

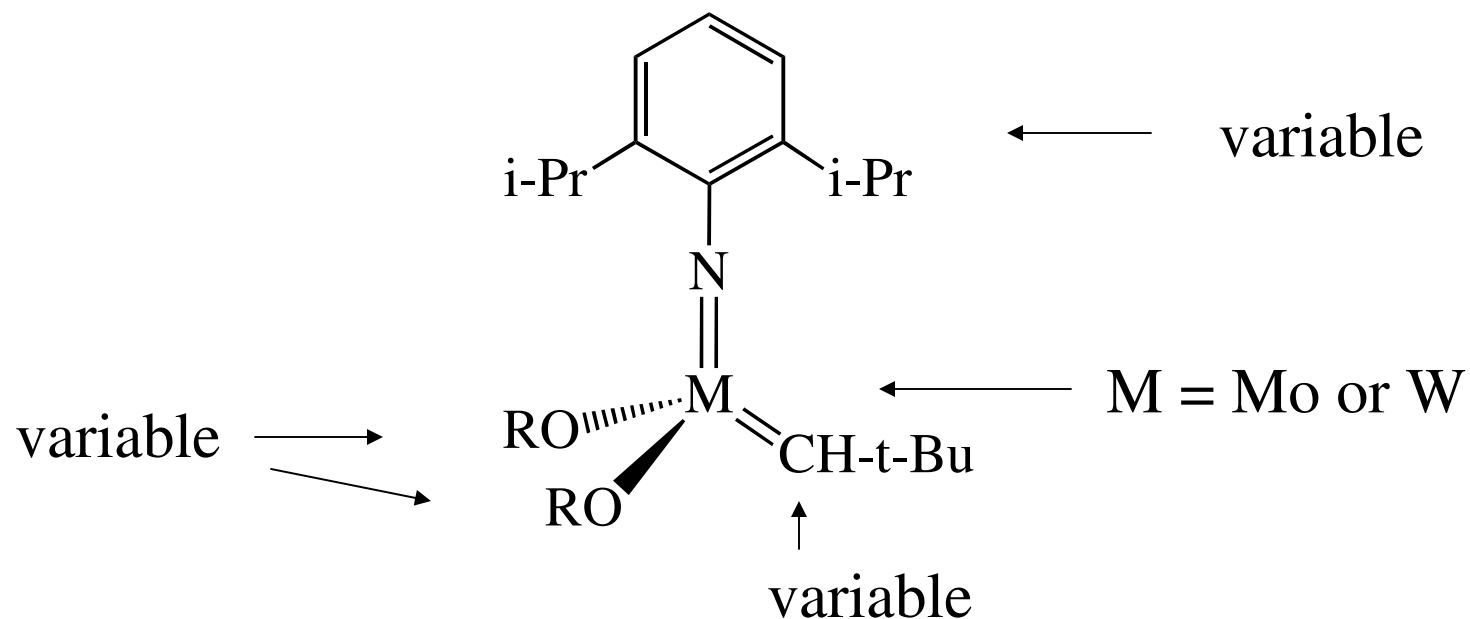
"New approaches to old and new Mo-based metathesis catalysts"

ISOM XVII
July 29, 2007

rrs@mit.edu

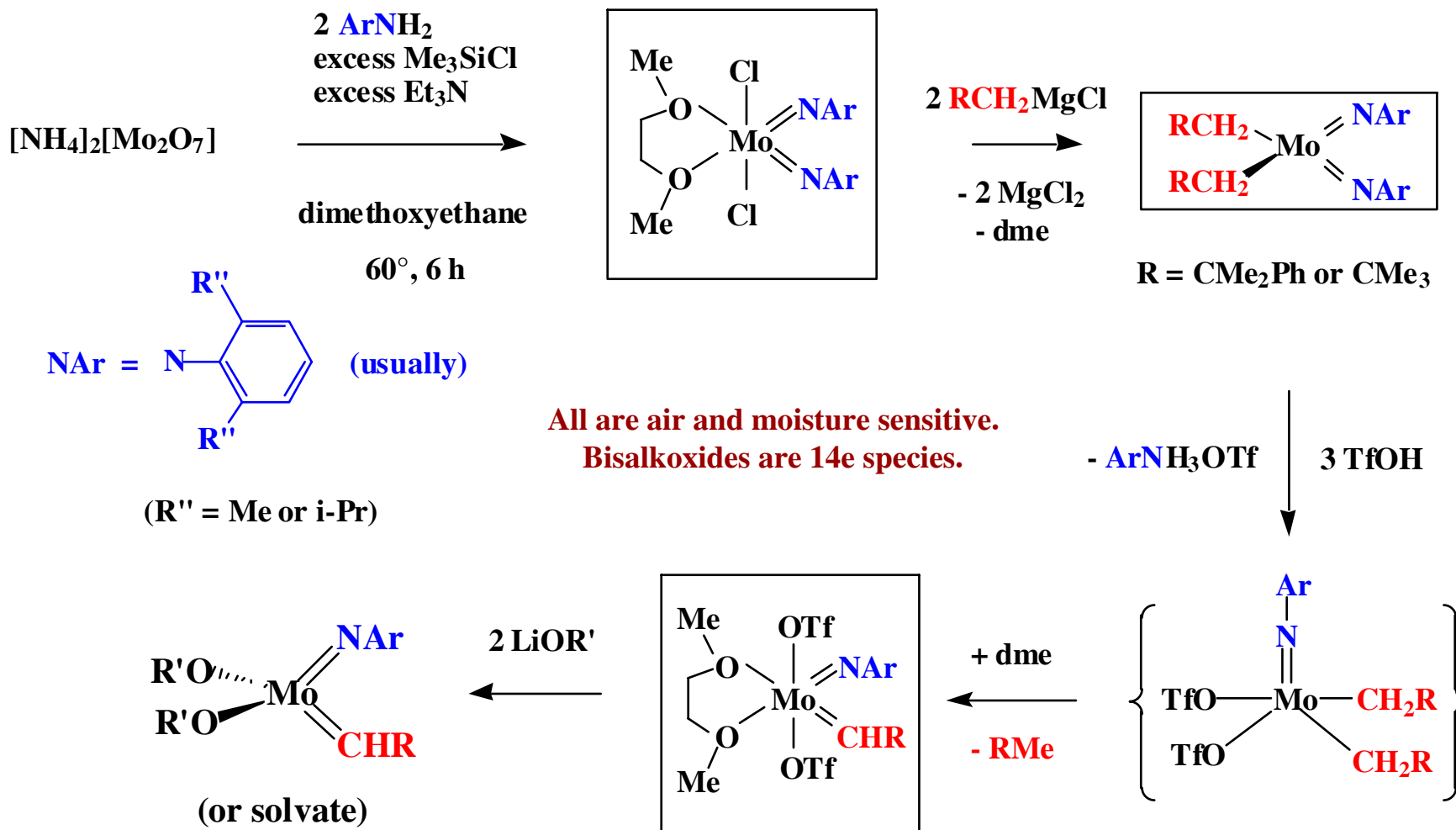


14e Bisalkoxide Metathesis Catalysts of W and Mo



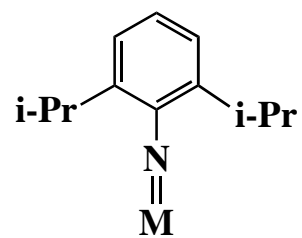
**The ability to use many imido (NR) and alkoxide (OR) groups is a great advantage.
Activities can be *controlled* through variations.**

Molybdenum Catalyst Synthesis

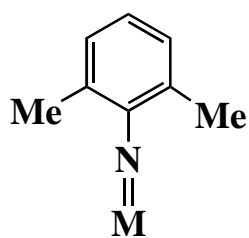


$\text{OR}' = \text{O-}t\text{-Bu, OCM}(\text{CF}_3)_2, \text{ bulky phenoxides, etc,}$
 (also chiral diolates)

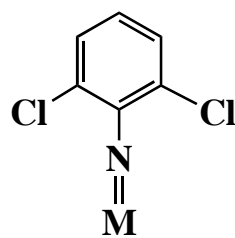
Some examples of imido groups, attached to M first.



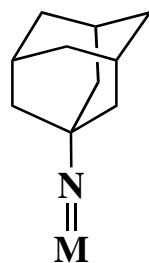
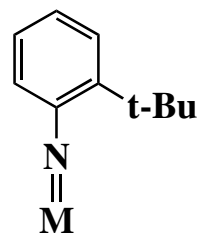
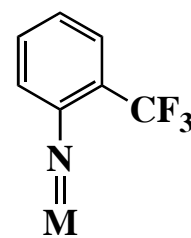
(Ar)



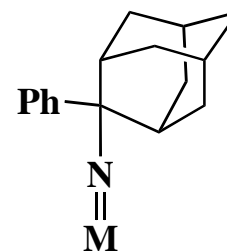
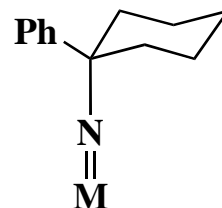
(Ar_{Me})



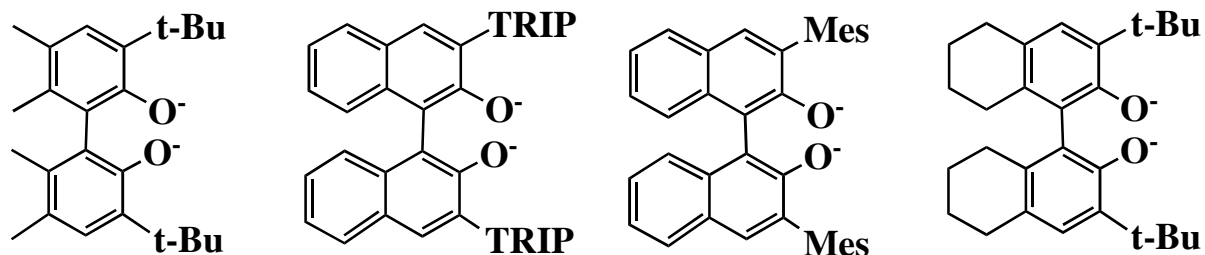
(Ar_{Cl})



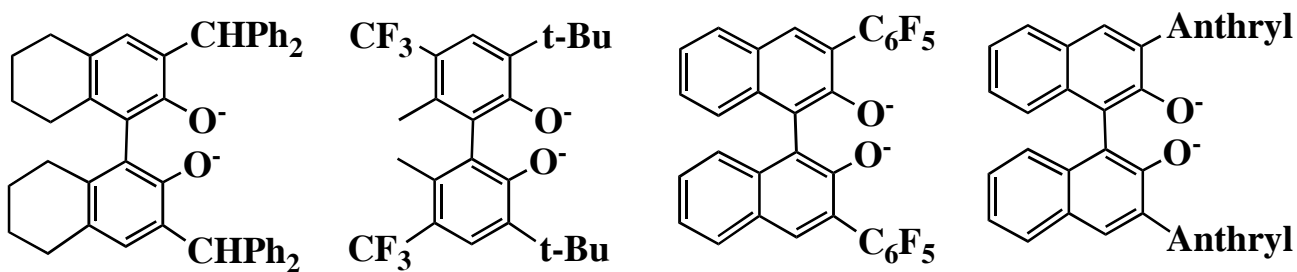
(Ad)



Some examples of diolate groups for enantiomorphous site control and asymmetric reactions.

