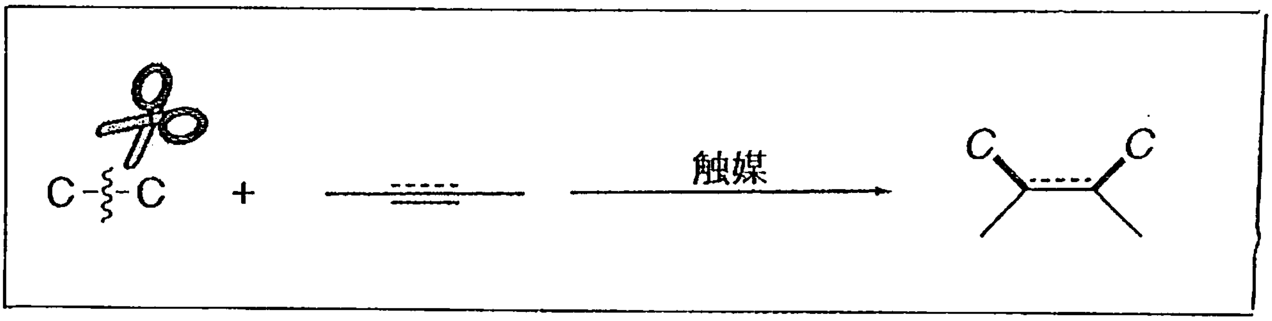
Literature Seminar (2005 Oct. 26th) Hisashi Mihara M2

Selective Carbon-Carbon Bond Cleavage Reaction and Insertion

Introduction



C-C bond cleavage + Alkene or Alkyne insertion

⇩

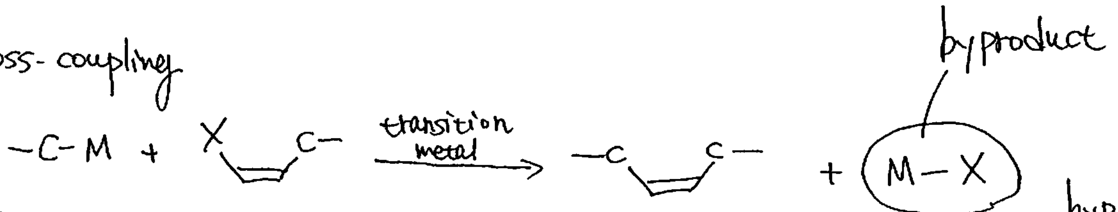
~ novel carbon-carbon bond-forming reaction ~

- advantage

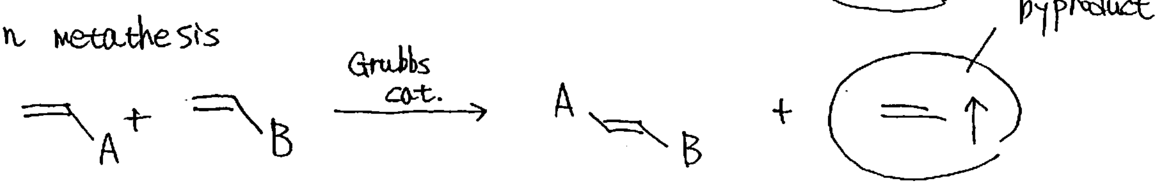
• No byproduct was obtained.

→ high atom economy

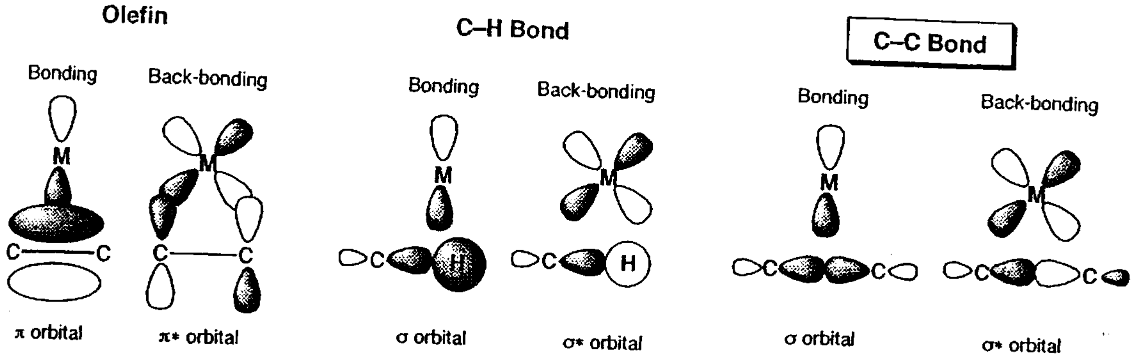
cross-coupling



olefin metathesis



○ Why is carbon - carbon bond cleavage difficlut?



