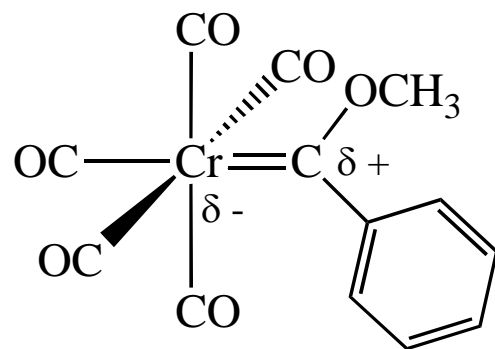


Multiple Metal-Carbon Bonds for Catalytic Metathesis Reactions

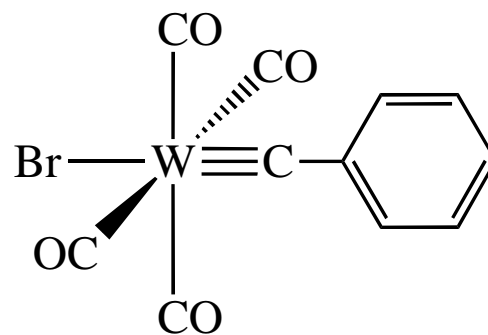
**Nobel Lecture
December 8, 2005**

Metal-carbon double and triple bonds in which the transition metal is in a "low oxidation state" were discovered by E. O. Fischer.



1964

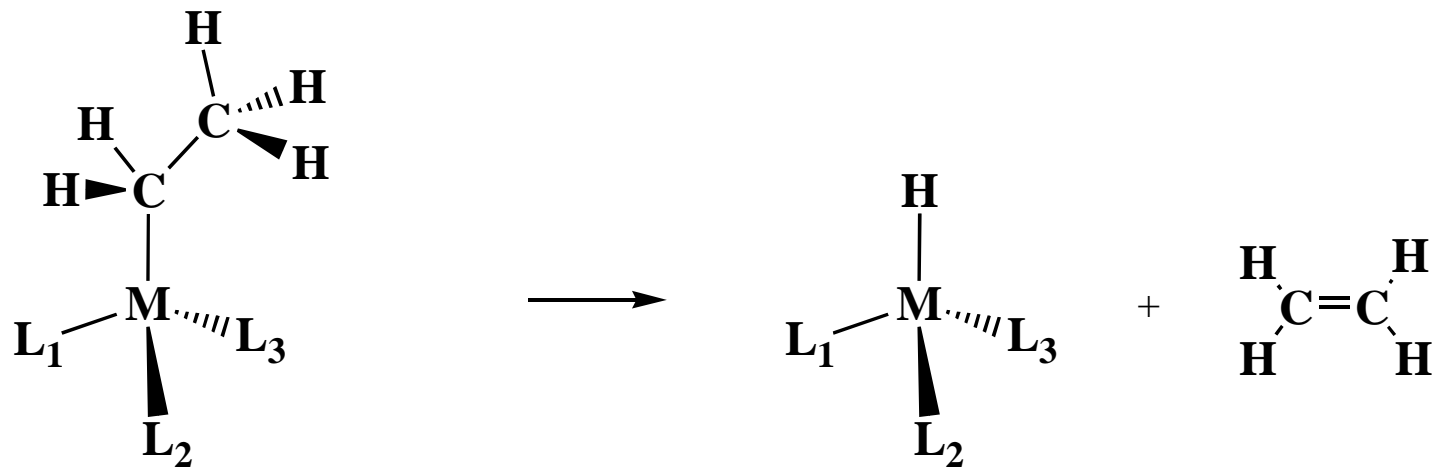
"carbene"



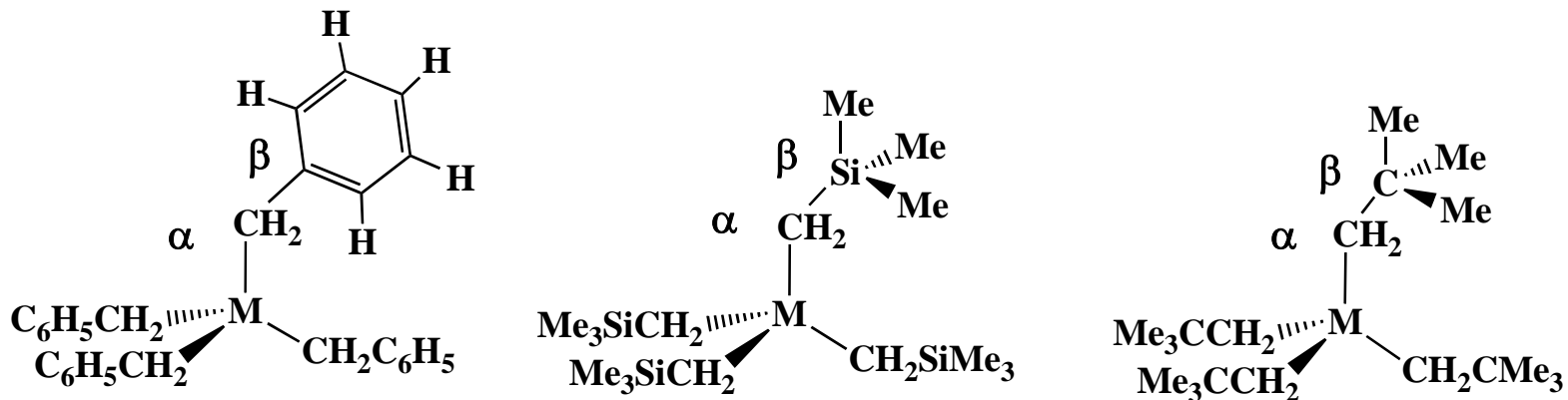
1973

"carbyne"

Beta hydride elimination in an ethyl complex

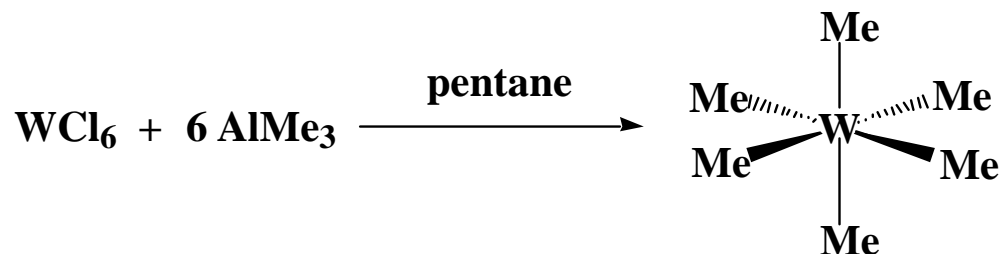


Known Group 4 Peralkyl Complexes (M = Ti, Zr, Hf) in 1973.



All alkyls lack one or more hydrogen atoms on the atom β with respect to the metal.

The first relatively stable permethyl complex



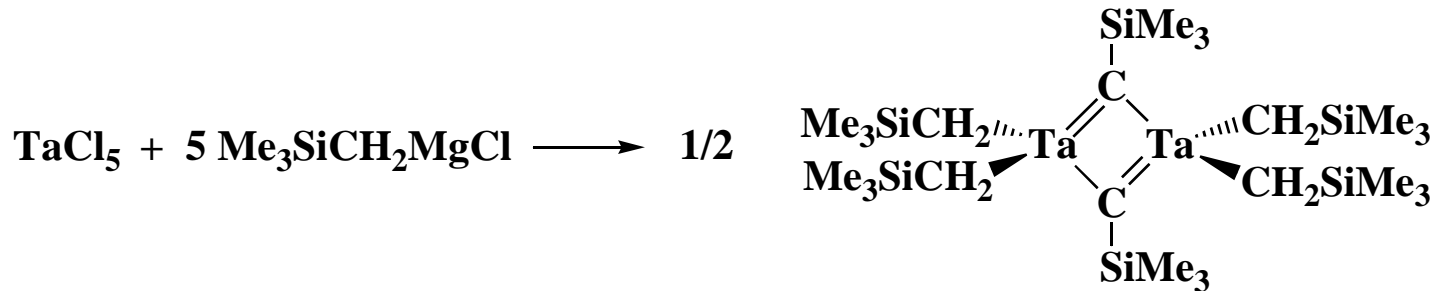
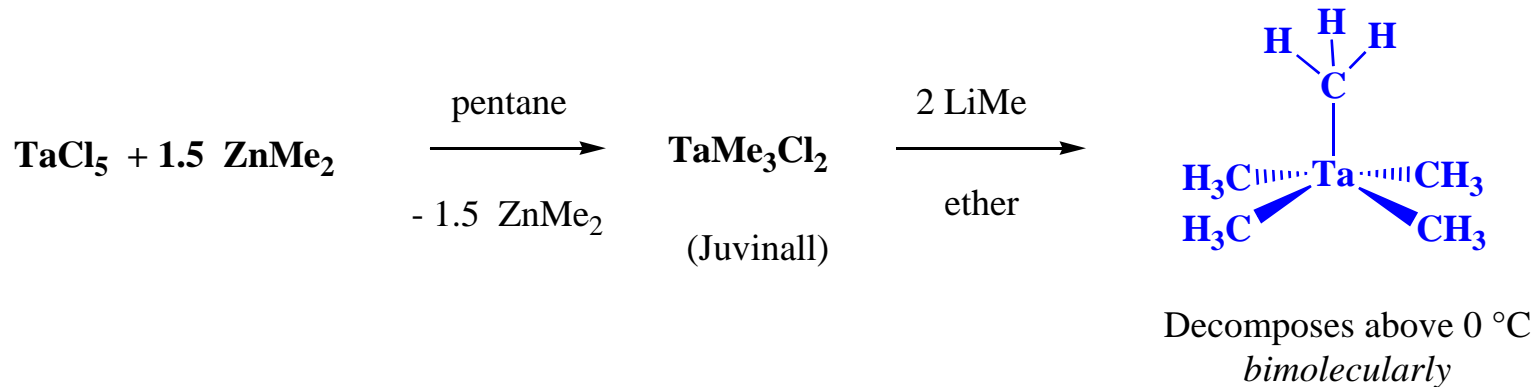
4	5	6	7	8
Ti	V	Cr	Mn	Fe
Zr	Nb	Mo	Tc	Ru
Hf	Ta	W	Re	Os

A. J. Shortland and G. Wilkinson
J. Chem. Soc., Dalton Trans. **1973**, 872.

“**Note added in proof.* Hexamethylrhenium (K. Mertis and G. Wilkinson) and pentamethyl[t]antalum (R. Schrock, DuPont, Wilmington, private communication) have recently been synthesized.”

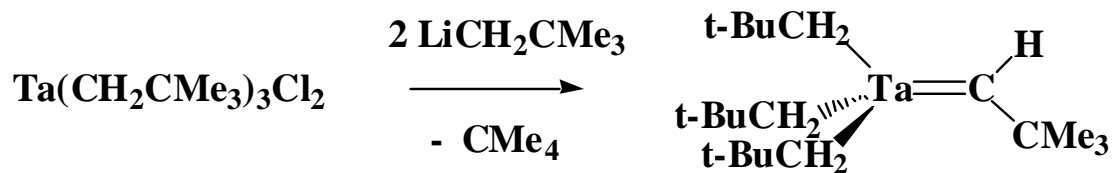
Geoffrey Wilkinson, Nobel Lecture, December 11, 1973

Synthesis of tantalum pentaalkyls



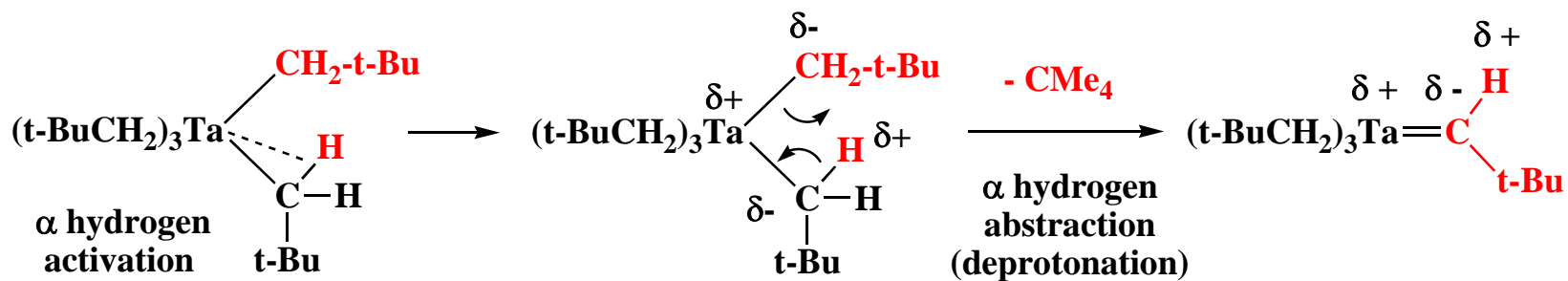
"It is assumed that a penta-alkyl complex cannot exist for steric reasons."
(Mowat, W.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1973**, 10, 1120.)

