are known to catalyze imine metathesis,[5] we conducted several control experiments to confirm that impurities were not catalyzing the metathesis reactions in our systems. Heating PhCH=NPh and *p*-TolCH=*N*-*p*-Tol in C_6D_6 for 59 h at 105 °C resulted in no observable metathesis. In addition, the complexes **1**, **6a**, and **7**, unlike acid, were not able to catalyze the metathesis of *N*-aryl and *N*-alkyl imines.
(12) The previously reported[7] value for the K_{eq} for the **6a**/**3a** interconversion is incorrect. Full details will be provided in a forthcoming full paper.

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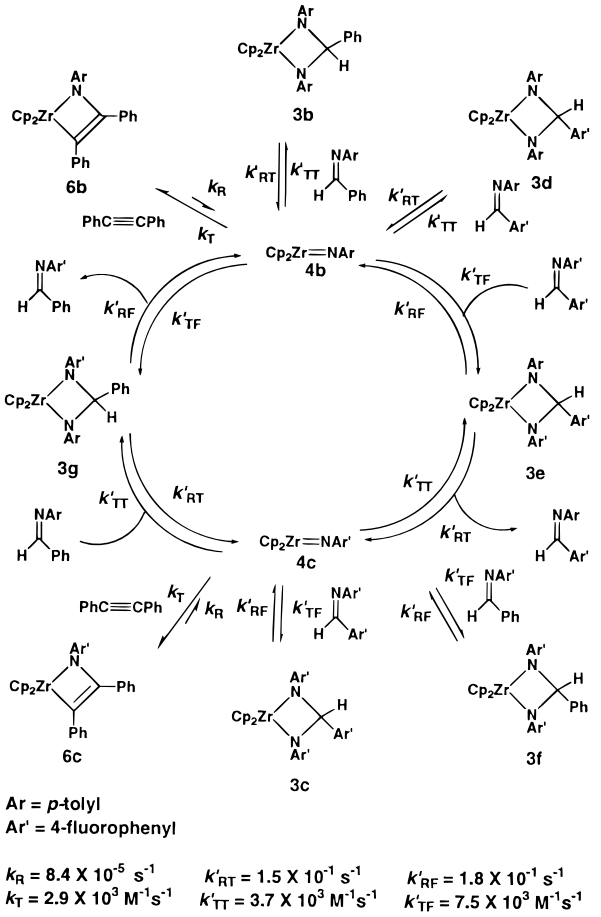
Scheme 2



metathesis products are resolved well enough to guarantee accurate quantification of concentrations by NMR integration. To maintain a constant concentration of diphenylacetylene throughout the reaction, the reactions were run with an added equivalent of alkyne relative to the catalyst.[14] Reactions were run at two different catalyst concentrations, several total imine concentrations, and several ratios of the two reactant imines.

We propose that the catalytic reaction proceeds by the cycle presented in Scheme 2.[6,7] Because of the complexity of the system, we used kinetic simulation software[15] to fit the experimental data to a model containing all of the species shown in the scheme. The concentration vs time data do not provide sufficient information to uniquely determine all 20 microscopic rate constants in the model, and therefore, reasonable assumptions were made that allowed us to reduce these to six distinguishable parameters for the purpose of fitting the experimental data. Specifically, the rates of reversion of azametallacyclobutene complexes **6b** and **6c**, k_R, were assumed to be equal; reversion of diazametallacyclobutane complexes **3c**, **e**−**g** to release *N*-*p*-F−C_6H_4 imines were set equal to the parameter k'_{RF}; likewise, the rates of reversion of complexes **3b**, **d**, **e**, **g** to release *N*-*p*-Tol imines were set equal to k'_{RT}. The rates of trapping of the transient imido complexes **4b** and **4c** with diphenylacetylene (k_T), *N*-*p*-F−C_6H_4 imines (k'_{TF}), and *N*-*p*-Tol imines (k'_{TT}) constituted the final three parameters.

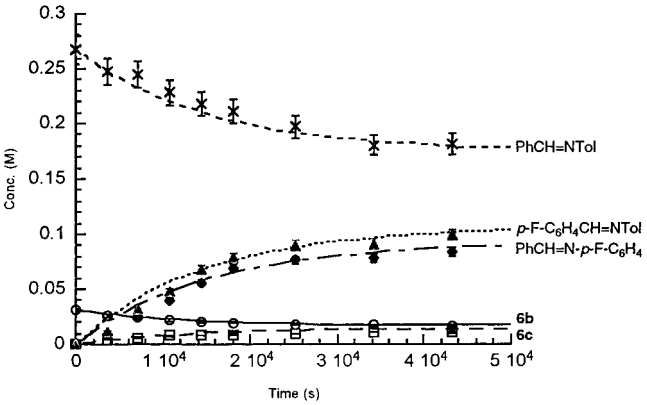


Figure 1. Experimentally determined (points) and simulated (lines) concentration vs time profiles for the reactant and product imines and the two azametallacyclobutene complexes **6b** and **6c** for a representative kinetic run. (For experimental details, see Supporting Information.)

Final optimization of the model was accomplished by application of a nonlinear least-squares fitting routine. The values of the parameters that gave a satisfactory fit to the experimental data under conditions of varying catalyst and imine concentrations are given in Scheme 2. A sample plot comparing experimental data with the simulated curves is given in Figure 1.

The quality of the model was explored by varying the final rate constants and determining the sensitivity of the fit to these changes. Changes in the parameter k_R produced the strongest effect on the goodness-of-fit of the simulation. This was consistent with the rate-determining steps of the cycle being the expulsion of diphenylacetylene from azametallacyclobutenes **6b** and **6c**. The rate of equilibration of **6b** and **6c** relative to the imine metathesis reaction was very sensitive to the *ratio* of the trapping rates of the free imidozirconocene intermediates **4** with imines (k'_{TF} and k'_{TT}) and diphenylacetylene (k_T). However, the *absolute* magnitude of these trapping rate constants did not noticeably affect the fit of the model. This is consistent with there being a partitioning of the highly reactive imido species between cycloaddition with imine (leading ultimately to metathesis) and reaction with alkyne to return to the resting state.

In conclusion we have shown that, by eliminating a detrimental side-reaction, imidozirconocene complexes are effective, long-lived catalysts for the metathesis of imines. By making use of kinetic simulation programs, we are able to describe this very complex system with a model involving imido and diazametallacyclobutane complexes that is consistent with the experimental observations. Given the potential utility of these catalysts, we are currently exploring their scope and selectivity for the metathesis of both acyclic and cyclic imines.

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Supporting Information Available: Characterization data for imines, complexes **3b**, **6b**, **6c**, **7**, Cp*CpZr(Me)Cl, and Cp*CpZr(Me)NH^{t}Bu; crystallographic data for **7**; kinetics data for the rate and simulation study (15 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(13) Complex **7** was not chosen as the catalyst precursor for the kinetic measurements because its imine adducts analogous to **3** exist as pairs of diastereomers. It was thought that this would further complicate the already complex system.

(14) The K_{eq} measurements in eq 2 predict that, at equilibrium, less than 10% of **6b** should be converted to diazametallacyclobutanes **3**.

(15) The FORTRAN programs GEAR and GIT (v. 2.1) were used for all kinetic simulations: (a) McKinney, R. J.; Weigert, F. J., Project SERAPHIM, program number IB-1407, 8. (b) Weigert, F. J. *Comput. Chem.* **1987**, *11*, 273. (c) Stabler, R. N.; Chesick, J. *Int. J. Chem. Kinet.* **1978**, *10*, 461−9.