Chapter 1

Introduction

The olefin metathesis reaction is an elegant chemical transformation that entails the metal–carbene catalyzed cleavage and re-assembly of carbon–carbon double bonds. Although simple at first glance, this reaction can be applied in an enormous variety of synthetically useful permutations, including ring-closing metathesis (RCM), cross metathesis (CM), acyclic diene metathesis polymerization (ADMET), and ring-opening metathesis polymerization (ROMP) (Figure 1.1).

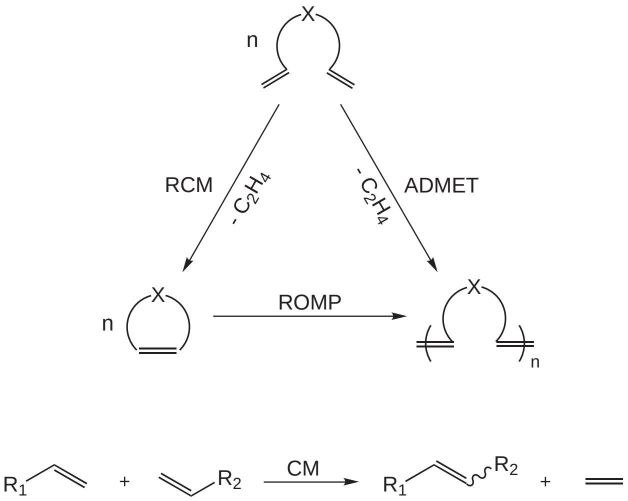

Figure 1.1

The field of olefin metathesis is currently in a period of renaissance, largely because of the success of well-defined ruthenium catalysts $(PCy_3)_2(Cl)_2Ru{=}CHPh$ (**1.1**)[1] and $(H_2IMes)(PCy_3)(Cl)_2Ru{=}CHPh$ (**1.2**; H_2IMes = 1,3-dimesityl-imidazolidine-2-ylidene).[2] The

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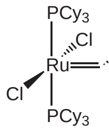
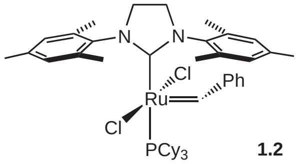
[1] Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100-110.
[2] Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953-956.

primary reasons for this success are the excellent functional group compatibility of ruthenium complexes, the relative ease with which they can be handled, and their wide range of catalytic activity.[3] In the past few years, the applications of ruthenium-based olefin metathesis catalysts have expanded to include the synthesis of molecules in organic, inorganic, biochemical, polymer, and materials chemistry.[4]



1.1



1.2

It is interesting to reflect on the origins of these developments. During the 1960s and 70s, olefin metathesis catalysts were usually multi-component systems that consisted of early transition metal salts and alkylating reagents.[5] Although these systems were limited in substrate scope, their catalytic activity was quite high, and this feature resulted in the commercialization of olefin metathesis (*e.g.*, in the SHOP and Phillips triolefin processes).[5] However, there were few advances in catalyst design until the isolation of the first metathesis-active metal–carbene complexes in the late 1970s. In particular, the Tebbe reagent $Cp_2Ti[(\mu\text{-}CH_2)(\mu\text{-}Cl)AlMe_2]$ (**1.3**)[6] and Schrock's molybdenum and tungsten alkylidene catalysts $(NAr)(OR)_2M{=}CHR'$ (**1.4**; M = Mo, W)[7] were responsible for revealing new vistas in olefin metathesis chemistry. For example,

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[3] Reviews of ruthenium-based olefin metathesis catalysts: (a) Grubbs, R. H.; Trnka, T. M.; Sanford, M. S. In *Fundamental Molecular Catalysis*, Yamamoto, A.; Kurosawa, H., Eds.; Elsevier, 2002, in press; chapter 4. (b) Sémeril, D.; Bruneau, C.; Dixneuf, P. H. *Adv. Synth. Catal.* **2002**, *344*, 585-595. (c) Frenzel, U.; Nuyken, O. *J. Poly. Sci. A: Poly. Chem.* **2002**, *40*, 2895-2916. (d) Herndon, J. W. *Coord. Chem. Rev.* **2002**, *227*, 1-58. (e) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18-29. (f) Dragutan, V.; Dragutan, I.; Balaban, A. T. *Platinum Metals Rev.* **2001**, *45*, 155-163. (g) Jafarpour, L.; Nolan, S. P. *J. Organomet. Chem.* **2001**, *617-618*, 17-27. (h) Dragutan, V.; Dragutan, I.; Balaban, A. T. *Platinum Metals Rev.* **2000**, *44*, 58-66. (i) Hafner, A.; van der Schaaf, P. A.; Mühlenbach, A. *Chimia* **1996**, *50*, 131-134.