Neopentyls yield a *stable* product of α hydrogen abstraction.

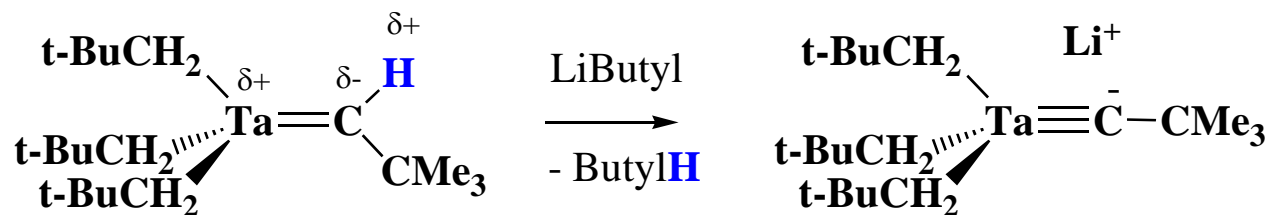


J. Am. Chem. Soc. **1974**, 96, 6796

Distills in a good vacuum at 75°C.

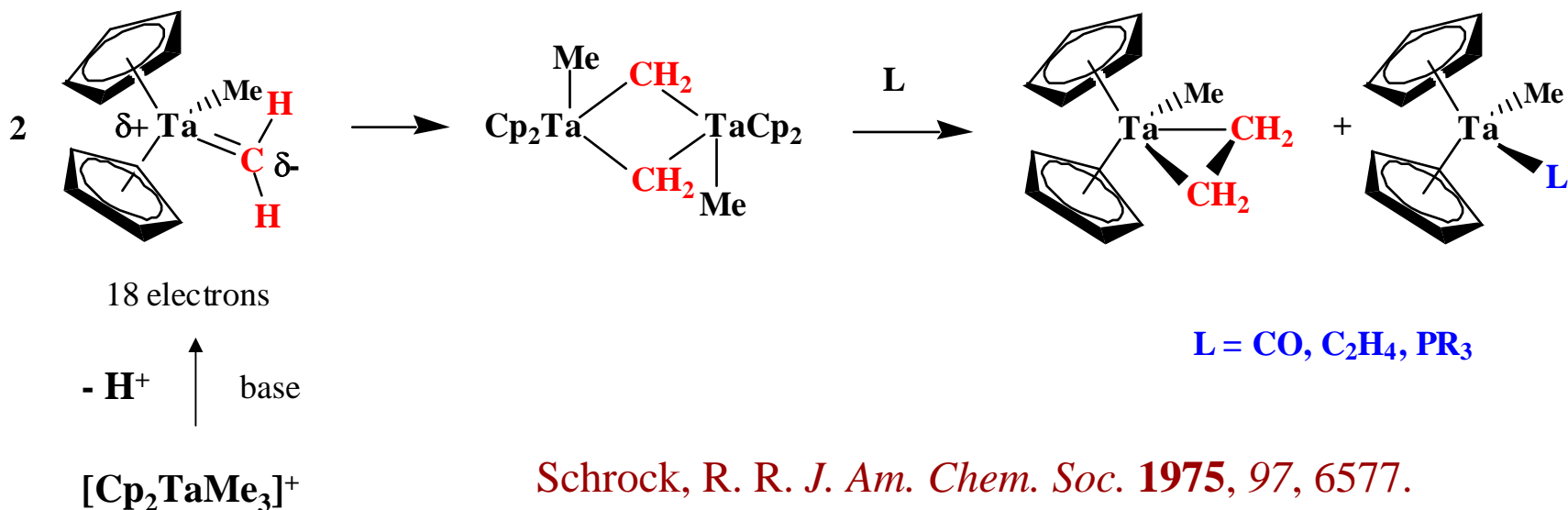


Alkylidenes can be deprotonated to yield tantalum-carbon triple bonds.



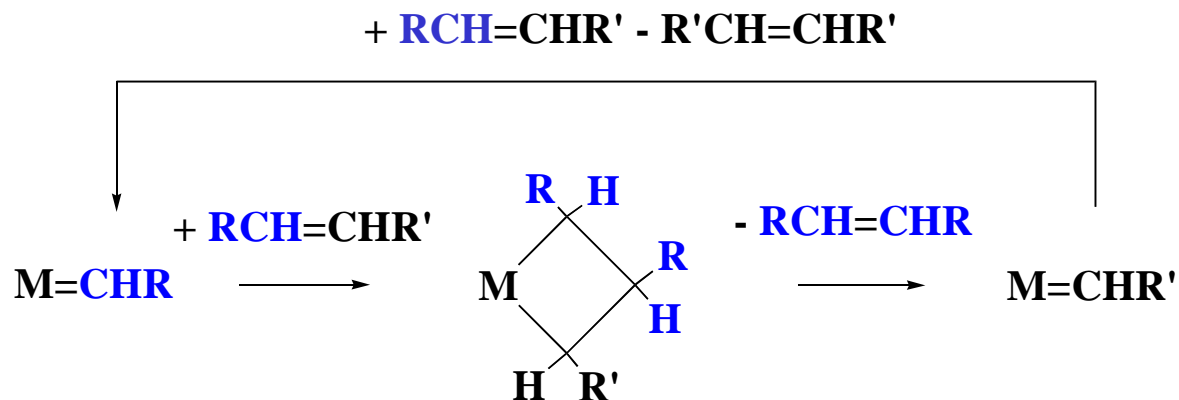
Guggenberger, L. J.; Schrock, R. R. *J. Am. Chem. Soc.* **1975**, *97*, 2935.

Alkylidenes decompose bimolecularly.



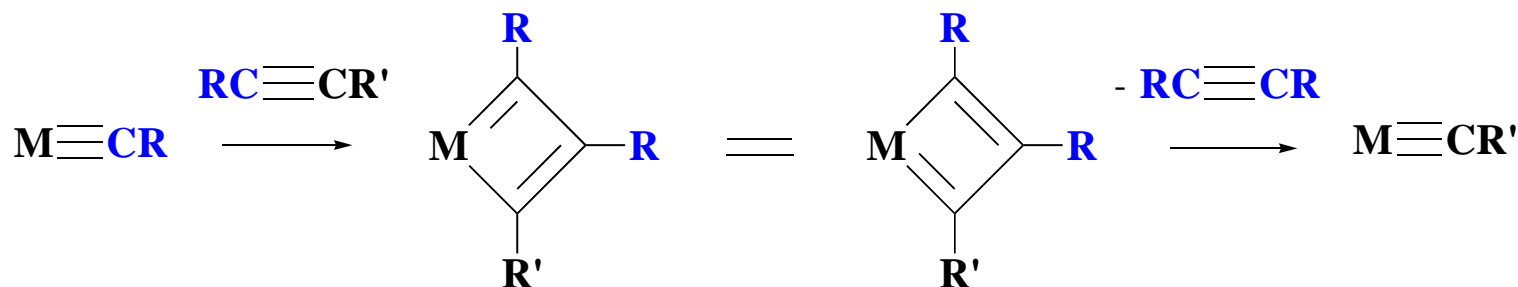
Bimolecular decomposition of alkylidenes, especially methylenes, is difficult to prevent, especially in electron deficient species.

Olefin metathesis and the Chauvin mechanism (1971)



$\text{M} = \text{Mo, W, or Re}$

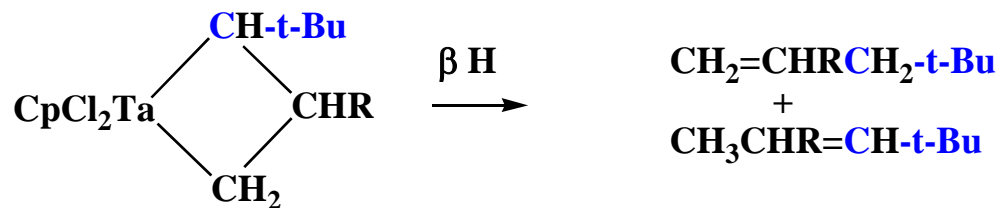
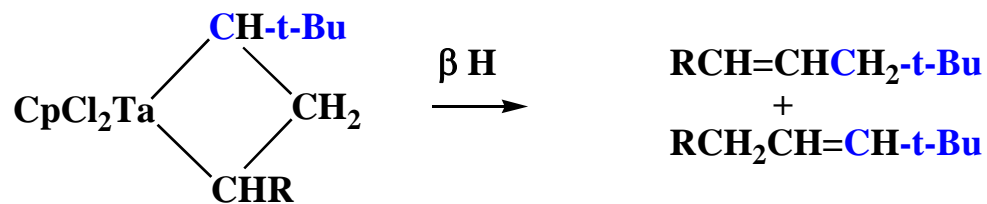
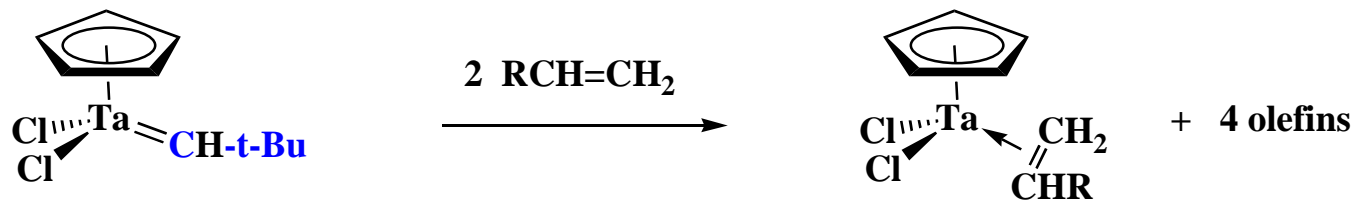
Alkyne metathesis and the metalacyclobutadiene mechanism



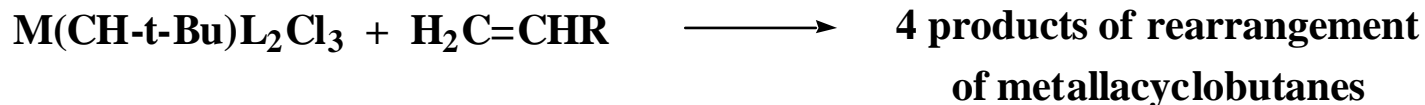
(suggested by
T. Katz; 1975)

$\text{M} = \text{Mo}, \text{W}$

Reaction of tantalum alkylidenes with olefins.



Modification of Nb and Ta yields metathesis catalysts



M = Nb or Ta

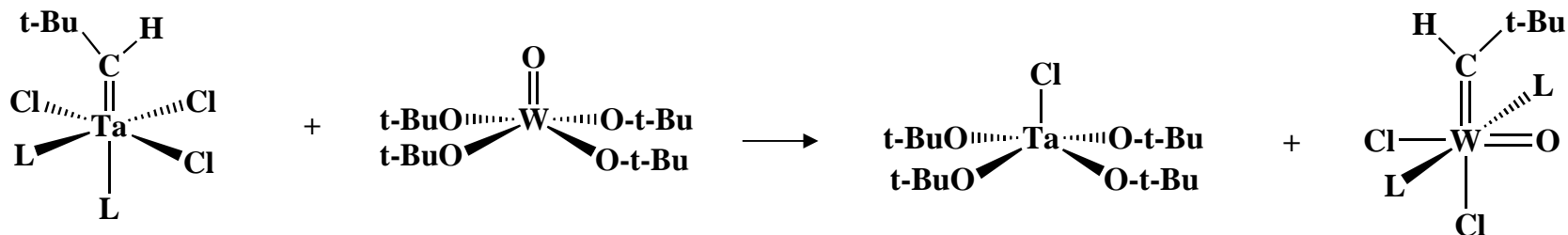
L = PMe₃



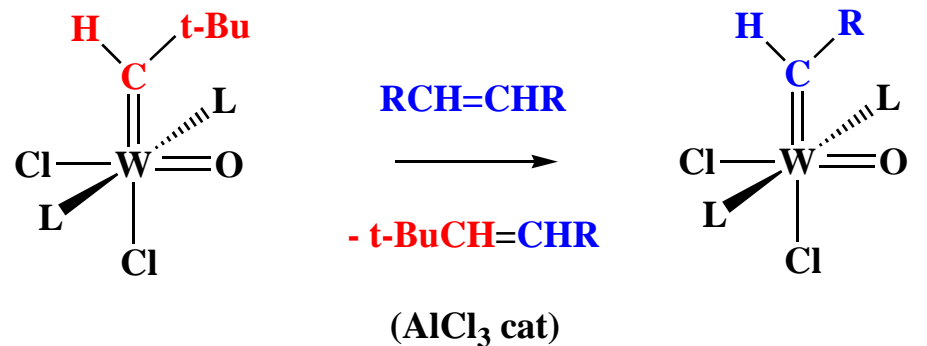
Alkoxides "prevent reduction" and "promote metathesis."