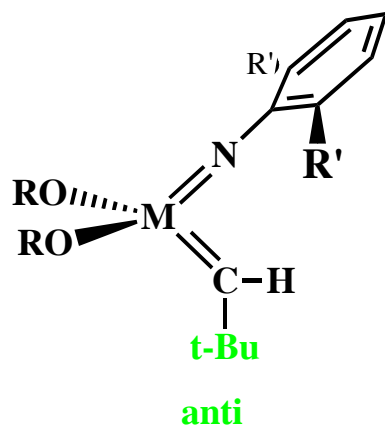


(Biphen²⁻)



(Benz₂Bitet²⁻)

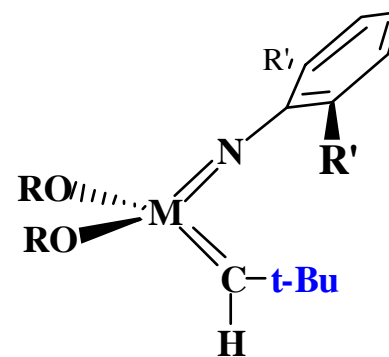
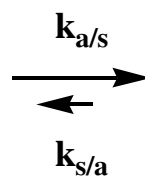
Syn and anti isomers create two potential 14e catalysts in any system, depending on their relative reactivities and rate of interconversion.



(favored for smaller OR, larger NR)

$$\delta H_{\alpha} = 13-14 \text{ ppm}$$

(Form stronger solvent adducts.)



syn (usually favored)

(favored for larger OR, smaller NR)

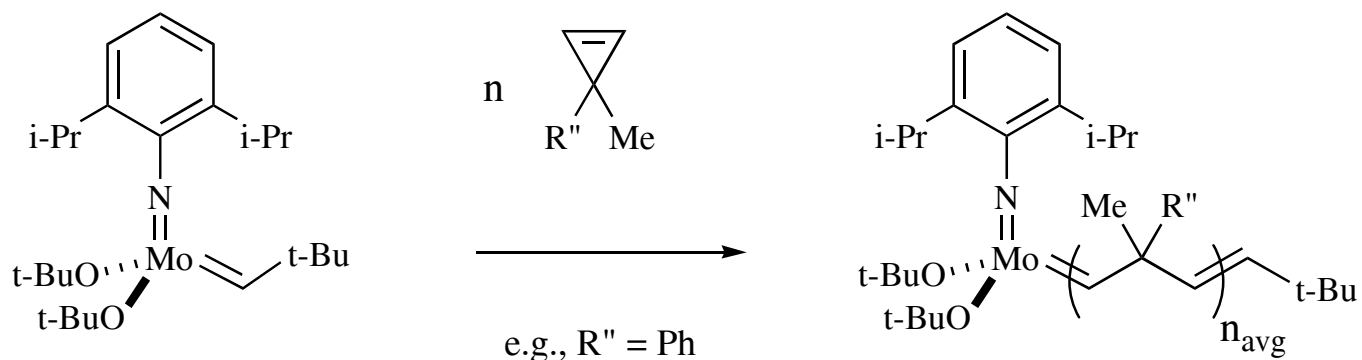
$$\delta H_{\alpha} = 11-13 \text{ ppm}$$

(Weak agostic CH_{α} interaction.)

Rate of interconversion of isomers can vary by 10^6 , from 1 to $\sim 10^{-5} \text{ s}^{-1}$, depending upon OR.

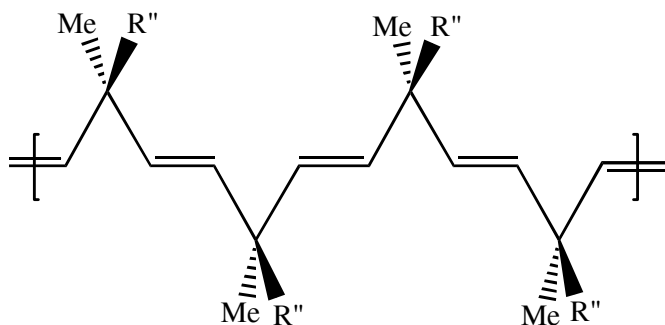
Anti isomer is more reactive than syn isomer (by several orders of magnitude).

A New Reaction, ROMP of Cyclopropenes

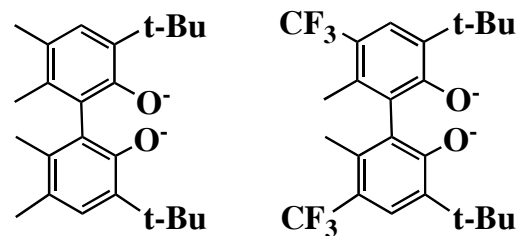


100 equivalents polymerized in 10 minutes; "perfectly living" and all *trans*
 (Singh, R.; Czekelius, C.; Schrock, R. R. *Macromolecules* **2006**, *39*, 1316-1317)

Ru second generation is slow (days) and incomplete (75%).



***Tacticity!* (syndio shown)**



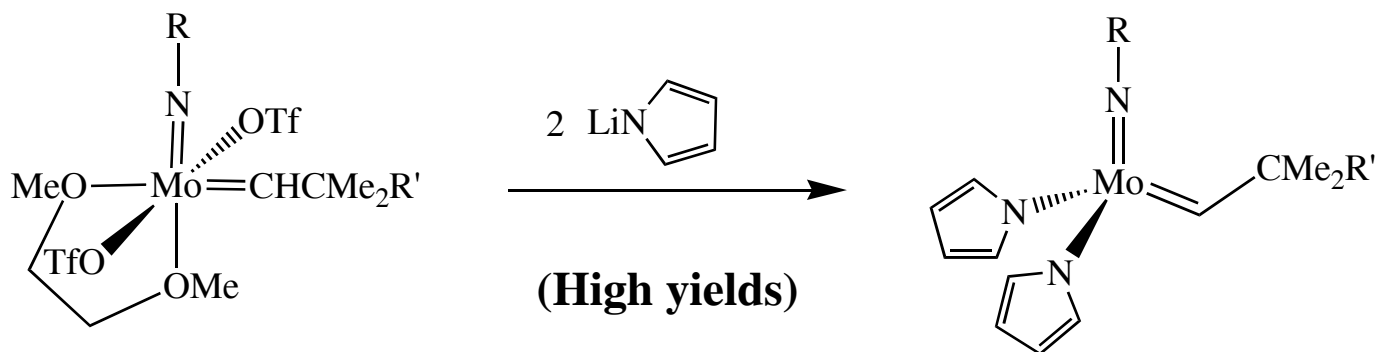
Atactic (T_g = 0°) >98% tactic (T_g = 100°)

Variations are the answer.

**The good news is that there are *hundreds* of variations.
*But there are too many catalysts to isolate each one.***

**The design and evaluation of an ever
increasing number of (especially asymmetric)
catalysts ultimately will require the synthesis
of catalysts *in situ*.**

Bispyrrolyl complexes can be prepared in high yield from bistriflates.

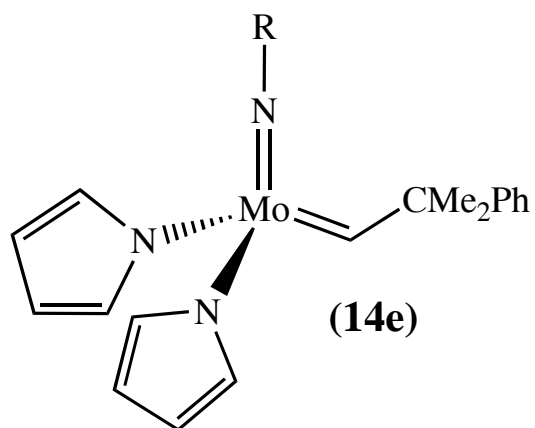


R = 2,6-*i*-Pr₂C₆H₃, adamantyl, 2,6-Br₂-4-MeC₆H₂; R' = Me or Ph

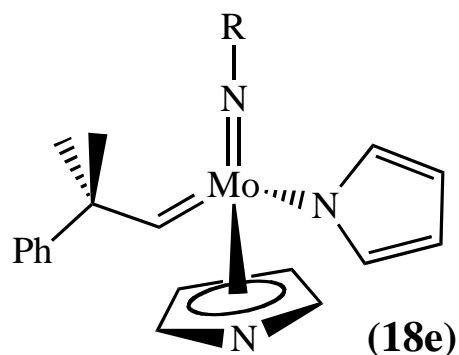
Adam Hock

Hock, A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 16373-16375.

