The Discovery and Development of Ruthenium-Catalyzed Olefin Metathesis

Zheng Xiang
Mar 18, 2005

Contents

- A Historical Retrospect of the Development of Olefin Metathesis Reactions
- The Discovery and Development of Well-Defined Ruthenium-base Olefin Metathesis Catalysts & Mechanism of Ruthenium-Catalyzed Olefin Metathesis
- Summary and Outlook
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Olefin Metathesis

A Variety of Olefin Metathesis Reactions

Ring-Opening Metathesis Polymerization (ROMP)
Ring-Closing Metathesis (RCM)
Acyclic Diene Metathesis Polymerization (ADMET)
Ring-Opening Metathesis (ROM)
Crossmetathesis (CM or XMET)

Ziegler Catalysts

Not only did Ziegler’s discovery of metal-catalyzed olefin polymerizations forever change polymer science, but also the science surrounding it supplied the motivation for many areas of modern organometallic chemistry research.

by Robert H. Grubbs

The Advent of Olefin Metathesis by Industrial Researchers

1956 H. S. Eleuterio, at Du Pont’s petrochemicals department
1960 W. L. Truett et al. at Du Pont’s polychemicals department
1964 R. L. Banks et al. at Phillips Petroleum
1967 N. Caldron et al. at Goodyear Tire & Rubber

\[
\begin{align*}
R_1 &\quad R_2 \\
\quad + \\
R_3 &\quad R_4 \\
&\quad \text{catalyst} \\
\end{align*}
\]


---

Explanation of the Mechanism

**WRONG TURNS**

Unusual intermediates proposed initially have since been rejected

M = metal

Rearranging metallacyclopentane
**Mechanism Proposed by Chauvin**

Chauvin's work gave the field "a chance to move away from its state of alchemy, although it took several years before the mechanism was experimentally supported and widely accepted."

by K. C. Nicolaou


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**Role of Metal-Carbene Complexes in Cyclopropanation and Olefin Metathesis Reactions**

**Katz’s Contribution**

"The mechanism suggests that initiators for olefin metathesis be sought by synthesizing simple alkyl-substituted metal-carbene species and four-membered rings."

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**Katz, T. J.; McGinnis, J. Am. Chem. Soc. 1975, 97, 1592.**

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**Comments**

- “Katz recognized that just because you have a highly active metal carbene does not mean that it’s not governed by the regular laws of organic chemistry.”  
  *by S. J. Danishefsky*

- "In particular, Katz proposed that initiators for olefin metathesis reactions be sought among isolable metal-carbene complexes and used such discrete compounds as initiators of olefin metathesis."  
  *by K. C. Nicolaou*

- Katz "actually put in a carbene--made by someone else to be sure, but it was a well-characterized carbene--and showed that it gave metathesis. No one can deny that. And then he proposed that this is the right way to do olefin metathesis."  
  *by S. J. Danishefsky*
The Third Period of Olefin Metathesis

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Why Ruthenium?

<table>
<thead>
<tr>
<th>Titanium</th>
<th>Tungsten</th>
<th>Molybdenum</th>
<th>Ruthenium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acids</td>
<td>Acids</td>
<td>Acids</td>
<td>Olefins</td>
</tr>
<tr>
<td>Alcohols, Water</td>
<td>Alcohols, Water</td>
<td>Acids, Water</td>
<td>Acids</td>
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<tr>
<td>Aldehydes</td>
<td>Aldehydes</td>
<td>Aldehydes</td>
<td>Aldehydes</td>
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<tr>
<td>Ketones</td>
<td>Ketones</td>
<td>Ketones</td>
<td>Ketones</td>
</tr>
<tr>
<td>Esters, Amides</td>
<td>Olefins</td>
<td>Esters, Amides</td>
<td>Esters, Amides</td>
</tr>
</tbody>
</table>

Increasing Reactivity


ROMP of 7-Oxanorbornene Derivatives

\[\text{RuCl}_3, \text{Ru(cod)Cl}_3, \text{OsCl}_3\]

Aqueous ROMP of 7-Oxanorbornene Derivatives


ROMP of Less-Strained Cyclic Monomers

**Synthesis of Tungsten Vinyl Alkylidene Complexes**


**The First Well-Defined, Metathesisactive Ruthenium Alkylidene Complex**

The First Well-Defined, Metathesisactive Ruthenium Alkyldene Complex


(PCy₃)₂Cl₂Ru=CH-CH=CPh₂, A Well-Defined Ruthenium Alkyldene Catalyst for the Metathesis of Acyclic Olefins

Catalytic Ring-Closing Metathesis of Functionalized Dienes

\[ \text{Ru-PCy}_3 \]

\[ \text{PCy}_3 \]

\[ \text{Ph} \]

\[ \text{Cl} \]

\[ \text{X} = \text{CF}_3 \]

