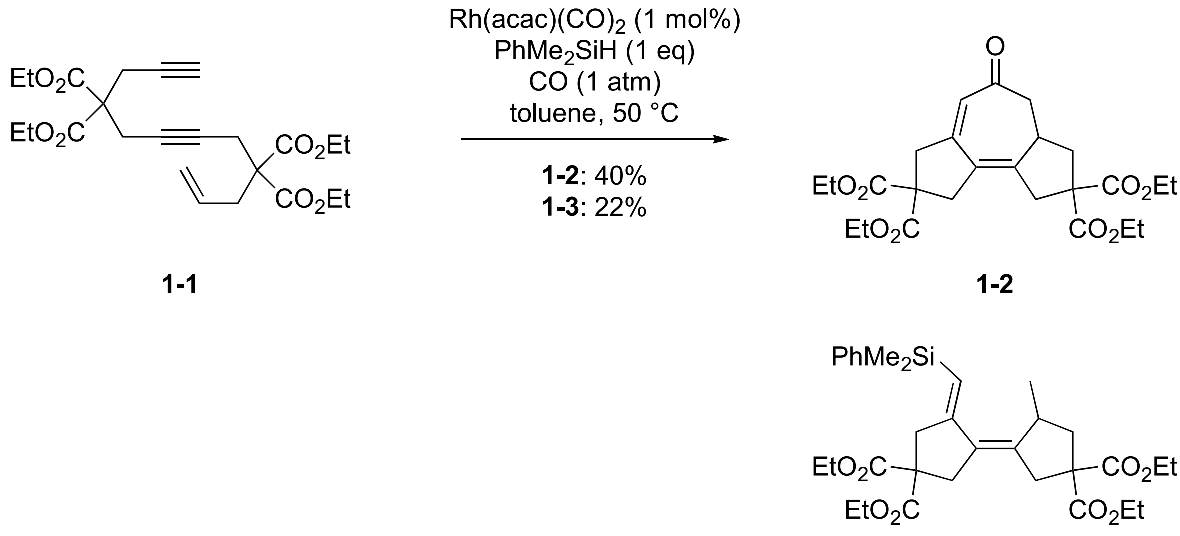
Problem Session (3)

2017/12/22 Akira Hirose

Please provide the reaction mechanisms.

1

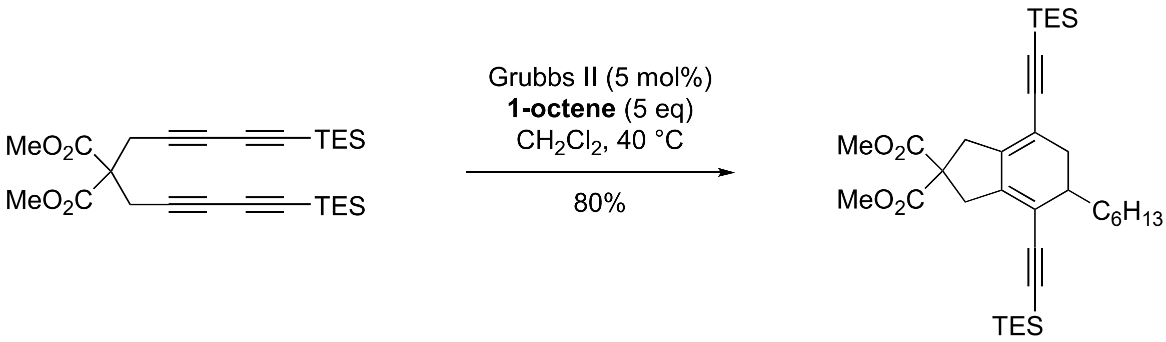


1-1

1-2

1-3

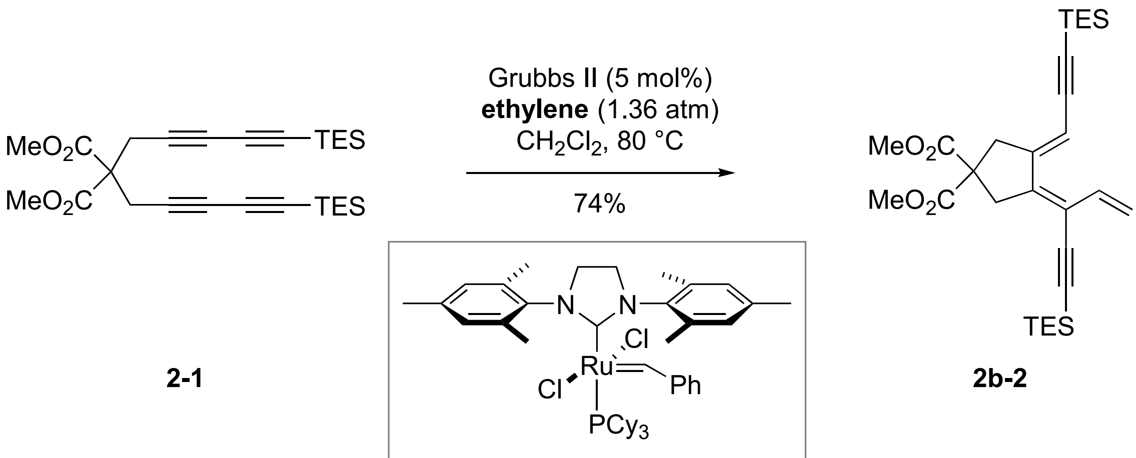
2 (a)



2-1

2a-2

(b)



2-1

Grubbs II

2b-2

3

3-1

3-2

Problem Session (3) -Answer-

2017/12/22 Akira Hirose

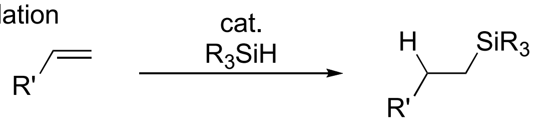
Topic: Metal-catalyzed cyclization of multiynes

related PS/LS -> 100904_PS_Hidenori_TODOROKI: Rh-catalyzed [5+2] cycloaddition
101127_PS_Shin_KAMIJO: Gold catalysis
110425_PS_Masanori NAGATOMO: Ynolate
120707_PS_Tomomi_GOTO: Ynamide
170127_PS_Tokumoto_Kotaro: Ynamide

121013_LS_Komei_Sakata: Aryne ene reaction
161024_LS_Takahiro_KAWAMATA: dehydro Diels-Alder reaction etc...

1 → **silicon-initiated carbometalation**

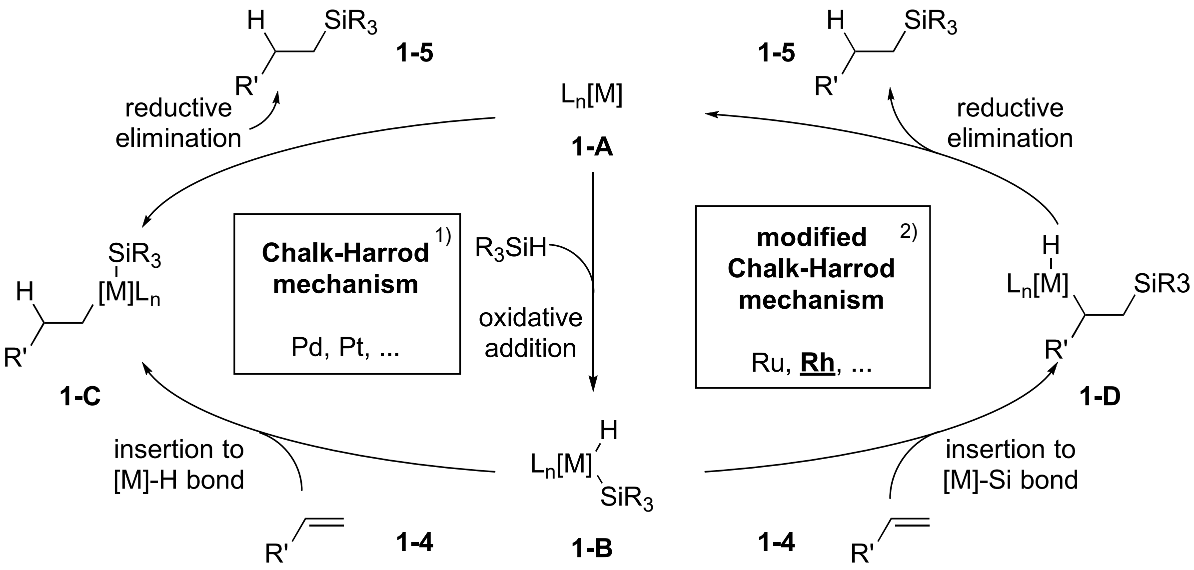
1. hydrosilylation



1-4 **1-5**

cat. = peroxide (1947~), metal (1949~)

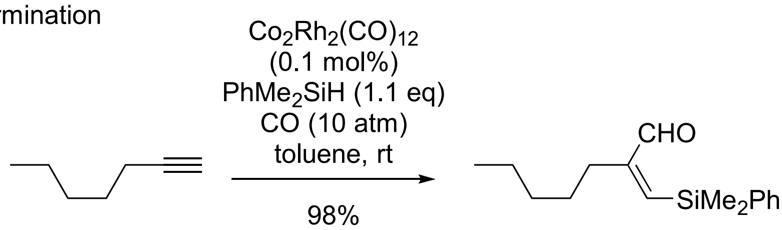
· reaction mechanisms



1) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16.
2) Schroeder, M. A.; Wrighton, M. S. *J. Organomet. Chem.* **1977**, *128*, 345.