J. Molec. Catal. **1980**, *8*, 73; *J. Am. Chem. Soc.* **1981**, *103*, 1440.

An oxo neopentylidene complex of tungsten

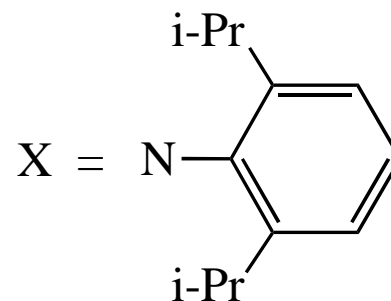
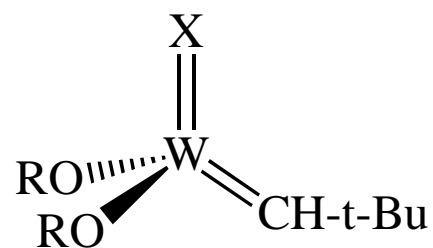


L = a phosphine, e.g. PEt_3



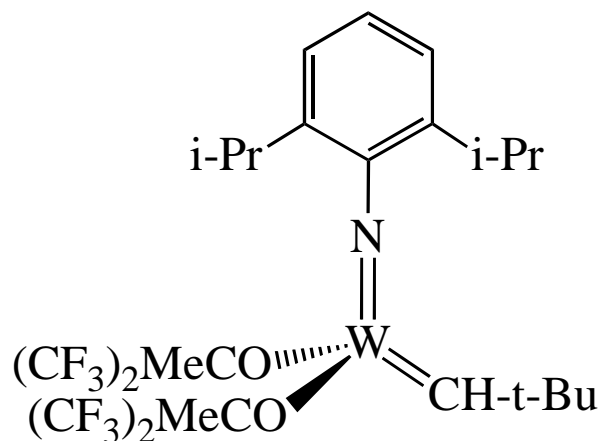
Even $\text{R} = \text{H}$

A sterically demanding diisopropylphenyl imido group might be a desirable "ancillary" ligand.



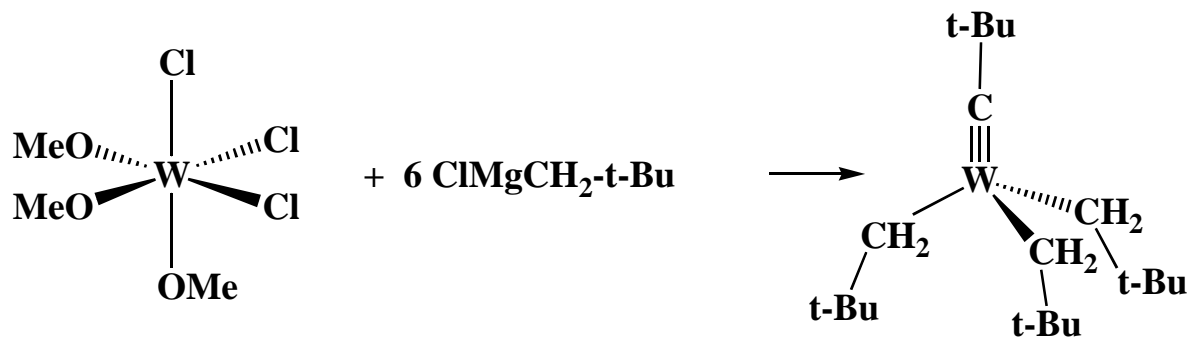
The OR group should be a sterically demanding tertiary alkoxide.

A sterically demanding diisopropylphenyl imido group might be a desirable "ancillary" ligand.



Hexafluoro-*t*-butoxide was chosen as a highly electron withdrawing alkoxide.

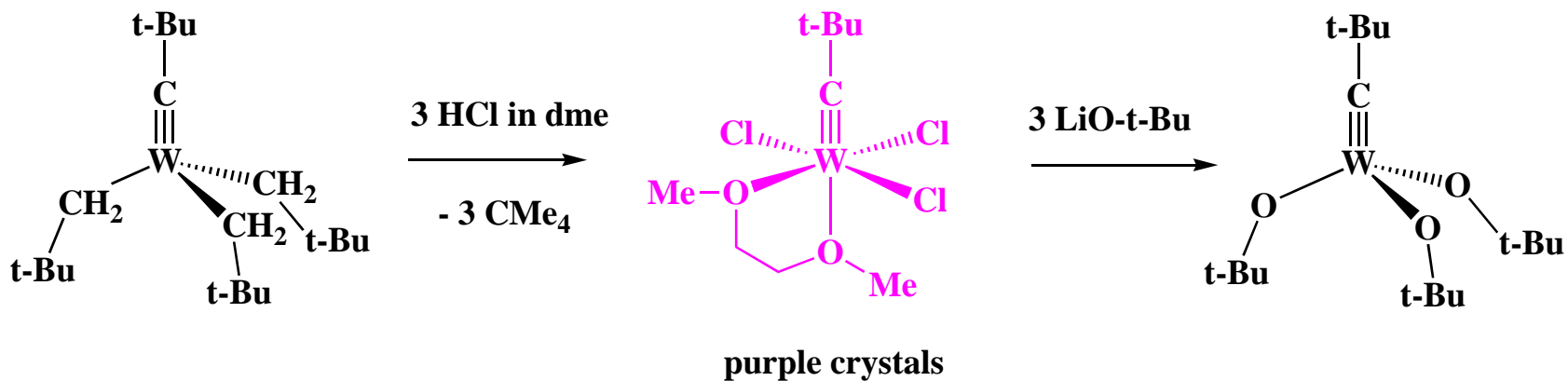
Synthesis of a tungsten neopentyldiyne complex



Volatile yellow crystals.
Thermally stable, distilling
at 75°C in a good vacuum.

(1978)

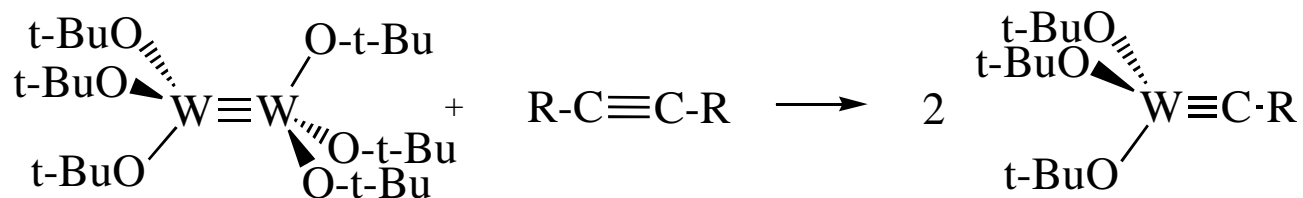
Tungsten-carbon triple bonds and alkyne metathesis



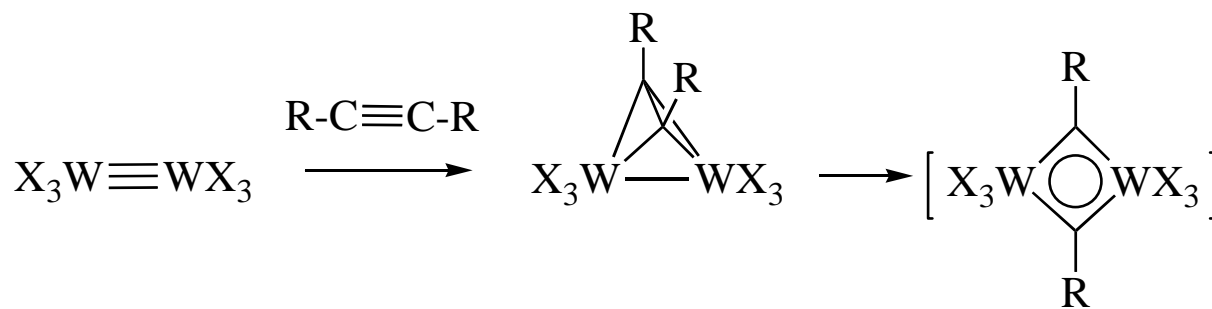
The tri-t-butoxide compound is a powerful catalyst for the alkyne metathesis reaction.



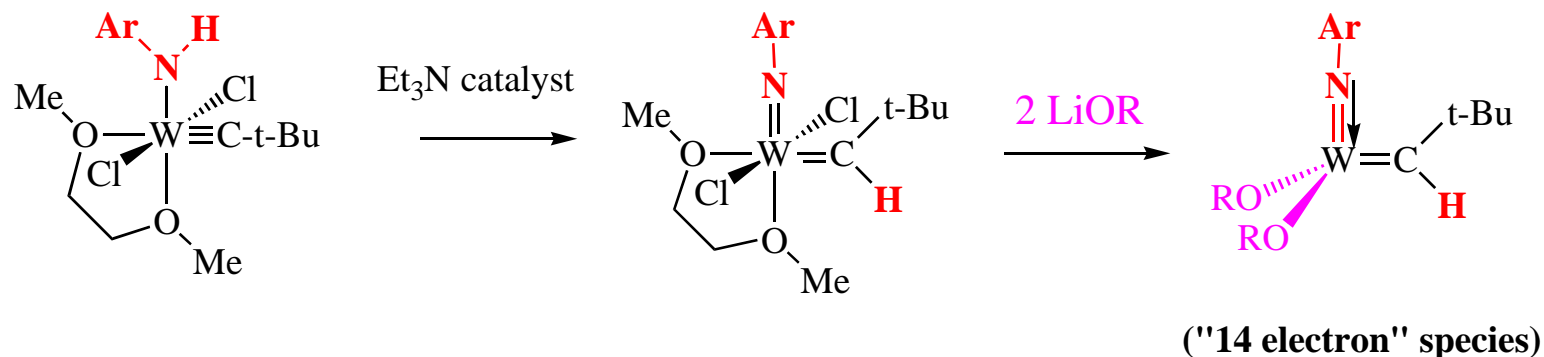
Metal-metal bonds and "metathesis" reactions.



(1982)

