

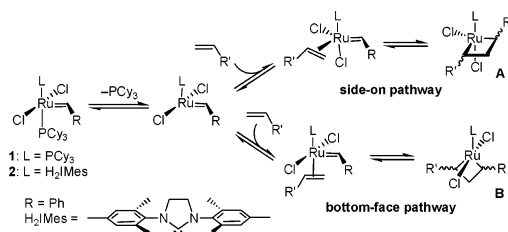
Ruthenium Metallacycles Derived from 14-Electron Complexes. New Insights into Olefin Metathesis Intermediates

Anna G. Wenzel^{†,§} and Robert H. Grubbs^{*,†}*Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, and Joint Science Department, Claremont McKenna, Pitzer, and Scripps Colleges, Claremont, California 91711*

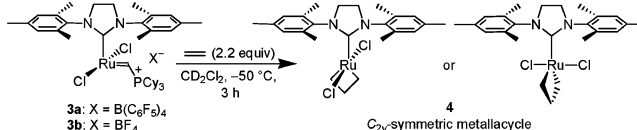
Received September 14, 2006; E-mail: rhg@caltech.edu

Since its discovery in the 1950s, olefin metathesis has emerged as a valuable synthetic tool for the construction of carbon–carbon bonds.¹ In particular, well-defined ruthenium catalysts **1** and **2** have received significant attention due to their high reactivity, commercial availability, and functional group tolerance.^{2,3}

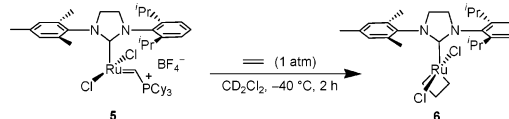
Extensive investigation into the mechanism of olefin metathesis has determined that the principal steps occur according to the Chauvin mechanism, where the reaction proceeds via the intermediacy of a metallacyclobutane complex, which subsequently collapses via a [2+2] cycloreversion to afford the olefinic product and the propagating metal carbene catalyst.⁴ However, for catalysts **1** and **2**, there is still an ongoing discussion as to the nature of the metallacyclobutane intermediate, particularly with regard to the stereochemical orientation of the ligands (Scheme 1).⁵ Unfortunately, acquiring detailed data on this has proven elusive, and until recently, experimental evidence supporting metallacycle orientation in ruthenium-based systems has been indirect, relying primarily upon the translation of stereochemistry from olefinic complexes.⁶ While compelling, the study of such complexes primarily indicates the thermodynamic preference for olefin binding (either side-on or bottom-face), not the kinetic preference for subsequent metallacycle formation.

Scheme 1. Initial Steps of the Olefin Metathesis Mechanism

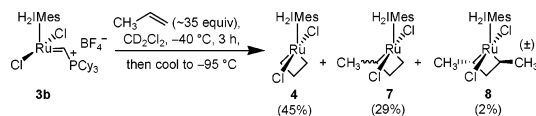
In 2005, Piers and co-workers reported the first direct observation of a ruthenium metallacycle. Upon the reaction of catalyst **3a** with 2.2 equiv of ethylene at $-50\text{ }^{\circ}\text{C}$, a C_{2v} -symmetric ruthenacyclobutane (**4**) was observed via ^1H NMR spectroscopy (Scheme 2).^{7,8} Piers's result is suggestive of bottom-face olefin coordination and metallacycle generation, as additional shifts that could be attributed to protons lying above and below the plane of a side-bound structure were not observed (Scheme 1, A vs B).⁹ Such an orientation is consistent with previous computational⁵ and crystallographic^{6a} evidence. However, the ligand dynamics of rotation about the ruthenium–*N*-heterocyclic carbene (NHC) bond as well as the stereochemical orientation of substituted metallacycles remained unknown. For these reasons, we initiated a comprehensive investigation to elucidate this information.

Scheme 2. Reaction of **3a** with Ethylene

To study the dynamics of the NHC ligand, we envisioned the preparation of an unsymmetrical catalyst, thereby breaking the C_{2v} symmetry previously observed with metallacycle **4**. To this effect, complex **5** was prepared in seven steps in 16% overall yield.⁹ Upon the reaction of **5** with ethylene (1 atm) at $-40\text{ }^{\circ}\text{C}$, complete conversion to metallacycle **6** was observed after 1.5 h (Scheme 3). Metallacycle **6** possesses a distinctive two-proton signal at -2.66 ppm that corresponds to the enantiotopic β -hydrogens.^{10,11} Analysis of the reaction mixture via 2D COSY and ROESY NMR identified the metallacycle α -hydrogen shifts at 6.75 and 6.60 ppm, indicating that Ru–NHC rotation is sufficiently slow on an NMR time scale at $-40\text{ }^{\circ}\text{C}$ that the α -methylene groups are diastereotopic. HMQC ^1H – ^{13}C analysis correlated the 6.75 and 6.60 ppm shifts with ^{13}C shifts at 94.9 and 93.7 ppm, respectively, allowing the assignment of each α -hydrogen signal to a unique carbon resonance. These results support the trigonal bipyramidal structure proposed by Piers and co-workers⁷ and computationally predicted by Chen.⁵