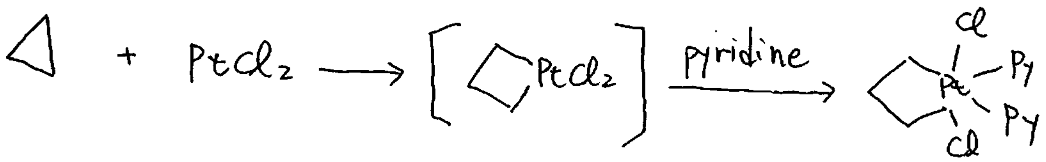
→ C – C single bond

- It has has high directionality.
- It is buried in substitutions of carbon atoms.

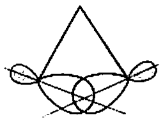
⇒ It is difficult to cleave carbon - carbon single bond.

○ For example carbon - carbon bond cleavage

· First example　Tipper et al. J. Chem. Soc. 1955, 2045

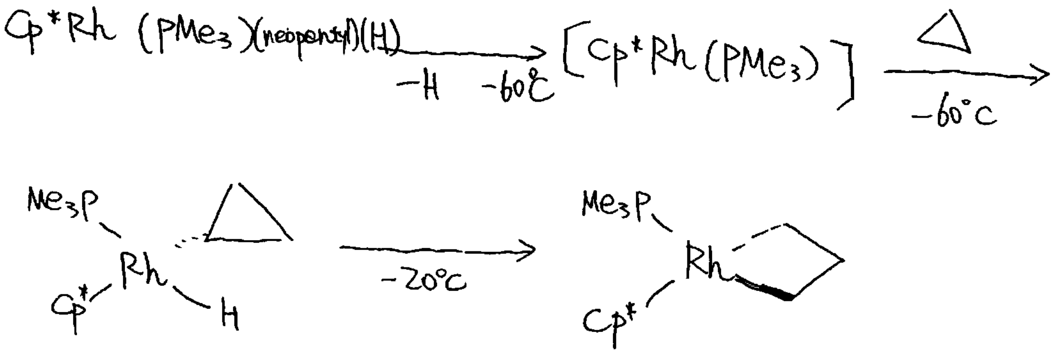


→ The C-C bond of cyclopropane has the character middle of σ bond and π bond.



シクロプロパンの湾曲結合

· Bergman J. Am. Chem. Soc. 1986, 108, 7346



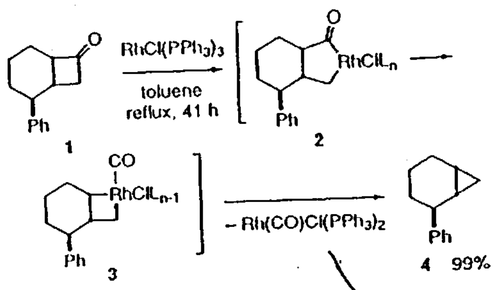
Selective activation of carbon–carbon bonds next to a carbonyl group

Masahiro Murakami, Hideki Amii & Yoshihiko Ito

→ Nature, 1994, 370, 540

J. Am. Chem. Soc. 1996, *118*, 8285−8290

Breaking of the C−C Bond of Cyclobutanones by Rhodium(I) and Its Extension to Catalytic Synthetic Reactions



○ Rh(I) undergoes an insertion into the bond between carbonyl carbon and α-carbon.

↓

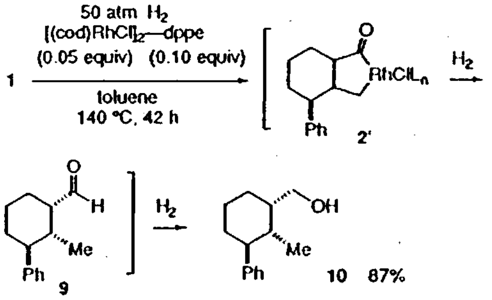
○ Extrution of the carbonyl group

↓

○ reductive elimination.

not active → RhCl(PPh$_3$)$_3$ was required stoichiometric amount.