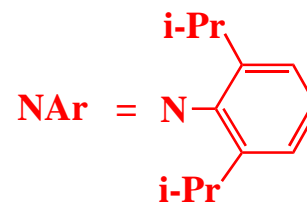


Synthesis of a tungsten imido alkylidene complex

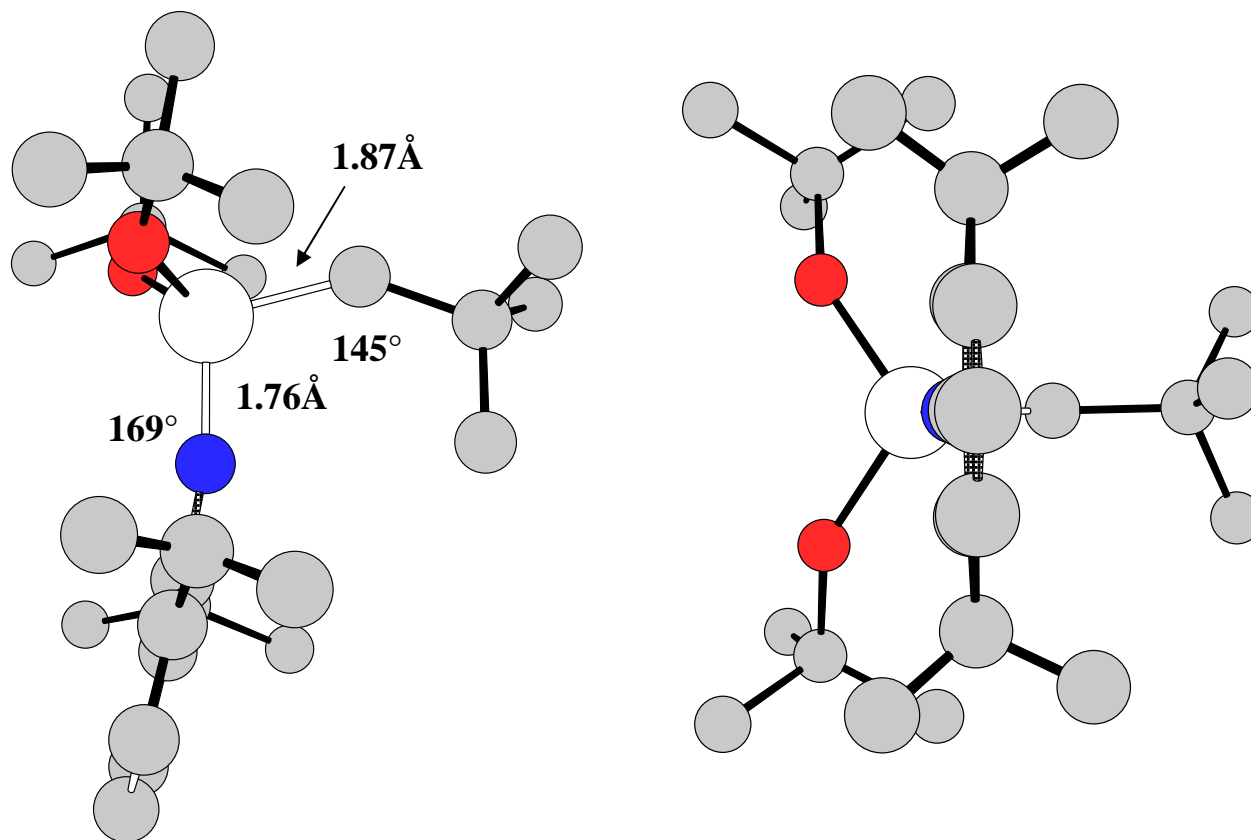


OR = O-t-Bu, OMe₂(CF₃), OMe(CF₃)₂,
and various bulky phenoxides

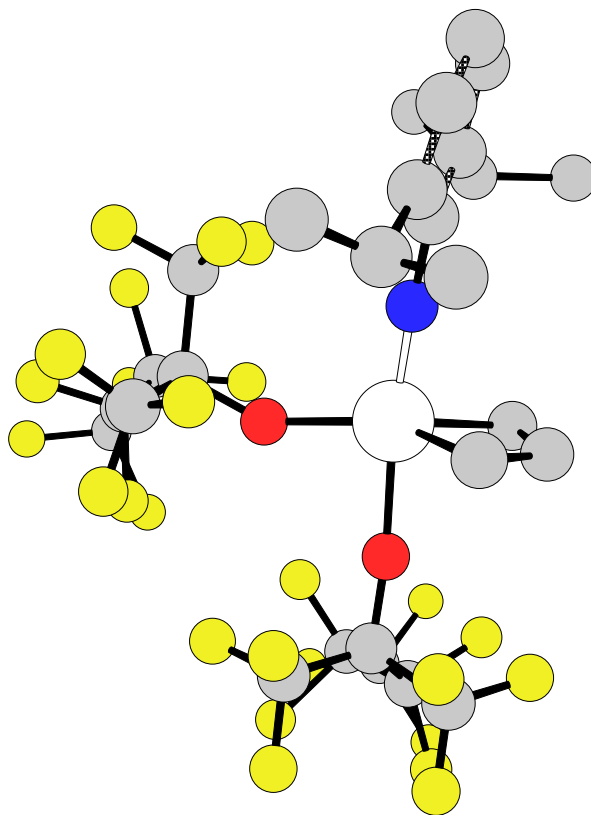
W(NAr)(CH-t-Bu)(OR)₂ species are "well-defined" catalysts for the metathesis of olefins and the activity can be varied systematically by varying OR.



Structure of *syn*-W(NAr)(CH-*t*-Bu)(O-*t*-Bu)₂

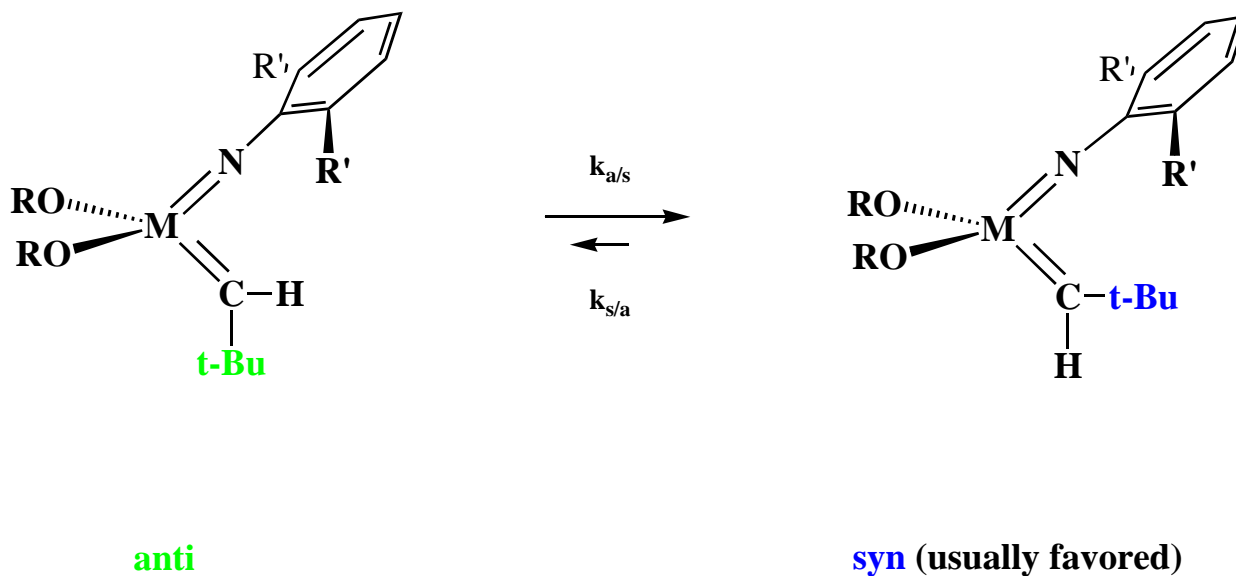


Tungstenacyclobutanes can be isolated, but can be too stable toward loss of olefin.

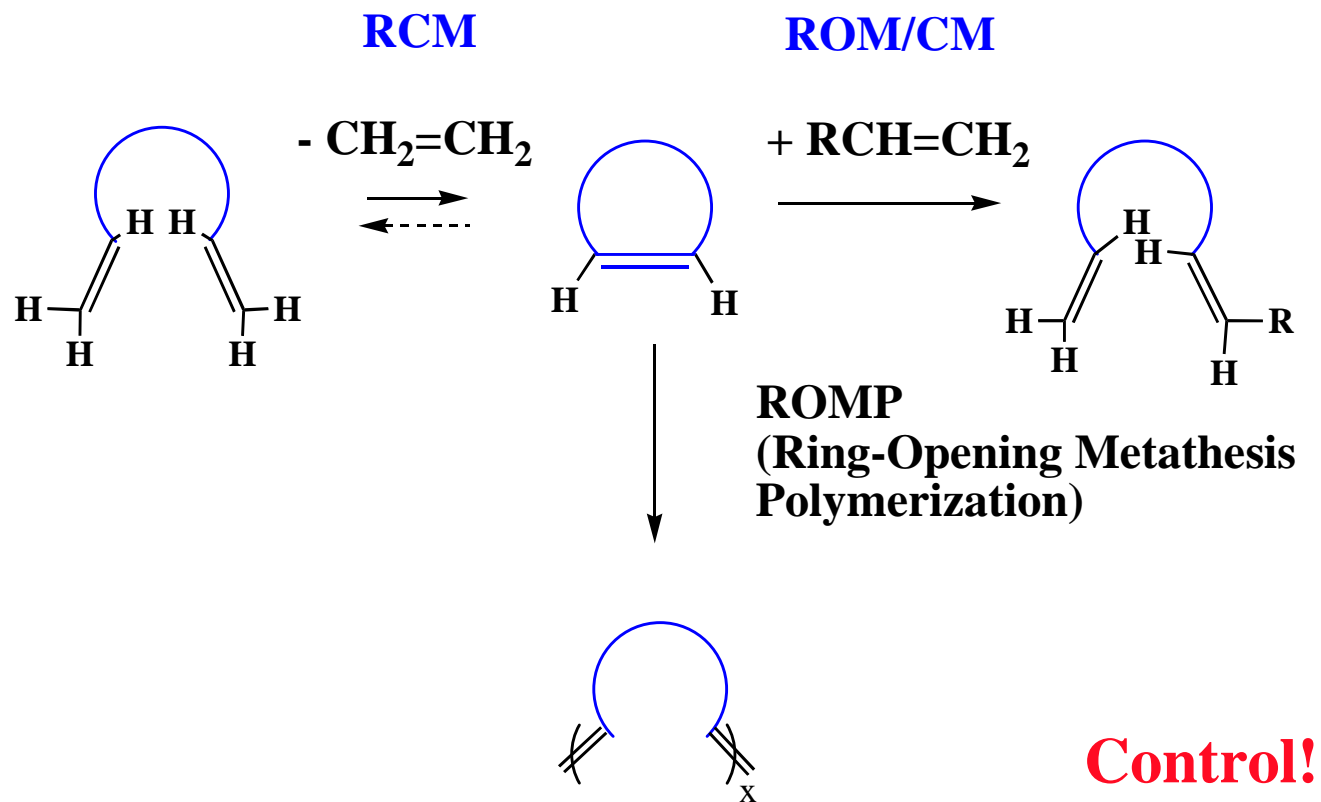


Molybdacyclobutane intermediates lose an olefin more readily.

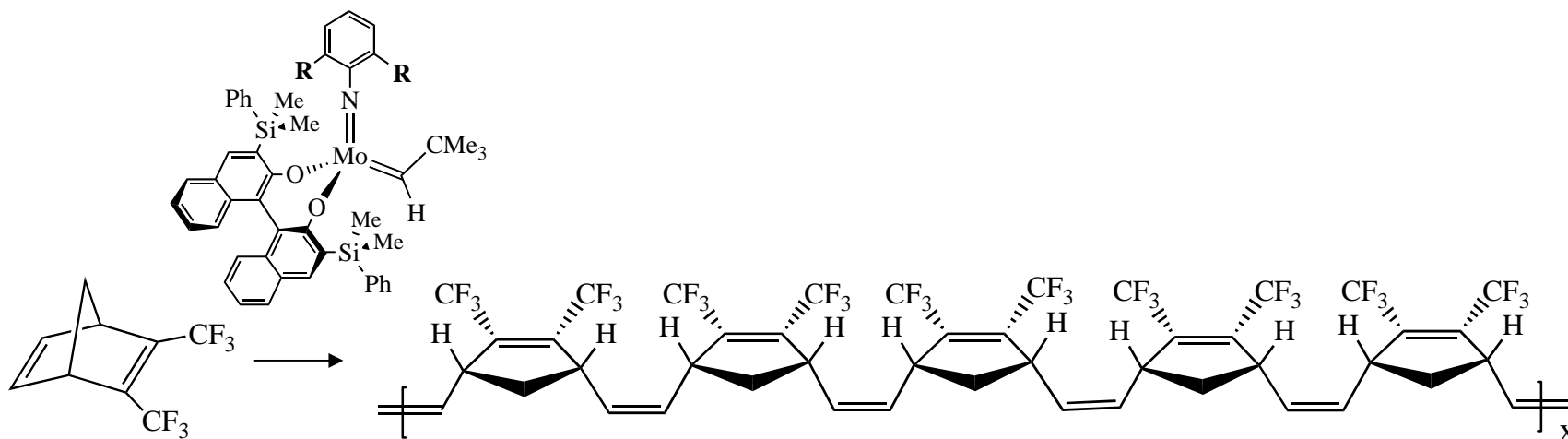
Two isomers (*anti* and *syn*) are available in any system through rotation about the M=C bond.



Olefin metathesis variations



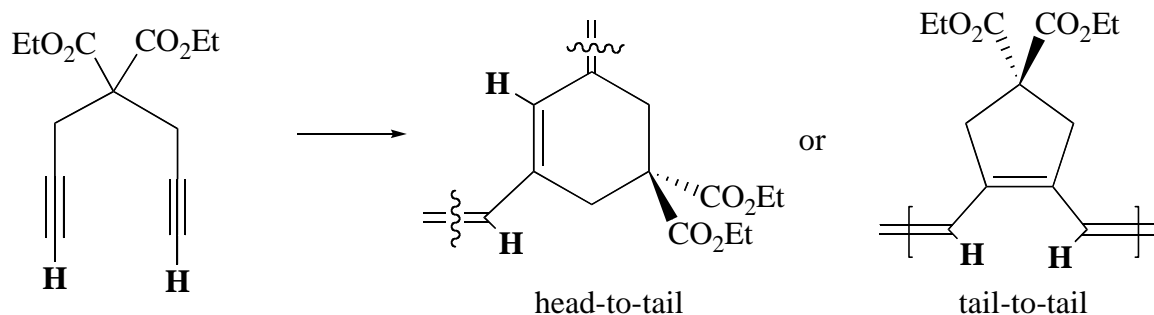
Polymerization of bistrifluoromethylnorbornadiene via enantiomorphic site control.



