

I. Basic Principles

I-J. Alkene Metathesis



Ring-Closing Metathesis (RCM) and Ring-Opening Metathesis (ROMP)



The Nobel Prize in Chemistry 2005

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Robert H. Grubbs
California Institute of Technology (Caltech),
Pasadena, CA, USA and

Richard R. Schrock
Massachusetts Institute of Technology
(MIT), Cambridge, MA, USA



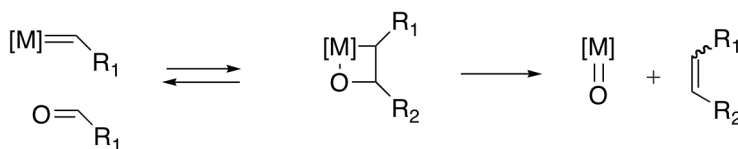
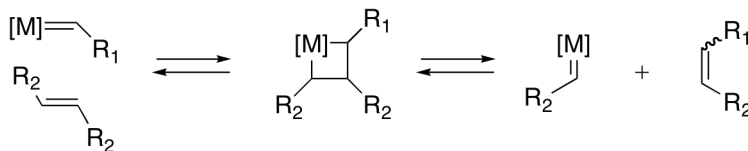
"for the development of the metathesis
method in organic synthesis".

<http://nobelprize.org/chemistry/laureates/2005/animation.html>

- **Introduction**
- **RCM**
- **Cross-Metathesis**
- **ROMP**

COVER STORY**December 23, 2002**Volume 80, Number 51
C&ENR 80 51 pp. 29-33
ISSN 0009-2347**OLEFIN METATHESIS: BIG-DEAL REACTION**

A boon to organic synthetic chemists, olefin metathesis also promises cleaner, cheaper, and more efficient industrial processes

A. MAUREEN ROUHI, C&EN WASHINGTON

Important types of metathesis reactions:

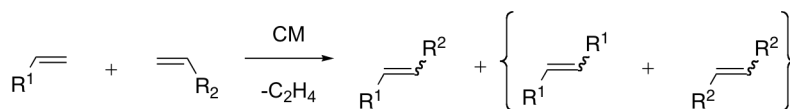
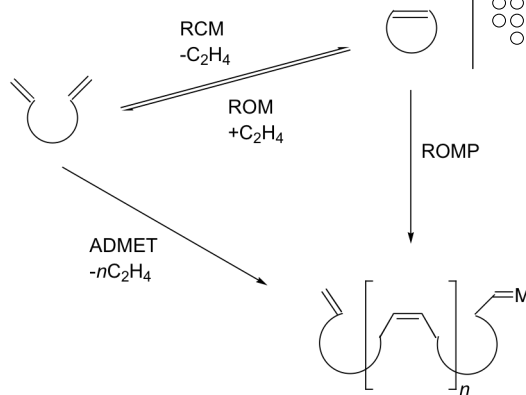
RCM = ring-closing metathesis

ROM = ring-opening metathesis

ROMP = ring-opening metathesis polymerization

ADMET = acyclic diene metathesis polymerization

CM = cross-metathesis



History of RCM

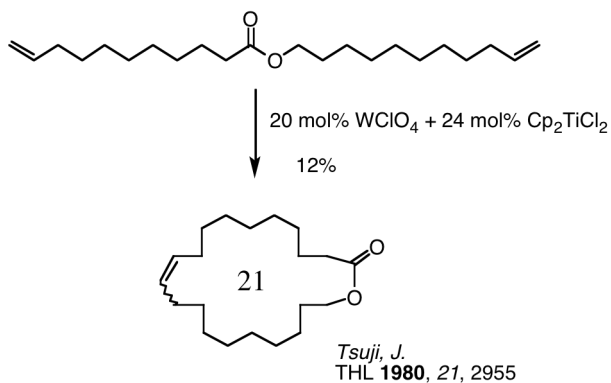


Stille, J. R.; Grubbs, R. H., "Synthesis of (+)-d9,12-capnellene using titanium reagents." *J. Am. Chem. Soc.* **1986**, *108*, 855-856.
Nicolaou, K. C.; Bulger, P. G.; Sarlah, D., "Metathesis reactions in total synthesis." *Angew. Chem., Int. Ed.* **2005**, *44*, 4490-4527.