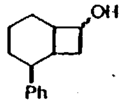
breaking of carbon - carbon bond + Hydrogenolysis



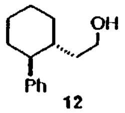
[(cod)RhCl]$_2$ - dppe … cat.

… Such complexes should bind CO much less strongly than RhCl(CO)(PPh$_3$)$_2$ owing to decreased Rh-CO π back-bonding.

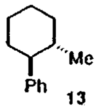
→ J. Am. Chem. Soc. 1978. 100, 7083 より.



11



12



13

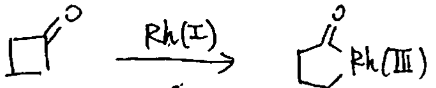
11 was not obtained.

→ oxidative addition of C-C bond proceeds faster than direct hydrogenation.

12 was not obtained

→ insertion of Rh(I) took place selectively into the less substituted C-C bond.

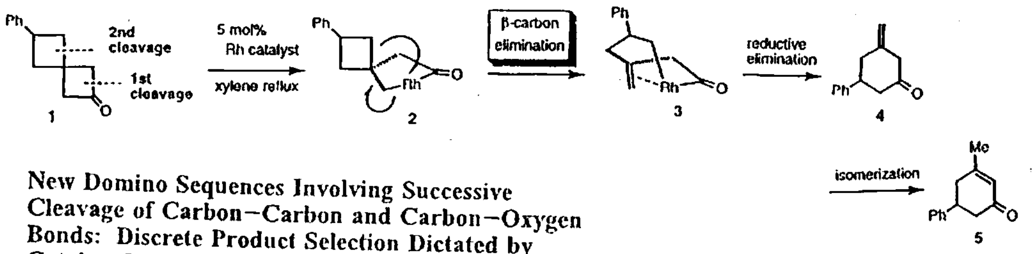
This chemistry is developing from cleavage of C-C bond to cleavage and reconstraction



- Nature, 1994, 370, 540
- J. Am. Chem. Soc. 1996, 118, 8285

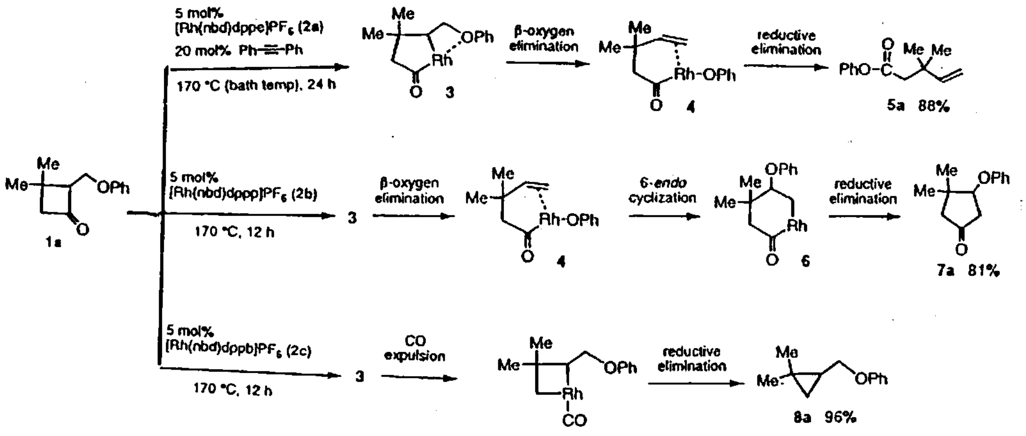
- J. Am. Chem. Soc. 1997, *119*, 9307

Rhodium(I)-Catalyzed Successive Double Cleavage of Carbon−Carbon Bonds of Strained Spiro Cyclobutanones



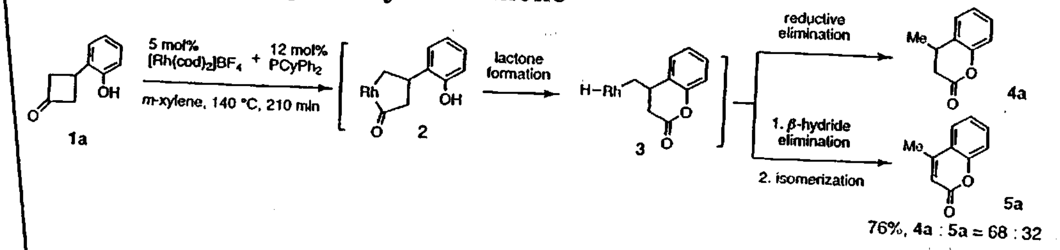
- J. Am. Chem. Soc. 1998, *120*, 9949

New Domino Sequences Involving Successive Cleavage of Carbon−Carbon and Carbon−Oxygen Bonds: Discrete Product Selection Dictated by Catalyst Ligands



