Olefin Metathesis
~Well-Defined Ru Catalysts~

3rd Literature Seminar

August 5, 2013

Soichi Ito (M2)

~Topics~

- Introduction
- Evolution of Ruthenium Catalysts

~from ill-defined catalysts to well-defined catalysts~

✓ill-defined Ruthenium catalysts

✓well-defined Ruthenium catalysts

➢First-Generation Grubbs Catalyst

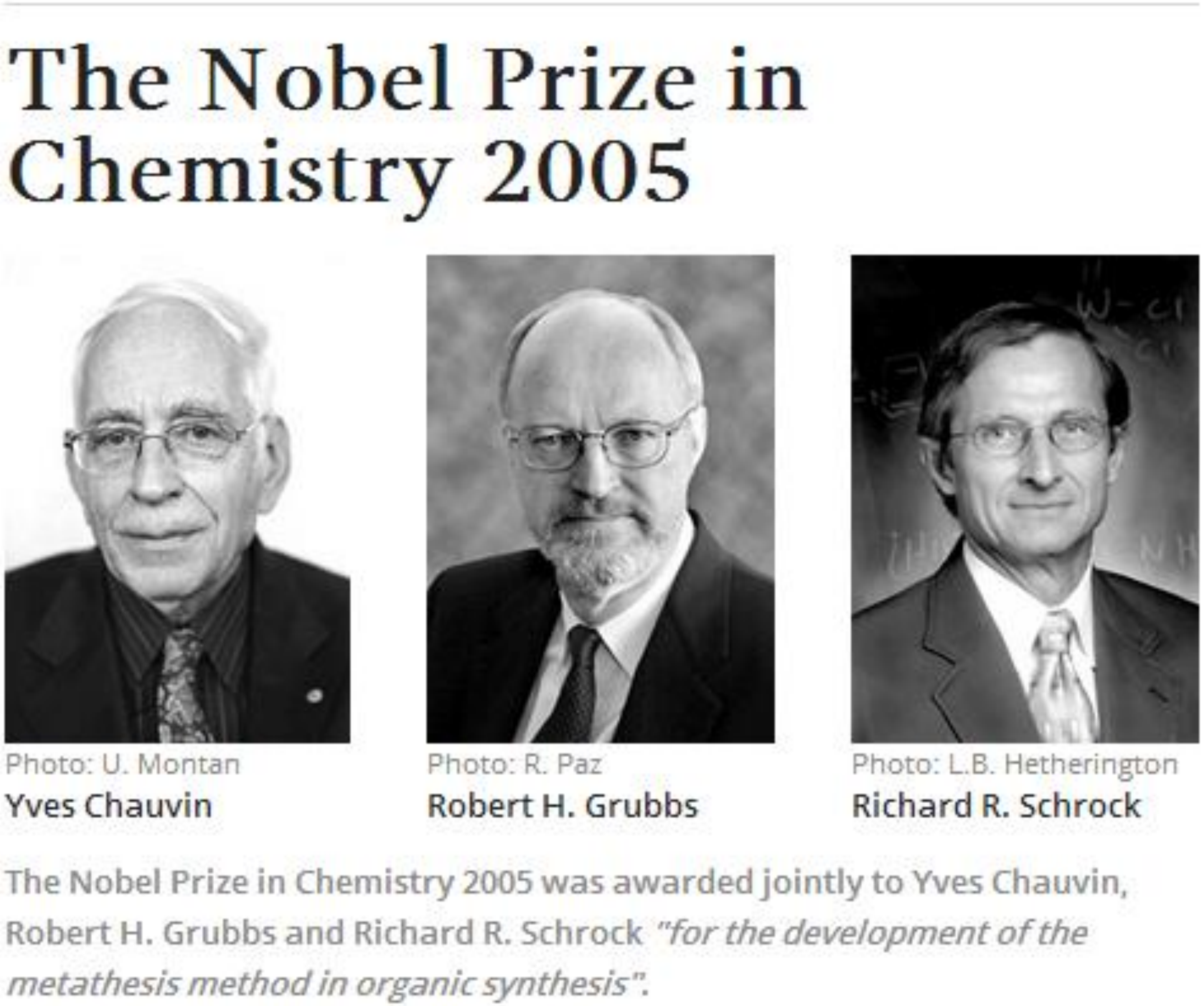
➢Mechanistic Study(1997)

➢Second-Generation Grubbs Catalyst

➢Mechanistic Study(2001)

Olefin Metathesis

A valuable Synthetic Tool for The Construction of Carbon-Carbon Bonds



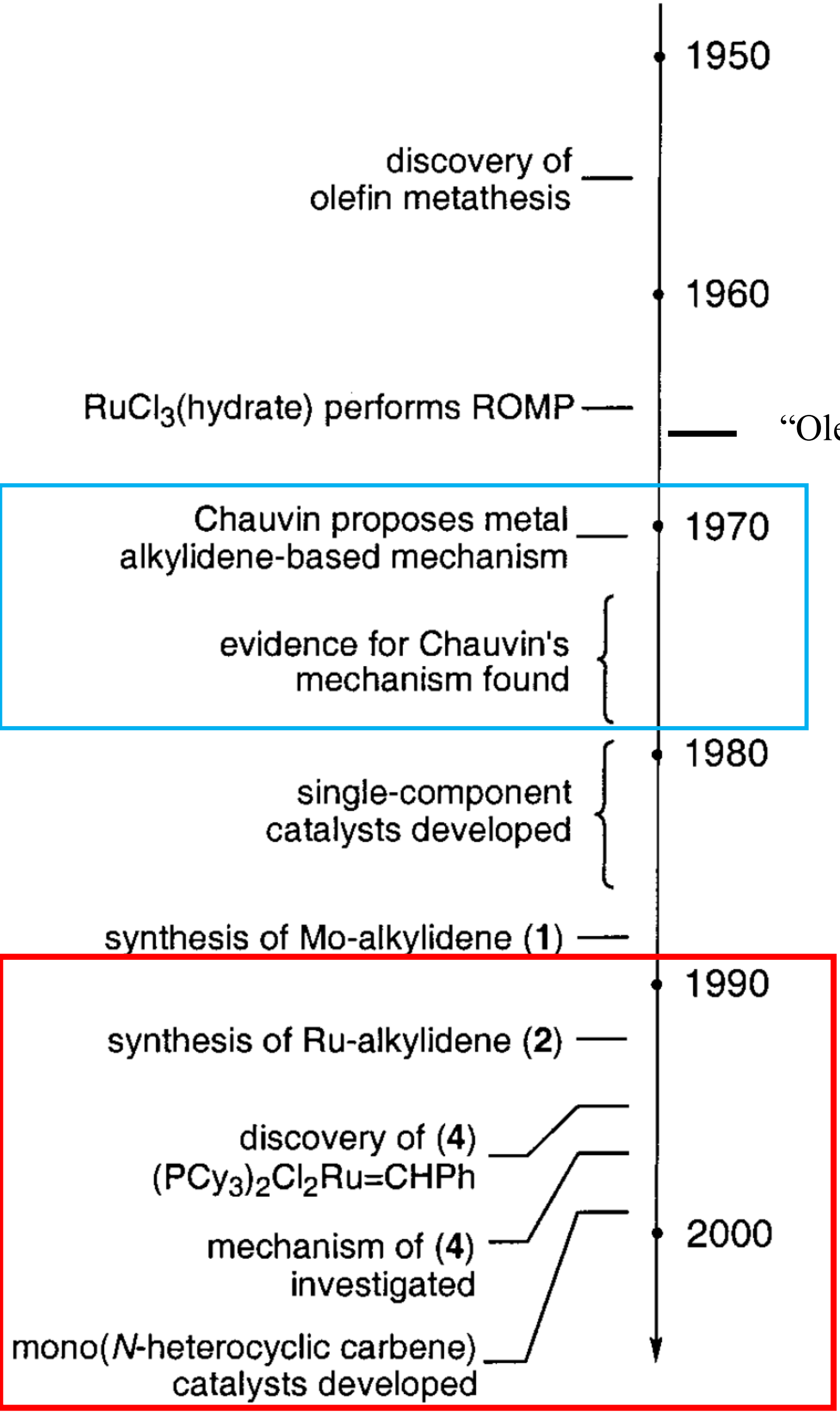
The Nobel Prize in Chemistry 2005

Photo: U. Montan
Yves Chauvin

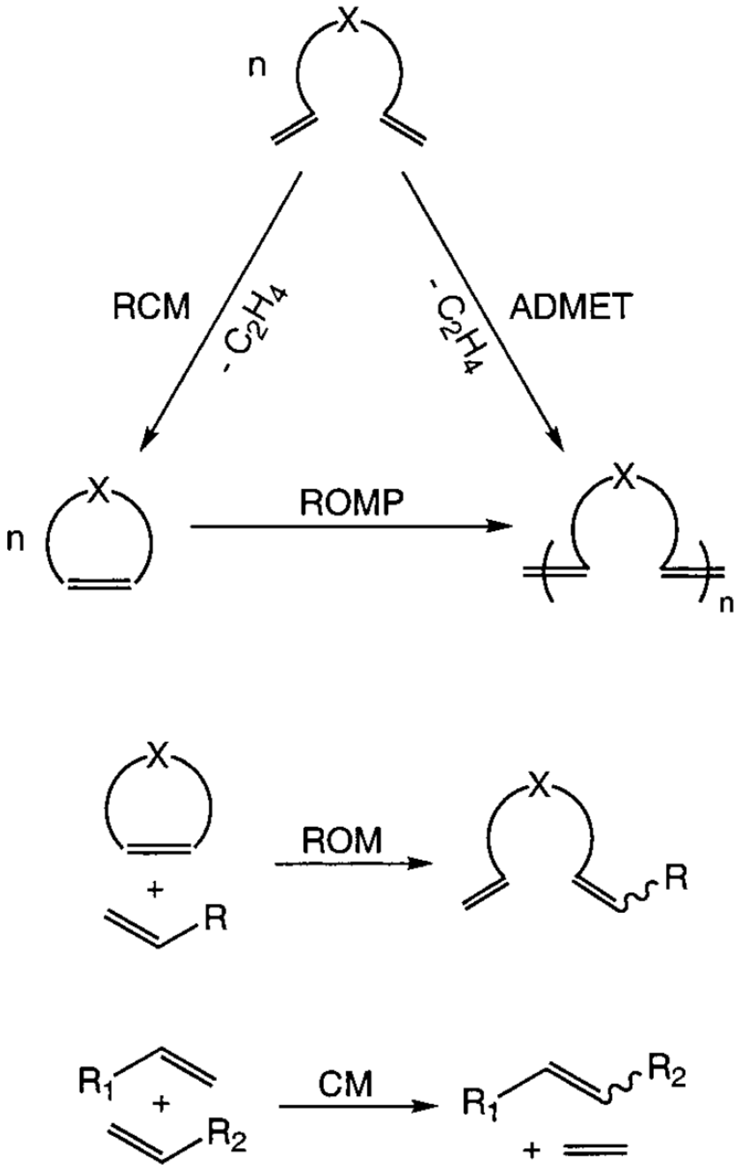
Photo: R. Paz
Robert H. Grubbs

Photo: L.B. Hetherington
Richard R. Schrock

The Nobel Prize in Chemistry 2005 was awarded jointly to Yves Chauvin, Robert H. Grubbs and Richard R. Schrock *"for the development of the metathesis method in organic synthesis".*



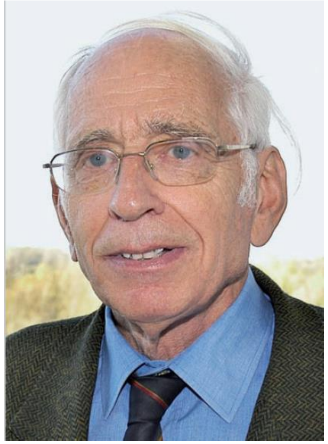
“Olefin Metathesis” by Calderon



A variety of olefin metathesis reactions.

Grubbs, R. H. *et al.*, *Acc. Chem. Res.* **2001**, *34*, 18.

Yves Chauvin



He was born on October 10, 1930 in Menin.
He joined Institut Français du Pétrole in 1960.
Motto
"If you want to find something new, look for something new!"

- *Dimersol Process (nickel-based catalyst): for gasoline*

✓ Dimerization of propylene into isohexenes: additive in gasoline as octane number booster.

✓ One of the first examples of application of homogeneous catalysts in refining

- *Dimersol Process: for chemistry*

✓ Dimerizing *n*-butenes to isooctenes

✓ Isooctenes are used as starting material for PVC plasticizer

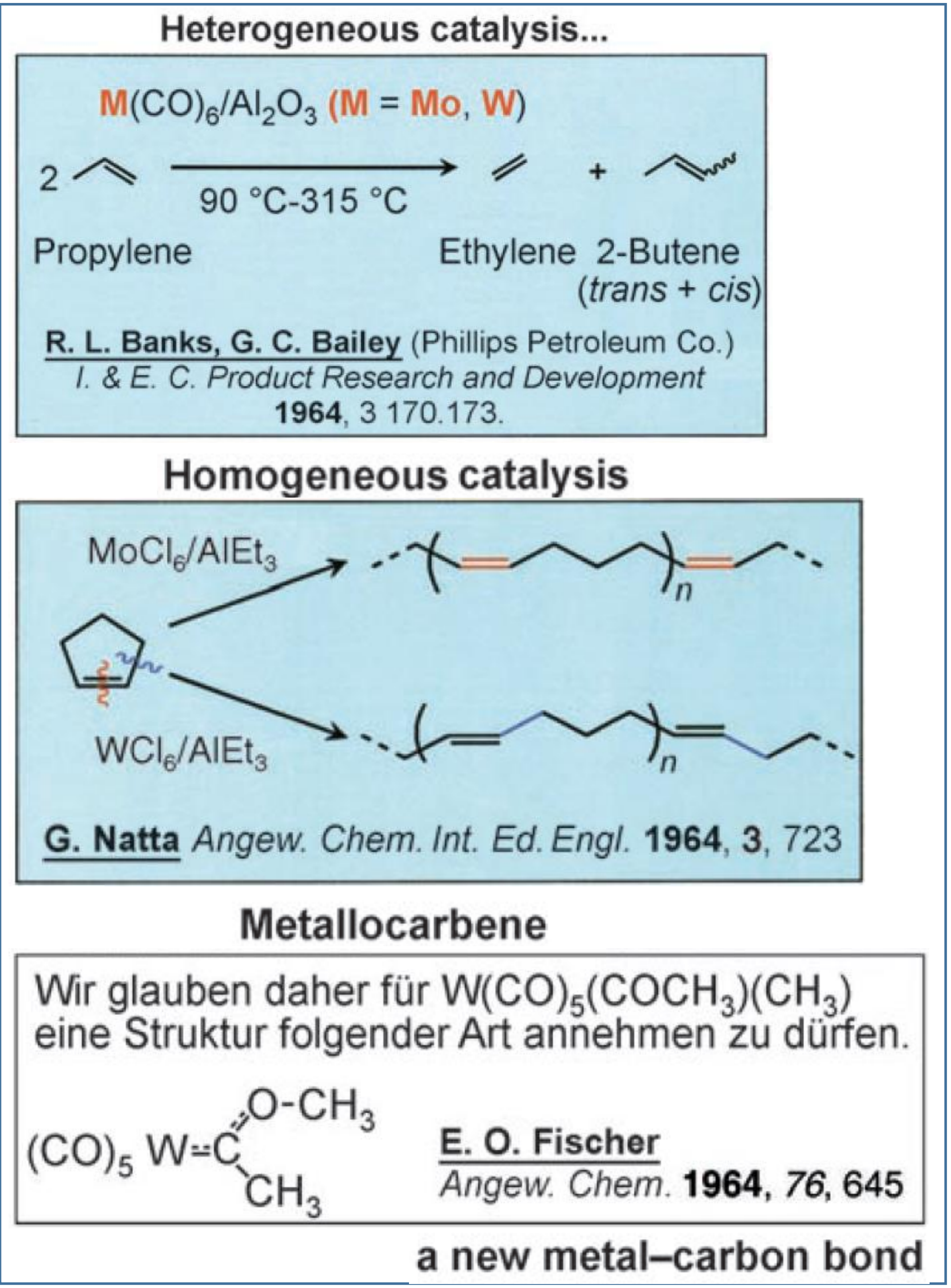
- *Alphabutol process (titanium based catalyst)*

✓ Dimerization of ethylene into 1-butene

✓ 1-butene is used as comonomer for polyethylene manufacture

- *Difasol Process* (improved Dimersol Process)

Non-Pair-Wise Mechanism



Heterogeneous catalysis...

$M(CO)_6/Al_2O_3$ (M = Mo, W)

2 Propylene $\xrightarrow[90\ °C-315\ °C]{}$ Ethylene + 2-Butene (*trans* + *cis*)

R. L. Banks, G. C. Bailey (Phillips Petroleum Co.)
I. & E. C. Product Research and Development
1964, 3 170.173.

Homogeneous catalysis

G. Natta *Angew. Chem. Int. Ed. Engl.* **1964**, **3**, 723

Metallocarbene

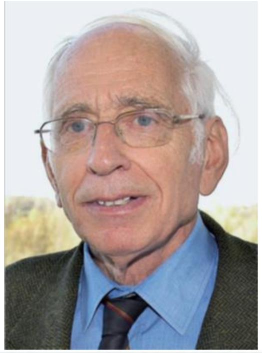
Wir glauben daher für $W(CO)_5(COCH_3)(CH_3)$ eine Struktur folgender Art annehmen zu dürfen.

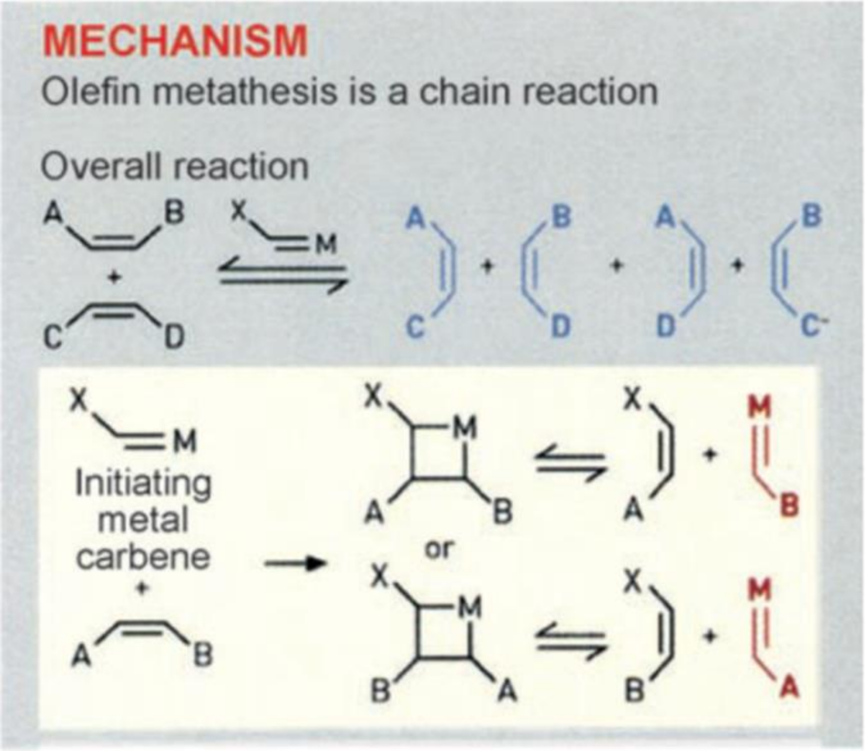
$(CO)_5W{=}C(O{-}CH_3)(CH_3)$

E. O. Fischer
Angew. Chem. **1964**, *76*, 645

a new metal–carbon bond

1964:
a magic year...





MECHANISM

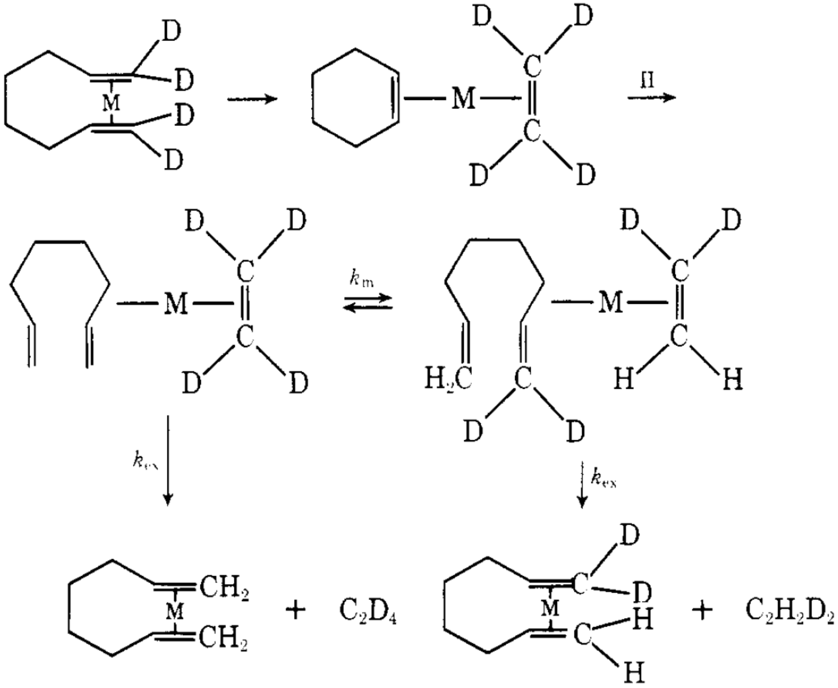
Olefin metathesis is a chain reaction

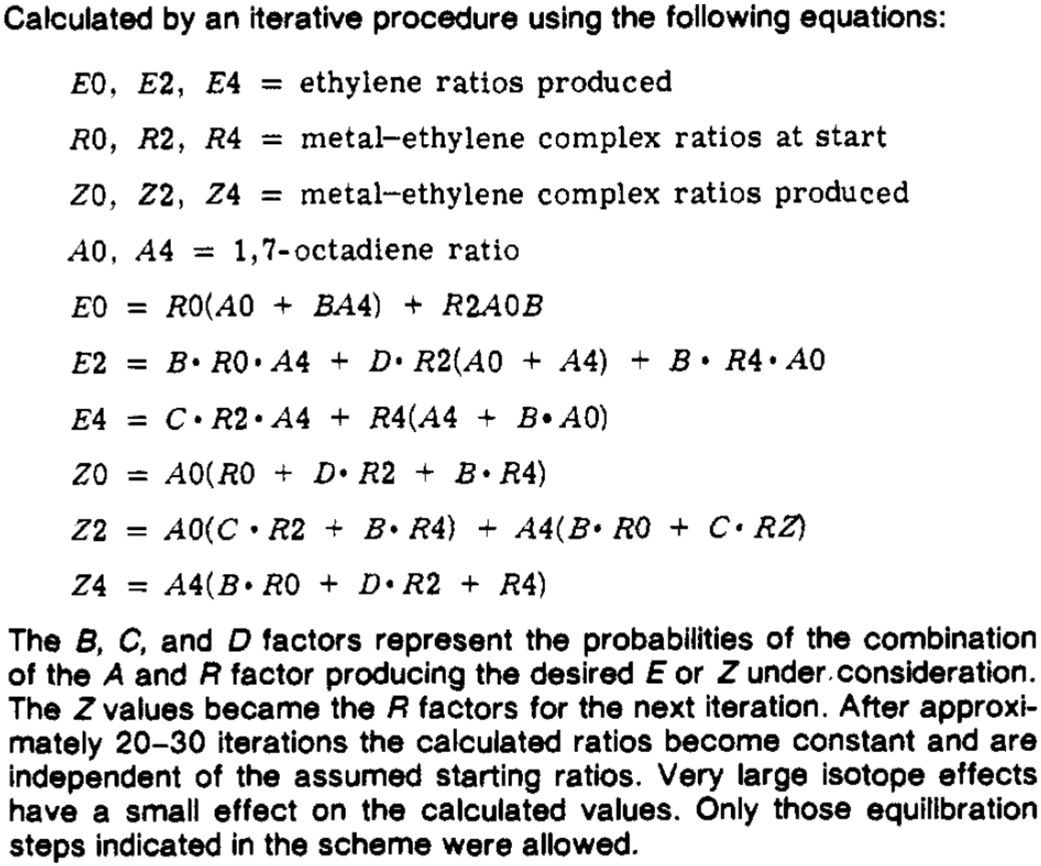
Overall reaction

Carbene mechanism

Chauvin, Y. *et al. Makromol. Chem.* **1971**, *141*, 161.
Chauvin, Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 3740.

Consideration of the Mechanism of the Olefin Metathesis Reaction





Calculated by an iterative procedure using the following equations:

$E0,\ E2,\ E4$ = ethylene ratios produced

$R0,\ R2,\ R4$ = metal–ethylene complex ratios at start

$Z0,\ Z2,\ Z4$ = metal–ethylene complex ratios produced

$A0,\ A4$ = 1,7-octadiene ratio

$$E0 = R0(A0 + BA4) + R2A0B$$

$$E2 = B \cdot R0 \cdot A4 + D \cdot R2(A0 + A4) + B \cdot R4 \cdot A0$$

$$E4 = C \cdot R2 \cdot A4 + R4(A4 + B \cdot A0)$$

$$Z0 = A0(R0 + D \cdot R2 + B \cdot R4)$$

$$Z2 = A0(C \cdot R2 + B \cdot R4) + A4(B \cdot R0 + C \cdot RZ)$$

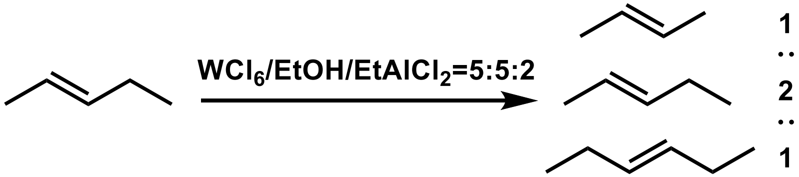
$$Z4 = A4(B \cdot R0 + D \cdot R2 + R4)$$

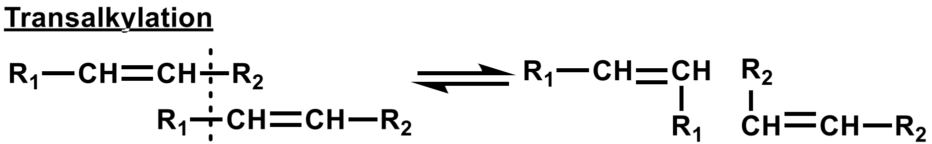
The *B*, *C*, and *D* factors represent the probabilities of the combination of the *A* and *R* factor producing the desired *E* or *Z* under consideration. The *Z* values became the *R* factors for the next iteration. After approximately 20–30 iterations the calculated ratios become constant and are independent of the assumed starting ratios. Very large isotope effects have a small effect on the calculated values. Only those equilibration steps indicated in the scheme were allowed.

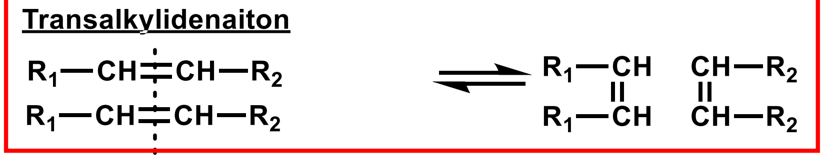
Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1975**, *97*, 3265.

Pair-Wise Mechanism

“Olefin Metathesis” was coined in this paper

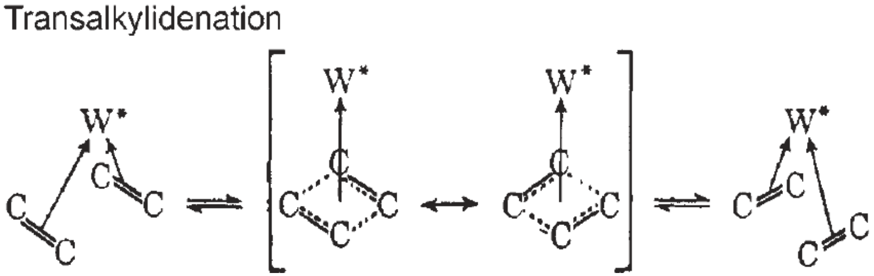






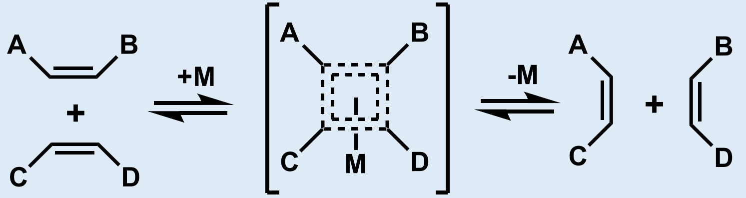
Calderon, N. *et al. Tetrahedron Lett.* **1967**, *34*, 3327

“Pairwise” mechanism

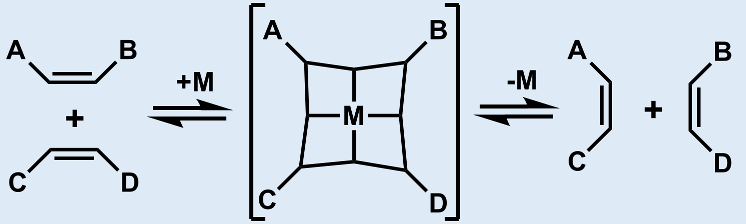


WRONG TURNS

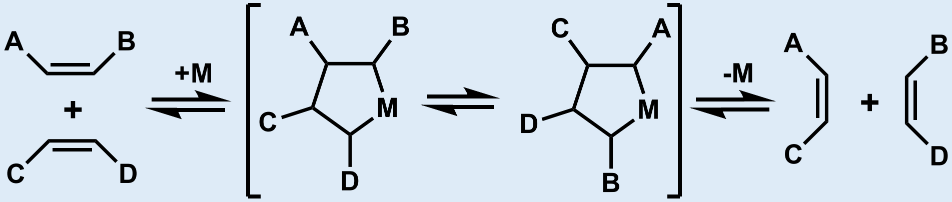
Unusual intermediates proposed initially have Since been rejected



Cyclobutane intermediate



Tetramethylene complex

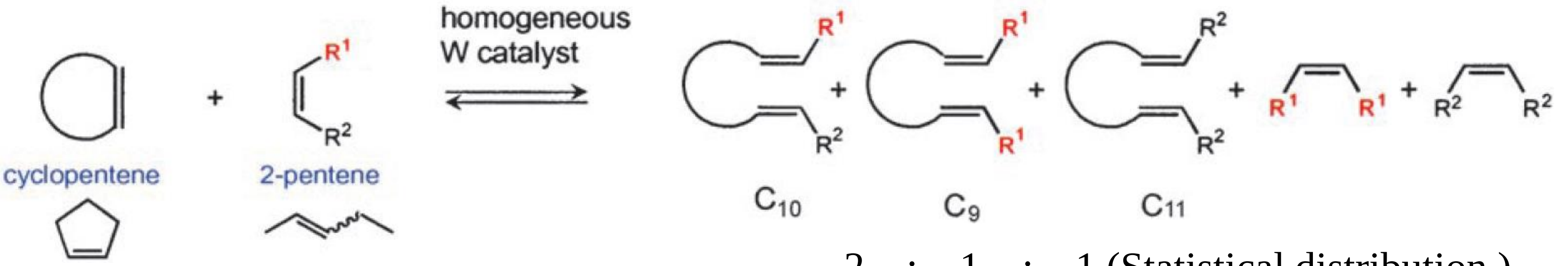


Rearranging metallacyclopentane

Chauvin,Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 3740.