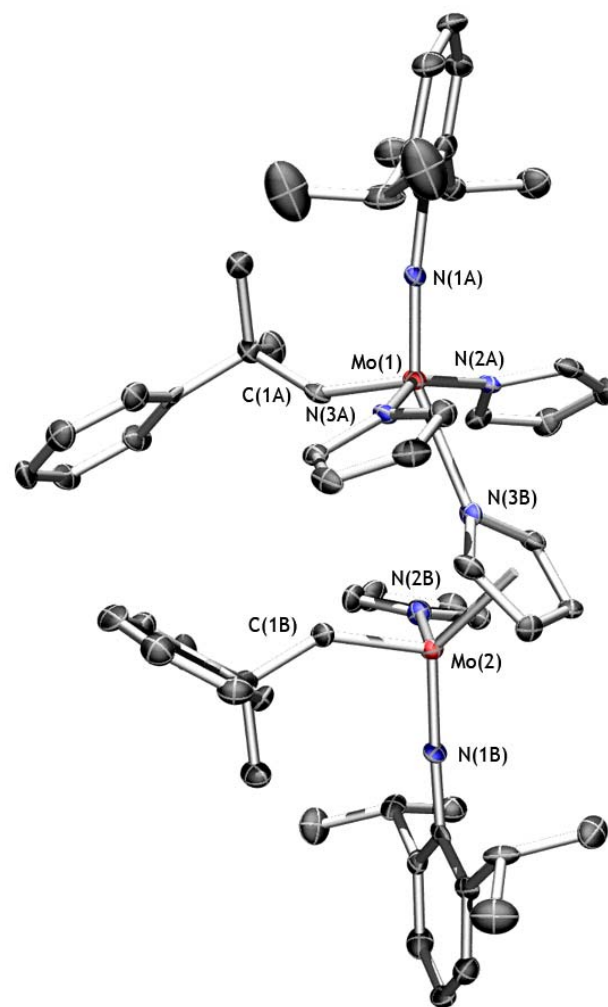
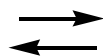
Bispyrrolyls are highly fluxional dimers



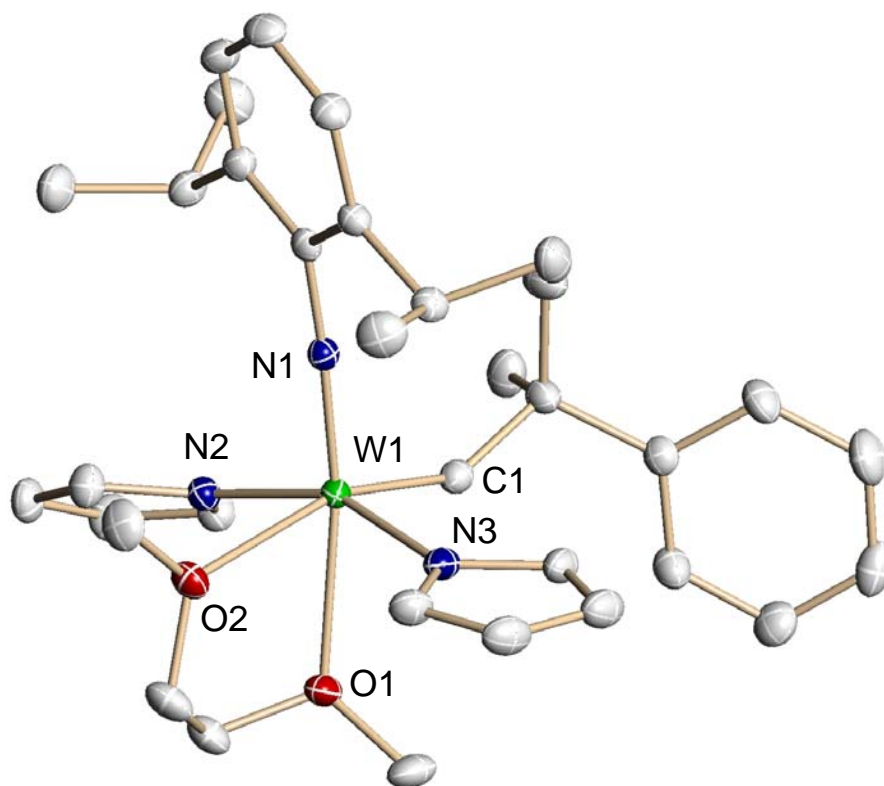
(14e)



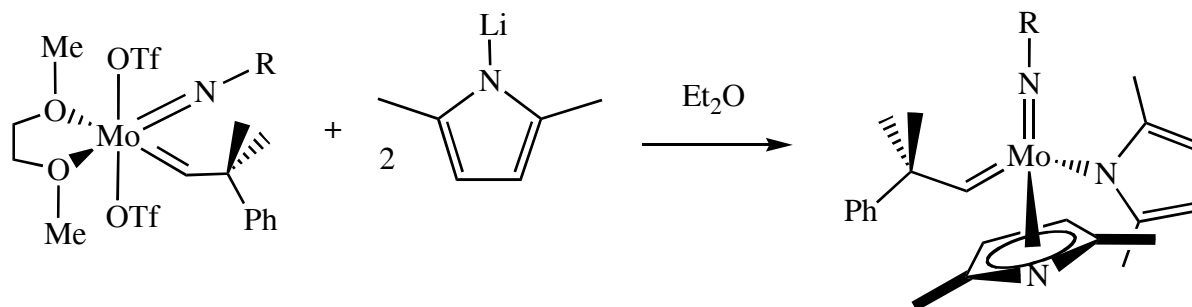
(18e)



Structure of $W(\text{NAr})(\text{CHMe}_2\text{Ph})(\text{NC}_4\text{H}_4)_2(\text{dme})$

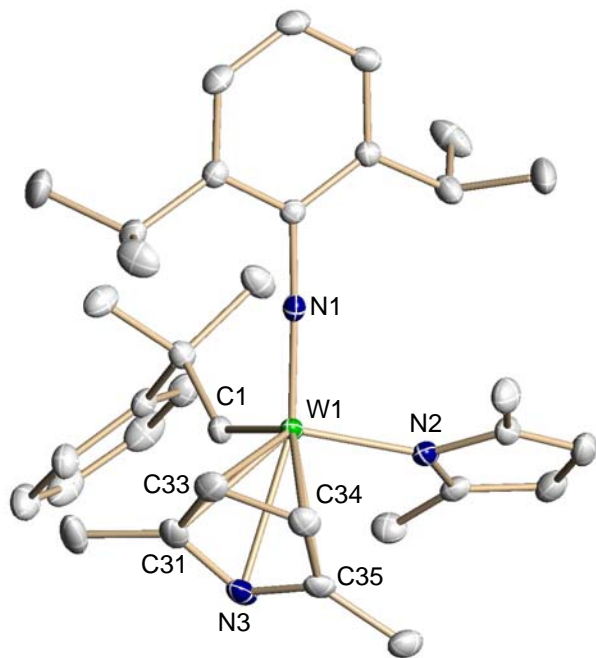


Bis(2,5-dimethylpyrrolyl) complexes are monomeric.



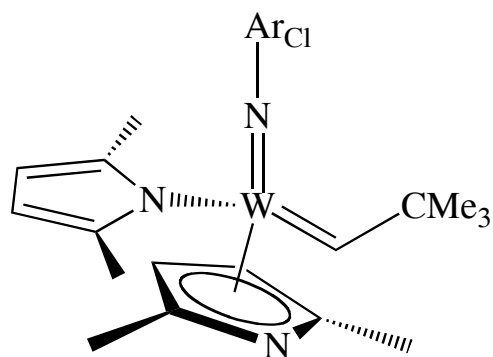
R = 2,6-*i*-Pr₂C₆H₃ (**1a**); 2,6-Me₂C₆H₃ (**1b**);
1-adamantyl (**1c**); 2-(CF₃)C₆H₄ (**1d**)

(**18e** species; fluxional)



Structure of W(NAr)(CHCMe₂Ph)(NC₄H₂Me₂)₂

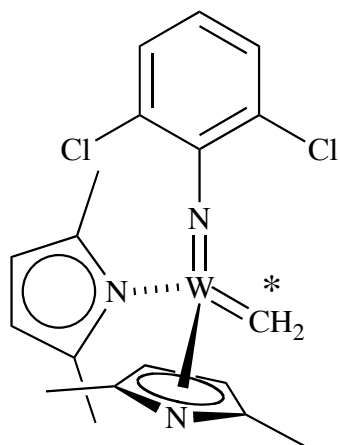
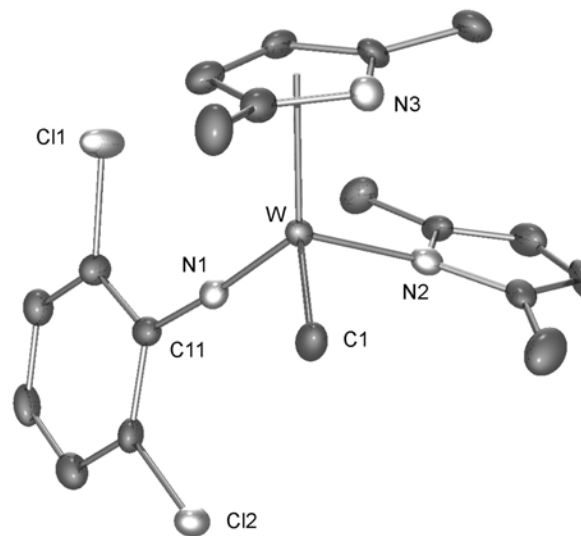
Bispyrrolides are relatively inactive (?) towards olefins, but a W methylene species can be isolated upon reaction with ethylene



+ C₂H₄
4 days



- CH₂=CHMe₃



*CH₂=*CH₂
immediate

No metallacyclobutane complexes observed.