2. Studies by Ojima

· silylformination



1-6 **1-7**

Ojima. et al., *Tetrahedron* **1993**, *49*, 5431.

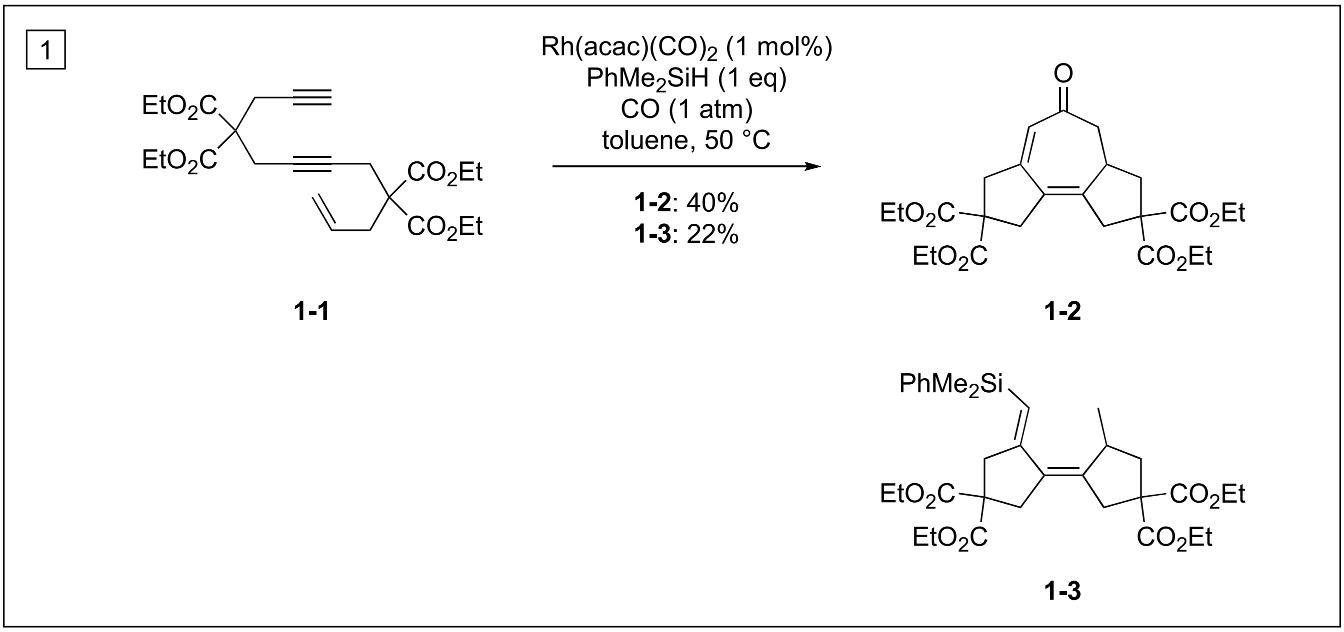
· <u>si</u>lyl<u>c</u>yclo<u>ca</u>rbonylation (SiCCa)

· <u>si</u>lyl<u>ca</u>rbo<u>c</u>yclization (SiCaC)

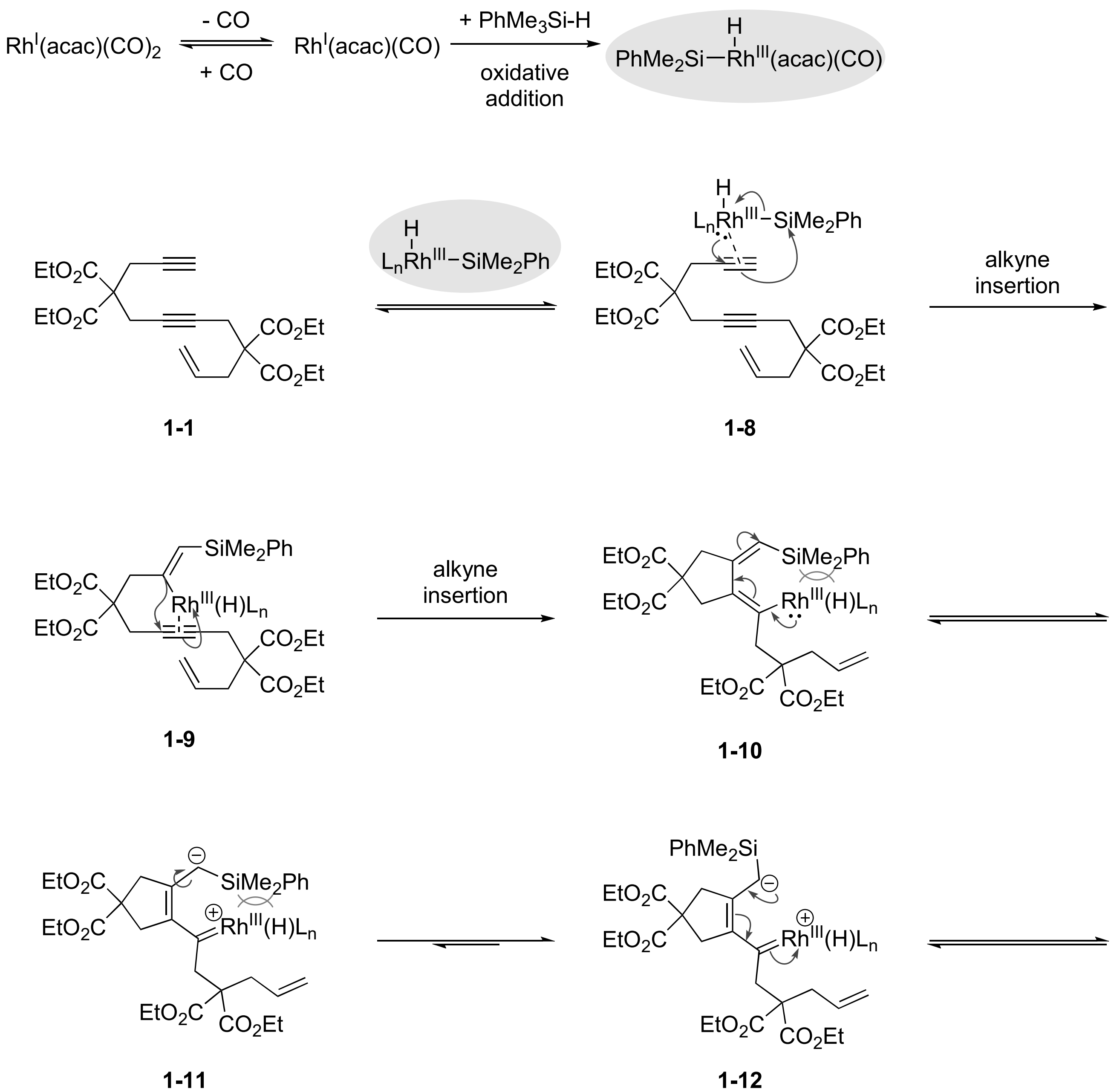
· <u>si</u>lyl<u>ca</u>rbo<u>b</u>icyclization (SiCaB)

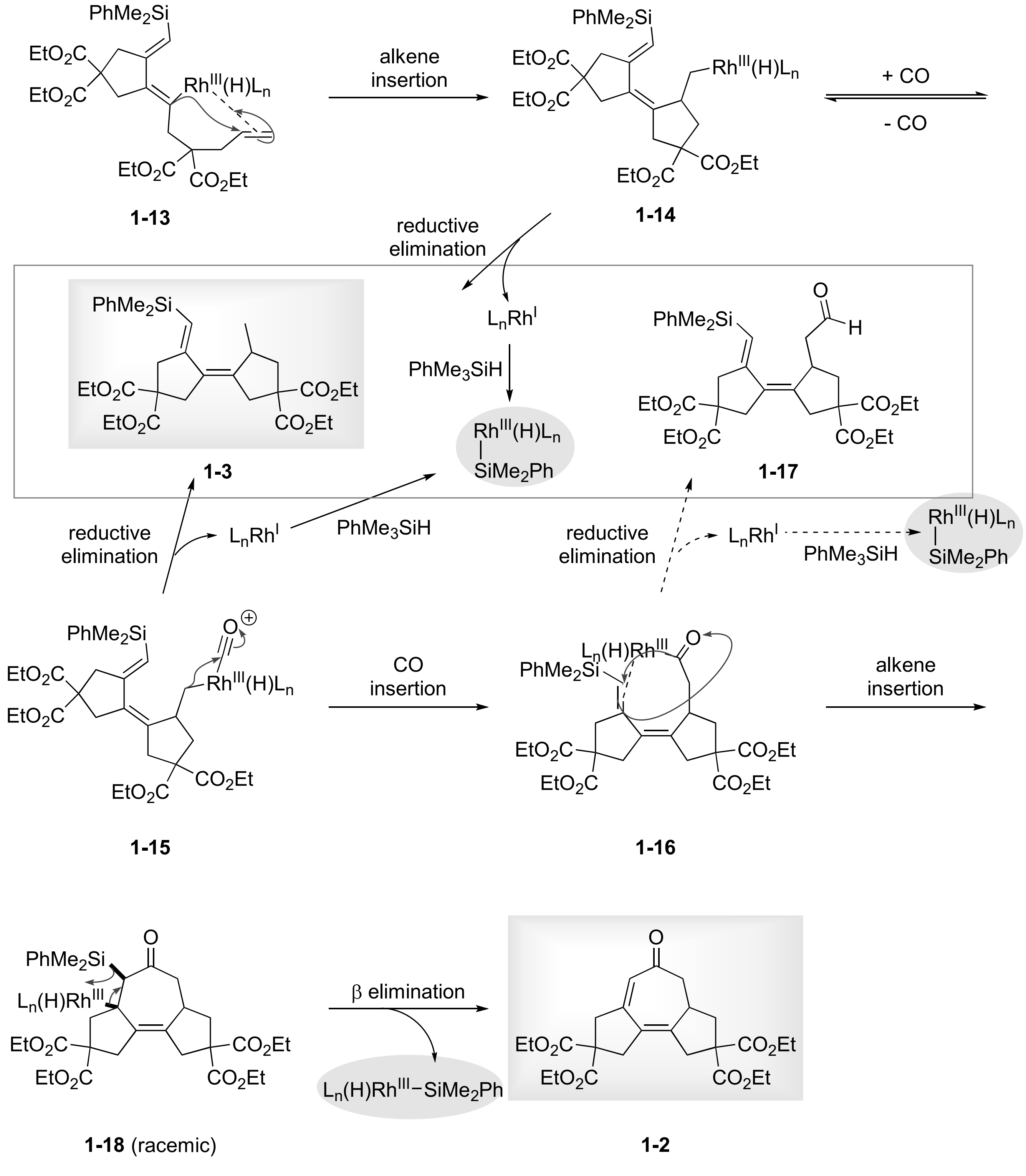
· <u>si</u>lyl<u>ca</u>rbo<u>t</u>ricyclization (SiCaT)