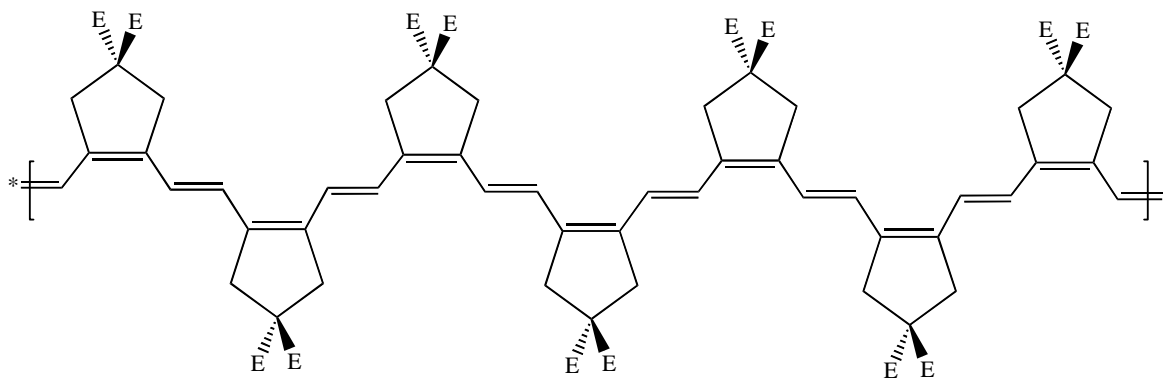
all *cis* and *isotactic* through enantiomeric site control when R = CH₃

When R = CH(CH₃)₂ the polymer structure has a relatively *random* (71% *cis*) structure.

Alkynes are polymerized to yield polyenes.



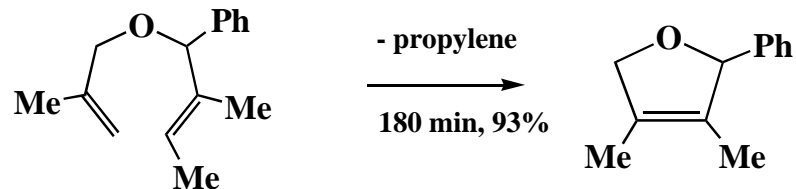
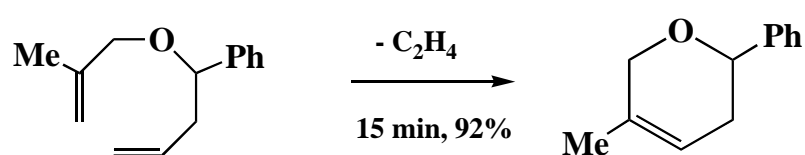
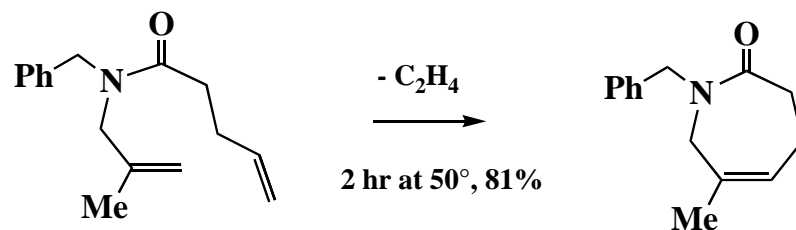
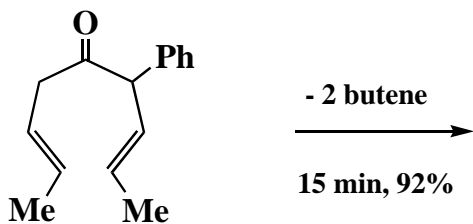
Soluble, highly conjugated (purple), and relatively air-stable;
both rings observed in polymer made with Mo(NAr)(OR_{F6})₂ catalyst.



>95% 5-membered rings produced with Mo(NAr)(O-t-Bu)₂ catalyst.

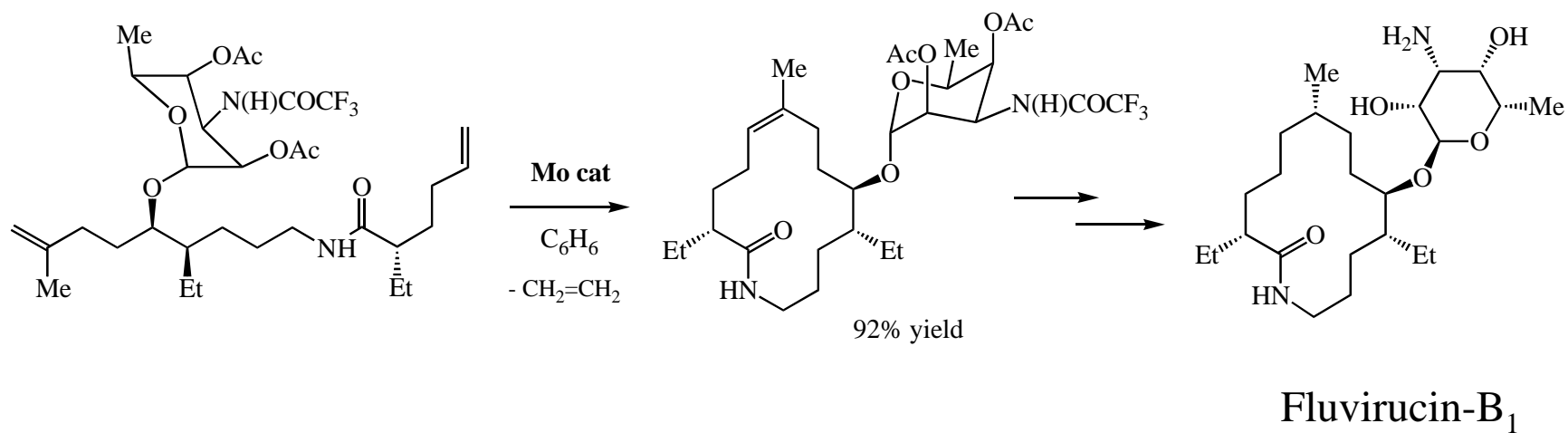
Ring-closing metathesis with Mo catalyst (4-5 mol%)

(Catalyst = Mo(NAr)(CHCMe₂Ph)[OCMe(CF₃)₂]₂)



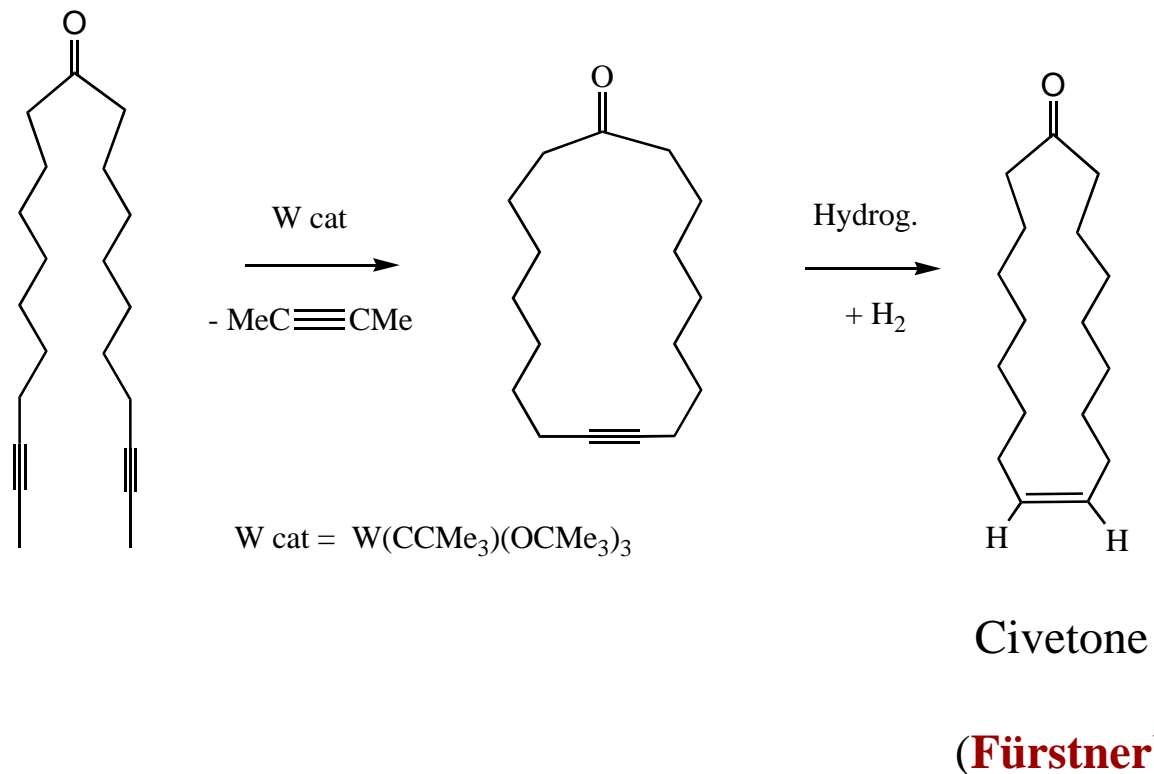
Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* 1992, 114, 5426; 7324.

Synthesis of Fluvirucin-B₁



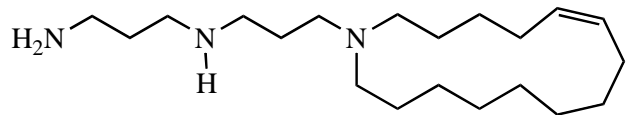
A. F. Houry, Z. M. Xu, D. A. Cogan, A. H. Hoveyda, *J. Am. Chem. Soc.* **1995**, *117*, 2943.

Mo or W catalyzed alkyne metathesis reactions are useful in organic chemistry.

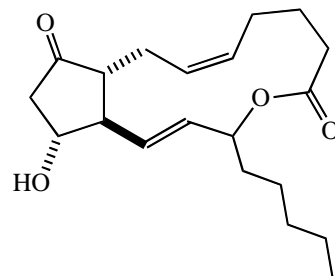


Olefins do not appear to react with M-C triple bonds.

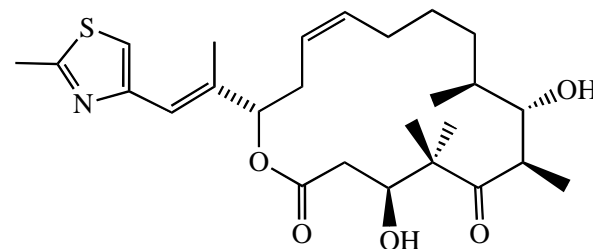
Other examples of alkyne metathesis in organic synthesis



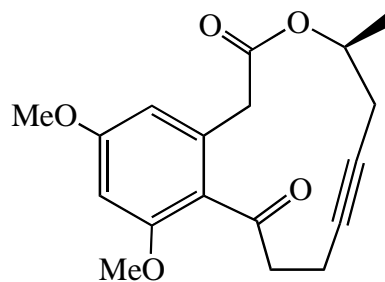
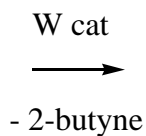
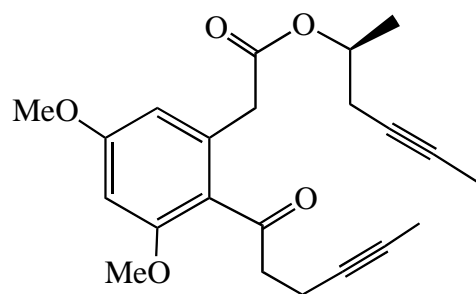
Motuporamine C



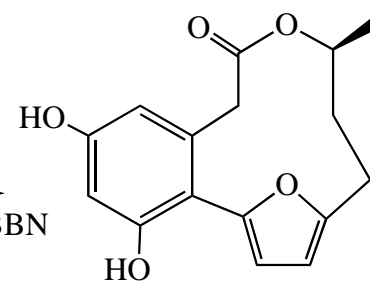
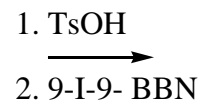
PGE₂-1,15-lactone