$\delta H_{\alpha} = 12.55$ and 10.98 ppm ($J_{HH} = 7.6$ Hz, $J_{CH} = 145$ Hz)

$\delta C_{\alpha} = 255.4$ ppm ($J_{WC} = 160$ Hz)

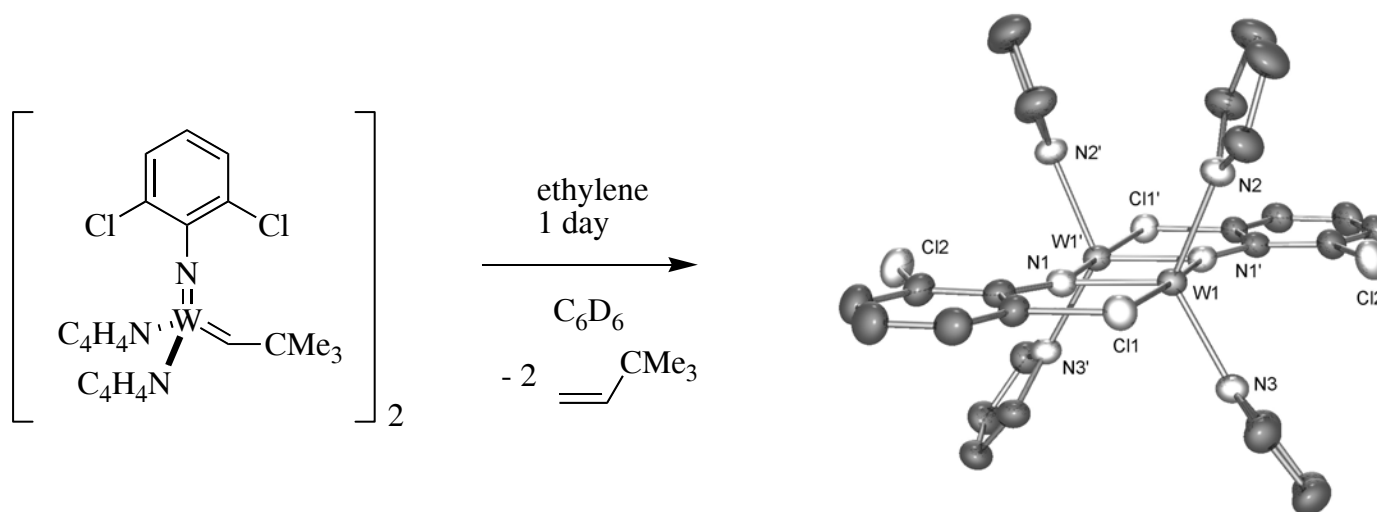
W-C(1) = 1.941(5) Å

W-N(1) = 1.754(4)

W-N(2) = 2.069(4)

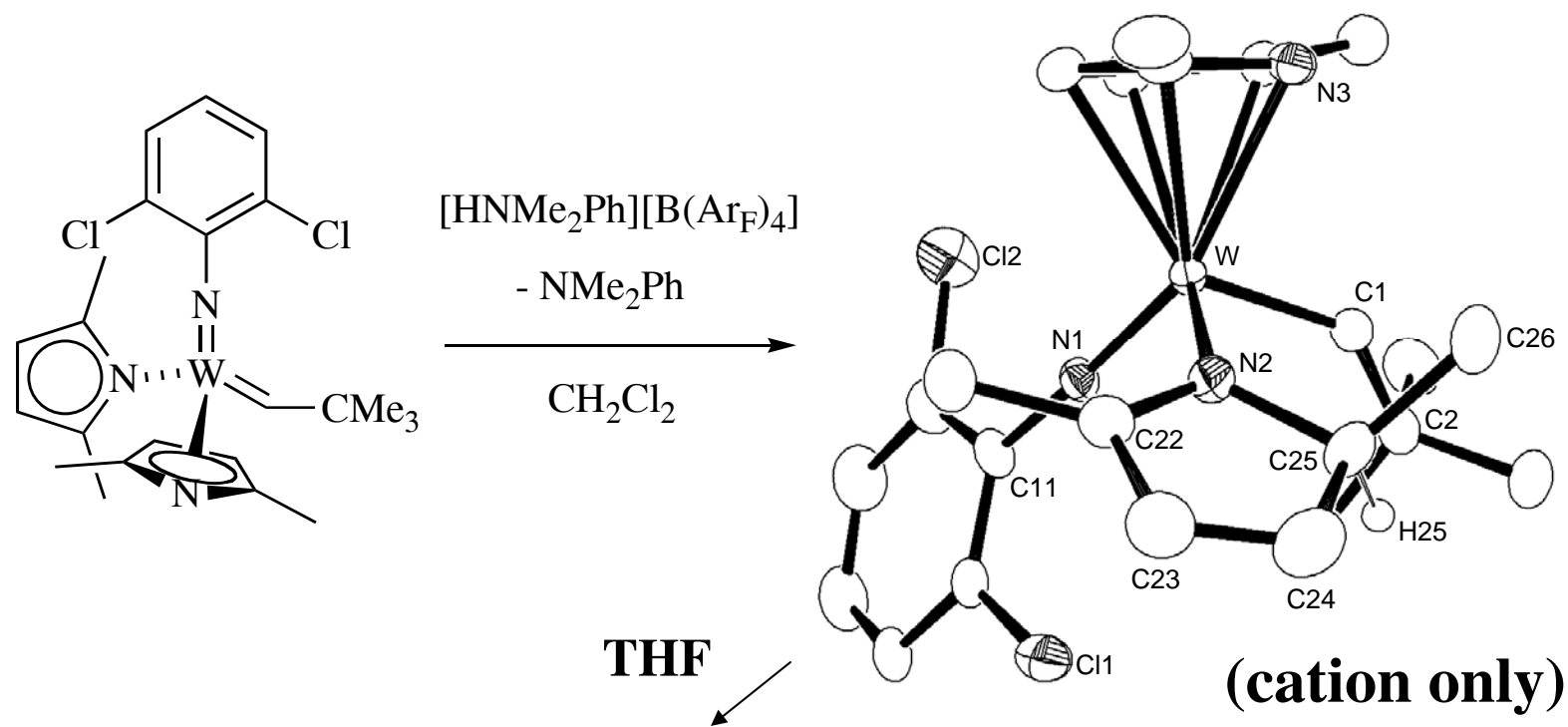
W(1)-N(1)-C(11)
= 175.5(4)°

The parent pyrrolide W methylene complex decomposes much more readily.

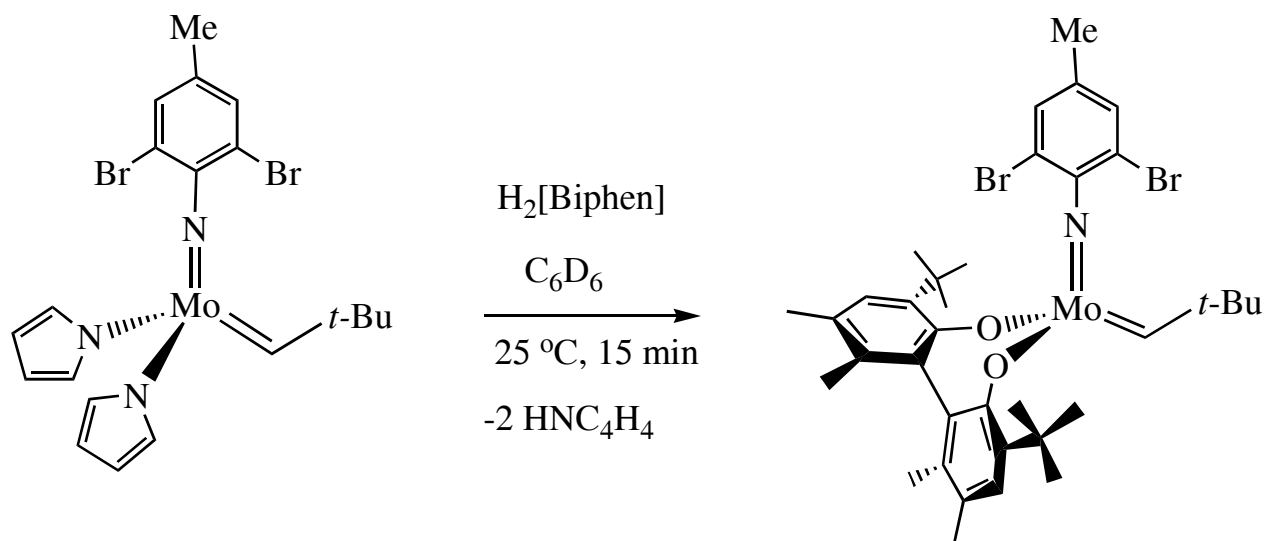


Dimethylpyrrolides (esp. η^5) provide internal protection of alkylidenes against bimolecular decomposition

Pyrroles protonate at C_α to give pyrrolenine complexes.



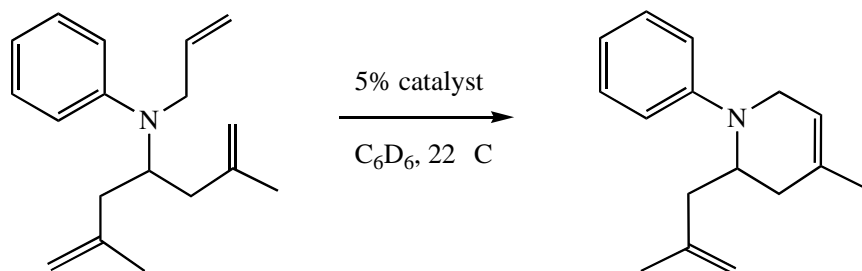
Dipyrrolyls react with all monoalcohols and diols with which we are familiar, even the H₂[Biphen]/Mo=NAr combination.



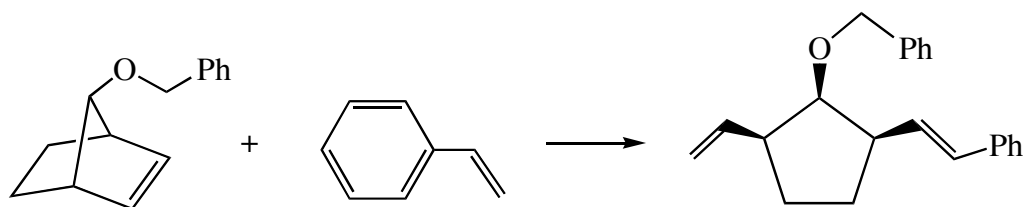
Catalysts can be prepared that could not be prepared through standard methods.

1. Reactions are generally fast (for pyrrolyl) and quantitative.
2. Pyrrolenine complexes can be intermediates.
3. 2,5-Dimethylpyrrolyl complexes react more slowly.
4. *In situ* diolate or bisalkoxide species are active catalysts.

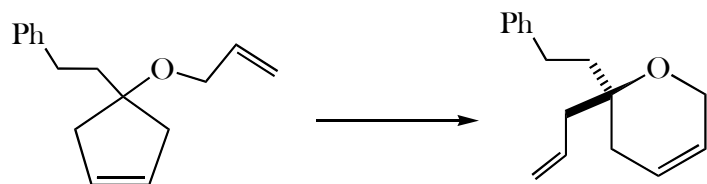
Asymmetric reactions with catalysts prepared *in situ*.