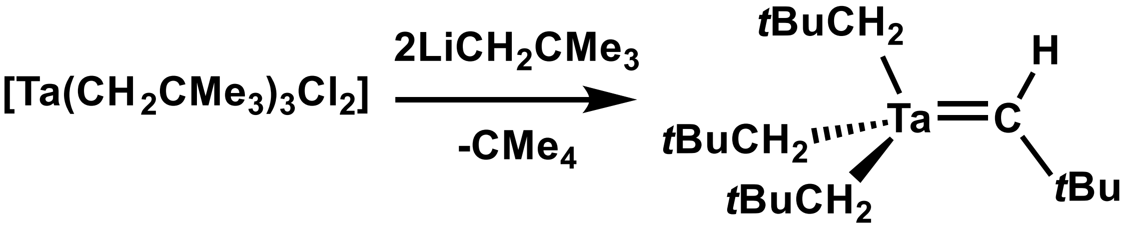
Evidence for Chauvin's Mechanism

Co-reaction of cyclopentene with 2-pentene



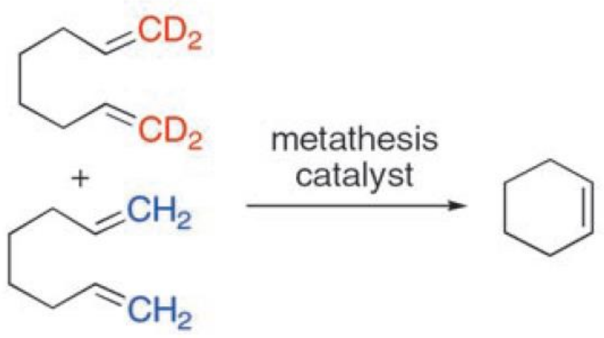
2 : 1 : 1 (Statistical distribution)

Chauvin,Y. *et al*. *Makromol. Chem.* **1971**, *141*, 161. Chauvin,Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 3740.



The first stable transition metal M=CHR species.

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



Predicted Ratio

	Chauvin	Pair-wise
$D_2C{=}CD_2$ +	1	1
$H_2C{=}CD_2$ +	2	0 -1.6
$H_2C{=}CH_2$	1	1

Scheme 1. Ring-closing metathesis of 1,7-octadiene.

Grubbs, R. H. *et al., J. Am. Chem. Soc.* **1975**, *97*, 3265. Grubbs, R. H. *et al., Acc. Chem. Res.* **2001**, *34*, 18.

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~from ill-defined catalysts to well-defined catalysts~

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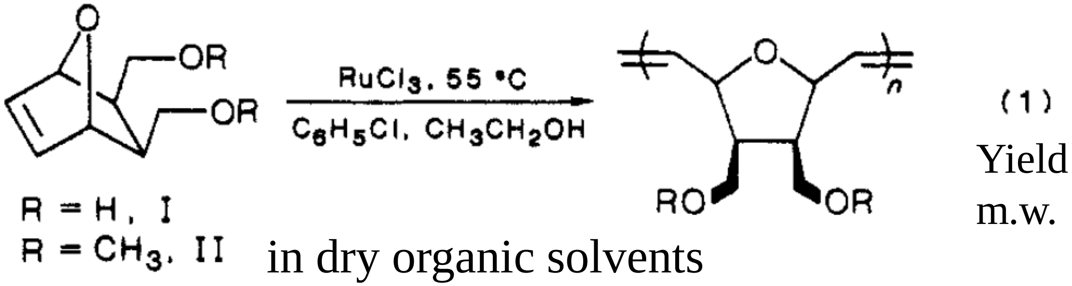
Ruthenium(Ⅲ) Salt for ROMP

At that time…

Oxophilic alkylidene ROMP catalyst ↔ Heteroatoms

In an effort to further the development of the polymerization of heterocyclic monomers…

7-oxa-norbornene derivative



Yield : 95%>

m.w. : 1 × 10^5

in dry organic solvents

$RuCl_3$(hydrate) and $OsCl_3$(hydrate) were successful.

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.*, **1988**, *110*, 960.

☹ Lengthy initiation period (on the order of hours to days) limited their usefulness. (Once initiated, the polymerization proceeded at a very high rate.)

Ⅱ was used as a monomer.

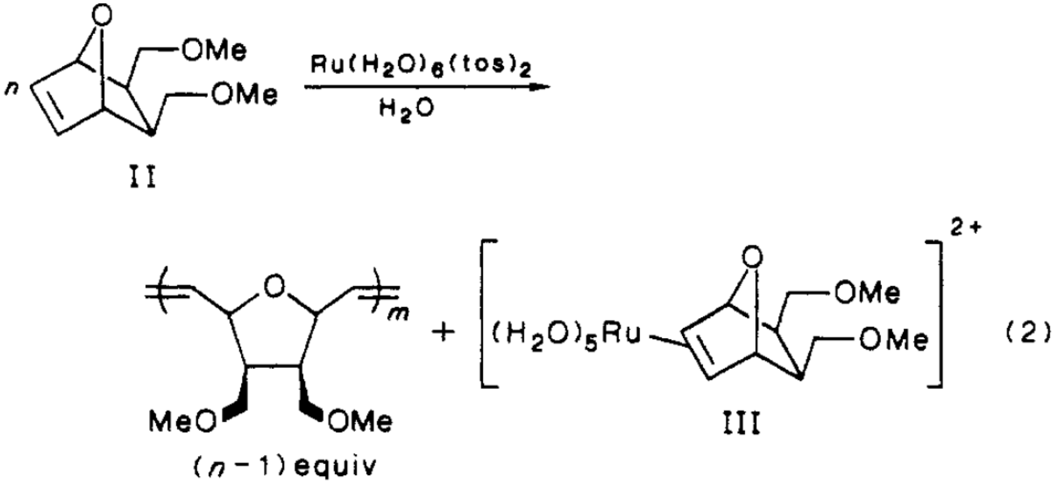
- ✓ Water dramatically decreased the initiation period. (yield was nearly quantitative)
  22-24 h/organic solvents→30-35 min/aqeous solution
- ✓ The used aqueous Ru solution was recyclable and became more active.
  37.5 min→10-12 s

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1988**, *110*, 7452.

Ruthenium(Ⅱ) Complex for ROMP

first recycled

$Ru(H_2O)_6(tos)_2$ was far more active. (initiation time: 50-55 s→10-12 s)



- ✓ The active solution from Ru^{3+} salts ($RuCl_3$, K_2RuCl_5) showed the identical olefin resonances of adduct Ⅲ.
- ✓ Ru^{3+} does not form stable olefin complexes.
- ✓ Ru^{4+} (as Ru Red) and Ru^{2+} olefin complex are formed when Ⅱ was polymerized by $Ru(NH_3)_5(H_2O)^{3+}$.

Proposed Mechanism

Ru^{3+}-Olefin Complex $\rightleftharpoons$ Ru^{2+}-Olefin Complex + Ru^{4+} spieces (trapped by Ru^{3+})

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1988**, *110*, 7452.

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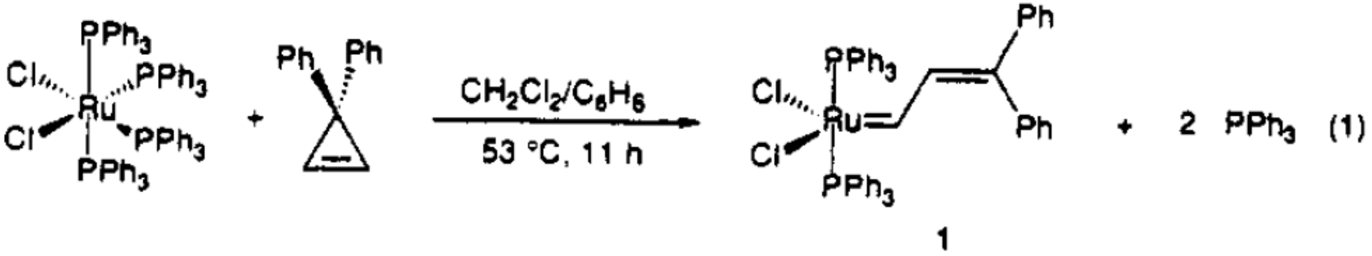
➢Mechanistic Study(2001)

ROMP by a Ruthenium Carbene Complex in Protic Media



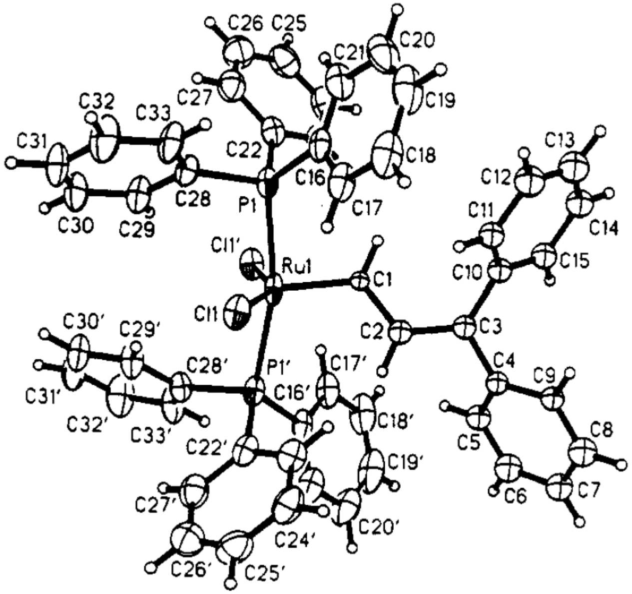
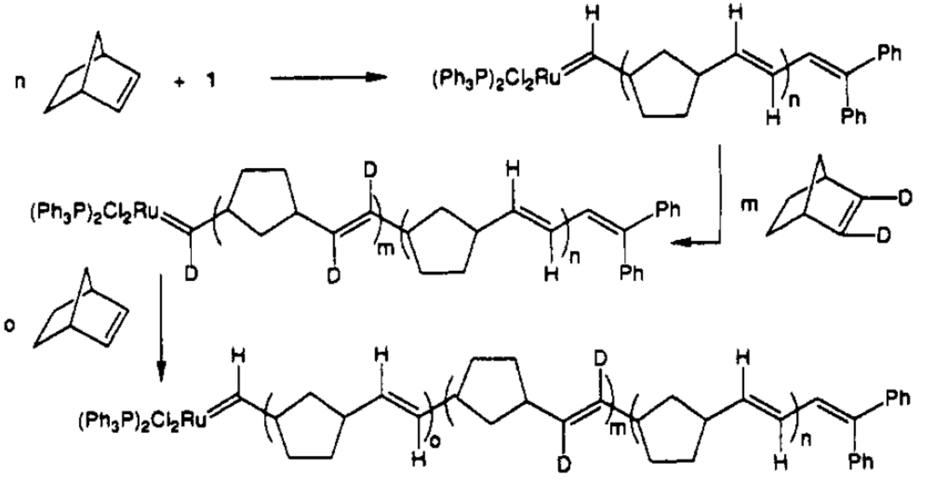


Figure 1. ORTEP diagram of **1**. The thermal ellipsoids are drawn at the 50% probability level.

Scheme I. The Block Copolymerization of 2,3-Dideuterionorbornene and Perprotionorbornene by **1**[16]



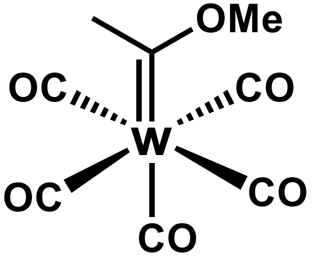
- ✓ Complex 1 was stable under inert atmosphere and several minutes in air.
- ✓ 1 was also stable for several days in C_2Cl_2/C_6H_6 in the presence of water, alcohol, or a diethyl ether solution of HCl.
- ✓ 1 did not undergo Wittig-type reactions with either ketone or an aldehyde.

Functional-Group Tolerance

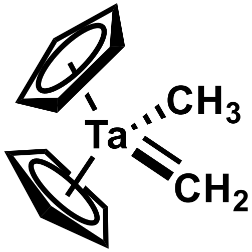
Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1992**, *114*, 3974.

ROMP by a Ruthenium Carbene Complex in Protic Media

low oxidation state
late transition metal
π-accepter ligands
electrophilic

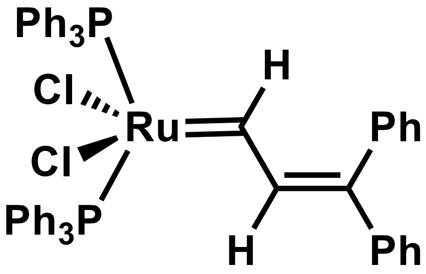


W(II), d^4, 18e
Fischer carbene complex



Ta(V), d^0, 18e
Schrock carbene complex

high oxidation state
early transition metal
nucleophilic



Ru(IV), d^4, 16e
Ruthenaolefin

＊酸化数はカルベンを
4電子供与体と見なした場合

"*Typically, high oxidation state metallaolefins are called alkylidene complexes while low oxidation state analogues are referred to as carbene complexes. The new complex described here does not show all of the characteristics of either of these two classes of complexes.*"

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1992**, *114*, 3974.

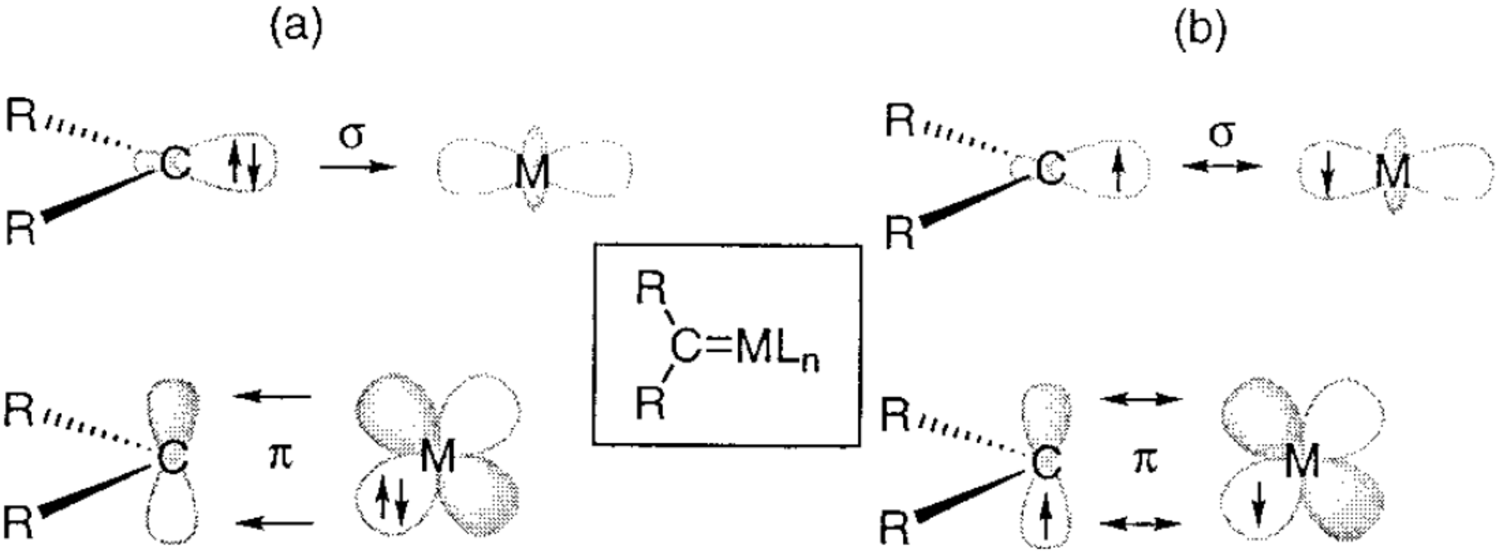
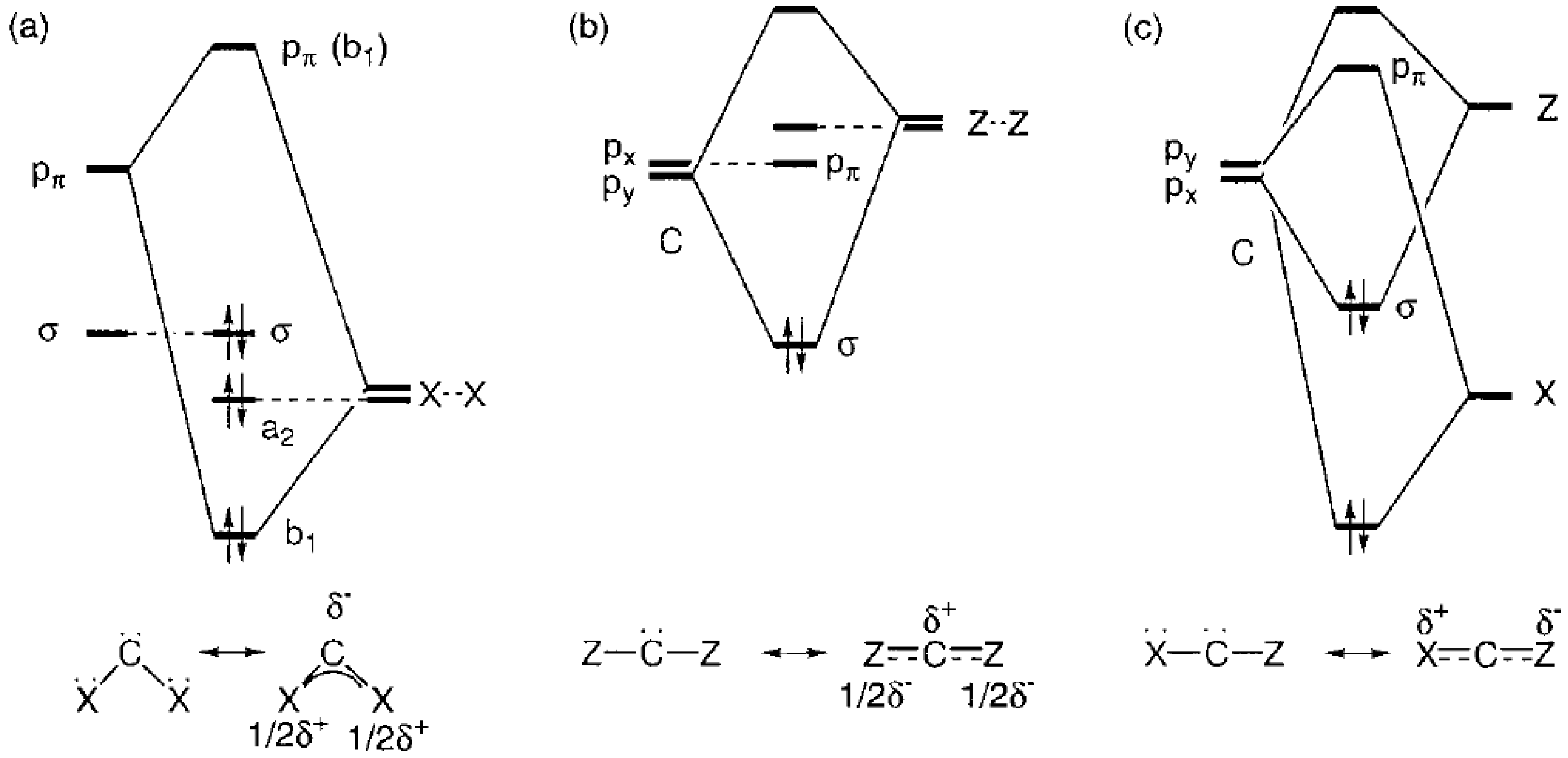


Figure 18. Schematic representations of (a) donor–acceptor bonding in Fischer carbene complexes and (b) covalent bonding in Schrock carbene complexes.

Fischer complexes are generally formed with a low-valent metal fragment and a carbene bearing at least a π-donor group, whereas Schrock complexes are usually formed with metals in a high oxidation state and carbene ligands bearing alkyl substituents.

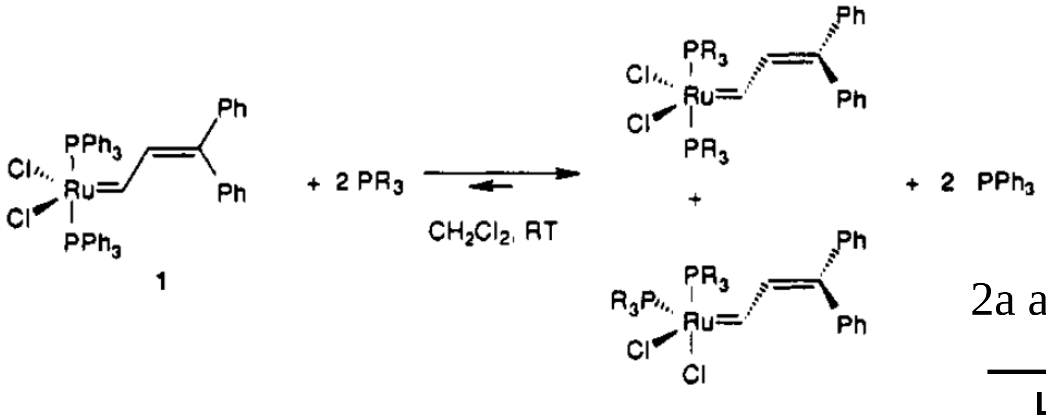
Chem. Rev. **2000**, *100*, 39



X: π-electron-donating substituents; Z: π-electron-withdrawing substituents

Chem. Rev. **2000**, *100*, 39

New Catalysts with high metathesis activity

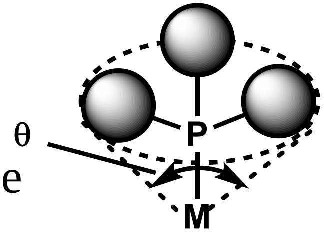


(1)

2a: R = Cy
2b: R = *i*-Pr

trans:*cis*=78:16 (2a)
67:20 (2b)

2a and 2b were moderately stable to air (≥1)



Ligand	Cone Angle	Metathesis of cis-2-penten	
PPh_3	145 °	not active	
$P(i\text{-}Pr)_3$	160 °	active	electron-rich
$P(CH_2Ph)_3$	165 °	not active	
PCy_3	170 °	active	electron-rich

Table I. Turnover Numbers[16] and Conditions for the Metathesis of *cis*-2-Pentene Catalyzed by **2a** and **2b**

entry	catalyst	solvent and catalyst concentration	turnover number[16] (equiv/h)
1	$(Cy_3P)_2Cl_2Ru{=}CHCH{=}CPh_2$ (**2a**)	6.06 mM in C_6D_6[a]	26
2	$(Cy_3P)_2Cl_2Ru{=}CHCH{=}CPh_2$ (**2a**)	6.06 mM in THF-d_8[a]	11
3	$(Cy_3P)_2Cl_2Ru{=}CHCH{=}CPh_2$ (**2a**)	6.06 mM in CD_2Cl_2[a]	103
4	$(Cy_3P)_2Cl_2Ru{=}CHCH{=}CPh_2$ (**2a**)	5.19 mM in (0.29:1) CD_3OD/CD_2Cl_2[b]	67
5	$[(i\text{-}Pr)_3P]_2Cl_2Ru{=}CHCH{=}CPh_2$ (**2b**)	6.06 mM in C_6D_6[a]	22

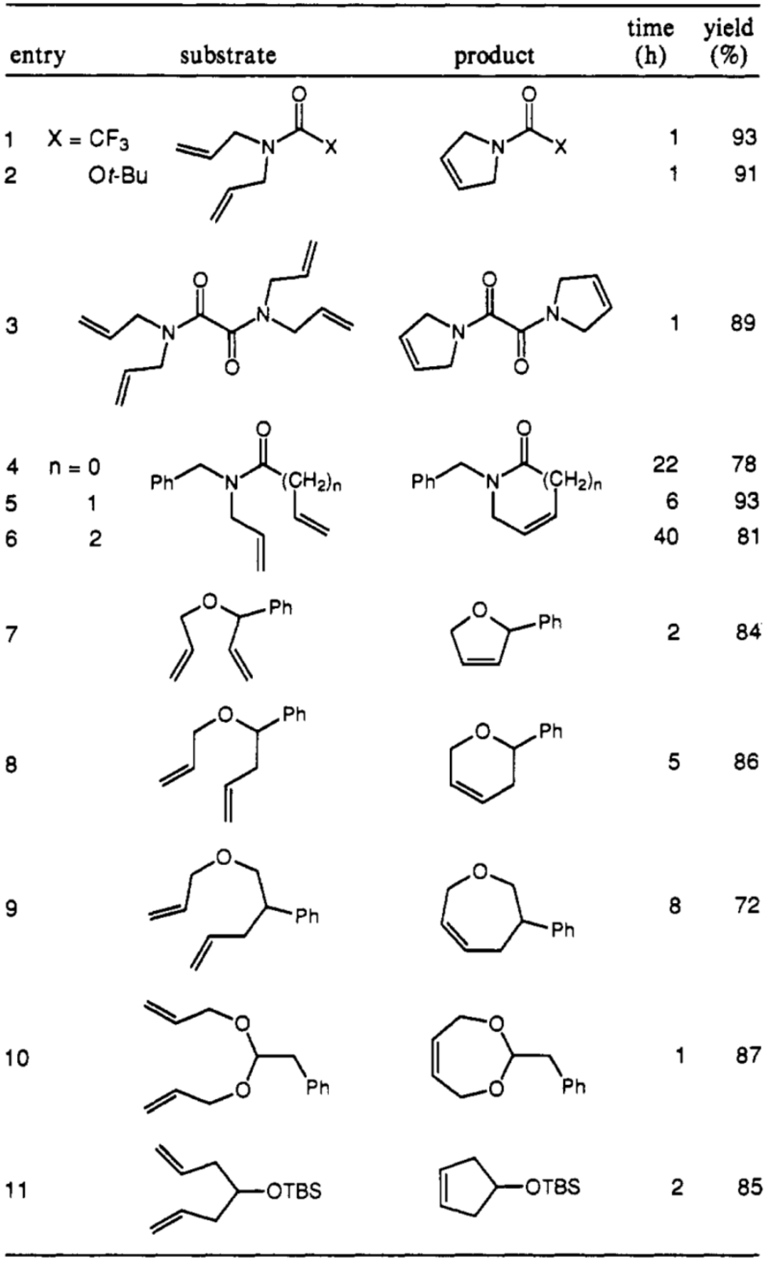
[a] Conditions: 0.5 mL of solution, 100 equiv of *cis*-2-pentene, room temperature. The reaction is carried out in an NMR tube with mesitylene as an internal standard. [b] Conditions: 0.59 mL of solution, 100 equiv of *cis*-2-pentene, room temperature. The turnover number is obtained by monitoring the first part of the *cis*-2-pentene metathesis reaction where the rate of metathesis is approximately pseudo-first-order; it is taken as the point at which 40% of the initial *cis*-2-pentene is consumed.

the first metathesis of acyclic olefin with well-defined Ru carbene complexes

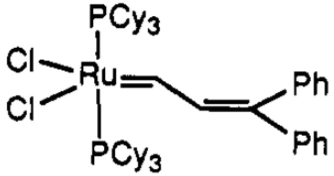
Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1993**, *115*, 9858.