Epothilone C

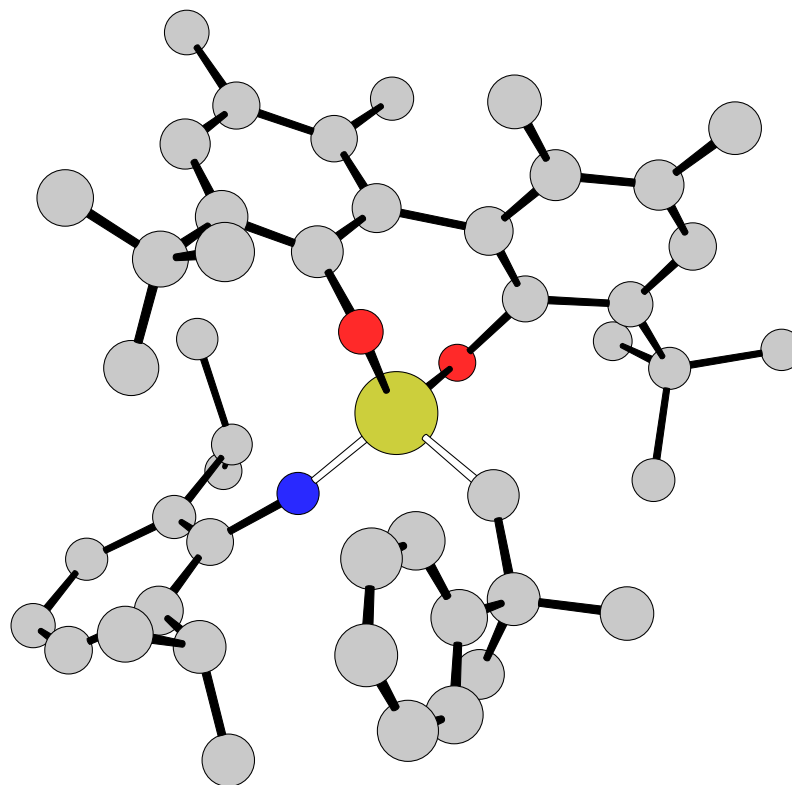


80%



S-(+)-citrefuran

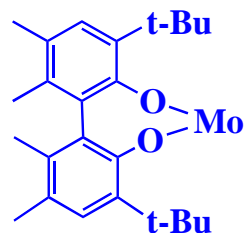
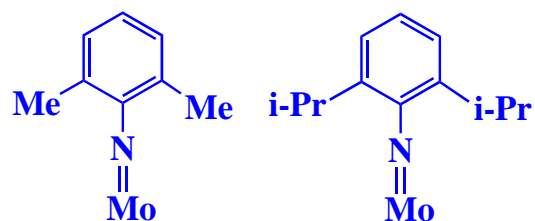
An enantiomerically pure Mo catalyst



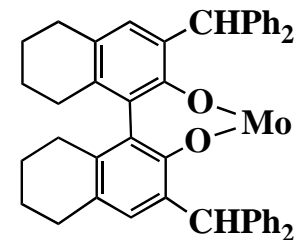
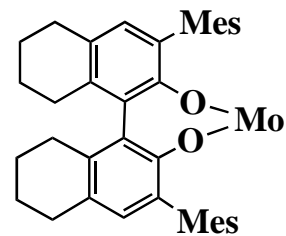
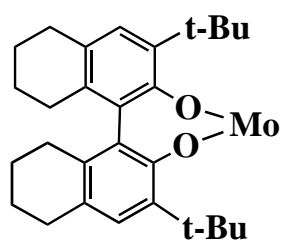
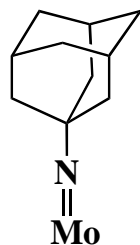
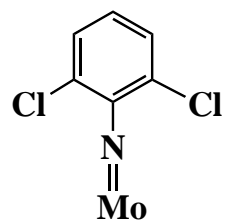
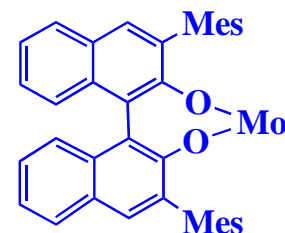
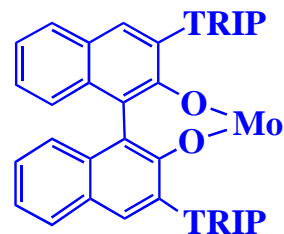
Alexander, J. B.; La, D. S.; Cefalo, D. R.; Hoveyda, A.; Schrock, R. R.
J. Am. Chem. Soc. **1998**, *120*, 4041.

Asymmetric catalyst design; a modular approach

Imido Groups

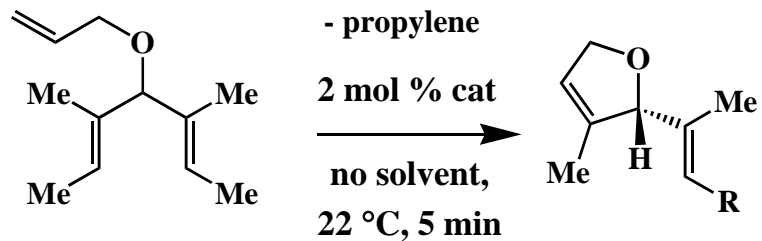
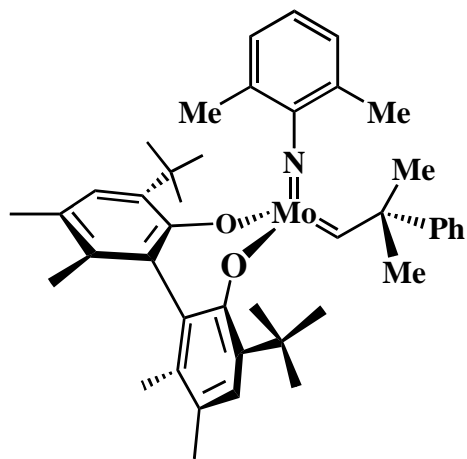


Diolates

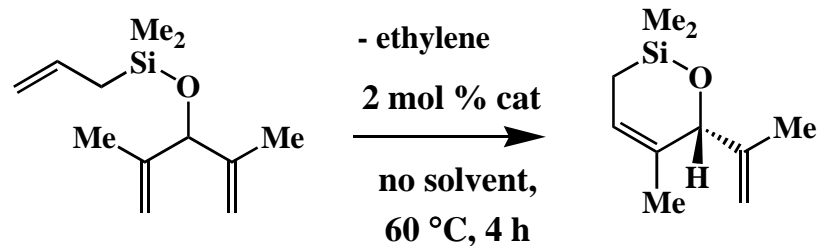
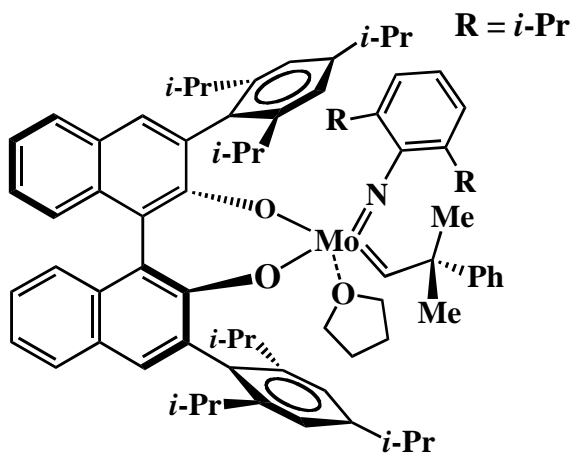


24 catalysts!

Asymmetric Ring-Closing Metathesis (ARCM)