**Ring-closing metathesis
desymmetrization of a
tertiary amine.**

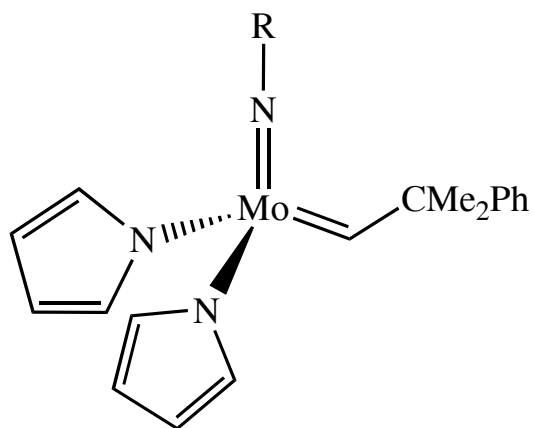


**Asymmetric
ring-opening/cross metathesis**



**Asymmetric
ring-opening/closing metathesis**

In situ catalyst synthesis and evaluation in drybox.

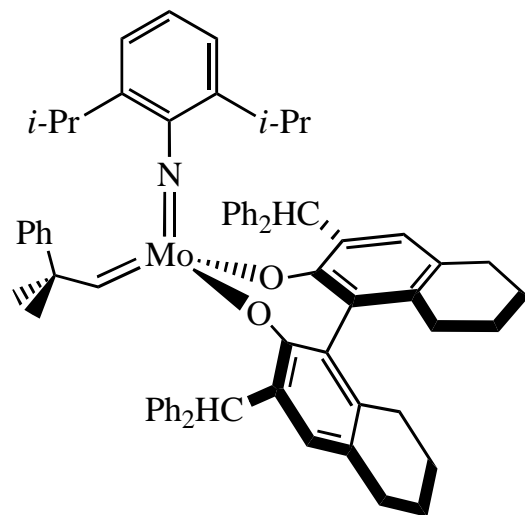


(in toluene)

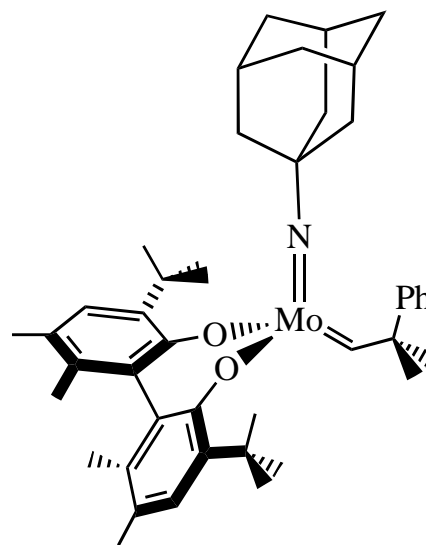
1. Add diol in toluene and wait x minutes.
2. Add substrate and monitor progress.
3. Evaluate conversion, yield, and ee.

(Bispyrrolylides are relatively inactive for olefin metathesis.)

Catalyst nomenclature

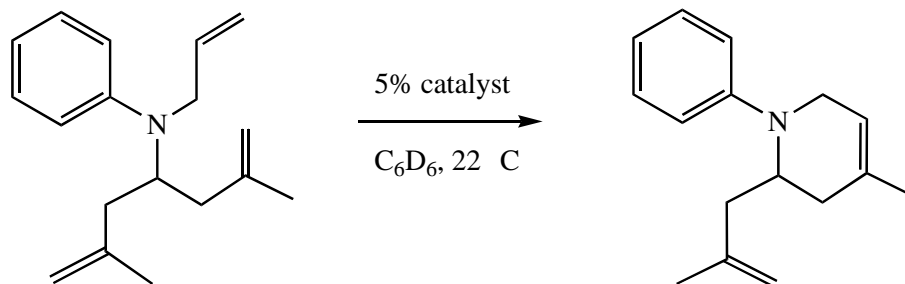


Ar/Benz₂Bitet



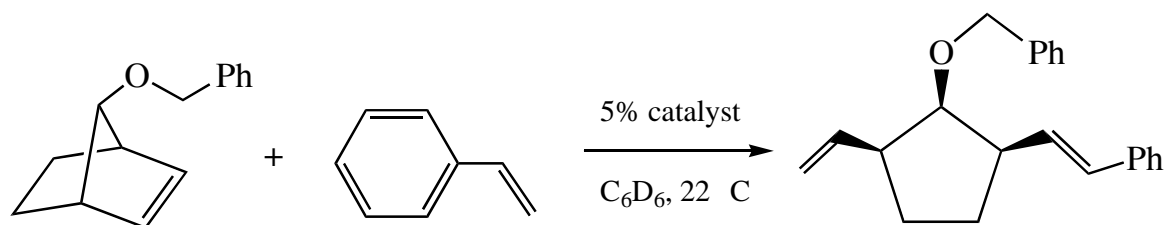
Ad/Biphen

Isolated vs. *in situ* catalyst in drybox



<u>Isolated catalyst</u>	<u>T(h)</u>	<u>Conv</u>	<u>Yield</u>	<u>ee</u>
Ar/Biphen	0.3	95	78	98
Ar/Benz ₂ Bitet	1	95	-	61
Ad/Biphen	2	98	80	98
<u><i>In situ</i> catalyst</u>	<u>T(h)</u>	<u>Conv</u>	<u>Yield</u>	<u>ee</u>
Ar + H ₂ Biphen	2	98	86	97
Ar + H ₂ Benz ₂ Bitet	2	98	77	60
Ad + H ₂ Biphen	2	95	90	97

Isolated vs. *in situ* catalyst in drybox



<u>Isolated catalyst</u>	<u>T(h)</u>	<u>Conv</u>	<u>ee</u>
Ar/Biphen	0.5	95	98
Ar/Benz ₂ Bitet	1	72	93
Ad/Biphen	2	76	97
<u>In situ catalyst</u>	<u>T(h)</u>	<u>Conv</u>	<u>ee</u>
Ar + H ₂ Biphen	2	80	98
Ar + H ₂ Benz ₂ Bitet	2	51	53 (solvent free))
Ad + H ₂ Biphen	2	79	98

In situ catalyst evaluation in a fume hood using solutions in dried solvents in N₂-flushed flasks

Stored in the **fume hood** in Schlenk flasks
C₆D₆ stock solutions of:

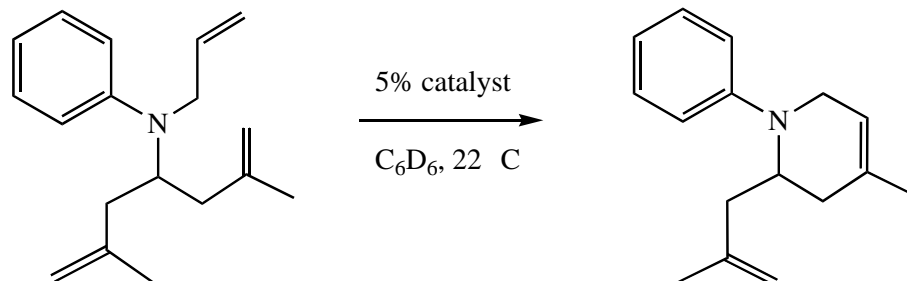
- Mo imido alkylidene bispyrrolide
- Chiral diol
- Substrates

Catalytic screenings performed on small scale (~2 mg cat, 20 mg substrate)

- After 3 days
- After 8 days
- After 2 weeks
- After a month
- ...

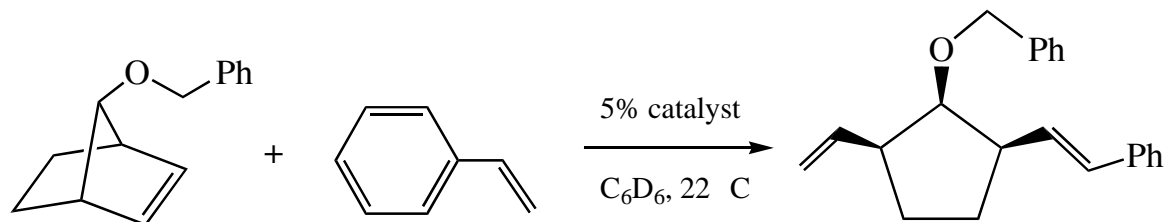


In situ catalyst in drybox vs. hood



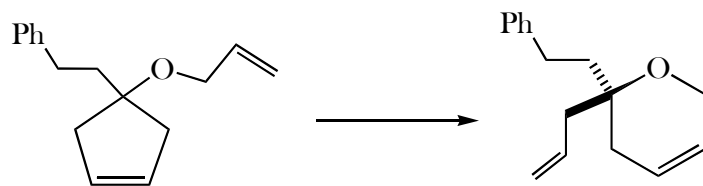
<u>Catalyst</u>		<u>T(h)</u>	<u>Conv</u>	<u>Yield</u>	<u>ee</u>
Ad/Biphen	Drybox	2	91	90	98
	Hood/3 days	2	96	94	96
	Hood/10 days	2	77	74	96
Ar/Biphen	Drybox	2	98	86	97
	Hood/3 days	2	98	95	97
	Hood/10 days	2	98	93	97
Ar/Benz₂Bitet	Drybox	2	98	77	60
	Hood/3 days	2	98	93	61
	Hood/10 days	2	98	91	62