History of RCM



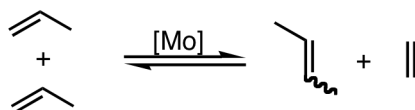
From the point of view of organic synthesis, the first noteworthy, but largely ignored, example of a ring closing diene metathesis reaction appeared in 1980:



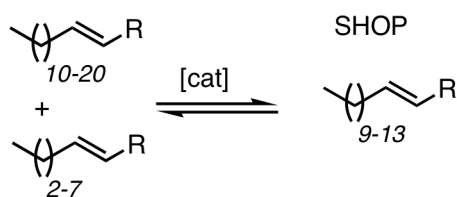
Important Technical Applications



Phillips triolefin process



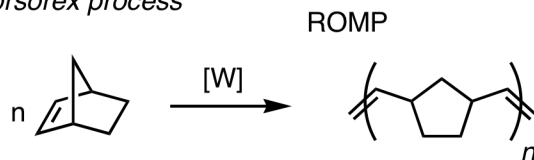
Shell higher olefin process



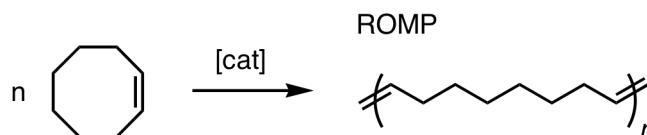
Important Technical Applications



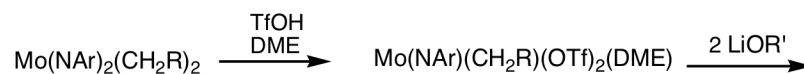
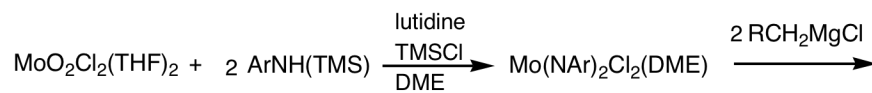
Norsorex process



Hüls-Vestnamer process



Molybdenum-Based Olefin Metathesis

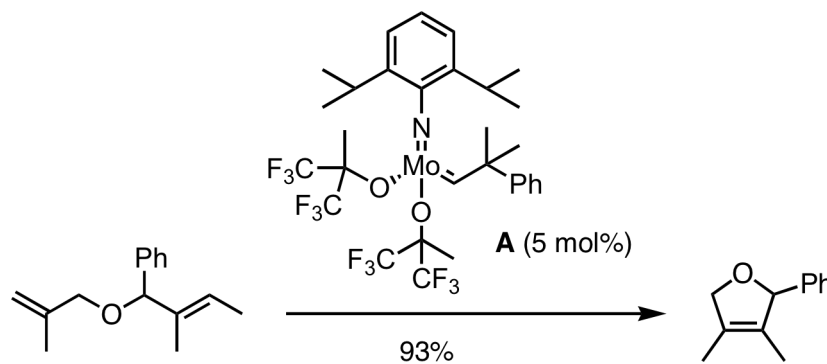


R: C(Me)₂Ph

R': C(Me)(CF₃)₂

Schrock, JACS **1990**, 112, 3875

Molybdenum-Based Ring-Closing Olefin Metathesis



Molybdenum-Based Ring-Closing Olefin Metathesis



Xu, Z.; Johannes, C. W.; Salman, S. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 10926.

Ruthenium-Based Olefin Metathesis

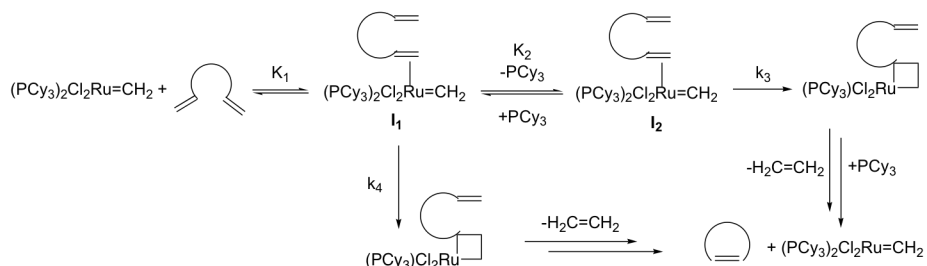


The synthesis of ruthenium vinylcarbene complexes allowed the development of well-defined, late transition metal, low oxidation state complexes that catalyze olefin metathesis. Ruthenium carbene complexes are significantly easier to make and handle than the Schrock molybdenum complex. In addition to 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



