Chem 1140; Ring-Closing Metathesis (RCM) and Ring-Opening Metathesis (ROMP)

- Introduction
- RCM
- Cross-Metathesis
- ROMP

Scheme 3. Important types of metathesis reactions: RCM = ring-closing metathesis; ROM = ring-opening metathesis; ROMP = ring-opening metathesis polymerization; ADMET = acyclic diene metathesis polymerization; CM = cross-metathesis.
From the point of view of organic synthesis, the first noteworthy, but largely ignored, example of a ring closing diene metathesis reaction appeared in 1980:

\[
\text{O} \quad \text{O} \\
\text{12\%} \\
\text{Tsuji, J. THL 1980, 21, 2955}
\]
Important Technical Applications

**Phillips triolefin process**

\[
\begin{align*}
\text{ethylene} + \text{ethylene} & \xrightleftharpoons{[\text{Mo}]} \text{polyethylene} + \text{H}_2 \\
n & \text{Norsorex process}
\end{align*}
\]

**Shell higher olefin process**

\[
\begin{align*}
\text{10-20} \text{ C-alkenes} & \xrightleftharpoons{[\text{cat}]} \text{SHOP} \\
\text{2-7} \text{ C-alkenes} & \xrightleftharpoons{[\text{cat}]} \text{9-13} \text{ C-alkenes}
\end{align*}
\]

**Hüls-Vestenamer process**

\[
\begin{align*}
\text{n} \text{ norbornene} & \xrightarrow{[\text{W}]} \text{norbornene polymer} \\
\text{n} \text{ norbornene} & \xrightarrow{[\text{cat}]} \text{linear polymer}
\end{align*}
\]

**Norsorex process**

\[
\begin{align*}
\text{ROMP}
\end{align*}
\]

**Hüls-Vestenamer process**

\[
\begin{align*}
\text{ROMP}
\end{align*}
\]
Molybdenum-Based Olefin Metathesis

\[
\text{MoO}_2\text{Cl}_2(\text{THF})_2 + 2 \text{ArNH(TMS)} \xrightarrow{\text{lutidine, TMSCl, DME}} \text{Mo(NAr)_2Cl}_2(\text{DME}) \xrightarrow{2 \text{RCH}_2\text{MgCl}} \\
\text{Mo(NAr)_2(CH}_2\text{R})_2 \xrightarrow{\text{TfOH, DME}} \text{Mo(NAr)(CH}_2\text{R)(OTf)}_2(\text{DME}) \xrightarrow{2 \text{LiOR'}}
\]

\[
\text{Mo(NAr)(CH}_2\text{R)(OR')}_2 \\
\text{R: C(Me)}_2\text{Ph} \\
\text{R': OC(Me)}_2\text{CF}_3
\]

Schrock, JACS 1990, 112, 3875

Molybdenum-Based Ring-Closing Olefin Metathesis

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{F}_3\text{C} & \quad \text{F}_3\text{C} \\
\text{F}_3\text{C} & \quad \text{F}_3\text{C} \\
\text{O} & \quad \text{O} \\
\text{Mo} & \quad \text{Mo} \\
\text{A (5 mol%)} & \quad 93\%
\end{align*}
\]

\[
\text{Ph} \quad \text{Ph}
\]

93%
The synthesis of ruthenium vinylcarbene complexes allowed the development of well-defined, late transition metal, low oxidation state complexes that catalyze olefin metathesis. Ruthenium carbene complexes are significantly easier to make and handle than the Schrock molybdenum complex. In addition to the metathesis of strained cyclic and exocyclic olefins, the remarkable functional group tolerance (alcohols, aldehydes, carboxylic acids) and stability toward air, water, and acid has made this class of compounds particularly attractive for practical applications (Grubbs, R. H.; Miller, S. J.; Fu, G. C. Acc. Chem. Res. 1995, 28, 446).
Ruthenium-Based Olefin Metathesis: Mechanism

Mechanistically, the major pathway (>95%) was found to involve phosphine dissociation from the metal center, such that a minor associative pathway in which both phosphines remain bound can be considered to operate only at higher phosphine concentrations. The formation of the 14-electron metallacyclobutane intermediate is the rate-determining step. The rate and catalyst activity are directly proportional to (a) $K_1$, the equilibrium constant for olefin binding, (b) $K_2$, the equilibrium constant for phosphine dissociation, (c) $k_3$, the rate constant for metallacyclobutane formation from the monophosphine olefin complex $I_2$. 

Ruthenium-Based Olefin Metathesis: Applications

Challenges for successful cross-metathesis include:
control of olefin geometry
suppression of homodimer formation
extending functional group compatibility

Cross-Metathesis

92% yield exclusively Z
Cross-Metathesis


Cross-Metathesis: Applications

Cross-Metathesis: Applications

1. PhSH, TEA  
2. (Ph₃P)₂RhCl, H₂  
3. DBU, THF; 76%

Tuberostemonine!  
27 steps/1.1% yield from Cbz-tyrosine
Figure 1. GPC trace for polymer blend obtained by tandem ROMP—hydrogenation—ROMP of 2b.
Living Ring Opening Metathesis Polymerization (ROMP)

- A way of making polymers from cyclic olefins
- Condition for prepare living polymers
  a. monomer is highly strained (irreversible)
  b. $R_2$ is slow
  c. organometallic intermediates in the polymerization reaction are stable
- Advantages of ROMP
  a. very narrow molecular weight distribution can be obtained: $M_n/M_W$ approaching 1.0
  b. living ROMP catalyst can tolerate a range of functionalities: most catalysts are destroyed in other types of living polymerization reactions
  c. new materials can be prepared under controlled design conditions

Brief history
- Calderon (1967): the discovery $\text{WCl}_5/\text{EtAlCl}_2/\text{EtOH}$ “olefin metathesis”
- Grubbs (1986): the first report of living ROMP of a cyclic olefin
- Richard R. Schrock (1980’s): molybdenum & tungsten catalysts

Living Polymerizations
- Absence of chain termination and chain transfer reaction provides polymers whose molecular weights are precisely predicted and controlled by stoichiometry of polymerization
  $M_n = (\text{g monomer}) / (\text{moles of initiator})$
- Polydispersity will decrease with increasing molecular weight
- Synthesis of macromonomers that retain the reactive chain ends when all the monomer has been consumed

ROMP

Why Carbene Ligands?

The nucleophilic carbenes are ‘phosphine-mimics’ and yet they are much more. They reside at the upper end of the Tolman electronic and steric parameter scales. From solution calorimetric studies, it became clear that nucleophilic carbenes (most of them) are better donors than the best donor phosphines.

Figure 2. ROMP of cycloocta-1,5-diene in the presence of catalysts 1 and 4. Conditions: 20°C, monomer/catalyst ratio 300:1, catalyst = 0.5 mM, CDCl₃ as solvent. Conversion was determined by ¹H NMR.
Why Carbene Ligands?

Fig. 13. Molecular structure of (PCyp)₂RuCl₂(=CHCH=CMe)₂(IMes) (15). Hydrogen atoms are omitted for clarity.

Don’t Miss....

Thursday, March 03, 2005
2:30 PM, Chevron Science Center 12 B
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Metathesis Enabled Combinatorial Chemistry for Drug Discovery

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