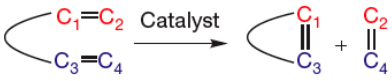
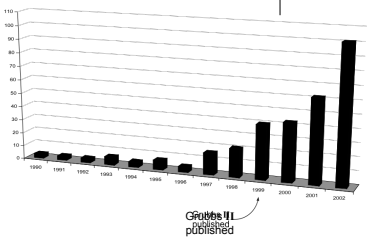
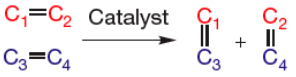
Alkene Metathesis

Ring-closing metathesis

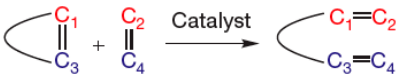




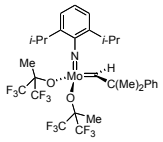
Cross metathesis



Ring-opening metathesis



The Catalysts



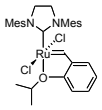
Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Reagan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875

Schrock I

$Cl_2(PCy_3)_2Ru{=}CHPh$

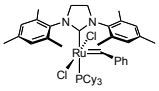
Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2039

Grubbs I



Kingsbury, J. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791

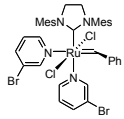
Green Grubbs



$(H_2IMes)(PCy_3)Cl_2Ru{=}CHPh$

Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953

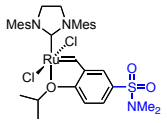
Grubbs II



$(H_2IMes)(3\text{-}Br\text{-}py)_2Cl_2Ru{=}CHPh$

Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2002**, *41*, 4035

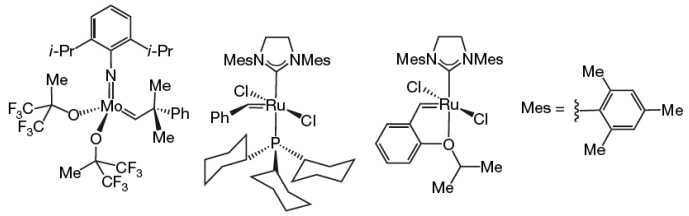
Grubbs III



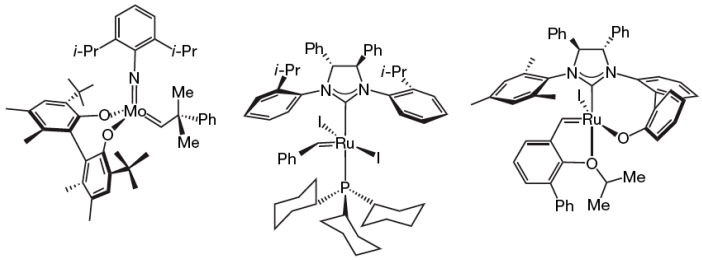
http://www.zannanpharma.com/english/products/

Zhan-1B

Achiral olefin metathesis catalysts



Chiral olefin metathesis catalysts



Hoveyda, A. H.; Zhugralin, A. R., "The remarkable metal-catalysed olefin metathesis reaction." *Nature* **2007**, *450*, 243-251.

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

The Nobel Prize in Chemistry 2005

Yves Chauvin
Institut Français du Pétrole, Rueil-Malmaison, France,

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

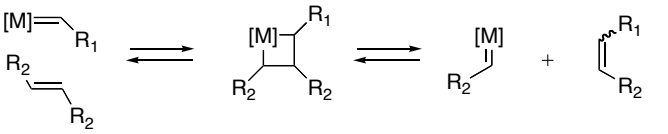
- ***Introduction***
- ***RCM***
- ***Cross-Metathesis***
- ***ROMP***

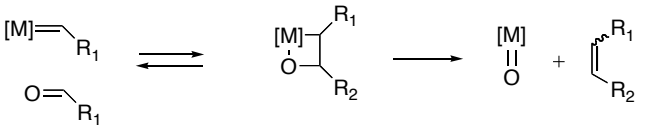
COVER STORY
December 23, 2002
Volume 80, Number 51
CENEAR 80 51 pp. 29-33
ISSN 0009-2347

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:

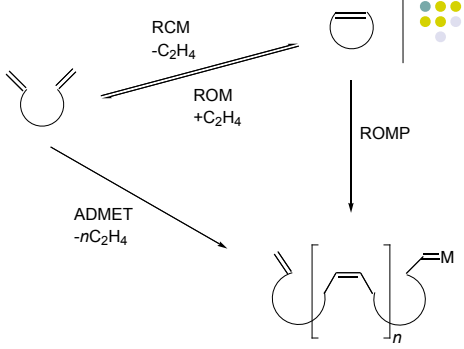
RCM = ring-closing metathesis

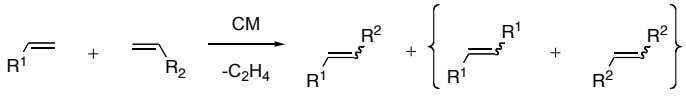
ROM = ring-opening metathesis

ROMP = ring-opening metathesis polymerization

ADMET = acyclic diene metathesis polymerization

CM = cross-metathesis

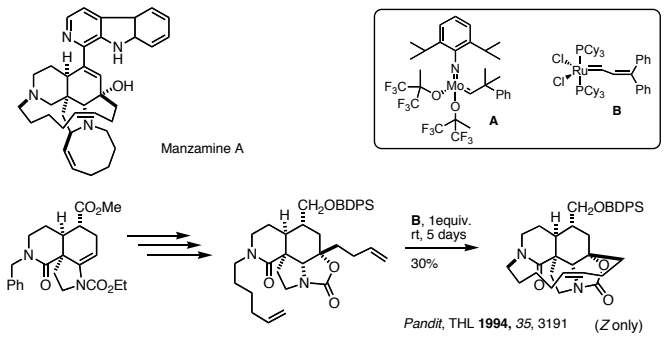




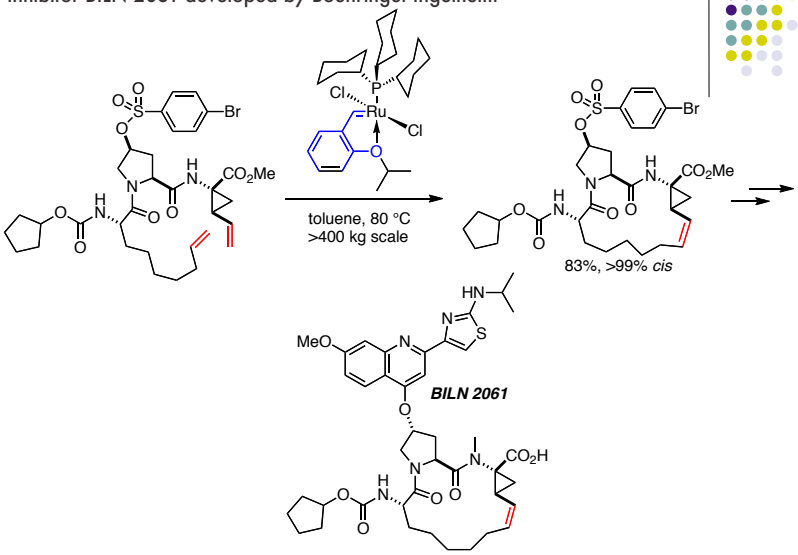
Ruthenium-Based Olefin Metathesis

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).

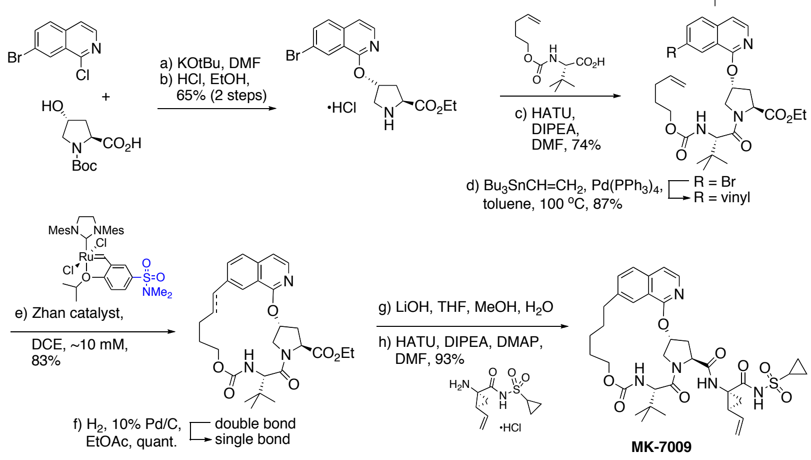
Ruthenium-Based Olefin Metathesis: Applications



Large-scale preparation of pharmaceutical candidates: Hepatitis C protease inhibitor BILN 2061 developed by Boehringer-Ingelheim

