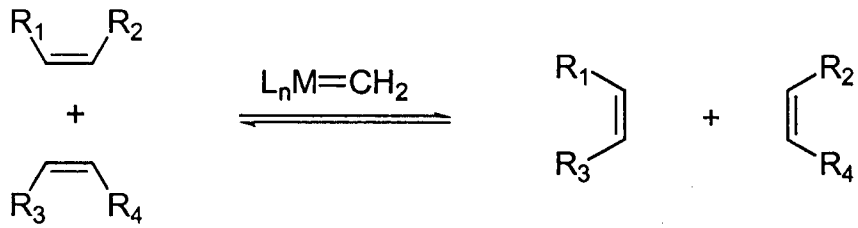
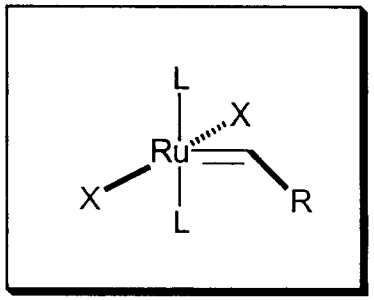
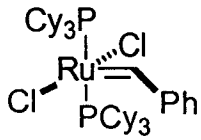
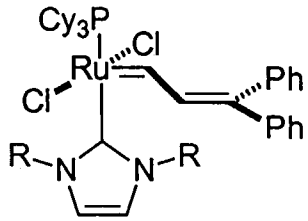
Mechanistic Studies of Olefin Metathesis

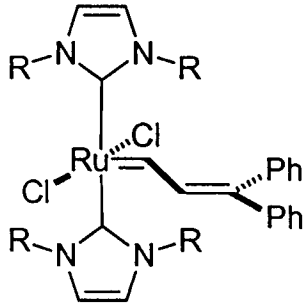
Jiping Fu April 10th, 2001







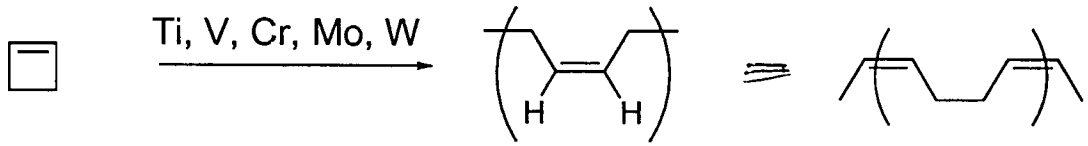




History of Olefin Metathesis

transition metal complexes

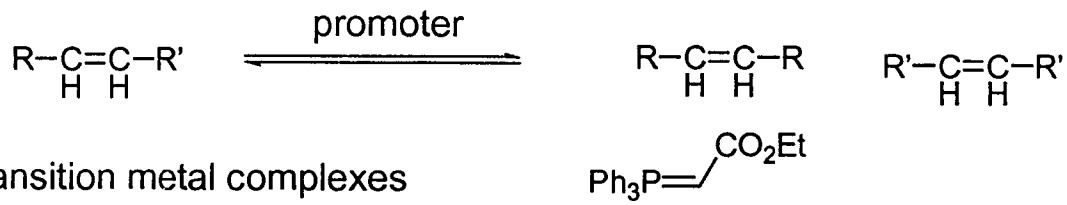
ring opening polymerization



Natta, G. *et al Makromol. Chem.* **1963**, *69*, 163.

Truett, W. L. *et al. J. Am. Chem. Soc.* **1960**, *82*, 2337

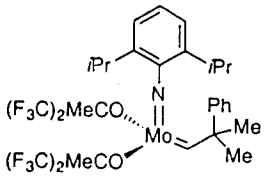
cross metathesis



transition metal complexes

well defined catalyst

ring-closing metathesis and ring-open metathesis

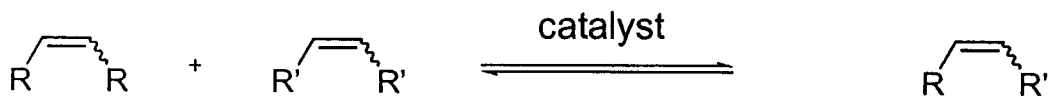


cross metathesis (synthetic useful)

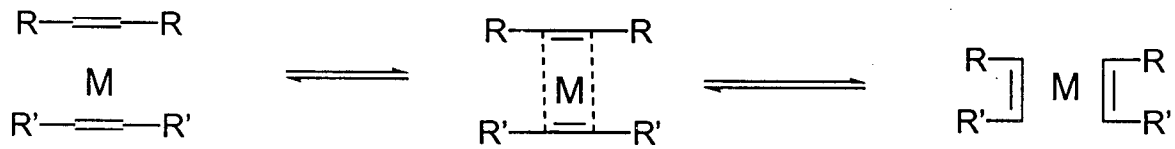
asymmetric metathesis & kinetic resolution

Possible Mechanisms

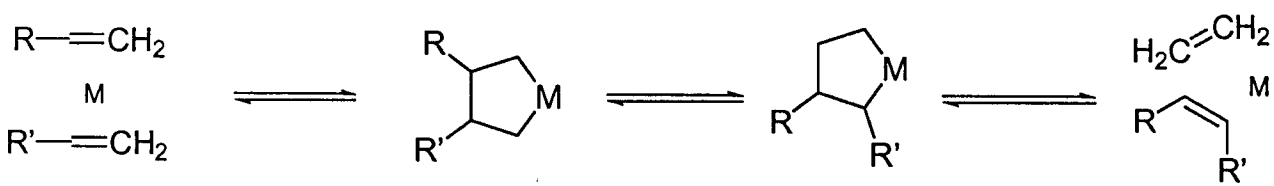
1. breaking C-C bonds or C=C bonds



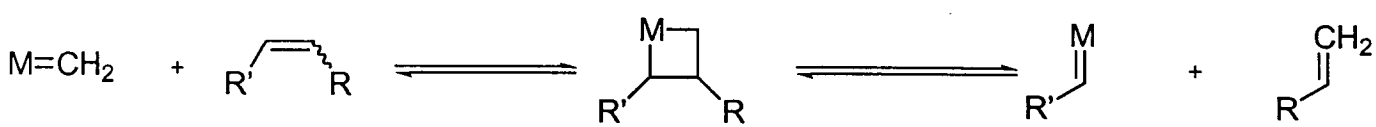
2. diolefin mechanisms



3. pairwise, nonconcerted mechanisms

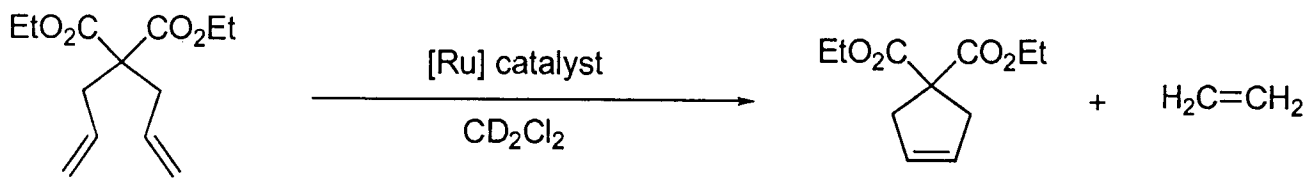


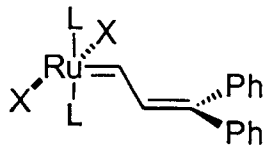
4. nonpairwise mechanisms



Chauvin, Y. *et al. Makrol. Chem.* **1970**, *141*, 161.