Application to RCM

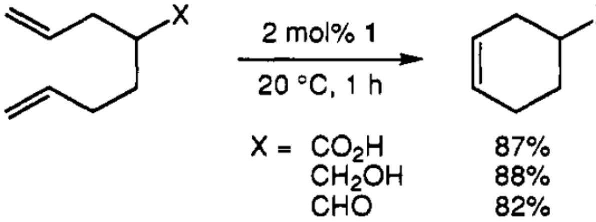
Table I. Catalytic Ring-Closing Metathesis of Dienes (2–4 mol % **1**, C_6H_6, 20 °C)



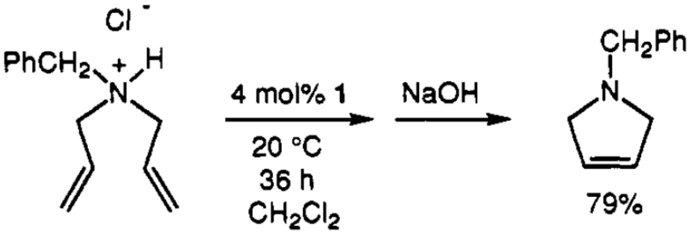
entry	substrate	product	time (h)	yield (%)
1	X = CF_3		1	93
2	O*t*-Bu		1	91
3			1	89
4	n = 0		22	78
5	1		6	93
6	2		40	81
7			2	84
8			5	86
9			8	72
10			1	87
11			2	85



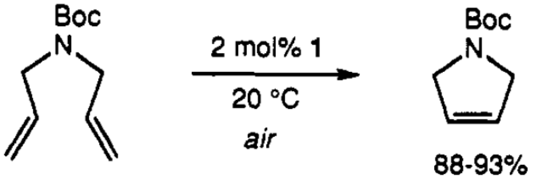
- ✓ insensitivity to atmospheric oxygen and moisture
- ✓ functional-group tolerance



(2)



(3)

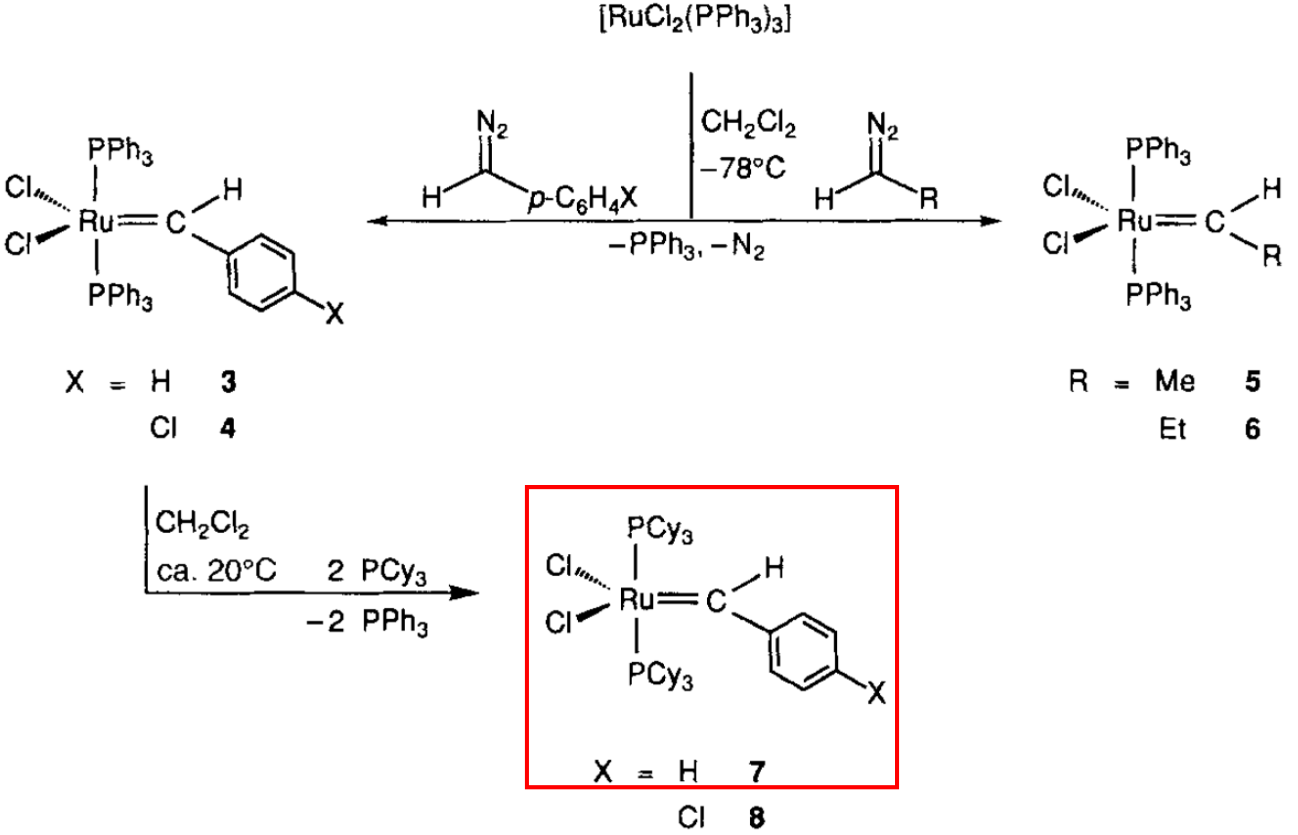


(4)

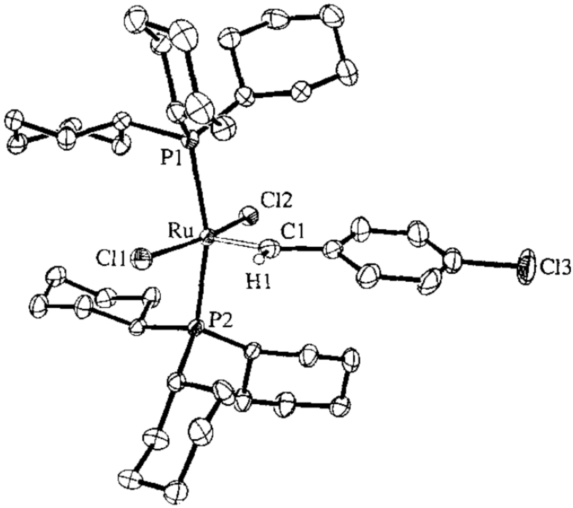
solvents: reagent-grade, undistilled
C_6H_6, CH_2Cl_2, THF, *t*-BuOH

Grubbs, R. H. *et al., J. Am. Chem. Soc.* **1993**, *115*, 9856.

First-Generation Grubbs Catalyst

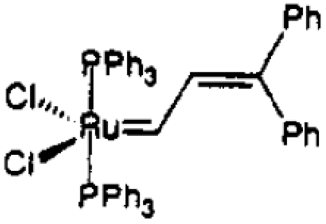


Scheme 1. Synthesis of alkylidene complexes from diazoalkanes and subsequent phosphane exchange. Cy = cyclohexyl.



crystal structure of 8

- ✓ 3-6 decomposed in solution(3 and 4 faster than 5 and 6) in several hours.
- ✓ However, 3-6 were efficient catalysts of living ROMP.
  (The initiation rate for 3 is about 1000 times greater than for 1).
- ✓ 7 and 8 were air-stable.

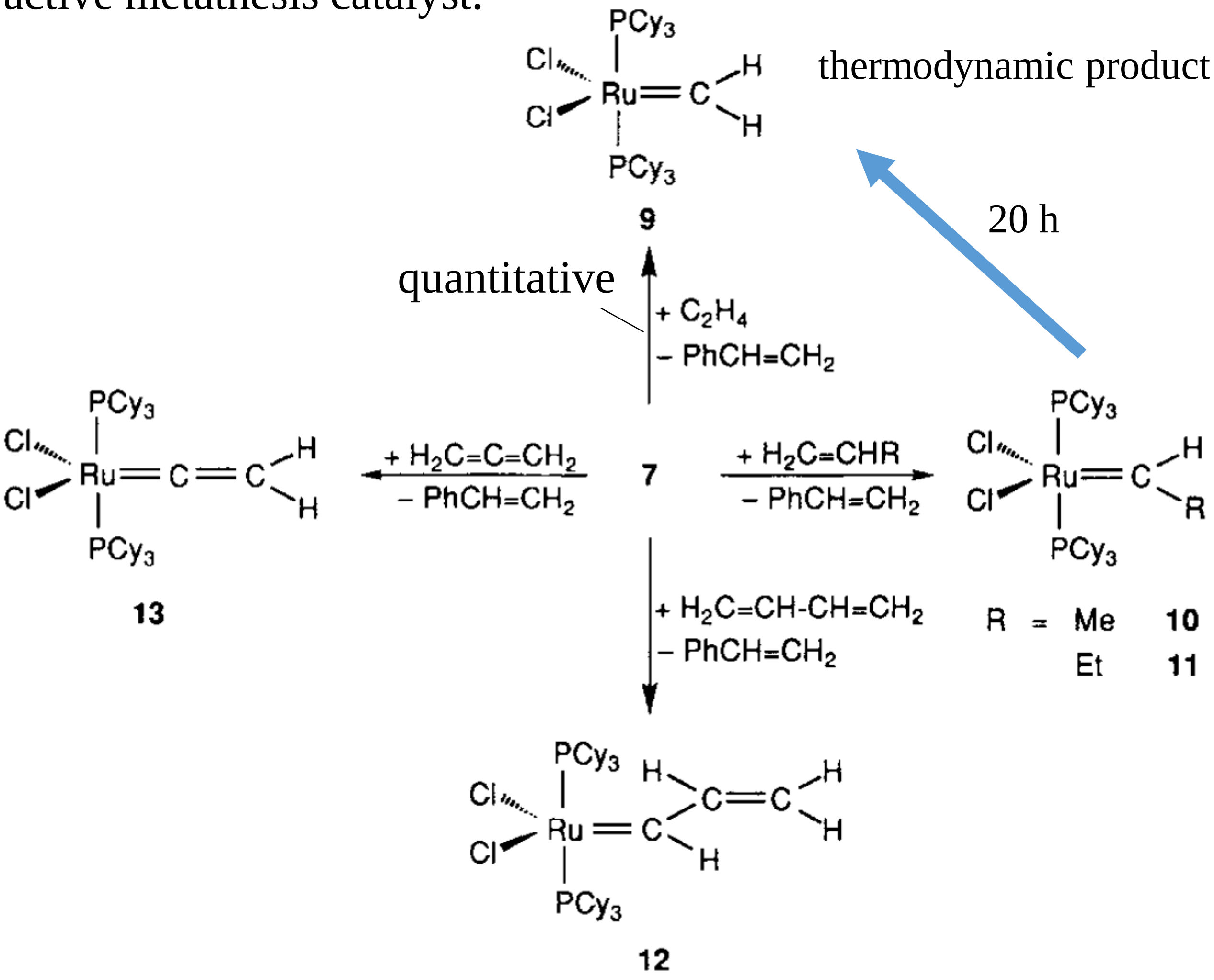


1

Grubbs, R. H. *et al.*, *Angew. Chem. Int. Ed.* **1995**, *34*, 2039.

Isolable Methylidene Complex

9 was the first isolable methylidene complex which is an active metathesis catalyst.



thermodynamic product

20 h

quantitative

kinetic products

Scheme 2. Methathesis of acyclic alkenes with **7** as catalyst.

Grubbs, R. H. *et al.*, *Angew. Chem. Int. Ed.* **1995**, *34*, 2039.

~Topics~

- Introduction
- Evolution of Ruthenium Catalysts

~from ill-defined catalysts to well-defined catalysts~

✓ill-defined Ruthenium catalysts

✓well-defined Ruthenium catalysts

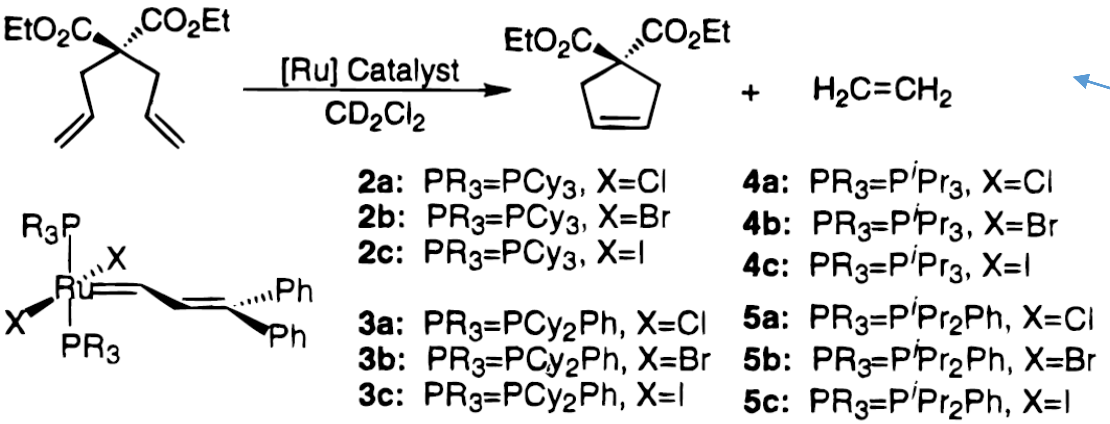
➢First-Generation Grubbs Catalyst

➢Mechanistic Study(1997)

➢Second-Generation Grubbs Catalyst

➢Mechanistic Study(2001)

Ligand Effect on Activity



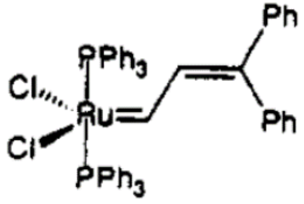
2a: $PR_3=PCy_3$, X=Cl
2b: $PR_3=PCy_3$, X=Br
2c: $PR_3=PCy_3$, X=I

3a: $PR_3=PCy_2Ph$, X=Cl
3b: $PR_3=PCy_2Ph$, X=Br
3c: $PR_3=PCy_2Ph$, X=I

4a: $PR_3=P^iPr_3$, X=Cl
4b: $PR_3=P^iPr_3$, X=Br
4c: $PR_3=P^iPr_3$, X=I

5a: $PR_3=P^iPr_2Ph$, X=Cl
5b: $PR_3=P^iPr_2Ph$, X=Br
5c: $PR_3=P^iPr_2Ph$, X=I

inactive



1

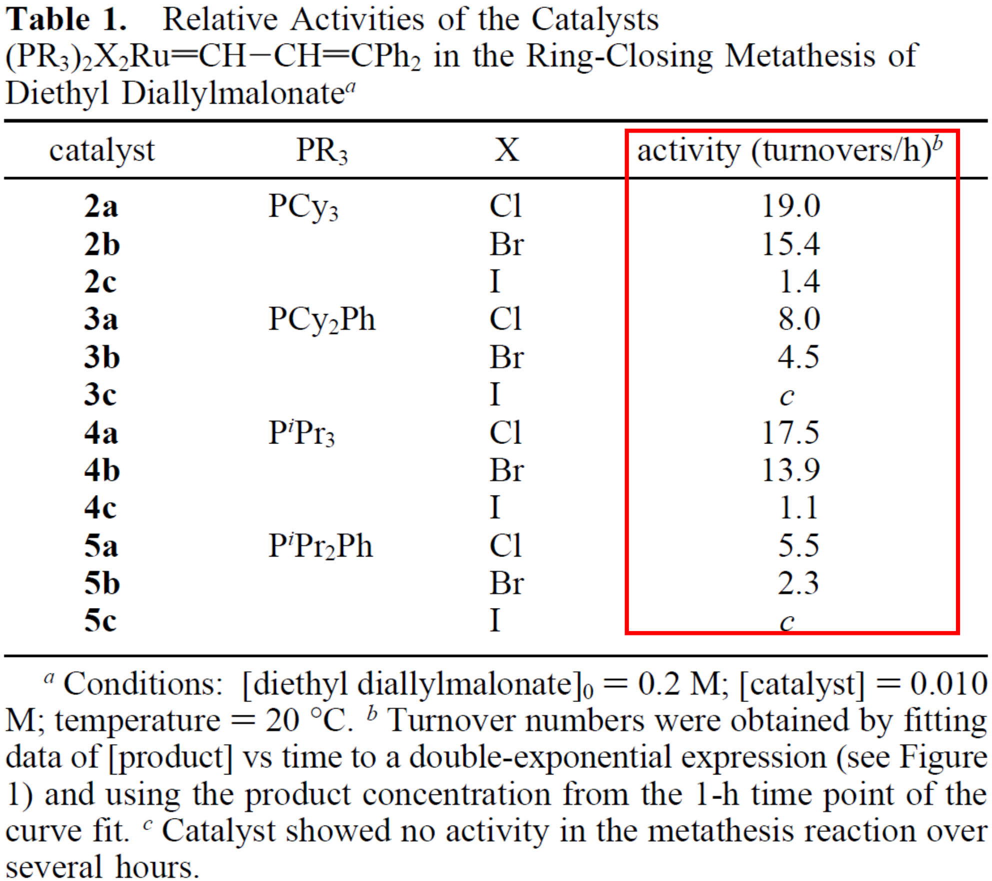


Table 1. Relative Activities of the Catalysts $(PR_3)_2X_2Ru{=}CH{-}CH{=}CPh_2$ in the Ring-Closing Metathesis of Diethyl Diallylmalonate[a]

catalyst	PR_3	X	activity (turnovers/h)[b]
2a	PCy_3	Cl	19.0
2b		Br	15.4
2c		I	1.4
3a	PCy_2Ph	Cl	8.0
3b		Br	4.5
3c		I	*c*
4a	P^iPr_3	Cl	17.5
4b		Br	13.9
4c		I	1.1
5a	P^iPr_2Ph	Cl	5.5
5b		Br	2.3
5c		I	*c*

[a] Conditions: [diethyl diallylmalonate]$_0$ = 0.2 M; [catalyst] = 0.010 M; temperature = 20 °C. [b] Turnover numbers were obtained by fitting data of [product] vs time to a double-exponential expression (see Figure 1) and using the product concentration from the 1-h time point of the curve fit. [c] Catalyst showed no activity in the metathesis reaction over several hours.

$X=I<Br<Cl$

→ activity

- ✓ more electron withdrawing
- ✓ smaller

$PR_3=PPh_3<<P^iPr_2Ph<PCy_2Ph<P^iPr_3<PCy_3$

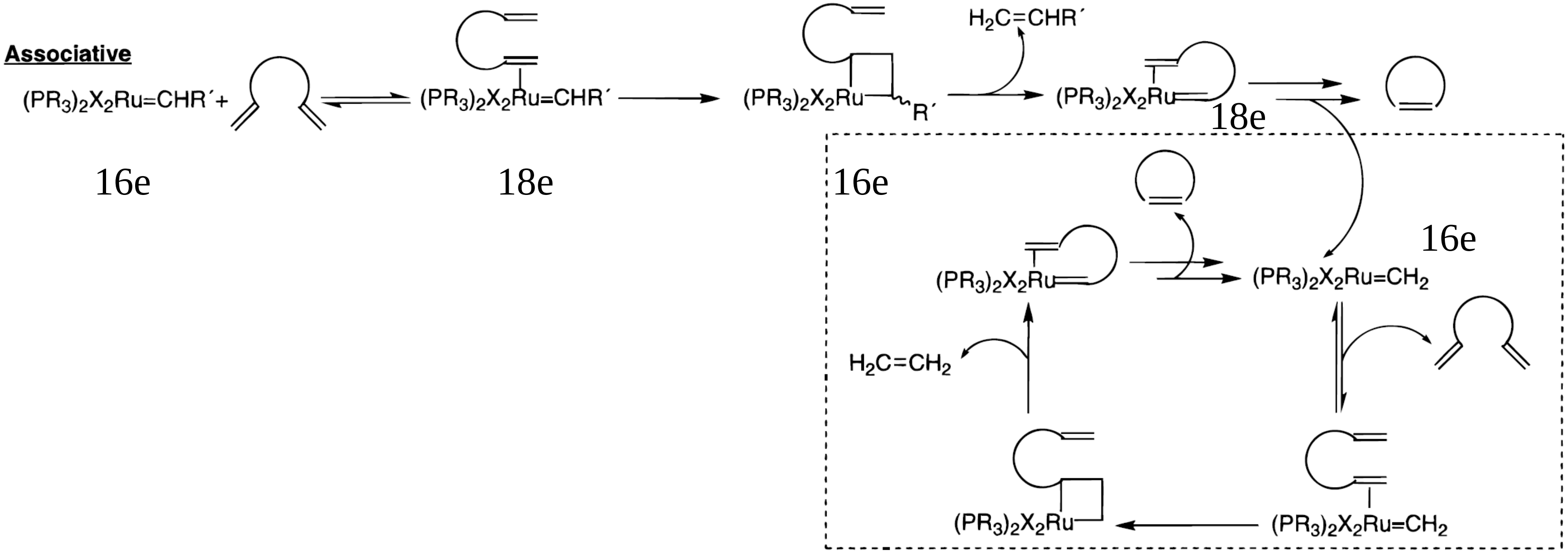
→ activity

- ✓ more electron-donating
- ✓ larger

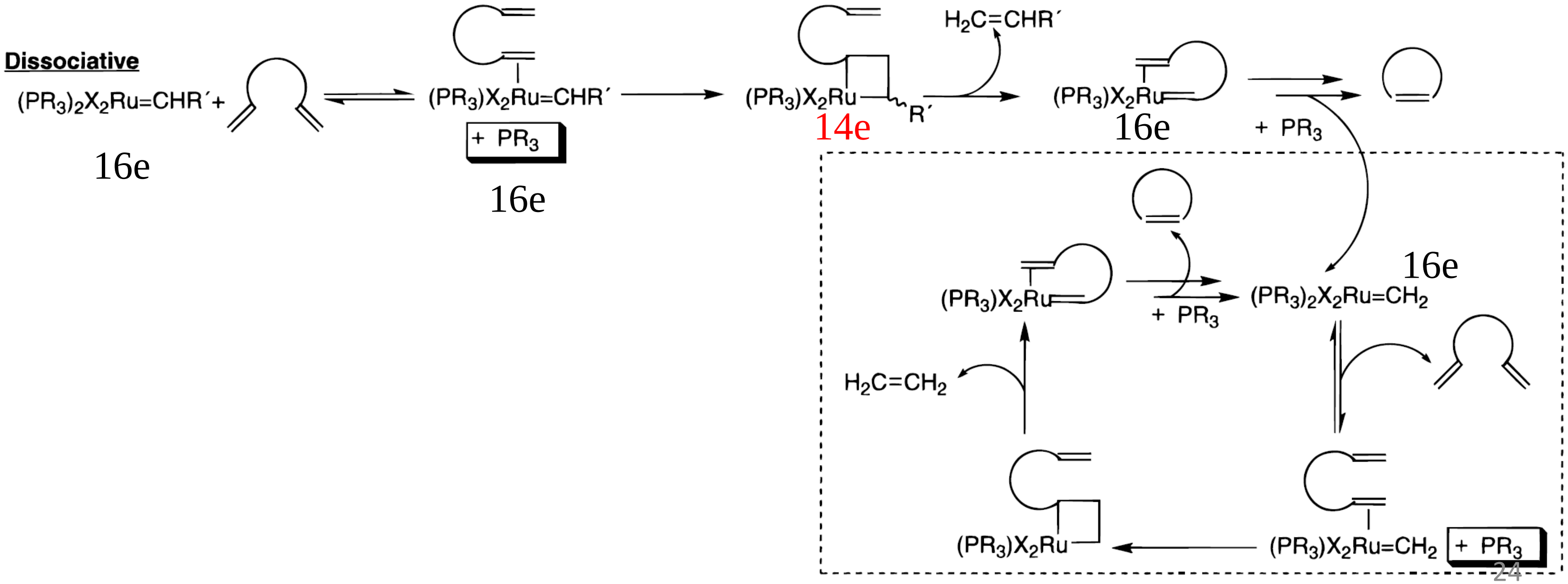
Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

“Associative” vs “Dissociative”

Associative

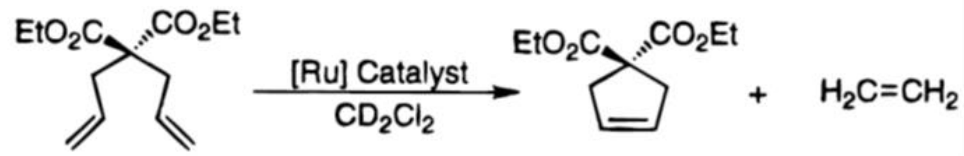


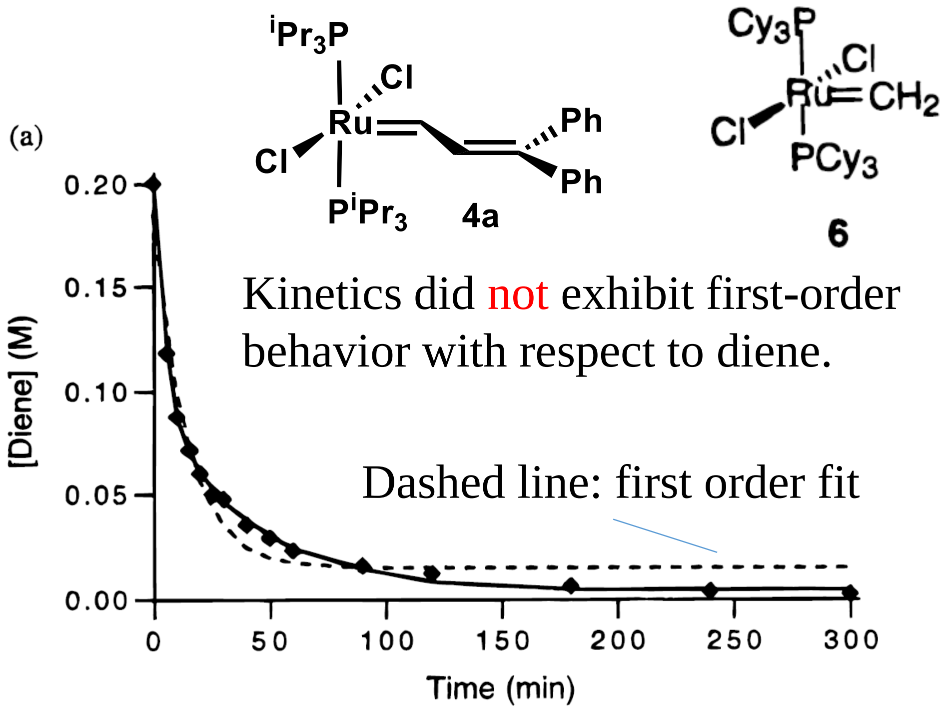
Dissociative



Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

Kinetics





Kinetics did not exhibit first-order behavior with respect to diene.

Dashed line: first order fit

Figure 1. (a) Representative plot of diene concentrations vs time for catalyst **4a**. The reaction was carried out with $[\text{diene}]_0 = 0.2$ M and $[\text{catalyst } (\mathbf{4a})] = 0.01$ M in CD_2Cl_2 at 20 °C. The filled diamonds are the data points, and the solid line is the double-exponential fit: $[\text{diene}](t) = K_0 + K_1 \exp(-K_2 t) + K_3 \exp(-K_4 t)$. The dashed line is the best first-order fit $[\text{diene}](t) = K_0 + K_1 \exp(-K_2 t)$. The constants K_n are generic constants that are calculated by the curve-fitting procedure. (b)

addition of phosphine (0.25-1.0 equiv)

slower rate

pseudo first order

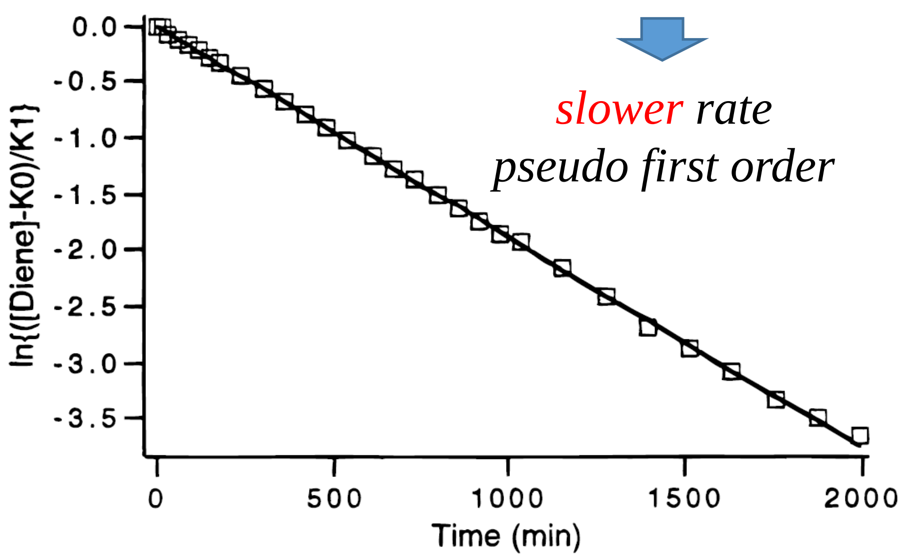
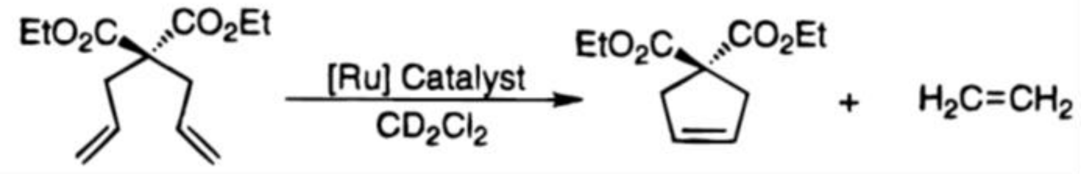


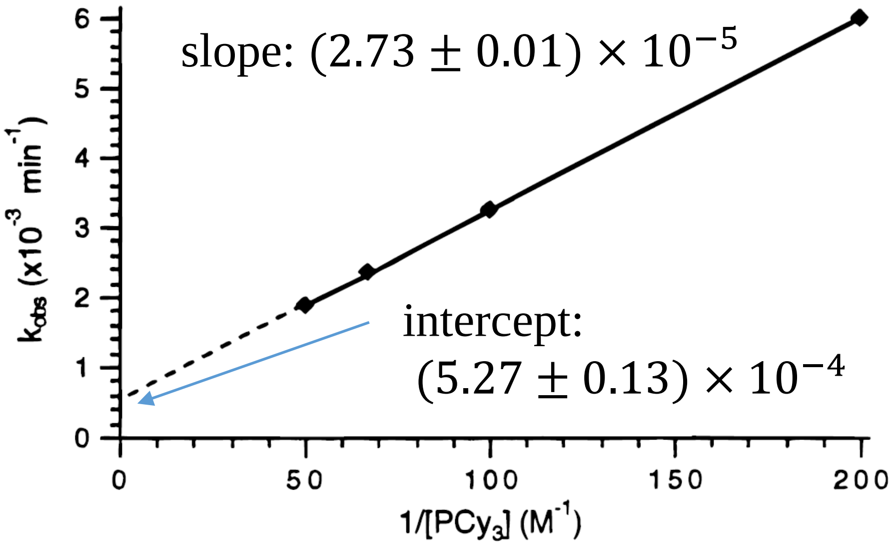
Figure 2. Log plot of diene concentration vs time for the ring-closing metathesis of diethyl diallylmalonate in the presence of 0.02 M PCy_3, where $[Ru]_0(\mathbf{6}) = 0.02$ M and $[\text{diene}]_0 = 0.2$ M. The reactions were carried out in CD_2Cl_2 at 30 °C. K_0 and K_1 are the constants from the first-order fit $[\text{diene}](t) = K_0 + K_1 \exp(-K_2 t)$, and K_2 is the slope of the line, where the constants K_n are generic constants calculated by the curve-fitting procedure. The boxes are the data points and the line is the linear fit. Intercept = $(6.45 \pm 7.64) \times 10^{-3}$; slope = $(-1.88 \pm 0.01) \times 10^{-3}$; linear correlation coefficient = 1.00.