In situ catalyst in drybox vs. hood



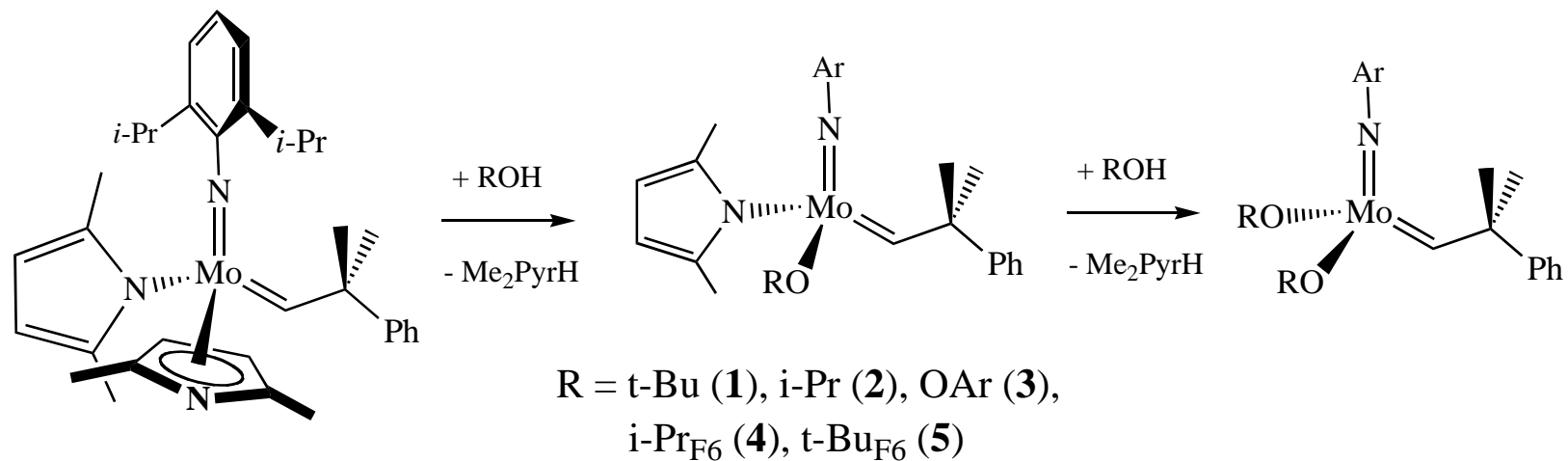
<u>Catalyst</u>		<u>T(h)</u>	<u>Conv</u>	<u>Yield</u>	<u>ee</u>
Ad/Biphen	Drybox	3	79	-	98
	Hood/4 days	2	92	80	>98
	Hood/10 days	2	91	89	>98
Ar/Biphen	Drybox	3	80	-	98
	Hood/4 days	2	68	60	98
	Hood/10 days	2	72	63	>98

In situ catalyst in drybox vs. hood



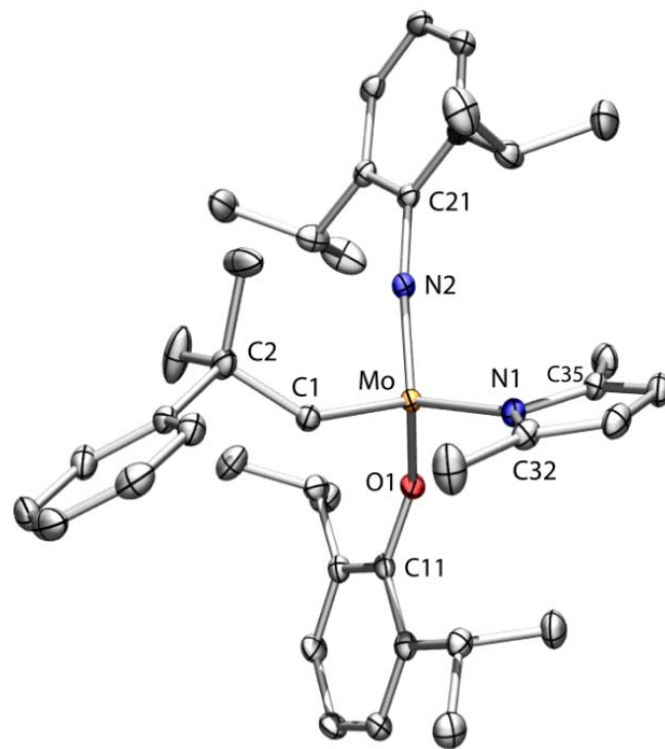
<u>Catalyst</u>		<u>T(h)</u>	<u>Conv</u>	<u>Yield</u>	<u>ee</u>
Ad/Biphen	Drybox	3	90	76	-12
	Hood/3 days (70 °)	3	93	77	-17
	Hood/10 days	3	91	68	-15
Ar/Biphen	Drybox	3	84	58	28
	Hood/3 days (70 °)	3	71	46	21
	Hood/10 days	3	81	53	24
Ar/Benz₂Bitet	Drybox	3	79	64	0
	Hood/3 days (70 °)	3	51	40	0
	Hood/10 days	3	85	56	0

It is possible to isolate monoalkoxide complexes.

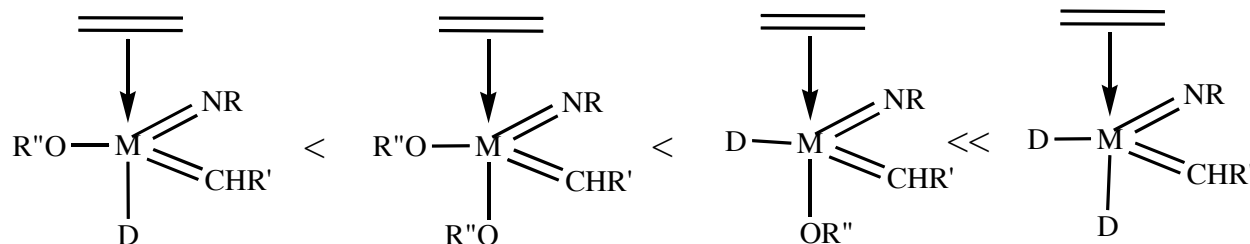


Structure of Mo(NAr)(CHCMe₂Ph)(Me₂Pyr)(OAr)

**Metal center
is asymmetric.**



Calculations (O. Eisenstein) suggest that E_a for formation of metallacycle is lowest in monoalkoxides!



D = donor (alkyl, amide, pyrrolide)

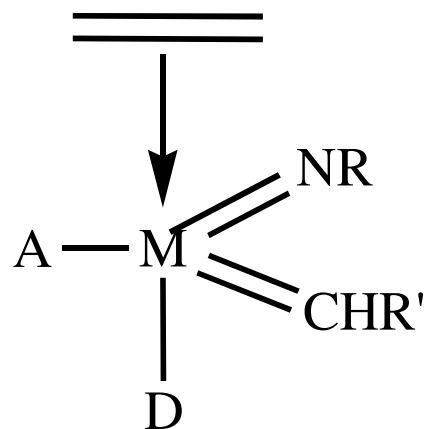
"prepared" for coordination
of olefin *trans* to donor

Distorted, "non-ideal" structures, including metallacyclobutanes, are less stable in unsymmetric (at M) systems.

Asymmetry at the metal raises a host of issues concerning asymmetric metathesis reactions by diastereomers.

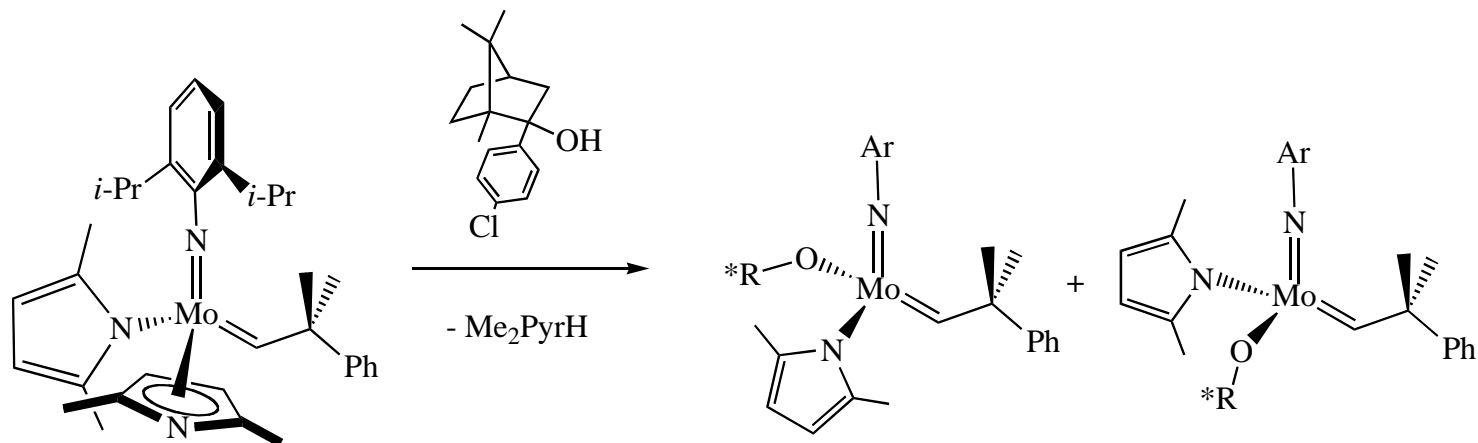
Poater, A., Solans-Monfort, X. ; Clot, E.; Copéret, C.; Eisenstein, O.
J. Am. Chem. Soc. **2007**, *129*, 8207-8216.

Principles are likely to be general.



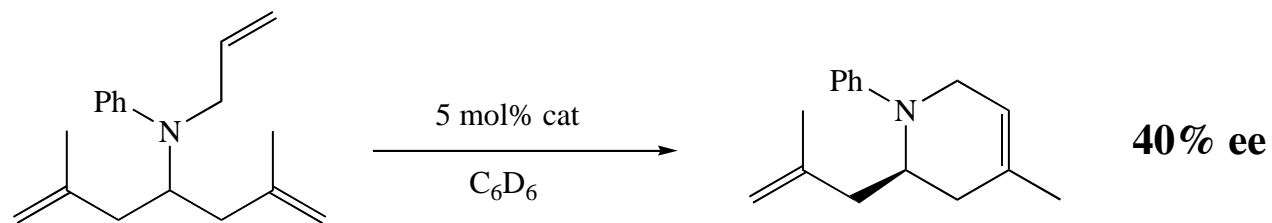
**"prepared" for coordination of olefin *trans* to donor (D),
cis to acceptor (A)**

Diastereomers that contain an epure alkoxide do not interconvert readily and can have significantly different reactivities.