· <u>carbonylative</u> <u>si</u>licon-initiated cascade <u>ca</u>rbo<u>t</u>ricyclization (CO-SiCaT) → problem 1

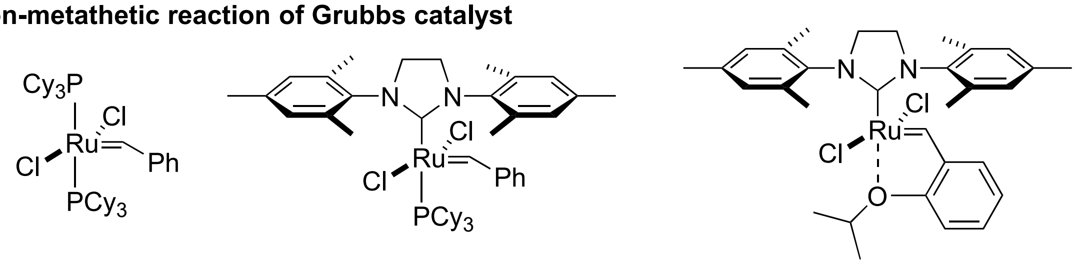


Ojima, I.; Lee, S.-Y. *J. Am. Chem. Soc*. **2000**. *122*, 2385.




PhMe2Si
EtO2C
EtO2C
RhIII(H)Ln
EtO2C
CO2Et
1-13
alkene
insertion
RhIII(H)Ln
CO2Et
1-14
+ CO
- CO
reductive
elimination
LnRhI
PhMe3SiH
RhIII(H)Ln
SiMe2Ph
1-3
O
H
1-17
reductive
elimination
LnRhI
PhMe3SiH
reductive
elimination
LnRhI
PhMe3SiH
RhIII(H)Ln
SiMe2Ph
CO
insertion
Ln(H)RhIII
alkene
insertion
1-15
1-16
β elimination
Ln(H)RhIII–SiMe2Ph
1-18 (racemic)
1-2

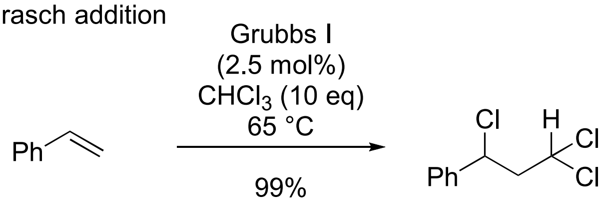
2 → **non-metathetic reaction of Grubbs catalyst**



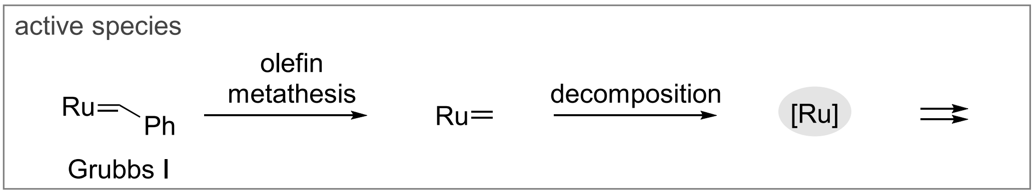
Grubbs I Grubbs II Hoveyda-Grubbs II

Example of non-metathetic reaction of Ru carbene

1. Kharasch addition

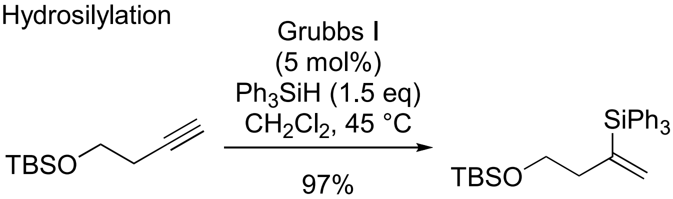


2-2 **2-3**

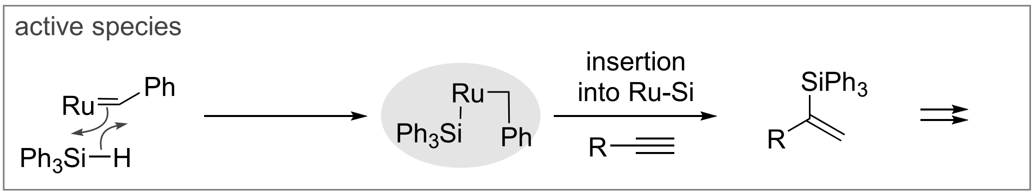


Tallarico, J. A.; Malnich, L. M.; Snapper, M. L. *J. Org. Chem.* **1999**. *64*, 344.

2. Hydrosilylation

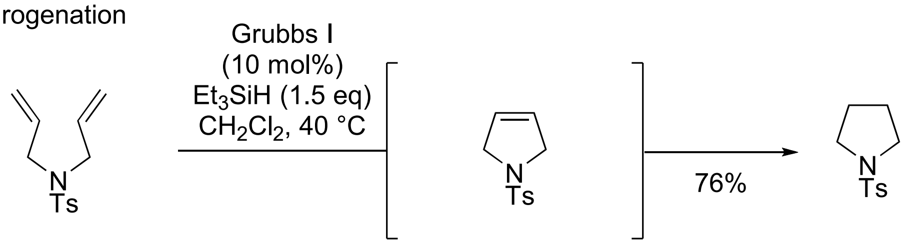


2-4 **2-5**

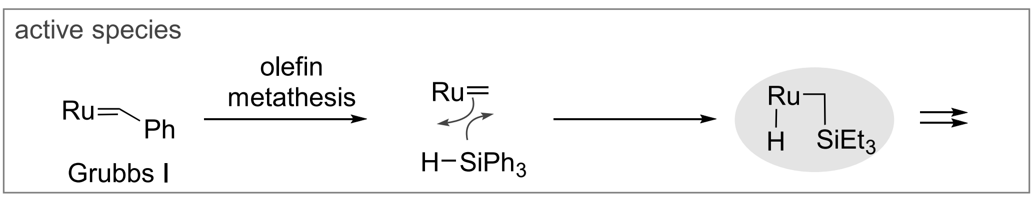


Menozzi, C.; Dalko, P. I.; Cossy, J. *J. Org. Chem.* **2005**. *70*, 10717.

3. Hydrogenation



2-6 **2-7** **2-8**

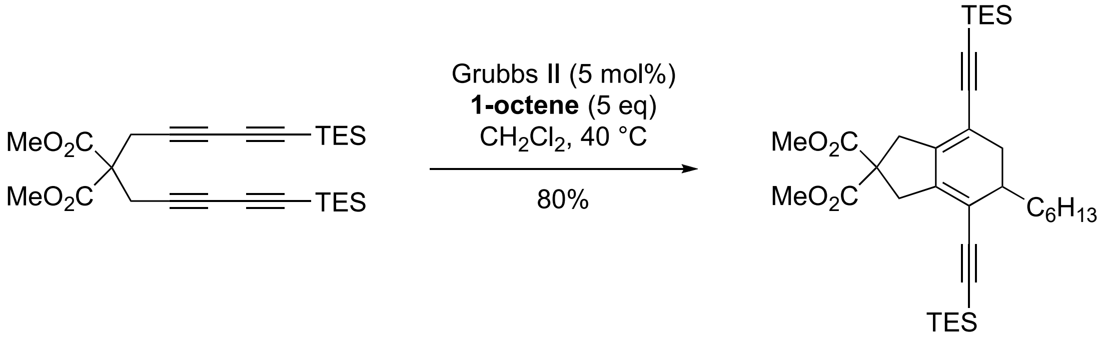


Menozzi, C.; Dalko, P. I.; Cossy, J. *Synlett* **2005**. 2449.