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

Pseudo-First-Order

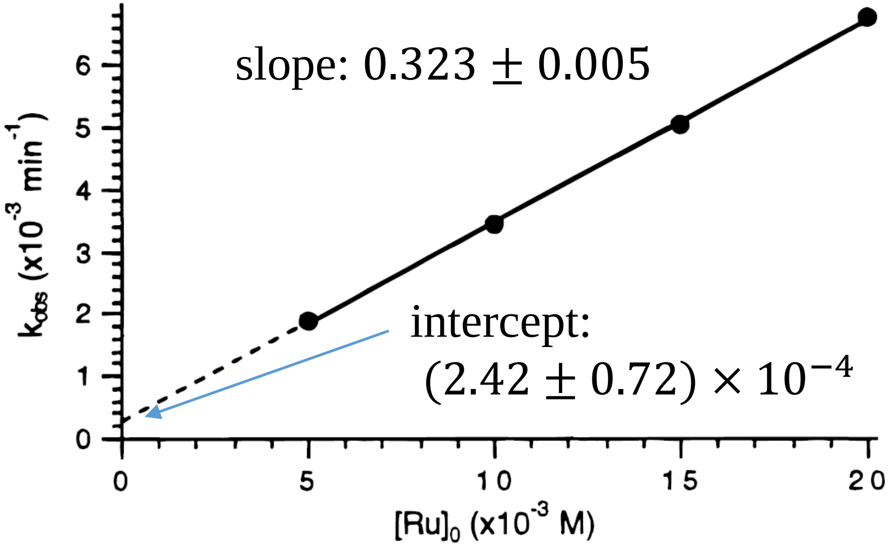


in the presence of additional PCy_3


slope: $(2.73 \pm 0.01) \times 10^{-5}$

intercept: $(5.27 \pm 0.13) \times 10^{-4}$

Figure 3. Plot of k_{obs} vs reciprocal phosphine concentration for the ring closing metathesis of diethyl diallylmalonate at varying phosphine concentrations, with $[diene]_0 = 0.2$ M and $[Ru]_0$ (**6**) = 0.02 M. The reactions were carried out in CD_2Cl_2 at 30 °C. The filled diamonds are the data points, the solid line is the linear fit $k_{obs} = K_0 + K_1(1/[PCy_3]$, where the constants K_n are generic constants calculated by the curve-fitting procedure, and the dashed line is the extrapolation of the linear fit to the intercept. Intercept = $(5.27 \pm 0.13) \times 10^{-4}$; slope = $(2.73 \pm 0.01) \times 10^{-5}$; linear correlation coefficient = 1.00.


slope: 0.323 ± 0.005

intercept: $(2.42 \pm 0.72) \times 10^{-4}$

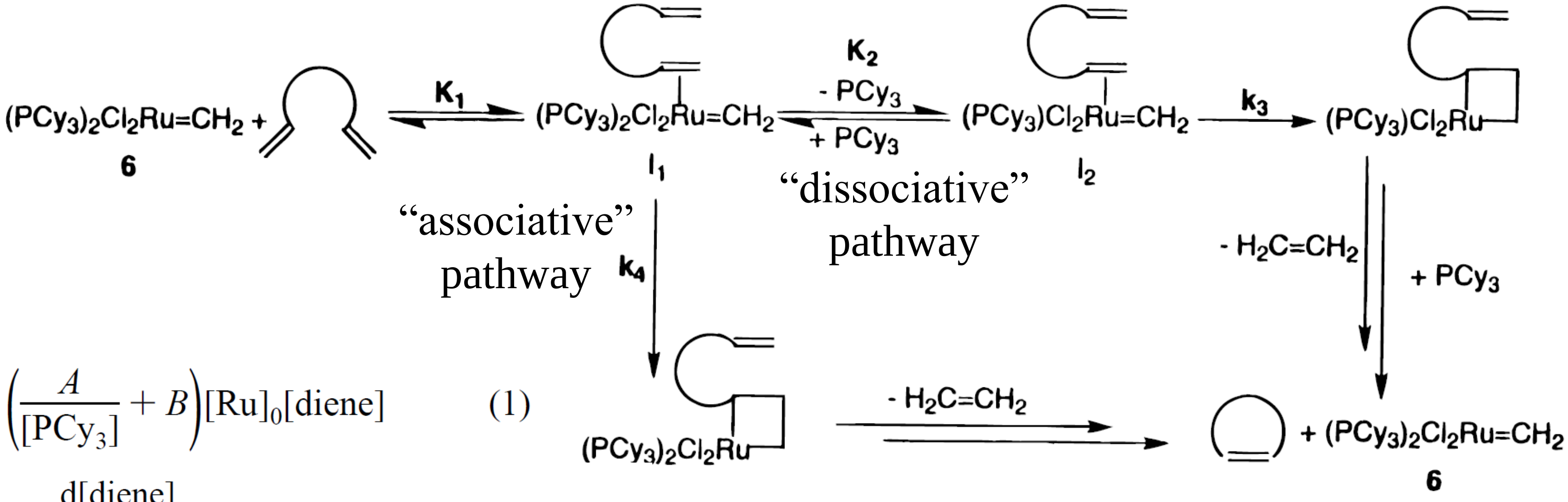
Figure 5. Plot of k_{obs} vs catalyst concentration for the ring-closing metathesis of diethyl diallylmalonate at varying catalyst concentrations in the presence of 0.005M PCy_3, with $[diene]_0 = 0.2$ M. The reactions were carried out in CD_2Cl_2 at 30 °C. The filled circles are the data points, the solid line is the linear fit $k_{obs} = K_0 + K_1([Ru]_0)$ where the constants K_n are generic constants calculated by the curve-fitting procedure, and the dashed line is the extrapolation of the linear fit to the intercept. Intercept = $(2.42 \pm 0.72) \times 10^{-4}$; slope = 0.323 ± 0.005; linear correlation coefficient = 1.00.

$$k_{obs} = K_0 + K_1(1/[PCy_3])$$

$$k_{obs} = K_0' + K_1'([Ru]_0)$$

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

“Associative” vs “Dissociative”



“associative” pathway

“dissociative” pathway

$$-\frac{\mathrm{d[diene]}}{\mathrm{d}t}=\left(\frac{A}{[\mathrm{PCy_3}]}+B\right)[\mathrm{Ru}]_0[\mathrm{diene}] \qquad (1)$$

$$-\frac{\mathrm{d[diene]}}{\mathrm{d}t}=k_3[\mathrm{I_2}]+k_4[\mathrm{I_1}] \qquad (2)$$

By solving the equilibria for the concentrations of $[\mathrm{I_1}]$ and $[\mathrm{I_2}]$, one easily obtains:

$$[\mathrm{I_1}]=K_1[\mathbf{6}][\mathrm{diene}] \qquad \text{and}$$

$$[\mathrm{I_2}]=K_2\frac{[\mathrm{I_1}]}{[\mathrm{PCy_3}]}=K_1K_2\frac{[\mathbf{6}][\mathrm{diene}]}{[\mathrm{PCy_3}]} \qquad (3)$$

Substituting eq 3 into eq 2 yields the final rate expression:

$$-\frac{\mathrm{d[diene]}}{\mathrm{d}t}=\left(k_3\frac{K_1K_2}{[\mathrm{PCy_3}]}+k_4K_1\right)[\mathbf{6}][\mathrm{diene}] \qquad (4)$$

By comparing eq 4 with the empirical rate expression in eq 1, where $[\mathbf{6}]=[\mathrm{Ru}]_0$, we find that the constants A and B are:

$$A=k_3K_1K_2 \qquad \text{and} \qquad B=k_4K_1 \qquad (5)$$

$A\rightarrow$ “dissociative” pathway
$B\rightarrow$“associative” pathway

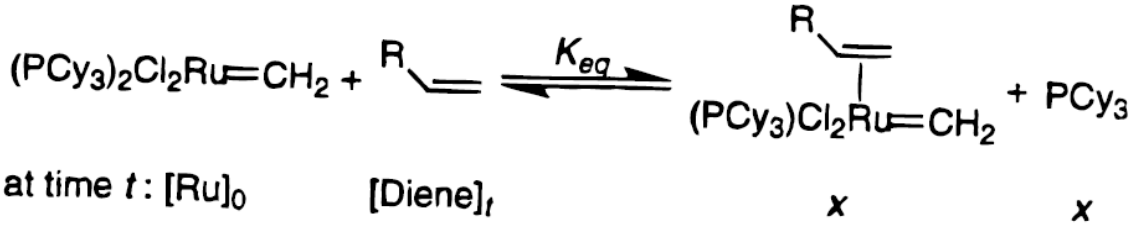
In the absence of excess phosphine,
$A/[\mathrm{PCy_3}] \gg B$ (>90-95%, Figure 3)

“dissociative” pathway ≫“associative” pathway

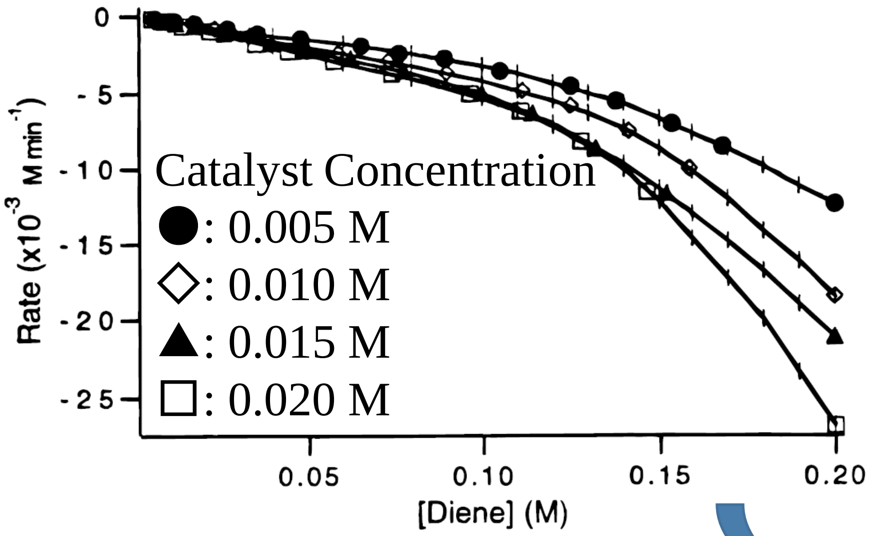
Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

Low Concentration of Active Species

Scheme 4



$$x = [PCy_3] = \sqrt{K_{eq}[Ru]_0[Diene]_t}$$



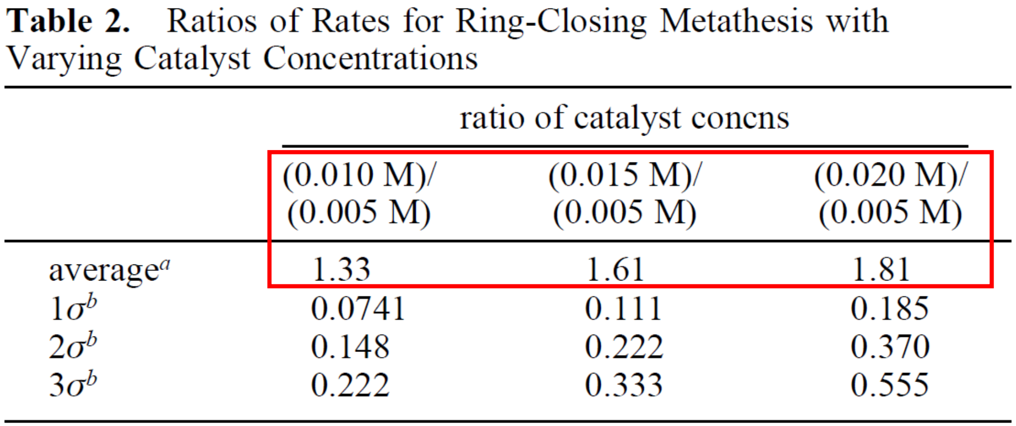


Table 2. Ratios of Rates for Ring-Closing Metathesis with Varying Catalyst Concentrations

	ratio of catalyst concns		
	(0.010 M)/ (0.005 M)	(0.015 M)/ (0.005 M)	(0.020 M)/ (0.005 M)
average[a]	1.33	1.61	1.81
1σ[b]	0.0741	0.111	0.185
2σ[b]	0.148	0.222	0.370
3σ[b]	0.222	0.333	0.555

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

Stereochemistry of Intermediate

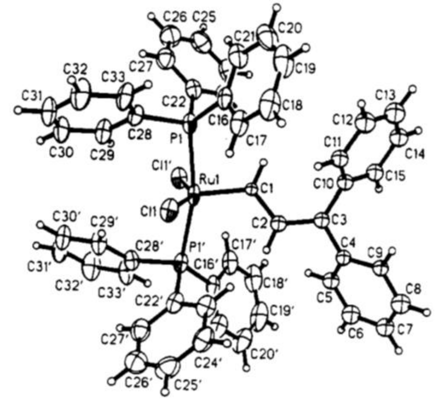
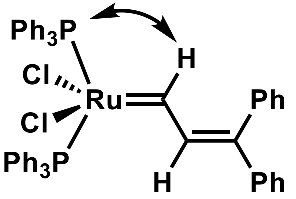
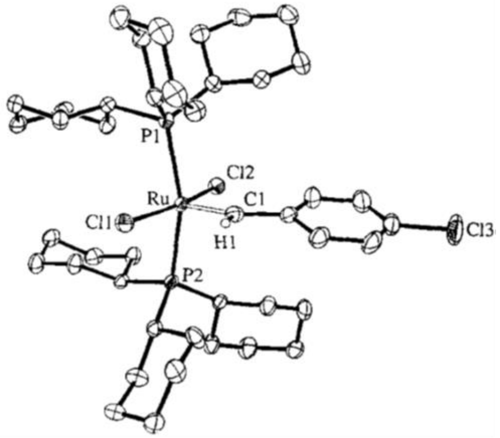


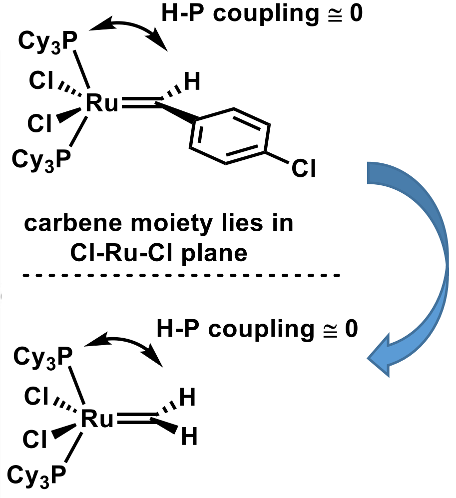
Figure 1. ORTEP diagram of 1. The thermal ellipsoids are drawn at the 50% probability level.

H-P coupling = 11-12Hz



carbene moiety lies in P-Ru-P plane





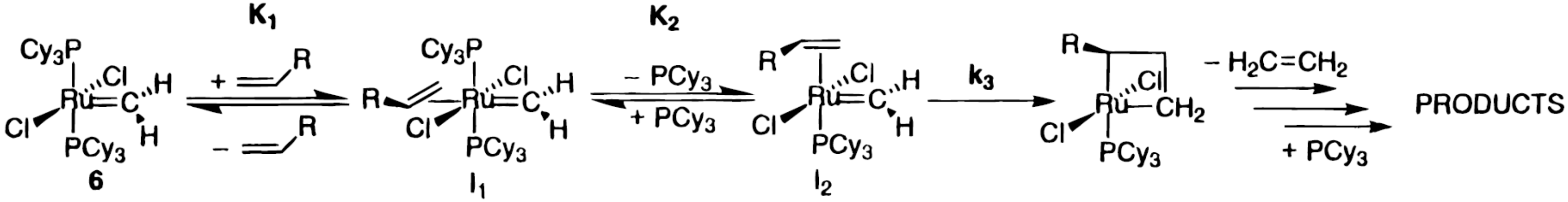
H-P coupling ≅ 0

carbene moiety lies in Cl-Ru-Cl plane

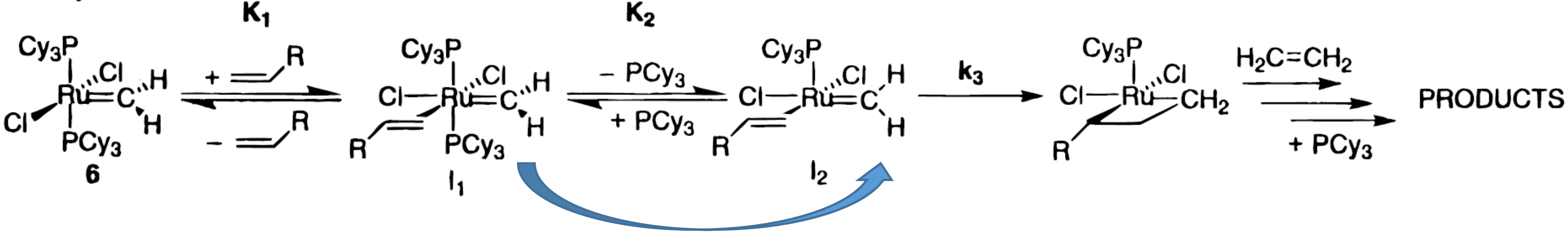
H-P coupling ≅ 0

carbene moiety should lie in Cl-Ru-Cl plane

Pathway 1



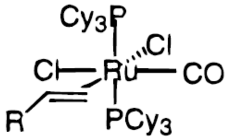
Pathway 2



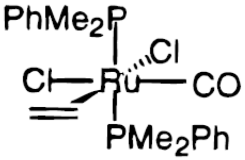
rotation

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

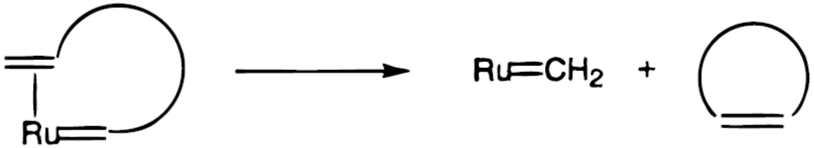
Stereochemistry of Intermediate



7a: olefin = acrylonitrile
7b: 1,2-dicyanoethylene

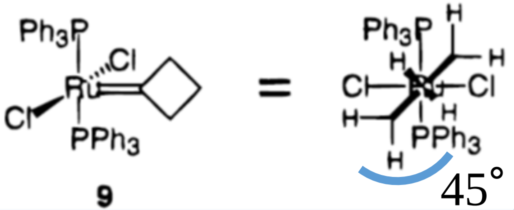


8



at the second step in RCM…

- ✓ Only *cis* coordination is possible. (small ring)
- ✓ *trans* coordination: strain energy

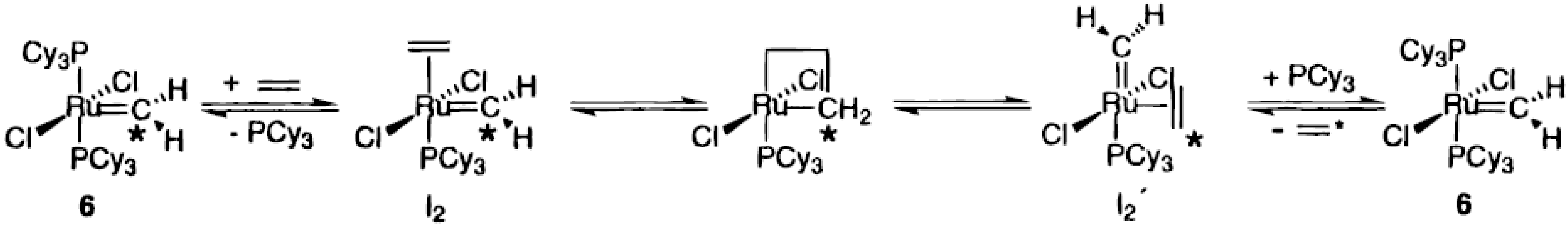


9

Rotation would be possible.

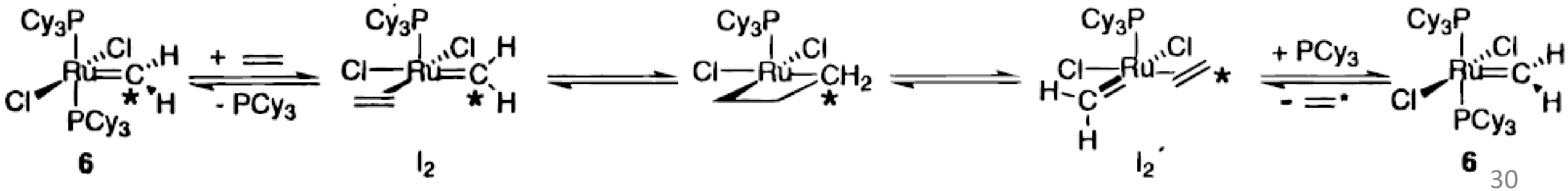
degenerate metathesis reaction

Pathway 1



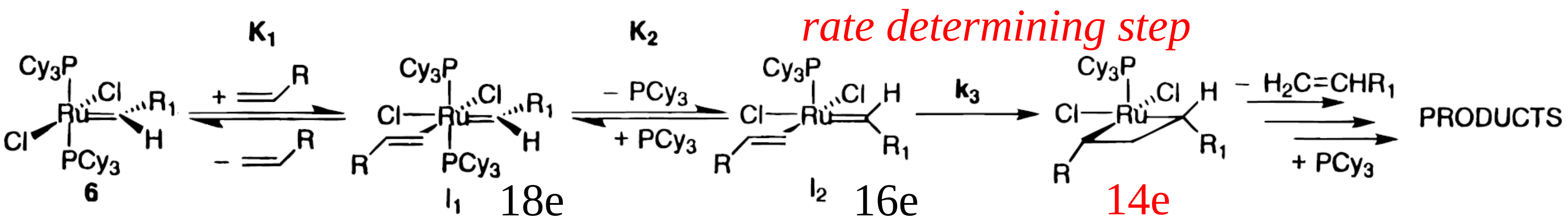
Pathway 2 was more likely

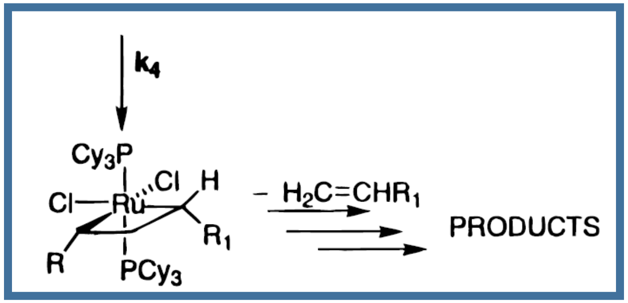
Pathway 2



Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

Summary of First Mechanistic Study





“associative” pathway can be ignored

$$-\frac{d[\text{diene}]}{dt} = \left(k_3\frac{K_1K_2}{[\text{PCy}_3]}\right)[\mathbf{6}][\text{diene}] \qquad (7)$$

Effect of Halogens

✓ *trans* influence: Cl < Br < I
Ru-olefin bond strength: Cl > Br > I
K_1: Cl > Br > I

✓ size: Cl < Br < I
steric repulsion(*cis* halogen): Cl < Br < I
K_1: Cl > Br > I

Effect of Phosphines

✓ cone angle: ↗
dissociation of phosphine: ↗
K_2: ↗ K_1: ↘ K_1K_2: ↗

✓ electron donating ability: ↗
trans influence: ↗
stabilization of I_2 and metallacyclobutane intermediate: ↗

Halogen: smaller and more electron withdrawing
Phosphine: larger and more electron donating

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

~Topics~

- Introduction
- Evolution of Ruthenium Catalysts

~from ill-defined catalysts to well-defined catalysts~

✓ill-defined Ruthenium catalysts

✓well-defined Ruthenium catalysts

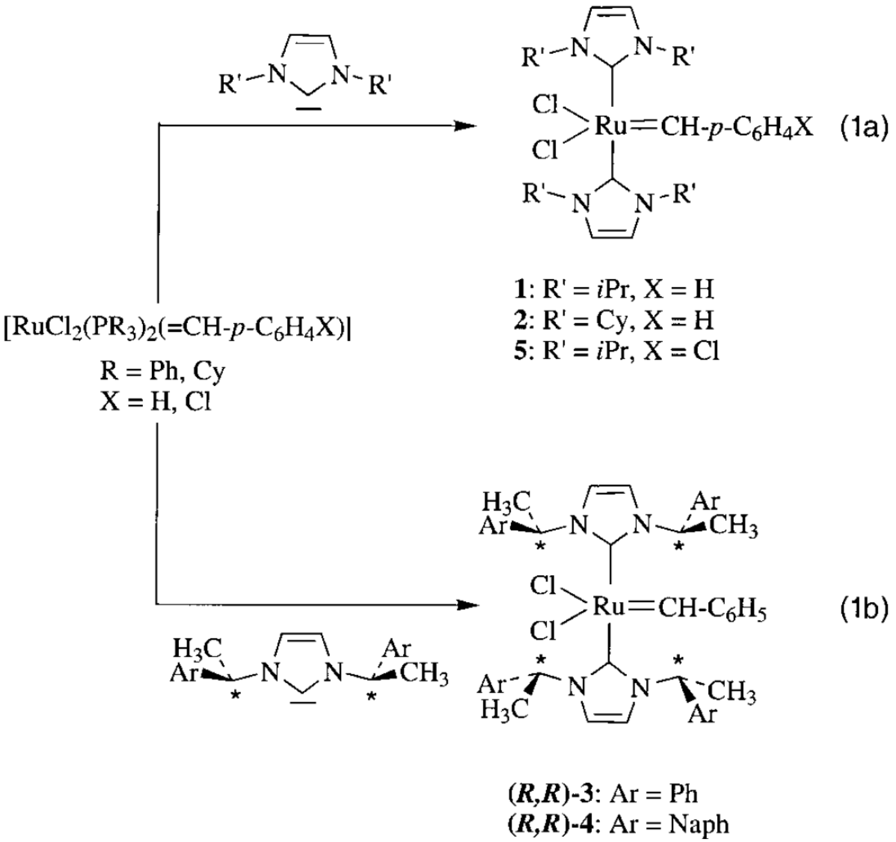
➢First-Generation Grubbs Catalyst

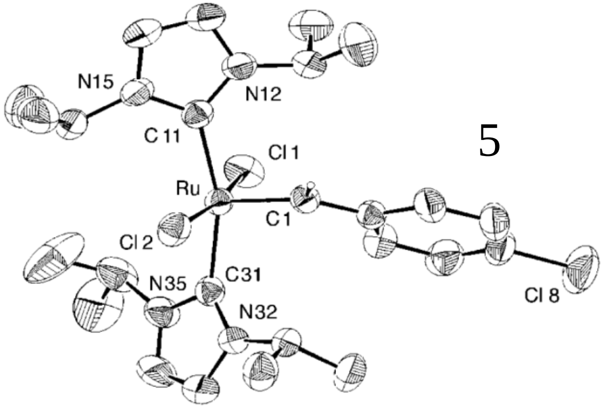
➢Mechanistic Study(1997)

➢Second-Generation Grubbs Catalyst

➢Mechanistic Study(2001)

Herrmann





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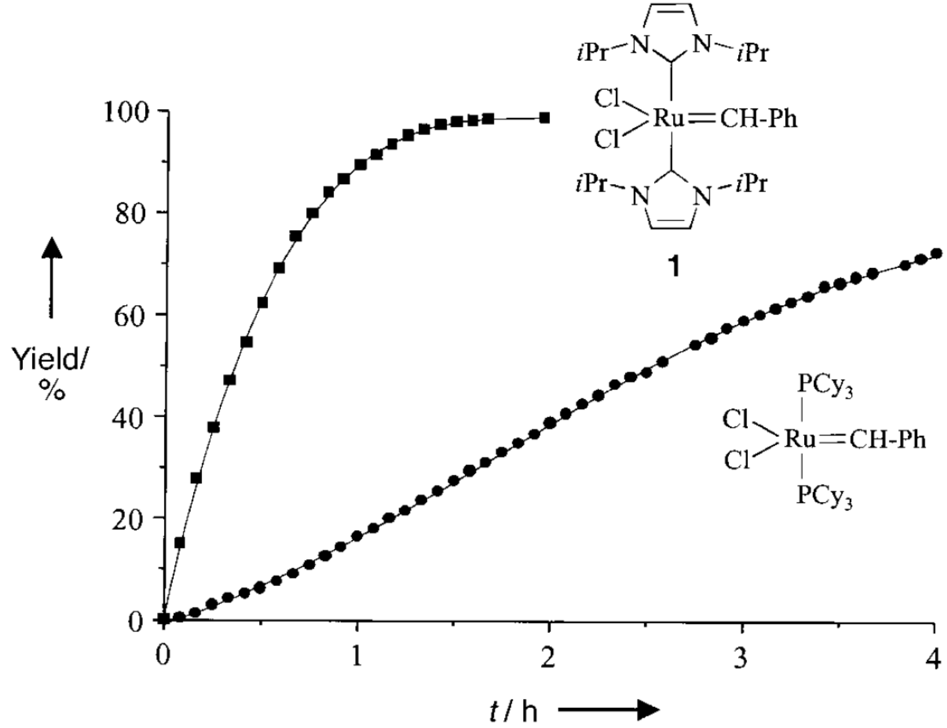


Figure 2. ROMP of cyclooctene. NMR-monitored comparison of **1** and a known ruthenium phosphane catalyst.[3d, 10] $T = 25\,^\circ C$, 2.50 µmol catalyst in 0.50 mL of CD_2Cl_2; [cyclooctene]/[catalyst] = 250/1.

Herrmann, W. A. *et al.*, *Angew. Chem. Int. Ed.* **1998**, *37*, 2490.