- Angew. Chem. Int. Ed. 2000, 39, 2494

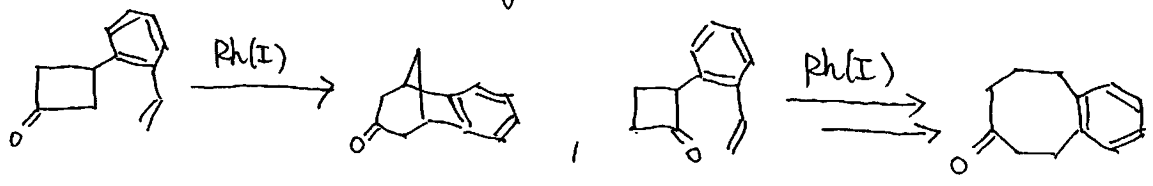
Lactone Formation by Rhodium-Catalyzed C−C Bond Cleavage of Cyclobutanone**



J. Am. Chem. Soc. 2002, 124, 13976

Chem. Lett. 2004, 33, 876

− cleavage and insertion −



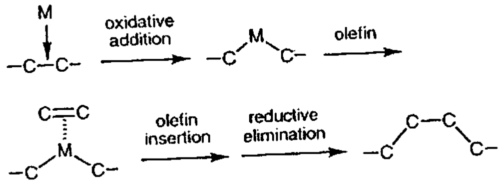
○ Intramolecular Olefin Insertion (C-C bond cleavage and insertion)

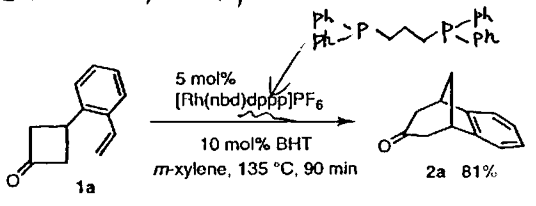
Catalyzed Intramolecular Olefin Insertion into a Carbon−Carbon Single Bond

Masahiro Murakami,* Tamon Itahashi, and Yoshihiko Ito

Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Yoshida, Kyoto 606-8501, Japan

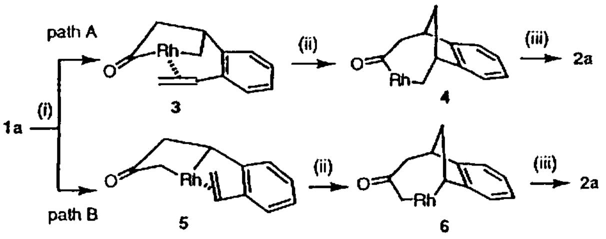
→ J. Am. Chem. Soc. 2002, 124, 13976.





The driving force of this reaction is the release of strain energy.

--- mechanism ---



○ rhodium (I) is inserted between the carbonyl carbon and α-carbon

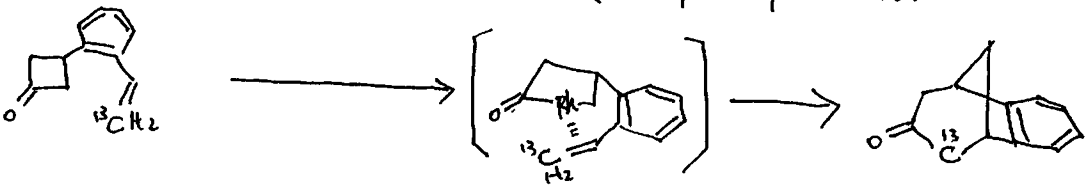
↓

generate 5-membered cyclic acylrhodium intermediate.

- ○ Mygratory insertion of the vinyl group into the rhodium-carbon bond
- ○ Reductive elimination

To determine which path the reaction follows.