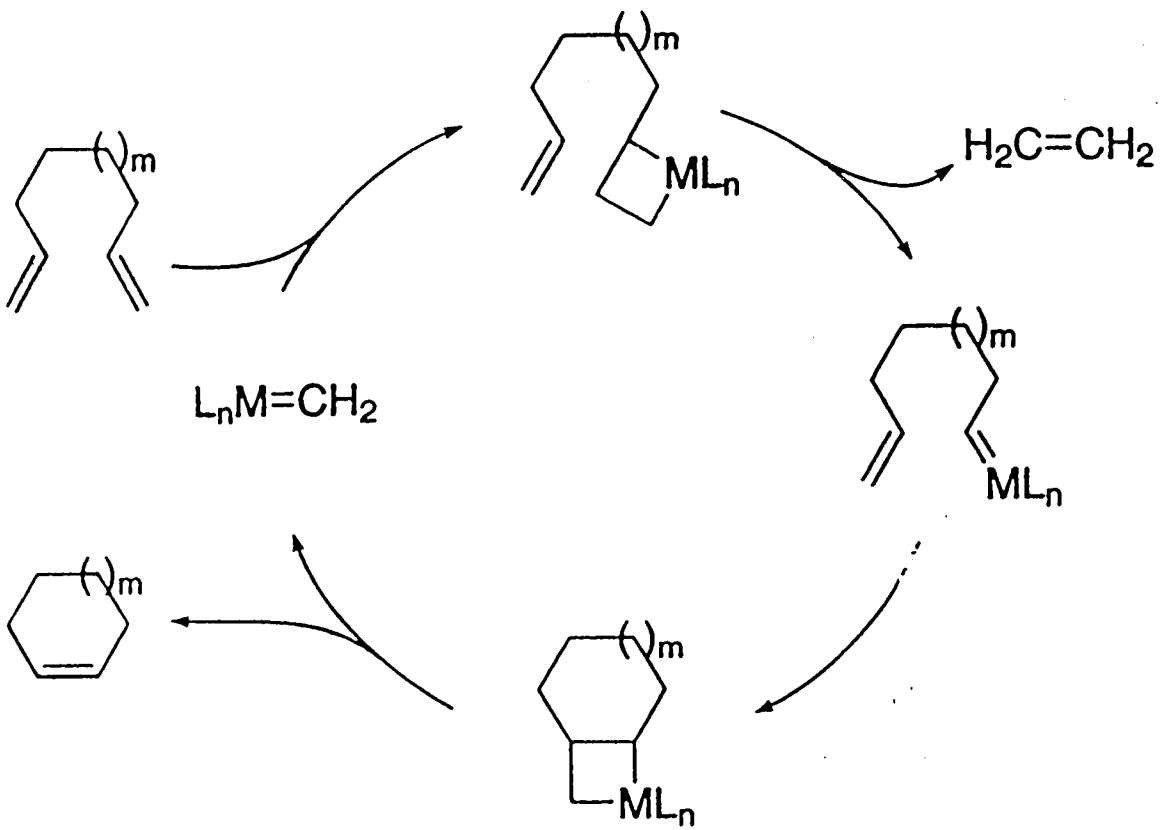
General Mechanism





X = Cl, Br, I

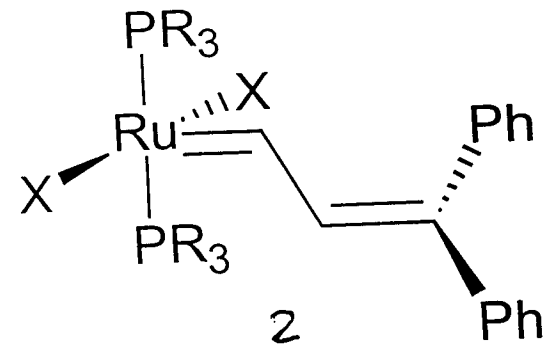
L = PCy_3, P*i*-Pr_3, PCy_2Ph, P*i*-Pr_2Ph



Ligand Effects of Catalysts

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.



- Larger and more electron donating phosphines produced more active catalysts,
  Smaller and more electron withdrawing halogens likewise produced more active catalysts.

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

kinetic Studies: Effect of Phosphine

1. reaction in absence of PCy_3

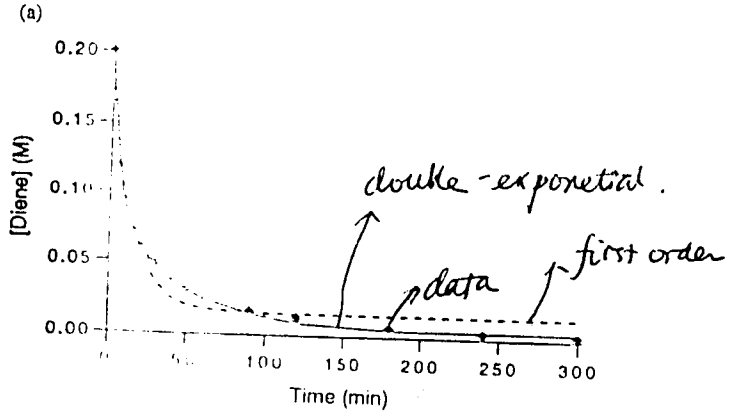
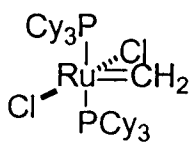


Figure 1. [illegible] Representative plot of diene concentrations vs time for catalyst 4a. The [illegible] was carried out with $[diene]_0 = 0.2$ M and [catalyst [illegible] 0.01 M in CD_2Cl_2 at 20 °C. The filled diamonds are the data poi[illegible] and the solid line is the double-exponential fit: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

because of initiation ?



behave the same way

2. reaction ½ order in [Ru]

reaction in presence of PCy_3

reaction become first order in diene

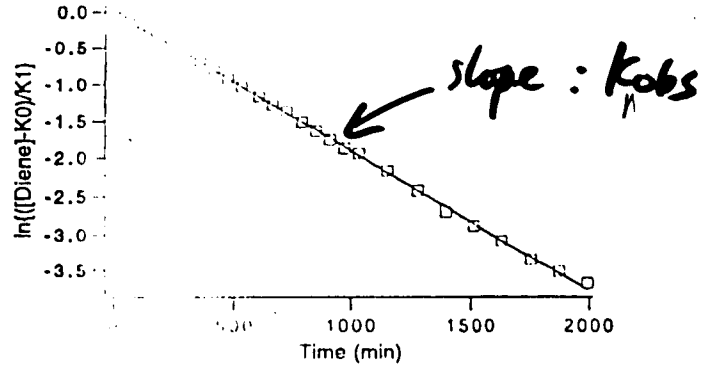


Figure 2. [illegible] plot of diene concentration vs time for the ring-closing metathesis of diethyl diallylmalonate in the presence of 0.02 M PCy_3, where $[Ru]_0 = 0.02$ M and $[diene]_0 = 0.2$ M. The reactions were carried out in CD_2Cl_2 at 30 °C. K_0 and K_1 are the constants from the first-order fit $[diene](t) = K_0 + K_1 \exp(-K_2 t)$, 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 linea[illegible] intercept = (0.45 ± 7.64) × 10^{-3}; slope = (−1.88 ± 0.01) × [illegible] linear correlation coefficient = 1.00

reaction 20 times slower

with 1equiv of [PCy_3] (to cat.)

Kinetic Studies in Presence of Phosphine

reaction order in phosphine

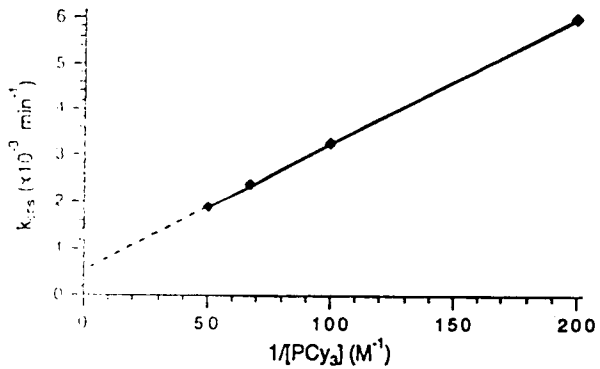


Figure 3. Plot of k_{obs} vs reciprocal phosphine concentration for the ring closing metathesis of diethyl diallylmalonate at varying phosphine concentrations, with $[diene]_0 = 0.2$ M and $[Ru]_0$ (6) = 0.02 M. The reactions were carried out in CD_2Cl_2 at 30 °C. The filled diamonds are the data points, 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 ± 0.13) × 10^{-4}; slope = (2.73 ± 0.01[illegible] × 1[illegible]; linear correlation coefficient = 1.00.

reaction order in [Ru$_0$]

