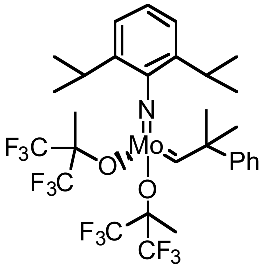
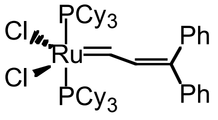
Synthesis of Ruthenium Olefin Metathesis Catalysts

Introduction

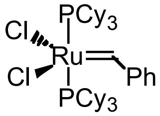
Well-defined metal alkylidene complexes are:



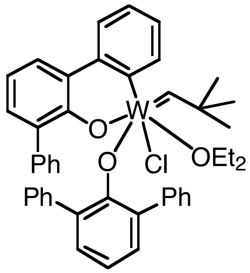
Schrock,
JACS **1990**, *112*, 3875



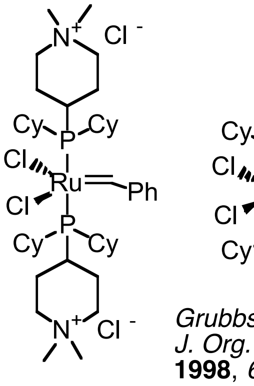
Grubbs,
JACS **1993**, *115*, 9858

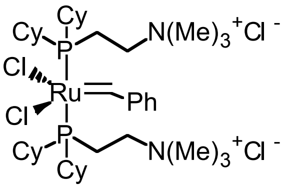


Grubbs,
ACE **1995**, *34*, 2039

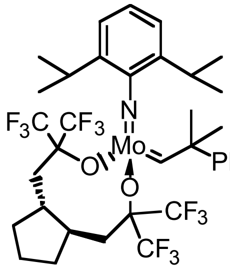


Couturier,
ACE **1992**, *31*, 628

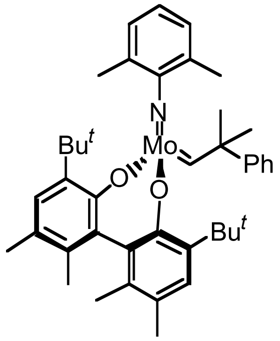




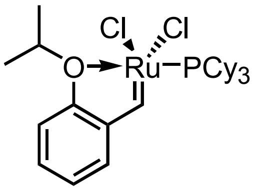
Grubbs
J. Org. Chem.
1998, *63*, 9904.



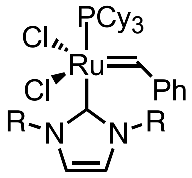
Grubbs,
Organometallics **1996**,
15, 1865



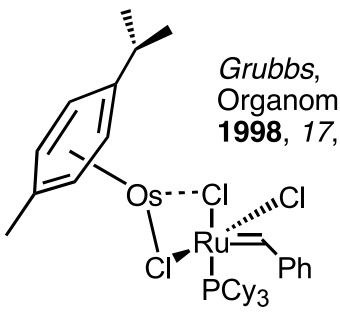
Hoveyda & Schrock
J. Am. Chem. Soc.
1998, *120*, 9720.



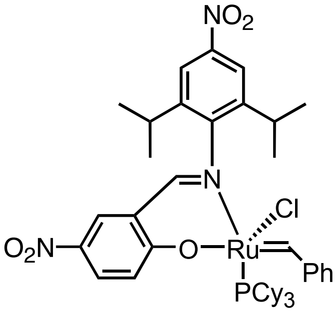
Blechert, Hoveyda
Tetrahedron Lett. **2000**,
41, 9973.
J. Am. Chem. Soc. **2000**,
122, 8168.



Herrmann,
Angew. Chem. Int. Ed.
1999, *38*, 2416.



Grubbs,
Organometallics
1998, *17*, 2758.



