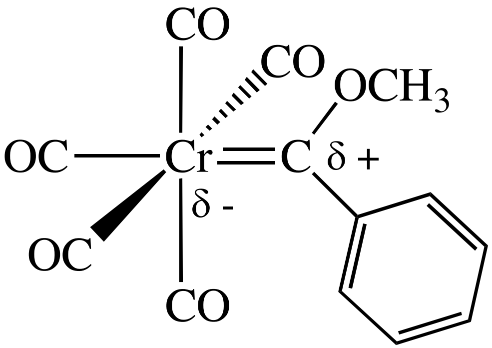
Multiple Metal-Carbon Bonds for Catalytic Metathesis Reactions

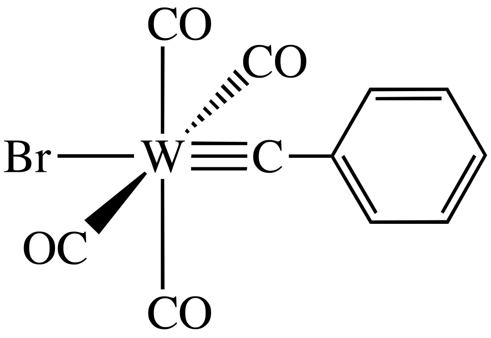
Nobel Lecture
December 8, 2005

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



1964

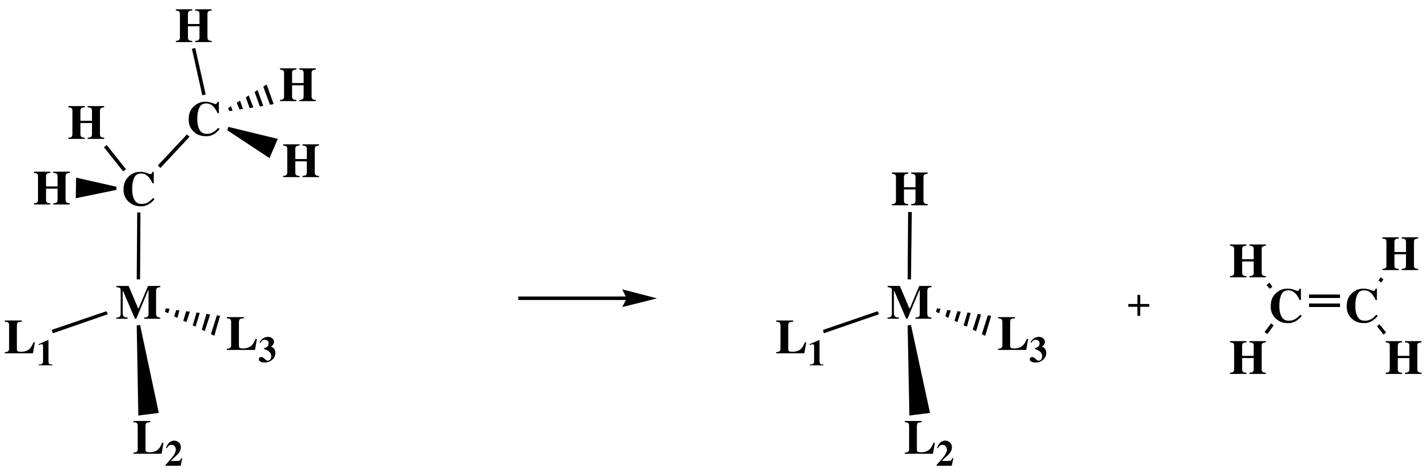
"carbene"



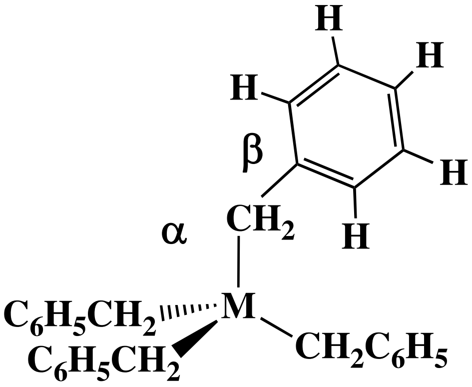
1973

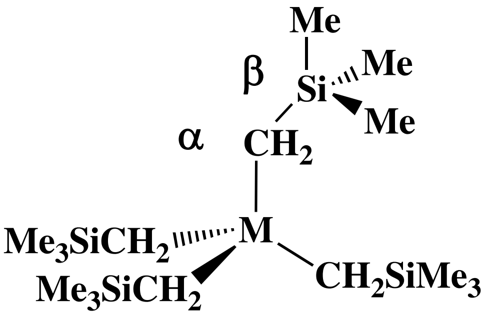
"carbyne"

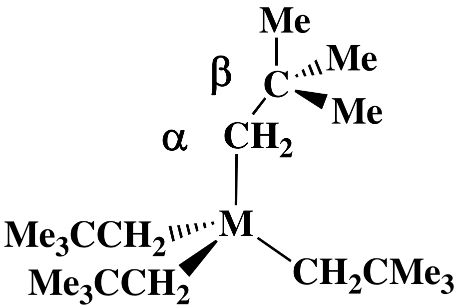
Beta hydride elimination in an ethyl complex



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

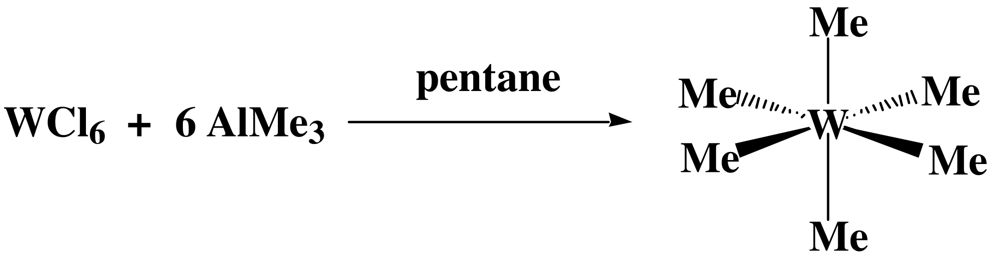






All alkyls lack one or more hydrogen atoms
on the atom β with respect to the metal.

The first relatively stable permethyl complex



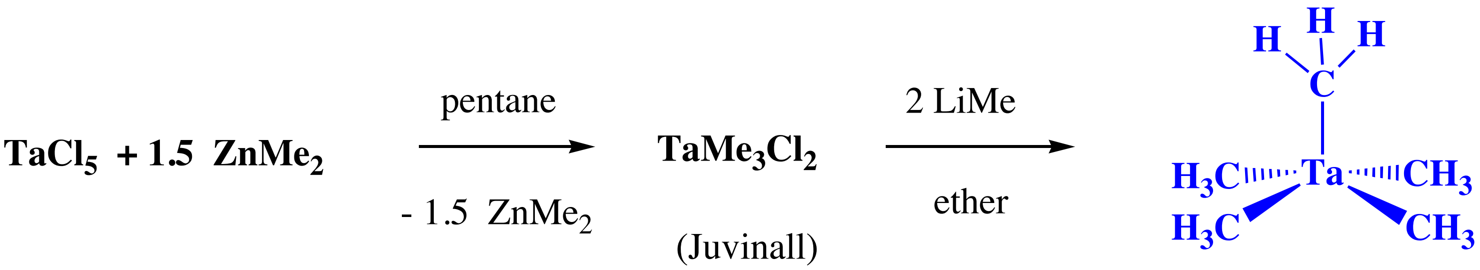
4	5	6	7	8
Ti	V	Cr	Mn	Fe
Zr	Nb	**Mo**	Tc	**Ru**
Hf	**Ta**	**W**	**Re**	Os

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

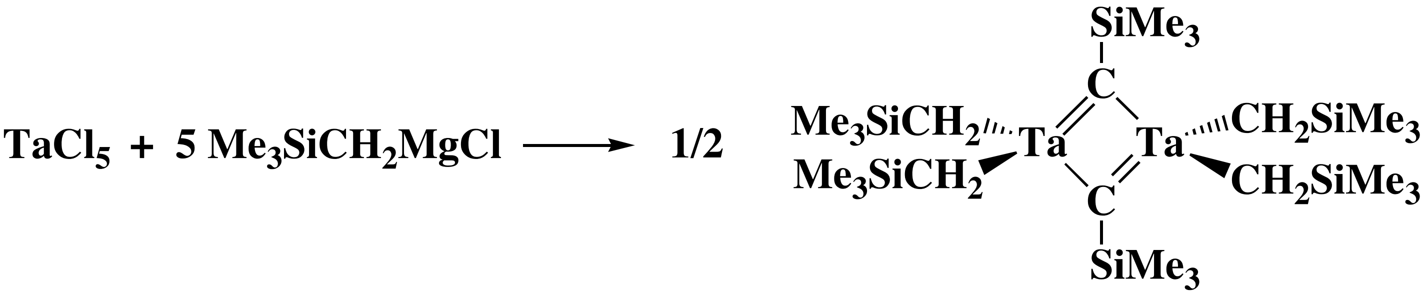
Synthesis of tantalum pentaalkyls



$TaCl_5 + 1.5\ ZnMe_2 \xrightarrow[-\ 1.5\ ZnMe_2]{\text{pentane}} TaMe_3Cl_2 \xrightarrow[\text{ether}]{2\ LiMe}$

(Juvinall)

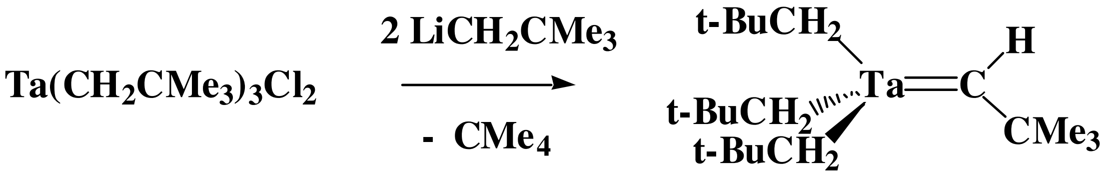
Decomposes above 0 °C
bimolecularly



$TaCl_5 + 5\ Me_3SiCH_2MgCl \longrightarrow$ 1/2

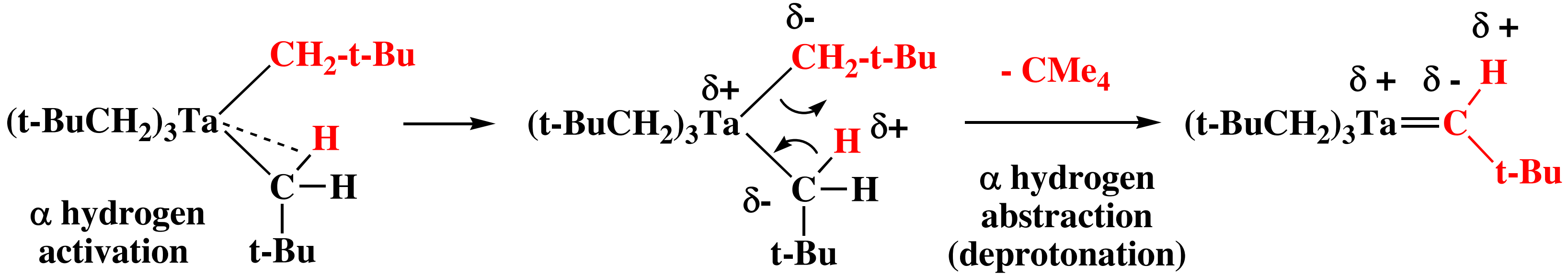
"It is assumed that a penta-alkyl complex cannot exist for steric reasons."
(Mowat, W.; Wilkinson, G. *J. Chem. Soc, Dalton Trans.* **1973**, *10*, 1120.)