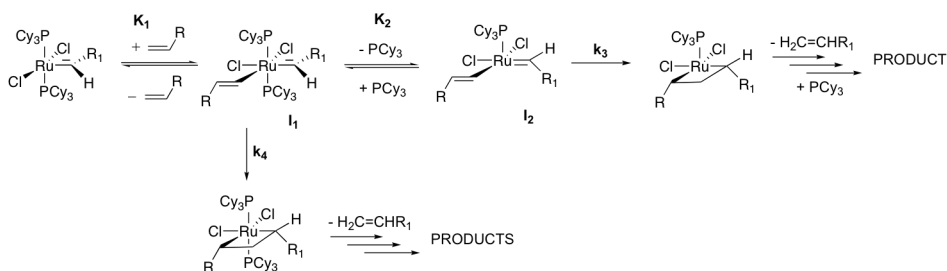
Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887.



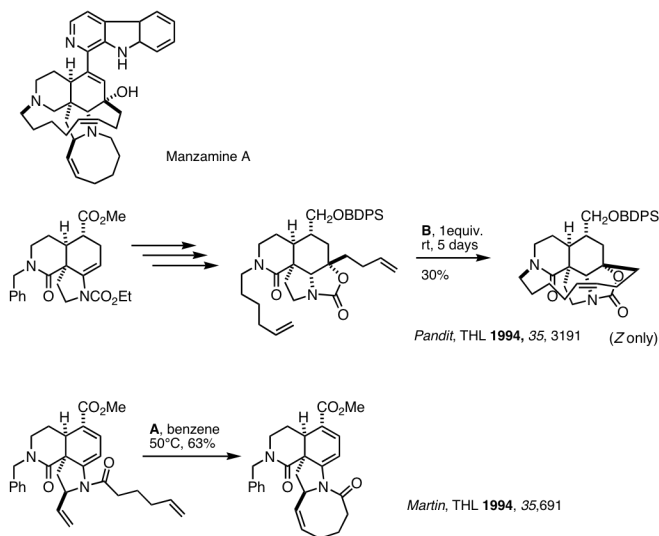
Ruthenium-Based Olefin Metathesis: Mechanism



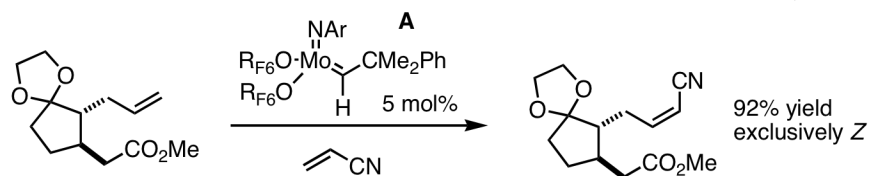
Mechanistically, the major pathway (>95%) was found to involve phosphine dissociation from the metal center, such that a minor associative pathway in which both phosphines remain bound can be considered to operate only at higher phosphine concentrations. The formation of the 14-electron metallacyclobutane 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



Cross-Metathesis



Challenges for successful cross-metathesis include:

- control of olefin geometry
- suppression of homodimer formation
- extending functional group compatibility

Cross-Metathesis

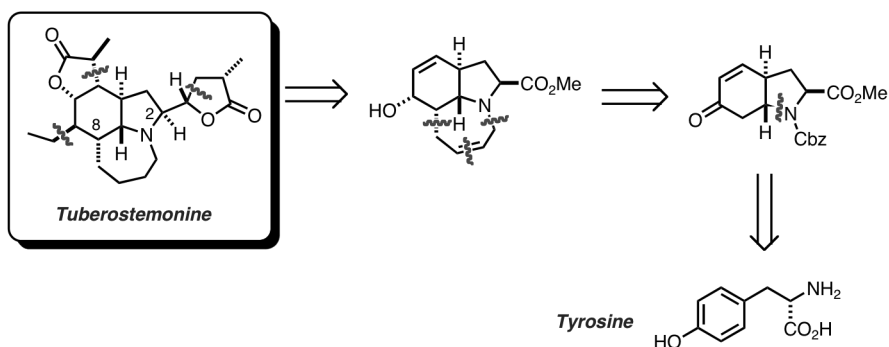


Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H., "Synthesis of functionalized olefins by cross and ring-closing metathesis." *J. Am. Chem. Soc.* **2000**, *122*, 3783.