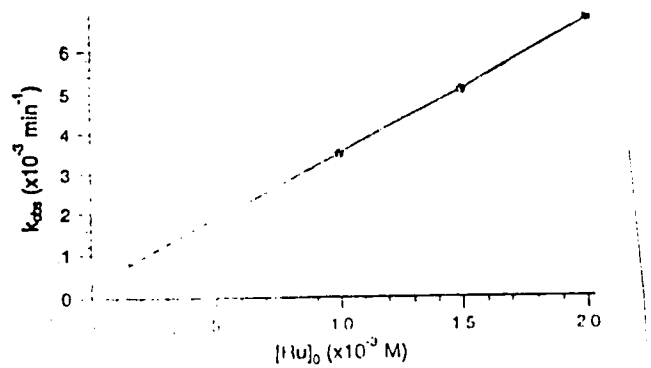


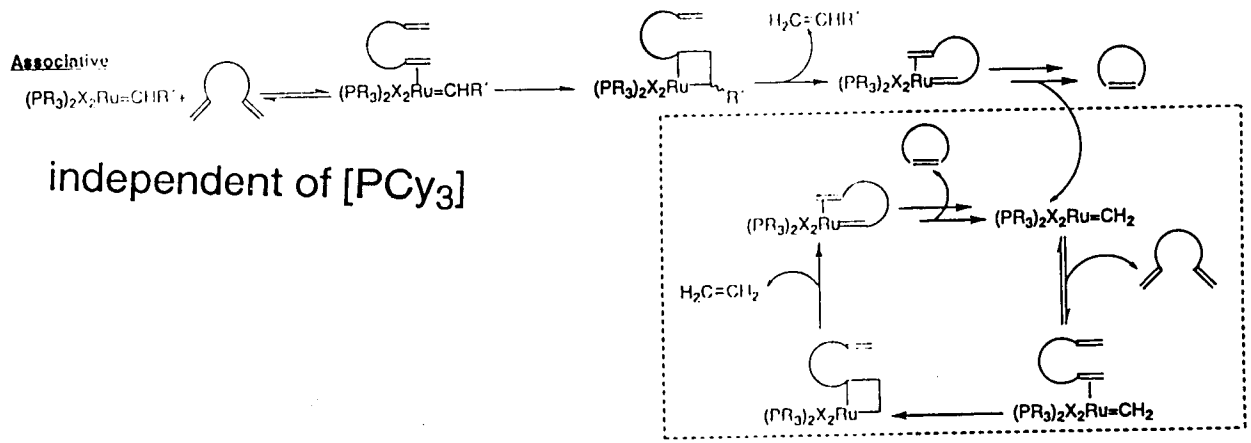
Figure 5. Plot of k_{obs} vs catalyst concentration for the ring-closing metathesis of diethyl diallylmalonate at varying catalyst concentrations in the presence of 0.0035 M PCy_3, with $[diene]_0 = 0.2$ M. The reactions were carried out in CD_2Cl_2 at 30 °C. The filled circles are the data points, the 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 ± 0.72) × 10^{-4}; slope = 0.323 ± 0.005; linear correlation coefficient = 1.00.

reaction is -1 order in PCy$_3$

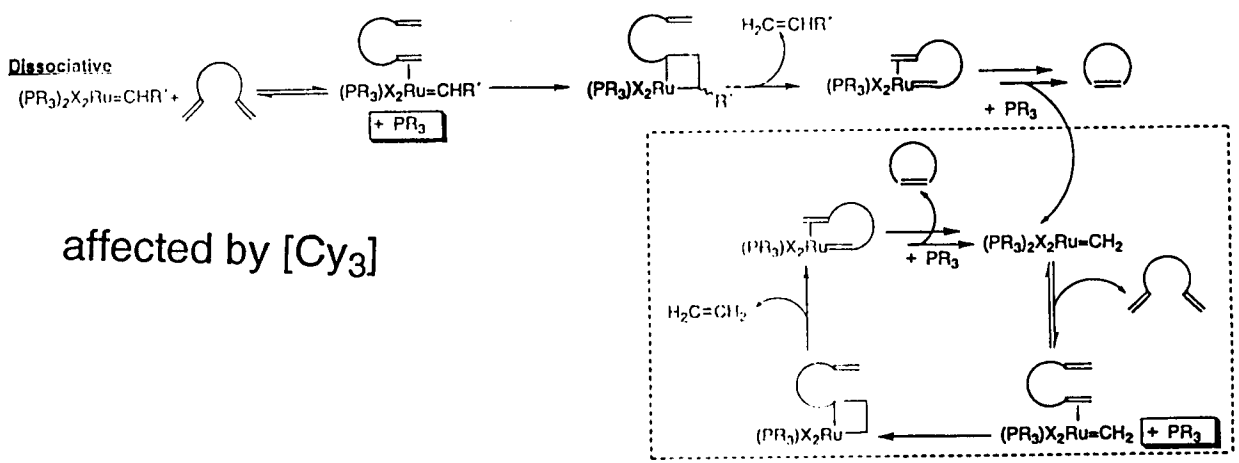
reaction is first order in [Ru$_0$]

There is an additional phosphine independent term in the rate expression

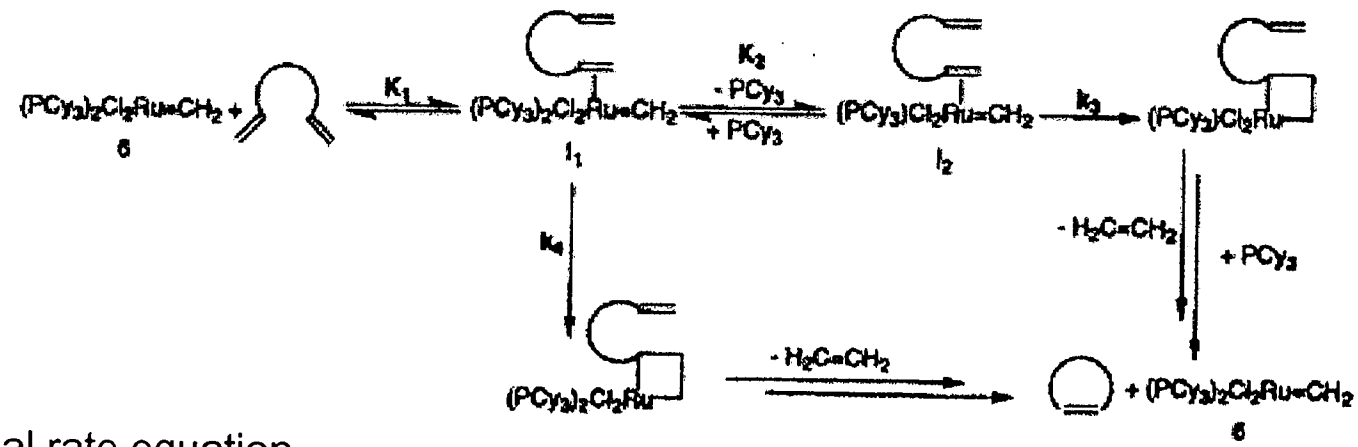
the Possibility of Dual Pathways



independent of [PCy_3]



affected by [Cy_3]



final rate equation

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

$$\boxed{-\frac{d[\text{diene}]}{dt} = \left(k_3\frac{K_1K_2}{[PCy_3]} + k_4K_1\right)[6][\text{diene}] \qquad (4)}$$

[PCy2] < 5% [Ru0]

major pathway dissociate pathw

in presence of additional phosphine

first order in [Ru], [diene], -1order in $[PCy_3]$

in absence of phosphine

Concentration at time t:	$[Ru]_0$	$[Diene]_t$	x	x

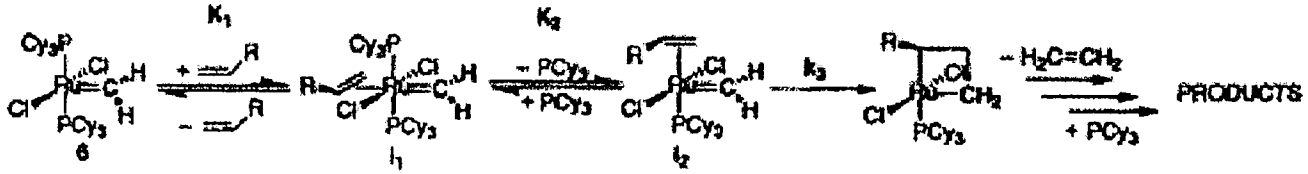
$$x = [PCy_3] = \sqrt{K_{eq}[Ru]_0[Diene]_t}$$