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

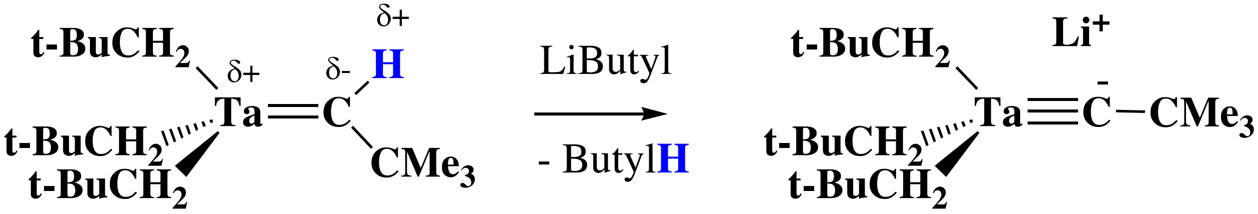


J. Am. Chem. Soc. **1974**, *96*, 6796

Distills in a good vacuum at 75°C.

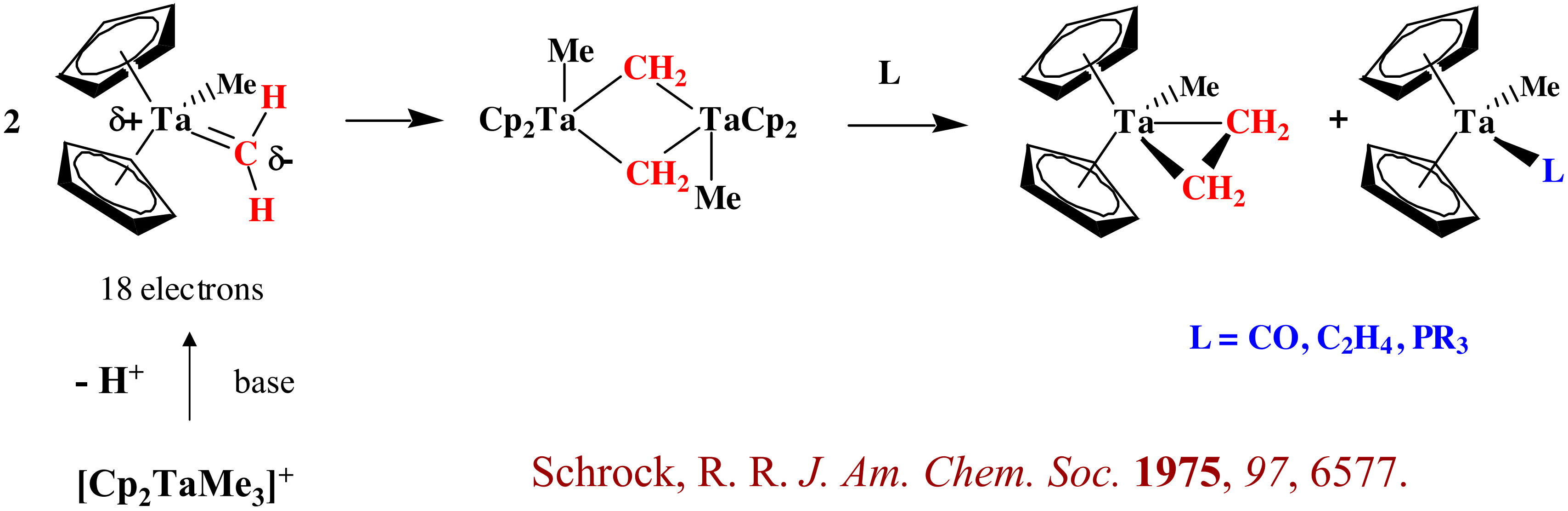


Alkylidenes can be deprotonated to yield tantalum-carbon triple bonds.



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

Alkylidenes decompose bimolecularly.

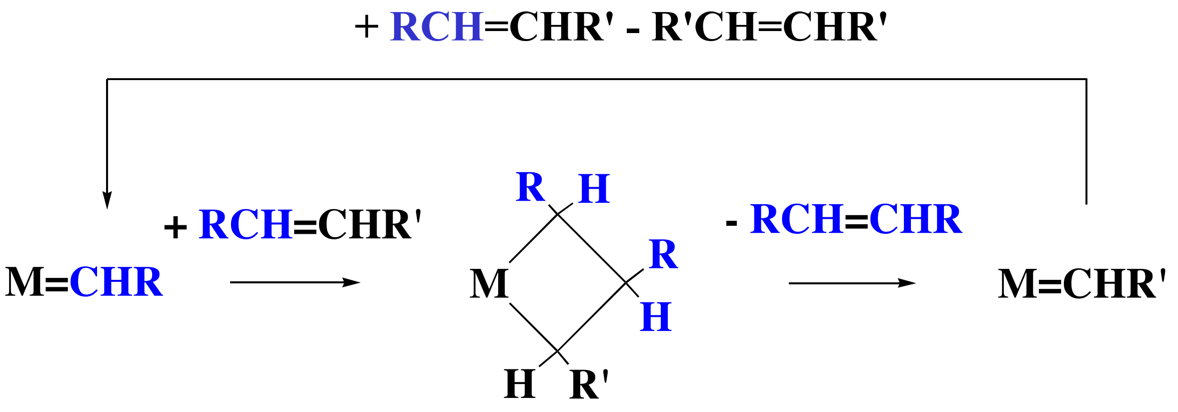


Schrock, R. R. *J. Am. Chem. Soc.* **1975**, *97*, 6577.

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

Olefin metathesis and the Chauvin mechanism (1971)

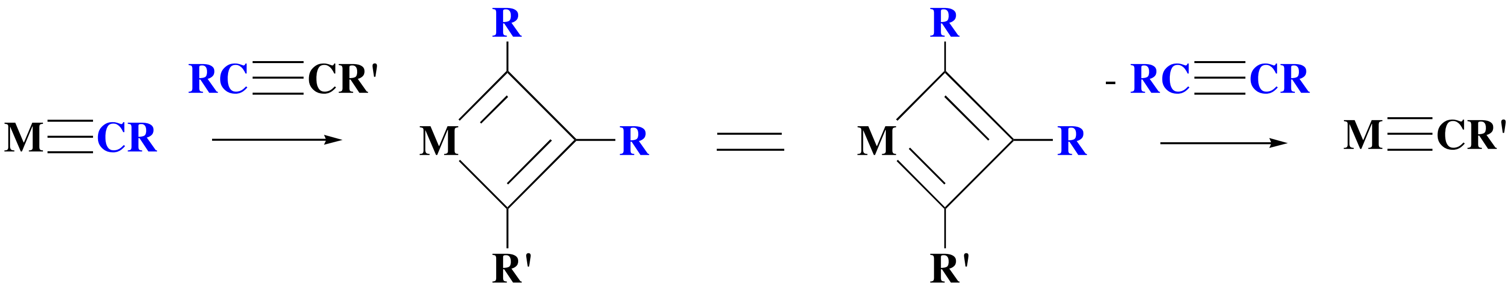
$$2\ \mathrm{RCH{=}CHR'} \rightleftharpoons \mathrm{RCH{=}CHR} + \mathrm{R'CH{=}CHR'}$$



M = Mo, W, or Re

Alkyne metathesis and the metalacyclobutadiene mechanism

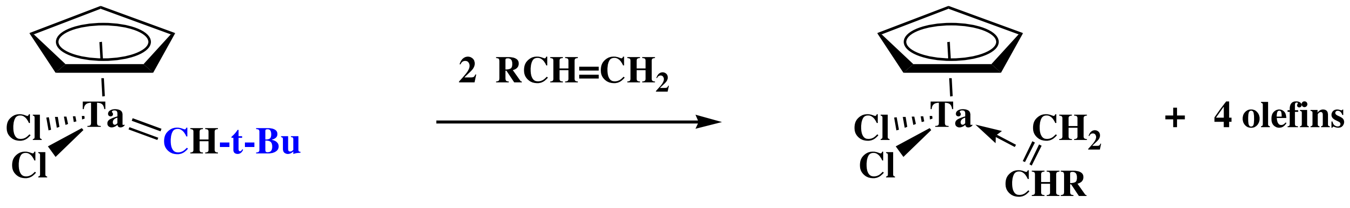
$$2\ RC{\equiv}CR' \rightleftharpoons R'C{\equiv}CR' + RC{\equiv}CR$$

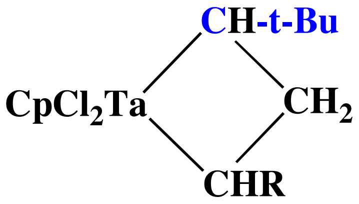


(suggested by
T. Katz; 1975)

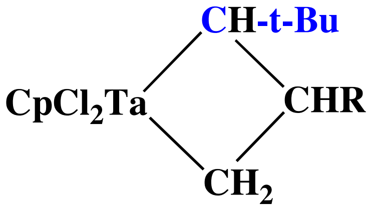
M = Mo, W

Reaction of tantalum alkylidenes with olefins.





$RCH{=}CHCH_2\text{-t-Bu}$
+
$RCH_2CH{=}CH\text{-t-Bu}$



$CH_2{=}CHRCH_2\text{-t-Bu}$
+
$CH_3CHR{=}CH\text{-t-Bu}$

Modification of Nb and Ta yields metathesis catalysts

$M(CH\text{-}t\text{-}Bu)L_2Cl_3 + H_2C{=}CHR \longrightarrow$ 4 products of rearrangement of metallacyclobutanes

M = Nb or Ta

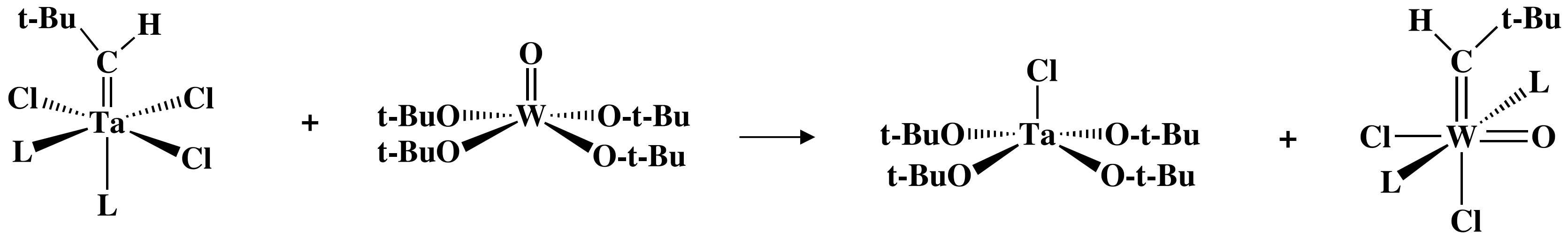
$L = PMe_3$

$M(CH\text{-}t\text{-}Bu)(O\text{-}t\text{-}Bu)_2Cl(PMe_3) +$ olefins $\longrightarrow$ also metathesis products (~35 turnovers for cis-2-pentene)

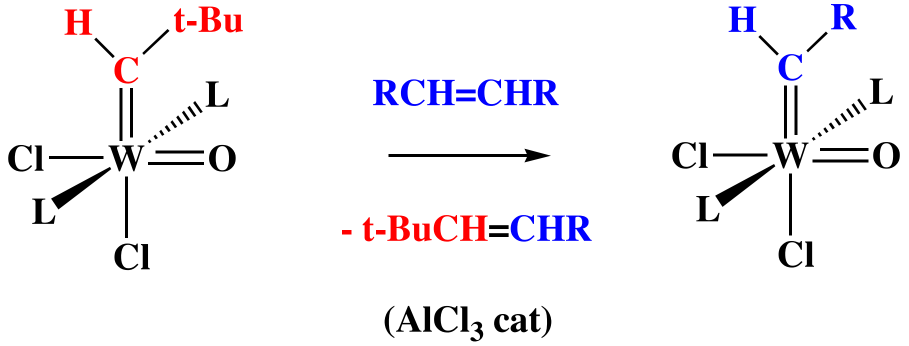
Alkoxides "prevent reduction" and "promote metathesis."

