OLEFIN METATHESIS
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Our goal is to create a comprehensive book that can be an everyday reference for synthetic chemists, with no prerequisite deep knowledge in inorganic and coordination chemistry, but at the same time providing the experts with a contemporary view on the theory and methods in the flourishing field of modern olefin metathesis.

The book comprises two major parts: the first one is devoted to the applications of metathesis (Targets), while the second one describes the metathesis Tools.

The most important types of the olefin metathesis reaction (cross metathesis (CM), ring-closing metathesis (RCM), enyne metathesis, ring-opening metathesis polymerization (ROMP), tandem processes, etc.) have been described in the first part of the book. This part also presents a short selection of the key applications of this methodology, for example, in the total synthesis of natural compounds, in the preparation of macromolecules and polymers, in medicinal chemistry, and in the conversion of renewable materials. The goal behind this part of the book is to present a detailed, yet clear description of all important flavors of the metathesis reaction.

The second part of the book describes the tools. A series of chapters introduce the most important classes of metal complexes that are active in metathesis, creating the user’s guide to the galaxy of known olefin metathesis catalysts. The same attention is paid to optimization of the reaction conditions, including discussion on effects of the solvent and additives, methods of catalysts immobilization and recovery, purification of the products, computational methods, and so on. This part of the book is used exactly similarly to the famous “The Hitch-Hiker’s Guide to the Galaxy,” a fictional travel guide, invented by the writer Douglas Adams. With “the words Don’t Panic inscribed in large friendly letters on its cover”(1), the second part of the book allows even the inexperienced end-user to select the most optimal catalyst and conditions for his or her important metathesis project easily and effectively.

I am delighted with the list of authors who have agreed to contribute, and I am honored to act as the editor. All chapters collected in this book come from the leading experts and practitioners in the area and nicely highlight the aspects mentioned above. I would like to thank all the authors for their excellent contributions. My personal wish is that the reader will savor the reading of this book as much as I personally enjoyed reading all chapters and editing the volume.

I want to give a special thanks to Polish artist, Ms. Katarzyna Felchnerowska (Effe.Fineart) who prepared the beautiful cover picture, presenting her personal idea of olefin metathesis—a change-your-partners dance (2). Last, but certainly not least, I want to thank the members of my research group who have reviewed the text at every stage of the editing process.

Altogether, I hope that this handy, one-volume book will take its common place on the desks and benches of researchers working in academic laboratories as well as in the industry.

Enjoy reading!

Karol Grela

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PART I

APPLICATIONS OF OLEFIN METATHESIS REACTIONS
SECTION 1

INTRODUCTION
OLEFIN METATHESIS REACTIONS: FROM A HISTORICAL ACCOUNT TO RECENT TRENDS

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1.1 INTRODUCTION

Metathesis (1–5) occupies a central place in the synthesis of complex organic molecules and polymers, and the major problems concerning the catalysts have been solved, including the presence of various functional groups in the organic substrates. Unlike palladium catalysis of cross carbon–carbon bond formation that is the other breakthrough in the formation of organic skeleton architectures, the metathesis reactions do not consume stoichiometric amounts of base, producing stoichiometric amounts of salts as wastes. In this sense, the metathesis reactions belong to the field of green chemistry, saving a number of steps in total syntheses and avoiding the handling and production of inorganic wastes. The discovery of homogeneous catalysis by Osborn and Wilkinson (6), allowing the hydrogenation of olefins, and its efficient asymmetric version by Kagan (7) considerably enhanced the possibilities of bringing about high selectivity and approaching a perfect knowledge of the molecular mechanisms leading to improvements and optimization. Thus, after the pioneering research of American industrial chemists in the 1960s, a significant advance in metathesis chemistry has been the mechanistic insight of Yves Chauvin in the early 1970s in disentangling the “black box” and the intense academic research by organometallic chemists at the end of the twentieth century (8), in particular by the groups of Robert Grubbs at Caltech and Richard Schrock at MIT in their quest for transition-metal-alkylidene (or benzylidene) and alkylidyne metathesis catalysts. Therefore, in this historical chapter, we wish to underline the role of the development of ideas and research efforts that have led to a success story in the advancement of metathesis chemistry and its applications. This chapter also includes examples of the most recent and major developments and applications of the various metathesis reactions, with emphasis on catalyst design and sustainable chemistry.