Grubbs,
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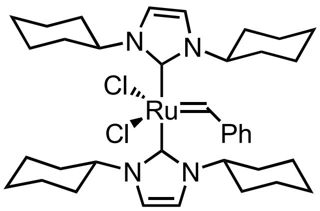
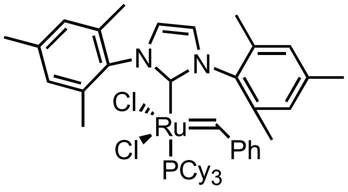
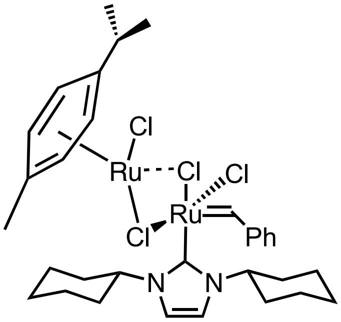
1998, *17*, 3460



Herrmann,
Angew. Chem. Int. Ed.
1999, *38*, 262.

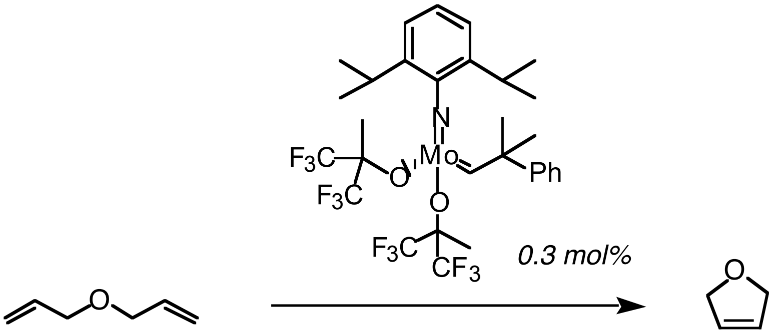


Herrmann, Grubbs, Nolan
THL **1999**, *40*, 2247.
JACS **1999**, *121*, 2674.



Herrmann,
J. Organomet. Chem.
1999, *582*, 362.

A typical example of a ring closing metathesis reaction is:



0.3 mol%

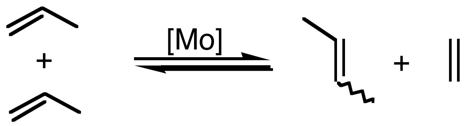
no solvent,
99% yield, 53% conversion

turnover number 180

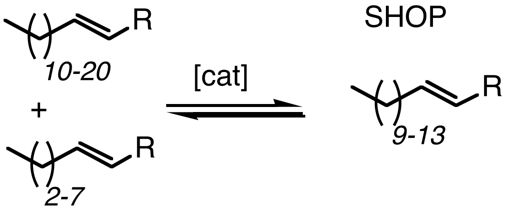
The mechanism involves a series of alternating [2+2] cycloadditions and cycloreversions between metal alkylidene and metallacyclobutane species. For terminal alkene substrates the reaction by-product is ethylene, and a partial vacuum may be used to drive the reaction. Several catalysts do not tolerate excessive steric hindrance.