Scheme 3. Reaction of **5** with Ethylene

With the Ru–NHC ligand dynamics better understood, we looked to investigate the influence of metallacycle substitution on ruthenium complex stability and stereochemistry. The exposure of propene to a metathesis catalyst results in the formation of butene and ethylene via cross-metathesis. Hence, when catalyst **3b** was reacted with an excess of propene at $-40\text{ }^{\circ}\text{C}$, the presence of the ethylene-derived metallacycle **4** in 45% conversion was readily explained (Scheme 4 and Figure 1a).^{9,12} However, much of the mass balance of the reaction remained to be accounted for, as $>95\%$ of the starting catalyst had been consumed.

Scheme 4. Reaction of **3b** with Propene¹⁶

During our ^1H NMR studies on metallacycle **4**, it had been observed that, upon warming the reaction mixture to $-20\text{ }^{\circ}\text{C}$,

[§] Joint Science Department, Claremont McKenna, Pitzer, and Scripps Colleges.[†] California Institute of Technology.

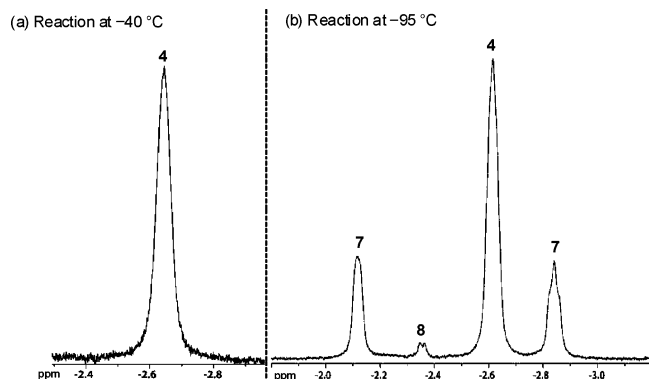


Figure 1. Reaction of catalyst **3b** with propene.

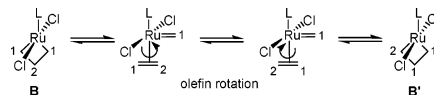
sufficient line broadening of the metallacycle peaks had occurred such that they disappeared into the baseline. Thinking that a similar scenario might be in effect, we observed the reaction of **3b** with propene at lower temperatures. Gratifyingly, three new peaks at -2.11 , -2.35 , and -2.84 ppm were observed in the upfield region of the ^1H NMR upon cooling the reaction to -95 °C (Figure 1b). The formation of these new species was found to be reversible, as warming the reaction mixture back to -40 °C afforded solely metallacycle **4** without any visible decomposition. In addition, the presence of these new peaks was found not to be solely due to ethylene, as cooling a solution of **4** to -95 °C afforded no new species. Instead, these new complexes were ultimately attributed to metallacycles derived from propene (Scheme 4).

2D COSY, ROESY, and HMQC analysis of the reaction mixture identified the protons at -2.11 and -2.84 ppm to occupy the same carbon on propene-derived metallacycle **7**, which was found to be present in 29% conversion. The doublet observed at -2.35 ppm was attributed the β -hydrogens of the C_2 -symmetric metallacycle **8**. As with **4**, metallacycles **7** and **8** lie in a bottom-face orientation. Repeating the reaction in the presence of $3\text{-}^{13}\text{C}$ -labeled propene confirmed that no metallacycles derived from either *cis*- or *trans*-2-butene are observable at these reaction temperatures—a result consistent with what Piers had observed in the reaction of **3a** with butene at -50 °C.⁷ It is important to note that the *trans* orientation of the methyl groups in metallacycle **8** is in marked contrast to the preferred *cis* orientation that had been previously postulated in analogy to cyclobutane puckering.^{1b} As the structure of **8** indicates, a *cis*/*trans* argument based solely upon the configurational preferences of cyclobutane is not entirely valid, particularly in view of experimental evidence that suggests the metallacycle ring is a distorted kite shape due to a $\text{M}\cdots\text{C}_\beta$ interaction.⁷