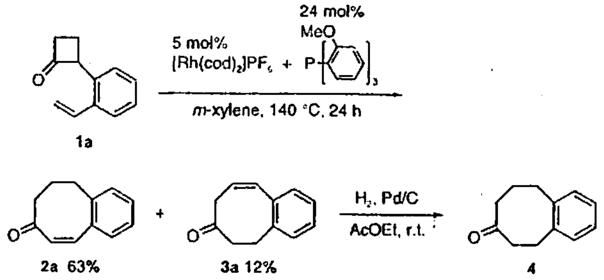
→ ^{13}C was installed at the terminal vinylic position.



→ initial insertion of rhodium occurred between the carbonyl carbon and the α-carbon of the cyclobutanone. (Path A)

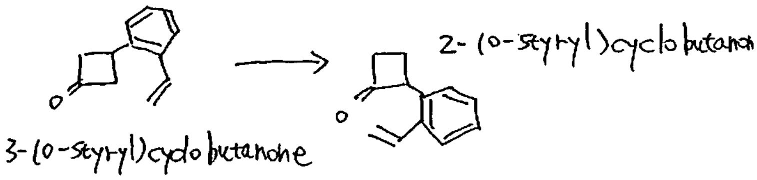
Changing the length of tether beeween the two phosphorus atm in the bidentate phosphine ligand gave a completely different result.

Eight-membered Ring Formation via Olefin Insertion into a Carbon–Carbon Single Bond

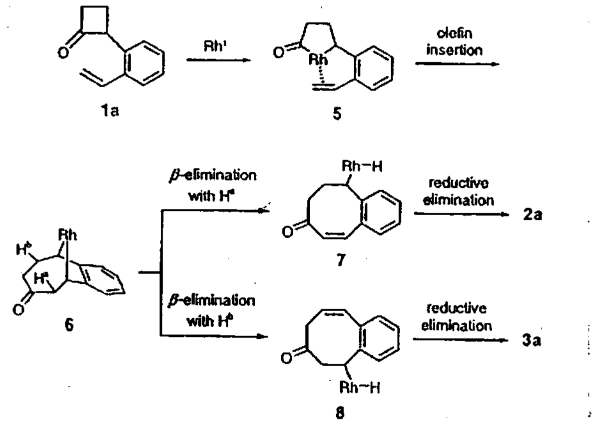


Scheme 1. Reaction of **1a** forming eight-membered ketones **2a** and **3a**.

Starting material was changed



mechanism



Scheme 2. Postulated mechanism for the formation of eight-membered ketones **2** and **3**.

∘ insertion of Rh(I)

↓

• five-membered acylrhodium intermediate

↓

∘ olefin insertion

↓

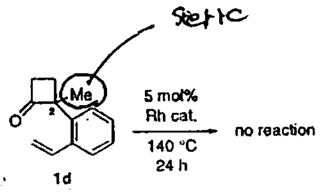
∘ β-elimination

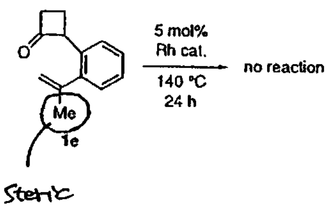
↓

• reductive elimination.

… Phosphine ligand … $P(o\text{-}MeOC_6H_4)_3$ is best. The reason is unclear.

$P(n\text{-}Bu)_3$, $P(c\text{-}Hex)_3$, $P(t\text{-}Bu)_3$ etc. resulted in the formation of a complex mixture.





1d … Fail to undergo Rh cat. insertion

1e … Fail to undergo olefin insertion

→ Steric reason

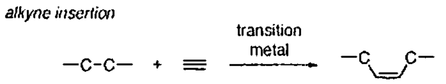
→ Those chemistry started since the bond between the carbonyl carbon and the α-carbon of cyclobutanone can be catalyticaly cleaved by rhodium (I) complex

° Intermolecular Alkyne Insertion

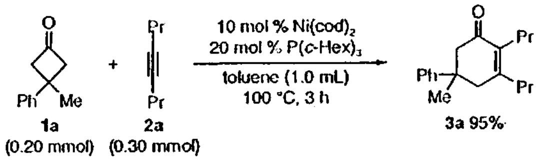
Nickel-Catalyzed Intermolecular Alkyne Insertion into Cyclobutanones

Masahiro Murakami,* Shinji Ashida, and Takanori Matsuda

→ J. Am. Chem. Soc. 2005, 127, 6933



… Next intra → intermolecular



(2)

(intermolecular insertion
rhodium catalyst have
all failur so far)

Rh (I) → Ni (0)

Recently, nickel(0)-catalyzed carbon-carbon bond forming reactions of an aldehyde with an alkyne via oxidative cyclization forming an oxanickelacyclopentene have been developed.