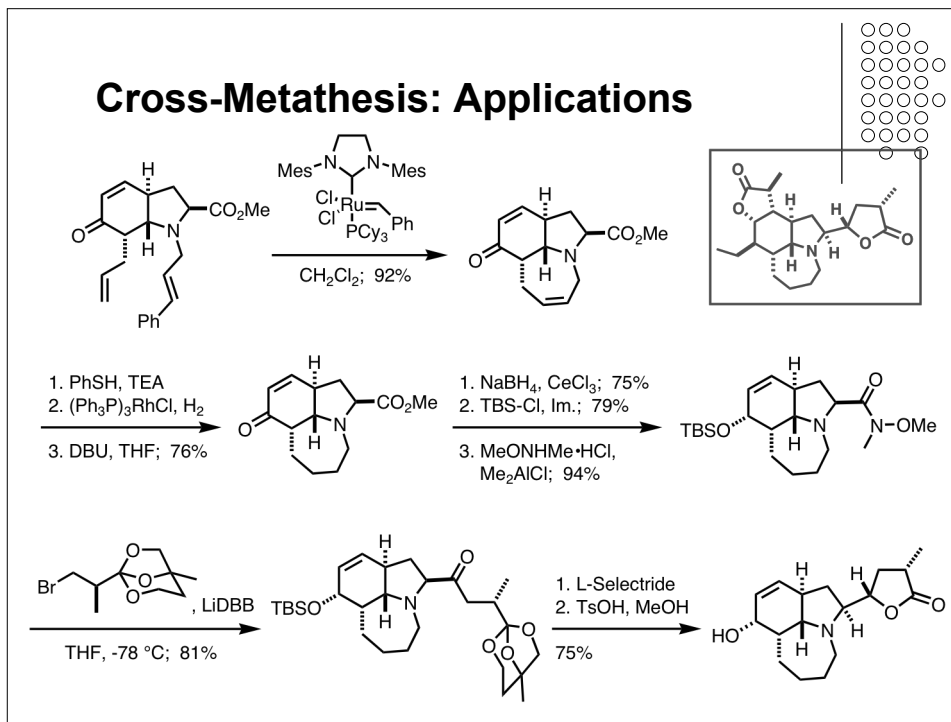
Cross-Metathesis: Applications



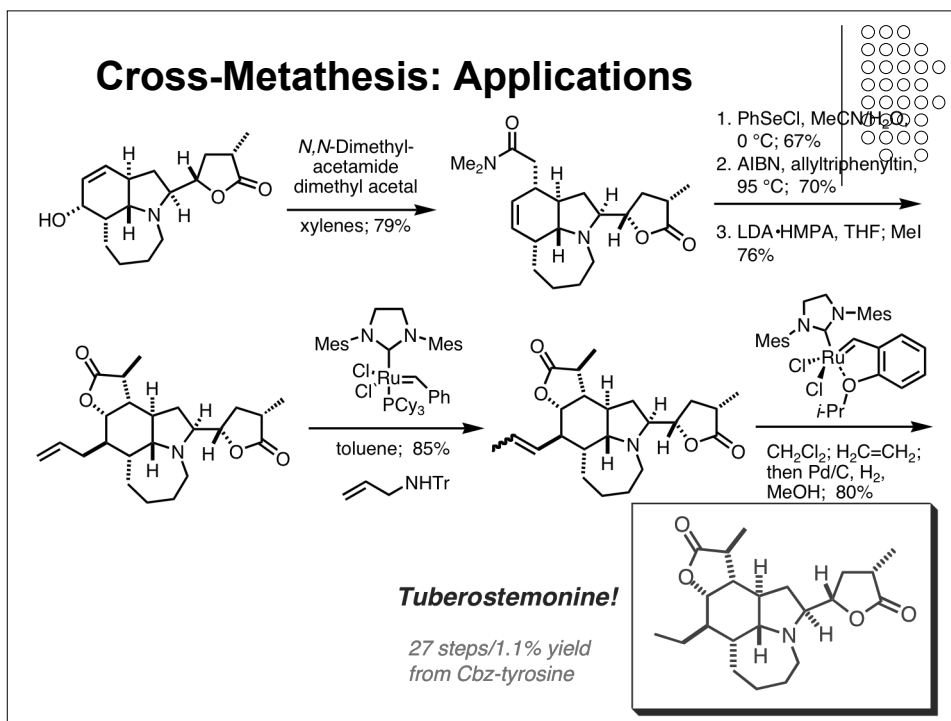
Wipf, P.; Spencer, S. R. "Asymmetric total syntheses of tuberostemonine, didehydrotuberostemonine, and 13-epituberostemonine." *J. Am. Chem. Soc.* **2005**, *127*, 225-235.