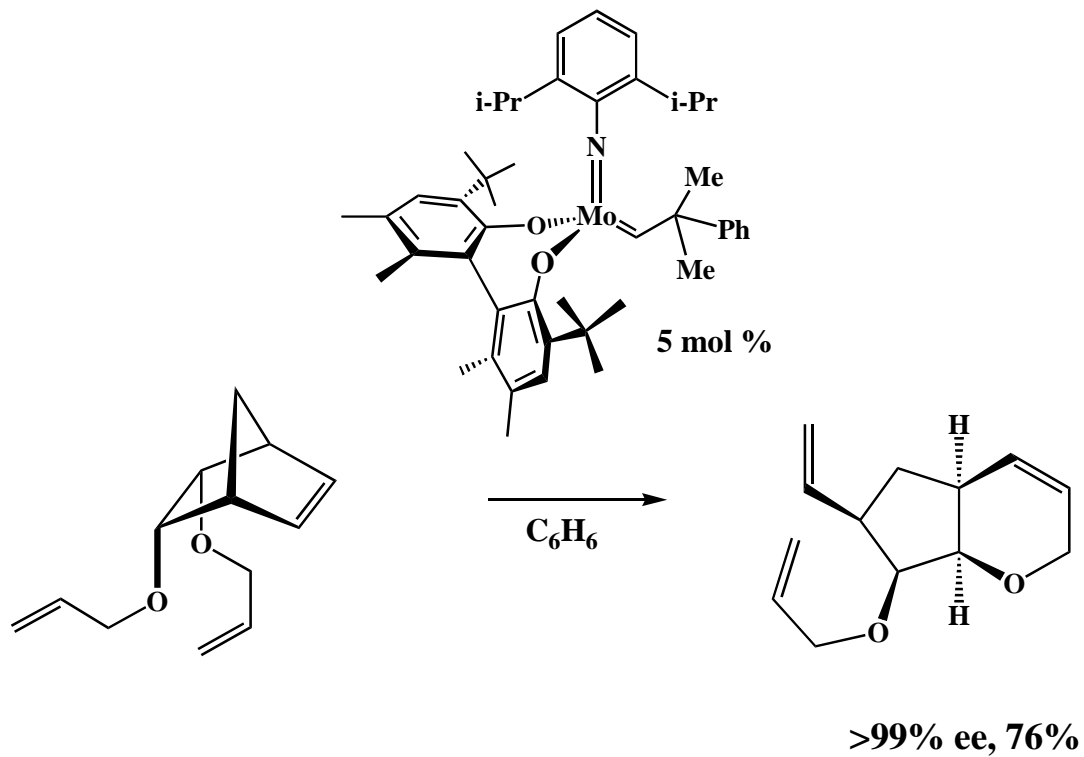


99% ee, 93%

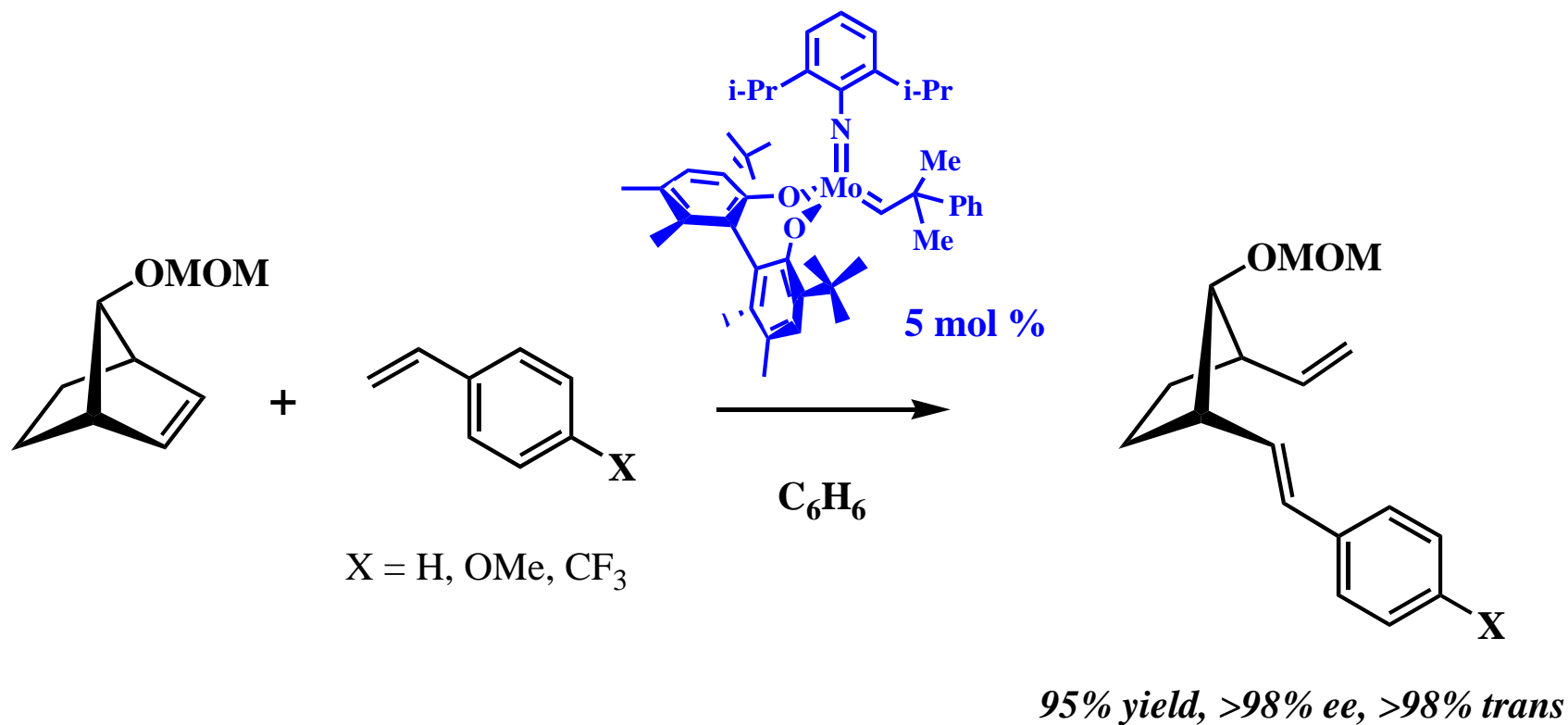


>99% ee, 98%

Ring-Opening / Ring-Closing Metathesis

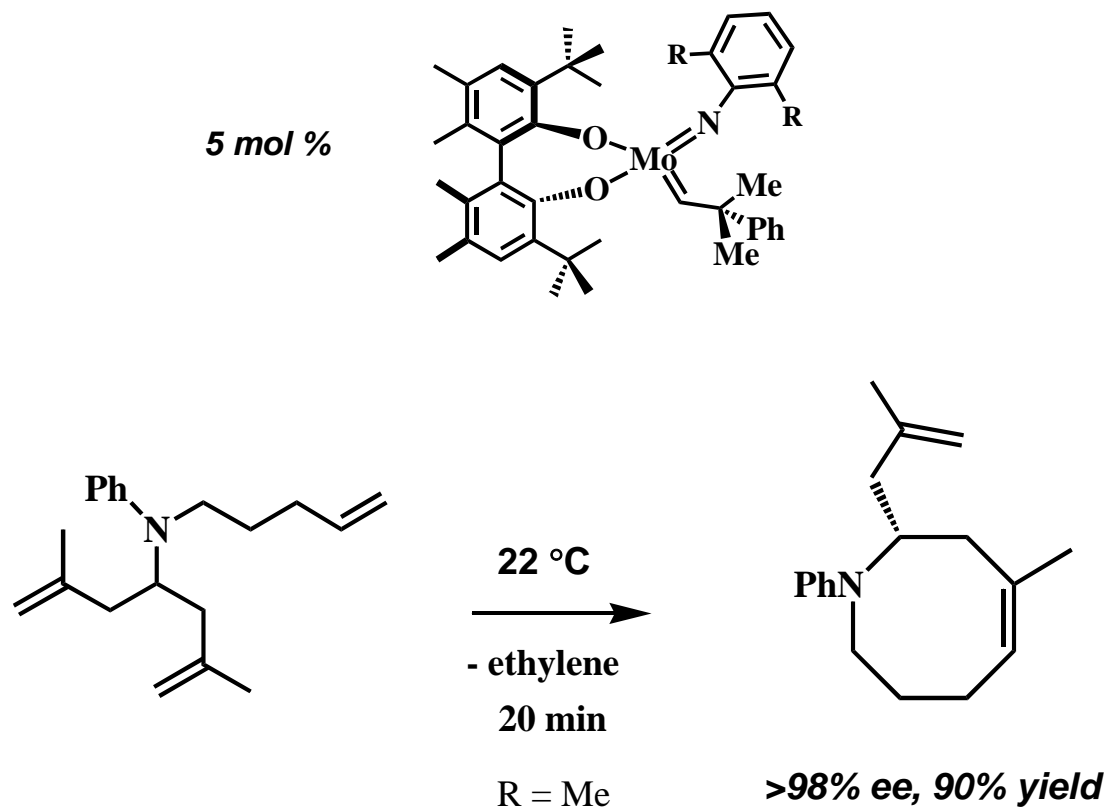


Ring-Opening / Cross Metathesis

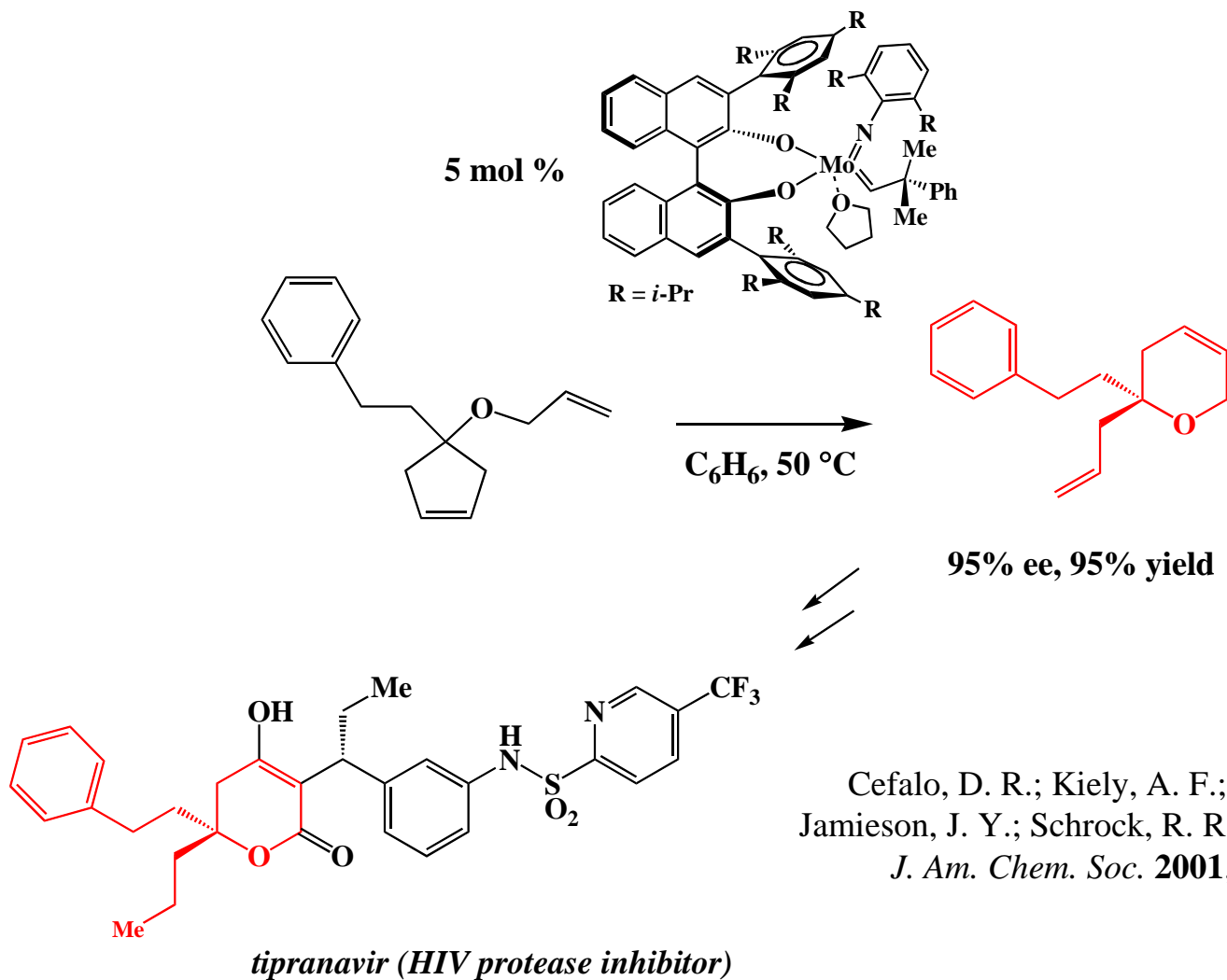


D. S. La; J. G. Ford; E. S. Sattely; P. J. Bonitatebus; R. R. Schrock;
A. H. Hoveyda *J. Am. Chem. Soc.* **1999**, *121*, 11603.

Nitrogen-Containing substrates

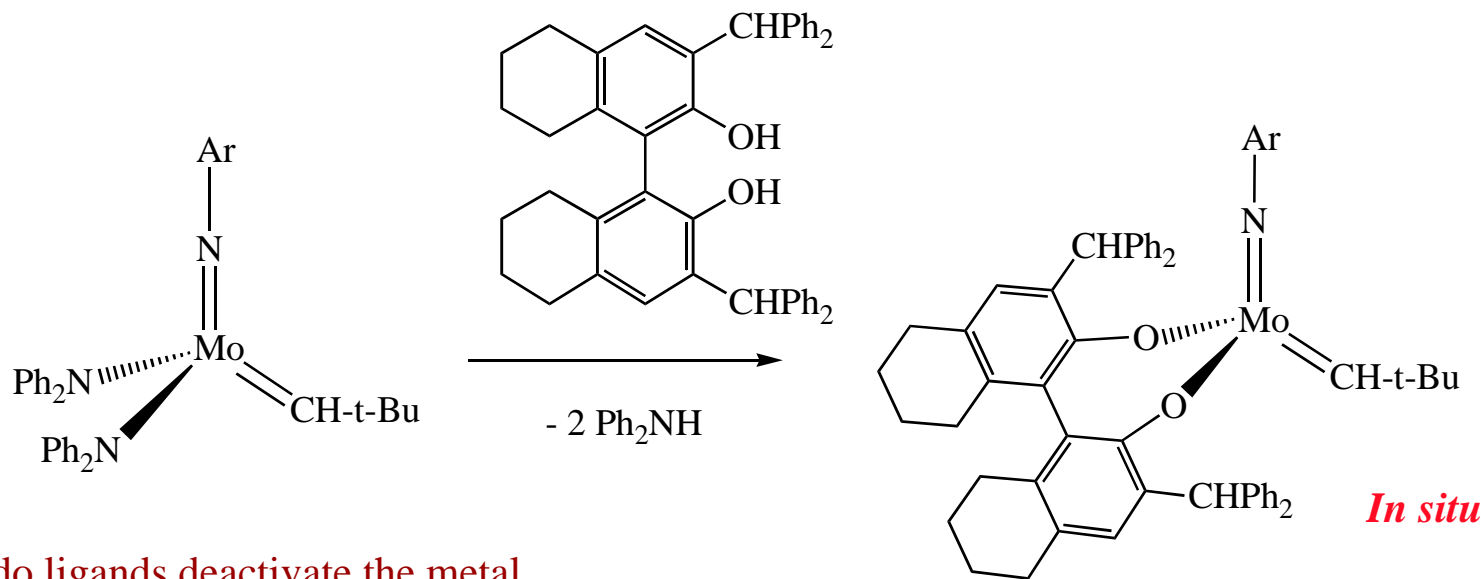


Enantioselective synthesis of a tertiary ether in a drug



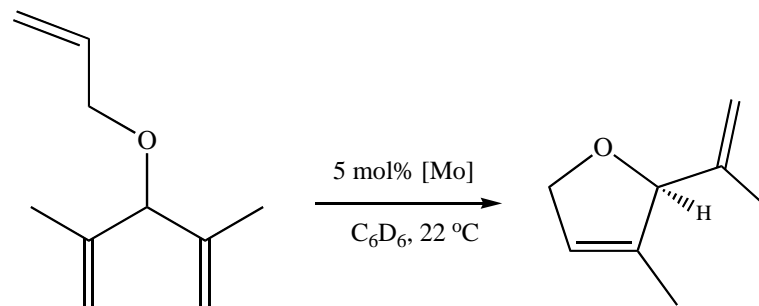
Cefalo, D. R.; Kiely, A. F.; Wuchrer, M.;
Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H.
J. Am. Chem. Soc. **2001**, *123*, 3139.

A bis amido alkylidene catalyst precursor.

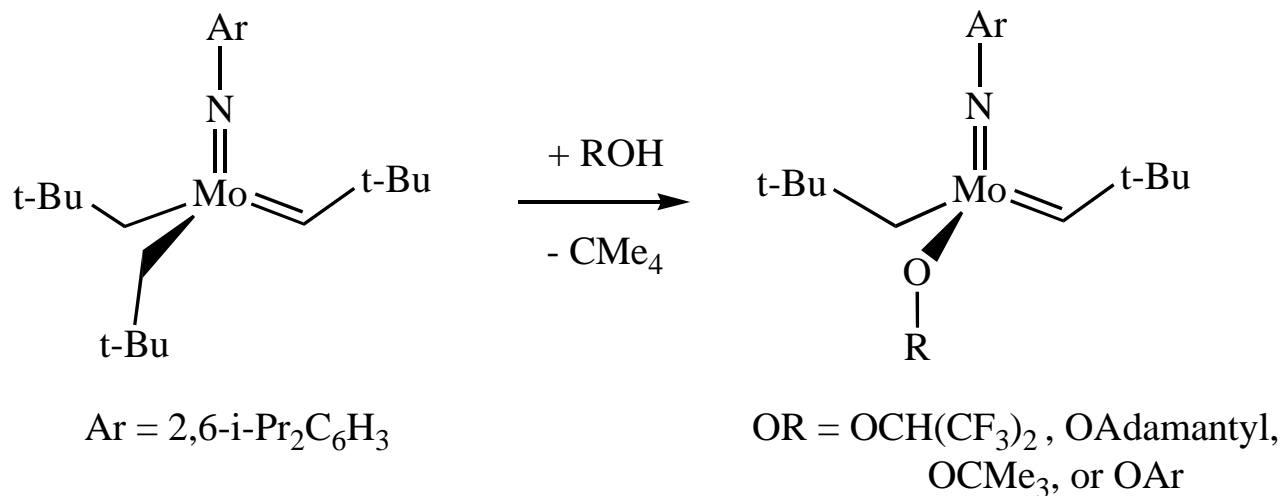


Amido ligands deactivate the metal toward metathesis reactions.