1.2 THE METATHESIS REACTIONS: EXCHANGES OF CARBENES AND CARBYNES

The word metathesis comes from the Greek μεταβεσίς that means transposition. Metathesis of ions between two ion pairs is a long-known example of metathesis in which two

\[ A^+ B^- + C^+ D^- \rightleftharpoons A^+ D^- + C^+ B^- \]  (1.1)

Likewise, the exchange of the two carbenes of an olefin with those of another olefin molecule (Eq. 1.2) was first called olefin metathesis by Calderon (9) in 1967, but this reaction requires a catalyst.

\[ 2 \begin{array}{c}
  R_1 \end{array} \begin{array}{c}
  R_2 \\
  R_1 \\
  R_2 \\
  R_1 \\
  R_2 \\
\end{array} \rightleftharpoons \begin{array}{c}
  [\text{cata}] \\
  R_1 \end{array} \begin{array}{c}
  R_2 \\
  R_1 \\
  R_2 \\
  R_1 \\
  R_2 \\
\end{array} + \begin{array}{c}
  R_1 \end{array} \begin{array}{c}
  R_2 \\
  R_1 \\
  R_2 \\
  R_1 \\
  R_2 \\
\end{array} \]  (1.2)

The principle is extended to the exchange of the two carbynes of alkyne molecules

\[ 2 \begin{array}{c}
  R_1 \end{array} \begin{array}{c}
  C \equiv R_2 \\
  C \equiv R_1 \\
  C \equiv R_2 \\
  C \equiv R_1 \\
  C \equiv R_2 \\
\end{array} \rightleftharpoons \begin{array}{c}
  \text{cata} \\
  R_1 \end{array} \begin{array}{c}
  C \equiv R_2 \\
  R_1 \\
  C \equiv R_2 \\
  R_1 \\
  C \equiv R_2 \\
\end{array} + \begin{array}{c}
  R_1 \end{array} \begin{array}{c}
  C \equiv R_2 \\
  R_1 \\
  C \equiv R_2 \\
  R_1 \\
  C \equiv R_2 \\
\end{array} \]  (1.3)
The metathesis reactions are under thermodynamic control, which means that the reactions of Eqs 1.2 and 1.3 present the inconvenient of being equilibrated. The problem is usually solved by using terminal olefins that produce gaseous ethylene as one of the metathesis products, which displaces the reaction toward the metathesis products. For alkyne metathesis, terminal alkyne metathesis is possible (see Section 1.15) but of little use due to competitive alkyne polymerization, so methyl-terminated alkynes are used for metathesis, which produces 2-butyne that is also removed according to the same principle.

1.3 THE EARLY DAYS OF OLEFIN METATHESIS IN AMERICAN INDUSTRY

The uncatalyzed reaction of propene upon heating at 852°C had been reported in 1931 by Schneider and Fröhlich (10) to give very low amounts of ethene and 2-butenes among other products, but the publication remained ignored for a long time. Ziegler and Natta’s discoveries of ethylene and propylene polymerization in 1953 induced considerable research interest in olefin polymerization reactions and their mechanisms. The first catalyzed metathesis reactions were reported in the late 1950s when industrial chemists at Du Pont, Standard Oil and Phillips Petroleum (H. S. Eleuterio, E. F. Peters, B. L. Evering, R. L. Banks, and G. C. Bailey) reported that propene led to ethylene and 2-butenes when it was heated with molybdenum [in the form of the metal, oxide, or (Mo(CO))₆ on alumina (Fig. 1.1)] (11–16).

The first polymerization of norbornene by the system WCl₆/AlEt₂Cl was independently reported in 1960 by Eleuterio (11,15) and by Truett et al. (13), but it was recognized only in 1967 by Calderon (9,17) at Goodyear that the polymerization of cyclic alkenes to polyalkenemers and the disproportionation of acyclic alkenes were the same type of reaction, the metathesis. The following year, labeling experiments by Calderon (9,17) at Goodyear and Mol (18) in Amsterdam confirmed this key finding.

1.4 UNSUCCESSFUL ATTEMPTS TO SOLVE THE MECHANISTIC PUZZLE

The first mechanistic suggestion to solve the mechanistic puzzle came in 1967 from Bradshaw et al. (19) who proposed a four-centered cyclobutane–metal intermediate. This hypothesis was supported the following year by Calderon (20). No other hypothesis appeared in the United States for three years, and this mechanism seemed to be adopted as being “conventional” by the metathesis community in the United States. Yet, cyclobutanes are not produced by metathesis, and they are not metathesis substrates either. Other mechanistic hypotheses by American chemists appeared only in the early 1970s. In 1971, the brilliant organometallic chemist Pettit (21,22), who had generated the first transition-metal

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**History of the olefin metathesis reactions**

