Chapter 1

Introduction

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Olefin (alkene) metathesis is a chemical reaction that involves the redistribution of carbon-carbon double bonds via their scission and reformation (Figure 1.1). Over the past 60 years, olefin metathesis has evolved from an unusual occurrence in petroleum distillation and cracking processes, to the standard method for the construction of new C-C double bonds. As such, olefin metathesis is now widely employed as a synthetic methodology in a variety of fields including synthetic organic chemistry, polymer and materials science, green chemistry, and biochemistry. The application of olefin metathesis to these fields has been facilitated by the development of a wide variety of increasingly advanced and well-defined catalysts tailored to suit these applications.

Early metathesis catalysts, first discovered in the 1950s, consisted of heterogeneous mixtures of tungsten (W) and molybdenum (Mo) oxides.[1] The subsequent discovery of stable metal carbenes[2] and their identification as metathesis active species[3] enabled the preparation of well-defined titanium (Ti), W, Mo, ruthenium (Ru), and rhenium (Re) catalysts (Figure 1.2). A variety of other metals in the transition metal block have exhibited metathesis activity, but they have not been explored to the same extent.[4] Our group focuses on the preparation, development, and study of Ru-based olefin metathesis catalysts.

Metathesis Reactions

The versatility of olefin metathesis is largely due to the diverse types of olefins that can be reacted in or formed by this reaction. These include terminal,

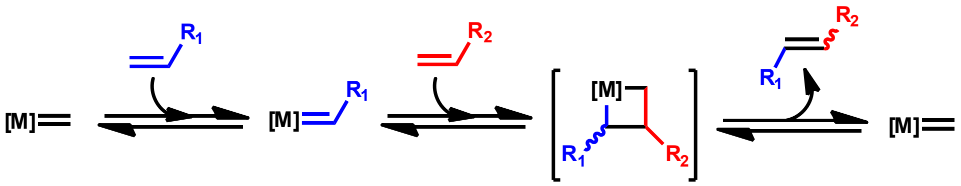

Figure 1.1. The olefin metathesis reaction

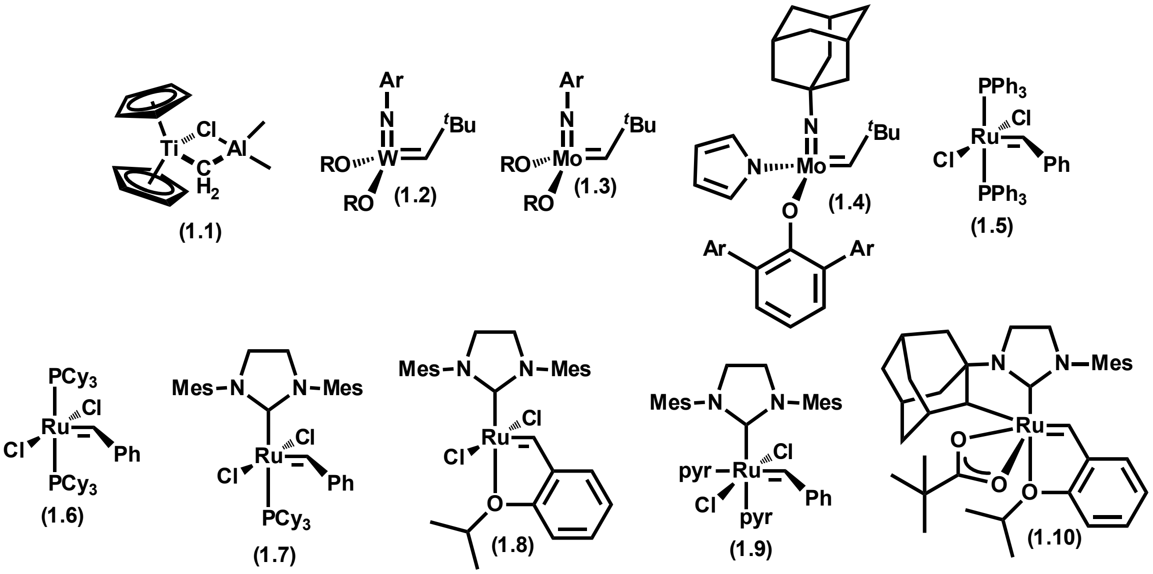

Figure 1.2. Common olefin metathesis catalysts. mes = 2,4,6-trimethylphenyl. ar = aryl. pyr = pyridine

internal, cyclic, macrocyclic, and polymeric olefins. In general, there are three major classes of metathesis reactions (Figure 1.3). For example, α,ω-dienes can undergo ring-closing metathesis (RCM) to form cyclic olefins. Strained cyclic or bicyclic olefins, such as norbornene, can undergo ring-opening metathesis polymerization (ROMP). Finally, cross-metathesis (CM), involves the intermolecular reaction of two terminal olefins to form a new internal olefin. These reactions are historically the most important and the most common, but several variations and combinations of ROMP, RCM, and CM are also known. For example, if the reaction concentration is high enough, α,ω-dienes will undergo *inter*molecular CM (instead of *intra*molecular