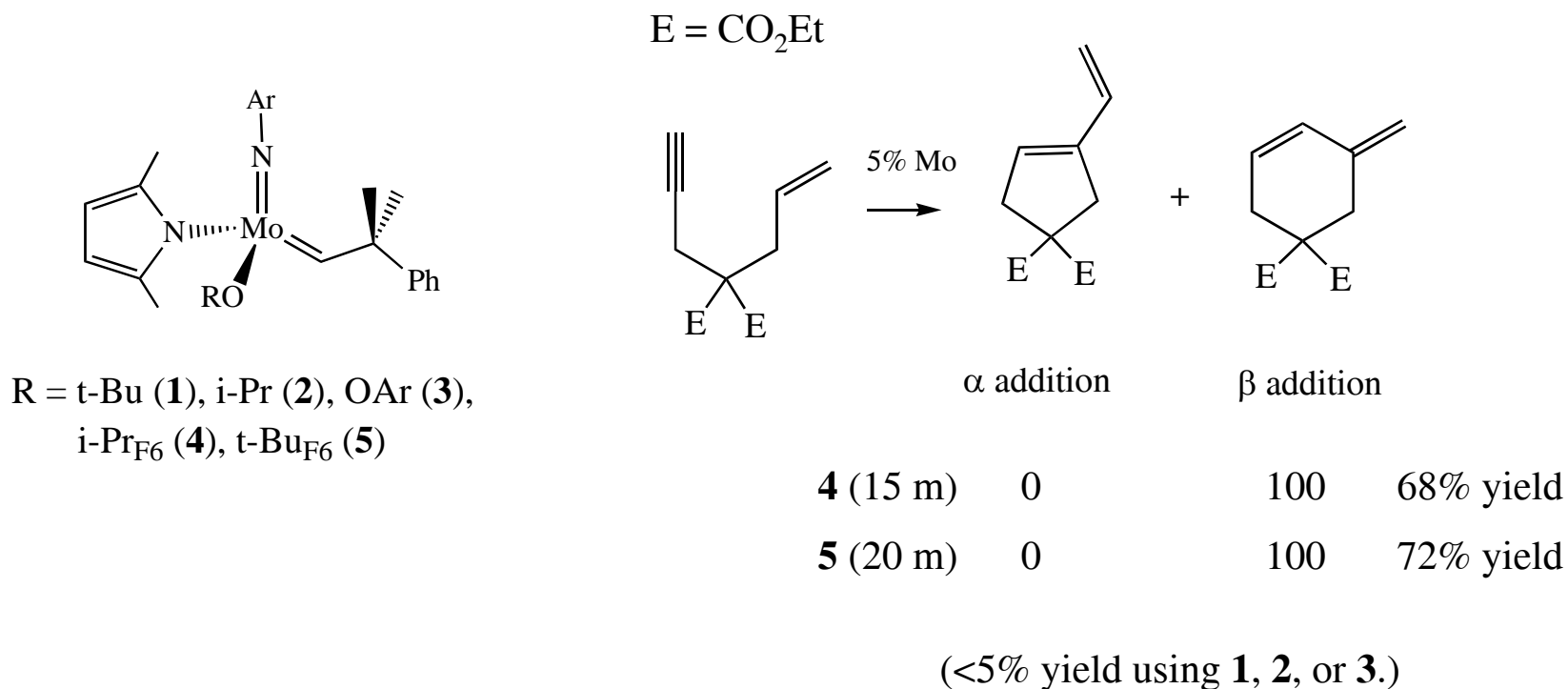
75:25 ratio (or *vice versa*)

(Diastereomeric ratios change upon recrystallization.)



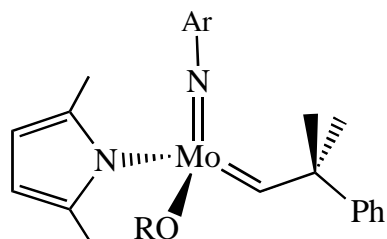
Largely *one* diastereomer (the minor one) is consumed.

Enyne metathesis is observed for the first time with Mo
(Bispyrrolide does not react and bisalkoxides produce a mess.)

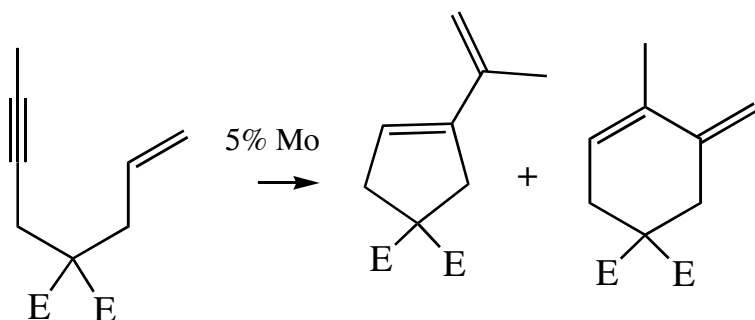


Only α addition observed using Ru.

An internal alkyne produces both
 "α" and "β" addition products.



R = t-Bu (**1**), i-Pr (**2**), OAr (**3**),
 i-Pr_{F6} (**4**), t-Bu_{F6} (**5**)



"α addition"

"β addition"

4 (20 m)

40

60

72%

5 (20 m)

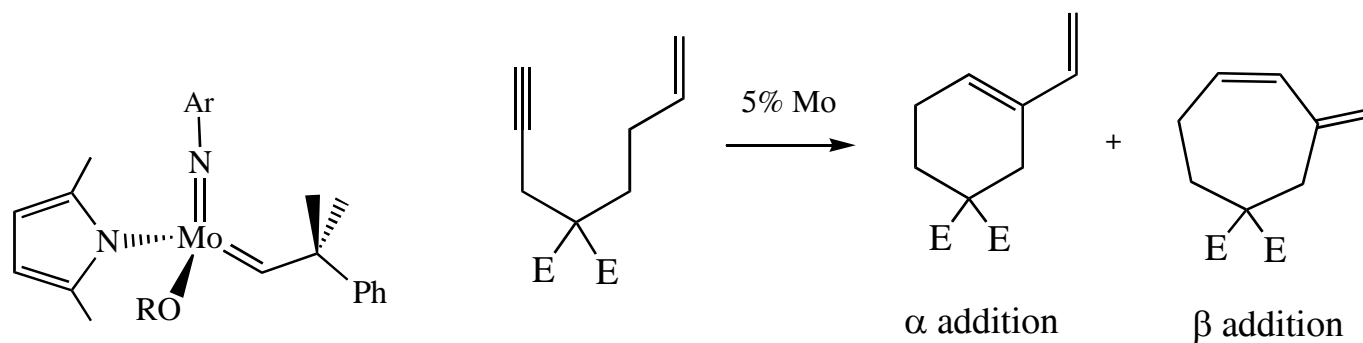
25

75

80%

(<5% yield using **2** or **3**.)

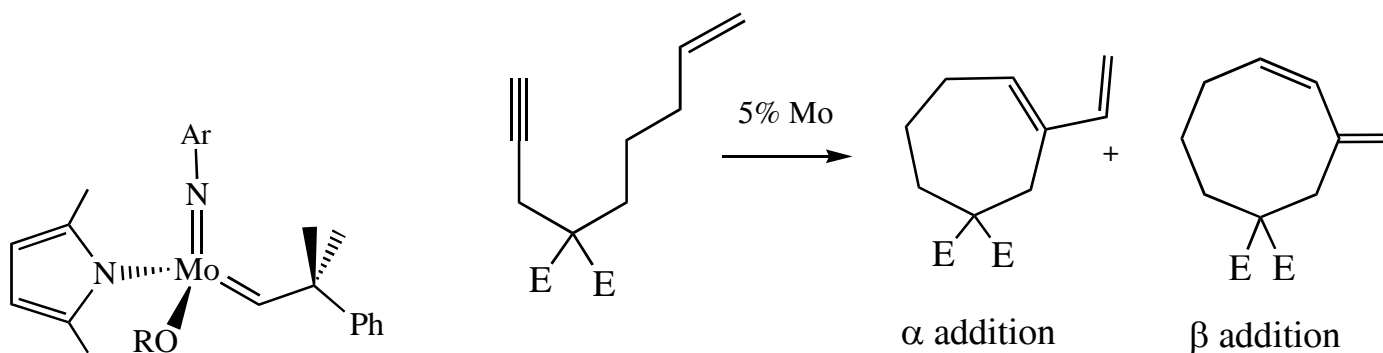
Enyne Metathesis Observed for the first time with Mo



R = t-Bu (**1**), i-Pr (**2**), OAr (**3**),
i-Pr_{F6} (**4**), t-Bu_{F6} (**5**)

1 (20 m)	60	40	77%
2 (20 m)	80	20	79%
3 (2 h)	0	100	70%
4 (20 m)	30	70	83%
5 (20 m)	0	100	70%