1/2 order in $[Ru_0]$,

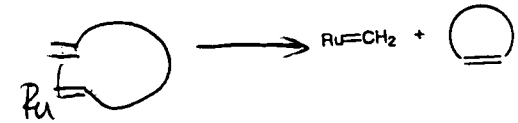
Approaches of Olefins

initial coordination of olefin

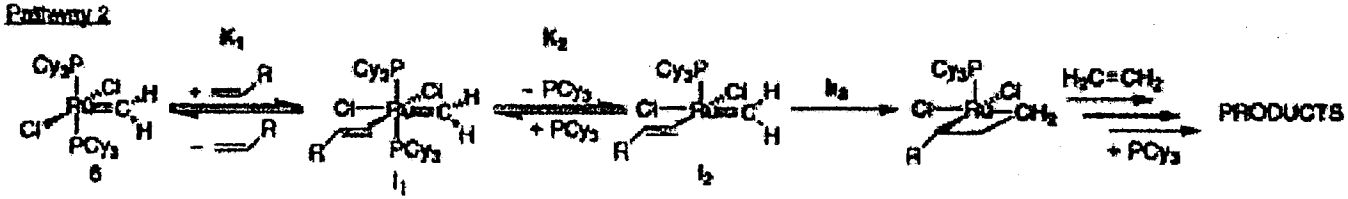
Pathway 1



supports for pathway 2:
RCM formation of small ring
only cis is possible



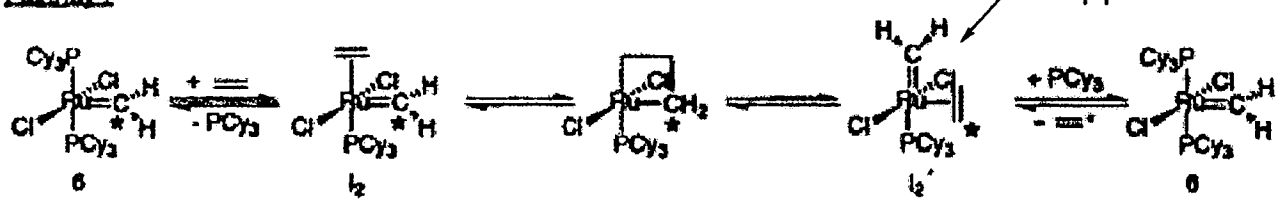
Pathway 2



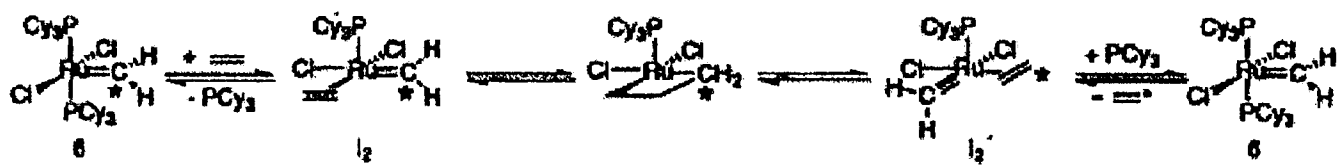
microscopic reversibility

ligands rearrangement must happen

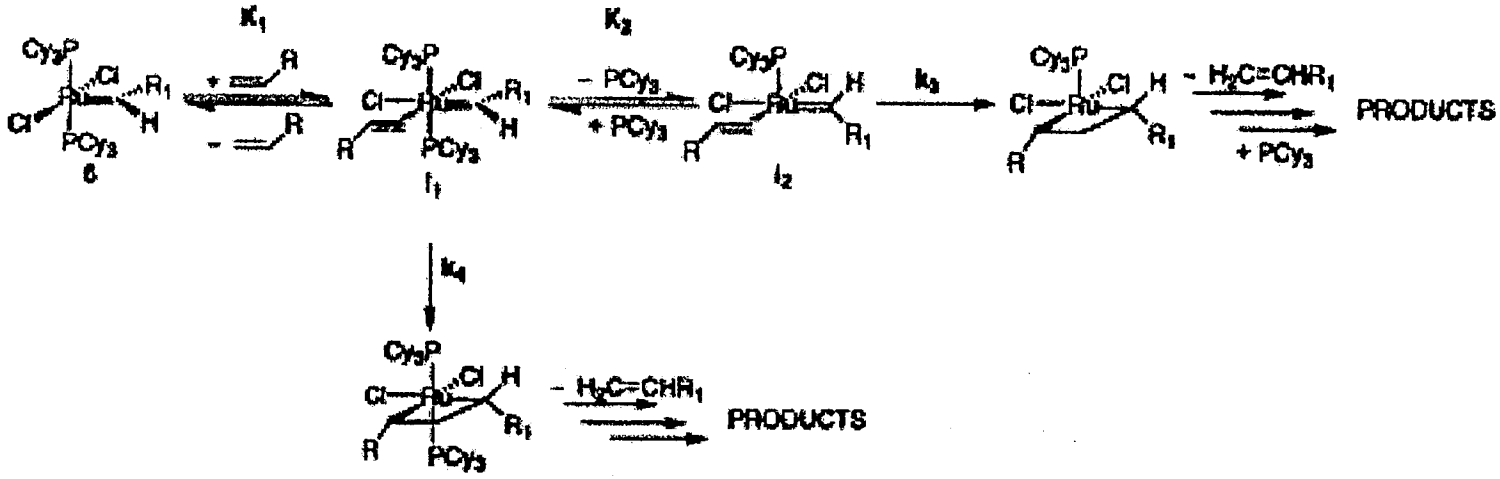
Pathway 1



Pathway 2



Explaination for the Effects of Ligands



effect of halogens

electronic: from Cl to I, olefin bond tighest for Cl, weakest for I due to the trans effect

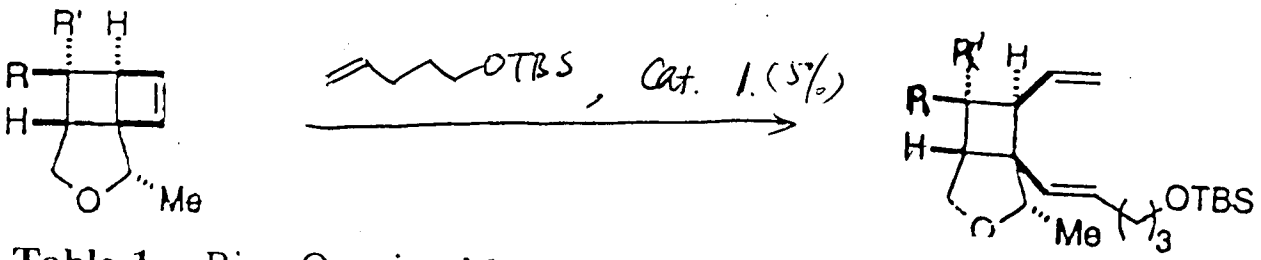
steric: one halogen cis to coming olefin, larger halogen disfavor binding

effect of phosphine

electron rich: help stabilizing 16 electron I2

steric: bulkier phosphine favor phosphine dissociation

Catalyst Caught in Act



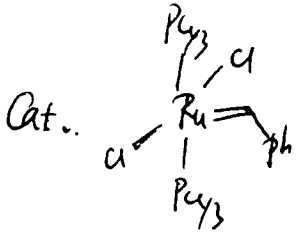
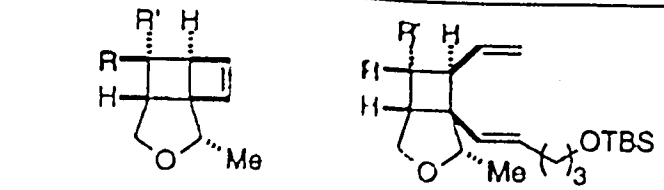
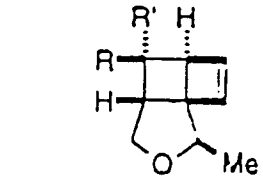


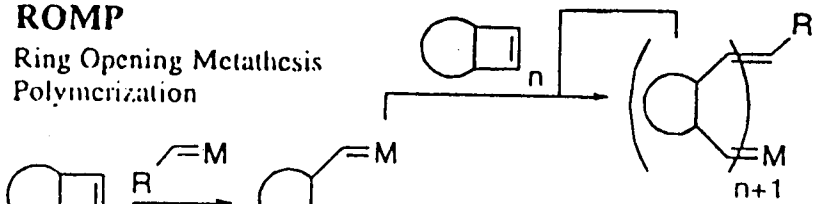
Table 1. Ring-Opening Metatheses[a]

entry	substrate	major product	yield[b]
1	5 R = Pr, R' = H	7 R = Pr, R' = H	72% (8:1) (trans : cis)
2	6 R = H, R' = Pr	8 R = H, R' = Pr	81% (7:1)
3	9 R = Pr, R' = H	–	0%
4	10 R = H, R' = Pr		0%



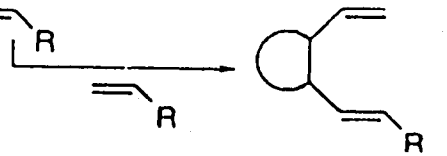


ROMP
Ring Opening Metathesis Polymerization



(1)

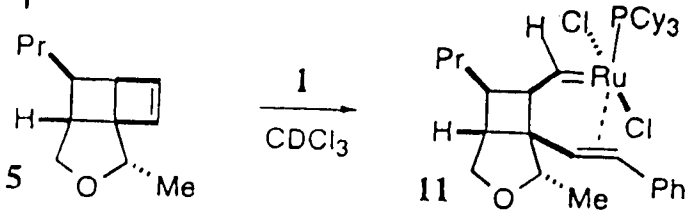
ROM
Ring Opening Metathesis



(2)

Snapper, M. L.; *et al. J. Am. Chem. Soc.* **1997**, *119*, 7157.