Nolan

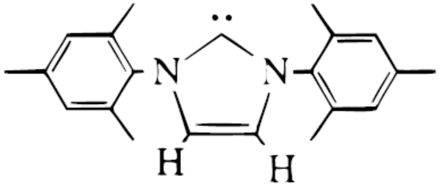
anaerobic solution calorimetry showed

$$[Cp^*RuCl]_4 + 4L \xrightarrow[RT]{THF} 4Cp^*Ru(L)Cl$$

$L = P^iPr_3$: $\Delta H = -37.4(0.3)$

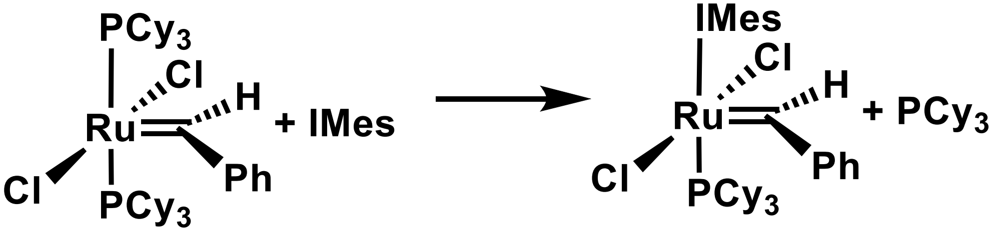
PCy_3: $\Delta H = -41.9(0.2)$

IMes: $\Delta H = -62.6(0.2)$



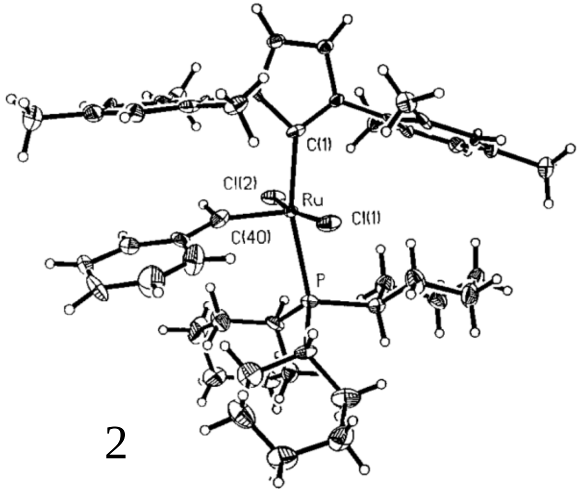
IMes

Ru-L stability ($-\Delta H$(kcal/mol):
IMes (15.6) > PCy_3 (10.5)

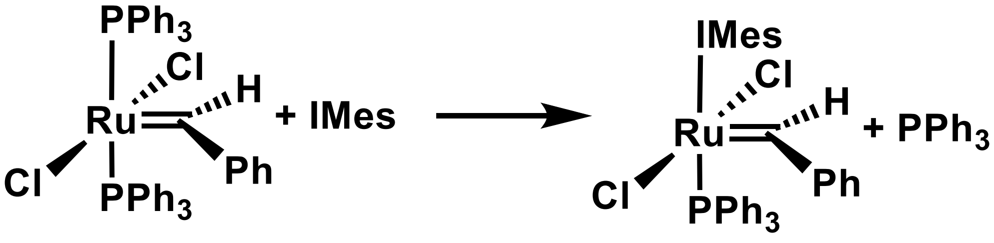


1

2: air-stable

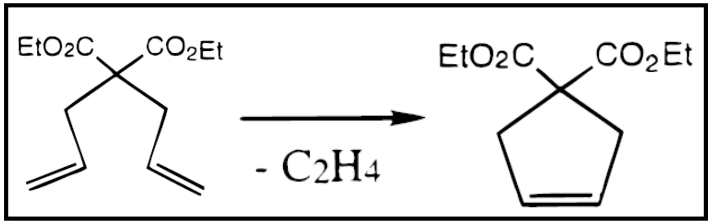


2



3

RCM test

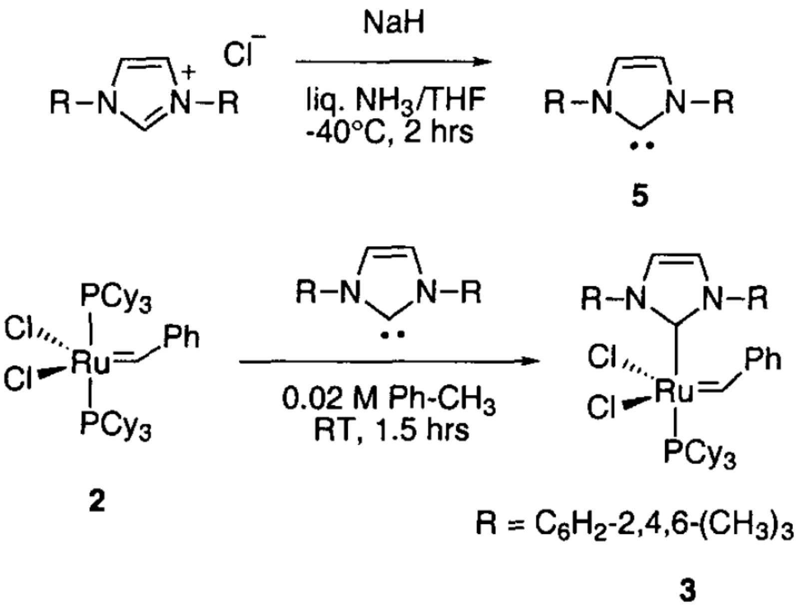


RCM activity: 3>2≅1
thermal stability (60℃): 2≫3>1

Nolan, S. P. *et al.*, *J. Am. Chem. Soc.* **1999**, *121*, 2674.

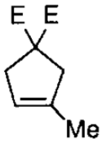
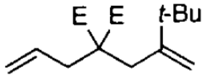
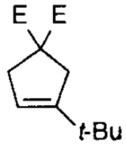
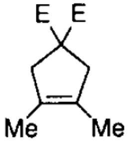
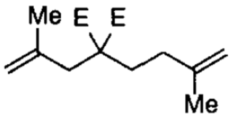
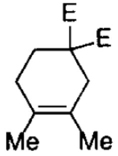
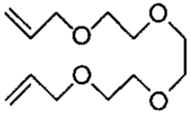
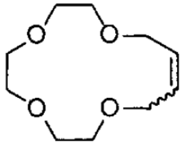
Grubbs

Scheme 1



The complex 3 is less reactive than the parent 2 at rt for RCM.

Table 1. Results of the RCM with 5 mol% **2** or **3** in 0.05M CD_2Cl_2 at reflux

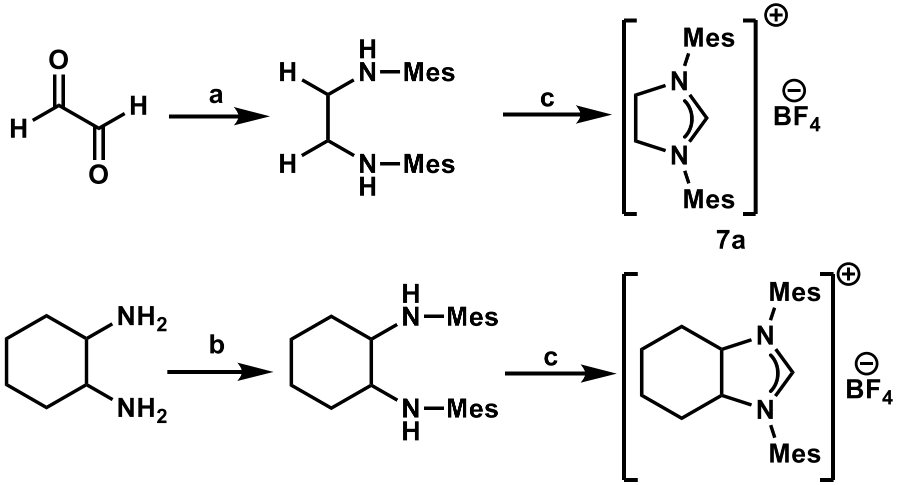
Entry	Substrate	Product	Time (min)	Yield with **2** (%)[a]	Yield with **3** (%)[a]
1	 E = CO_2Et		30	100	100
2			30	82	100
3			60	N.R.	100
4			90	N.R.	40
5			90	N.R.	95
6			60	39[b]	55 (45)[c]

[a] Yields represent the conversion to product as determined by ^1H NMR. [b] E:Z = ~1.6:1

[c] Isolated yield in parentesis; E:Z~2:1.

Grubbs, R. H. *et al.*, *Tetrahedron Lett.* **1999**, *40*, 2247.

Second-Generation Grubbs Catalyst



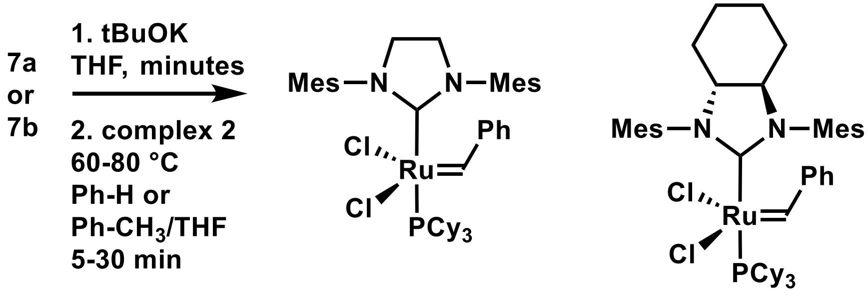
7a

7b

(a): (i) 2,4,6-$(CH_3)_3$-C_6H_2-NH_2, acetone/water, (ii)H_2, Pd/C, EtOH

(b): 2,4,6-$(CH_3)_3$-C_6H_2-Br, Pd_2dba_3, (±)BINAP, NaO^{t}Bu, Ph-CH_3, 100 °C

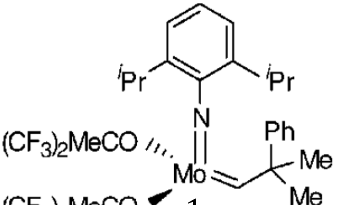
(c): $HC(OEt)_3$, NH_4BF_4, 120 °C



9a

9b

air- and water- tolerant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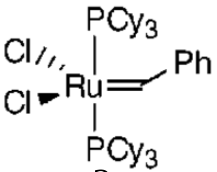
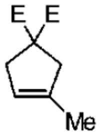
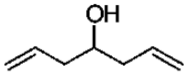
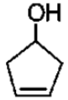
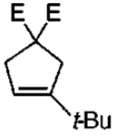
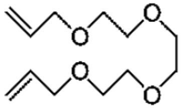
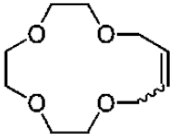
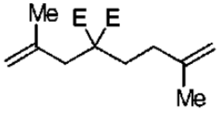
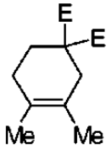
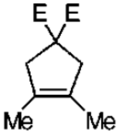

2

Table 1. Results of Ring-Closing Metathesis at 45 °C Utilizing 5 mol % of Catalysts **1**, **2**, and **9a**,**b**

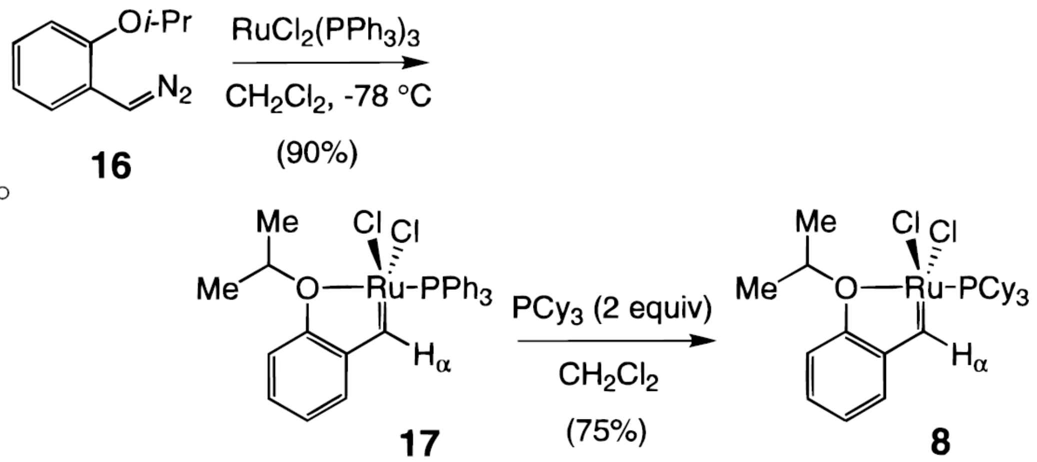
Entry	Substrate	Product	Time	Yield of product (%) using:			
				1	2	7a	7b
1.			10 min	quant.	quant.	quant.	quant.
2.	 **10**		10 min	quant.	20	quant.	quant.
3.			10 min	N.P.	N.P.	quant.	quant.
4.	 **11**		60 min	37	N.P.	quant.	quant.
5.			60 min	(15)[a]	(39)[a]	(35)[b]	(45)[b]
6.			90 min	52	N.P.	90	87
7.			24 hrs	93	N.P.	31	55

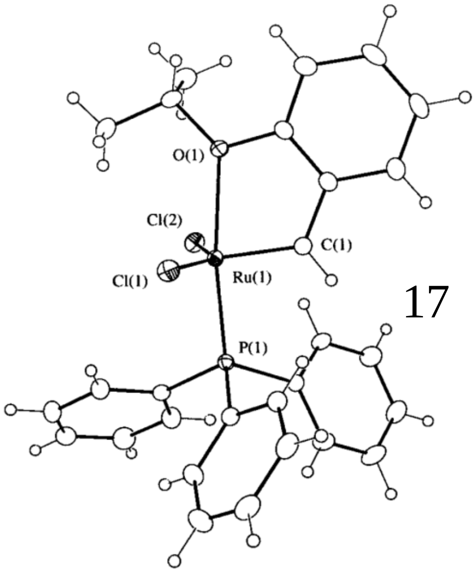
E=CO_2Et, ^{a}*E*:*Z*=1.6:1, ^{b}*E*:*Z*=2.0:1

Grubbs, R. H. *et al.*, *Org. Lett.* **1999**, *1*, 953.

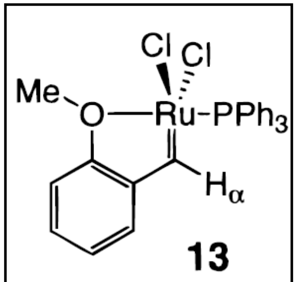
First-Generation Hoveyda-Grubbs Catalyst

Scheme 4





17



13

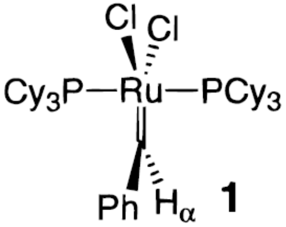
inactive

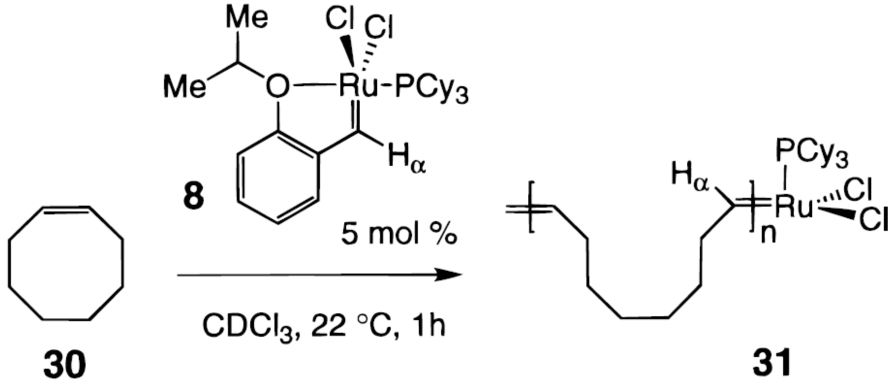
- ➢ Excellent stability to air and moisture
- ➢ High recyclability

Kinetic Study

Complex 8 shows

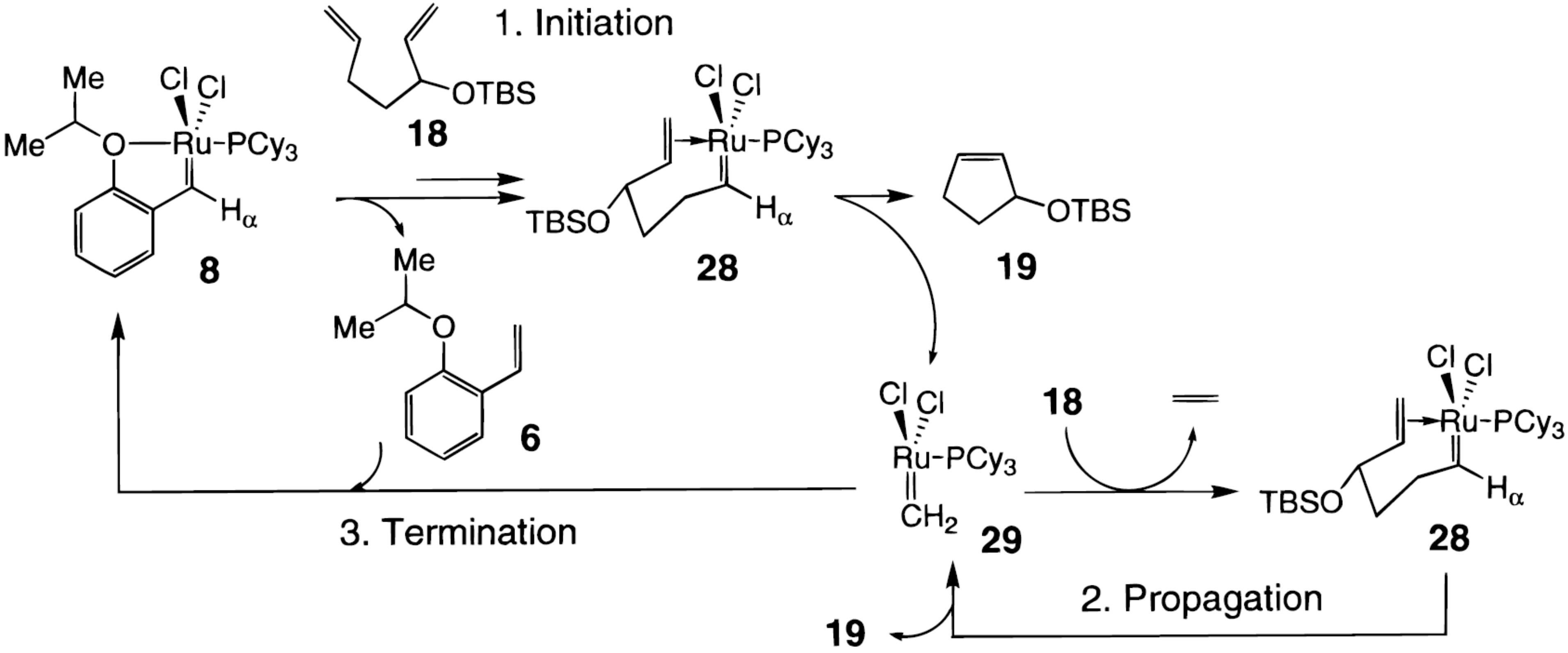
- ✓ ca. 30 times slower initiation
  (less facile dissociation of the smaller ligand)
- ✓ 4 times faster propagation
  (without rate-retarding excess phosphine)





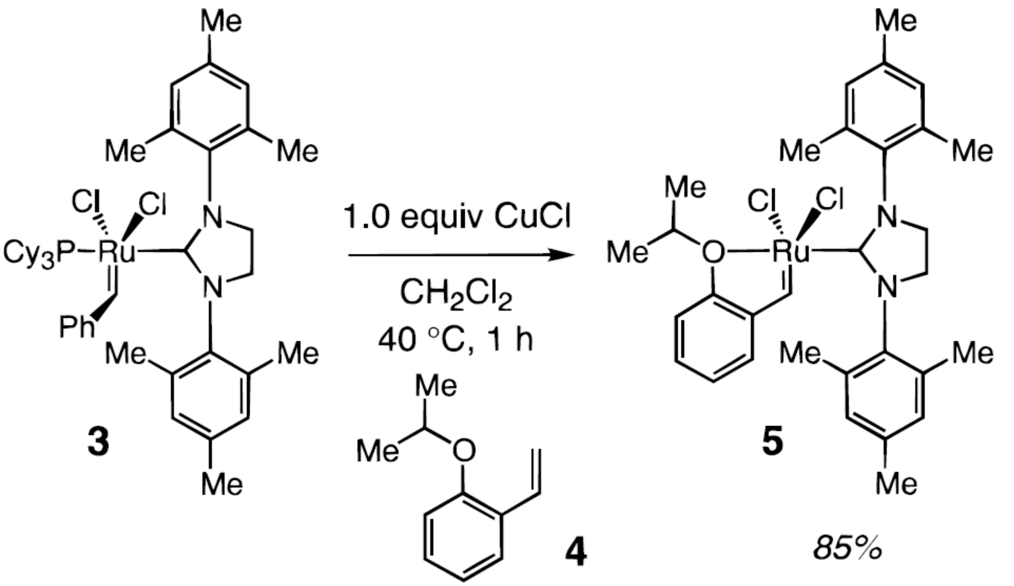
Hoveyda, A. H. *et al.*, *J. Am. Chem. Soc.* **1999**, *121*, 791.

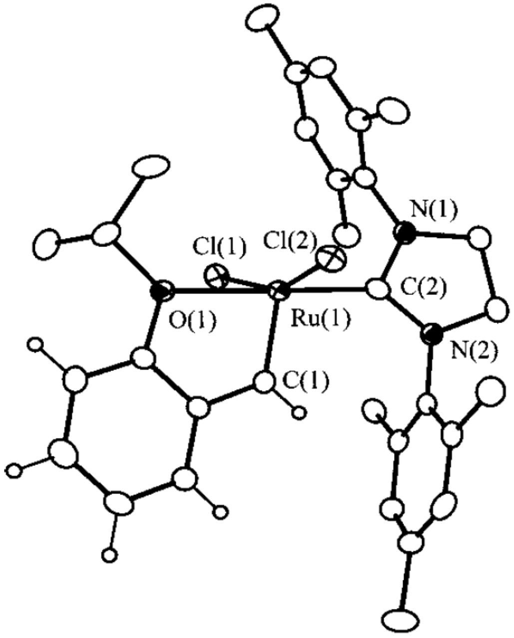
First-Generation Hoveyda-Grubbs Catalyst



Hoveyda, A. H. *et al.*, *J. Am. Chem. Soc.* **1999**, *121*, 791.

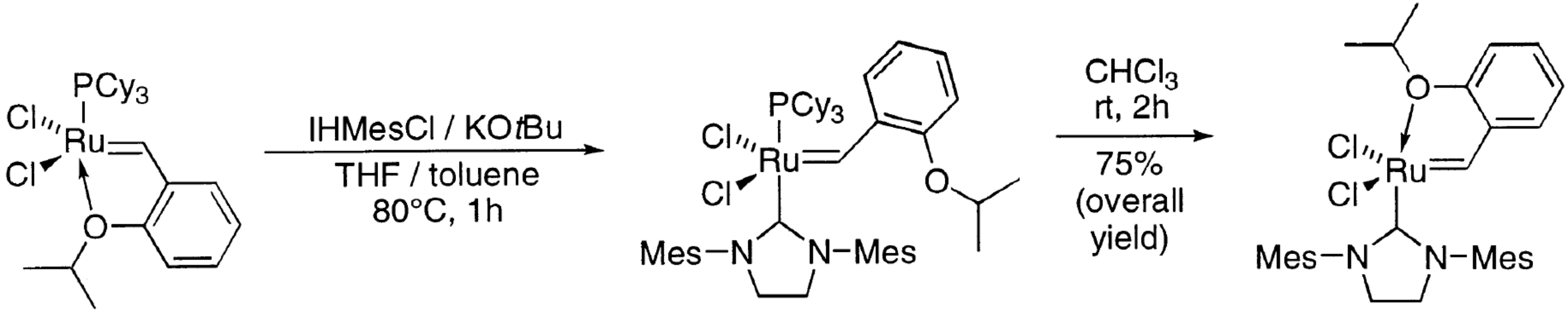
Second-Generation Hoveyda-Grubbs Catalyst





Hoveyda, A. H. *et al.*, *J. Am. Chem. Soc.* **2000**, *122*, 8168.

Publication Date: August 12, 2000

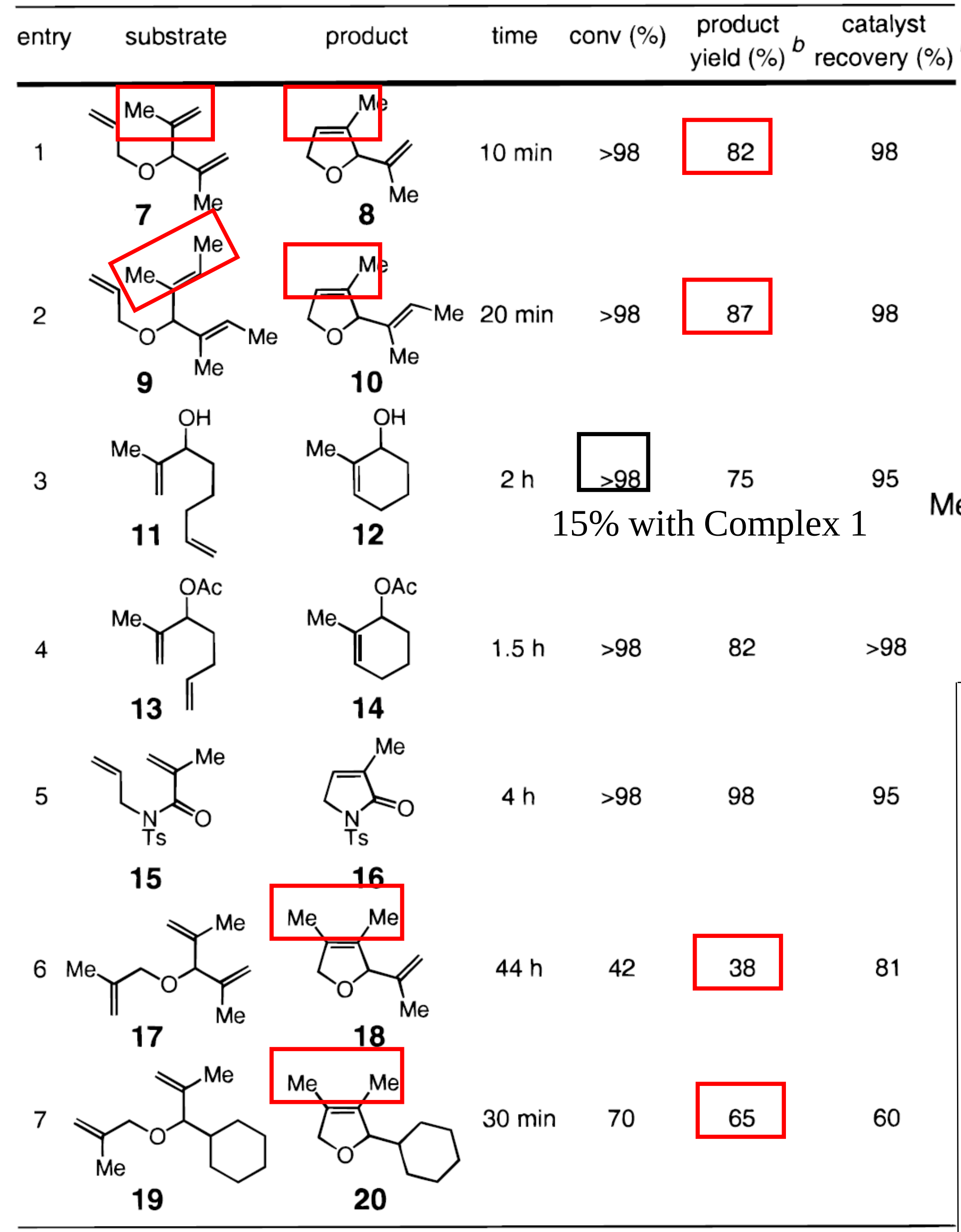


Received: September 8, 2000

Blechert, S. *et al.*, *Tetrahedron. Lett.* **2000**, *41*, 9973.

Second-Generation Hoveyda-Grubbs Catalyst

Table 2. Ring-Closing Metathesis of Acyclic Dienes by Ru Complex **5**[a]



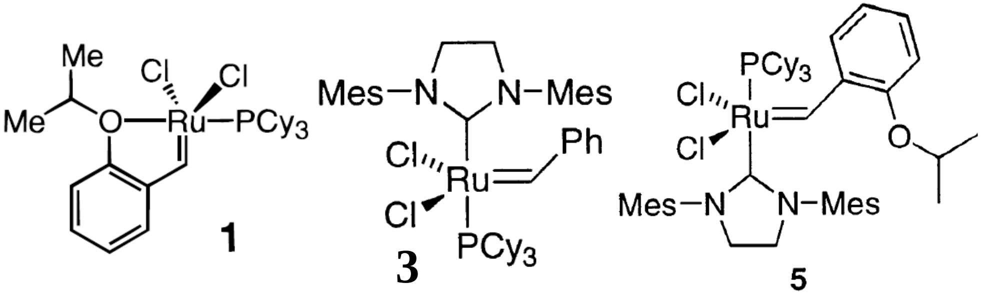
entry	substrate	product	time	conv (%)	product yield (%)[b]	catalyst recovery (%)
1	**7**	**8**	10 min	>98	82	98
2	**9**	**10**	20 min	>98	87	98
3	**11**	**12**	2 h	>98	75	95
4	**13**	**14**	1.5 h	>98	82	>98
5	**15**	**16**	4 h	>98	98	95
6	**17**	**18**	44 h	42	38	81
7	**19**	**20**	30 min	70	65	60

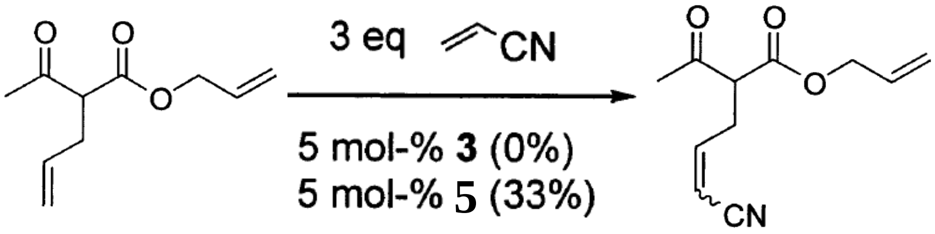
15% with Complex 1

[a] Conditions: 5 mol % **5** for entries 1 and 3−7, 1 mol % **5** for entry 2, 22 °C, CH_2Cl_2 (entries 1−5); 24 h at 22 °C and 20 h at 40 °C, CH_2Cl_2 for entry 6; toluene, 80 °C for entry 7. [b] Isolated yields after silica gel chromatography.

Complex 5 showed similar reactivity with Complex 3(high reactivity) in RCM.

Hoveyda, A. H. *et al.*, *J. Am. Chem. Soc.* **2000**, *122*, 8168.





5 seems to be a promising catalyst especially for CM.

Blechert, S. *et al.*, *Tetrahedron. Lett.* **2000**, *41*, 9973.