problem 2(a) → **enyne metathesis**

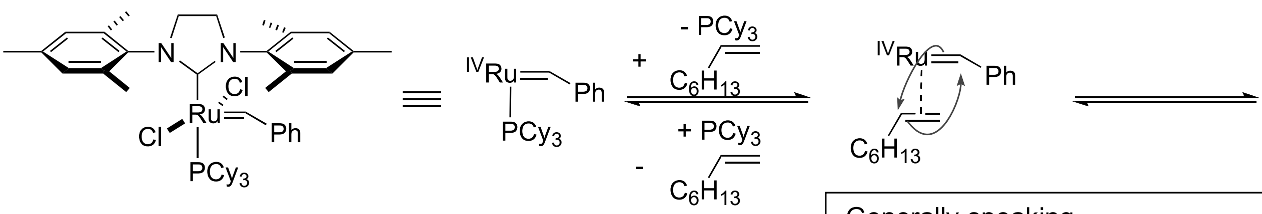
2(b) → **hydrovinylative cyclization via ruthenacycle**

2 (a)

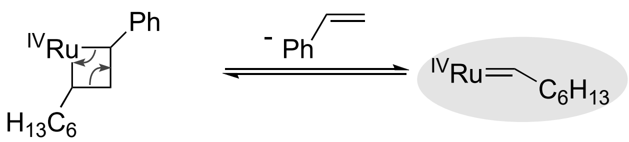


2-1 2a-2

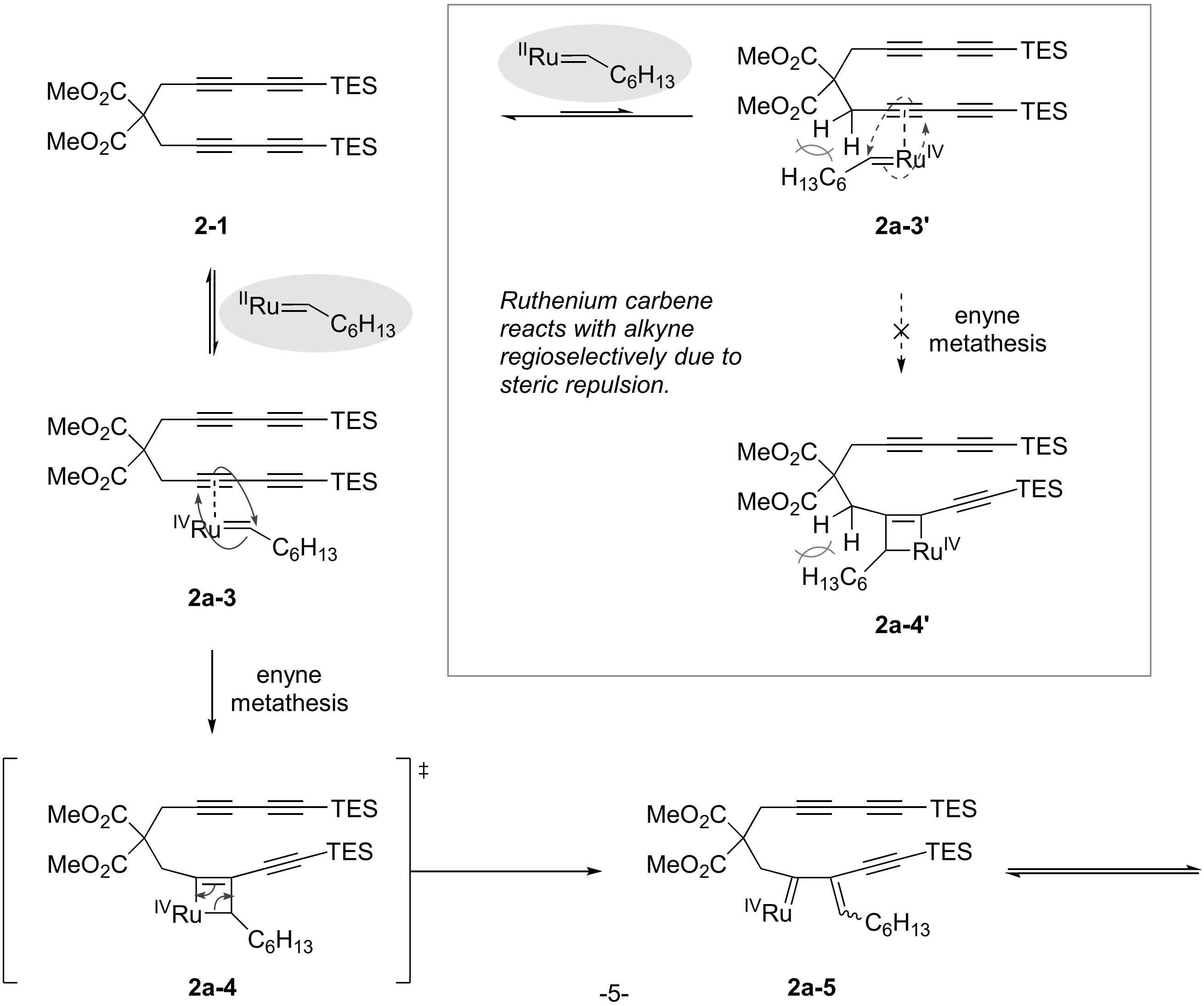
Yun, S. Y.; Wang, K.-P.; Kim, M.; Lee, D. *J. Am. Chem. Soc.* **2013**. *135*, 4668.



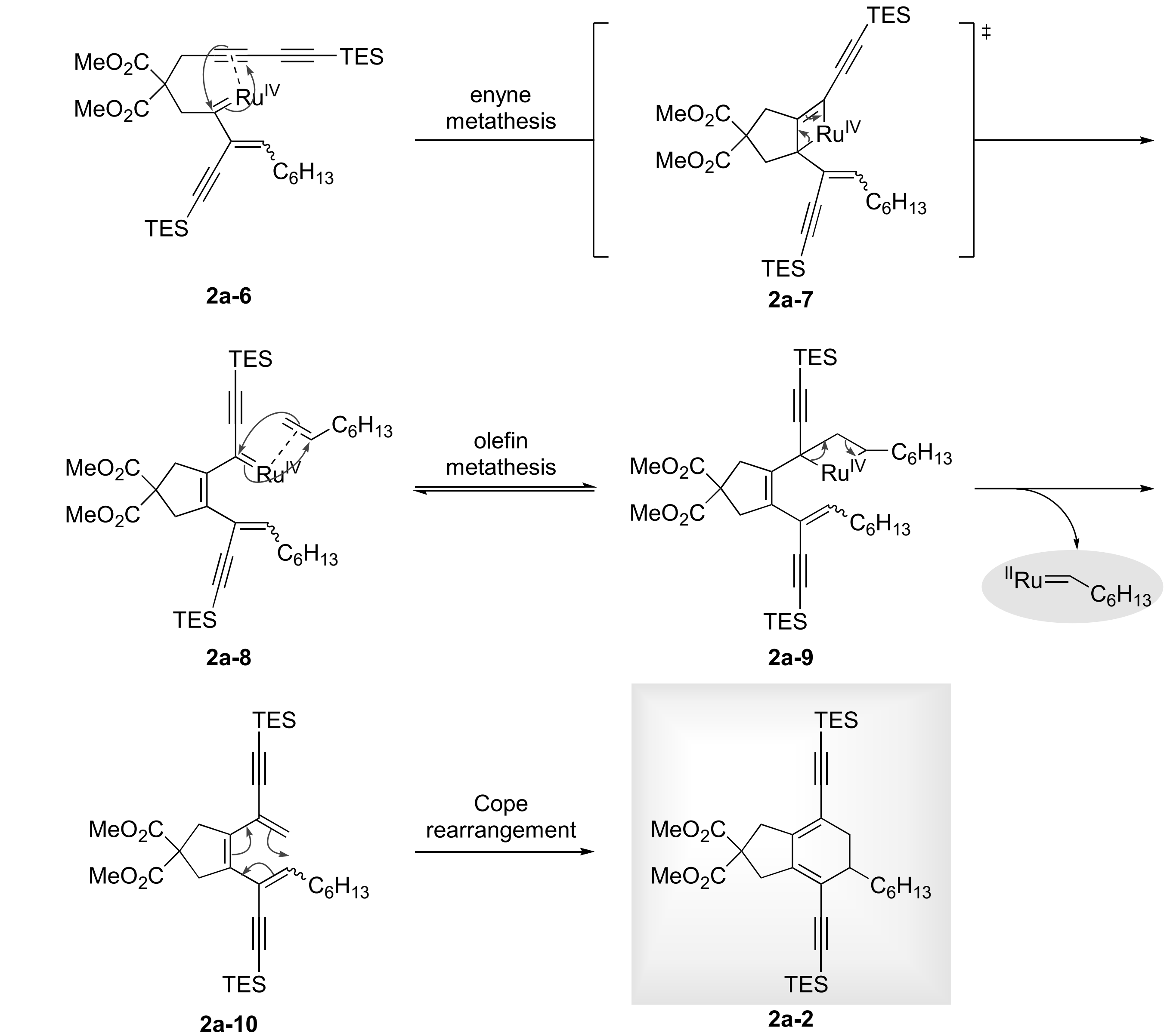
Grubbs II



Generally speaking,
Ru of Ru carbene complex
(e.g. Grubbs catalyst) is bivalent (II).
In this PS, however, carbene complex is regarded as double bond between metal and anionic ligands.
→ **Ru is defigned as tetravalent (IV).**

