

## C–H Bond Activation of Hydrocarbons by an Imidozirconocene Complex

Helen M. Hoyt, Forrest E. Michael, and Robert G. Bergman\*

Department of Chemistry, University of California, Berkeley, Berkeley, California 94720

Received September 18, 2003; E-mail: bergman@cchem.berkeley.edu

Monomeric imidozirconocene complexes of the type Cp<sub>2</sub>(L)-Zr=NCMe<sub>3</sub> (Cp = cyclopentadienyl, L = Lewis base) have been shown to undergo reversible dissociation of L upon thermolysis to form a transient 16-electron imido (Cp<sub>2</sub>Zr=NCMe<sub>3</sub>) intermediate.<sup>1</sup> This reactive species undergoes cycloaddition reactions with a variety of unsaturated organic molecules<sup>1</sup> and activates the carbon–hydrogen bonds of benzene.<sup>2a</sup> Wolczanski and co-workers have reported a series of nonmetallocene imidozirconium and -titanium complexes bearing (Me<sub>3</sub>C)<sub>3</sub>SiNH and “silox” ligands that react with saturated hydrocarbons,<sup>2b–d</sup> but, to our knowledge, this singularly important class of C–H activation reactions has never been observed in imidozirconocene systems. We now report a metallocene system whose [Zr]=NCMe<sub>3</sub> bond cleanly and quantitatively activates a wide range of *n*-alkane, alkene, and arene C–H bonds.

In an attempt to isolate or detect a base-free imido complex, the imido precursor racemic ethylenebis(tetrahydro)indenyl (ebthi) methyl *tert*-butylamide complex (**1a**) was heated in hexanes. Surprisingly, clean and quantitative activation of *n*-hexane to give complex **1b** was observed (Scheme 1). The dramatic increase in reactivity of the intermediate formed from complex **1a** toward saturated hydrocarbons, as compared with that of the parent zirconocene analogue, prompted our investigations into the scope, selectivity, and mechanism of this new C–H activation reaction.

Starting (methyl)(amido)zirconium complex **1a** was synthesized by metathesis of the known ebthi zirconium methyl chloride complex<sup>3</sup> with lithium *tert*-butylamide. When **1a** was heated at 75 °C in neat *n*-hexane, a <sup>1</sup>H NMR spectrum of the isolated product (**1b**) showed diagnostic resonances for the C–H bond activation reaction: a new amide proton signal and two upfield triplet of doublet resonances for the diastereotopic methylene protons α to the zirconium center. This reaction was extended to a variety of hydrocarbons using similar conditions (Table 1). Connectivity was confirmed for the analogous *n*-pentyl (**1c**) and silylmethyl (**1d**) complexes by X-ray crystallography (Figure 1).

Activation of substrates containing different types of C–H bonds was carried out to gauge the intramolecular selectivity of this reaction (Table 1). The formation of complexes **1e–g** demonstrated the preferential activation of sp<sup>2</sup> alkenyl C–H bonds over sp<sup>3</sup> primary or secondary C–H bonds. Both **1f** and **1g** formed as the sterically favorable *trans* products, assigned by the large vinyl proton coupling constants (*J* ≈ 18 Hz). When sp<sup>2</sup> aryl C–H bonds were less sterically accessible than benzylic sp<sup>3</sup> C–H bonds, C–H bond activation occurred exclusively at the sp<sup>3</sup> position, as illustrated by the formation of mesityl complex **1h**.<sup>4</sup> The formation of **1i** resulted from clean activation of a cyclopropyl C–H bond in favor of an aryl C–H bond.

Clean C–H activation reactions were also observed with more highly branched saturated hydrocarbons, leading to alkyl complexes **1j–l**. Unfortunately, a 1:1 mixture of diastereomers is observed for complexes **1l** and **1i**, presumably because the substituents are not large enough to cause unfavorable interactions with the ebthi ligand. Reaction of **1a** with bulkier hydrocarbons containing the “isopropyl” moiety, such as 2,3-dimethylbutane and 2,4-dimeth-