~Topics~

- Introduction
- Evolution of Ruthenium Catalysts

~from ill-defined catalysts to well-defined catalysts~

✓ill-defined Ruthenium catalysts

✓well-defined Ruthenium catalysts

➢First-Generation Grubbs Catalyst

➢Mechanistic Study(1997)

➢Second-Generation Grubbs Catalyst

➢Mechanistic Study(2001)

14-Electron, Mono-Phosphine Intermediate

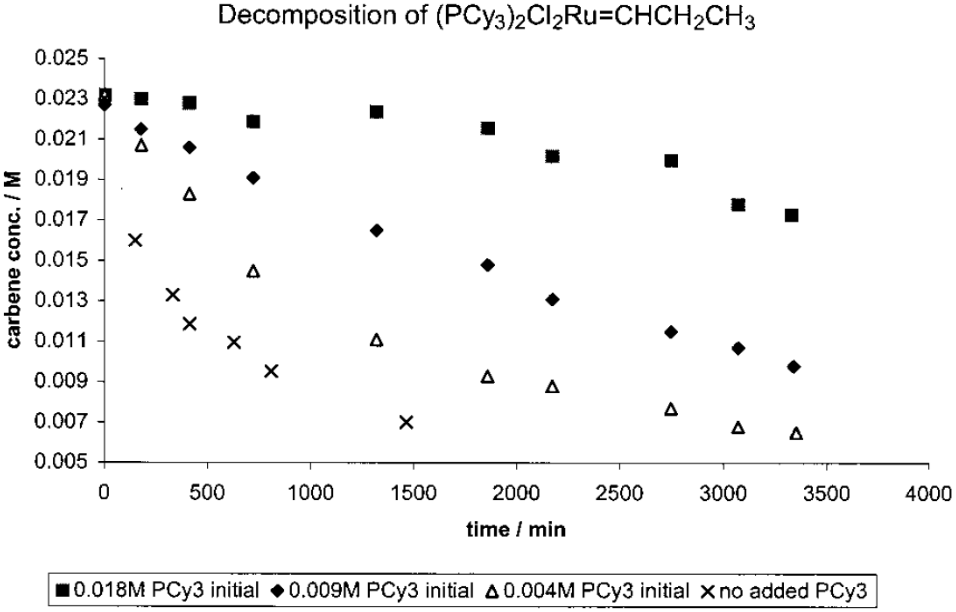
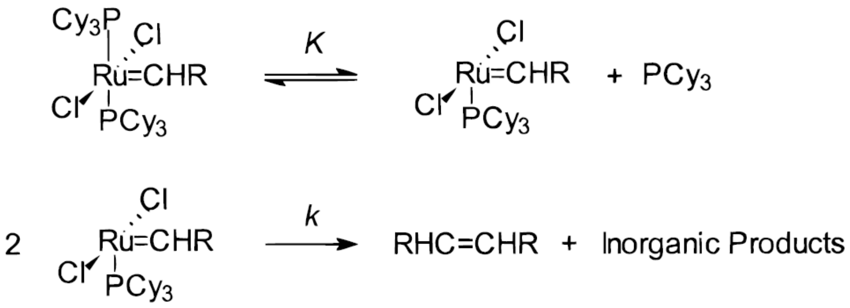


Figure 1. Phosphine dependence of decomposition at 55 °C.

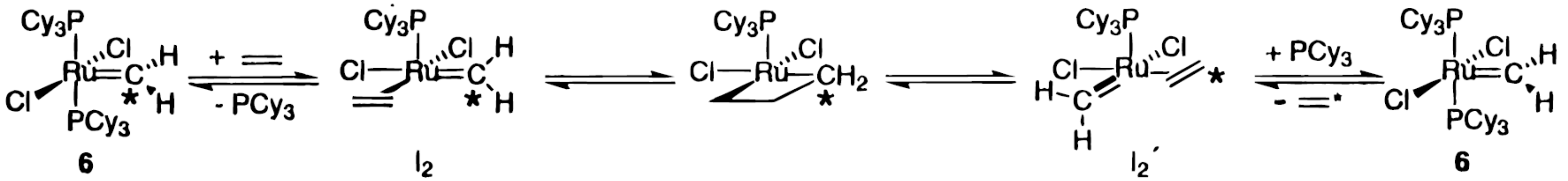
The rate of decomposition slowed significantly in the presence of excess phosphine.

Scheme 2. Proposed Pathway for Alkylidene Decomposition



Grubbs, R. H. *et al., J. Org. Chem.* **1999**, *64, 7202.*

Pathway 2



Simulations (Car-Parrinello dynamics simulations) reveal and lend support to the mechanism proposed by Grubbs.

Their results showed that mono-phosphine complex was the active species.

Francesco Buda *et al. J. Am. Chem. Soc*. **1998**, *120*, 7174.

14-Electron, Mono-Phosphine Intermediate

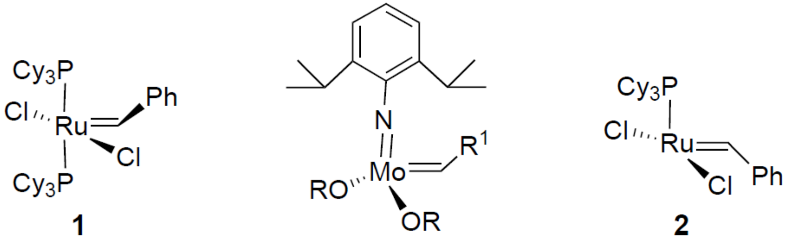
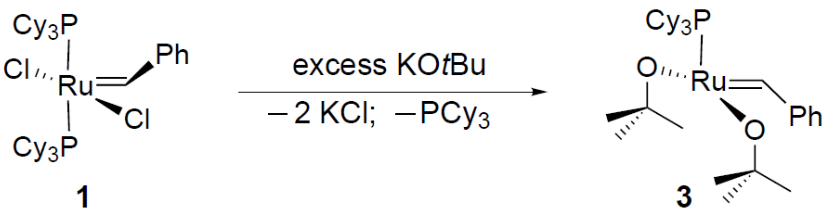
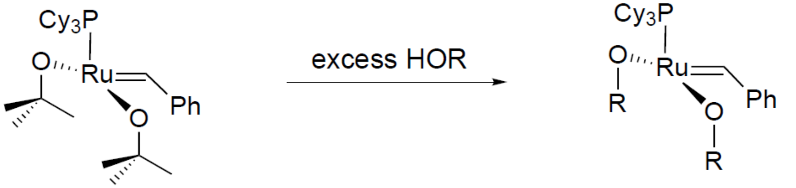
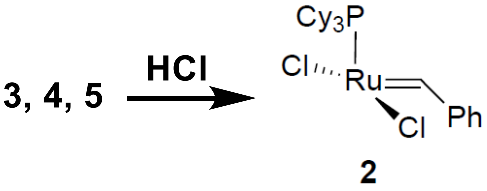


Figure 1. Olefin metathesis catalysts and the proposed intermediate **2**.

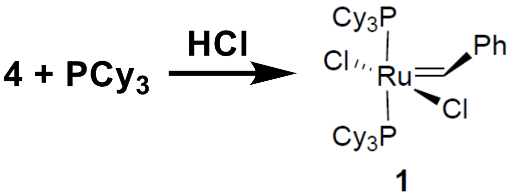




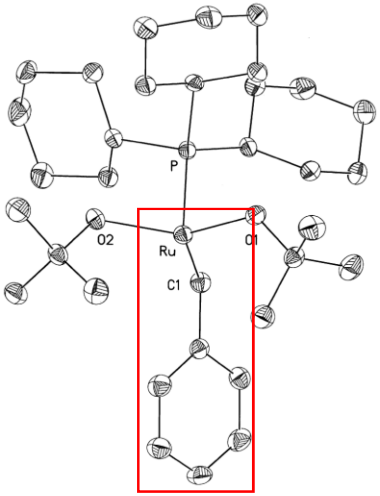
R = $C(CF_3)_2(CH_3)$ **4**
R = $C(CF_3)_3$ **5**



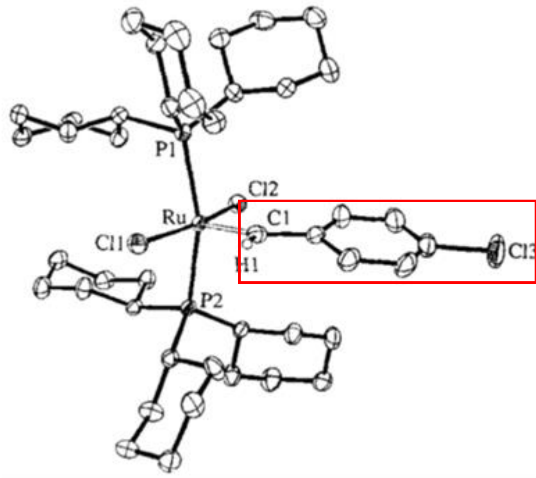
was generated?



support



Structure of 3



rotation of carbene moiety

Table 1. Ring-closing metathesis reactions of diethyl diallylmalonate with complexes **1** and **3**–**5**.[a]

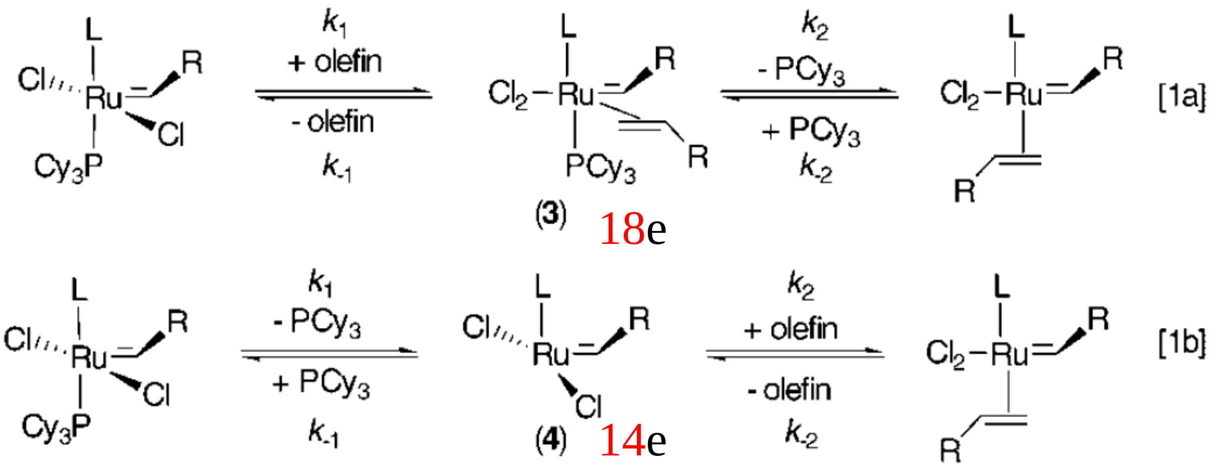
Catalyst	Additive	T [°C]	t [h]	Yield [%]
3	none	60	96	< 5
4	none	60	96	70
5	none	60	12	40
4	HCl[b]	25	0.65	> 96
1	none	25	1.5	> 96[c]

[a] Reactions of five equivalents of substrate in C_6D_6; [catalyst] = 0.01–0.02 M; yields were estimated by integration of the ^1H NMR spectrum; unless indicated catalyst decomposition terminated the reaction. [b] Two equivalents of HCl were added as a 2 M solution in diethyl ether. [c] Catalyst remains at the end of the reaction.

Grubbs, R. H. *et al.*, *Angew. Chem. Int. Ed.* **2000**, *39*, *3451*.

Phosphine Exchange

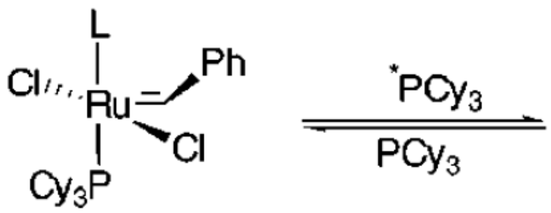
Scheme 1

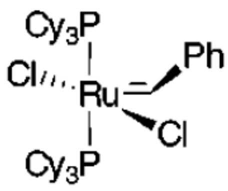


"associative" pathway

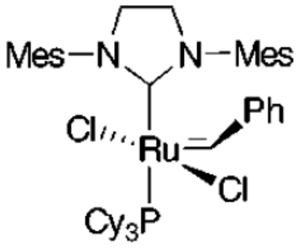
"dissociative" pathway

Model Study for the Phosphine/Olefin Substitution





(1)



(2)

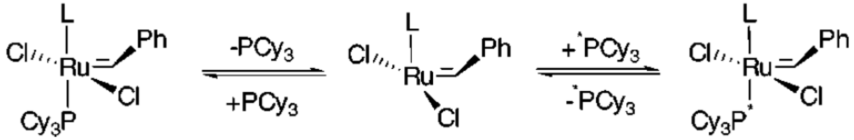
exchange rate constants (k_B) at 80℃
(per coordinated phosphine ligand)

$9.6 \pm 0.2\ s^{-1}$ > $0.13 \pm 0.01\ s^{-1}$!!

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 749.

Eyring Plot

- ✓ k_B is independent of [PCy_3]
- ✓ $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are large and positive



“dissociative” pathway

Table 1. Activation Parameters for Phosphine Exchange

catalyst	k_B (s^{-1}) 80 °C	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal mol^{-1} K^{-1})	$\Delta G^{\ddagger}$ (298 K) (kcal mol^{-1})
1	9.6 ± 0.2	23.6 ± 0.5	12 ± 2	19.88 ± 0.06
2	0.13 ± 0.01	27 ± 2	13 ± 6	23.0 ± 0.4

$$ln\frac{k}{T} = ln\kappa\frac{k_B}{h} - \frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R}$$

$$= ln\frac{k_B}{h} - \frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R}$$

$$(\because \kappa \cong 1)$$

- Eyring plot

A certain chemical reaction is performed at different temperatures and the reaction rate is determined. The plot of ln(*k*/T) versus 1/T gives a straight line with slope $-\Delta H^{\ddagger}/R$ from which the enthalpy of activation can be derived and

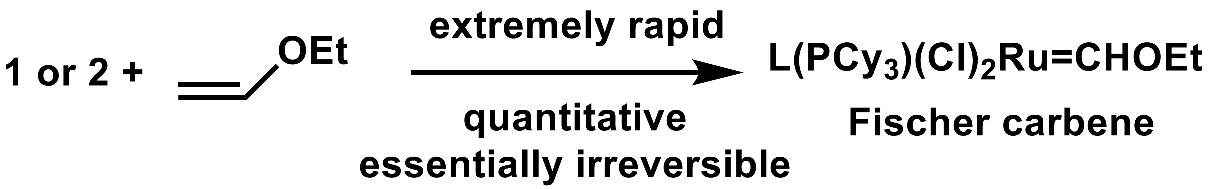
with intercept $\ln(k_B/h) + \Delta S^{\ddagger}/R$ from which the entropy of activation is derived.

wikipedia

*Here, k_B is Boltzmann's constant

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 749.

Model for the Initial Event


1 or 2 + OEt $\xrightarrow[\text{quantitative}]{\text{extremely rapid}}$ $L(PCy_3)(Cl)_2Ru{=}CHOEt$

essentially irreversible

Fischer carbene

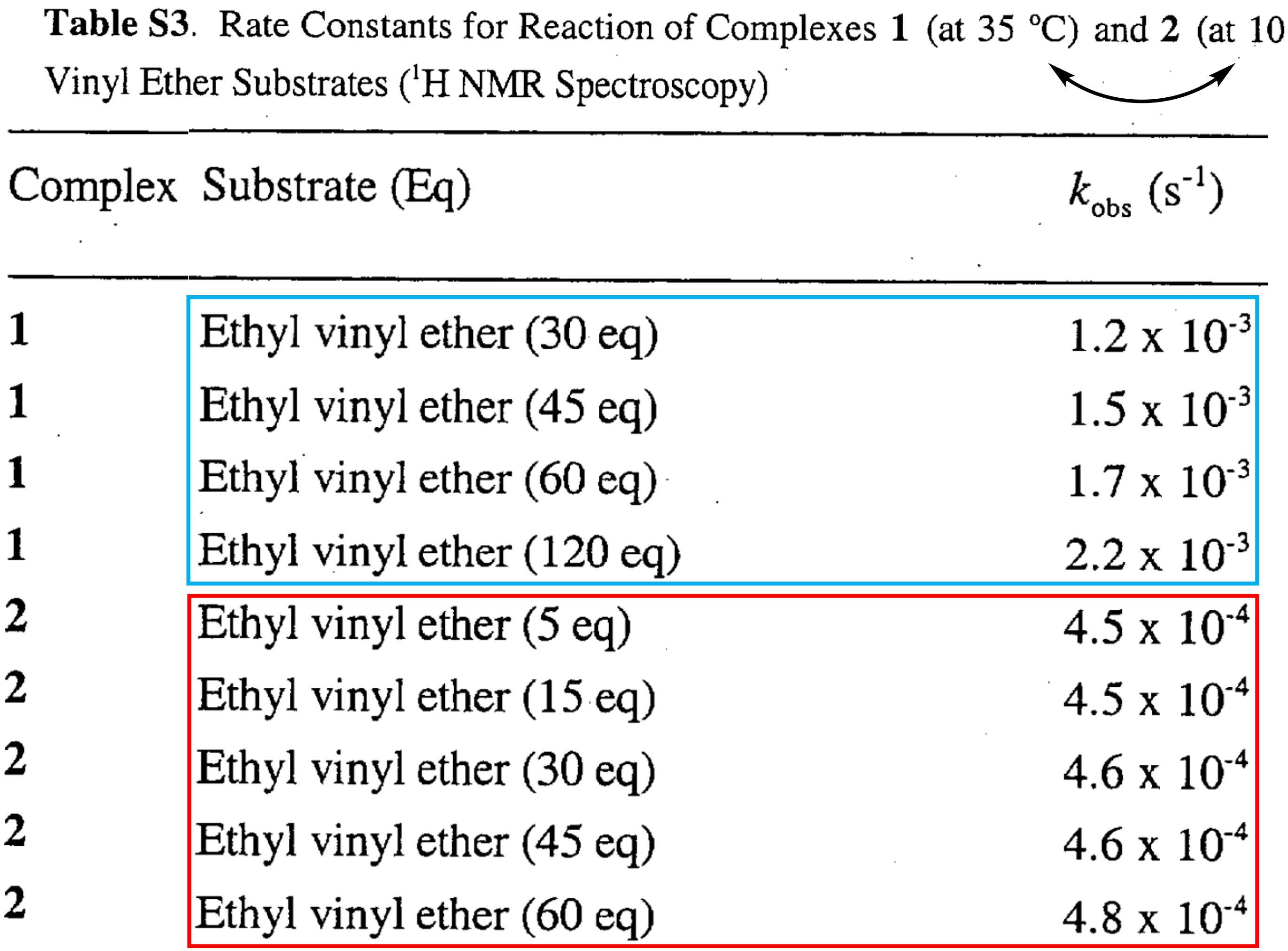
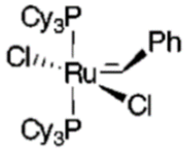
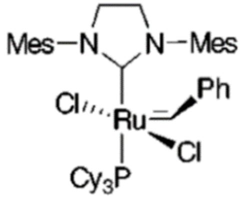


Table S3. Rate Constants for Reaction of Complexes **1** (at 35 °C) and **2** (at 10 °C) with Vinyl Ether Substrates (^{1}H NMR Spectroscopy)

Complex	Substrate (Eq)	k_{obs} (s^{-1})
1	Ethyl vinyl ether (30 eq)	1.2×10^{-3}
1	Ethyl vinyl ether (45 eq)	1.5×10^{-3}
1	Ethyl vinyl ether (60 eq)	1.7×10^{-3}
1	Ethyl vinyl ether (120 eq)	2.2×10^{-3}
2	Ethyl vinyl ether (5 eq)	4.5×10^{-4}
2	Ethyl vinyl ether (15 eq)	4.5×10^{-4}
2	Ethyl vinyl ether (30 eq)	4.6×10^{-4}
2	Ethyl vinyl ether (45 eq)	4.6×10^{-4}
2	Ethyl vinyl ether (60 eq)	4.8×10^{-4}



(1)



(2)

k_{obs} is dependent on olefin concentration

k_{obs} is independent of olefin concentration.
$k_{obs} = (4.6 \pm 0.3) \times 10^{-4}\ s^{-1}$

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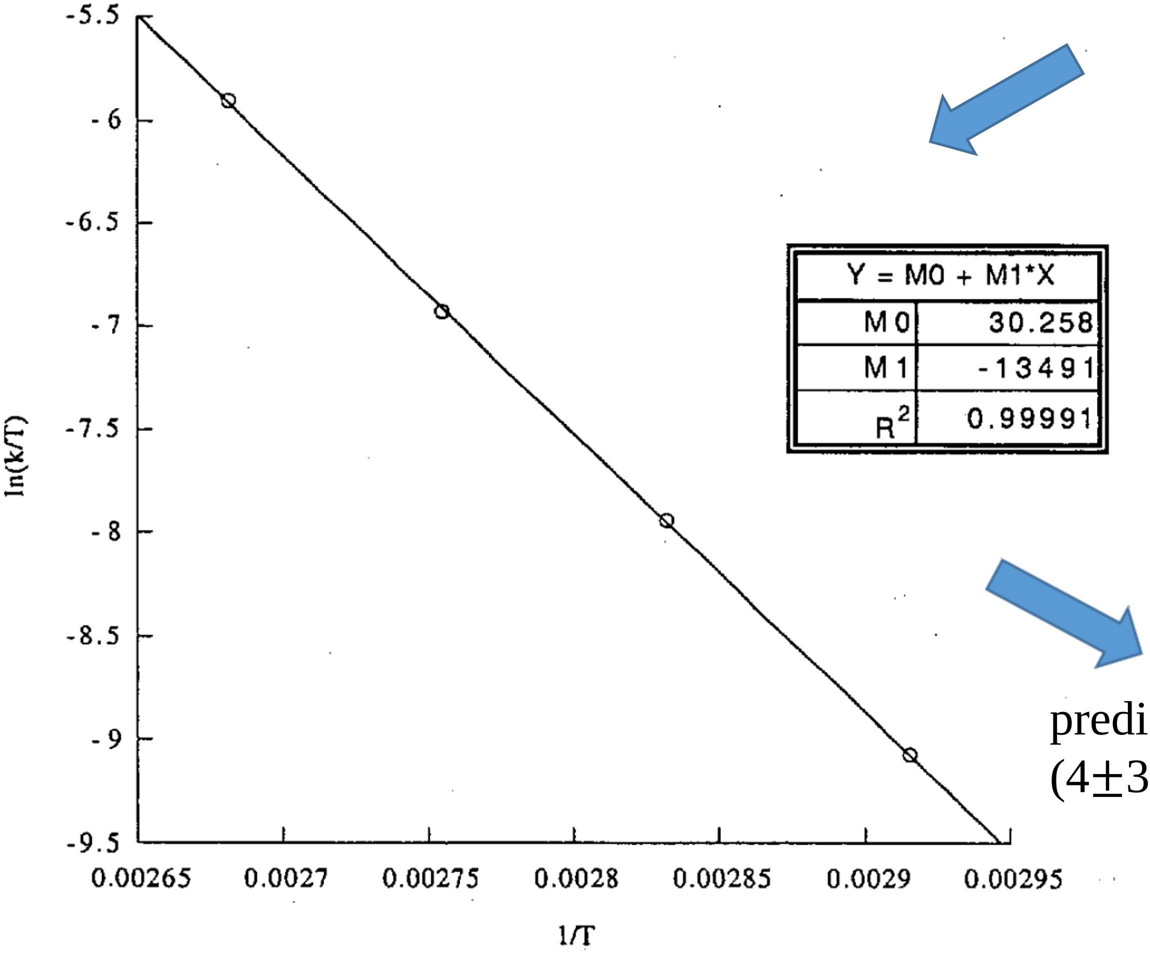
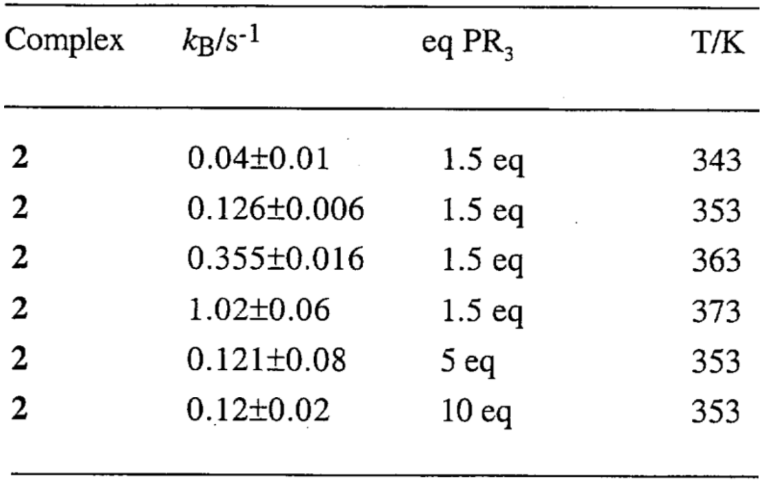
Complex 2

even at low olefin concentration…

Figure S4. Eyring Plot for Complex 2



Observed Rate Constants
for Phosphine Exchange



Complex	k_B/s^{-1}	eq PR_3	T/K
2	0.04±0.01	1.5 eq	343
2	0.126±0.006	1.5 eq	353
2	0.355±0.016	1.5 eq	363
2	1.02±0.06	1.5 eq	373
2	0.121±0.08	5 eq	353
2	0.12±0.02	10 eq	353

predicted k_B at 35℃
$(4\pm3)\times10^{-4}\ s^{-1} \cong\ \ k_{obs}\ (4.6\pm0.3)\times10^{-4}\ s^{-1}$

Rate-determining step of the reaction is phosphine dissociation.

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Complex 1

at much higher olefin concentration…

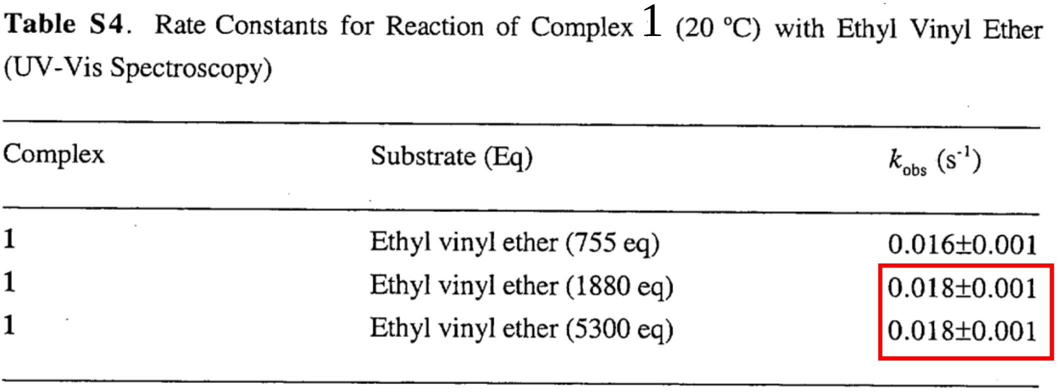
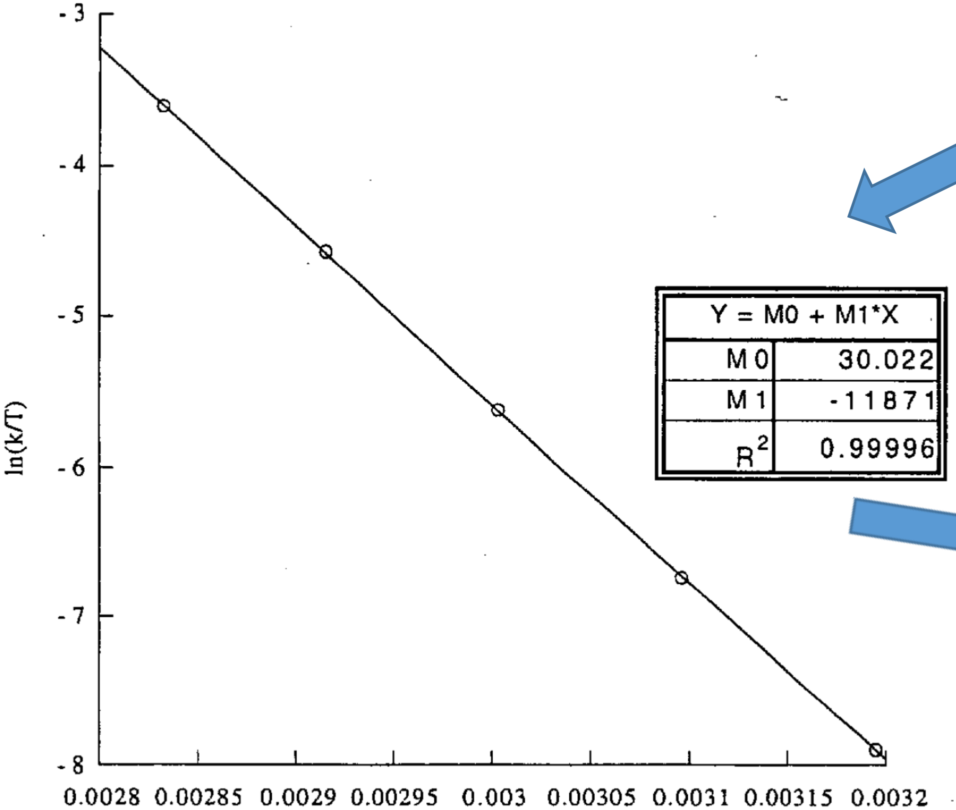


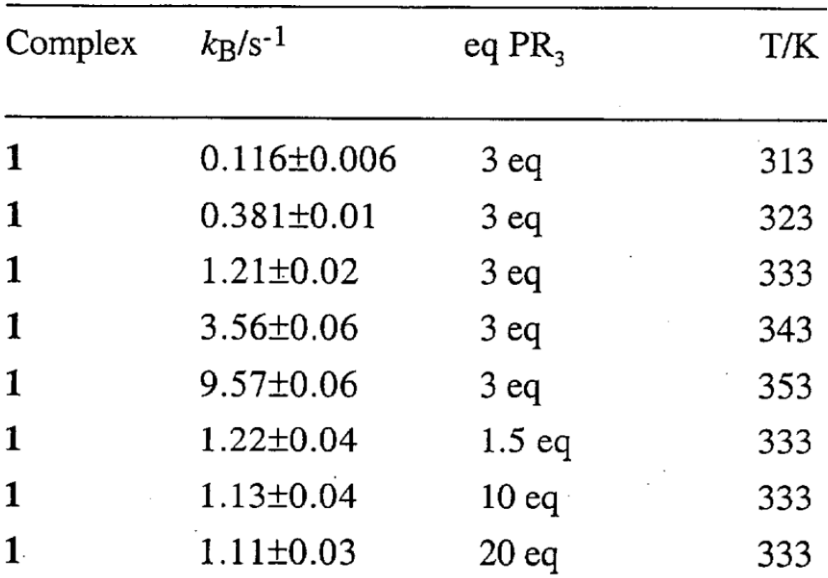
Table S4. Rate Constants for Reaction of Complex 1 (20 °C) with Ethyl Vinyl Ether (UV-Vis Spectroscopy)

Complex	Substrate (Eq)	k_{obs} (s^{-1})
1	Ethyl vinyl ether (755 eq)	0.016±0.001
1	Ethyl vinyl ether (1880 eq)	0.018±0.001
1	Ethyl vinyl ether (5300 eq)	0.018±0.001

Figure S3. Eyring Plot for Complex 1



Observed Rate Constants for Phosphine Exchange



Complex	k_B/s^{-1}	eq PR_3	T/K
1	0.116±0.006	3 eq	313
1	0.381±0.01	3 eq	323
1	1.21±0.02	3 eq	333
1	3.56±0.06	3 eq	343
1	9.57±0.06	3 eq	353
1	1.22±0.04	1.5 eq	333
1	1.13±0.04	10 eq	333
1	1.11±0.03	20 eq	333

predicted k_B at 20℃

$0.016 \pm 0.002\ s^{-1} \cong\ k_{obs}\ 0.018 \pm 0.001\ s^{-1}$

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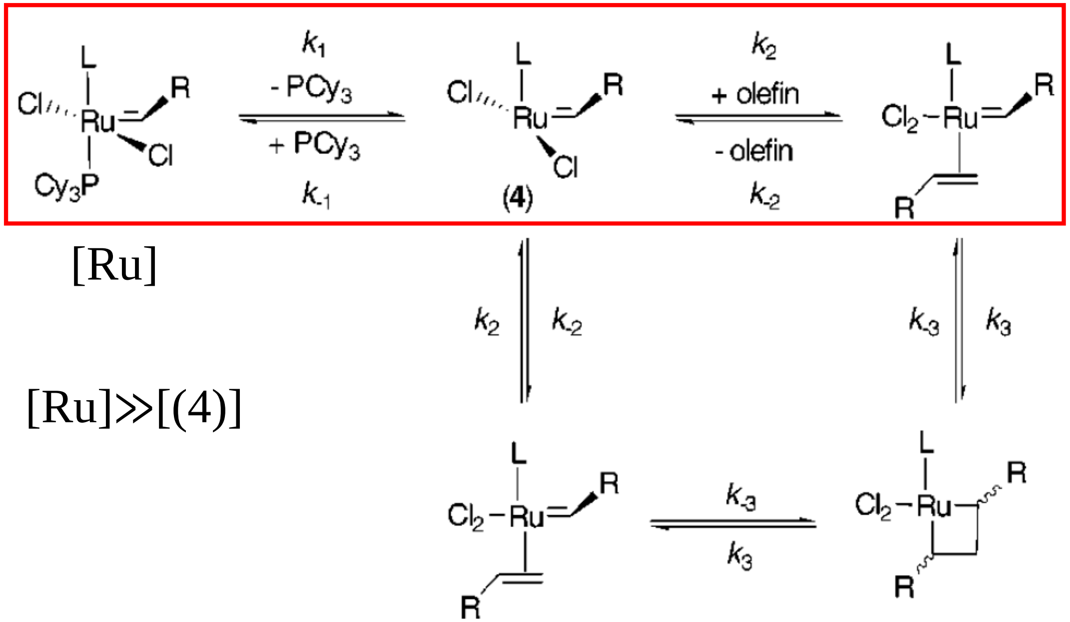
Suggested Mechanism



[Ru]

[Ru]≫[(4)]

Steady-state approximation: $k_2 \gg k_{-2}$, [(4)] is constant, $k_{obs}[\mathrm{Ru}]=k_2[(4)][\mathrm{Olefin}]$

$$k_1[\mathrm{Ru}]=k_2[(4)][\mathrm{Olefin}]+k_{-1}[(4)][\mathrm{PCy_3}]$$
$$=[(4)](k_2[\mathrm{Olefin}]+k_{-1}[\mathrm{PCy_3}])$$

$$\therefore \frac{k_1[\mathrm{Ru}]}{k_2[(4)][\mathrm{Olefin}]}=1+\frac{k_{-1}[\mathrm{PCy_3}]}{k_2[\mathrm{Olefin}]}$$

$$k_{obs}=\frac{k_2[(4)][\mathrm{Olefin}]}{[\mathrm{Ru}]}=\frac{k_1}{\frac{k_{-1}[\mathrm{PCy_3}]}{k_2[\mathrm{Olefin}]}+1}$$

➡

k_1 and k_{-1}/k_2 can be obtained from k_{obs} and $[\mathrm{PCy_3}]/[\mathrm{Olefin}]$.