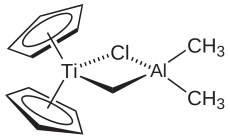
[4] Recent reviews of olefin metathesis applications: (a) Pederson, R. L.; Fellows, I. M.; Ung, T. A.; Ishihara, H. *Adv. Synth. Catal.* **2002**, *344*, 728-735. (b) Mecking, S.; Held, A.; Bauers, F. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 544-561. (c) Coates, G. W. *J. Chem. Soc., Dalton Trans.* **2002**, 467-475. (d) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3013-3043. (e) Tsuji, J. *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: Chichester, 2000; chapter 8. (f) Maier, M. E. *Angew. Chem., Int. Ed.* **2000**, *39*, 2073-2077. (g) Roy, R.; Das, S. K. *Chem. Commun.* **2000**, 519-529. (h) Jørgensen, M.; Hadwiger, P.; Madsen, R.; Stütz, A. E.; Wrodnigg, T. M. *Curr. Org. Chem.* **2000**, *4*, 565-588. (i) Yet, L. *Chem. Rev.* **2000**, *100*, 2963-3007. (j) Cook, G. R. *Curr. Org. Chem.* **2000**, *4*, 869-885. (k) Buchmeiser, M. R. *Chem. Rev.* **2000**, *100*, 1565-1604. (l) Grubbs, R. H.; Khosravi, E. and Davidson, T. A.; Wagener, K. B. In *Synthesis of Polymers: A Volume of the Materials Science and Technology Series*, Schlüter, A.-D.; Cahn, R. W.; Haasen, P.; Kramer, E. J., Eds.; Wiley-VCH: Weinheim, 1999; chapter 3, pp. 65-104 and chapter 4, pp. 105-122. (m) Zaragoza Dörwald, F. *Metal Carbenes in Organic Synthesis*; Wiley-VCH: Weinheim, 1999. Phillips, A. J.; Abell, A. D. *Aldrichimica Acta*, **1999**, *32*, 75-89. (n) Wright, D. L. *Curr. Org. Chem.* **1999**, *3*, 211-240. (o) Kingsbury, C. L.; Mehrman, S. J.; Takacs, J. M. *Curr. Org. Chem.* **1999**, *3*, 497-555.

[5] Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: London, 1997.

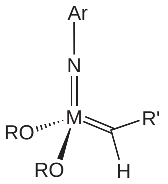
[6] (a) Grubbs, R. H.; Pine, S. H. *Comprehensive Organic Chemistry*, Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, Chapter 9.3. (b) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611-3613.

[7] (a) Schrock, R. R. *Tetrahedron*, **1999**, *55*, 8141-8153. (b) Schrock, R. R. In *Alkene Metathesis in Organic Synthesis*, Fürstner, A., Ed.; Springer: Berlin, 1998; pp 1-36. (c) Schrock, R. R. *The Strem Chemiker* **1992**, *14*, 1-14. (d) Feldman, J.; Schrock, R. R. *Prog. Inorg. Chem.* **1991**, *39*, 1-6. (e) Schrock, R. R. *Acc. Chem. Res.* **1990**, *23*, 158-165.

these complexes enabled the first living ROMP reactions, the first ROMP reactions with sterically hindered substrates, and the first RCM applications.[8]



1.3



1.4

However, the main drawback of **1.3** and **1.4** was one of limited substrate scope, caused by their oxophilic, early transition metal centers. Olefin metathesis catalysts composed of late transition metal salts, on the other hand, were characterized by low activity but high functional group tolerance, especially toward water and other protic solvents. These features led Grubbs and coworkers to re-investigate ruthenium catalyst systems and ultimately develop the first well-defined, ruthenium–carbene olefin metathesis catalyst in 1992.[9]

Since that time, a wide variety of ruthenium-based catalysts have been studied. The examples include **1.1**, **1.2**, bimetallic derivatives, Schiff-base complexes, vinylidenes, N-heterocyclic carbene (NHC) complexes, and isopropoxide-coordinated species, among others (Figure 1.2).[10,11] A number of *in situ* generated and solid-supported ruthenium catalysts have