Complex: intermediate could be isolated.



70%

stable, purified by silicagel.

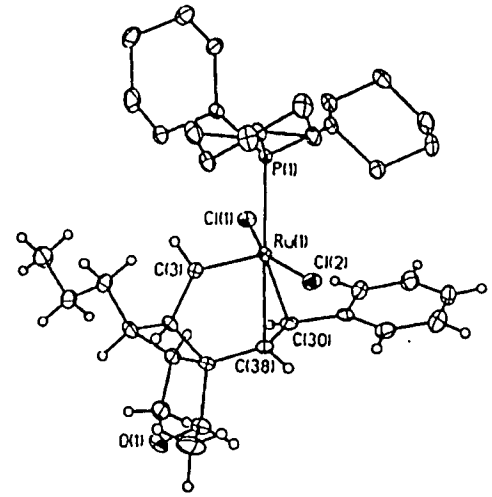
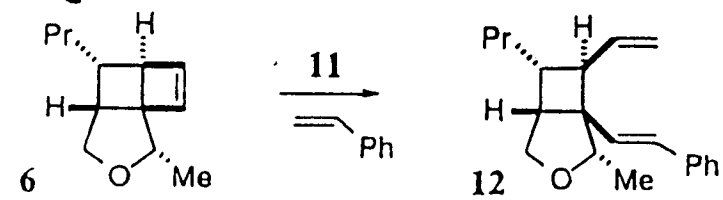


Figure 1. ORTEP drawing of **11** with 30% thermal ellipsoids.[6]

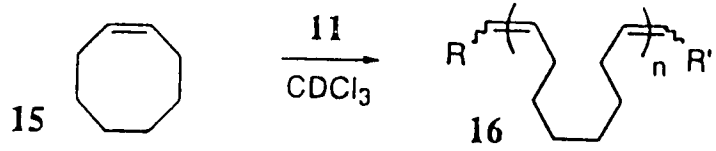
- 11 as catalyst in RCM, ROM.



(4) 74%

(5) 84%

- Kinetic studies.

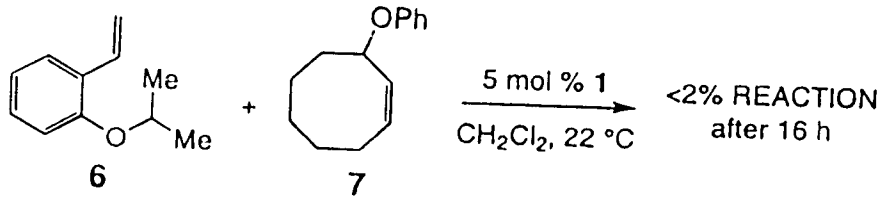


(6)

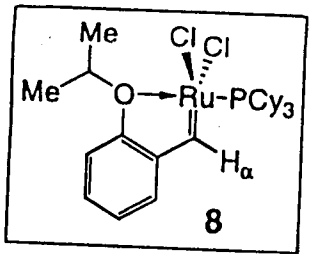
initiation rate 4 times slower than

propagation rate 8 times faster the

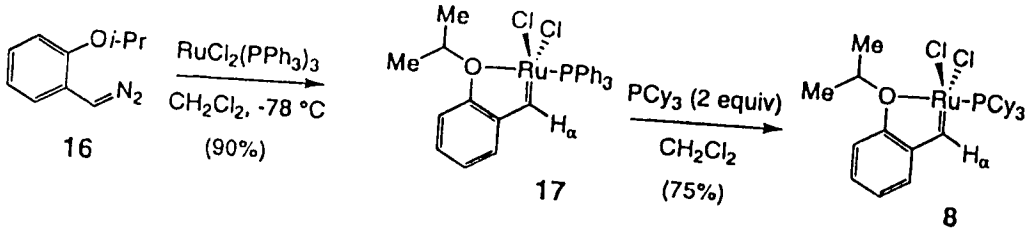
Chelating Carbene

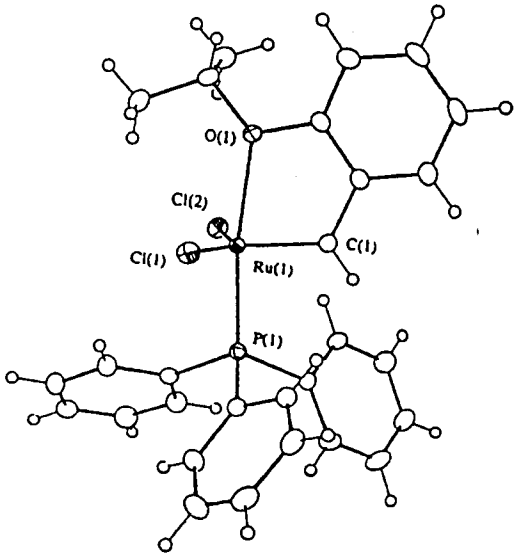


possible explanation for slow reaction



independent synthesis of 8.