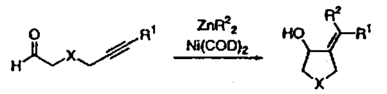
- oxanickelacyclopenten

① Montgomery et al.

A New Stereoselective Method for the Preparation of Allylic Alcohols

J. Am. Chem. Soc. 1997, 119, 9065

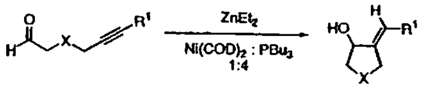
Table 1. Ynal Alkylative Cyclizations



entry	X	R^1	R^2	yield (%)[a]
1	CH$_2$	H	CH$_3$	70[b]
2	CH$_2$	H	Ph	72
3	CH$_2$	H	n-Bu	62
4	CH$_2$	CH$_3$	Ph	64
5	CH$_2$	CH$_3$	n-Bu	76
6	CH$_2$	Ph	CH$_3$	73
7	CH$_2$	Ph	Et	67
8	NCOPh	H	CH$_3$	72

[a] Products were obtained as single stereoisomers by 500 MHz ^{1}H NMR analysis. [b] Isolated as the benzoate ester (two-step yield is reported).

Table 2. Ynal Reductive Cyclizations



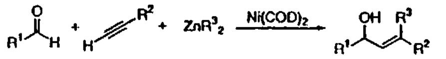
entry	X	R^1	yield (%)[a]
1	CH$_2$	H	74[b]
2	CH$_2$	CH$_3$	67[b]
3	CH$_2$	Ph	62
4	NCOPh	H	70[c]

[a] Products were obtained as single stereoisomers by 500 MHz ^{1}H NMR analysis. [b] Isolated as the benzoate ester (two-step yield is reported). [c] Isolated as a mixture with 9% of the ethyl-substituted alkylative cyclization product.

↳ with PBu$_3$

reductive cyclization
∨
alkylative cyclization

Table 3. Three-Component Couplings

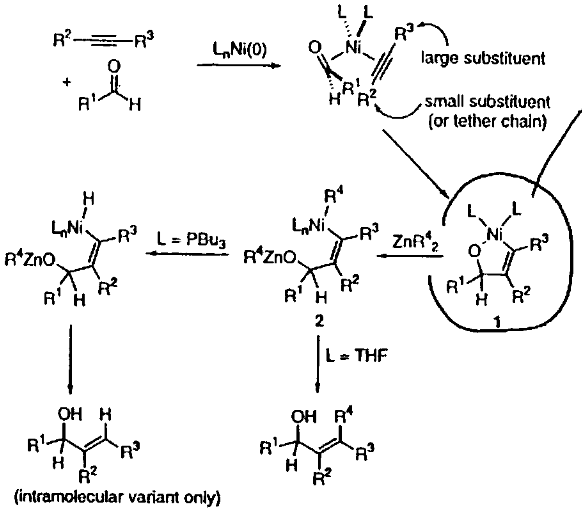


entry	R^1	R^2	R^3	yield (%)[a]
1	Ph	Ph	Me	60
2	Ph	C$_6$H$_{13}$	Me	74
3	Ph	C$_6$H$_{13}$	n-Bu	71
4	i-pr	Ph	Me	21[b]
5	Ph	Ph	C(CH$_3$)=CH$_2$	0[c]

[a] Products were obtained as single regio- and stereoisomers by 500 MHz ^{1}H NMR analysis. [b] Isolated as the acetate ester (two-step yield is reported). [c] The alcohol derived from isopropenyl addition to benzaldehyde was isolated in 90% yield.