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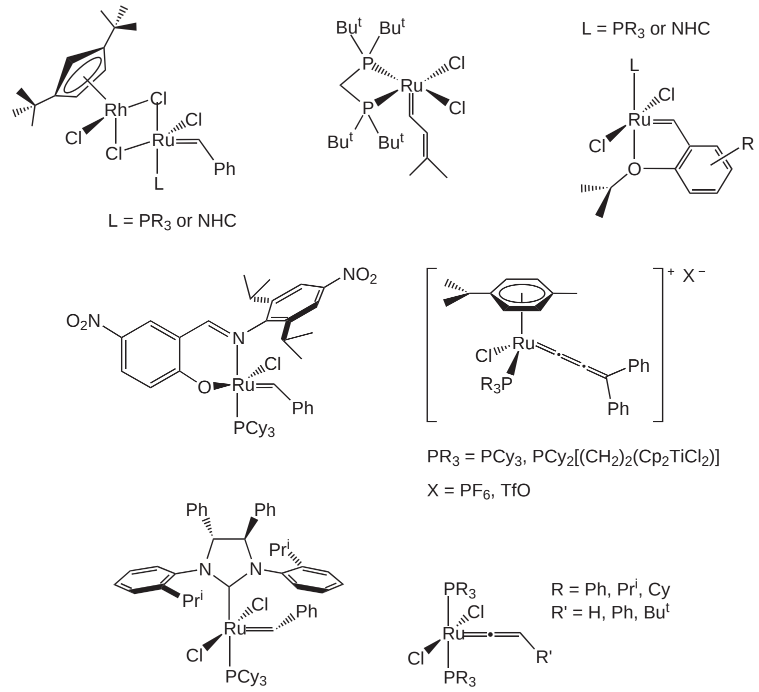
[8] (a) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 3800-3801. (b) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 7324-7325. (c) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426-5427. (d) Schrock, R. R.; Feldman, J.; Cannizzo, L. F.; Grubbs, R. H. *Macromolecules* **1987**, *20*, 1169-1172. (e) Gilliom, L. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1986**, *108*, 733-742.

[9] Nguyen, S. T.; Johnson, L. K.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 3974-3975.

[10] Examples from the Grubbs laboratory: (a) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225-3228. (b) Ulman, M.; Belderrain, T. R.; Grubbs, R. H. *Tetrahedron Lett.* **2000**, *41*, 4689-4693. (c) Lynn, D. M.; Mohr, B.; Grubbs, R. H.; Henling, L. M.; Day, M. W. *J. Am. Chem. Soc.* **2000**, *122*, 6601-6609. (d) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247-2250. (e) Sanford, M. S.; Henling, L. M.; Grubbs, R. H. *Organometallics* **1998**, *17*, 5384-5389. (f) Chang, S.; Jones, L.; Wang, C.; Henling, L. M.; Grubbs, R. H. *Organometallics* **1998**, *17*, 3460-3465. (g) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887-3897. (h) Wu, Z.; Nguyen, S. T. Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 5503-5511. (i) Nguyen, S. T.; Johnson, L. K.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 3974-3975.

[11] Examples from other research groups: (a) Denk, K.; Fridgen, J.; Herrmann, W. A. *Adv. Synth. Catal.* **2002**, *344*, 666-670. (b) De Clercq, B.; Verpoort, F. *Adv. Synth. Catal.* **2002**, *344*, 639-648. (c) Stüer, W.; Wolf, J.; Werner, H. *J. Organomet. Chem.* **2002**, *641*, 203-207. (d) Buchowicz, W.; Ingold, F.; Mol, J. C.; Lutz, M.; Spek, A. L. *Chem. Eur. J.* **2001**, *7*, 2842-2847. (e) Coalter, J. N.; Caulton, K. G. *New J. Chem.* **2001**, *25*, 679-684. (f) Fürstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem. Eur. J.* **2001**, *7*, 3236-3253. (g) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168-8179. (h) Katayama, H.; Urushima, H.; Nishioka, T.; Wada, C.; Nagao, M.; Ozawa, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 4513-4515. (i) Leung, W.-H.; Lau, K.-K.; Zhang, Q.-F.; Wong, W.-T.; Tang, B. *Organometallics* **2000**, *19*, 2084-2089. (j) Saoud, M.; Romerosa, A.; Peruzzini, M. *Organometallics* **2000**, *19*, 4005-4007. (k) van der Schaaf, P. A.; Kolly, R.; Kirner, H.-J.; Rime, F.; Mühlebach, A.; Hafner, A. *J. Organomet. Chem.* **2000**, *606*, 65-74. (l) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674-2678. (m) Weskamp, T.; Kohl, F. J.; Herrmann, W. A. *J. Organomet. Chem.* **1999**, *582*, 362-365. (n) Hansen, S. M.; Volland, M. A. O.; Rominger, F.; Eisenträger, F.; Hofmann, P. *Angew. Chem. Int. Ed.* **1999**, *38*, 1273-1276. (o) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791-799. (p) Weskamp, T.; Schattenmann, W. C.; Spiegler, M.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **1998**, *37*, 2490-2493.