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

An oxo neopentylidene complex of tungsten

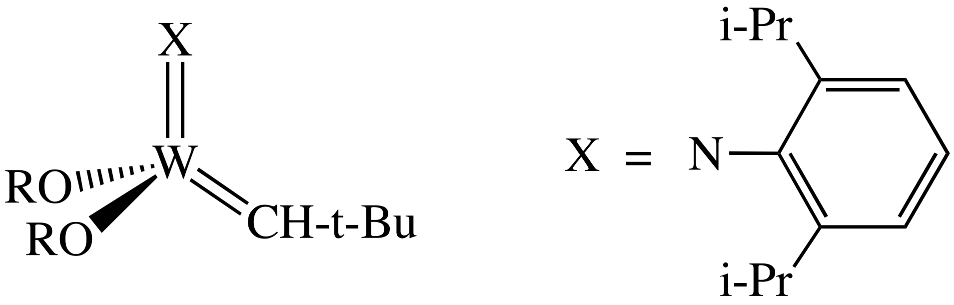


L = a phosphine, e.g. PEt_3



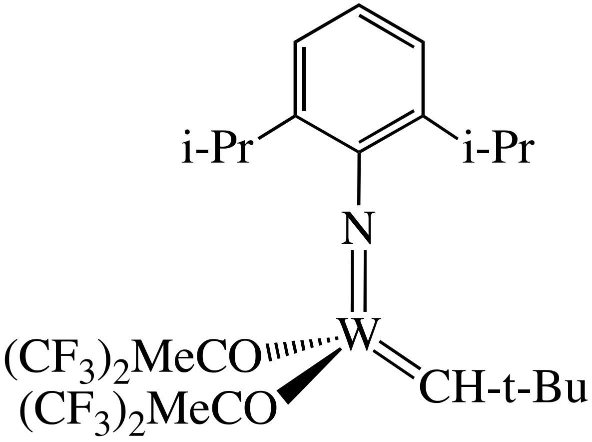
Even R = H

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



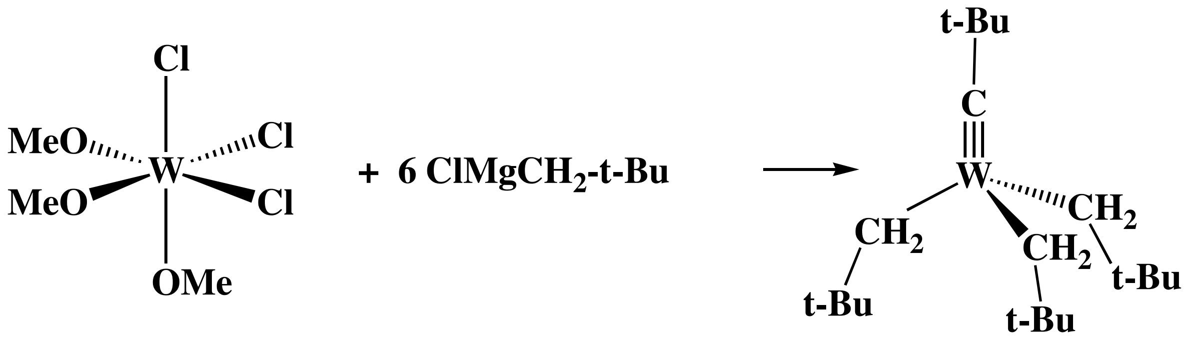
The OR group should be a sterically demanding tertiary alkoxide.

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



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

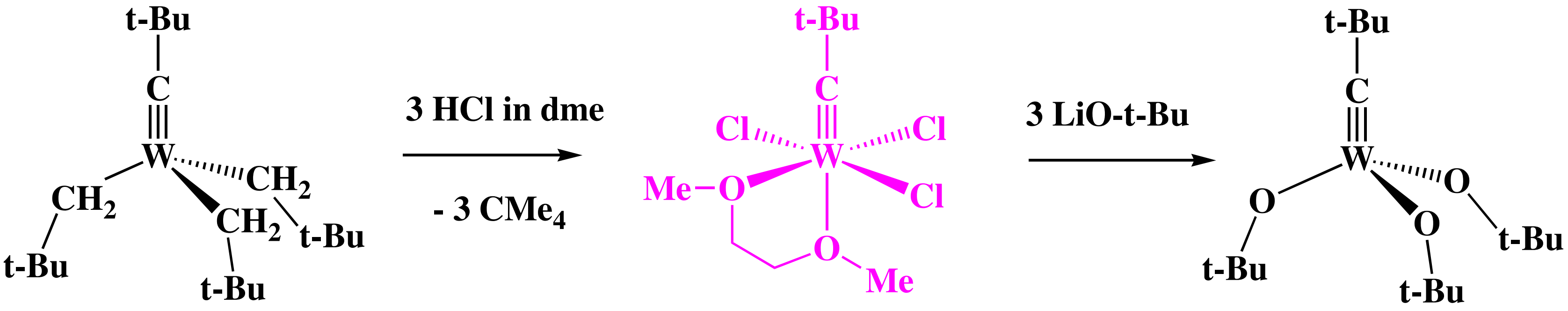
Synthesis of a tungsten neopentylidyne complex



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

(1978)

Tungsten-carbon triple bonds and alkyne metathesis

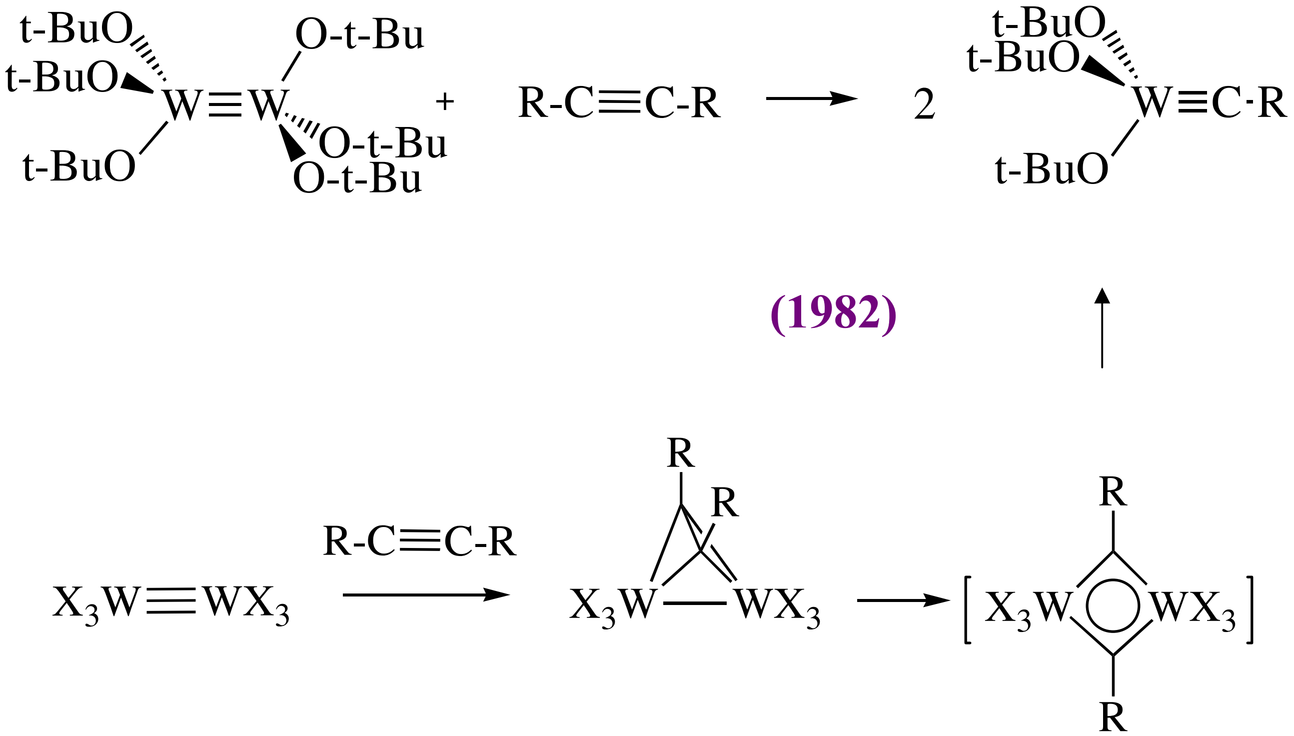


purple crystals

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

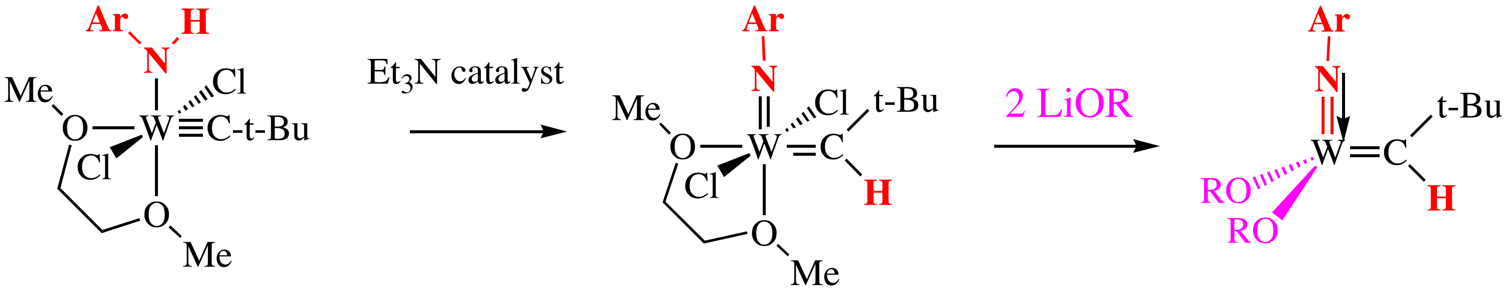
$$2\ RC{\equiv}CR' \rightleftharpoons R'C{\equiv}CR' + RC{\equiv}CR$$

Metal-metal bonds and "metathesis" reactions.