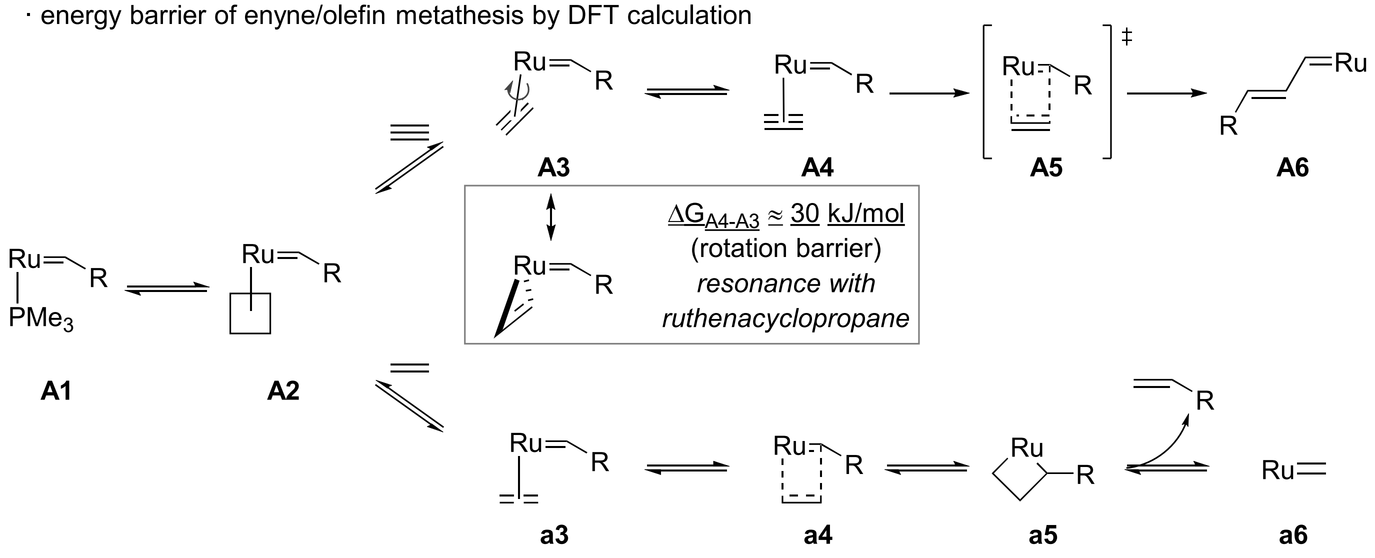


2-1, 2a-3, 2a-3', 2a-4', 2a-4, 2a-5



Note: *reactivity of alkene vs alkyne with ruthenium carbene*

· energy barrier of enyne/olefin metathesis by DFT calculation

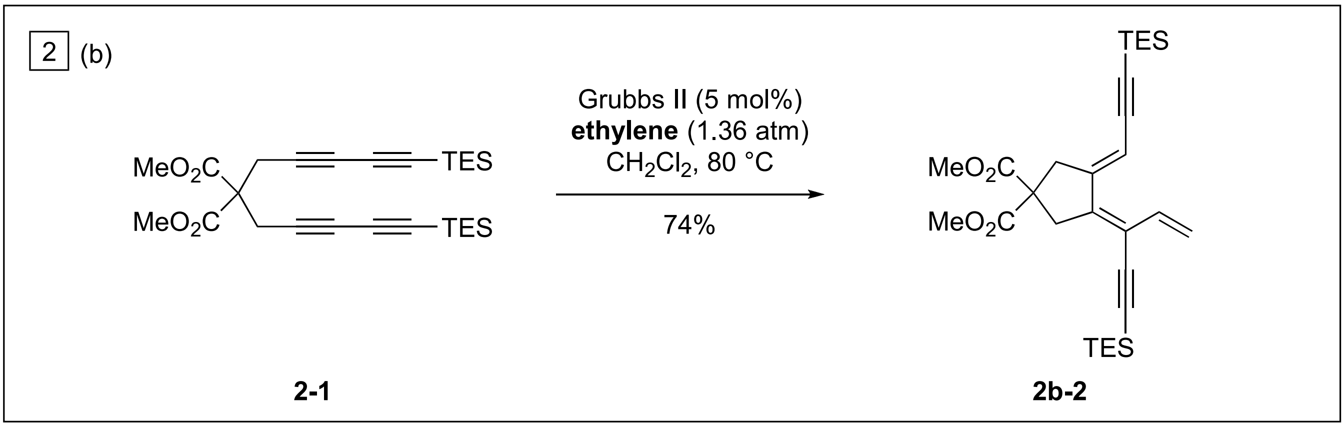


Lippstreu, J. J.; Straub, B. F. *J. Am. Chem. Soc.* **2005**, *127*, **7**444.

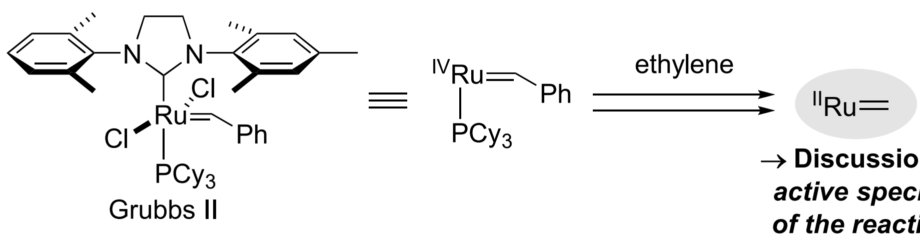
· energy barrier of enyne metathesis (= $\Delta G_{A5\text{-}A1}$) > olefin metathesis (= $\Delta G_{a4\text{-}A1}$)

→ **Enyne metathesis** is disfavor.

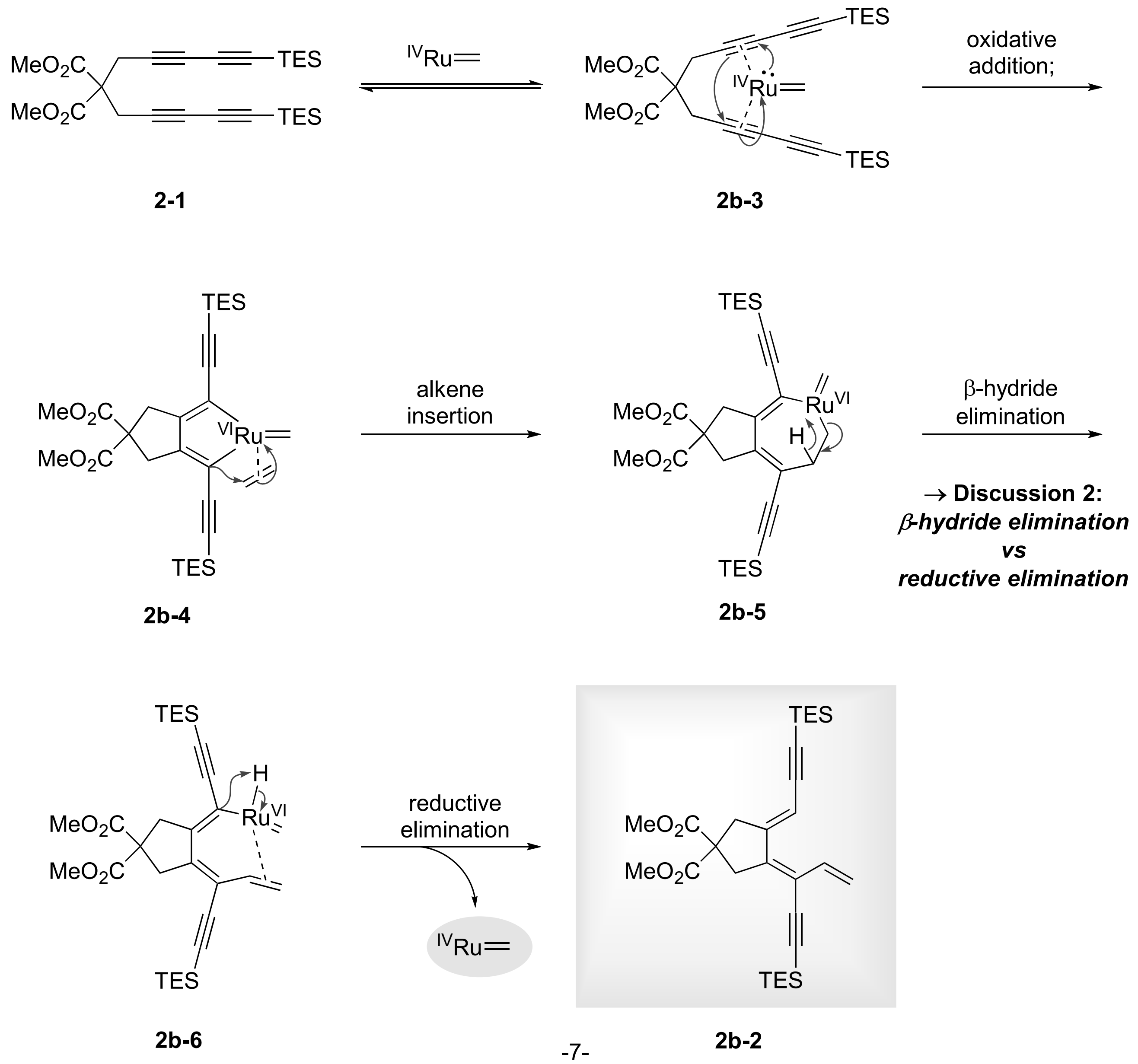
Grubbs II primary reacted with octene.



Yun, S. Y.; Wang, K.-P.; Kim, M.; Lee, D. *J. Am. Chem. Soc*. **2013**. *135*, 4668.