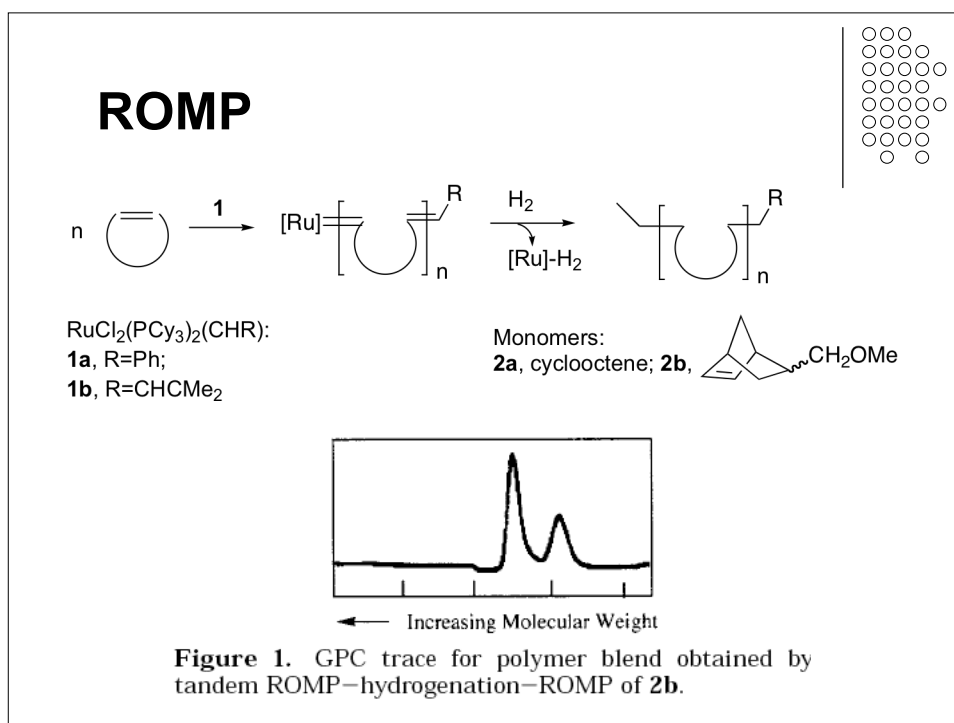
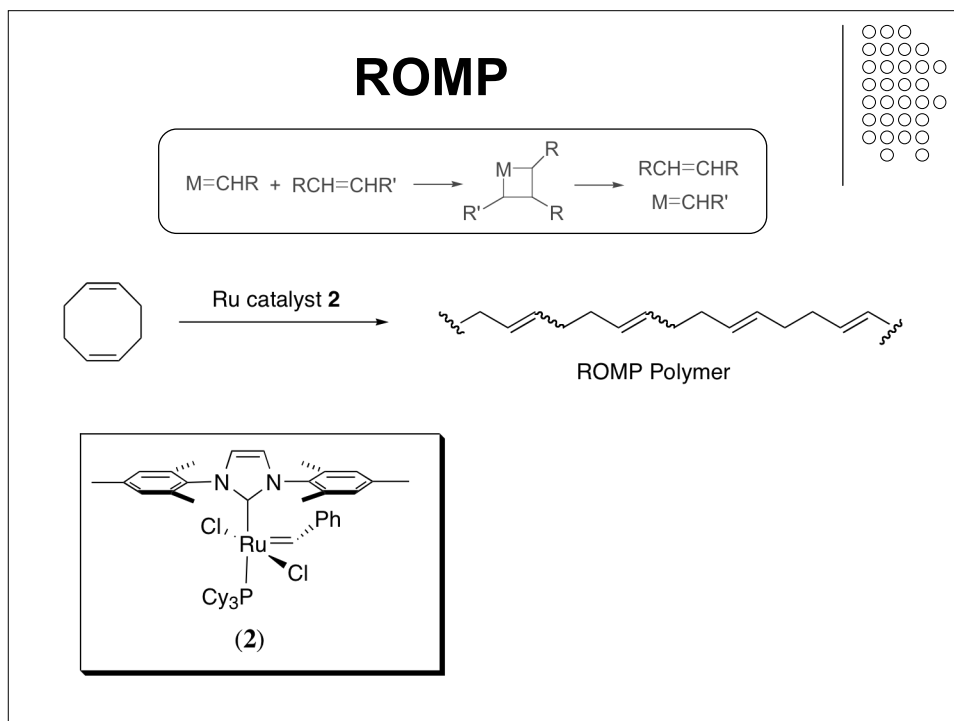