(1982)

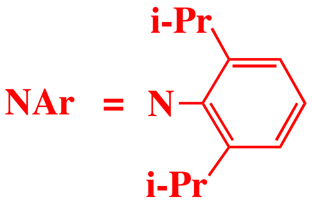
Synthesis of a tungsten imido alkylidene complex



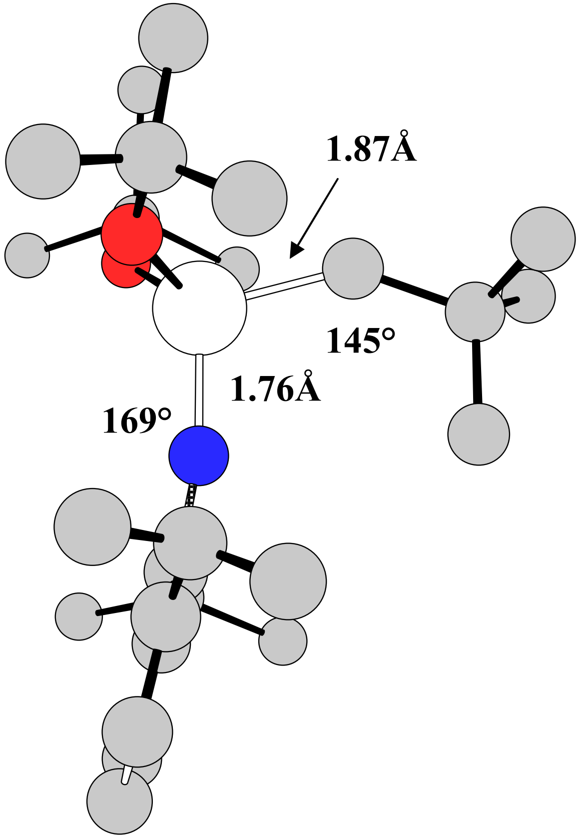
("14 electron" species)

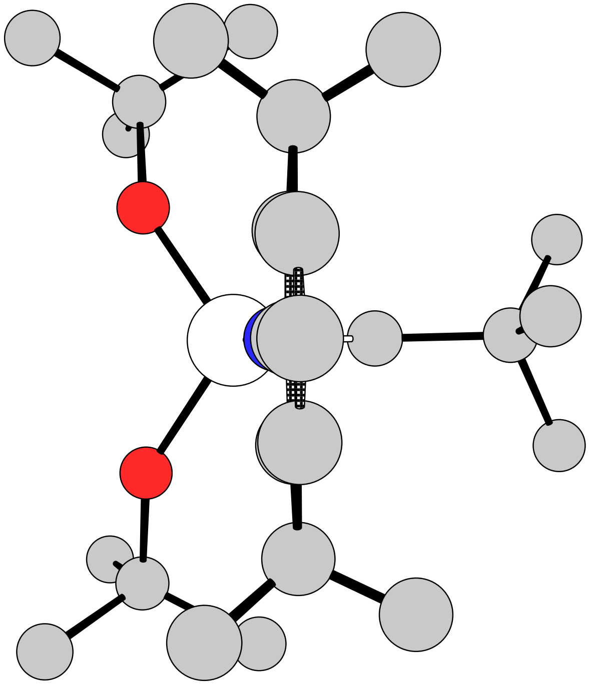
OR = O-t-Bu, $OCMe_2(CF_3)$, $OCMe(CF_3)_2$,
and various bulky phenoxides

$W(NAr)(CH\text{-}t\text{-}Bu)(OR)_2$ species are "well-defined" catalysts for the metathesis of olefins and the activity can be varied systematically by varying OR.

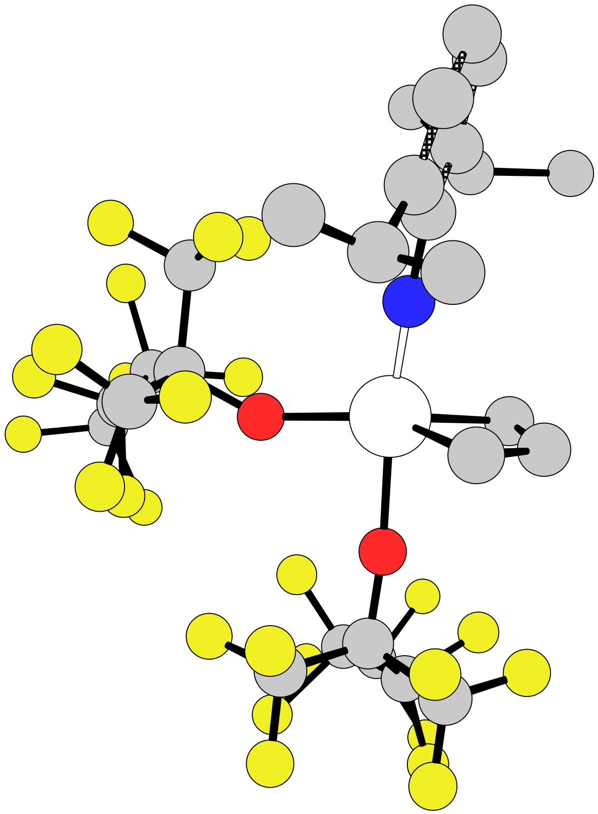


Structure of *syn*-W(NAr)(CH-t-Bu)(O-t-Bu)$_2$



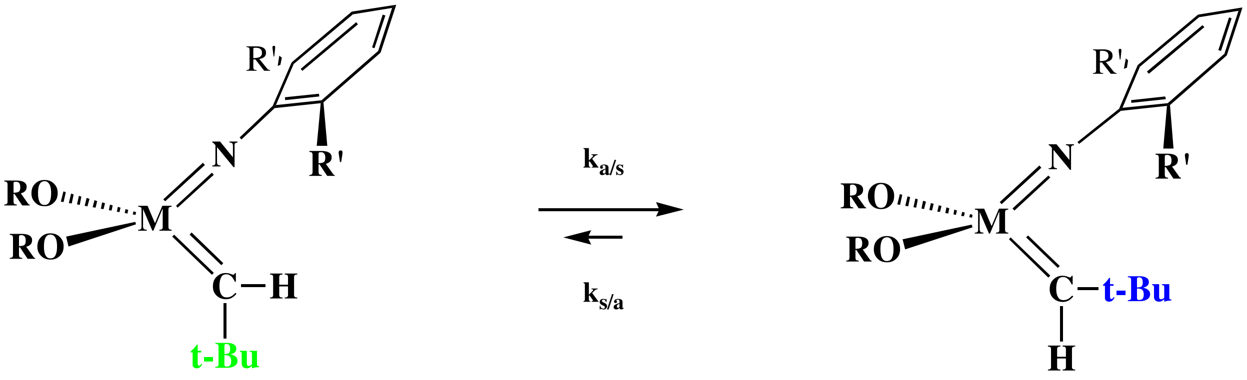


Tungstenacyclobutanes can be isolated, but can be too stable toward loss of olefin.



Molybdacyclobutane intermediates lose an olefin more readily.

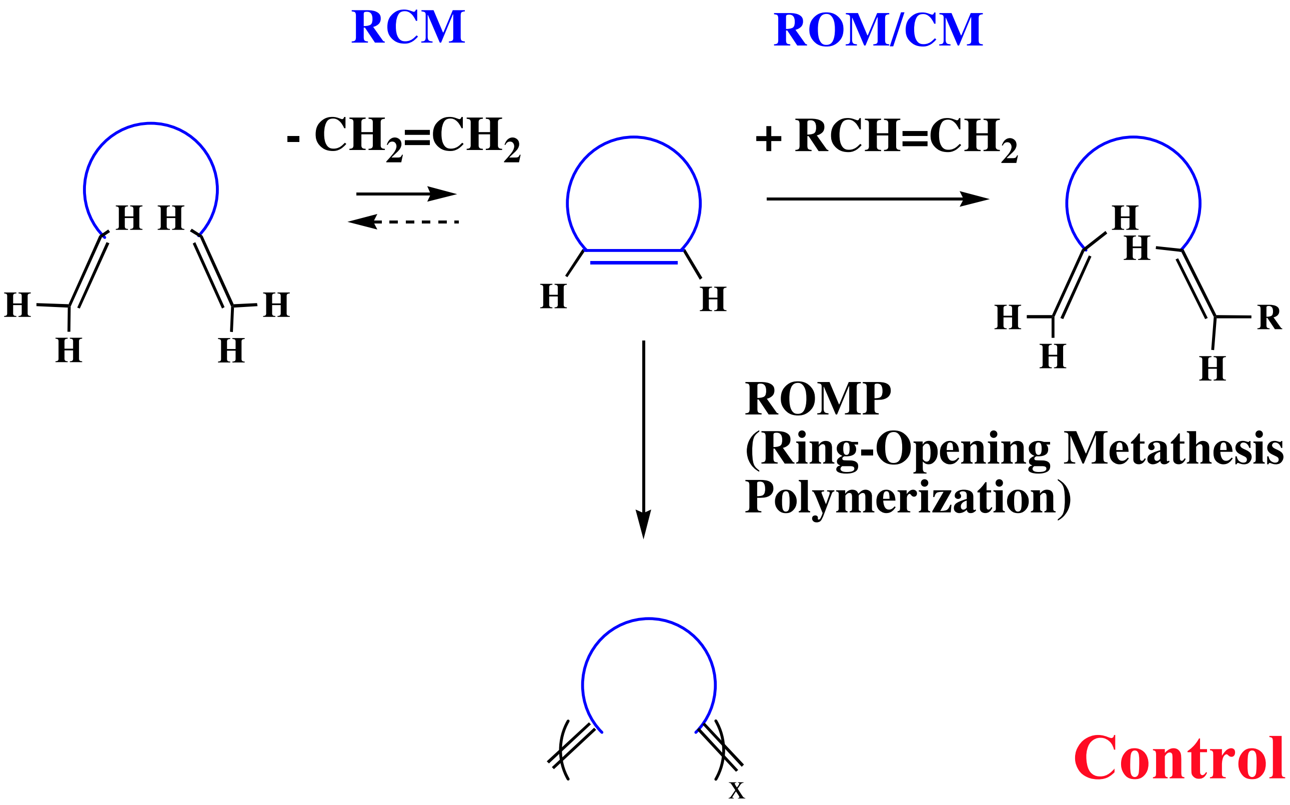
Two isomers (*anti* and *syn*) are available in any system through rotation about the M=C bond.



anti

syn (usually favored)

Olefin metathesis variations



RCM

$- CH_2{=}CH_2$

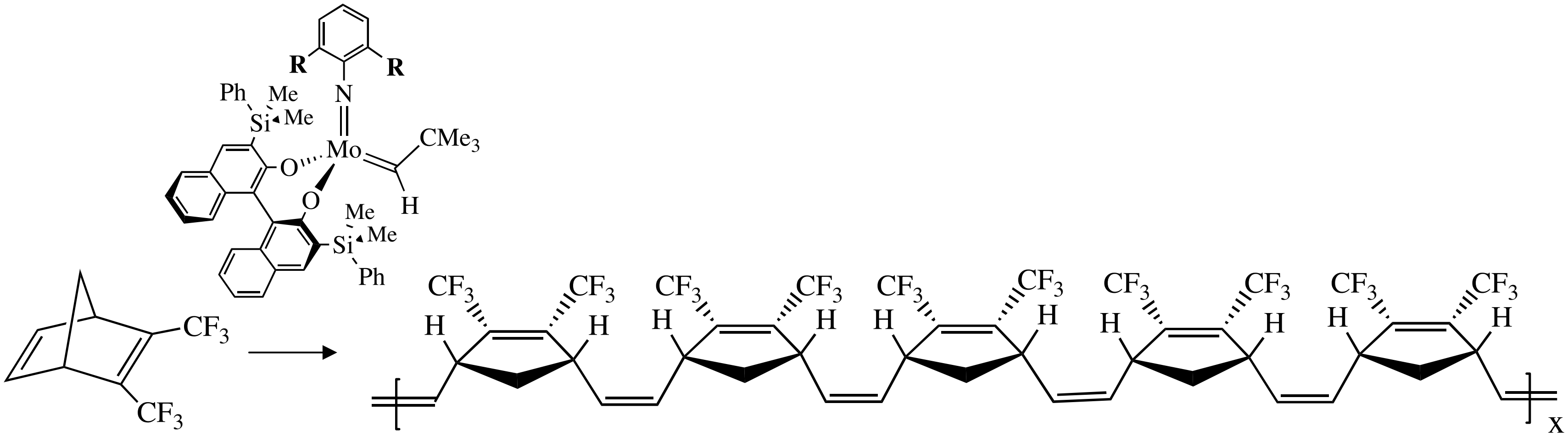
ROM/CM

$+ RCH{=}CH_2$

ROMP
(Ring-Opening Metathesis
Polymerization)

Control!