- Ethylene and 2-butenes are found in small amounts upon heating propene at 852°C: Schneider and Fröhlich (1931)
- Heterogeneous metathesis catalysts: M(CO)₆ (M = Mo or W) on alumina or silica, or Re₂O₇ (150–500°C): Eleuterio (1956) and Bank (1964)
- Chauvin mechanism: metal–alkylidene + olefin and metallacyclobutane intermediate, 1971
- First stoichiometric metathesis reaction between a metal–carbene and an olefin, Casey (1974)
- First isolated metal–alkylidene complex, [Ta=CHBu(CH₂Bu)₃]: Schrock (1974)
- First catalytic metathesis reaction using a unimolecular catalyst, [LaTa=CHBu]: Schrock (1980)
- First unimolecular ruthenium–carbene metathesis catalyst, [Ru=C=CHPh(PR₃)₂Cl₂]: Grubbs (1992)
- First ruthenium–benzylidene metathesis catalyst: [Ru=C=CHPh(PCy₃)₂Cl₂]: Grubbs (1995)
- Robust isopropoxybenzylidene Ru catalysts: Hoveyda, Blechert (with NHC), Grela (with NO₂), 2000–2002

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**Figure 1.1** Dates of the history of olefin metathesis.
methylene species \([\text{Fe}(\eta^5-C_5H_5)(\text{CO})_2(=\text{CH}_2)]\text{BF}_4\), suggested the possibility of a tetra(methylene)metal intermediate in which the four methylene units were bonded to the transition metal (23–25). Double oxidative addition to a transition-metal center is not possible, however (24,25). Grubbs (26) proposed rearranging metallocyclopentane intermediates and cyclobutane complexed to a carbene (27). Neither of the mechanisms mentioned above (Fig. 1.2) fit the data, and the olefin metathesis mechanism remained rather mysterious in the United States until the mid 1970s.

1.5 THE CHAUVIN MECHANISM: A METATHESIS DANCE

Chauvin from the Institut Français du Pétrole, had three key findings in mind when he envisaged the mechanism of olefin metathesis: the report of Fischer (28) on the synthesis of a tungsten–carbene complex, \([\text{W}(\text{CO})_5\{\text{C}(\text{CH}_3)(\text{OCH}_3)\}]\), that of Natta (29) on the polymerization of cyclopentene by ring-opening catalyzed by a mixture of \(\text{WCl}_6\) and \(\text{AlEt}_3\), and that of Banks and Bailey (14) on the formation of ethylene and 2-butene from propene catalyzed by \([\text{W}(\text{CO})_6]\) on alumina. Consequently, Chauvin and his student Hérisson published their proposition of metathesis mechanism in 1971 (Scheme 1.1) (30).

![Scheme 1.1](image-url)  
Scheme 1.1 Linear representation of the Chauvin mechanism (including the degenerate metathesis steps).
The Chauvin mechanism involves a metal–carbene species (or more precisely metal–alkylidene), the coordination of the olefin onto the metal atom of this species, followed by the shift of the coordinated olefin to form the metallocyclobutane intermediate, and finally the topologically identical shift of the new coordinated olefin in the metallocyclobutane in a direction perpendicular to the initial olefin shift. This forms a metal–alkylidene to which the new olefin is coordinated, then liberated. This new olefin contains a carbene from the catalyst and the other carbene from the starting olefin. The new metal–alkylidene contains one of the two carbenes of the starting olefin and it can re-enter a catalytic cycle of the same type as the first one (Schemes 1.1 and 1.2).

In fact, depending on the orientation of the coordinated olefin, the new catalytic cycle can give two different metallacyclobutenes, one leading to the symmetrical olefin and the other leading to the starting olefin. This latter cycle is said to be degenerate olefin metathesis. Thus, the catalytic cycles alternatively involve both metal–alkylidene species resulting from the combination of the metal with each of the two carbenes of the starting olefin (Scheme 1.1).

When the Chemistry Nobel prize was announced on October 5, 2005, Chauvin’s metathesis mechanism was compared in a video to a dance in which couples exchange partners, which represents the two carbene fragments of the olefin. The dancers cannot exchange their partner directly, but they have to do the exchange by coupling with a master of ceremony that is the metal center. The master of ceremony also has a partner and, with the entering couple they form a circle so that the master of ceremony can exchange partners within the circle by taking a new partner from the couple. Then with his new partner, he can go to another couple for another exchange, and so on (31).