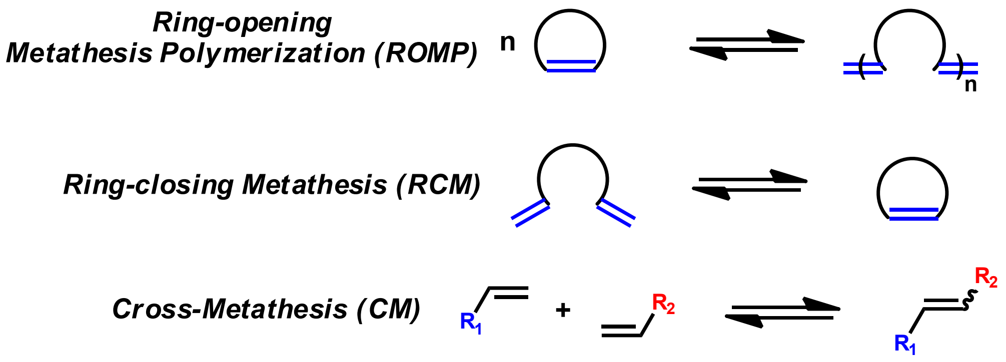

Figure 1.3. Common metathesis reactions

RCM) to form polymers in a process known as acyclic diene metathesis (ADMET). Similarly, when ROMP is performed in the presence of a large excess of terminal olefin, a ring-opening cross-metathesis reaction (ROCM) reaction may occur.

All metathesis reactions are thermodynamically controlled.[5] Thus, they require a driving force to give a single product. In the case of ROMP, the driving force is the release of ring-strain in the monomer. For RCM and CM, the driving force for reaction is the release of a volatile product (e.g., ethylene) or the formation of a more stable olefin. However, the thermodynamic product of a metathesis reaction is not always desired because a synthetic chemist may wish to form the thermodynamically disfavored *cis*- or *Z*-olefin via metathesis. The formation of kinetic products, such as *Z*-olefins, has persisted as a significant challenge for olefin metathesis since its discovery.

Mechanism and Mechanistic Intermediates in Ru-Based Olefin Metathesis

The general mechanism of olefin metathesis, as proposed by Chauvin and Herrison, involves the formation of a metallocyclobutane from a metal alkylidene and subsequent cycloreversion to generate a different metal alkylidene

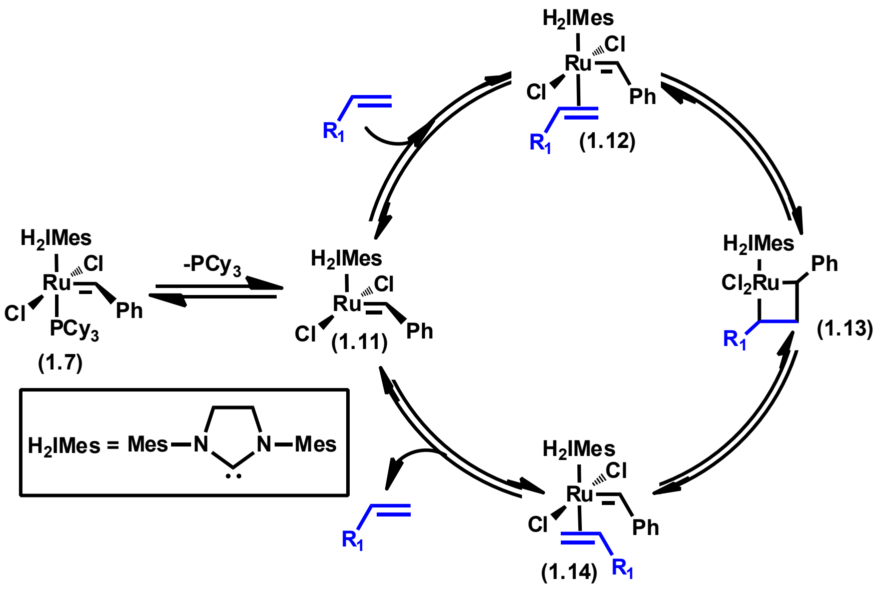

Figure 1.4. Catalytic cycle for Ru-based olefin metathesis including important intermediates

and an olefin product (Figure 1.4). All metathesis catalysts proceed through this mechanism, including Ru-based catalysts. However, there are a number of specific factors and reactions that change depending on the construction of the catalyst.

Prototypical Ru-based metathesis catalysts are 16 electron (e^-) Ru(II) species that require ligand dissociation in order to access the 14 e^- intermediate required for ruthenacyclobutane formation. Kinetic studies have established that phosphine dissociation in catalysts such as **1.7** is rate-determining.[6] For catalysts with chelating alkylidenes, either oxygen dissociation or olefin binding is rate-determining depending on the nature of the catalyst and reacting olefin.[7] Although catalyst initiation is well-understood, very little is known about the Ru-olefin (**1.12**) and ruthenacycle species (**1.14**) in the metathesis catalytic cycle.