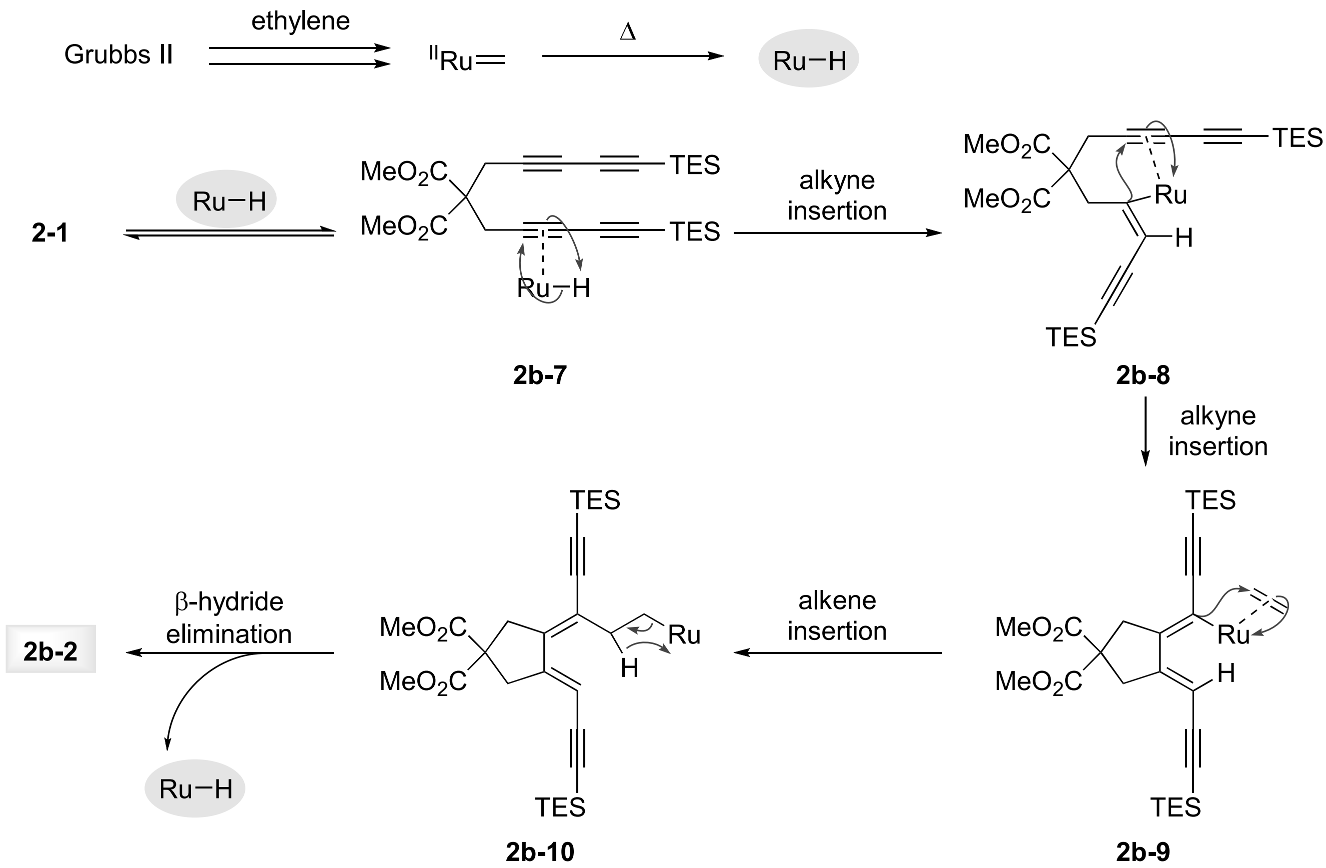
→ **Discussion 1:**
active species
of the reaction



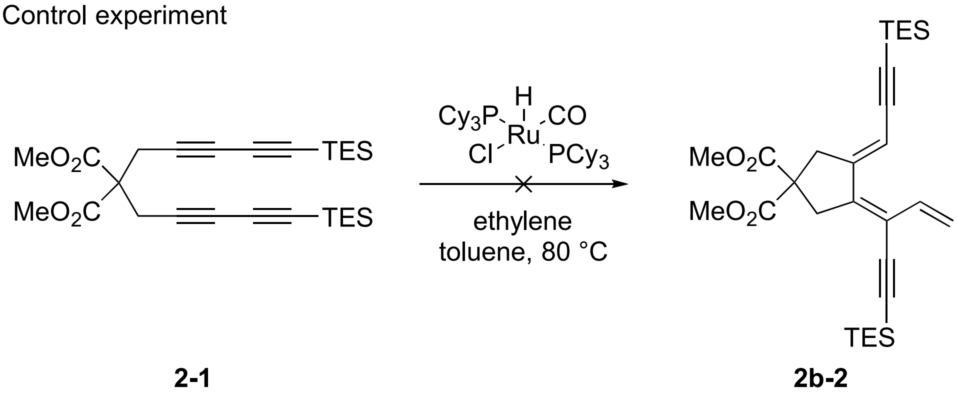
Discussion:

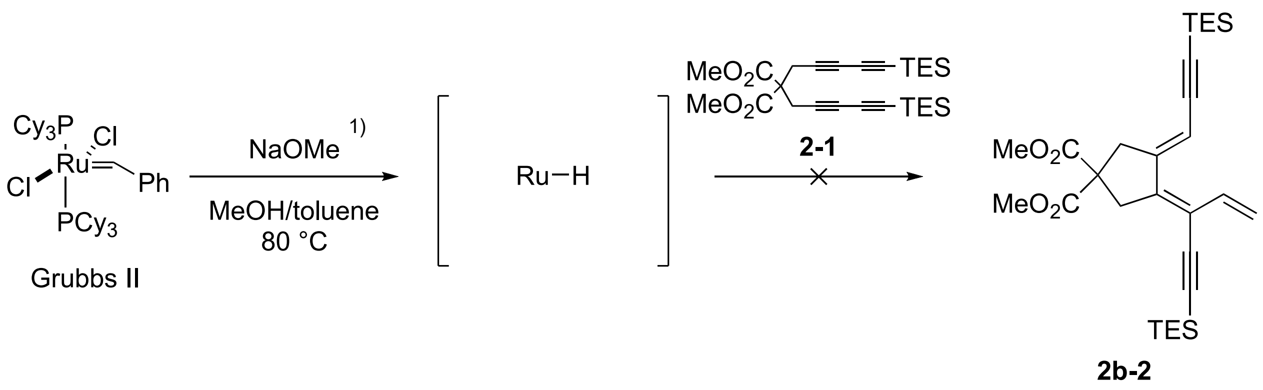
1. Active species of the reaction

1-1. Another possible mechanism: path 2 (cf. 170916 PS_Fujisawa)



1-2. Control experiment





1) Snapper et al., *Chem. Commun.* **2010**, *46*, 5692.

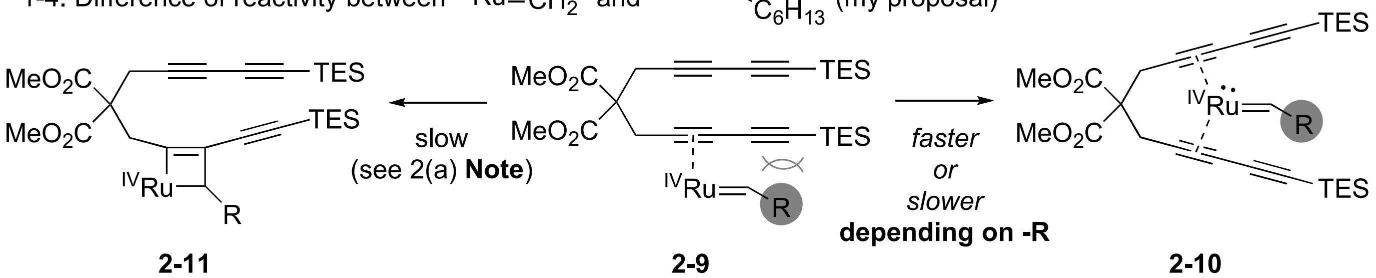
The reaction did not proceed by ruthenium hydride (both synthesized and *in situ*).

→ Path 2 is not correct.