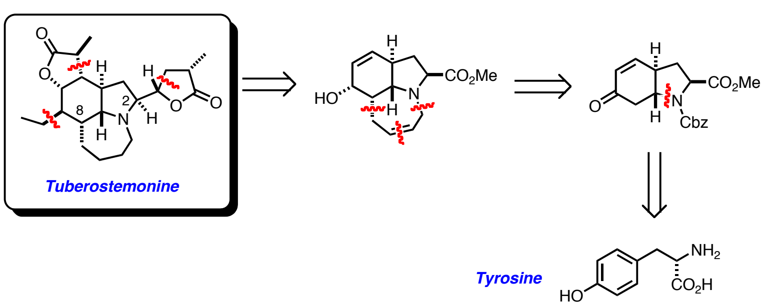


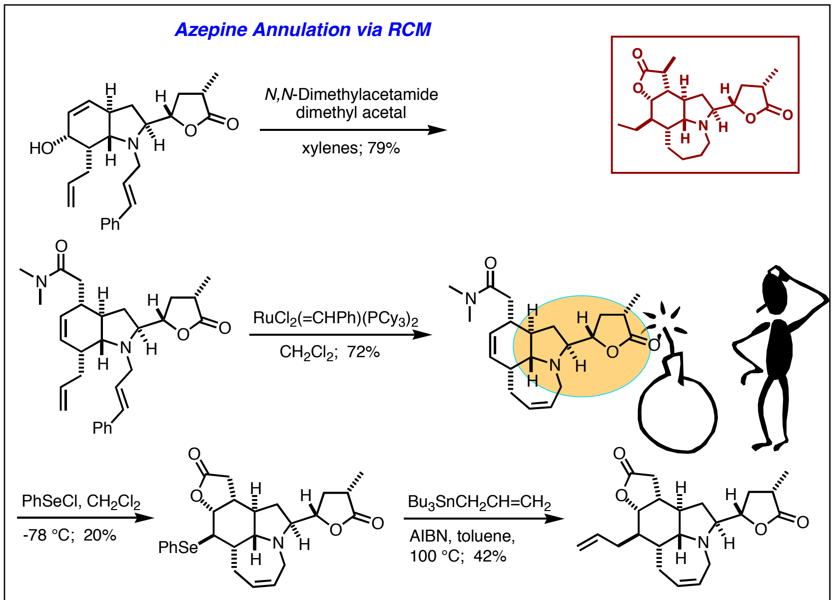
Liverton, N. J.; Holloway, M. K.; Mccauley, J. A.; Rudd, M. T.; Butcher, J. W.; Carroll, S. S.; Dimuzio, J.; Fandozzi, C.; Gilbert, K. F.; Mao, S.-S.; Mcintyre, C. J.; Nguyen, K. T.; Romano, J. J.; Stahlhut, M.; Wan, B.-L.; Olsen, D. B.; Vacca, J. P., "Molecular modeling based approach to potent P2-P4 macrocyclic inhibitors of hepatitis C NS3/4A protease." *J. Am. Chem. Soc.* **2008**, *130*, 4607-4609.



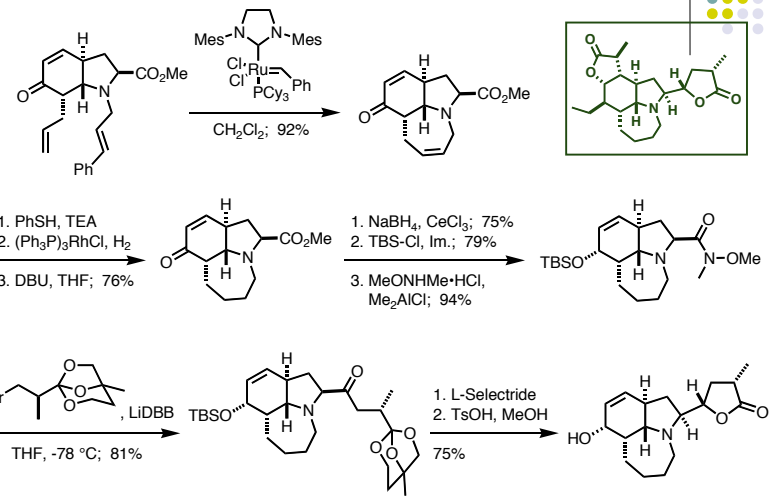
Cross-Metathesis: Applications

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

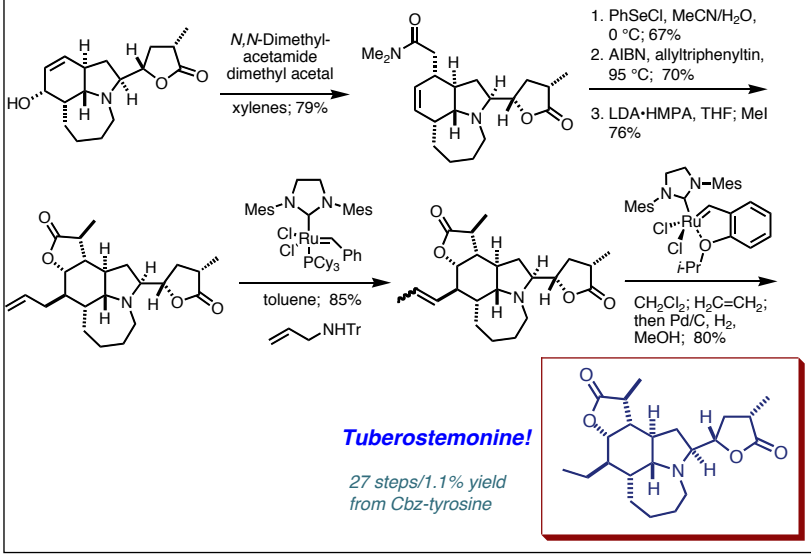




Cross-Metathesis: Applications



Cross-Metathesis: Applications

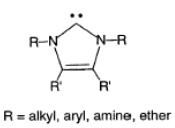


Tuberostemonine!

27 steps/1.1% yield from Cbz-tyrosine

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.



R = alkyl, aryl, amine, ether