Important Technical Applications

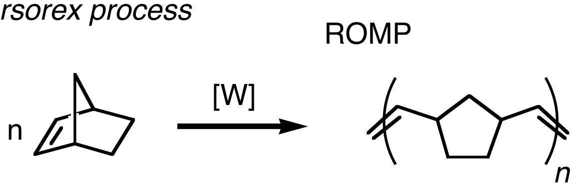
Phillips triolefin process



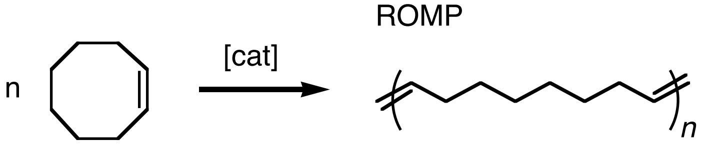
Shell higher olefin process



Norsorex process



Hüls-Vestenamer process



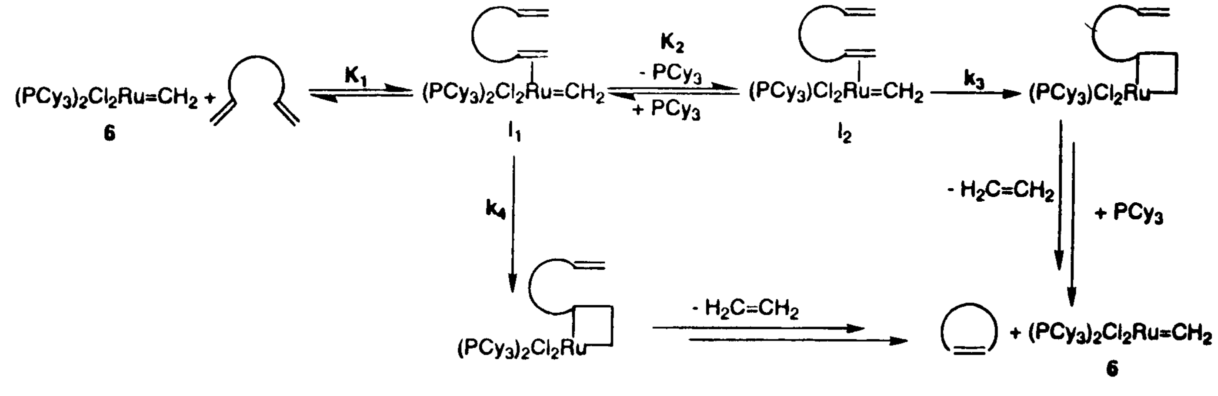
Ruthenium-Based Olefin Metathesis

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.

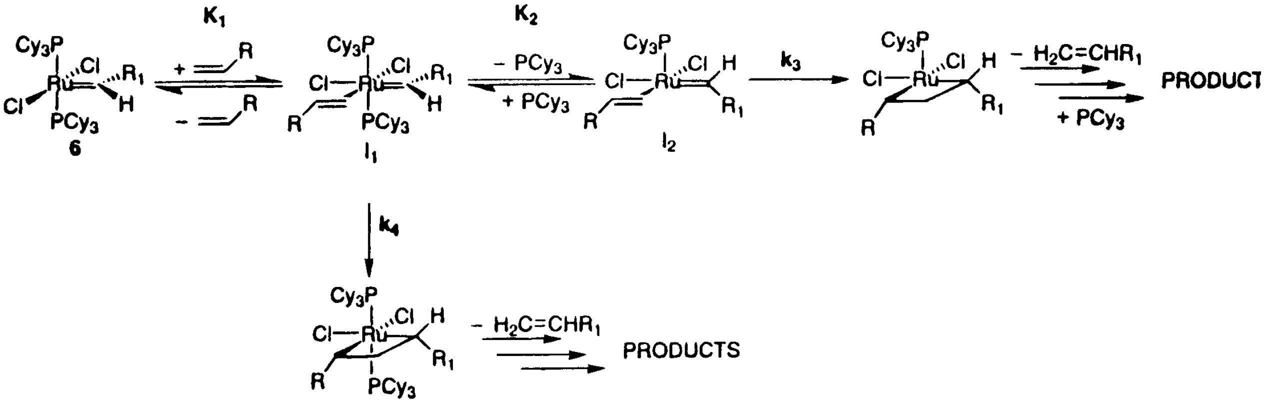
In addition to the metathesis of strained cyclic and exocyclic olefins, the remarkable functional group tolerance (alcohols, aldehydes, carboxylic acids) and stability toward air, water, and acid has made this class of compounds particularly attractive for practical applications

(Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446). However, the cyclization of 1,1-disubstituted alkenes and enol ethers is problematic.