Of particular interest is the geometry of the ruthenacyclobutane intermediate and whether it is primarily side-bound (*cis* to the NHC) or bottom-bound (*trans* to the NHC). Studies on model complexes intended to mimic typical reaction intermediates have provided evidence for side-bound ruthenacycles.[8] On the other hand, the majority of theoretical and experimental studies on actual metathesis-active species support a bottom-bound ruthenacycle.[9,10] Based on this discrepancy, it is likely that the difference in energy between side-bound and bottom-bound structures is very small and dependent on the exact reaction conditions. The study of these structures remains important in order to resolve the exact nature of the intermediate. Moreover, greater understanding of this issue would facilitate improvements in selectivity during olefin metathesis.

Ligand Effects

Like many organometallic catalysts, the development of more efficient olefin metathesis catalysts has been facilitated by the preparation of new ligand frameworks. The majority of Ru-based catalysts have the general formula $X_2L_2Ru{=}CHR$ where X and L represent anionic and neutral donors, respectively. The first well-defined Ru-based catalysts was $Cl_2(PPh_3)_2Ru{=}CHPh$ (**1.5**), which showed good reactivity for the polymerization of norbornene and other strained monomers.[11] A significant improvement in catalyst activity was discovered when the PPh_3 in **1.5** was replaced with PCy_3 to generate **1.6**.[12] Both **1.5** and **1.6** were less reactive than their Mo counterparts (**1.3**), but demonstrated an impressive stability towards both dioxygen (O_2) and water that enabled their use on the benchtop without the need for an inert atmosphere.

The next major advance in catalytic activity occurred when one PCy_3 ligand in **1.6** was replaced with an N-heterocyclic carbene (NHC) ligand to yield complex **1.7**.[13] With the NHC ligand, catalyst **1.7** displayed activities comparable to Mo- and W-based catalysts. The subsequent exchange of the other phosphine in **1.7** with a chelating ether moiety resulted in catalyst **1.8**, which possessed enhanced stability.[14] It is also worth noting that the PCy_3 in **1.7** has also been replaced with pyridine to prepare a fast initiating catalyst (**1.9**) that is exceptional at catalyzing ROMP.[15] In addition to improving catalyst reactivity, the use of an NHC ligand has enabled the rigorous study of steric and electronic effects on Ru-based metathesis catalysts. Along these lines, a wide variety of catalysts containing both traditional (e.g., substituted, unsaturated) and relative exotic NHCs (e.g., abnormal, cyclic alkyl amino carbene) have been prepared and studied.[16]

Recently, a new class of Ru-based catalysts, formed via carboxylate-induced C-H activation of the NHC ligand, has emerged (**1.10**).[17] These catalysts have displayed remarkable kinetic selectivity for the selective formation of *Z*-olefins and rival their Mo- and W-based counterparts in both activity and selectivity. The C-H activated catalysts also exhibit several interesting reactivity trends that will make them interesting to study for years to come.

Future Outlook

A convincing argument could be made that the continued development of Ru-based and other olefin metathesis catalysts is no longer necessary. Indeed, researchers have developed a number of ingenious methods for adapting the current ‘family’ of catalyst to their specific needs. However, while certain fields may no longer require catalysts that are more stable or more active, the development of such catalysts has facilitated the proliferation of the metathesis methodology into other synthetic disciplines. In other words, there will always be a need for new catalysts in niche, but important applications, many of which are only starting to be explored.

One example of a new application is *Z*-selective olefin metathesis, and new, selective olefin metathesis catalysts based on Mo, W, and Ru have only recently been reported. The development of these catalysts has finally enabled the preparation of *Z*-olefins using metathesis. Despite this progress, significant improvements in both catalytic activity and selectivity are necessary for these catalysts to become industrially relevant. Moreover, mechanistic studies focused on catalyst stability and the origin of Z-selectivity will be essential to developing improved catalysts, just as they were in the development of previous generations of metathesis catalysts.

New catalysts for use in polymer synthesis and materials science will also be required. The importance of metathesis in these areas has been demonstrated by its inclusion as the basis for self-healing materials,[18] as a method for the facile preparation of polymer photonic crystals[19] and the development of advanced polymer composites.[20] Some of these applications require extremely fast initiating and active catalysts while others need slow, but stable catalysts. Clearly, one catalyst is not suitable for all materials science applications. The development of new metathesis catalysts has traditionally focused on the needs of synthetic organic chemists, but many of these catalysts are not suited to polymer applications. Therefore, the preparation of new catalysts with previously neglected attributes such as enhanced stability and slow initiation may prove beneficial to the materials science community.

A final area where the development of new catalysts can make an impact is in the industrial use of metathesis in processes such as ethenolysis. Compared to other metathesis applications, ethenolysis is extremely difficult since it requires a catalyst that is both very stable and kinetically selective. Despite this challenge, the results in this thesis hint that an improved understanding of degenerate metathesis combined with the knowledge of the factors governing catalyst stability will facilitate the development of new catalysts for industrial-scale ethenolysis.

In conclusion, metathesis is among the most powerful methodologies for the preparation of new C-C bonds. Thus, the development of new catalysts with improved activity, selectivity, and stability will continue to expand the metathesis methodology into new areas of chemistry while rewarding the students and postdoctoral fellows who invest in this field.

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