1-3. NMR monitoring of the reaction

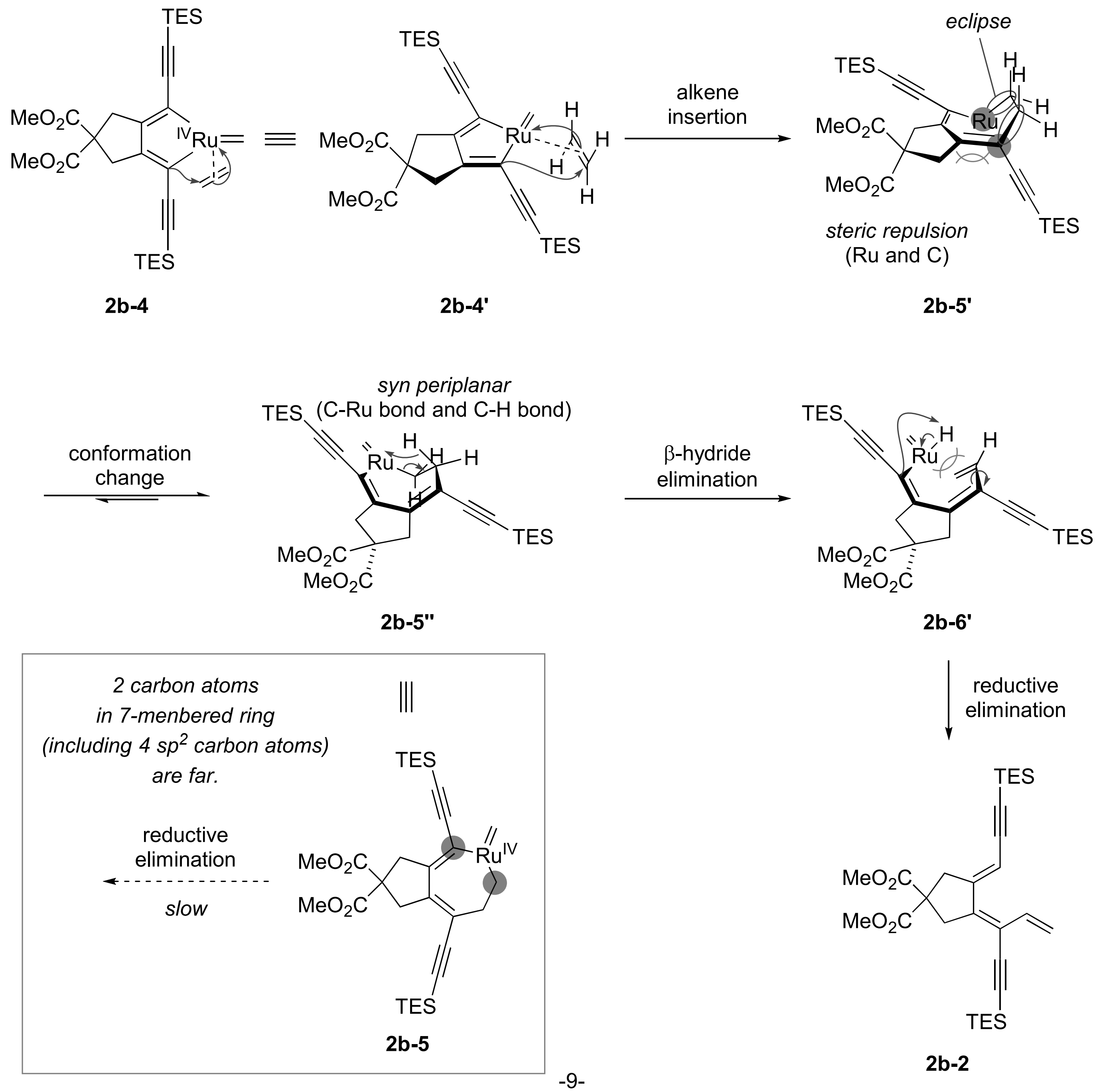
Ruthenium methylidene complex was observed as the major Ru species.
→ Authors concluded that Ru=CH_2 is involved in hydrovinylative cyclization.

1-4. Difference of reactivity between $^{IV}Ru{=}CH_2$ and $^{IV}Ru{=}CH{-}C_6H_{13}$ (my proposal)

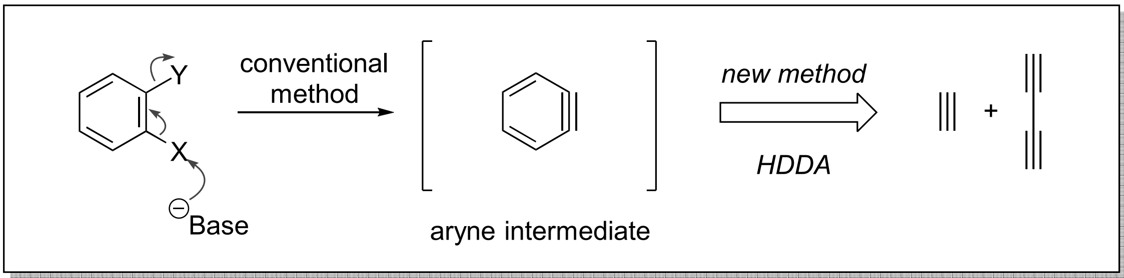


· R = CH_2 (small): 2nd alkyne coordination is faster than enyne metathesis.
· R = C_6H_{13} (large): 2nd alkyne coordination is slower than enyne metathesis.

2. β-hydride elimination vs reductive elimination

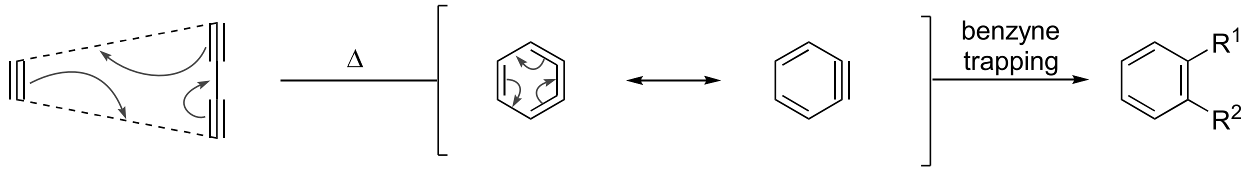


3 → **hexadehydro-Diels-Alder (HDDA) reaction** (cf. 161024_LS_Takahiro_KAWAMATA)



Hoye, T. R.; Baire, B.; Niu, D.; Willoughby, P. H.; Woods, B. P. *Nature* **2012**. *490*, 290.