Formation of the eight-membered ring is problematic

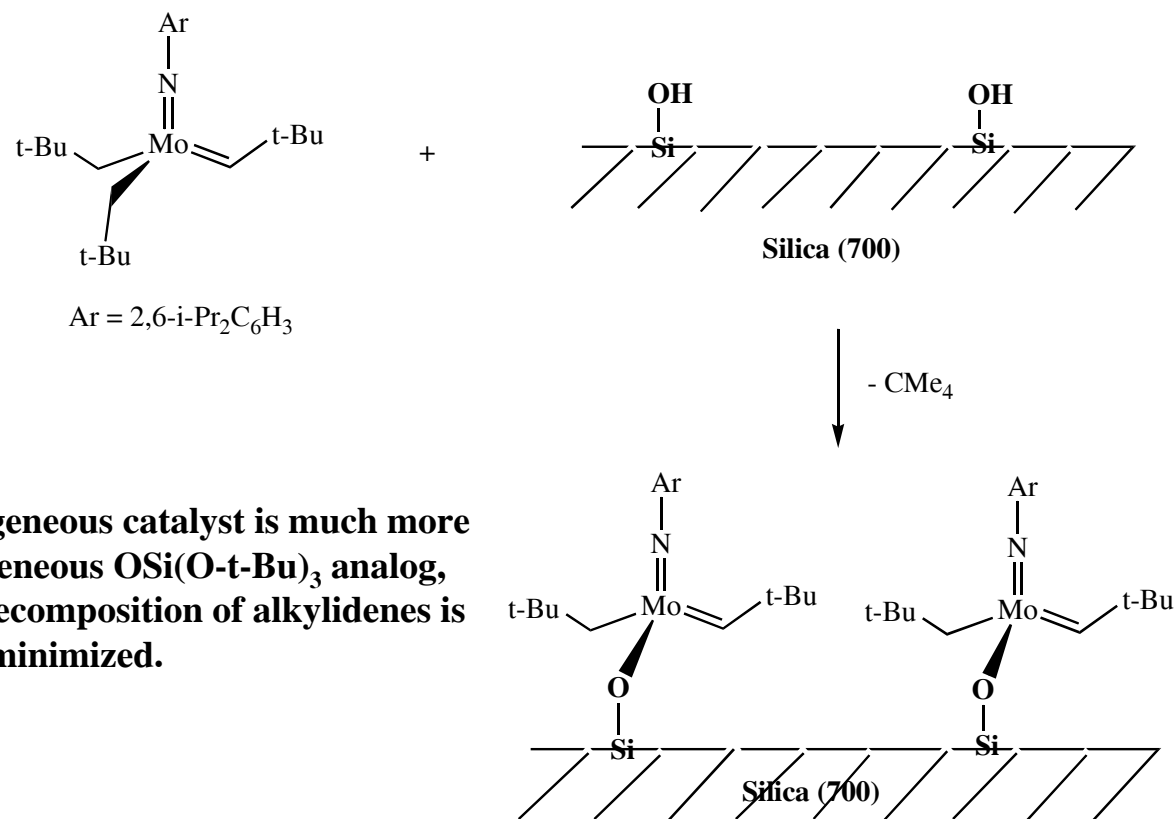


R = t-Bu (**1**), i-Pr (**2**), OAr (**3**),
i-Pr_{F6} (**4**), t-Bu_{F6} (**5**)

1 and 2 40-50% consumption of substrate
but <5% products

3, 4, and 5 <5% products

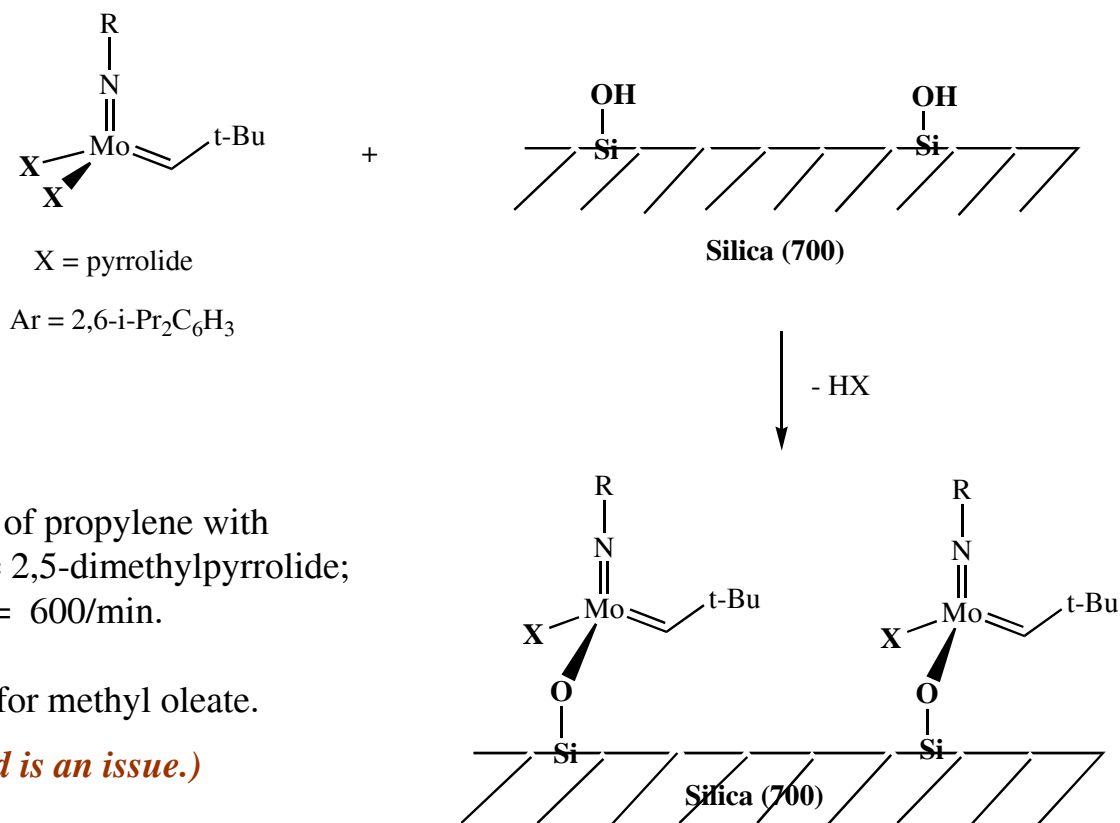
"Well-defined" heterogeneous catalysts can be prepared on silica.



100% active heterogeneous catalyst is much more active than homogeneous OSi(O-*t*-Bu)₃ analog, since bimolecular decomposition of alkylidenes is minimized.

F. Blanc, A. Baudouin, C. Copéret, J. Thivolle-Cazat, J.-M. Basset,
A. Lesage, L. Emsley, A. Sinha, R. R. Schrock,
Angew. Chem. Int. Ed. **2006**, 45 1216.

"Well-defined" heterogeneous catalysts can be prepared on silica.



180,000 turnovers of propylene with
R = adamantyl and X = 2,5-dimethylpyrrolide;
initial rate = 600/min.

10,000 turnovers for methyl oleate.

(Purity of feed is an issue.)

Blanc, R.; Berthoud, R.; Salameh, A.; Basset, J.-M.; Copéret, C.; Singh, R.; Schrock, R. R.
J. Am. Chem. Soc. 2007, 129, 8434-8435.

Goals

- 1. Learn how to control catalyst decomposition (inter and intramolecular) completely.**
- 2. Prepare supported "well-defined" alkene metathesis catalysts.**
- 3. Exploit new alkylidenes that are asymmetric at the metal center for high reactivity or enantioselectivity.**
- 4. Explore and exploit *in situ* catalysts.**
- 5. Explore new cationic catalysts.**

Acknowledgements

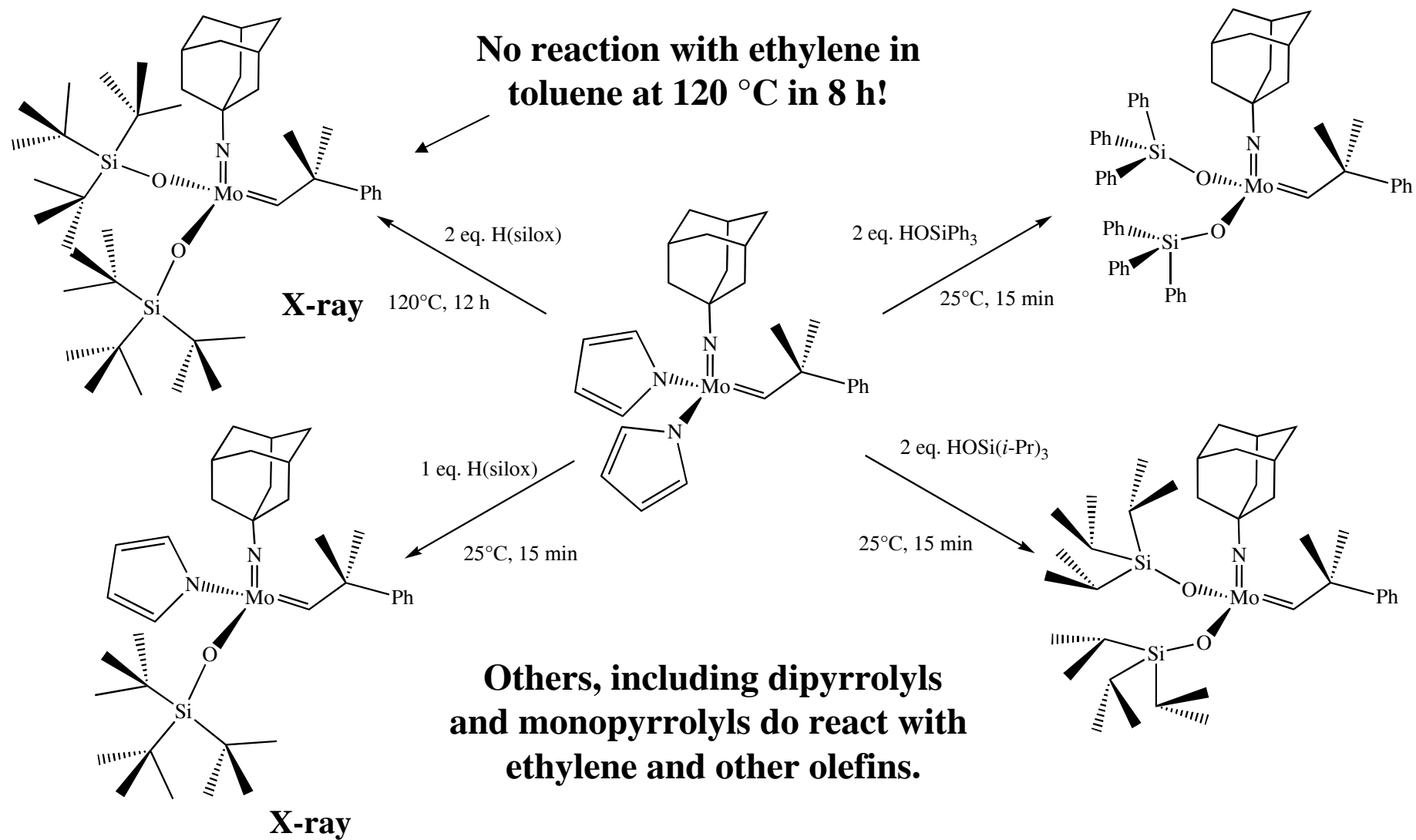
National Science Foundation
(Fundamental studies)

National Institutes of Health
(Asymmetric metathesis reactions)

A. Hoveyda and group (Boston College)

**Constantin Czekelius,
Adam Hock, Rojendra Singh, Thorsten Kreickmann,
Zach Tonzetich, Stephan Arndt, Tanya Pilyugina**

Siloxides



Alkylidenes decompose primarily in two ways