At this point, we had acquired significant insight into the Ru–NHC ligand dynamics and the configurational preferences of ruthenium metallacycles. During the course of our 2D NMR investigations, however, we had additionally found the α - and β -positions of metallacycles **4** and **6** to possess exchange cross-peaks,^{13,9} raising the issue of metallacycle dynamics. Taking previous mechanistic studies into account,^{1,4} the presence of exchange cross-peaks was strongly indicative that metallacycle cycloreversion and re-formation was occurring on the NMR time scale, leading to an equilibrium between **B** and **B'** (Scheme 5). In addition, as no exchange was observed between the metallacycle and free olefin within this time period, exchange between the α - and β -positions must be attributed to rotation of the π -bound olefin between successive reaction cycles. Two-dimensional EXSY experiments on **4** were utilized to determine the rate constant ($k_{\text{B} \leftrightarrow \text{B}'}$)¹⁴ for this process to be $26 \pm 2 \text{ s}^{-1}$, corresponding to $\Delta G^\ddagger_{233\text{K}} = 12.18 \pm 0.04 \text{ kcal/mol}$. Experimental evidence indicates that metallacycles derived from propene are also dynamic structures;

however, further investigation is required to fully ascertain their exchange behavior. The extension of these studies to include the dynamics of substituted metallacycles derived from **5** also remains to be investigated.¹⁵

Scheme 5. Dynamics of Ruthenium Metallacycles



In summary, we have shown evidence supporting the bottom-face orientation of ruthenium(IV) metallacycles derived from both ethylene and propene. The metallacycle structures derived from propene represent the first observed examples of substituted ruthenacyclobutanes and offer new insight into the preferred stereochemical orientation of metathesis intermediates. In addition, we have presented new evidence that suggests that ruthenacyclobutanes derived from ethylene and propene are dynamic structures that proceed through a series of nonproductive metallacycle formations/cycloreversions prior to olefin exchange. Current efforts are underway to apply these data to the rational design of additional olefin metathesis catalysts, particularly those directed at the still unsolved problem of olefin diastereocontrol.

Acknowledgment. The authors thank Dr. Phillip Dennison and the U.C. Irvine NMR Facility for the generous donation of instrument time for the propene VT NMR experiments. Theodor Agapie is acknowledged for his instruction on Schlenk techniques for quantitated gas additions. Special thanks also goes to Professor Daniel O'Leary of Pomona College for invaluable research discussion. Funding was provided by NIH. Postdoctoral funding for A.G.W. was provided by NIH (NRSA GM070147-02) and UNCF-Pfizer.

Supporting Information Available: Experimental procedures and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) (a) *Handbook of Metathesis*, Vols. 1–3; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003. (b) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, CA, 1997.
- (2) (a) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100–110. (b) Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 9858–9859.
- (3) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.
- (4) Hérisson, J. L.; Chauvin, Y. *Makromol. Chem.* **1971**, *141*, 161–176.
- (5) Adlhart, C.; Chen, P. *J. Am. Chem. Soc.* **2004**, *126*, 3496–3510.
- (6) (a) Tallarico, J. A.; Bonitatebus, P. J., Jr.; Snapper, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 7157–7158. (b) Anderson, D. R.; Hickstein, D. D.; O'Leary, D. J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 8386–8387.
- (7) Romero, P.; Piers, W. E. *J. Am. Chem. Soc.* **2005**, *127*, 5032–5033.
- (8) We have subsequently confirmed the presence of **4** under these conditions via mass spectrometry. Refer to the Supporting Information.
- (9) Refer to the Supporting Information.
- (10) Mashima, K.; Kaidzu, M.; Nakayama, Y.; Nakamura, A. *Organometallics* **1997**, *16*, 1345–1348.
- (11) Howard, T. R.; Lee, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 6878–6880.
- (12) Relative to anthracene as an internal standard.
- (13) Neuhaus, D.; Williamson, M. P. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*, 2nd ed.; Wiley-VCH: New York, 2000; Chapter 8.
- (14) The $k_{\text{B} \leftrightarrow \text{B}'}$ rate constant includes the rates of metallacycle cycloreversion, olefin rotation, and metallacycle formation to interconvert positions 1 and 2 in Scheme 5.
- (15) Examples of additional olefins that we have thus far investigated: 1,1-difluoroethylene, vinyl fluoride, ethyl vinyl ether, neohexene, acenaphthylene, 2-butyne, and methyl acrylate.
- (16) Propene was added in excess (35 equiv) to both minimize the conversion of **3b** into a bis-ruthenium μ -Cl decomposition product and prevent the reaction mixture from freezing.

JA0666598