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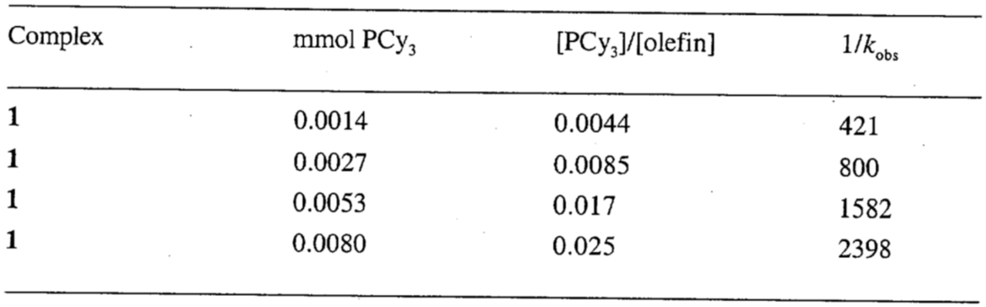
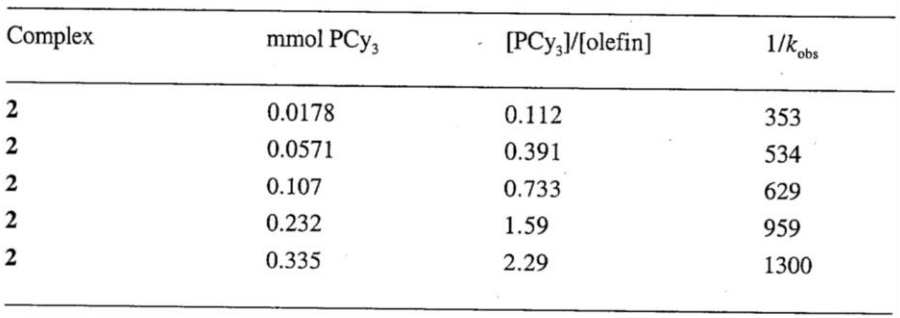
$1/k_{obs}$ versus $[PCy_3]$/[Olefin]

Table S5. $[PCy_3]$/[Olefin] Experiments for **1**.



Complex	mmol PCy_3	$[PCy_3]$/[olefin]	$1/k_{obs}$
1	0.0014	0.0044	421
1	0.0027	0.0085	800
1	0.0053	0.017	1582
1	0.0080	0.025	2398

Table S6. $[PCy_3]$/[Olefin] Experiments for **2**.



Complex	mmol PCy_3	$[PCy_3]$/[olefin]	$1/k_{obs}$
2	0.0178	0.112	353
2	0.0571	0.391	534
2	0.107	0.733	629
2	0.232	1.59	959
2	0.335	2.29	1300

Figure S7. $1/k_{obs}$ versus $[PCy_3]$/[Olefin] for Complex 1

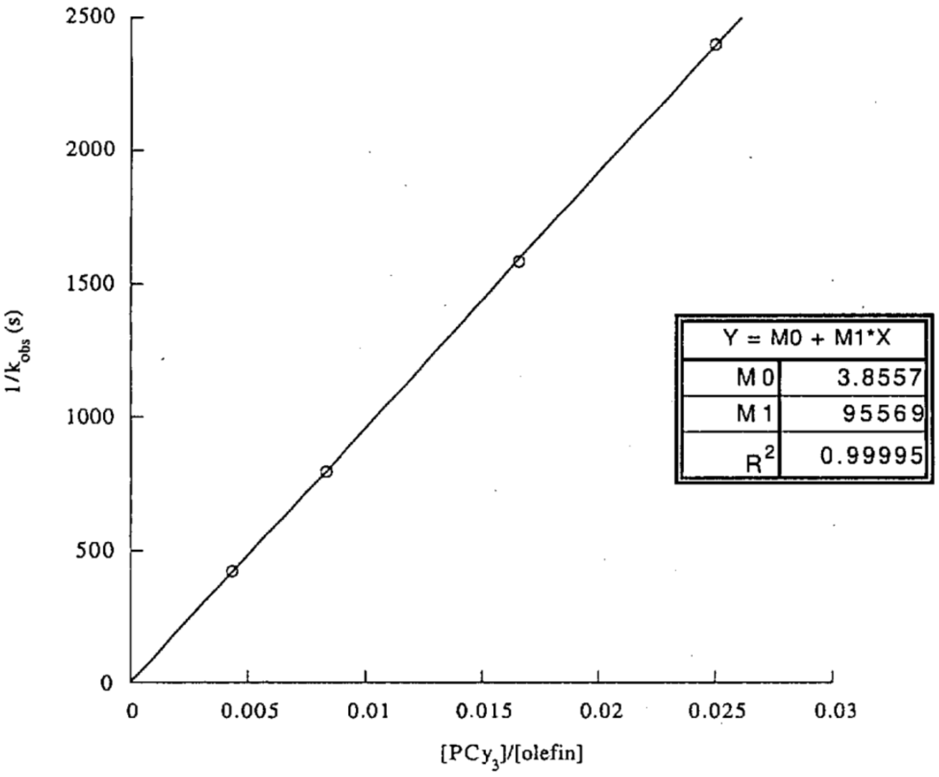
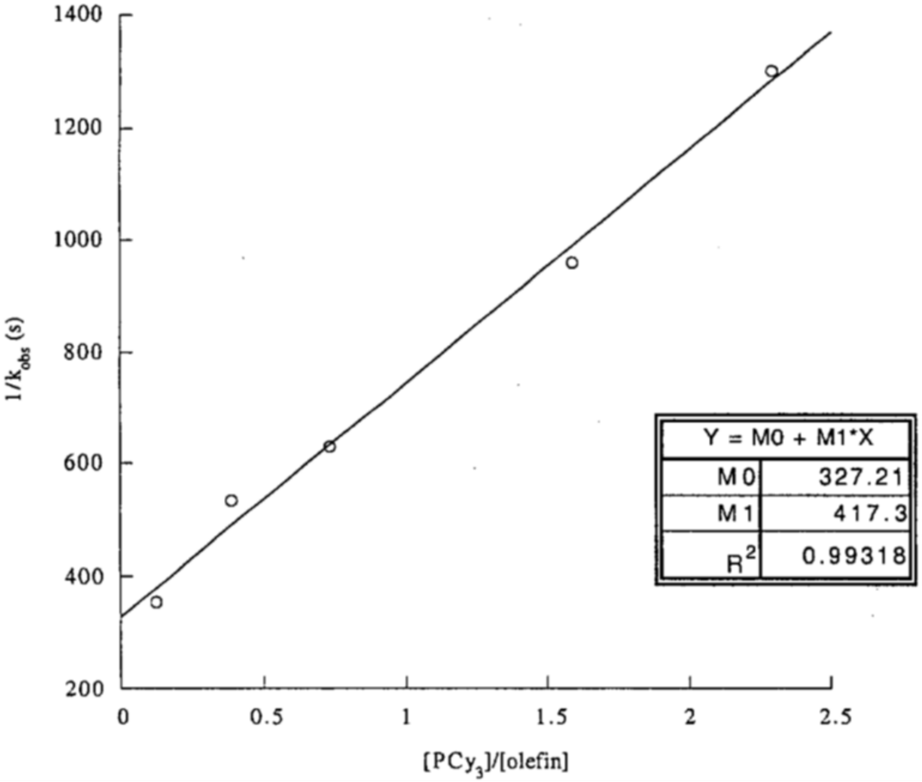


Figure S8. $1/k_{obs}$ versus $[PCy_3]$/[olefin] for Complex 2



Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 749.

What This Mechanistic Study Indicated

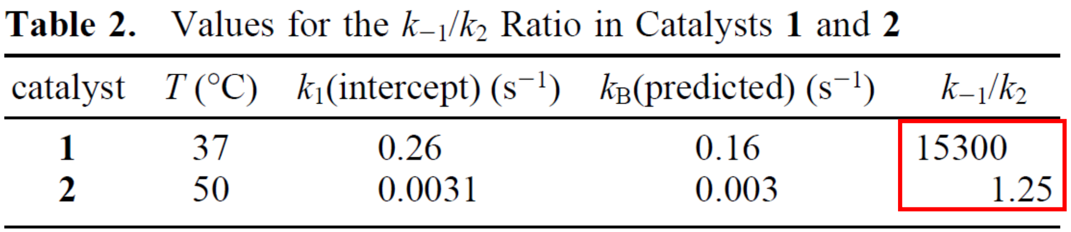


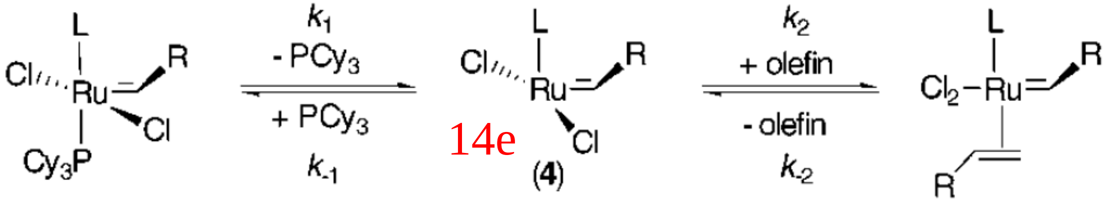
Table 2. Values for the k_{-1}/k_2 Ratio in Catalysts **1** and **2**

catalyst	T (°C)	k_1(intercept) (s^{-1})	k_B(predicted) (s^{-1})	k_{-1}/k_2
1	37	0.26	0.16	15300
2	50	0.0031	0.003	1.25

Olefin Metathesis Activity
Catalyst 2≫Catalyst 1

Catalyst 1: Relatively rapid initiation; Relatively few turnovers of 14-electron intermediate
Catalyst 2: Relatively slow initiation; Relatively many turnovers of 14-electron intermediate

Summary



14e

rate-determining step

Dissociative pathway
14-electron intermediate

The high activity of N-heterocyclic carbene-coordinated catalyst 2 is due to...

✓ Its improved selectivity for binding π-acidic olefinic substrates in the presence of phospnine →decreasing k_{-1}/k_2

✓ Not its ability to promote phosphine dissociation (increasing k_1, previous assumption)

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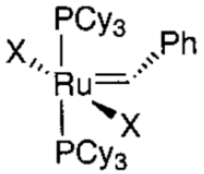
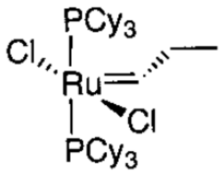
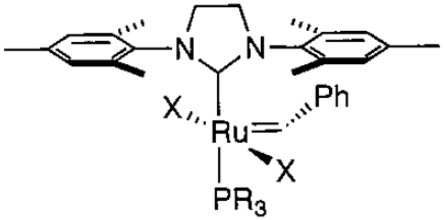
Phospnine Exchange



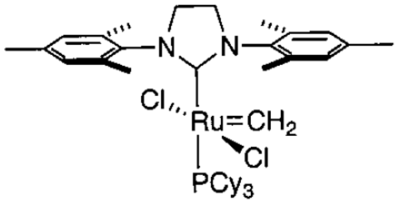
X = Cl (**1**)
X = Br (**2**)
X = I (**3**)



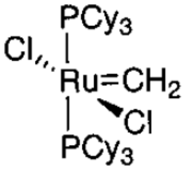
(**5**)



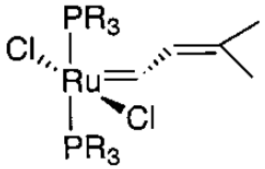
X = Cl; R = Cy (**8**)
X = Br; R = Cy (**9**)
X = I; R = Cy (**10**)
X = Cl; R = Ph (**11**)
X = Cl; R = Bn (**12**)



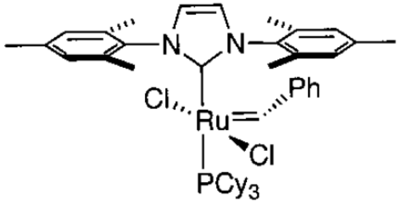
(**13**)



(**4**)



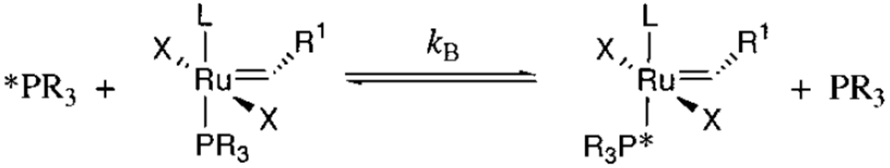
R = Cy (**6**)
R = Cp (**7**)



(**14**)

Table 1. Rate Constants and Activation Parameters for Phosphine Exchange[a]

catalyst	k_B (s^{-1}) 80 °C[b]	$\Delta H^\ddagger$ ($kcal/mol^{-1}$)	$\Delta S^\ddagger$ (eu)	$\Delta G^\ddagger$(298 K) ($kcal/mol^{-1}$)
1	9.6 ± 0.2	23.6 ± 0.5	12 ± 2	19.88 ± 0.06
2	30 ± 2	23.1 ± 0.3	13 ± 1	19.11 ± 0.03
3	1660 ± 220[c]	19.0 ± 0.5	10 ± 2	16.12 ± 0.01
4[d]				
5	19.4 ± 0.8	24.3 ± 0.6	16 ± 2	19.6 ± 0.1
6	0.33 ± 0.02	24 ± 1	8 ± 3	22.0 ± 0.2
7	1.42 ± 0.06	24 ± 1	11 ± 3	21.1 ± 0.1
8	0.13 ± 0.01	27 ± 2	13 ± 6	23.0 ± 0.4
9	0.52 ± 0.02	27 ± 2	15 ± 6	22.0 ± 0.4
10	29 ± 3	23 ± 4	12 ± 11	19.0 ± 0.5
11	7.5 ± 0.5[c]	21 ± 3	5 ± 9	19.6 ± 0.3
12	0.165 ± 0.006	27 ± 1	13 ± 4	22.7 ± 0.3
13[d]				
14	0.03 ± 0.01[c]	25 ± 4	6 ± 11	24 ± 1



[a] Reactions were carried out in toluene-d_8 with 1 equiv of Ru ([Ru] = 0.04 M) and 1.5 equiv of free PR_3 (relative to bound PR_3). [b] Values for k_B are reported per coordinated PR_3 ligand. [c] Values for k_B at 80 °C were extrapolated from Eyring plots. [d] Values for k_B in complexes **4** and **13** could not be determined due to catalyst decomposition at the elevated temperatures required for these experiments.

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Initiation Kinetics (Reaction with Ethyl Vinyl Ether)

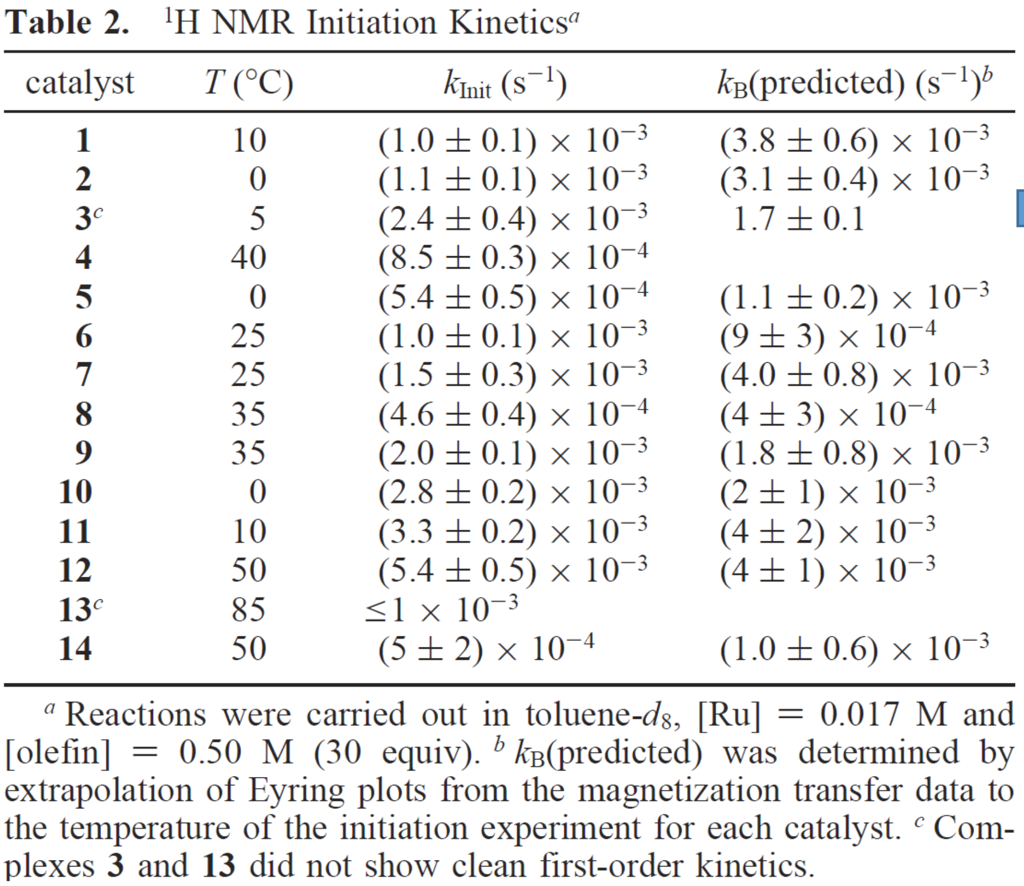

Table 2. ^{1}H NMR Initiation Kinetics[a]

catalyst	T (°C)	k_{Init} (s^{-1})	k_B(predicted) (s^{-1})[b]
1	10	$(1.0 \pm 0.1) \times 10^{-3}$	$(3.8 \pm 0.6) \times 10^{-3}$
2	0	$(1.1 \pm 0.1) \times 10^{-3}$	$(3.1 \pm 0.4) \times 10^{-3}$
3[c]	5	$(2.4 \pm 0.4) \times 10^{-3}$	1.7 ± 0.1
4	40	$(8.5 \pm 0.3) \times 10^{-4}$	
5	0	$(5.4 \pm 0.5) \times 10^{-4}$	$(1.1 \pm 0.2) \times 10^{-3}$
6	25	$(1.0 \pm 0.1) \times 10^{-3}$	$(9 \pm 3) \times 10^{-4}$
7	25	$(1.5 \pm 0.3) \times 10^{-3}$	$(4.0 \pm 0.8) \times 10^{-3}$
8	35	$(4.6 \pm 0.4) \times 10^{-4}$	$(4 \pm 3) \times 10^{-4}$
9	35	$(2.0 \pm 0.1) \times 10^{-3}$	$(1.8 \pm 0.8) \times 10^{-3}$
10	0	$(2.8 \pm 0.2) \times 10^{-3}$	$(2 \pm 1) \times 10^{-3}$
11	10	$(3.3 \pm 0.2) \times 10^{-3}$	$(4 \pm 2) \times 10^{-3}$
12	50	$(5.4 \pm 0.5) \times 10^{-3}$	$(4 \pm 1) \times 10^{-3}$
13[c]	85	$\leq 1 \times 10^{-3}$	
14	50	$(5 \pm 2) \times 10^{-4}$	$(1.0 \pm 0.6) \times 10^{-3}$

[a] Reactions were carried out in toluene-d_8, [Ru] = 0.017 M and [olefin] = 0.50 M (30 equiv). [b] k_B(predicted) was determined by extrapolation of Eyring plots from the magnetization transfer data to the temperature of the initiation experiment for each catalyst. [c] Complexes **3** and **13** did not show clean first-order kinetics.

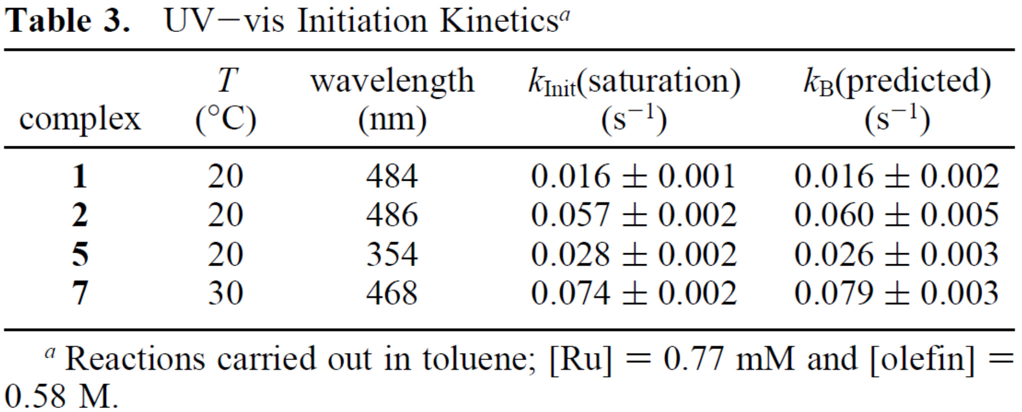

Table 3. UV−vis Initiation Kinetics[a]

complex	T (°C)	wavelength (nm)	k_{Init}(saturation) (s^{-1})	k_B(predicted) (s^{-1})
1	20	484	0.016 ± 0.001	0.016 ± 0.002
2	20	486	0.057 ± 0.002	0.060 ± 0.005
5	20	354	0.028 ± 0.002	0.026 ± 0.003
7	30	468	0.074 ± 0.002	0.079 ± 0.003

[a] Reactions carried out in toluene; [Ru] = 0.77 mM and [olefin] = 0.58 M.

at low [ethyl vinyl ether],
1,2,3,5 and 7 showed
$k_B \propto$[ethyl vinyl ether] (approximately)

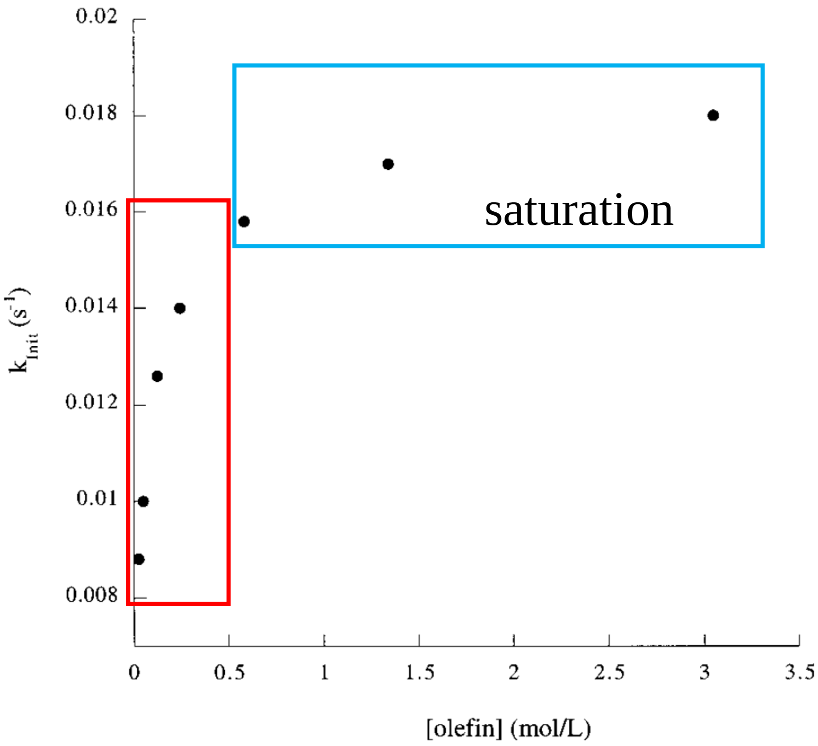

Figure 3. k_{Init} vs [olefin] for catalyst **1**.

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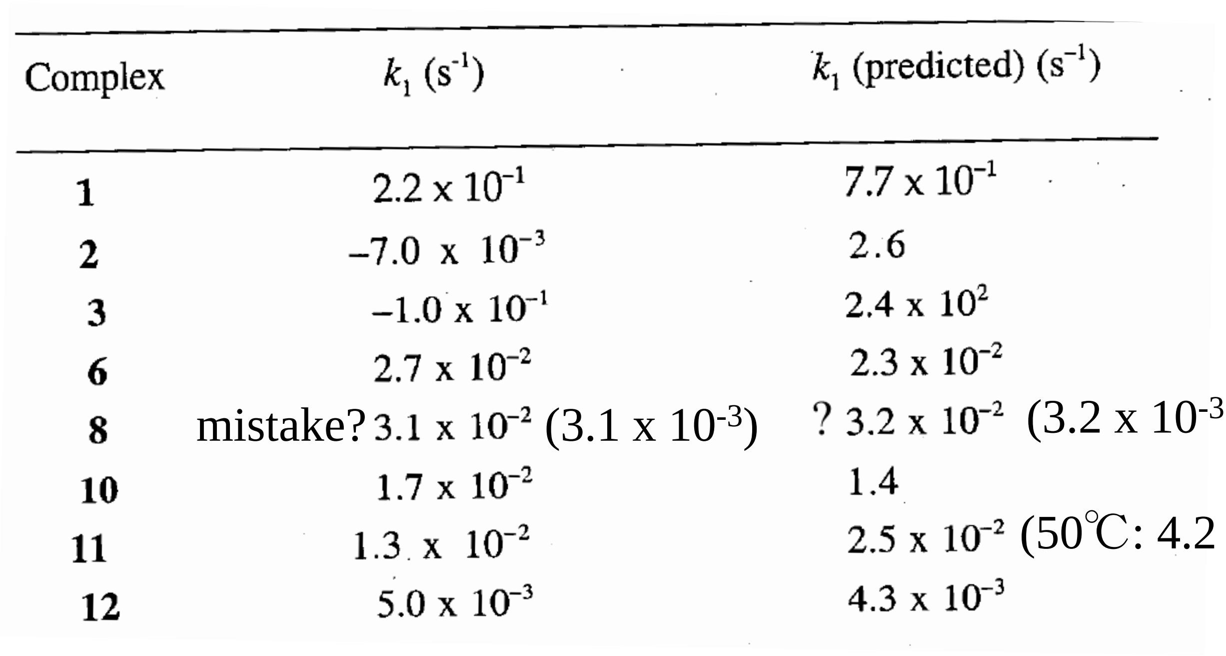
$$1/k_{obs}=k_{-1}[PR_3]k_1k_2[\text{Olefin}]+1/k_1$$



Complex	k_1 (s^{-1})	k_1 (predicted) (s^{-1})
1	2.2×10^{-1}	7.7×10^{-1}
2	-7.0×10^{-3}	2.6
3	-1.0×10^{-1}	2.4×10^{2}
6	2.7×10^{-2}	2.3×10^{-2}
8	mistake? 3.1×10^{-2} (3.1×10^{-3})	? 3.2×10^{-2} (3.2×10^{-3})
10	1.7×10^{-2}	1.4
11	1.3×10^{-2}	2.5×10^{-2} (50℃: 4.2×10^{-1})
12	5.0×10^{-3}	4.3×10^{-3}

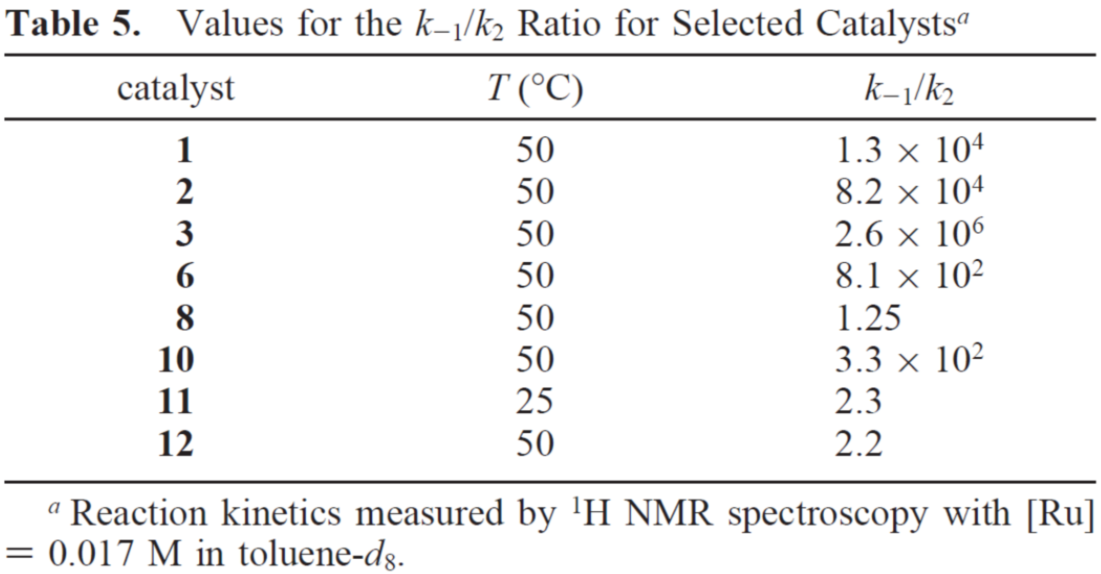


Table 5. Values for the k_{-1}/k_2 Ratio for Selected Catalysts[a]

catalyst	T (°C)	k_{-1}/k_2
1	50	1.3×10^{4}
2	50	8.2×10^{4}
3	50	2.6×10^{6}
6	50	8.1×10^{2}
8	50	1.25
10	50	3.3×10^{2}
11	25	2.3
12	50	2.2

[a] Reaction kinetics measured by ^{1}H NMR spectroscopy with [Ru] = 0.017 M in toluene-d_8.