Chauvin and Hérisson not only suggested the metallacyclobutane mechanism, but also published several experiments to confirm it. For instance, they reported that reaction of a mixture of cyclopentene and 2-pentene led to C-9, C-10, and C-11 dienes in the ratio 1 : 2 : 1. Also, the reaction of a mixture of cyclooctene and 2-pentene led almost exclusively to the C-13 product. The latter reaction, but not the first one, was compatible with Calderon’s mechanism. In 1973 and 1976, Chauvin (32,33) published other results showing that the mixture of WCl₆ + MeLi catalyzes the formation of propene by reaction of 2-butene, which was proposed to proceed via methylation of tungsten, followed by the α-elimination in the tungsten–carbon bond of W–CH₃ to form a W(=CH₂)(H) species, then metathesis. Here again, Chauvin’s intuition was remarkable, because at that time, σ-bond metathesis in d⁰ meta-alkyl complexes, that is the only available mechanism to activate such α-C–H bonds, was unknown and was disclosed only more than a decade later by the groups of Watson (Lu) (34), Bercaw (Sc) (35), and Marks (Th) (25,36,37).

The first recognition of Chauvin’s valuable mechanism together with an elegant confirmation came from Casey and Burkhardt (38) when they reported that the carbene complex

Scheme 1.2  Cyclic representation of the Chauvin metathesis mechanism.
[W(CO)₅(=CPh₂)] reacted with isobutene to form a new olefin, 1,1-diphenylethene (Eq. 1.4), as the major product and that the same complex reacted with H₂C=Ĉ(OCH₃)Ph to form 1,1-diphenylethene and the metal–carbene complex [W(CO)₅(=C(OCH₃)Ph)] (Eq. 1.5), just as predicted in the Chauvin mechanism.

\[
\begin{align*}
\text{H}_2\text{C} &= \text{C} = \text{CH}_2 \\
\text{H}_3\text{C} &= \text{C} = \text{CH}_2 \\
\text{H}_3\text{C} &= \text{C} = \text{CH}_2 \\
\text{H}_3\text{C} &= \text{C} = \text{CH}_2
\end{align*}
\]

Later, labeling experiments by the groups of Grubbs and Katz (39–41) demonstrated that alkenes underwent non-pairwise exchange as required by the Chauvin mechanism. In particular, Grubbs (39) showed that a mixture of 1,7-octadiene and its analog that was deuterated on both methylene termini underwent metathesis to yield a statistical mixture of d₀-, d₂-, and d₄-ethylene, and that d₀- and d₄-ethylene were not scrambled after their formation. At that point, however, the actual catalytically active species was unknown, because the precatalysts used were 18-electron metal–carbene complexes such as [W(CO)₅(=CPh₂)] or [W(CO)₅(C(OMe)Ph)] or eventually metal precursors that did not contain a carbene ligand (38–41). Such complexes cannot bind olefins because the metal valence electron shell does not rise to 20 electrons; hence some decomposition of these pre-catalysts had to occur. Casey had nicely shown that the decomposition was partly limited to a single carbonyl ligand with the complex, but also half of the starting material decomposed. The second complex that was sometimes used by Katz is more problematic, because carbenes bearing a heteroatom are, like CO itself, singlet carbenes. Thus, contrary to common usage, a double bond between this carbene and the metal should not be used in Fischer-type carbene complexes (28) such as this one (in the same way as the representation of the metal–carbonyl bond that is not written as M=Ĉ=O). Accordingly, we now know that the Fisher-type metal–carbene complexes are poor metathesis pre-catalysts, and that good tungsten olefin metathesis catalysts systematically have a high oxidation state (4).

### 1.6 The Importance of the Chauvin Mechanism for Overall Organometallic Catalysis

Chauvin’s mechanism introduced several new ideas. First, he proposed a metal–carbene complex to initiate the catalysis of the metathesis reaction. This idea first suggested that one could just synthesize unsaturated metal–alkylidene complexes (i.e., with 16 valence electrons on the metal or less) and let them react as catalysts or pre-catalysts with olefins to carry out the metathesis reaction. Of course, many authors later engaged in such research directions, first delineated by Chauvin. The induction time was long, however. Relatively few chemists became interested in such a route in the first half of the decade following Chauvin’s proposal.

The second key point mentioned above was the explanation of the “black box” of the American industrial chemists: a d⁰ metal–alkyl complex formed using such a mixture undergoes the formation of a metal–methylene or metal–alkylidene species that serves as a catalyst for alkene metathesis. For that purpose, Chauvin included in his metathesis mechanism the crucial proposition of an α-H elimination, a pioneering idea that was reactivated and rationalized by its σ-bond mechanism only much later.

Another very important aspect of the Chauvin mechanism concerns the intermediacy of the metallacyclobutane. Such metallocyclobutane complexes are sometimes stable, and some stable metallacyclobutenes have indeed been shown to be involved in metathesis. Elegant studies by Grubbs’ group in 1980 showed that Tebbe’s complex [Cp₂Ti(CH₂)(ClAlMe₂)], reported in 1978 (42), reacted with olefins in the presence of dimethylaminopyridine to give titanacyclobutenes that slowly catalyze metathesis and could be used to identify all the intermediates in olefin metathesis (43–45).