93%

\[ \text{X} = \text{O-t-Bu} \]

91%

\[ \text{X} = \text{N} \]

89%

\[ \text{X} = \text{N-Ph} \]

89%

\[ n = 0 \]

78%

\[ n = 1 \]

93%

\[ n = 2 \]

81%

\[ \text{Ph} \]

84%

\[ \text{O} \]

86%

\[ \text{Ph} \]

72%

\[ \text{Ph} \]

72%

\[ \text{OTBS} \]

85%

\[ \text{X} = \text{CO}_2\text{H} \]

87%

\[ \text{CH}_2\text{OH} \]

88%

\[ \text{CHO} \]

82%

\[ \text{Boc} \]

88-93%

\[ \text{solvents: reagent-grade, undistilled} \]

\[ \text{C}_6\text{H}_6, \text{CH}_2\text{Cl}_2, \text{THF}, \text{t-BuOH} \]

(PCy3)2Cl2Ru=CH-CH=CPh2, A Well-Defined Ruthenium Alkylidene Catalyst for the Metathesis of Acyclic Olefins

September 28, 1992


Synthesis of RuCl2(=CH-p-C6H4X)(PR3)2

Improvements in Catalyst Synthesis


Synthesis of RuCl₂(=CH-p-C₆H₄X)(PR₃)₂

X-ray Diffraction Study of RuCl$_2$(=CH-p-C$_6$H$_4$Cl)(PCy$_3$)$_2$


Relative Activities of the Catalysts (PR$_3$)$_2$X$_2$Ru=CH-CH=CPh$_2$

in the Ring-Closing Metathesis of Diethyl Diallylmalonate

**Critical Mechanistic Insight into Olefin Metathesis**

- The rate of product formation was dramatically depressed by the addition of free PCy₃.
- A plot of \( k_{\text{obs}} \) (RCM) versus 1/[PCy₃] was linear with an intercept very close to zero.
- The ring-closing reaction proceeded with first-order kinetics in both catalyst and diene.

A Ruthenium Catalyst Caught in the Act


Other Information Which Supports the Dissociative Mechanism

- The observation of mono(phosphine) intermediates by electrospray ionization tandem mass spectrometry
- Quantum molecular dynamics studies


Relative Activities of the Catalysts $(PR_3)_2X_2Ru=CH-CH=CPh_2$ in the Ring-Closing Metathesis of Diethyl Diallylmalonate

Developments in Catalyst Design

*Organometallics* 1998, 17, 2758-2767.
*Organometallics* 1998, 17, 5384-5389.

A Novel Class of Ruthenium Catalysts for Olefin Metathesis

2nd-Generation Grubbs Catalyst


<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield with 2 (%)</th>
<th>Yield with 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E, E</td>
<td>E, E</td>
<td>30</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>E, E, Me</td>
<td>E, E</td>
<td>30</td>
<td>62</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>E, E, t-Bu</td>
<td>E, E</td>
<td>60</td>
<td>N.R.</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>Me, E, Me</td>
<td>E, E</td>
<td>90</td>
<td>N.R.</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>Me, E, Me</td>
<td>Me, Me</td>
<td>90</td>
<td>N.R.</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td>60</td>
<td>35&lt;sup&gt;a&lt;/sup&gt;</td>
<td>55 (45)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
**2nd-Generation Grubbs Catalyst**


![Chemical Reaction Diagram](attachment:image1.png)

**New Insights into the Mechanism of Ruthenium-Catalyzed Olefin Metathesis Reactions**

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Time Line of Milestones in the Development of Olefin Metathesis

- 1957: Fischer Carbene
- 1964: Calderon Olefin Metathesis
- 1970: Chauvin proposed alkylidene based mechanism
- 1974, 1975: C. P. Casey, Katz, Grubbs Single component catalyst developed
- 1992: Schrock's catalyst
- 1995: Grubbs' second generation catalyst
- 1999: Grubbs' first generation catalyst
- 2000: Tebbe Reagent

Chemical Structures:

- R= Ph, OMe
- Yee Reagent
- Schrock, 1990
- Grubbs' first generation catalyst
- Herrmann, 1990
- Grubbs' second generation catalyst
Outlook

- Further catalyst to increase the activity and functional group tolerance
- Stereoselective olefin metathesis
- Novel catalysts

Following the development of olefin metathesis from an interesting reaction that was only useful for unfunctionalized olefins, used ill-defined catalysts, and proceeded by a totally unknown mechanism to the present highly active, well-defined, functional group tolerant, and mechanistically well understood catalyst systems has been fun. A number of times along the way, I thought the journey was complete. However, the reaction keeps fooling me. It will be interesting to see where it leads next.

Acknowledgement

- Prof. Yang and Prof. Chen
- Prof. Yu and Prof. Shi
- Dr. Mengwei Huang

Thank You for Your Attention!