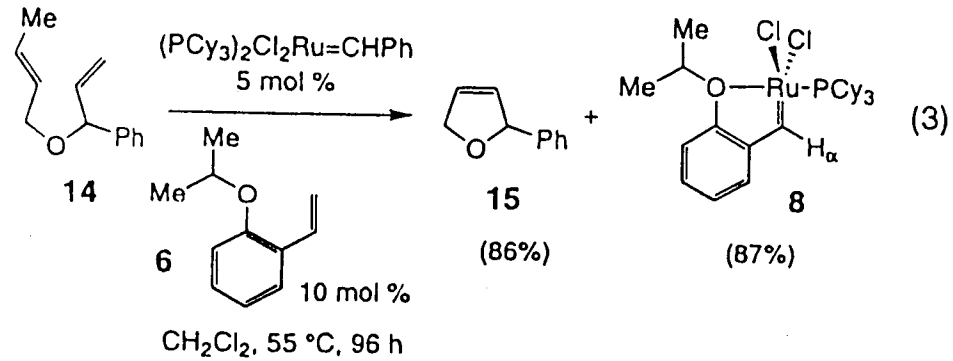


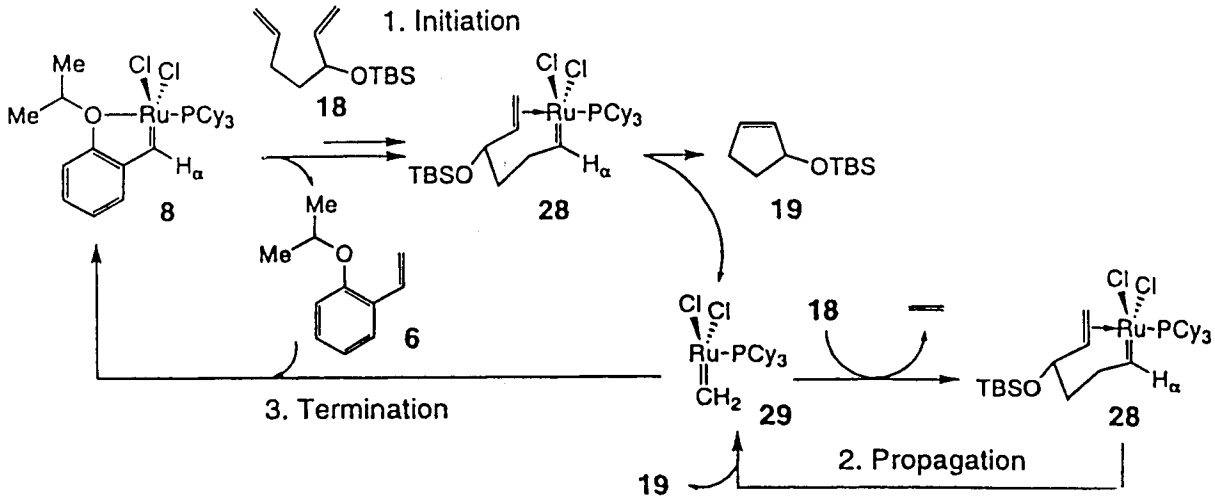


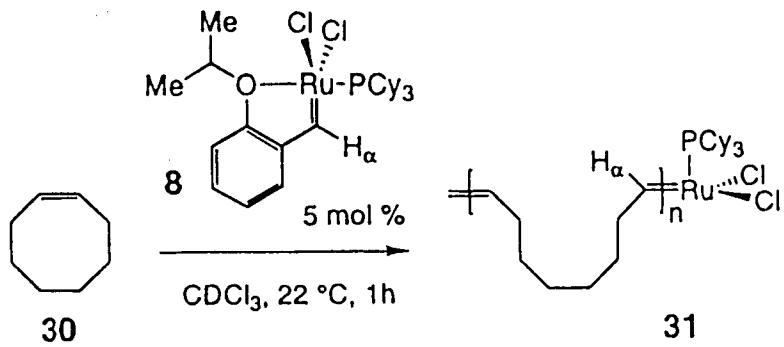
X-Ray of 17.

Hoveyda, A. H.; *et al. J. Am. Chem. Soc.* **1999**, *21*, 791.

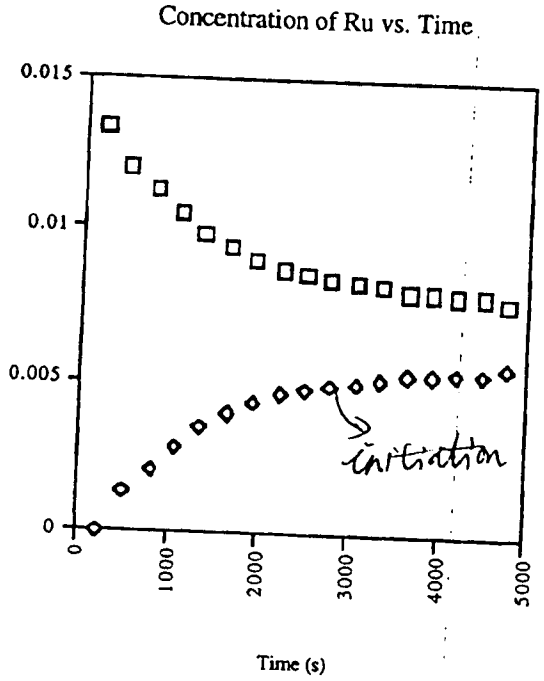
Recyclable Catalyst

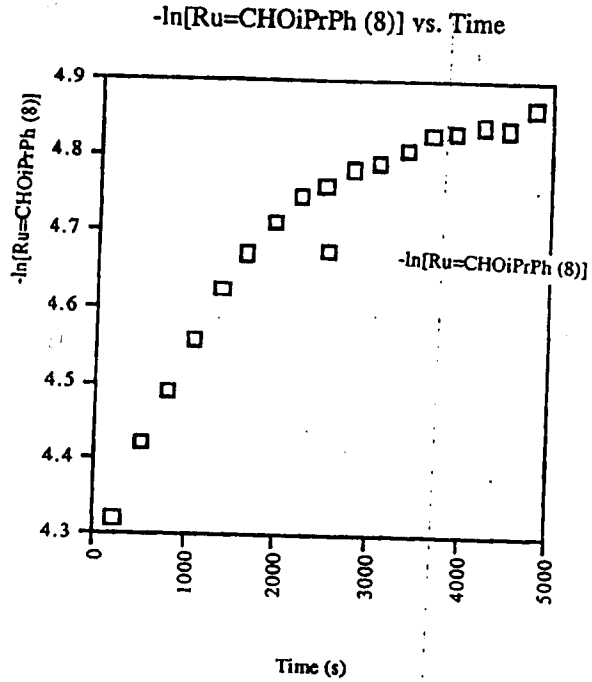


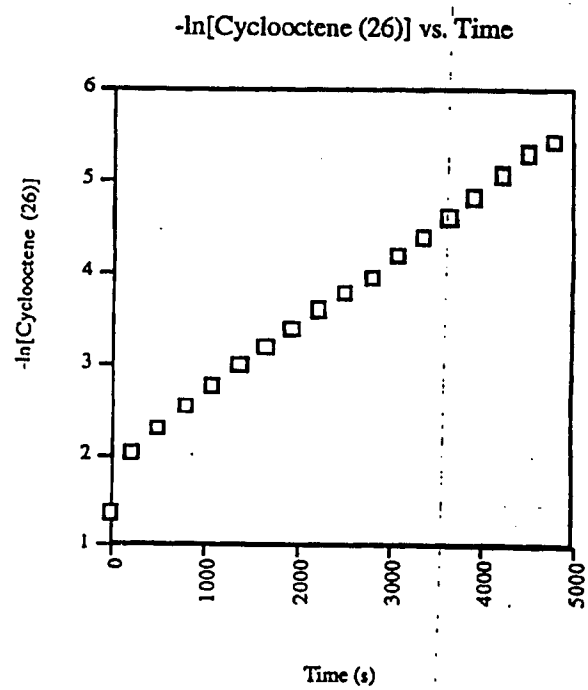




(4)







□ [Ru=CHOiPrPh (8)] (mol/L)

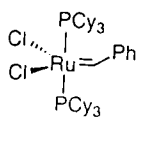
◇ [Propagating Ru-Carbene] (mol/L)

Compared to 1. 8 initiate 30 times slower

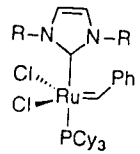
8 propagate 4 times faster

propagation

Second Generation Catalyst



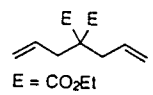
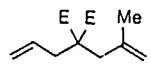
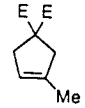
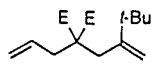
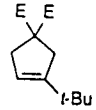
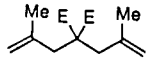
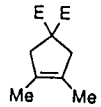
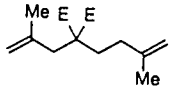
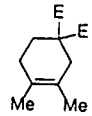
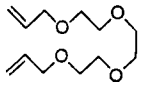
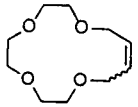
2



R = C_6H_2-2,4,6-$(CH_3)_3$

3

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

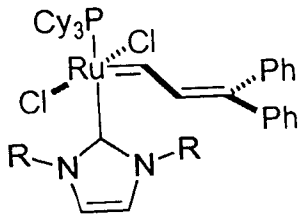
Entry	Substrate	Product	Time (min)	Yield with **2** (%)[a]	Yield with **3** (%)[a]
1	 E = CO_2Et		30	100	100
2			30	82	100
3			60	N.R.	100
4			90	N.R.	40
5			90	N.R.	95
6			60	39[b]	55 (45)[c]

[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.

the IMes Ligand

Calorimetric investigation:



2

$$1/4[Cp^*RuCl]_4 + \text{IMes} \xrightarrow[\text{RT}]{\text{THF}} Cp^*Ru(IMes)Cl \quad (1)$$

3

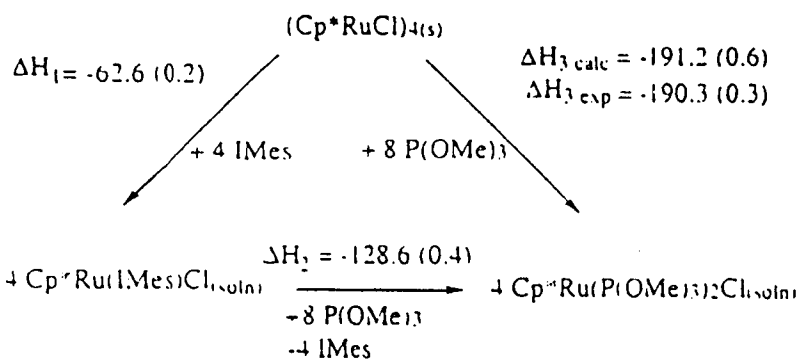
$$2 + 4L \xrightarrow[\text{RT}]{\text{THF}} 4Cp^*Ru(L)Cl \quad (2)$$

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

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

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

Consistency of data



$$\underset{4}{Cp^*Ru(PCy_3)Cl} + \text{IMes} \xrightarrow[\text{RT}]{\text{THF}} \underset{3}{Cp^*Ru(IMes)Cl} + PCy_3 \quad (3)$$

$\Delta H_{calcd} = -5$ kcal/mol

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

π Acceptor Ability

Table 3. The ν(CO) absorptions [cm^{-1}] in carbene complexes *fac*-[$MoL_3(CO)_3$] [139, 140].