Chauvin’s mechanism applies to the whole range of olefin metathesis reactions, including cross metathesis (CM), ring-closing metathesis (RCM), acyclic diene metathesis polymerization (ADMEP), ring-opening metathesis polymerization (ROMP), enyne metathesis (EYM), and ring-opening cross metathesis (ROCM) (Fig. 1.3) (1–4).

Finally, it is possible to represent a generalization of the metallosquare formed by the shift of the olefin coordinated to the metal in the metal–alkylidene species (25). The metallosquare is not only involved as an intermediate or transition state in alkene metathesis, but also in many other catalytic organometallic mechanisms. Indeed, the metathesis of alkynes and the metathesis polymerization of cycloalkenes and alkynes formulated by Katz (41) are completely analogous. Moreover, it is possible to represent by a metallo-square scheme the mechanisms of σ-bond metathesis and β-elimination. Scheme 1.3 gathers together the different organometallic reactions involving a metallo-square (that can eventually have puckered shapes).
(a) Cross Metathesis (CM)

(b) Ring Closing Metathesis (RCM)

(c) Acyclic Diene Metathesis Polymerization (ADMEP)

(d) Ring Opening Metathesis Polymerization (ROMP)

(e) Enyne Metathesis (EYM)

(f) Ring-Opening Cross Metathesis (ROCM)

Figure 1.3 Various types of olefin metathesis reactions (all proceeding according to the Chauvin mechanism).

1.7 SCHROCK’S HIGH OXIDATION STATE ALKYLIDENE AND ALKYLIDYNE COMPLEXES

From the middle of the nineteenth century to the middle of the twentieth century, chemists believed that metal–alkyl compounds were intrinsically unstable, because of the supposedly too low energy of the metal–carbon bond. Wilkinson (46–48) then synthesized stable binary metal–alkyl complexes that did not contain β-hydrogen, showing that this instability was in fact kinetic, due to β-H elimination, because chemists had been trying to make binary metal–ethyl complexes. Organometallic chemists could then synthesize a whole series of thermally stable binary (and other) metal–alkyl complexes with alkyl groups lacking β-hydrogens, such as methyl, benzyl, neopentyl, trimethylsilylmethyl, and mesityl, even if the metal had less than 18 valence electrons in the valence shell (47,48). Such binary metal–poly(alkyl) complexes have indeed a low number of valence electrons in conflict with the 18-electron rule (49).

Richard Schrock was a PhD student at Harvard of John Osborn, who had been a PhD student of Geoffrey Wilkinson, who was at Imperial College, London, after Harvard had turned down his promotion for tenure. The influence of Wilkinson on his scientific grandson Schrock is seen clearly. Also inspired by Schmidbauer’ synthesis of pentaalkyl phosphorous and arsenic derivatives, Schrock, then at Du Pont, synthesized [TaMe5], [Ta(CH2Ph)5] (47) and tried to synthesize [Ta(CH2CMe3)5], which, analogously, would not contain β-hydrogens and thus, according to this principle, should have been stable. An α-elimination reaction occurred, however, upon attempting to coordinate the fifth neopentyl group, which produced one mole of neopentane and led to the isolation of the first stable metal–alkylidene complex, [Ta(CH2CMe3)3(=CHCMe3)] that was reported in 1974 (Scheme 1.4) (50).

Schrock’s group subsequently showed that the α-elimination reaction was quite general when the coordination sphere became crowded in these Ta and Nb complexes. This yielded a rich family of high oxidation state Ta and Nb alkylidene complexes in which the carbenic carbon is nucleophilic, somewhat resembling phosphorus ylids (51,52). At the time of this finding, the detailed mechanism of this reaction was unknown, but as stated above, the σ-bond metathesis that takes the α-elimination reaction into account was recognized 8 years later (34–37). Neither the 18-electron Fischer-type metal–carbene complexes (see above) nor the 10-electron Schrock-type Ta- or Nb-alkylidene complexes gave olefin metathesis upon
Square schemes for the transformations of single, double, and triple bonds

<table>
<thead>
<tr>
<th>Reaction Type</th>
<th>Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>4e: σ-bond metathesis</td>
<td><img src="image" alt="4e Scheme" /></td>
</tr>
<tr>
<td>6e: olefin insertion</td>
<td><img src="image" alt="6e Scheme" /></td>
</tr>
<tr>
<td>8e: olefin metathesis</td>
<td><img src="image" alt="8e Scheme" /></td>
</tr>
<tr>
<td>10e: alkyne polymerization</td>
<td><img src="image" alt="10e Scheme" /></td>
</tr>
<tr>
<td>12e: alkyne metathesis</td>
<td><img src="image" alt="12e Scheme" /></td>
</tr>
</tbody>
</table>

**Scheme 1.3** Square schemes involved in the mechanisms of catalytic organometallic reactions (the metallosquares can eventually have puckered shapes).