been developed in addition to these well-defined, homogeneous catalysts.[12,13] Each of these catalysts has a distinctive reactivity profile, and even small changes in the ruthenium coordination sphere can have profound and largely unpredictable effects on catalytic activity, stability, and selectivity. For instance, compared to **1.1**, the diiodide derivative $(PCy_3)_2(I)_2Ru{=}CHPh$ exhibits enhanced initiation properties whereas **1.2** exhibits reduced initiation properties.[14] At this time, it is only possible to speculate about the origins of these effects.



L = PR_3 or NHC

L = PR_3 or NHC

PR_3 = PCy_3, $PCy_2[(CH_2)_2(Cp_2TiCl_2)]$

X = PF_6, TfO

R = Ph, Pr^i, Cy

R' = H, Ph, Bu^t

Figure 1.2

Thus, despite significant advances in the development of ruthenium-based catalysts for olefin metathesis applications, many aspects of their reactivity are poorly understood, and the "design" of new derivatives remains largely a trial-and-error endeavor. For these reasons, the

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[12] *In situ* generated examples: (a) De Clercq, B.; Verpoort, F. *Tetrahedron Lett.* **2001**, *42*, 8959-8963. (b) Sémeril, D.; Cléran, M.; Bruneau, C.; Dixneuf, P. H. *Adv. Synth. Cat.* **2001**, *343*, 184-187. (c) Jan, D.; Delaude, L.; Simal, F.; Demonceau, A.; Noels, A. F. *J. Organomet. Chem.* **2000**, *606*, 55-64. (d) Fürstner, A.; Ackermann, L. *Chem. Commun.* **1999**, 95-96. (e) Hamilton, J. G.; Rooney, J. J.; DeSimone, J. M.; Mistele, C. *Macromolecules* **1998**, *31*, 4387-4389.

[13] Solid-supported examples: (a) Jafarpour, L.; Heck, M.-P.; Baylon, C.; Lee, H. M.; Mioskowski, C.; Nolan, S. P. *Organometallics* **2002**, *21*, 671-679. (b) Kingsbury, J. S.; Garber, S. B.; Giftos, J. M.; Gray, B. L.; Okamoto, M. M.; Farrer, R. A.; Fourkas, J. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4251-4256. (c) Mayr, M.; Mayr, B.; Buchmeiser, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 3839-3842. (d) Nieczypor, P.; Buchowicz, W.; Meester, W. J. M.; Rutjes, F. P. J. T.; Mol, J. C. *Tetrahedron Lett.* **2001**, *42*, 7103-7105. (e) Nguyen, S. T.; Grubbs, R. H. *J. Organomet. Chem.* **1995**, *497*, 195-200.

[14] (a) Sanford, M. S.; Ulman, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 749-750. (b) Sanford, M. S., Love, J. A., Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543-6554.

objectives of the work described in this dissertation were (1) to further improve the properties of these ruthenium catalysts, and (2) to obtain a better understanding of how these catalysts operate.

As described in Chapters 2 and 3, the first problem was addressed by varying the ligand sphere within the $L_2X_2Ru{=}CHR$ framework. In particular, Chapter 2 explores the question of why the metathesis of directly functionalized olefins is such a challenging reaction. The properties of ruthenium carbene complexes with α-functionality reveal the reasons for this effect. Chapter 3 explores other ligand variations, such as L = phosphines, N-heterocyclic carbenes (NHCs), imidazoles, or pyridines, as well as derivatives that contain cyclic carbene ligands. The trends in catalytic activity, stability, and selectivity yield valuable information that allows ruthenium catalysts to be tuned for particular olefin metathesis applications. Chapter 4 addresses the issue of alkyne polymerization with ruthenium alkylidene complexes. This topic is explored through reactivity studies, which reveals why these complexes are largely ineffective in this transformation. Finally, Chapter 5 is concerned with the structure and bonding of metal–phosphine and –NHC complexes, which is of fundamental importance in understanding the widely varied properties of ruthenium alkylidene catalysts.