1. Reaction mechanisms

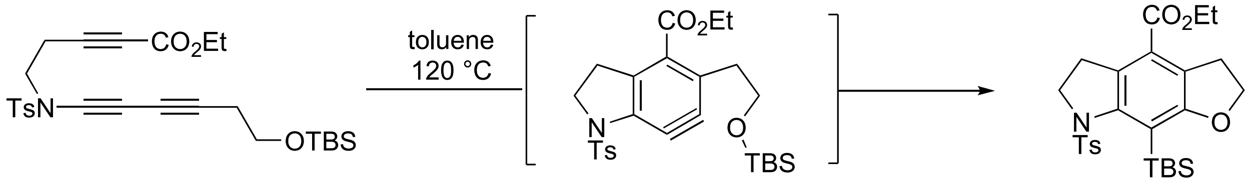


→ ***in situ* aryne synthesis**

→ **Discussion 1:**
elucidation of reaction mechanisms

2. Synthetic applications

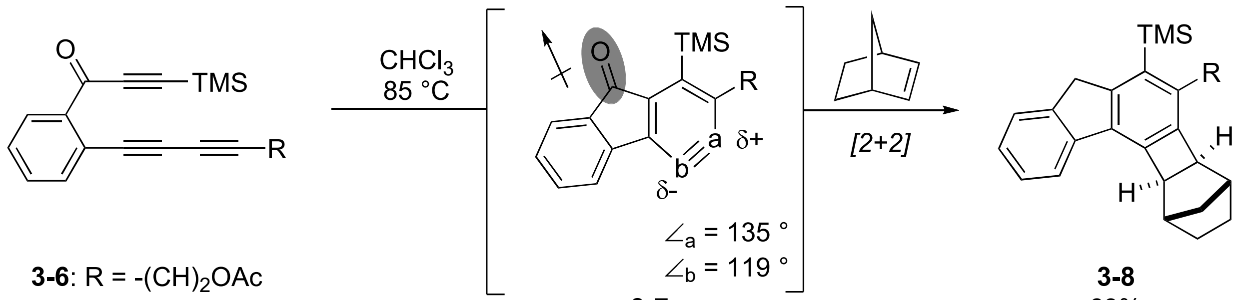
2-1. Intramolecular aryne trapping



3-3 **3-4** **3-5**

· Metal catalyst stabilizes aryne intermediate. → ***problem 3***

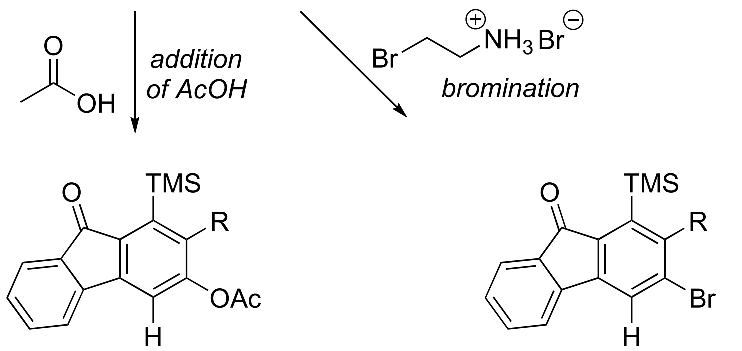
2-2. Intermolecular aryne trapping



3-6: R = -(CH)$_2$OAc

3-7

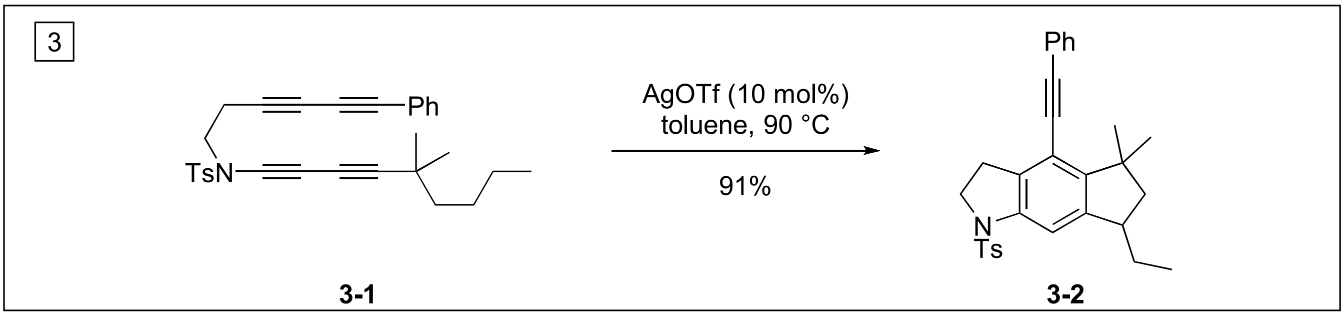
3-8
63%



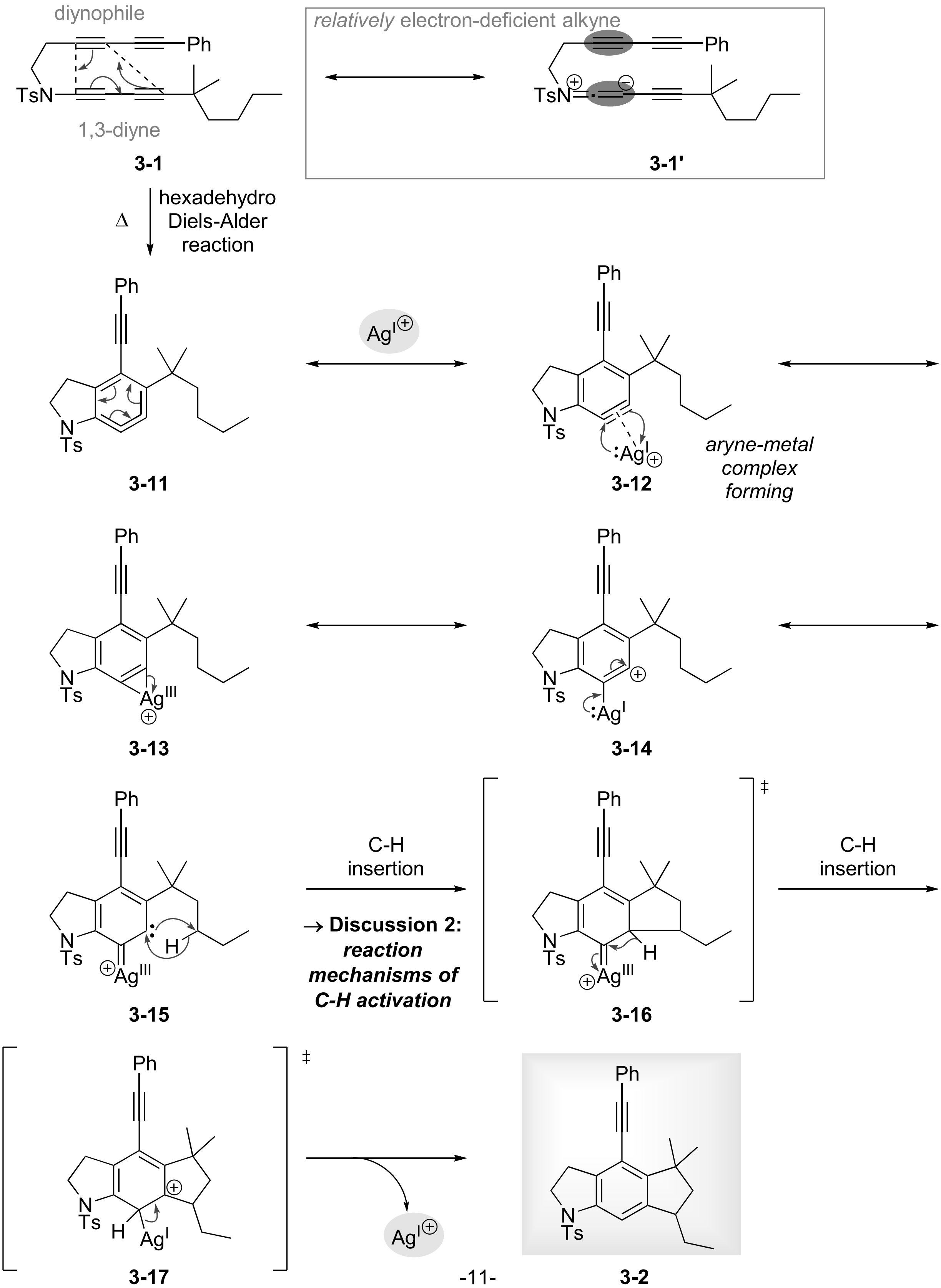
* Regioselectivity of the reaction of aryne intermediate **3-7** can be explained by,
1. electoronic effect (by carbonyl group)
2. distortion effect ($\angle_a$ = 135 °, $\angle_b$ = 119 °)

3-9
89%

3-10
72% (regioselectivity 6:1)



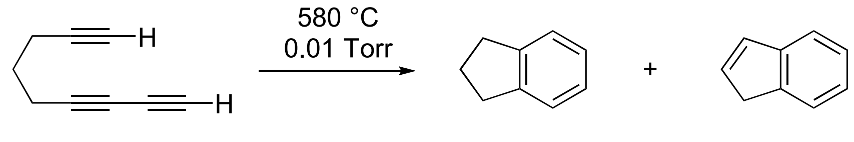
Yun, S. Y.; Wang, K.-P.; Lee, N.-K.; Mamidipalli, P.; Lee, D. *J. Am. Chem. Soc*. **2013**. *135*, 4668.



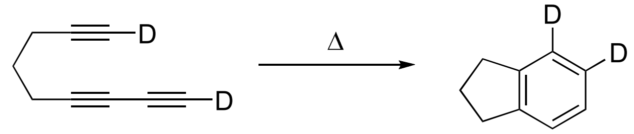
Discussion:

1. Elucidation of reaction mechanisms

Deuterium labeling study (the first example of this type Diels-Alder reaction)



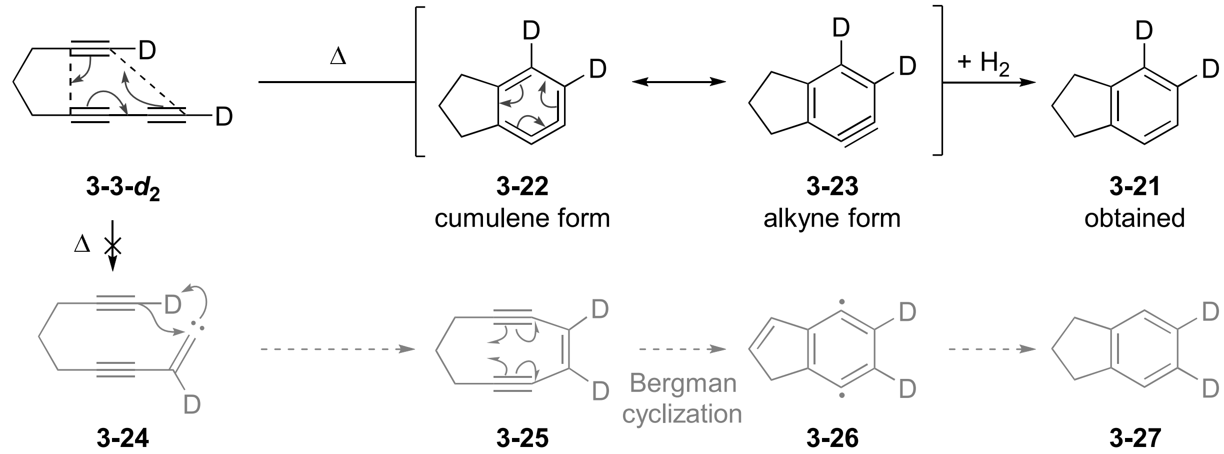
3-18 **3-19** 86% **3-20** 14%



3-3-d_2 **3-21**

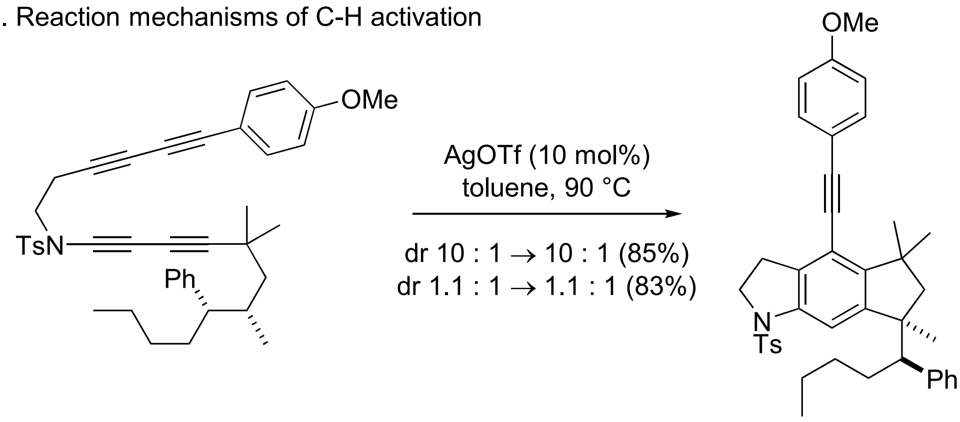
Bradley, A. Z.; Johnson, R. P. *J. Chem. Am. Soc.* **1997**, *119*, 9917.

→ The path via vinylidene **3-24** was rejected.



not obtained

2. Reaction mechanisms of C-H activation



3-28 **3-29**

Stereochemistry of starting material **3-28** was completely conserved.

→ This step is a cocerted mechanism than stepwise process.

× radical

× cathionic intermediate