**Scheme 1.4** σ-bond metathesis mechanism in the formation of Schrock’s first neopentylidene complex.
reaction with olefins, however, because the metallocyclobutane intermediates gave other products. Fischer-type metal–carbene complexes react with some olefins to give cyclopropanes eventually (but not always) by reductive elimination of intermediate metallacyclobutanes (53), whereas metallacyclobutanes resulting from the reaction of olefins with Schrock-type complexes gave \( \beta \)-H elimination, because they had less than 18 electrons in the Ta valence shell (Scheme 1.5). The metal–alkenyl hydride species formed in the latter case gave reductive elimination. Then, the free coordination sites allowed reaction with 2 mol of olefins giving tantalacyclopentane intermediate that also underwent \( \beta \)-H elimination followed by reductive elimination to yield for instance 1-butene, when the olefin was ethylene. The metal species thus catalyzed olefin dimerization. Interestingly, Chauvin (54, 55) also discovered extremely efficient and selective titanium-based olefin dimerization catalysts that are used industrially. In 1975, Schrock (56) also synthesized at Du Pont the first stable transition-metal–methylen complex, \([\text{TaCp}_2(\text{CH}_3)(=\text{CH}_2)]\) by deprotonation of the cationic Ta-methyl precursor \([\text{TaCp}_2(\text{CH}_3)_2][\text{BF}_4]\), and this methylen complex was characterized \textit{inter alia} by its X-ray crystal structure.

It was only in 1980 that Schrock’s group at MIT reported a tantalum–alkylidene complex, \([\text{Ta} (=\text{CH}-\text{t-Bu})(\text{Cl})(\text{PMe}_3)(\text{O-t-Bu}_2)]\), 1 (Fig. 1.4, also Nb and W complexes), that catalyzed the metathesis of \( \text{cis}-2 \)-pentene (57).

After Casey’s finding in 1974 and stereochemical arguments from the Grubbs and Katz groups, this provided another evidence for Chauvin’s mechanism of olefin metathesis with well-defined high oxidation state alkylidene complexes, almost a decade after Chauvin’s proposal. The reason that these complexes catalyzed the metathesis reaction, whereas the other members of the family of niobium– and tantalum–alkylidene complexes failed to do so, was the presence of ancillary alkoxide ligands in the catalysts. Molybdenum and tungsten, however, were obviously the most active metals in alkene metathesis and, around 1980, Schrock and his group considerably increased their efforts in the search for stable molecular alkylidene and alkylidyne complexes of these metals including alkoxide ligands that would catalyze the metathesis of unsaturated hydrocarbons. This search was successful (58) and eventually produced a whole family of molybdenum– and tungsten–alkylidene complexes of the general formula \([\text{M}(=\text{CHMe}_2\text{Ph})(\text{N–Ar})(\text{OR}_2)]\), \(\text{R}\) and \(\text{Ar}\) being bulky groups. In these complexes, the imido ligand is supposed to be a four-electron ligand, because the lone pair of the nitrogen atom is engaged in a vacant tungsten orbital, so that these four-coordinate pseudo-tetrahedral complexes are best considered as 14-electron complexes. These compounds presently are the most active alkene metathesis catalysts (Fig. 1.4). Their metathesis mechanism involves direct (weak) coordination of the olefin to provide 16-electron \(\text{M}(=\text{CH}-\text{t-Bu})(\text{olefin})\) intermediates, presumably of trigonal bipyramidal structure that form 14-electron metallacyclobutanes according to the Chauvin (59–61) mechanism and further continue to give olefin metathesis.

Other chemists such as John Osborn in Strasbourg (26) and Jean-Marie Basset (27) in Lyon played an important role in the history of olefin metathesis by reporting tungsten complexes that were active as olefin metathesis catalysts in the 1980s. Osborn reported a well-defined W(VI) alkylidene metathesis catalysts, 2 (Fig. 1.4) and showed the living character of the polymerization system and the intermediacy

### Scheme 1.5

The three modes of evolution of metallacyclobutanes formed by reaction between a metal–carbene complex and an olefin.
of a tungstacyclobutane by $^1$H NMR spectroscopy (62–65). Basset (66–68) reported aryloxoalkoxoalkylidene W(VI) catalysts and one of the first examples of Lewis-acid-free initiators, 3 (Fig. 1.4) that allowed the polymerization of substituted norbornenes following the ROMP mechanism.