$[Mo(PPh_3)_3(CO)_3]$	1835	1934
$[Mo(CH_3CN)_3(CO)_3]$	1783	1915
$[Mo(CH_3CN)(L-L)(CO)_3]$[a]	1780	1896
$[Mo(py)(L-L)(CO)_3]$[a]	1772	1891
$[MoL_3(CO)_3]$[a]	1764	1881
$[Mo(py)_3(CO)_3]$	1746	1888

[a] L and L–L are heterocyclic mono- and dicarbene ligands, respectively.

Table 4. The ν(CO) absorptions in *trans*-[$RhL^1L^2(CO)X$] complexes [65].

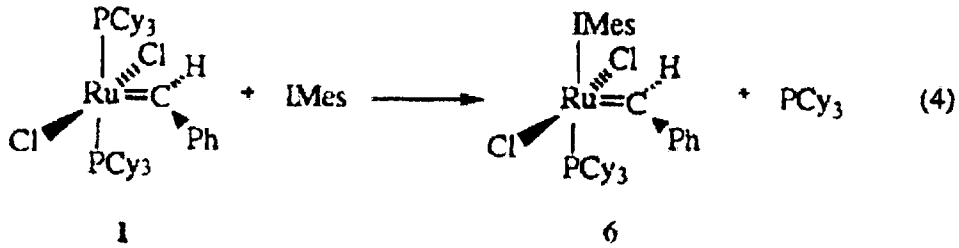
L^1, L^2[a]	X	$\tilde{\nu}$ [cm^{-1}] (medium)
L^{Me}, L^{Me}	Cl	1924 (KBr)
L^{Cy}, L^{Cy}	Cl	1929 (KBr)
PCy_3, PCy_3	Cl	1939 (benzene)
PMe_3, PMe_3	Cl, Br, I	1957, 1958, 1960 (benzene)
L^{CHPh_2}, PPh_3	Br	1968 (KBr)
PPh_3, PPh_3	Cl	1983 (benzene)
$L^{CHPh_2}, P(OPh)_3$	Br	1994 (KBr)
$P(C_6F_5)_3, P(C_6F_5)_3$	Cl	2003 (benzene)
$P(OPh)_3, P(OPh)_3$	Cl, Br	2018, 2020 (benzene)

[a] L^{Me} = 1,3-Dimethyl-2,3-dihydro-1*H*-imidazol-2-ylidene, L^{Cy} = 1,3-bis(cyclohexyl)-2,3-dihydro-1*H*-imidazol-2-ylidene, L^{CHPh_2} = 1,3-bis(diphenylmethyl)-2,3-dihydro-1*H*-imidazol-2-ylidene.

π acceptor ability: NO > CO > RNC > PF_3 > $P(OPh)_3$ > P(aryl) > P(alkyl) > RCN > N-heterocycle > Py

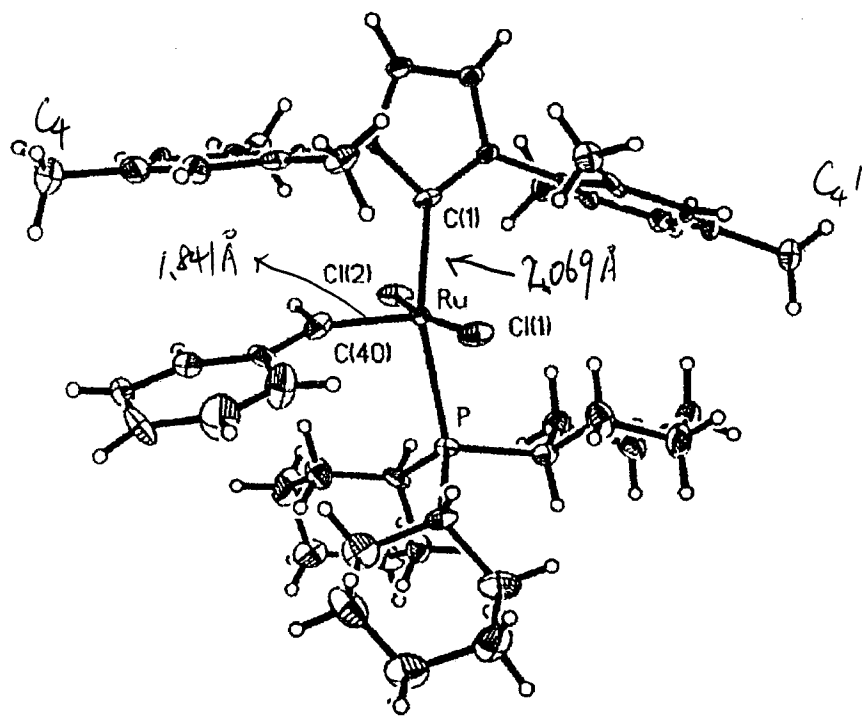
Herrmann, W. A.; *et al. Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2162.

the IMes Ligand



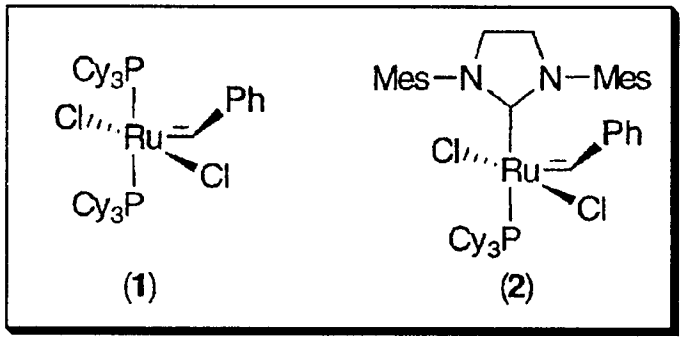
only one PCy3 could be replaced even in presence of 10 equiv. of IMes

$\angle C_4 - Ru - C_{4'} = 150.7°$

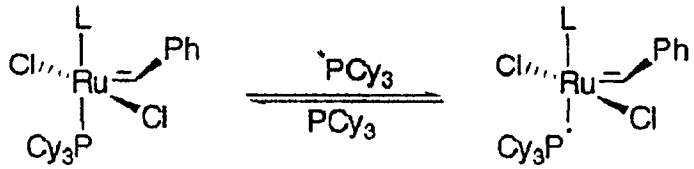


6

the Kinetic Studies



phosphine exchange reaction



^{31}P magnetization transfer reaction

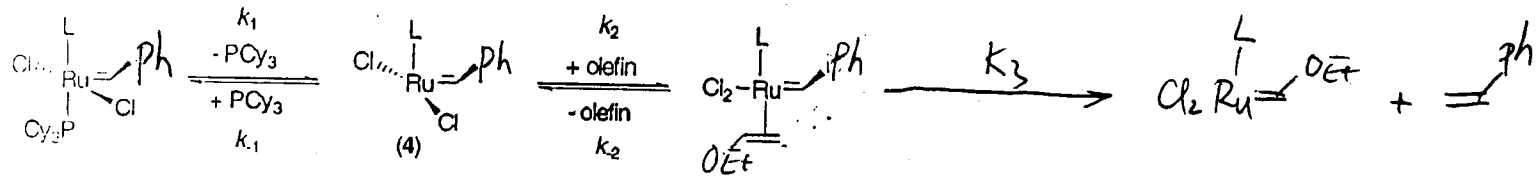
exchange rate constant

1 9.6 S^{-1} **2** 0.13 S^{-1}

the dessociation of PCy_3 can not account for the reacivity

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

the Kinetic Studies



- apply steady state to 4,
- all steps following olefin binding is fast
- pseudo-first order in olefin.

rate equation.