Cross-Metathesis: Applications



Cross-Metathesis: Applications

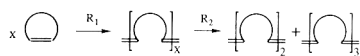




Living Ring Opening Metathesis Polymerization (ROMP)



- A way of making polymers from cyclic olefins



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

Brief history

- Calderon (1967): the discovery $WCl_6/EtAlCl_2/EtOH$ "olefin metathesis"
- Grubbs (1986): the first report of living ROMP of a cyclic olefin
- Richard R. Schrock (1980's): molybdenum & tungsten catalysts

Living Polymerizations

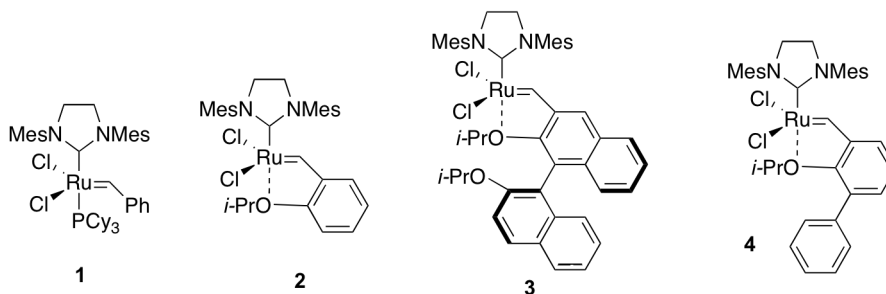
- Absence of chain termination and chain transfer reaction provides polymers whose molecular weights are precisely predicted and controlled by stoichiometry of polymerization

$$M_n = (\text{g monomer}) / (\text{moles of initiator})$$
- Polydispersity will decrease with increasing molecular weight
- Synthesis of macromonomers that retain the reactive chain ends when all the monomer has been consumed

ROMP



Wakamatsu, H.; Blechert, S. "A new highly efficient ruthenium metathesis catalyst." *Angew. Chem. Int. Ed.* **2002**, *41*, 2403-2405



ROMP

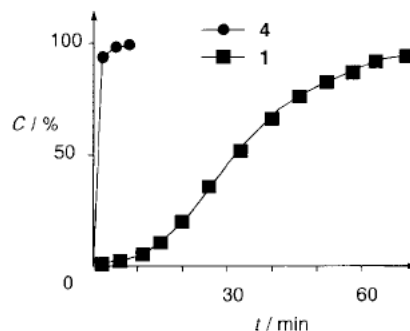
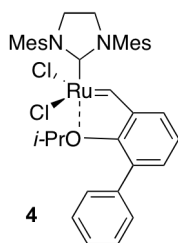
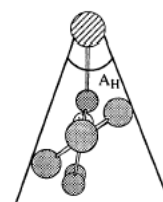
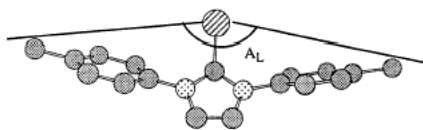
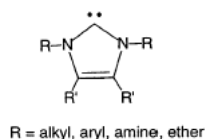


Figure 2. ROMP of cycloocta-1,5-diene in the presence of catalysts **1** and **4**. Conditions: 20°C, monomer/catalyst ratio 300:1, catalyst = 0.5 mM, CD₂Cl₂ as solvent. Conversion was determined by ¹H NMR.

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.



Why Carbene Ligands?

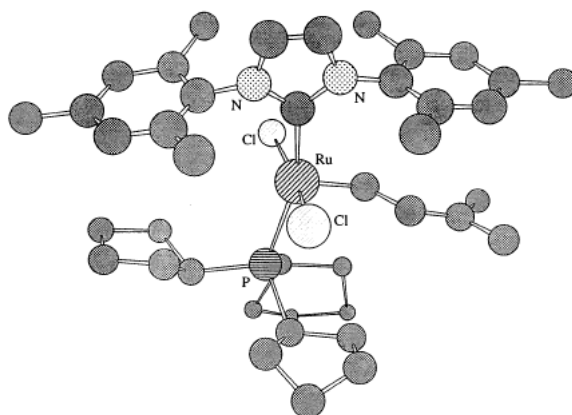


Fig. 13. Molecular structure of (PCyp₃)RuCl₂(=CHCH=CMe₂)(IMes) (15). Hydrogen atoms are omitted for clarity.