The advantage of Schrock’s (59–61) catalysts, whose most efficient members 4 and 5 (Fig. 1.3) were reported in 1990–1991, was that even though they are extremely active, they are molecular (without additives) and also provided a commercial catalyst and chiral versions for the first examples of asymmetric metathesis catalysis (69–76).

In 1975, Schrock (77) also reported the first high oxidation state alkylidyne complex, [Ta(C–t-Bu)(CH$_2$–t-Bu)$_3$]. As its alkylidene analog and the Fischer-type carbyne complex [W(CO)$_3$(Br)(C–Ph)], however, this Ta complex was inactive in metathesis. Schrock (78) applied the same principles as with olefin metathesis and thus turned to W complexes with alkoxide ancillary ligands. In 1982, his group reported a very active catalyst, [W(C–t-Bu)(O–t-Bu)$_3$] for the metathesis of internal alkynes. Schrock’s W-alkylidyne complexes do not react with olefins, but they selectively and efficiently metathesize alkenes without the need for a co-catalyst. For instance, the prototype [W(CCMe$_3$)(O–t-Bu)$_3$] effects several hundred turnovers per minute of 2-heptyne metathesis under mild conditions. Some reactions even proceed at 25 °C. Here again, the alkoxide ligands are indispensible for the catalysis of the metathesis reactions.

1.8 GRUBBS’ APPROACH AND THE RU OLEFIN METATHESIS CATALYSTS

Among the late transition metals, ruthenium is known as a magic metal by organometallic chemists. Despite a promising start with Pettit’s (21,53) elusive methylene complex and its cyclopropanation chemistry upon reaction with olefins, an iron-based metathesis catalyst has not yet been discovered. The first ruthenium carbene complex, [RuCp{=C(Me)OMe}(CO)(PCy$_3$)][PF$_6$], an 18-electron complex of Fischer-type, was synthesized by Malcolm Green’s group in Oxford (78) but did not show any metathesis activity. The success of Grubbs’ approach to stable benzylidene complexes containing the electrophilic benzylidene ligand may appear, by comparison, somewhat surprising, but it is due to the neutrality of the complexes, thus affording a considerably reduced electrophilicity of the carbene ligand compared to cationic complexes, and the great versatility of ruthenium that forms stable 16-electron complexes.

Grubbs (26,27) had been interested for a long time in the metathesis reaction, as indicated by his mechanistic proposals early on. He had eventually noticed Natta’s 1965 publication on the catalysis by RuCl$_3$ of the polymerization of cyclobutene and 3-methylcyclobutene by ring opening (79). This process (in butanol) had been developed by Norsorex. In this context, the Ziegler–Natta polymerization of olefins under mild conditions obviously had a considerable
impact on polymer chemistry (80). The delineation of a new polymerization mechanism, however, was not a simple task. Greatly inspired by this approach, Grubbs published in 1988 the polymerization of 7-o xoanorboprene into a high molecular weight monodisperse polymer \( \left( M_n = 1.3 \times 10^6 \text{ g mol}^{-1}; M_w/M_n = 1.2 \right) \) by RuCl\(_3\)-xH\(_2\)O or \([\text{Ru(H}_2\text{O})_6]\)(OTs)\(_2\) (OTs = toluene sulfonate), 6 (Fig. 1.5).

This catalytic reaction was all the more remarkable as it was conducted in water (81). Shortly afterward, he could show, in the course of the same reaction, the formation of a Ru-alkylidene intermediate, then the polymerization of cyclooctene, an olefin with little constraints, when the alkylidene ligand source was ethyl diazoacetate added to the aqueous solution of \([\text{Ru(H}_2\text{O})_6]\)(OTs)\(_2\) (82). Consecutively and according to the same logic, a great step forward was accomplished by Grubbs in 1992. He reported the first molecularly well-defined ruthenium–carbene complex that promoted the ROMP of low strain olefins as well as the catalytic RCM of functionalized dienes without the need of a co-catalyst (83). Grubbs showed that these vinylidene complexes, \([\text{RuCl}_2(\text{PR}_3)_2](=\text{CH}–\text{CH}=\text{CHPh})) (R = \text{Ph}, 7, or Cy), were efficient molecular catalysts for these polymerization reactions and other metathesis reactions such as those involving ring closing of terminal diolefins (83,84).