Scheme 1

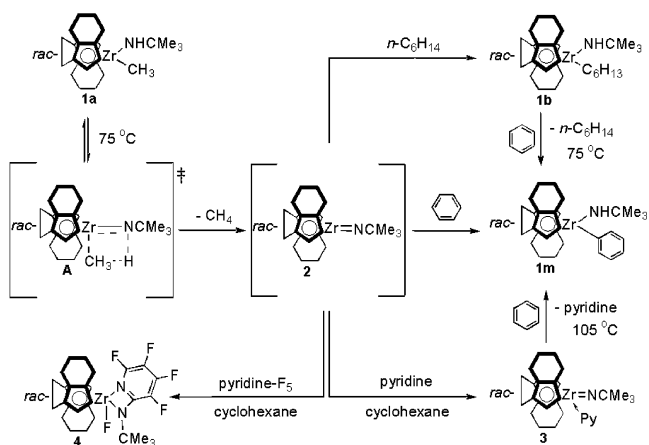


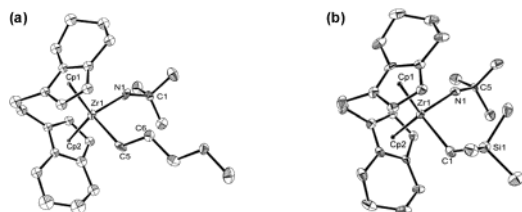
Table 1. Regiochemistry and Substrate Scope of Carbon–Hydrogen Bond Metathesis

Pdt	R-H <sup>a</sup>	% Yield <sup>b</sup>	Pdt	R-H <sup>a</sup>	% Yield <sup>b</sup>
<b>1b</b>		93	<b>1i</b>		81 <sup>c</sup>
<b>1c</b>		92	<b>1j</b>		98
<b>1d</b>		89	<b>1k</b>		92
<b>1e</b>		93	<b>1l</b>		90 <sup>c</sup>
<b>1f</b>		92	<b>1m</b>		93
<b>1g</b>		99	<b>1n</b>		68
<b>1h</b>		96	<b>1o</b>		81

<sup>a</sup> Regiochemistry of substrate activation indicated explicitly by drawn hydrogen atoms. <sup>b</sup> Isolated yield. <sup>c</sup> No diastereoselectivity observed between newly generated stereocenter and asymmetric ebthi-Zr fragment.

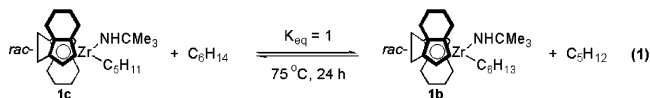
ylpentane, resulted in thermal decomposition. These results again indicate the presence of strong steric constraints on the C–H activation reaction of simple alkyl groups: methyl hydrogens react preferentially, and a relatively unhindered group such as a methylene unit must be adjacent to the methyl position undergoing attack.

Heating the *n*-hexyl adduct **1b** in benzene yielded the phenyl adduct **1m**, demonstrating the reversibility of the C–H activation reaction (Scheme 1). Furthermore, when **1a**, **1b**, and **1c** were independently heated at 75 °C in a 1:1 mixture of *n*-pentane and *n*-hexane, a 1:1 product mixture of **1b**:**1c** was observed. This



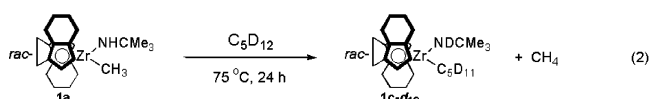
**Figure 1.** ORTEP diagrams for (a) complex **1c** and (b) complex **1d** with hydrogen atoms omitted for clarity.

suggests that equilibrium was reached between **1b** and **1c** with a calculated  $K_{\text{eq}} \approx 1$  at 75 °C (eq 1). We therefore believe that the selectivities that we have observed so far reflect the relative thermodynamic stabilities of the products.<sup>5</sup>



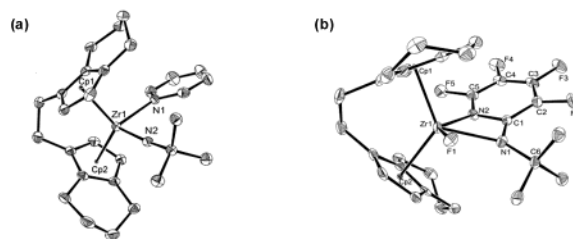
Intermolecular competition experiments were conducted by heating complex **1a** in mixtures of hydrocarbons. The relative thermodynamic selectivity was found to be formation of: **1g**  $\gg$  **1i**  $>$  **1n**  $\approx$  **1o**  $\approx$  **1m**  $\gg$  **1c**.<sup>6</sup> The thermodynamic selectivity, with a calculated statistical correction for differing numbers of reactive C–H bonds, between activation of cyclopropylbenzene versus benzene is notably large (44:1).<sup>2d</sup> Conversely, the difference between the product ratio of **1n** to **1o** is negligible (3:2), suggesting a remarkably small electronic effect.

To establish the origin of the amide proton in the products of C–H activation, the thermolysis of **1a** was monitored in *n*-pentane-*d*<sub>12</sub> (eq 2). Throughout the course of this reaction, no “N–H” resonance was observed for **1c-d**<sub>12</sub> in the <sup>1</sup>H NMR spectra. This indicated that the N–H proton of starting material **1a** did not exchange with the N–D deuterium in the product **1c-d**<sub>12</sub>, including when **1a** and **1c-d**<sub>12</sub> were present in an equimolar proportion. These results, coupled with the prevalence of intramolecular addition/elimination mechanisms described for similar systems,<sup>2</sup> lead us to propose a four-centered transition state (e.g., **A**) for these  $\sigma$ -bond metathesis reactions (Scheme 1).