In situ catalyst prepared with gives same ee (93-94%) as the isolated catalyst.



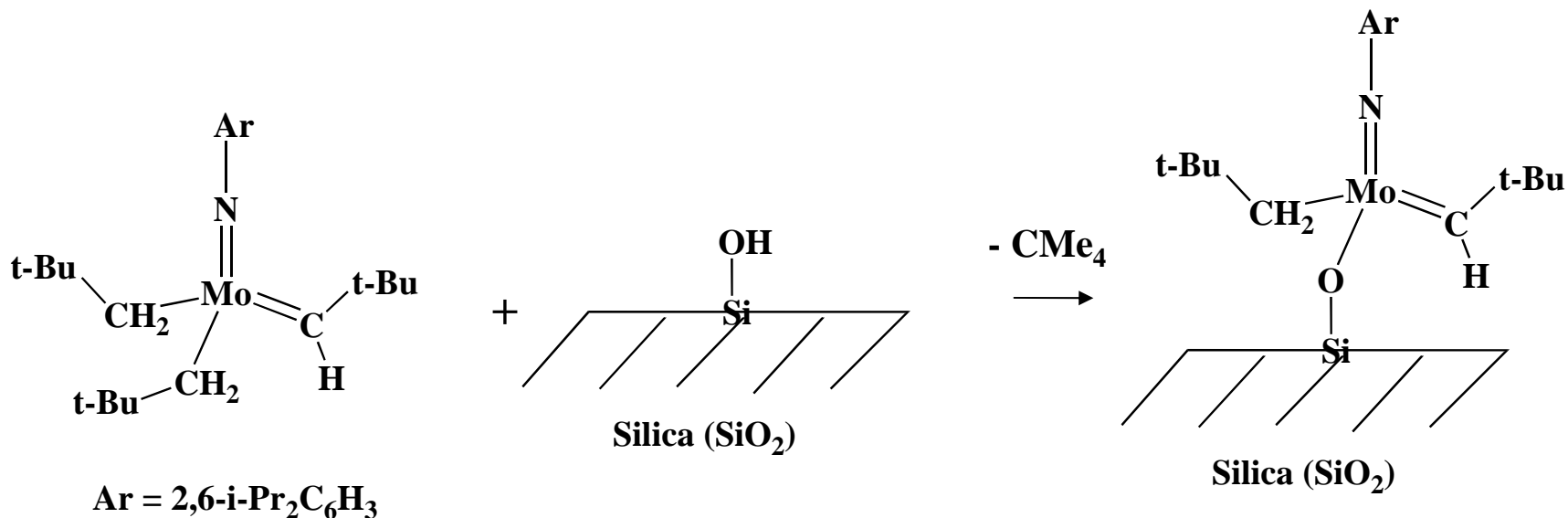
Dineopentyl species were examined as bisalkoxide catalyst precursors.



Preliminary results suggest that monoalkoxides are at least as active as bisalkoxides!

(Surprising since dineopentyl species are essentially inactive.)

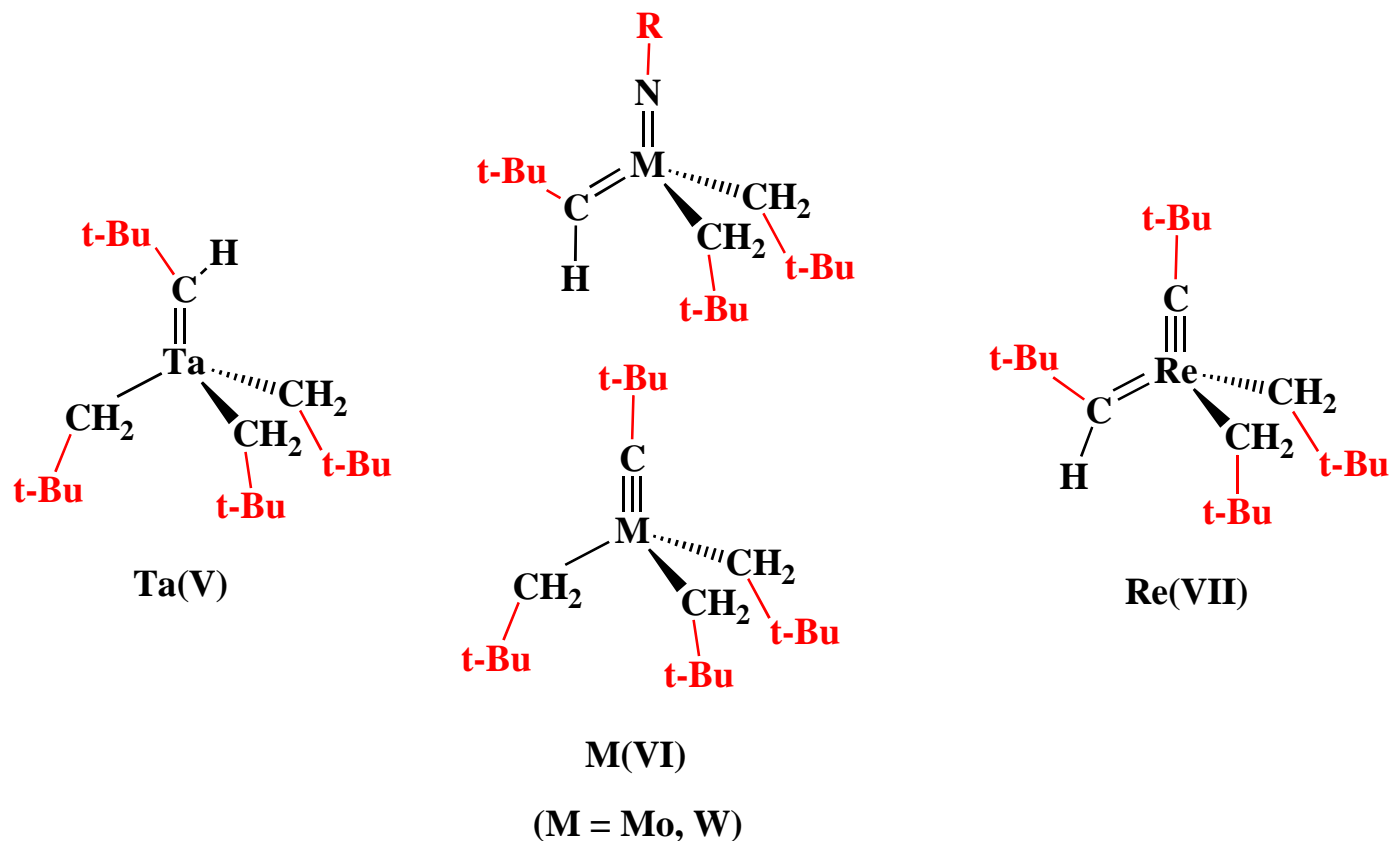
"Well-defined" catalysts can be prepared on a silica surface.



Bimolecular decomposition of alkylidenes is not possible.

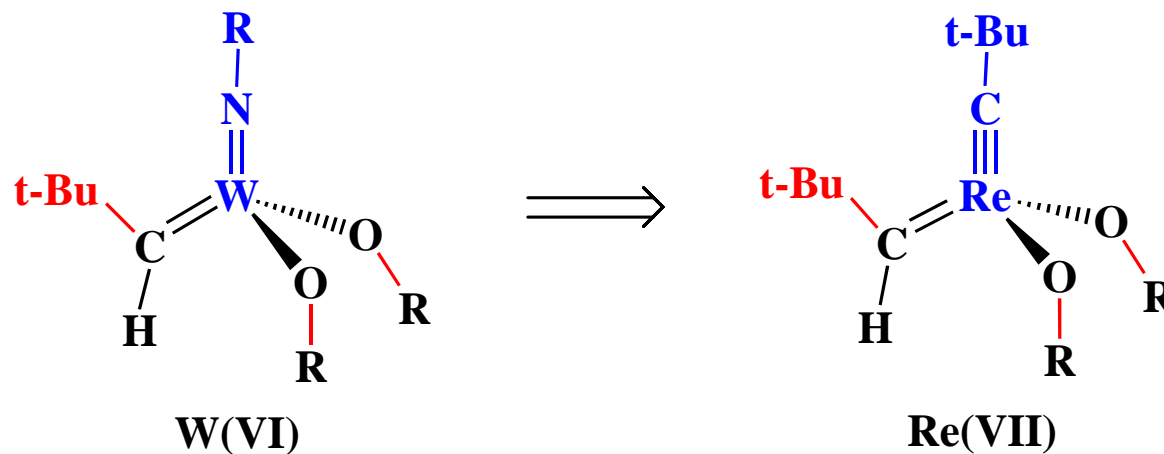
Frédéric Blanc, Anne Baudouin, Christophe Copéret, Jean Thivolle-Cazat, Jean-Marie Basset, Anne Lesage, Lyndon Emsley, Amritanshu Sinha, Richard R. Schrock, *Angew. Chem. Int. Ed.*, in press.

Well-defined catalysts can be prepared on a silica surface using other "clean" neopentyl sources.



Cóperet, C.; Chabanas, M.; Saint-Arroman, R. P.; Basset, J.-M.
Angew. Chem. Int. Ed. **2003**, 42, 156.

The principles of high oxidation state alkylidene and alkylidyne chemistry extend to Re(VII)

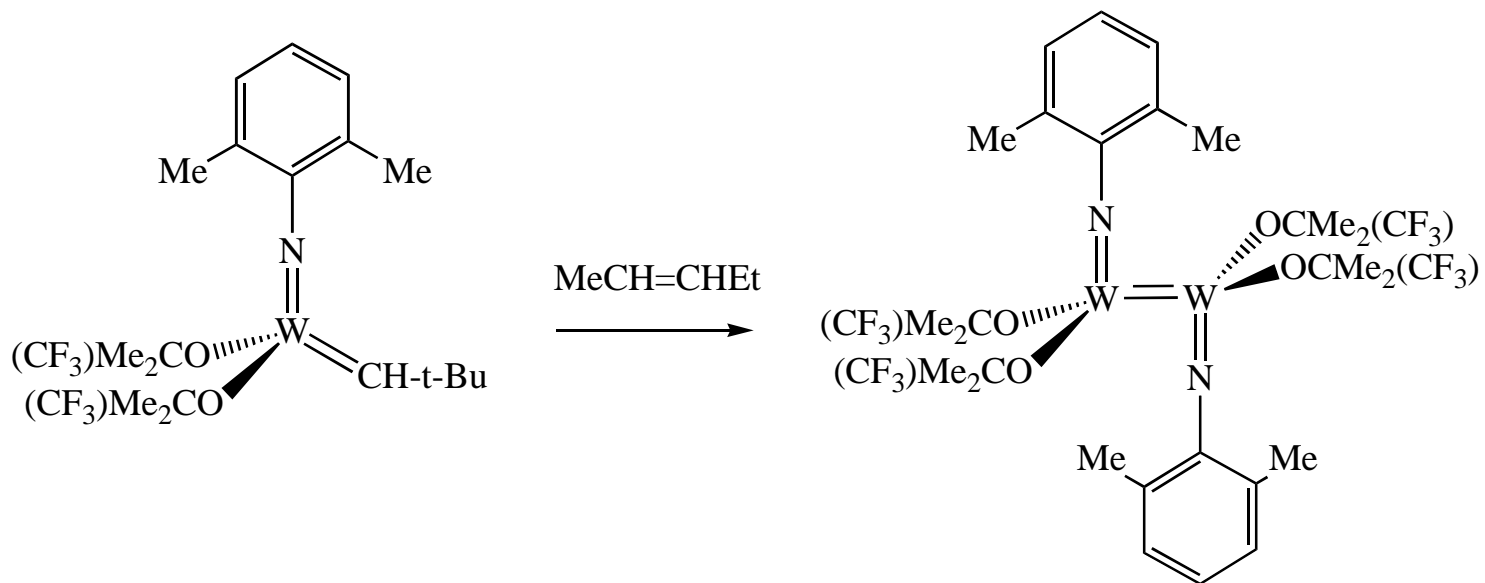


Olefins react with the Re=CHR bond selectively, *not* the Re≡C-t-Bu bond.
These Re species are active olefin metathesis catalysts.

Present and future challenges

1. **Prevent** catalyst decomposition completely and/or find ways to **regenerate** catalysts from decomposition products.
2. Find ways to generate and evaluate all catalysts *in situ* from one precursor.
3. Synthesize **new catalysts** and aim for *additional selectivity and efficiency* in metathesis reactions.

"Unsupported" M=M bonds are formed in bisalkoxide systems



A W=W species (**W=W = 2.49 Å**)
that does *not* contain
bridging groups.