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

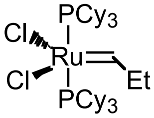
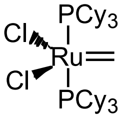
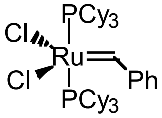
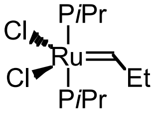
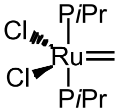
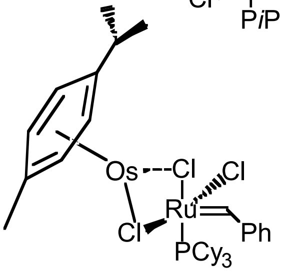


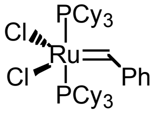
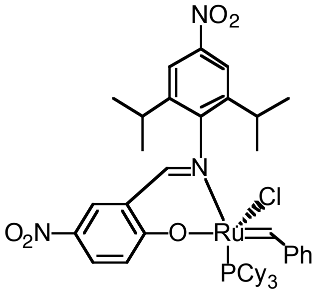
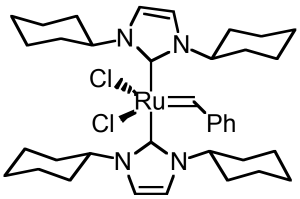
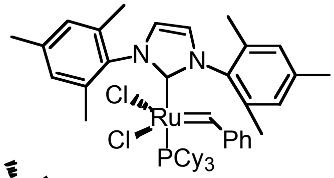
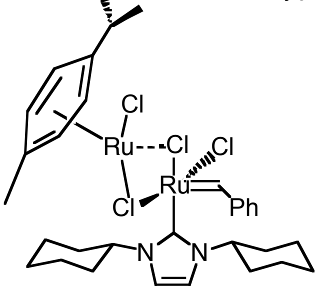
Mechanistically, the major pathway (>95%) was found to involve phosphine dissociation from the metal center, such that a minor associative pathway in which both phosphines remain bound can be considered to operate only at higher phosphine concentrations



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.

- Ulman, M.; Grubbs, R. H., "Ruthenium carbene-based olefin metathesis initiators: Catalyst decomposition and longevity." *J. Org. Chem.* **1999**, *64*, 7202-7207. Alkylidene decomposition is predominantly second order, requiring phosphine dissociation, while methylidene decomposition is primarily first order. The exact nature of the inorganic decomposition products is not known. The fact that substrates that are difficult to cyclize require high catalyst loadings can now be explained by the unimolecular decomposition of the propagating methylidene catalyst. For most applications, the utility of a catalyst is determined by the ratio of the rate of catalysis to the rate of decomposition.

	half-lives at 23 mM conc.	time at which reaction progress ceased (yield)
	8 h / 55 °C	
	40 min / 55 °C	
	8 d / 55 °C	5 d /25 °C (91%) 8 h /55 °C (80%)
	10 h / 55 °C	2 d /25 °C (67%) 1 h /55 °C (51%)
	30 min / 25 °C	
	30 min / 55 °C	10 min /25 °C (18%) 4 min /55 °C (18%)

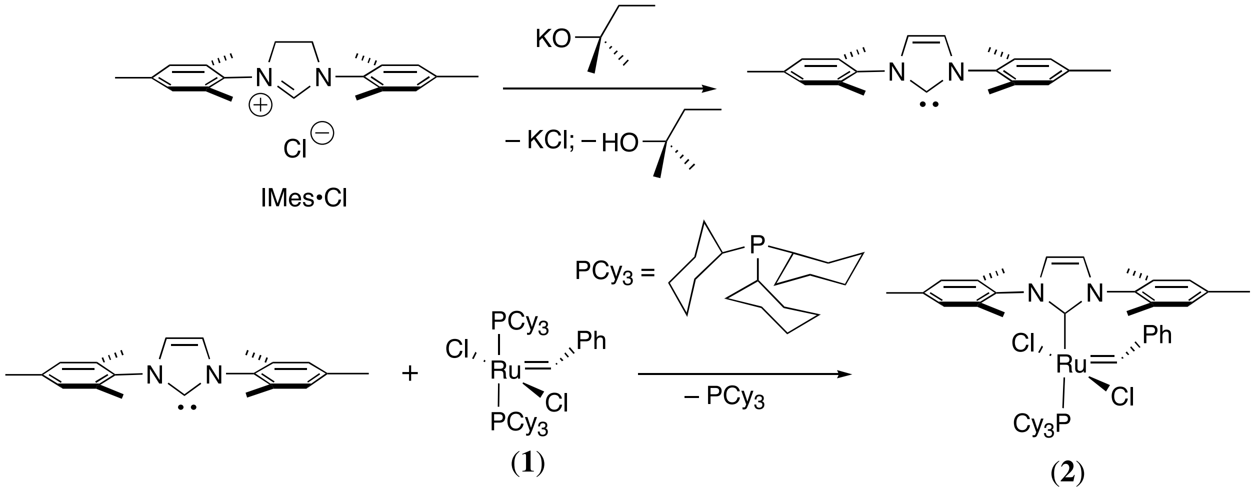
	half-lives at 23 mM conc.	time at which reaction progress ceased (yield)
 + CuCl	10 min / 55 °C	1.5 h /25 °C (55%) 0.5 h /55 °C (65%)
		2 d /55 °C (100%)
		4 h /25 °C (20%) 3 h /55 °C (33%)
		4 h /55 °C (98%)
		15 min /55 °C (86%)