$$1/k_{obs} = k_{-1}[PCy_3]/k_1k_2[olefin] + 1/k_1 \qquad (1)$$

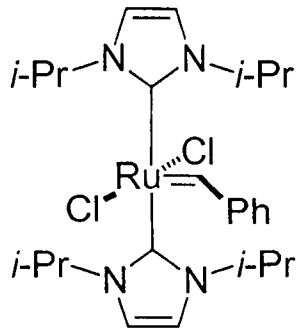
$k_{-1}/k_2 = 15300$ **1**

$k_{-1}/k_2 = 1.25$ **2**

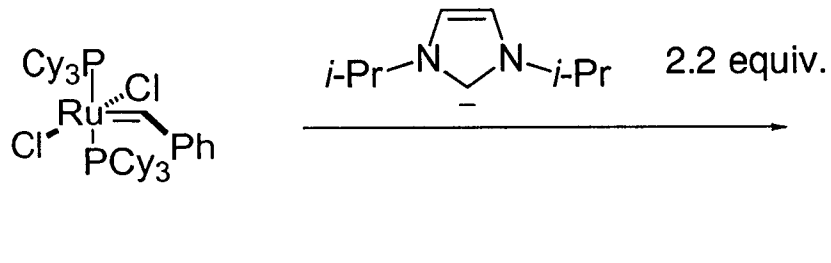
result of kinetic studies: the catalyst bind olefin more favorable

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

Bis-carbene Catalyst



biscarbene catalyst



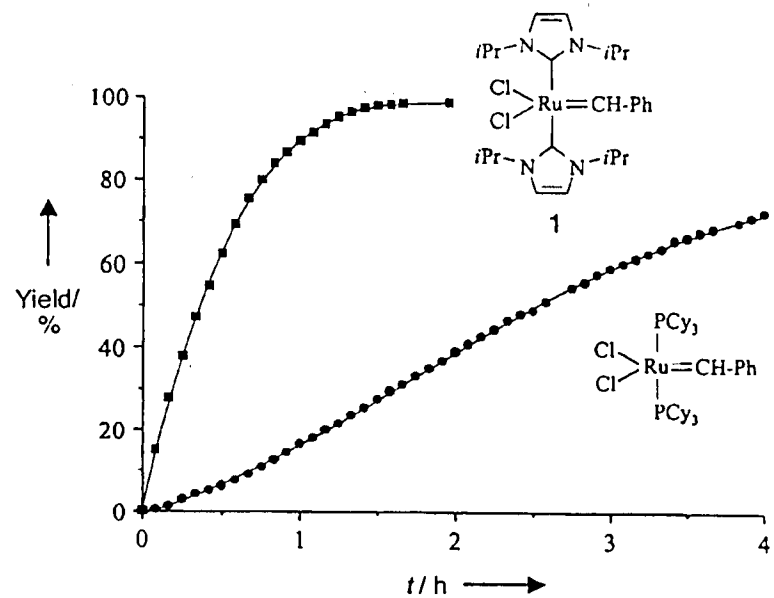


Figure 2. ROMP of cyclooctene. NMR-monitored comparison of **1** and a known ruthenium phosphane catalyst.[3d, 10] $T = 25\,°C$, 2.50 μmol catalyst in 0.50 mL of CD_2Cl_2; [cyclooctene]/[catalyst] = 250/1.

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

Reactivities of Olefins

Metathesis of Terminal Olefins with Ruthenium Benzylidene

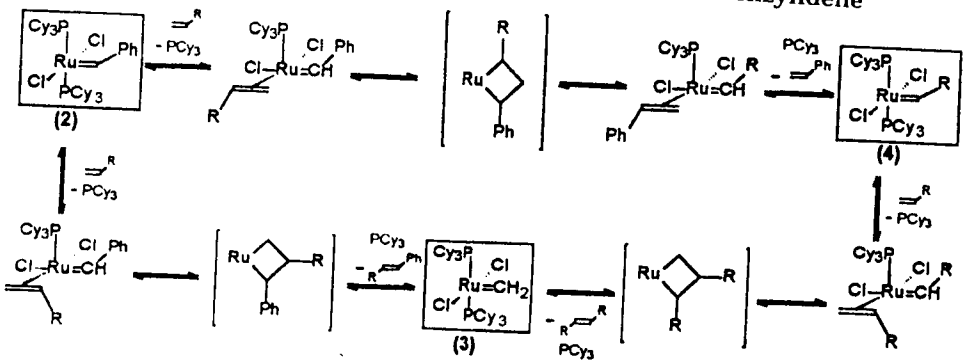


Table 1. Second-Order Rate Constants (k) for Metathesis Reactions Using 31 equiv of Olefin

	olefin	initiator	product	Temp / °C	k ± SDOM[a] / L/mole•sec
1	styrene-d_8	Ru=Ph	Ru=CD Ph-d_5	7	$1.3 \pm 0.4 \times 10^{-3}$
2	styrene-d_5	Ru=Ph	Ru=CH Ph-d_5	7	$2.15 \pm 0.01 \times 10^{-3}$
3	styrene	Ru=C_4H_7	Ru=Ph	7	$7.6 \pm 0.2 \times 10^{-3}$
4		Ru=Ph	Ru=C_4H_7	7	$1.48 \pm 0.04 \times 10^{-3}$
5		Ru=Ph	Ru=C_4H_7	35	$\sim 10^{-2}$
6		Ru=Ph	Ru=	7	$1.02 \pm 0.06 \times 10^{-3}$
7		Ru=Ph	Ru=CH_2	35	$2.5 \pm 0.2 \times 10^{-4}$
8		Ru=Ph	Ru=CH_2	35	minor in 4 days
9		Ru=Ph		35	no rxn.
10	Ph	Ru=Ph		35	no obs. Rxn.
11		Ru=Ph	Ru=C_2H_5	35	$3.0 \pm 0.4 \times 10^{-4}$
12		Ru=Ph	Ru=C_2H_5	35	$7.6 \pm 0.8 \times 10^{-4}$
13		Ru=CH_2	Ru=C_4H_7	25	$1.64 \pm 0.1 \times 10^{-4}$ (6000 sec)
14		Ru=CH_2	Ru=C_4H_7	35	$6.10 \pm 0.04 \times 10^{-4}$ (1000 sec)
15		Ru=C_2H_5	Ru=C_4H_7	7	$\sim 7 \times 10^{-3}$

[a] SDOM = Standard Deviation of the Mean

Grubbs, R. H.; *et al. Organometallics* **1998**, *17*, 2484.

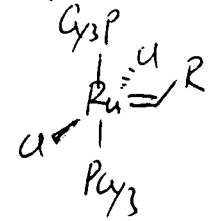
① Steric:

entry 6. 7. 8. 9.

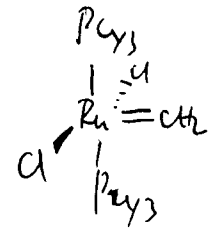
② trans react slower.

11, 12

③ Kinetic product for non-steric hinde olefin



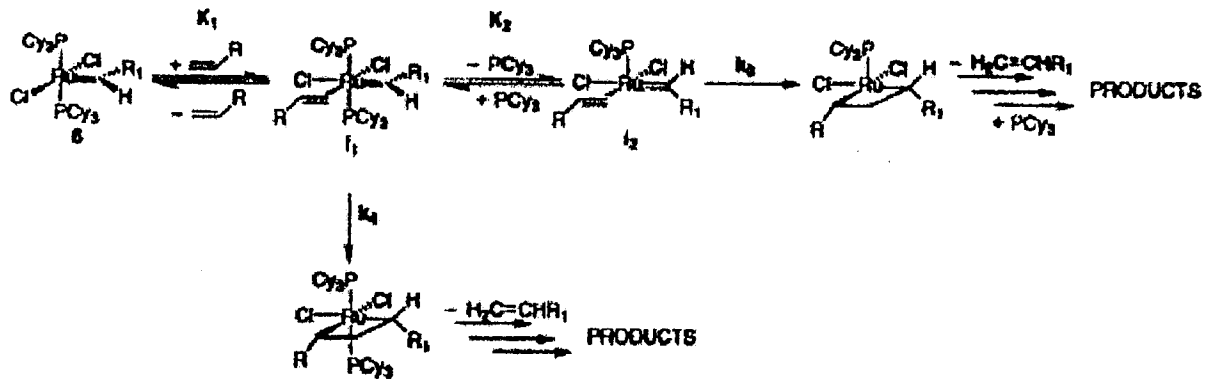
④ steric hindered olefin product



⑤ Ru=Ph initiate faster than R=CH2

Conclusion

dual pathways dissociative pathway major



IMes: steric hindered ligand, strong σ donor; weak π acceptor

Origin of increased reacitivity: strong binding of olefin not due to the dissociation of phosphine.