Although this labeling experiment demonstrates that the amide deuterium in complex **1c-d**<sub>12</sub> originated on the perdeutero substrate, it does not rule out an intermolecular process which might place the R and H/D groups from the reacting hydrocarbon on different metal centers in the final product. To test for a pathway of this type, **1a** was heated in a 1:1 mixture of *d*<sub>0</sub>:*d*<sub>12</sub> *n*-pentane. If intermolecular pathways were being followed, a statistical distribution of *n*-pentane-*d*<sub>*x*</sub> (*x* = 0–12) would be incorporated into the solvent mixture at the completion of the reaction, because the system is in equilibrium at 75 °C. However, no change in isotope distribution was observed in the resulting solvent mixture by <sup>1</sup>H NMR spectroscopy. These results are consistent with the proposal that complex **1a** undergoes 1,2-methane elimination to form the transient imido intermediate **2** followed by 1,2-C–H bond addition of a hydrocarbon substrate and that both are intramolecular processes.

Additional support for the proposed mechanism was found when the 16-electron imido intermediate **2** was trapped with pyridine to form the pyridine imido complex **3** (Figure 2). Complex **3** reacts



**Figure 2.** ORTEP diagrams for (a) complex **3** and (b) complex **4** with hydrogen atoms omitted for clarity.

with benzene to form the phenyl complex **1m**, although at a much slower rate than the analogous reaction with **1a** (Scheme 1). Remarkably, when a less electron-donating Lewis base, pentafluoropyridine, was heated with complex **1a**, carbon–fluorine bond activation occurred (Scheme 1). Activation of the *ortho* C–F bond yielded complex **4**, which was characterized by X-ray crystallography (Figure 2). This C–F activation reaction is likely driven by the inherent reactivity of the 2-fluoropyridyl bond<sup>7</sup> and the formation of a strong Zr–F bond.

In conclusion, the reactive *rac*-(*ebthi*)Zr(NHCMe<sub>3</sub>)(Me) complex has been shown to activate a variety of hydrocarbons with primary alkyl, alkenyl, and aryl C–H bonds. Products formed by activation of sp<sup>2</sup> C–H bonds are generally more thermodynamically stable than those formed by activation of sp<sup>3</sup> C–H bonds, and those resulting from reaction at primary C–H bonds are preferred over secondary sp<sup>3</sup> C–H activation products. There is also evidence that thermodynamic selectivity among C–H bonds is strongly sterically influenced, while substrate inductive electronic effects only slightly influence the relative product stability. Mechanistic experiments support the proposal of intramolecular elimination of methane followed by a concerted addition of the hydrocarbon C–H bond. Continuing work is aimed at measuring the kinetic selectivities in these reactions and preparing analogues of **1a** with other substituted cyclopentadienyl ligands to understand the factors that determine when alkane C–H activation will occur in metallocene systems.

**Acknowledgment.** This work was supported by the National Institutes of Health through grant no. GM-25459. We thank Dr. Fred Hollander and Dr. Allen Oliver of the UC Berkeley CHEXRAY facility and Dennis Leung for the X-ray structure determinations.

**Supporting Information Available:** Experimental procedures and characterization for all new compounds (PDF). X-ray crystallographic data for **1c**, **1d**, **3**, and **4** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- (1) Duncan, A. P.; Bergman, R. G. *Chem. Rev.* **2002**, *2*, 431.
- (2) (a) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729. (b) Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731. (c) Schaller, C. P.; Cummins, C. C.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1996**, *118*, 591. (d) Bennett, J. L.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1997**, *119*, 10696. (e) For a V(=NR)<sub>2</sub> example, see: De With, J.; Horton, A. D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 903.
- (3) (a) Sweeney, Z. K.; Salsman, J. L.; Andersen, R. A.; Bergman, R. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 2339. (b) Diamond, G. M.; Jordan, R. F.; Petersen, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 8024.
- (4) Activation of benzylic sp<sup>3</sup> and aryl sp<sup>2</sup> C–H bonds is often competitive; preference for aryl or benzylic activation is highly system dependent (see refs 2c–6a; Adams, C. S.; Legzdins, P.; Tran, E. *Organometallics* **2002**, *21*, 1474).
- (5) We presume that secondary products, if formed, are less thermodynamically stable than primary products and are thus not observed.
- (6) Selectivities fall qualitatively in line with those observed for both early (see ref 2c–e) and late metal systems: (a) Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* **1989**, *22*, 91. (b) Arndsten, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (c) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.
- (7) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373 and references therein.

JA0385944