

Chapter 1

Current Frontiers in Olefin Metathesis

Olefin metathesis has emerged as a versatile and powerful tool for organic and polymer chemistry.¹ The development of commercially available catalysts **1–4** (Figure 1.1) has been essential to the widespread use of this reaction. The early ruthenium-based complex **2**² is significantly more stable towards water, air and functionality than molybdenum-based complex **1**, but **1** has greater activity, especially toward sterically demanding and electron-deficient olefins.³

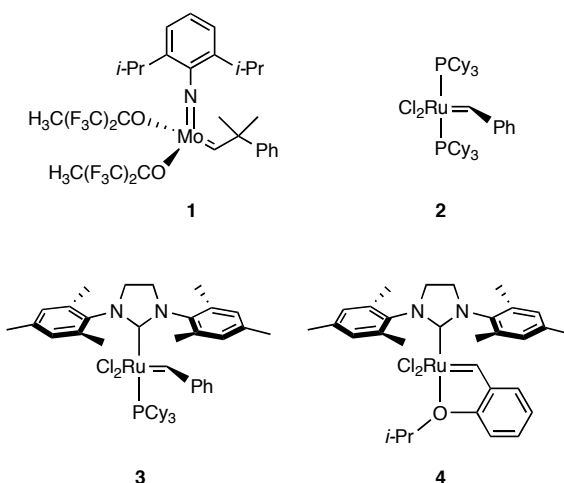


Figure 1.1. Commercially available catalysts for olefin metathesis.

The use of *N*-heterocyclic carbenes (NHCs) as ligands for ruthenium closed the gap between molybdenum and ruthenium systems.⁴ Ruthenium-based NHC complexes, such as **3**, possess activity similar to molybdenum-based complexes yet maintain the high functional group tolerance and stability of **2**.⁵ This combination of stability (toward air and moisture), selectivity (for olefins over other functional groups) and activity has led to ruthenium-based systems being those most commonly used. Nevertheless, challenges remain in all three areas for ruthenium catalysts. This thesis will describe efforts to design and synthesize more selective ruthenium-based olefin metathesis catalysts and more active ruthenium-based olefin metathesis catalysts. Investigation of different

catalysts' stabilities and efforts to design more stable catalysts lies outside of the scope of this thesis.⁶

There are three areas of selectivity that are current topics of interest for ruthenium-based olefin metathesis catalysts: enantioselectivity, diastereoselectivity (E/Z ratios), and chemoselectivity (selective reactions with differentially substituted olefins). The work described in this thesis has focused on the development of enantioselectivity in ruthenium systems. Chapter 2 describes the synthesis of ruthenium catalysts for enantioselective olefin metathesis. The application of these catalysts to asymmetric ring-closing metathesis is described in Chapter 3. The application of these catalysts to asymmetric cross and ring-opening cross metathesis is described in Chapter 4.

The development of more active ruthenium-based olefin metathesis catalysts is an area of ongoing research. It is widely accepted that there are two phases to the olefin metathesis catalytic cycle: initiation and propagation (Figure 1.2).⁷

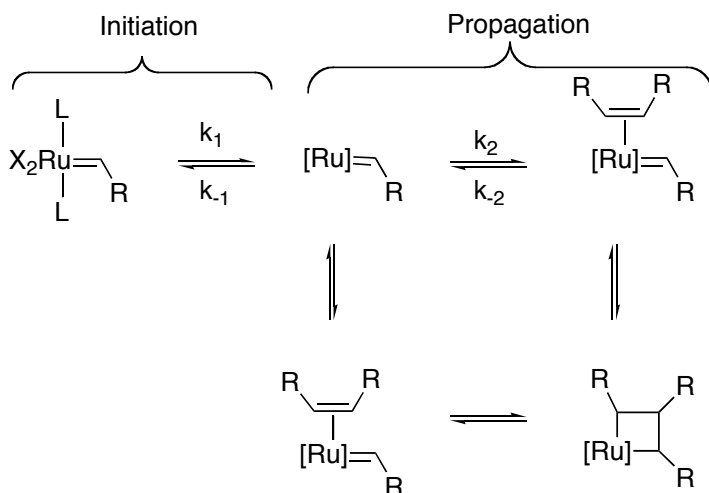


Figure 1.2. Catalytic cycle of olefin metathesis.

There are three methods to increasing the activity of the system: increasing the initiation rate (k_1) as that is the rate-limiting step, increasing the amount of catalyst that is

propagating (k_2/k_1), or expanding the scope of olefins that can react with the catalyst (k_2/k_2 for a class of olefins). Replacing one of the phosphine ligands of **2** with an NHC in **3** resulted in a 75-fold decrease in k_1 but a 1000-fold increase in the ratio k_2/k_1 .⁷ This decrease in k_1 has been offset by a great deal of successful research focused on increasing the initiation rates of NHC-containing catalysts.⁸ In addition, the use of NHC-containing catalysts expanded the substrate scope of ruthenium-catalyzed olefin metathesis, as, for the first time, electron deficient olefins such as acrylates were viable substrates.⁹ Nevertheless, continued expansion of the substrate scope remains essential as ruthenium-catalyzed olefin metathesis reactions with very hindered substrates remain challenging. Examples include: RCM and CM to form tetrasubstituted olefins, CM of olefins with bulky substitution at the allylic position, and polymerization of very sterically encumbered olefins. The design and synthesis of a family of ruthenium catalysts with increased activity for RCM to form tetrasubstituted olefins is described in Chapter 5.

¹ For recent reviews on olefin metathesis, see: (a) Grubbs, R. H. *Handbook of Metathesis*; Wiley-VCH: Weinheim, 2003. (b) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012. (c) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413.

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⁴ (a) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783. (b) Morgan, J. P.; Grubbs, R. H. *Org. Lett.* **2000**, *2*, 3153. (c) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953. (d) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247.

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⁶ Soon Hong has performed a great deal of work in this area, and his thesis should include a complete discussion of recent work on catalyst stability.

⁷ Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543 and references therein.

⁸ (a) Love, J. A.; Sanford, M. S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 10103. (b) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J., Jr.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791. (c) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.;

Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168. (d) Van Veldhuizen, J. J.; Garber, S. B.; Kingsbury, J. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 4954. (e) Randl, S.; Gessler, S.; Wakamatsu, H.; Blechert, S. *Synlett* **2001**, *3*, 430. (f) Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 9973. (g) Wakamatsu, H.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 794. (h) Wakamatsu, H.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2403. (i) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035.

⁹ Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783.