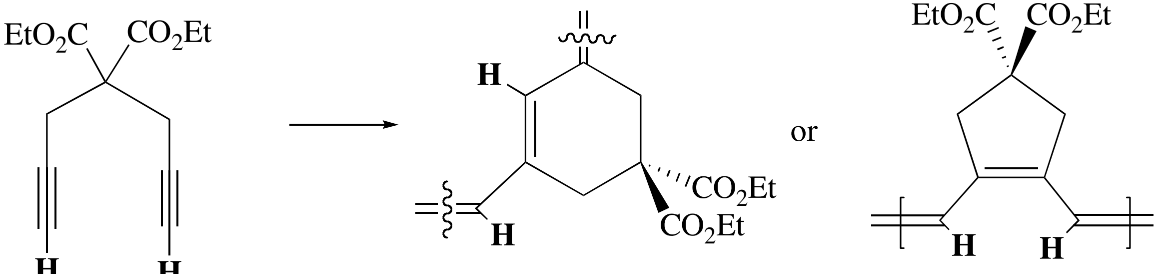
Polymerization of bistrifluoromethylnorbornadiene via enantiomorphic site control.



all *cis* and *isotactic* through enantiomeric site control when R = CH_3

When R = $CH(CH_3)_2$ the polymer structure has a relatively *random* (71% cis) structure.

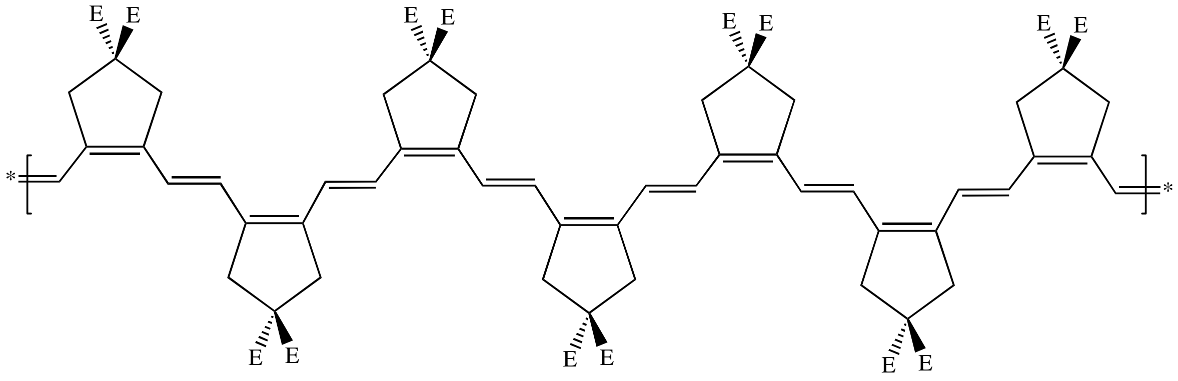
Alkynes are polymerized to yield polyenes.



head-to-tail

tail-to-tail

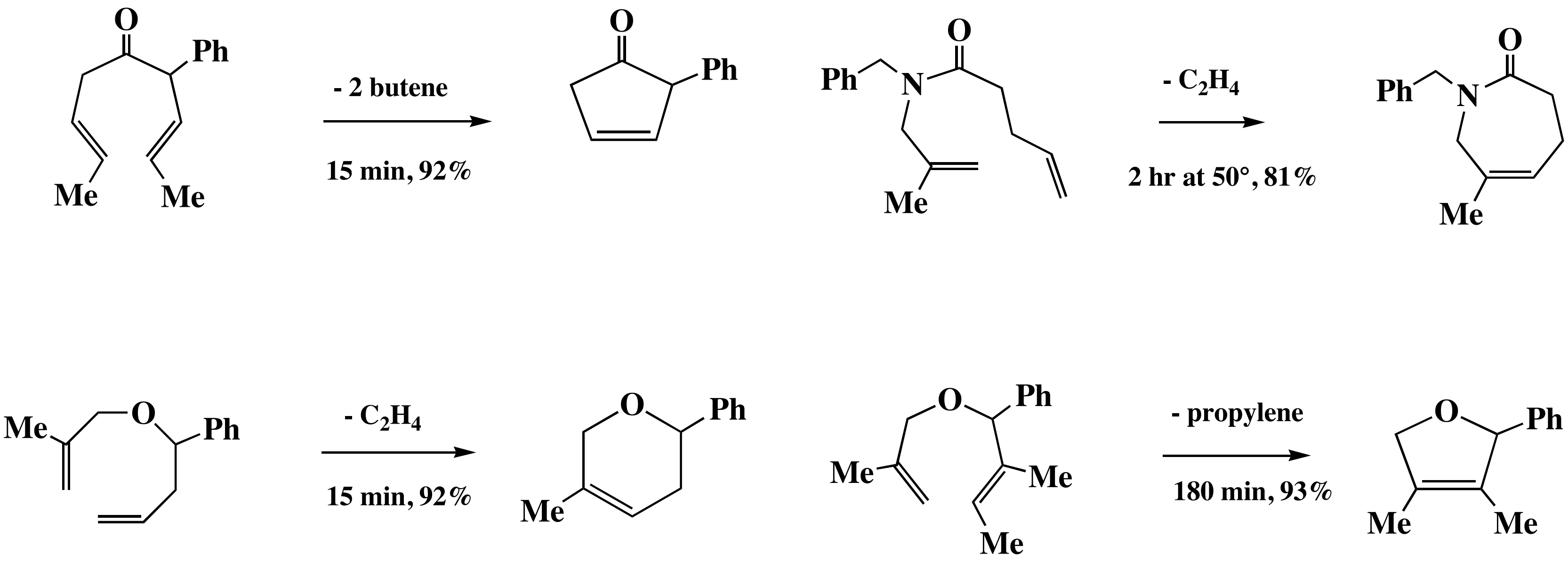
Soluble, highly conjugated (purple), and relatively air-stable; both rings observed in polymer made with Mo(NAr)(OR_{F6})$_2$ catalyst.



>95% 5-membered rings produced with Mo(NAr)(O-t-Bu)$_2$ catalyst.

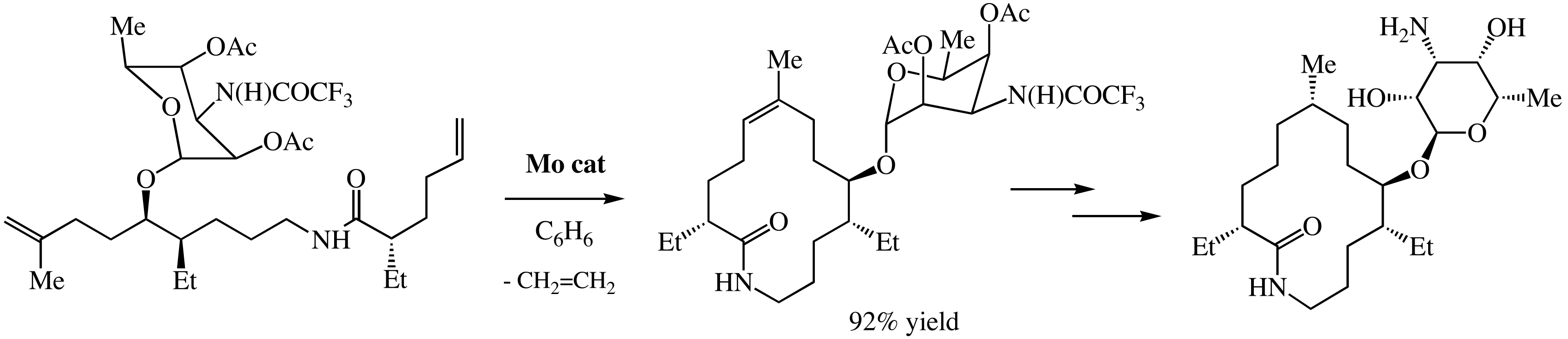
Ring-closing metathesis with Mo catalyst (4-5 mol%)

(Catalyst = $Mo(NAr)(CHCMe_2Ph)[OCMe(CF_3)_2]_2$)



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

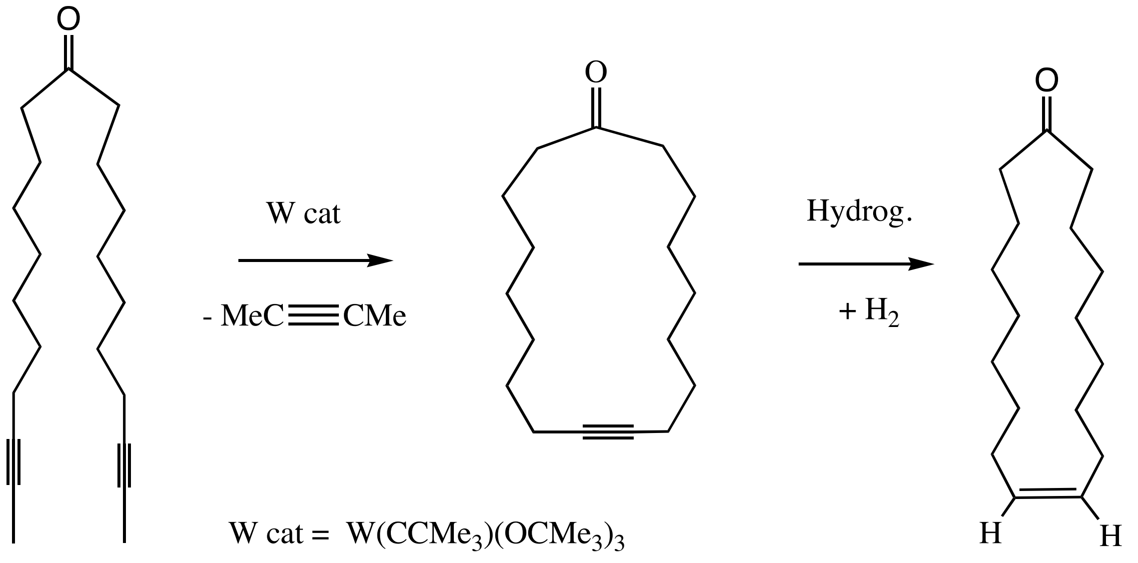
Synthesis of Fluvirucin-B_1



Fluvirucin-B_1

A. F. Houri, 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.



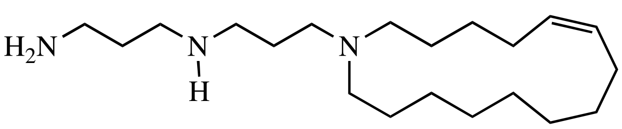
W cat = $W(CCMe_3)(OCMe_3)_3$

Civetone

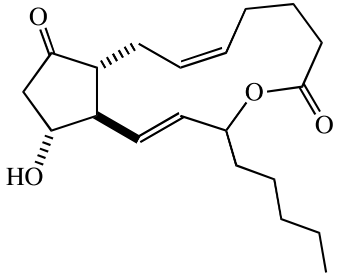
(Fürstner)

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

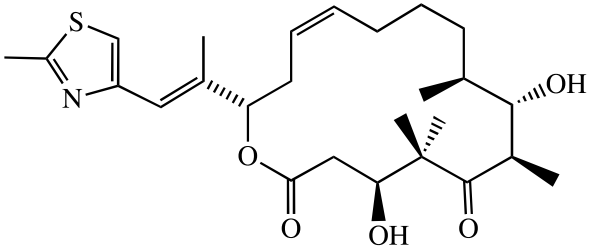
Other examples of alkyne metathesis in organic synthesis