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 6543.

Solvent Effects on Initiation

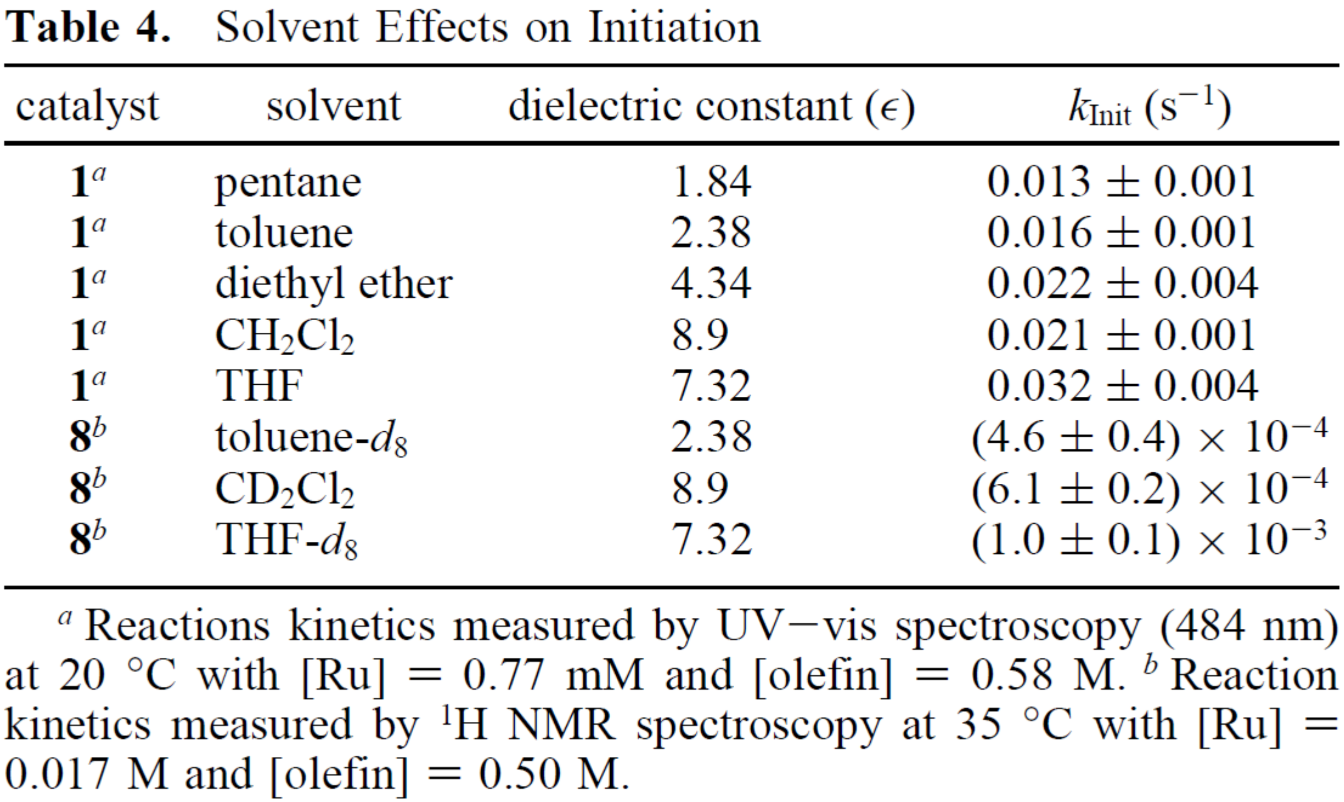
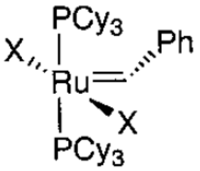


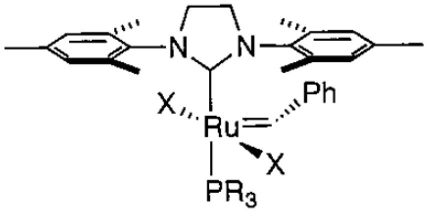
Table 4. Solvent Effects on Initiation

catalyst	solvent	dielectric constant (ϵ)	k_{Init} (s^{-1})
1[a]	pentane	1.84	0.013 ± 0.001
1[a]	toluene	2.38	0.016 ± 0.001
1[a]	diethyl ether	4.34	0.022 ± 0.004
1[a]	CH_2Cl_2	8.9	0.021 ± 0.001
1[a]	THF	7.32	0.032 ± 0.004
8[b]	toluene-d_8	2.38	$(4.6 \pm 0.4) \times 10^{-4}$
8[b]	CD_2Cl_2	8.9	$(6.1 \pm 0.2) \times 10^{-4}$
8[b]	THF-d_8	7.32	$(1.0 \pm 0.1) \times 10^{-3}$

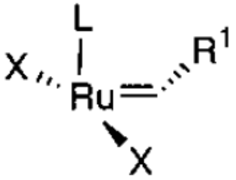
[a] Reactions kinetics measured by UV−vis spectroscopy (484 nm) at 20 °C with [Ru] = 0.77 mM and [olefin] = 0.58 M. [b] Reaction kinetics measured by ^{1}H NMR spectroscopy at 35 °C with [Ru] = 0.017 M and [olefin] = 0.50 M.



X = Cl (**1**)



X = Cl; R = Cy (**8**)



(**B**)

- ✓ $k_{\mathrm{Int}} \propto$ dielectric constant
- ✓ Increased stabilization of the 4-coordinate B intermediate and/or free PCy_3? (Both are expected to be more polar than the Ru starting material.)
- ✓ The stabilization of B may involve coordination of solvent to the electron-deficient Ru(Ⅱ) center. (THF, diethyl ether, however no evidence)

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Relative Catalyst Activities

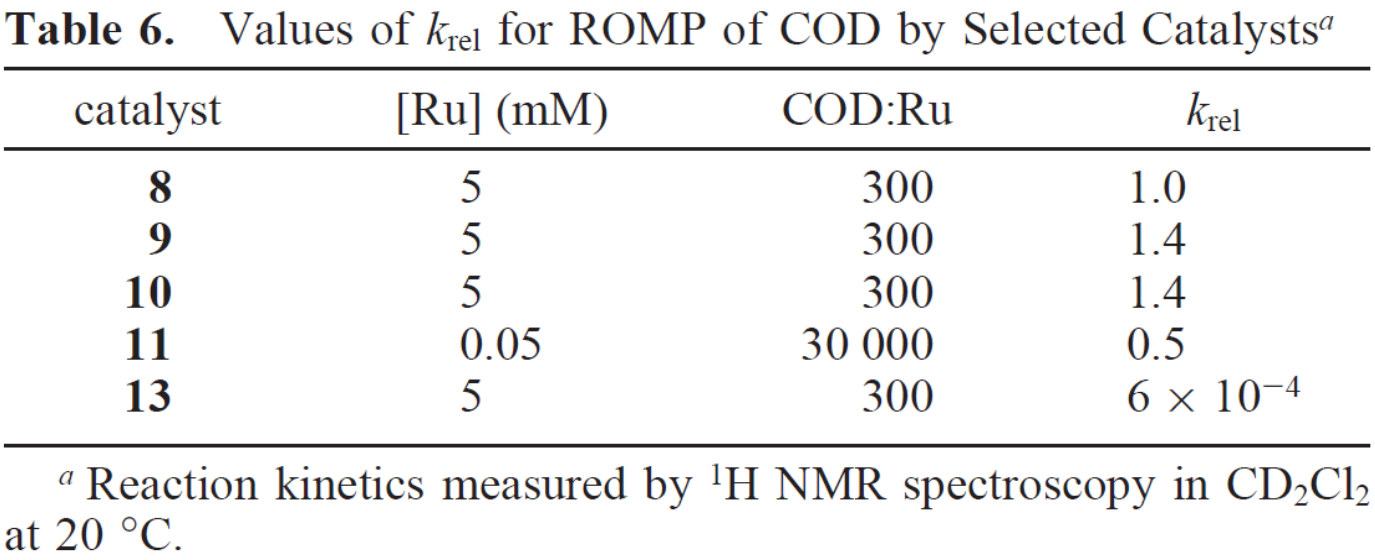
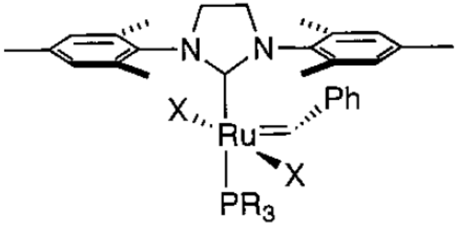


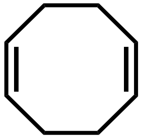
Table 6. Values of k_{rel} for ROMP of COD by Selected Catalysts[a]

catalyst	[Ru] (mM)	COD:Ru	k_{rel}
8	5	300	1.0
9	5	300	1.4
10	5	300	1.4
11	0.05	30 000	0.5
13	5	300	6×10^{-4}

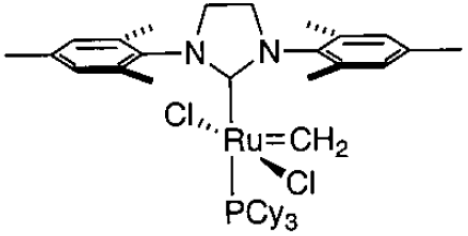
[a] Reaction kinetics measured by ^{1}H NMR spectroscopy in CD_2Cl_2 at 20 °C.



X = Cl; R = Cy (**8**)
X = Br; R = Cy (**9**)
X = I; R = Cy (**10**)
X = Cl; R = Ph (**11**)



COD: serve as a benchmark for comparing the *relative activities*



(**13**)

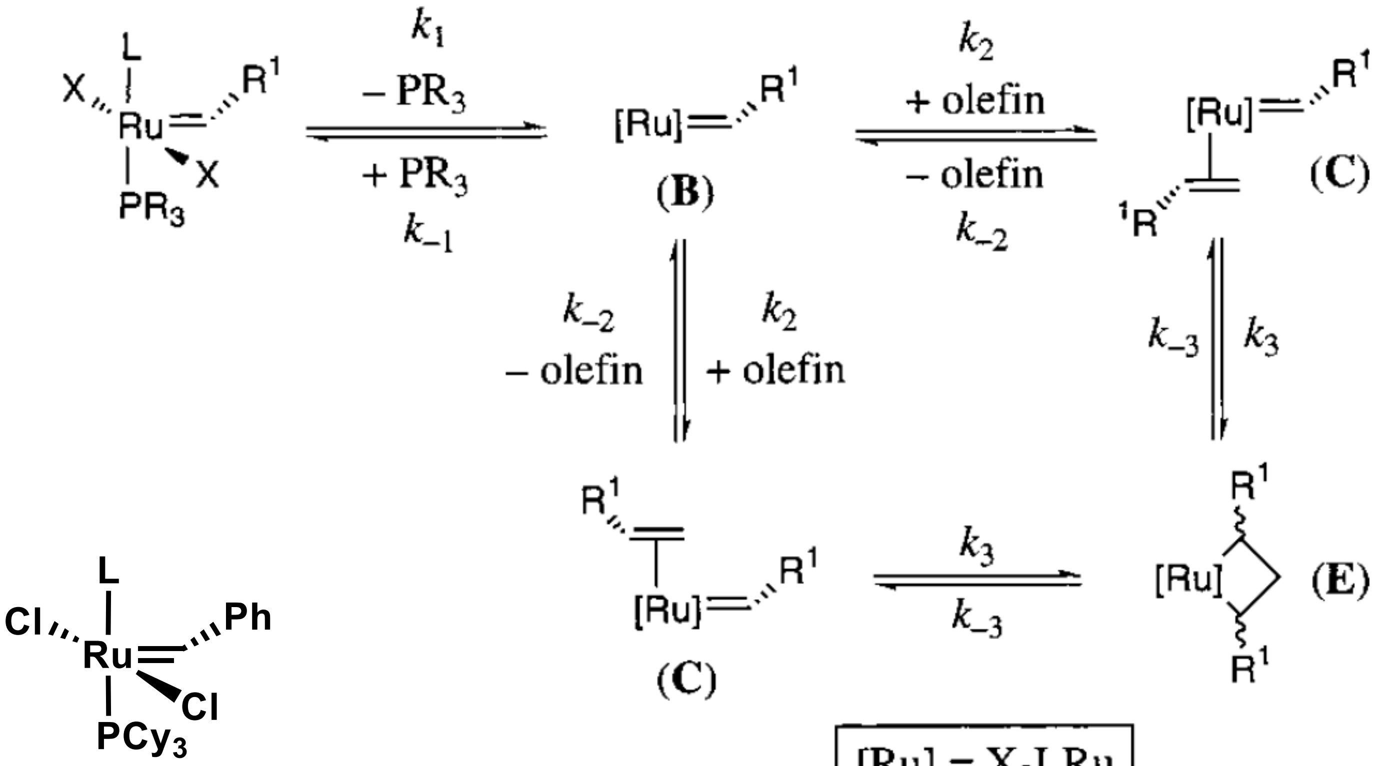
Initiation (k_1): 8<9<10 (10 initiates almost quantitatively)
Propagation (k_{-1}/k_2): 8>9>10

Comparison of 8 and11 showed that
11 initiates more than 50 times faster than 8. (8 and 11 generate the same propagating species)
→The loading of catalyst can be reduced significantly.

13 reacts especially slowly because of the slow rate of phosphine dissociation.
(13 is a crucial intermediate during RCM and CM…)

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 6543.

Mechanism of Ru-Catalyzed Olefin Metathesis



$[Ru] = X_2LRu$

(1) L=PCy_3
k_1(rel)=~10^2
k_{-1}/k_2(rel)=~10^4

(8) L=H_2IMes
k_1(rel)=1
k_{-1}/k_2(rel)=1

- ✓ Bis-phosphine system (1-7): k_1 is large, but $k_{-1}/k_2 \gg 1$ (few catalytic turnover)
- ✓ NHC-complex (8-14): k_1 is small, but $k_{-1}/k_2 \sim 1$ (many catalytic turnover)

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 6543.

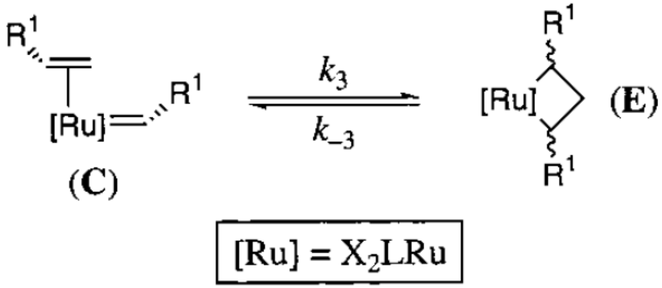
Ligand Effects

- *L-Type Ligand*

➢ Selectivity for binding π-acidic olefinic substrates over σ-donating phosphine (k_2/k_{-1})
NHC-substituted Ru center ≫ phosphine-substituted Ru center

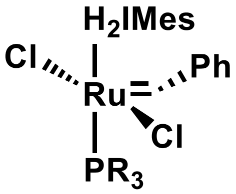
➢ As a electron donor ligand
NHC(IMesH_2 > IMes) ≫ P(alkyl)$_3$

➢ Electron donation of NHC's is expected to…
stabilize the olefin complex C
accelerate the oxidative addition for matallacyclobutane formation



[Ru] = X_2LRu

- *Phosphine Ligand*



(8) R=Cy
k_1(rel)=1
k_{-1}/k_2=1.25

(11) R=Ph
k_1(rel)=~10^2
k_{-1}/k_2=2.3

p*K*a's of the conjugate acids
PCy_3: 9.7
PPh_3: 2.73
→the lower basicity, the higher k_1
((**12**)PBn_3: 6.0, k_1(rel)=~10^2)???

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 6543.

Phosphine Ligand

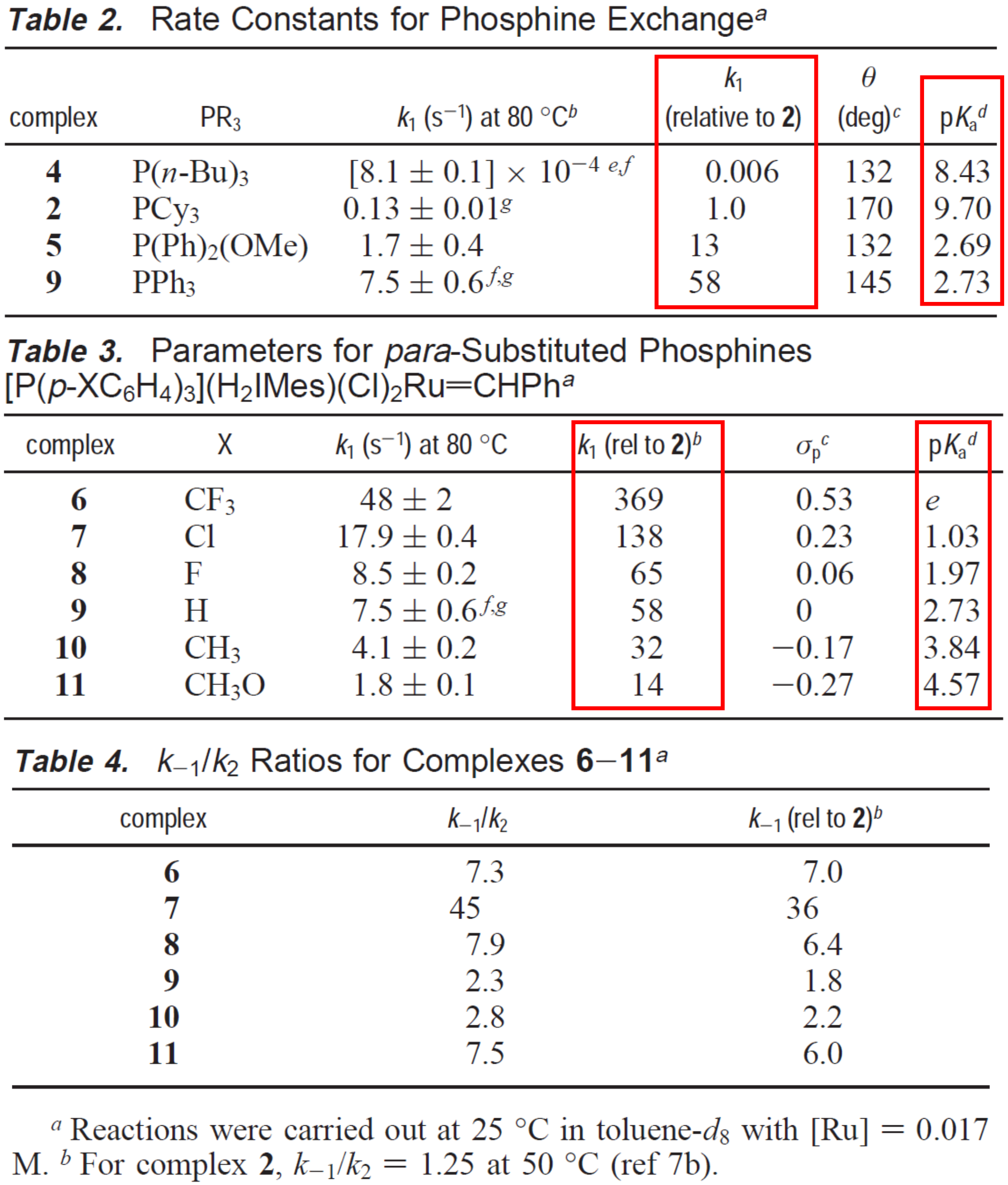


Table 2. Rate Constants for Phosphine Exchange[a]

complex	PR_3	k_1 (s^{-1}) at 80 °C[b]	k_1 (relative to **2**)	θ (deg)[c]	pK_a[d]
4	$P(n\text{-}Bu)_3$	$[8.1 \pm 0.1] \times 10^{-4}$ [e,f]	0.006	132	8.43
2	PCy_3	0.13 ± 0.01[g]	1.0	170	9.70
5	$P(Ph)_2(OMe)$	1.7 ± 0.4	13	132	2.69
9	PPh_3	7.5 ± 0.6[f,g]	58	145	2.73

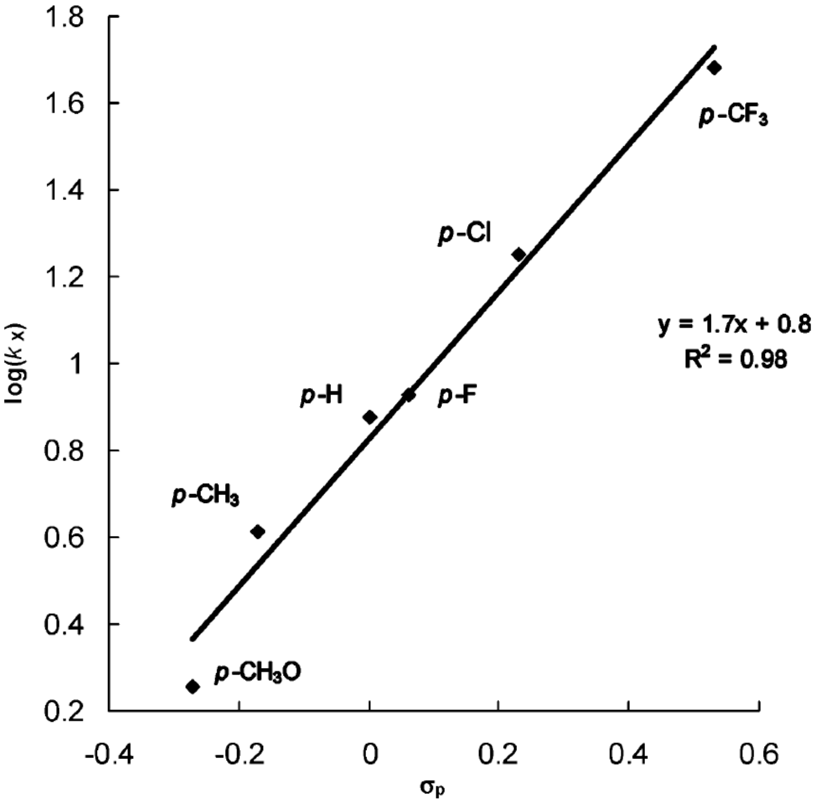
Table 3. Parameters for *para*-Substituted Phosphines $[P(p\text{-}XC_6H_4)_3](H_2IMes)(Cl)_2Ru{=}CHPh$[a]

complex	X	k_1 (s^{-1}) at 80 °C	k_1 (rel to **2**)[b]	σ_p[c]	pK_a[d]
6	CF_3	48 ± 2	369	0.53	*e*
7	Cl	17.9 ± 0.4	138	0.23	1.03
8	F	8.5 ± 0.2	65	0.06	1.97
9	H	7.5 ± 0.6[f,g]	58	0	2.73
10	CH_3	4.1 ± 0.2	32	−0.17	3.84
11	CH_3O	1.8 ± 0.1	14	−0.27	4.57

Table 4. k_{-1}/k_2 Ratios for Complexes **6**–**11**[a]

complex	k_{-1}/k_2	k_{-1} (rel to **2**)[b]
6	7.3	7.0
7	45	36
8	7.9	6.4
9	2.3	1.8
10	2.8	2.2
11	7.5	6.0

[a] Reactions were carried out at 25 °C in toluene-d_8 with [Ru] = 0.017 M. [b] For complex **2**, $k_{-1}/k_2 = 1.25$ at 50 °C (ref 7b).



Hammett constant

the more electron-poor, the faster dissociation

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2003**, *125*, 10103.

Ligand Effects

- *Halide Ligand*

➢ Cl→I: 250-fold increase in initiation (**1**→**3**, **8**→**10**)

✓ This would be due to the increase in steric bulk.

Ionic radii: Cl$^-$ 167pm, I$^-$ 206pm, Covalent radii: Cl$^-$ 99pm, I$^-$ 133pm

the larger size of I$^-$ →steric crowding→promotion of PR_3 dissociation

✓ Electronics may play a role, but cis electronic effect on dissociative ligand substitution is generally relatively small.

➢ Cl→I: 100-fold increase in k_{-1}/k_2 (poorly understood)

➢ Olefin metathesis activities: Cl→I, comparable or even lower

- *Carbene Ligand*

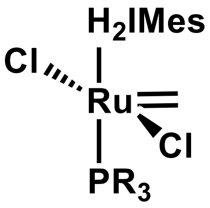
➢ k_1: H (**4**)<CHCHC(Me)$_2$ (**6**) <Ph (**1**) <CH_2CH_3 (**5**)

✓ sterically bulky and electron-donating→effective promotion of phosphine dissociation

➢ Complex **4** and especially **13** are extremely poor initiators.

✓ Phosphine-free **13** is an active olefin metathesis catalyst.

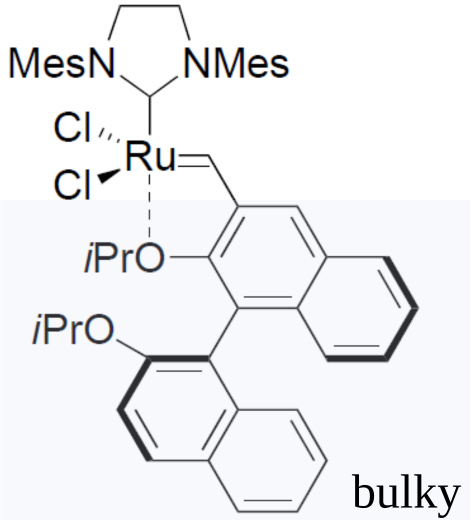
→The formation of these complex should be avoided.(substrate design)



13

Grubbs, R. H. *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 6543.

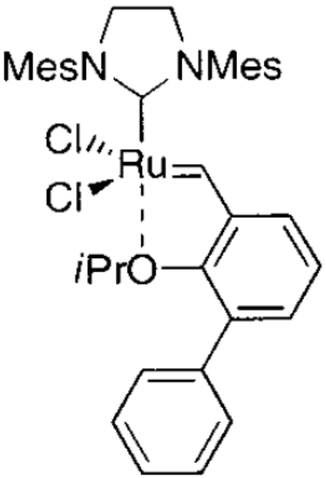
Improved Catalysts Rush



A

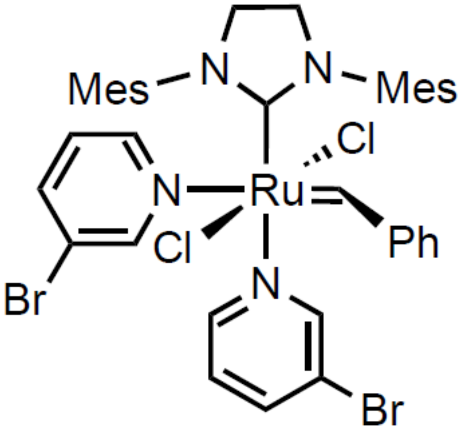
Activity in RCM
>2nd generation
Grubbs catalyst

Blechert, S. *et al.*, *Angew. Chem. Int. Ed.* **2002**, *41*, 794.



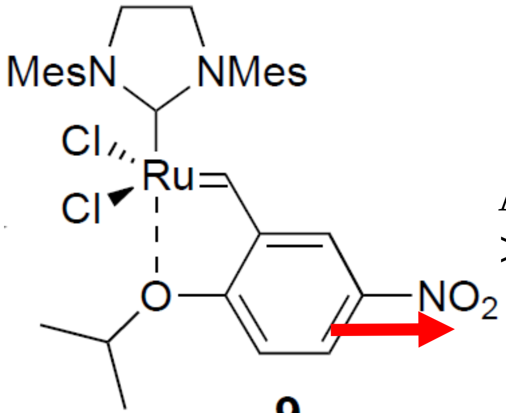
Activity in RCM
>complex A

Blechert, S. *et al.*, *Angew. Chem. Int. Ed.* **2002**, *41*, 2403.



k_{int} (at 5℃)[$\times 10^{-3} s^{-1}$]
4000
(2nd generation Grubbs cat.
0.0032)

Grubbs, R. H. *et al.*, *Angew. Chem. Int. Ed.* **2002**, *41*, 4035.



9

Activity in RCM
>2nd generation
Hoveyda-Grubbs
catalyst

Grela, K. *et al.*, *Angew. Chem. Int. Ed.* **2002**, *41*, 4038.