Interestingly, Noels’ group (85) reported, also in 1992, the Ru-catalyzed ROMP of cycloolefins initiated by diazoesters. In 1995, this group showed that addition of such diazoesters to \([\text{Ru}(\eta^5-\text{cymene})\text{PR}_3] (R = \text{Cy or t-Bu}) produces very active arene-free ruthenium–carbene catalysts in which the carbene proton could be observed by \(^1\text{H}\) NMR, shedding light onto the catalyst structure (86). In 1995, the new molecularly well-defined catalysts \([\text{Ru} (=\text{CHPh})\text{Cl}_2(\text{PR}_3)_2], R = \text{Ph or Cy}, whose structures are closely related to the vinylidene ones published 3 years earlier, were reported by the Grubbs group and commercialized with R = Cy.

The complex \([\text{Ru} (=\text{CHPh})\text{Cl}_2(\text{PCy}_3)_2], 8, \) is now known as the first-generation Grubbs catalyst and is even today the metathesis catalyst most used by organic chemists, because of its stability in air and compatibility with a large variety of functional groups (except for amines, nitriles, and basic media) (87). Subsequently, the best organometallic research groups also offered astute alternative syntheses to Grubbs’ catalysts in the late 1990s (88–91).

Fine mechanistic studies with this catalyst led Grubbs’ group to conclude that the mechanism first involved the dissociation of one phosphine to generate the reactive 14-electron ruthenium intermediate for coordination of the olefin. In order to supposedly favor this dissociative step, Grubbs introduced, in place of one phosphine, an N-heterocyclic (NHC) bis-amino carbene ligand that is relatively stable, even in the free form obtained by deprotonation of the corresponding imidazolium cation (92). These NHC ligands are excellent σ-donors without π-acceptor properties and have been known for several decades, but they have only recently become very popular in organometallic chemistry and catalysis (92–95). It was Herrmann’s group (93) that first synthesized ruthenium complexes with two such NHC carbene ligands in the context of the catalysis of olefin metathesis, but their catalytic activity was shown to be modest. In Grubbs’ second-generation catalysts 9 and 10 containing only one such ligand, the electron density at the ruthenium center is increased, which favors alkene coordination from the 14-electron intermediate. Thus, the second generation of Grubbs catalysts \([\text{RuCl}_2\{\text{N(mesityl)}\text{CH}_2\}_2](\text{PCy}_3)(=\text{CHPh})\) containing a single NHC carbene ligand and its catalytic activity in metathesis were successively proposed within a few months by the groups of Grubbs (96,97), Nolan (98), and, with a variation of the NHC ligand, Fürtner and Herrmann (99) (Fig. 1.5). The complex 10, and the third-generation of Grubbs’ catalyst 15, simply obtained upon addition of a pyridine to 10, are presently the most used catalysts for efficient cross-metathesis reactions. These commercially available catalysts are even more active than Grubbs’ first-generation catalyst 8, although they are also more thermally stable than 8 (Fig. 1.5) (100–107).

In the late 1990s, other ruthenium olefin metathesis catalysts were reported (108–113) including that of Peter Hofmann. The latter, also very active, was obtained by chloride abstraction providing a dicaticionic dimer from a ruthenium analog bearing a cis-diphosphine (108–110).

Hoveyda (114,115), Grela (116,117), Buchmeiser (118), Misutani (119), and Blechert (120–122) reported other related, very active, stable, and functional group-tolerant ruthenium metathesis catalysts of this family in the early 2000s. Some of the best catalysts are represented in Figure 1.4. The first Hoveyda metathesis catalyst 12 is derived from Grubbs’ first-generation catalyst 8, and the chelating benzylidene ligand improved the stability compared to 8. It bears only one phosphine and a chelating carbene ligand. In 2000, Blechert and Hoveyda independently reported a more active and more stable complex 13, also bearing a NHC ligand instead of the phosphine. Both catalysts are now commercially available, although expensive. Grela reported variations of the Hoveyda catalyst with increased efficiency (active even at 0°C) when the aryl group of the benzylidene ligand bears a nitro group in the meta or para positions or two methoxy substituents (14, Fig. 1.5).

Grela’s successful idea was to destabilize the Ru–O(ether) bond in order to favor the ether decoordination that generates the catalytically active 14-electron species (116,117). This key finding was further confirmed by Grela’s group upon reporting the poorer catalytic performances of this catalyst in which the nitro group was replaced by the electron-releasing NEt\(_3\) group at the para position, whereas the introduction of the related electron-withdrawing diethyl methyl ammonium substituent brought about a remarkably excellent activity. This family of Grubbs–Hoveyda–Grela catalysts, whose