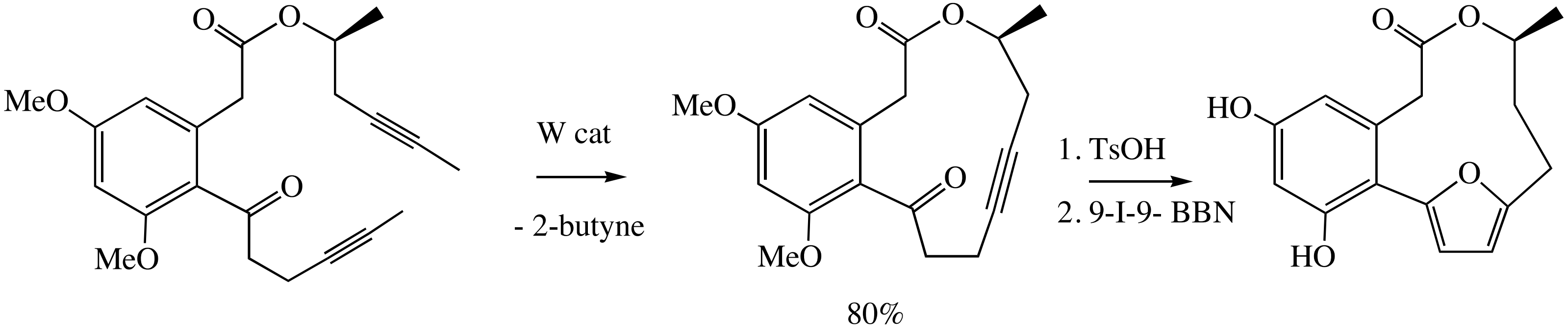
Motuporamine C



PGE$_2$-1,15-lactone

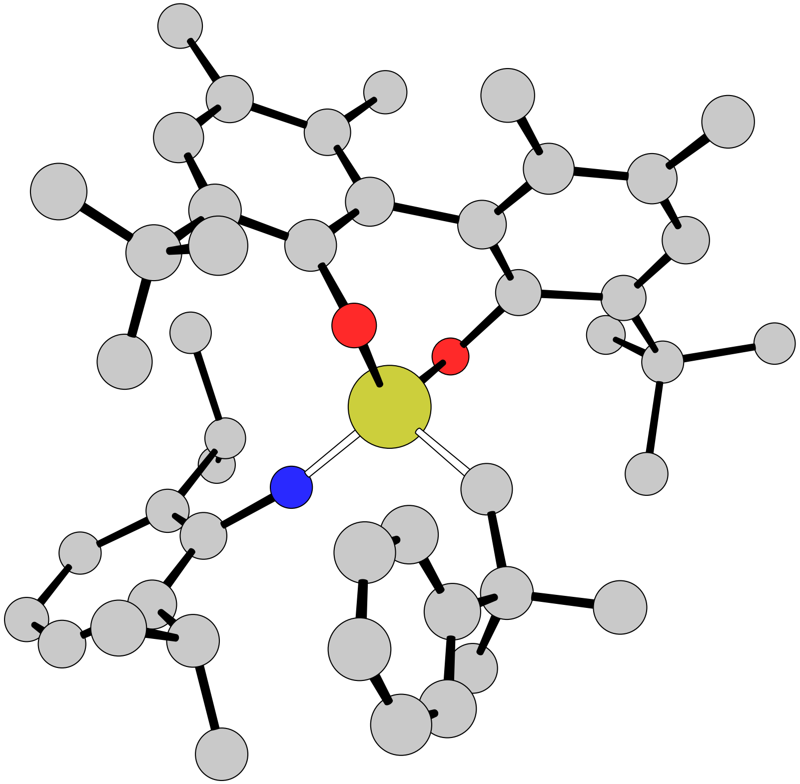


Epothilone C



S-(+)-citreofuran

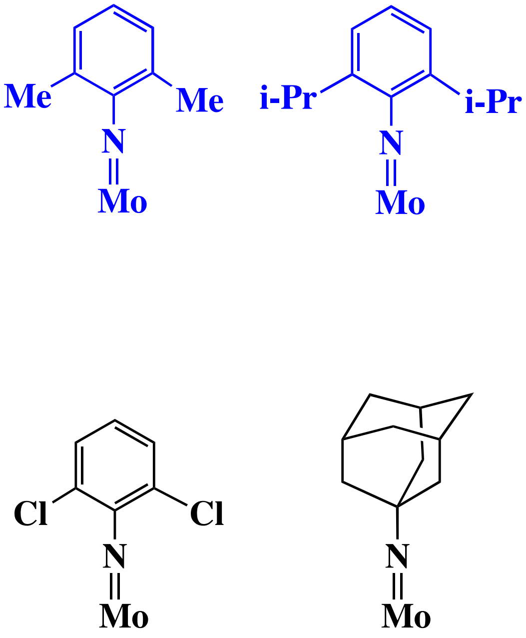
An enantiomerically pure Mo catalyst



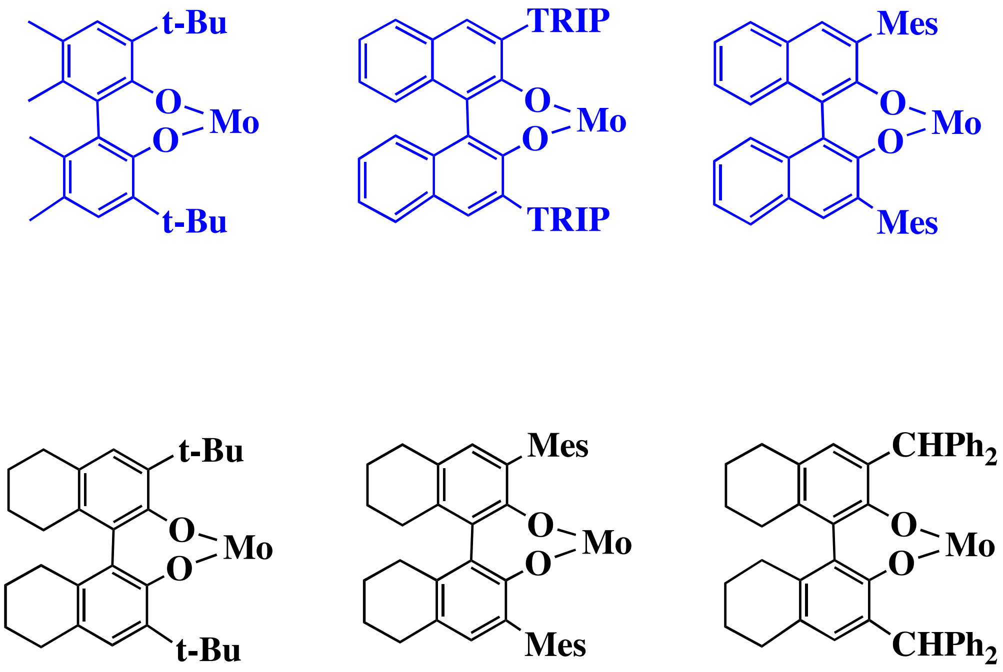
Alexander, J. B.; La, D. S.; Cefalo, D. R.; Hoveyda, A.; Schrock, R. R.
J. Am. Chem. Soc. **1998**, *120*, 4041.

Asymmetric catalyst design; a modular approach

Imido Groups

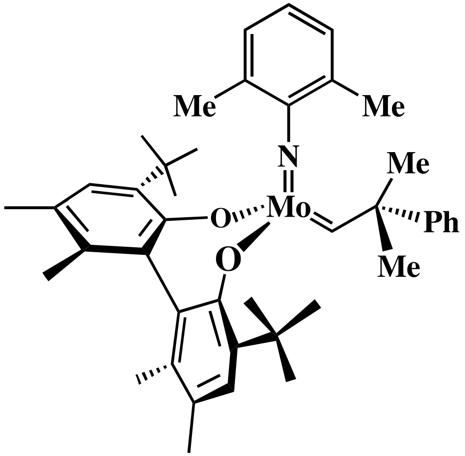


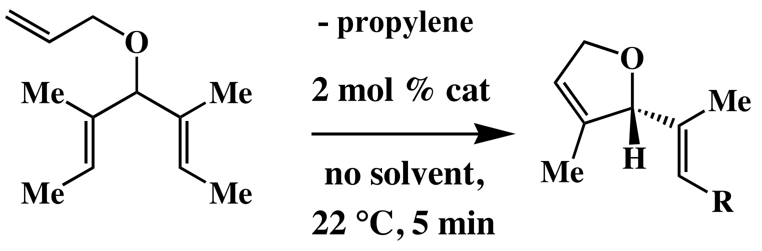
Diolates



24 catalysts!

Asymmetric Ring-Closing Metathesis (ARCM)