Prior Reading and Techniques: Szafran Chapter 5. Lecture notes on “Handling of Air-Sensitive Compounds”.

Experimental Section

This experimental section is based on work by Prof. Steve Nolan at the University of New Orleans, and Prof. Melanie Sanford at the University of Michigan, who are gratefully acknowledged for sharing this information with us.

Part A: Preparation of Ruthenium Olefin Metathesis Catalysts



Safety Recommendations: Potassium *tert*-amylate is a strong base than needs to be handled with care. IMes•Cl and ruthenium catalysts are harmful if swallowed, inhaled, or absorbed through skin.

Chemical Data: Complete this table using a current Aldrich or Strem catalog *before* running the experiment.

Compound	**FW**	**Amount**	**Mmol**	**Mp [°C]**	**Density**
IMes•Cl					
K *tert*-amylate					
Ru-catalyst **1**					

Required Equipment: Glassware for this reaction – 10 mL vials containing a stir bar – should be dried in the oven for at least 8 h before starting the experiment. Glove bag. Septa. Magnetic stirrer.

Synthesis of Complex 2. In a glove box/bag, IMes•Cl (124 mg, 0.365 mmol, pre-weighed in a vial) and potassium *tert*-amylate (0.58 mL, 0.55 mmol, as a ~15 wt% solution in cyclohexane) were suspended in dry and degassed cyclohexanes (4 mL). The flask was capped with a rubber septum and stirred in the glove bxo/bag for 1 hour. The ruthenium complex **1** (200 mg, 0.243 mmol, pre-weighed in a vial) was added slowly to the reaction mixture as a solid in two batches during 30 min in the glove box/bag. The solution was stirred at room temperature under N_2 for at least 48 h during which time a pink solid precipitated from solution. The flask was removed from the glove box/bag, and the pink precipitate was collected on a fritted filter, washed with a 50%/50% mixture of methanol and H_2O (3 x 5 mL) and dried under vacuum to afford the product as a pink solid. Samples for ^1H NMR spectroscopy may be be weighed and handled as a solid in an air atmosphere, but the complex should not be exposed to air for longer than 5 minutes.

Characterization of Product. ^1H NMR; IR. How do your data compare to the literature on complex **2**?

Questions. **1.** How does the C(2) carbon in the imidazoline change its electron configuration? **2**. Why is the phosphine ligand displaced, and not one of the chlorines? **3**. Why does the reaction stop after a single displacement? **4**. Why are the methyl groups on the benzene rings of the ligand important? **5**. Based on your literature reading, what is the advantage of catalyst **2** over catalyst **1**?

References:

M. Scholl *et. al. Org. Lett.* **1999**, *1*, 953-956.
L. Jafarpour and S. P. Nolan, *Organometallics* **2000**, *19*, 2055-2057.
L. Jafarpour, A. F. Hillier, S. P. Nolan, *Organometallics* **2002**, *21*, 442-444.
J. A. Love, J. P. Morgan, T. M. Trnka, R. H. Grubbs, *Angew. Chem, Int. Ed.* **2002**, *41*, 4035-4037.