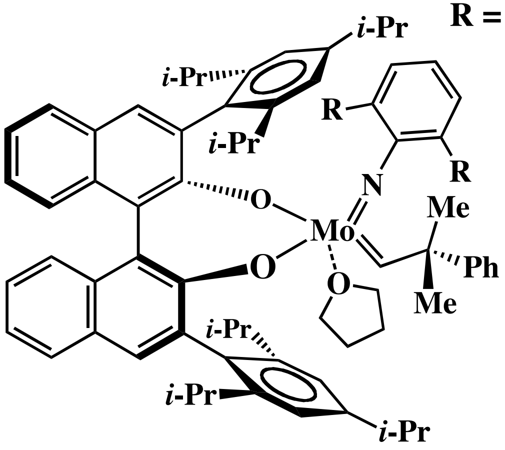


- propylene

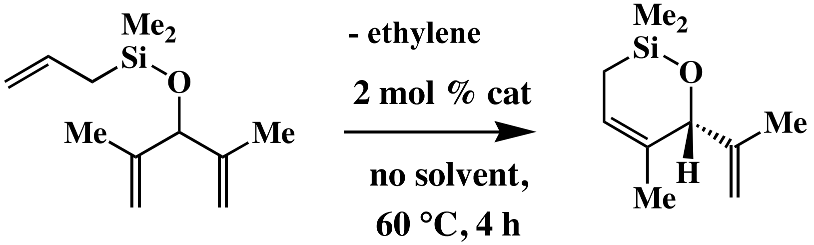
2 mol % cat

no solvent,
22 °C, 5 min

99% ee, 93%



R = i-Pr



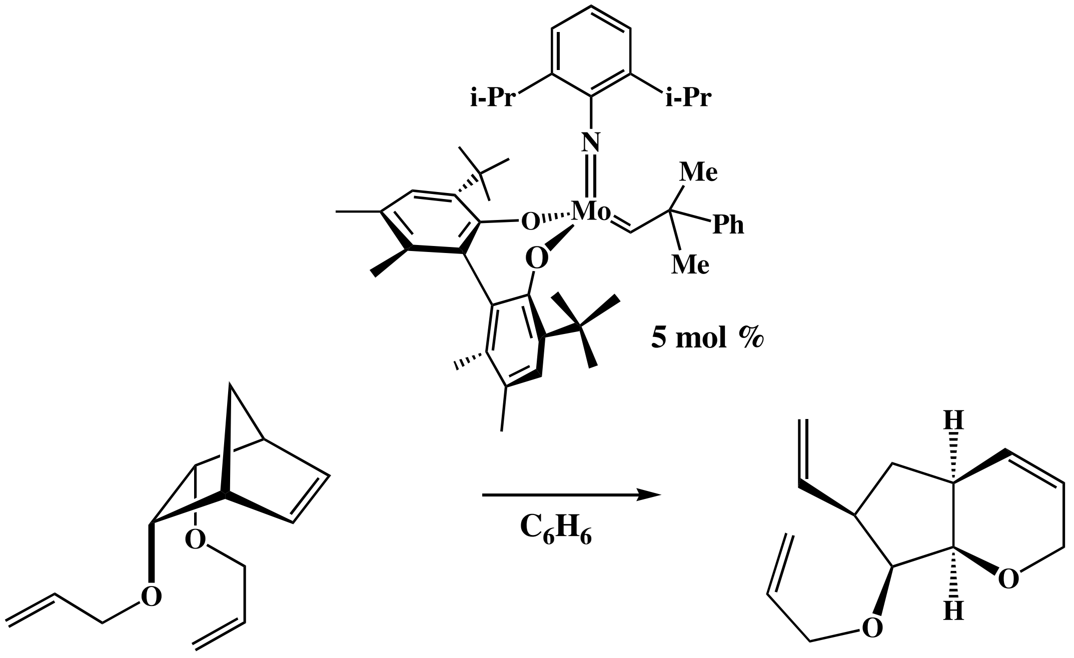
- ethylene

2 mol % cat

no solvent,
60 °C, 4 h

>99% ee, 98%

Ring-Opening / Ring-Closing Metathesis

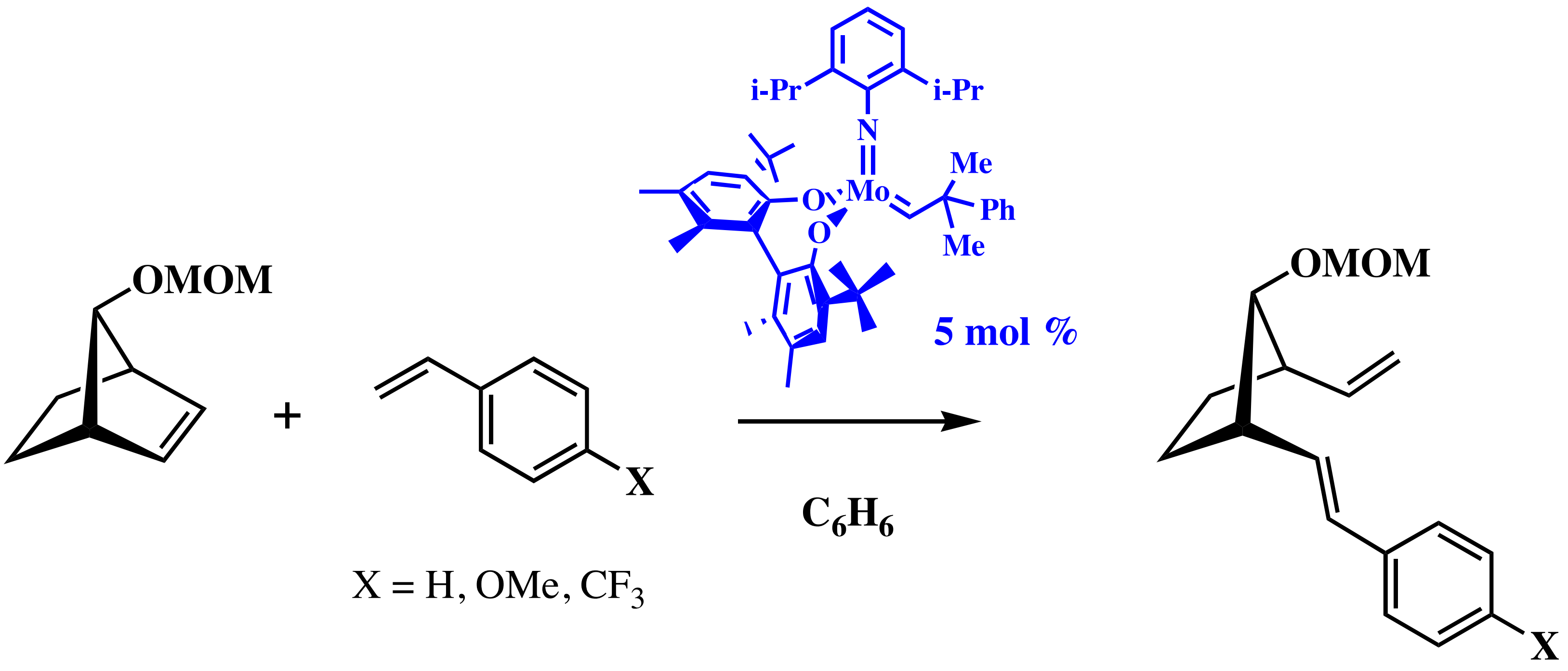


5 mol %

C_6H_6

>99% ee, 76%

Ring-Opening / Cross Metathesis

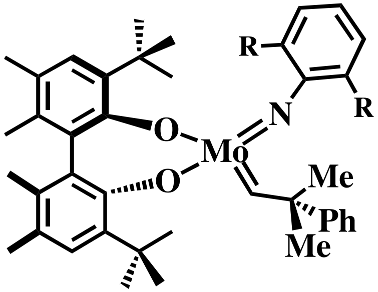


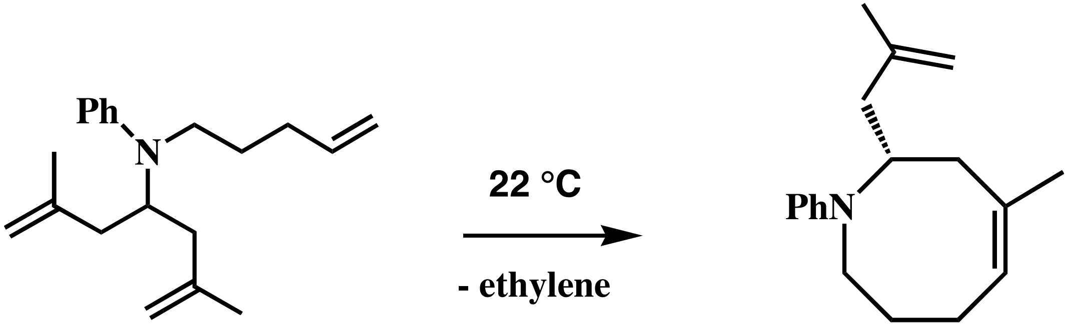
95% yield, >98% ee, >98% trans

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

5 mol %





22 °C

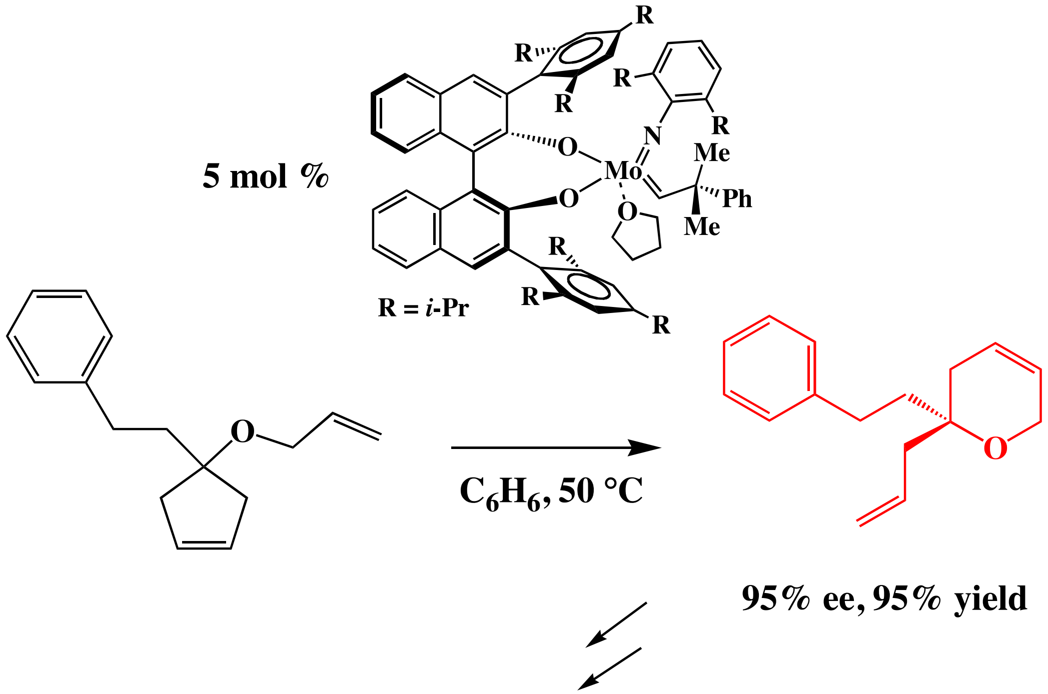
- ethylene

20 min

R = Me

>98% ee, 90% yield

Enantioselective synthesis of a tertiary ether in a drug

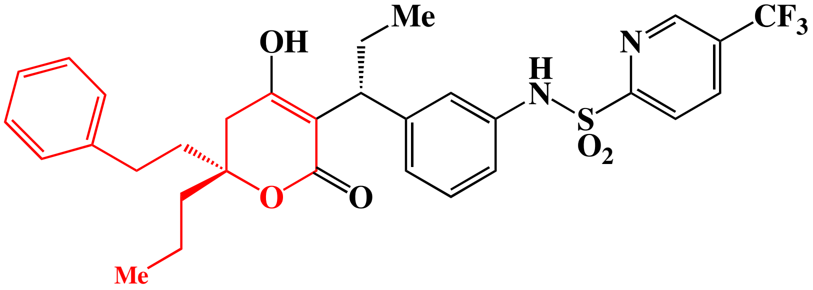


5 mol %

R = *i*-Pr

C_6H_6, 50 °C

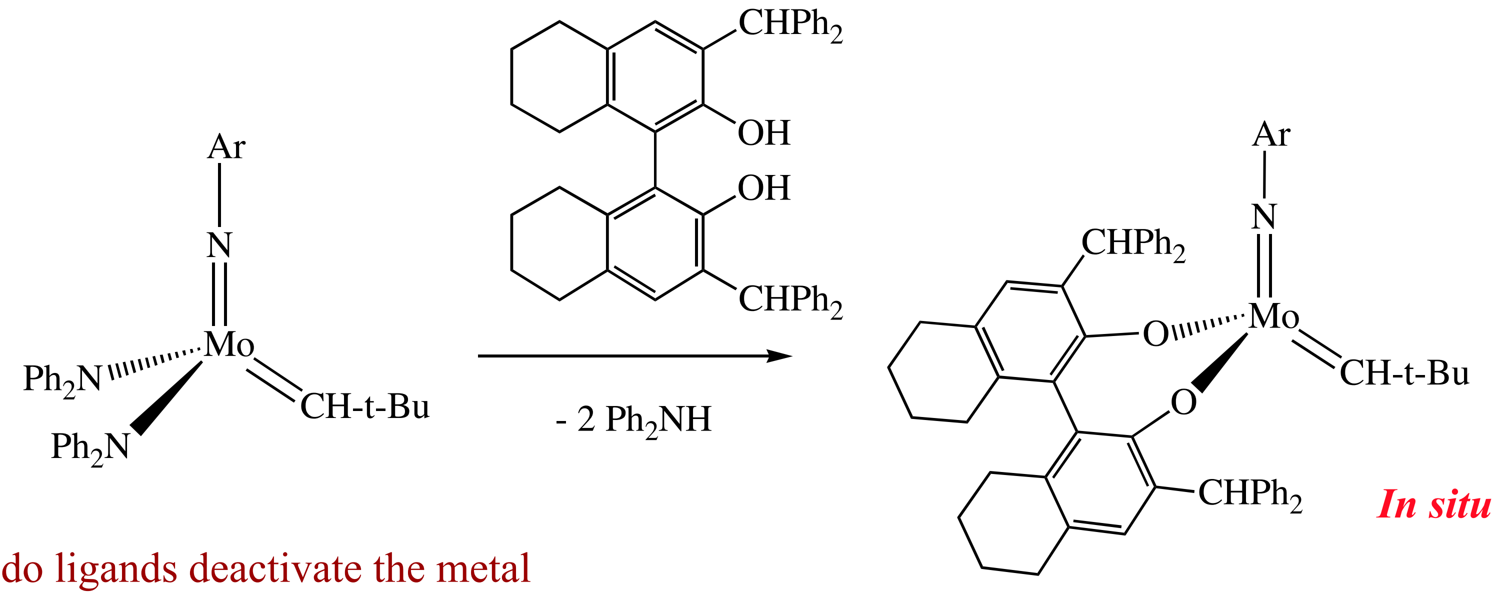
95% ee, 95% yield



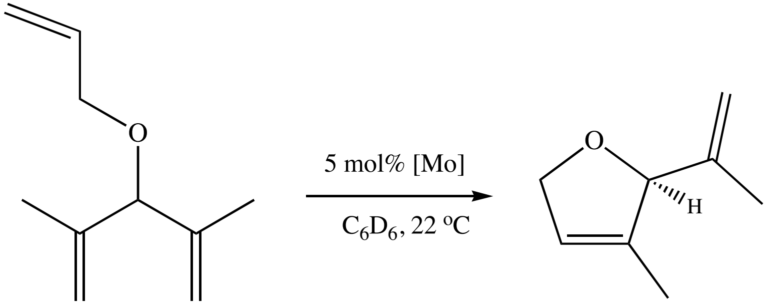
tipranavir (HIV protease inhibitor)

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.

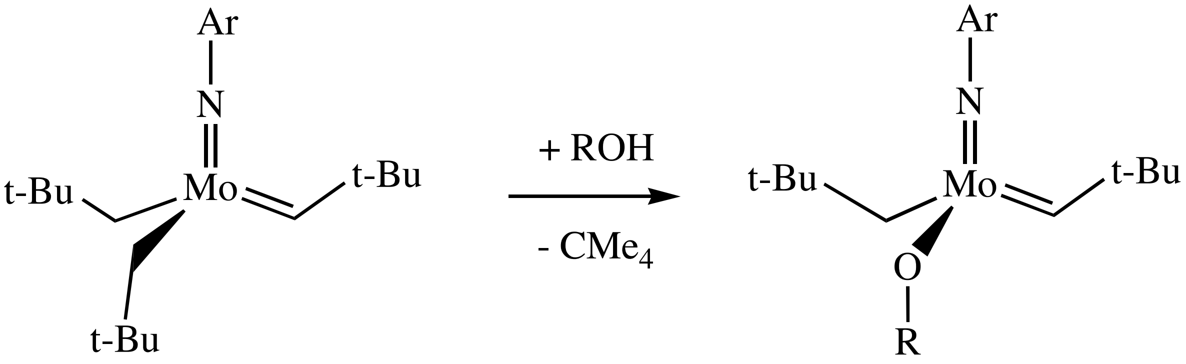


Amido ligands deactivate the metal toward metathesis reactions.



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

Dineopentyl species were examined as bisalkoxide catalyst precursors.



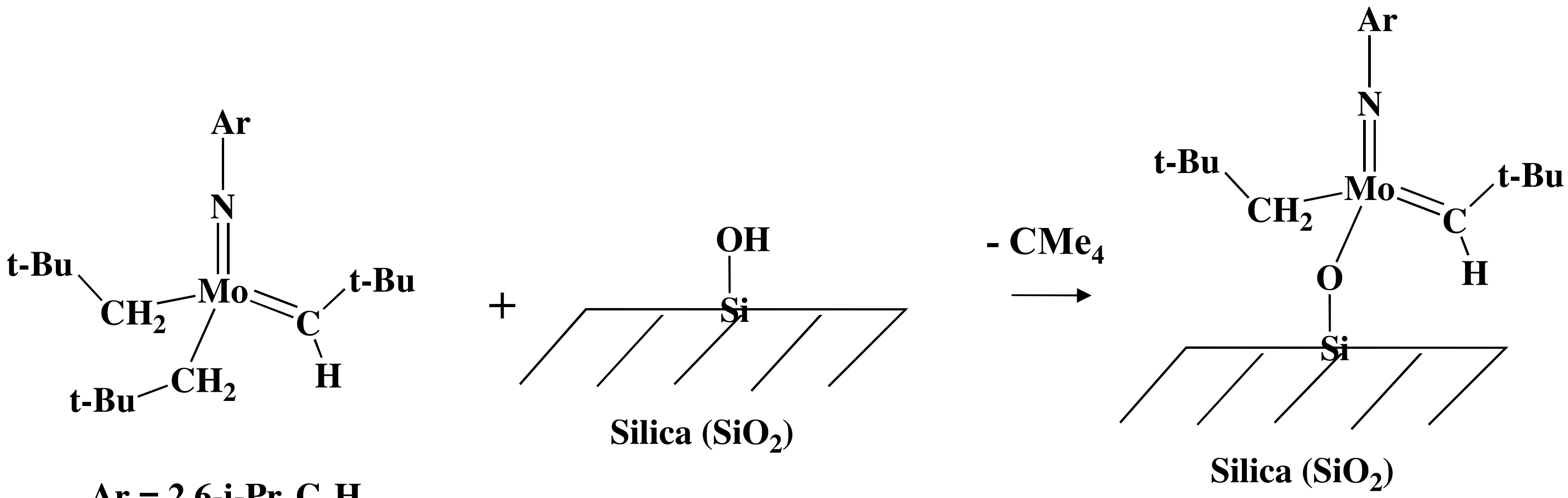
Ar = 2,6-i-$Pr_2C_6H_3$

OR = $OCH(CF_3)_2$, OAdamantyl,
$OCMe_3$, or OAr

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.

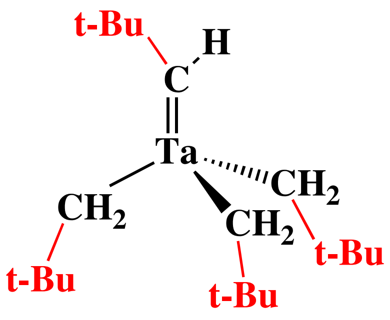


Ar = 2,6-i-$Pr_2C_6H_3$

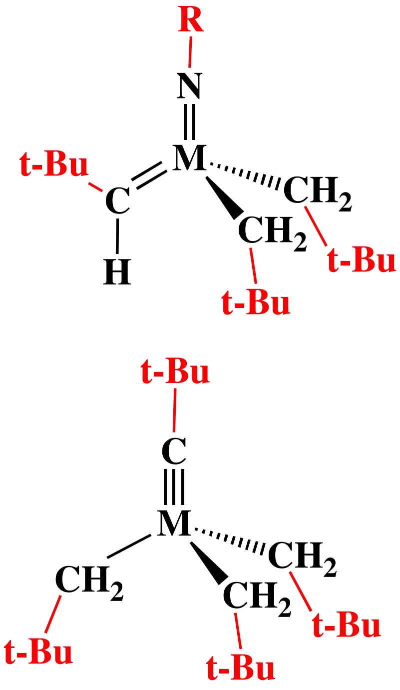
Bimolecular decomposition of alkylidenes is not possible.

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.

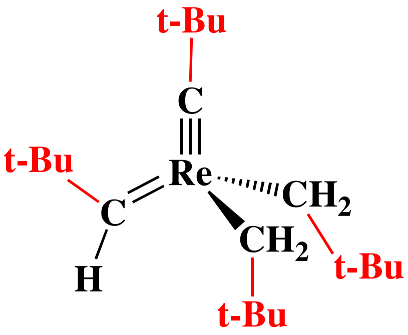


Ta(V)



M(VI)

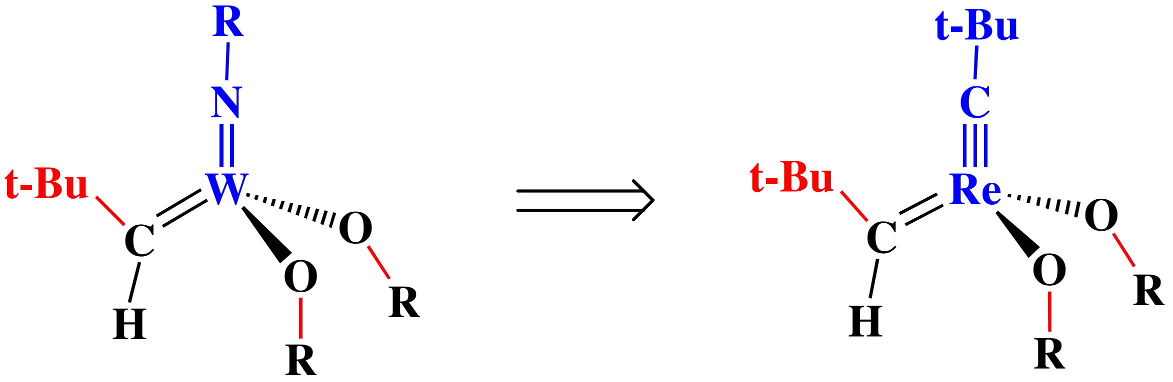
(M = Mo, W)



Re(VII)

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)



W(VI) 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.

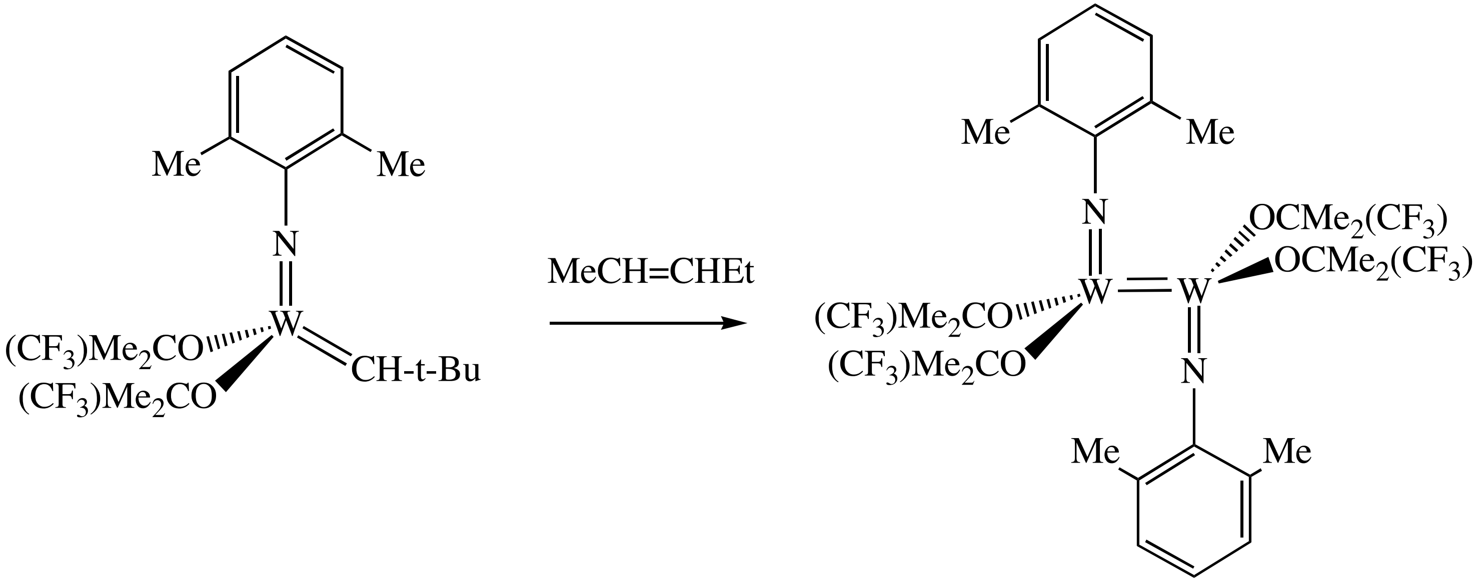
Present and future challenges

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.