mechanism

Scheme 1. Proposed Mechanism for Ynal Cyclizations and Three-Component Couplings



oxanickelacyclo penten

↓

Transmetalation of the organozinc

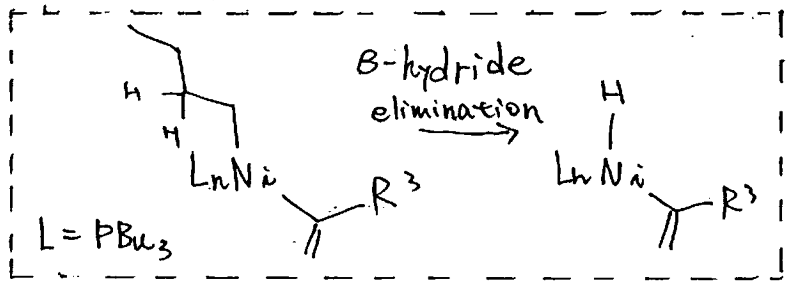
↓

① L = THF

Reductive elimination

② L = PBu3

β-hydride elimination



○ reaction of aldehyde with alkyne

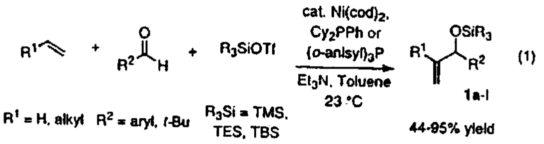
→ Allylic alcohol

② Jamison et al.

Simple Alkenes as Substitutes for Organometallic Reagents: Nickel-Catalyzed, Intermolecular Coupling of Aldehydes, Silyl Triflates, and Alpha Olefins

… J. Am. Chem. Soc. 2005, 127, 14194

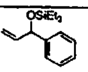
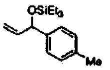
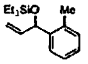
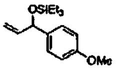
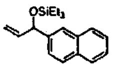
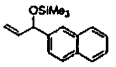
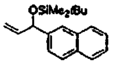
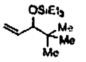
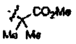
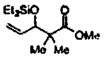
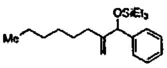
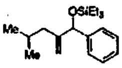
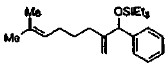
Sze-Sze Ng and Timothy F. Jamison*



→ 600 mol% Et3N was needed

mono substituted olefin undergo.

Table 1. Nickel-Catalyzed, Three-Component Coupling of Alkenes, Aldehydes, and Silyl Triflates [a]

entry	R1 (alkene)	R2 (aldehyde)	R3SiOTf	product		isolated yield (%)
1	H (ethylene, 1 atm)	Ph	Et3SiOTf		1a	82
2	"	*p*-tolyl	Et3SiOTf		1b	88
3	"	*o*-tolyl	Et3SiOTf		1c	93
4	"	*p*-anisyl	Et3SiOTf		1d	95
5	"	2-naphthyl	Et3SiOTf		1e	95
6	"	2-naphthyl	Me3SiOTf		1f	60
7	"	2-naphthyl	*t*BuMe2SiOTf		1g	67
8	"	piv	Et3SiOTf		1h	70
9	"		Et3SiOTf		1i	81
10	*n*-hexyl	Ph	Et3SiOTf		1j	48 [b]
11	isobutyl	Ph	Et3SiOTf		1k	44 [b]
12		Ph	Et3SiOTf		1l	50 [b]

[a] See eq 1. Standard conditions (entries 1−9): To a solution of Ni(cod)$_2$ (20 mol %) and tris(*ortho*-methoxyphenyl)phosphine (40 mol %) in toluene at 23 °C under ethylene (balloon, 1 atm) were added triethylamine (600 mol %), the silyl triflate (175 mol %), and the aldehyde (100 mol %). The mixture was stirred 2−8 h at room temperature, and purification by chromatography (SiO$_2$) afforded products 1a−i. For entries 10−12, dicyclohexylphenylphosphine and the alkene shown were used in place of tris(*ortho*-methoxyphenyl)phosphine and ethylene, respectively (reaction under Ar). See Supporting Information. [b] A silyl ether of a homoallylic alcohol was also isolated in 10−20% yield. See Supporting Information.

→ Et3SiOTf is the superior silyl triflate than Me3SiOTf and tBuMe2SiOTf.

※ Di- and tetrasubstituted olefin do not react.

- mechanism
- major product   minor product   formed in trace amount

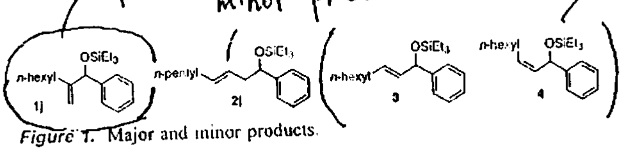
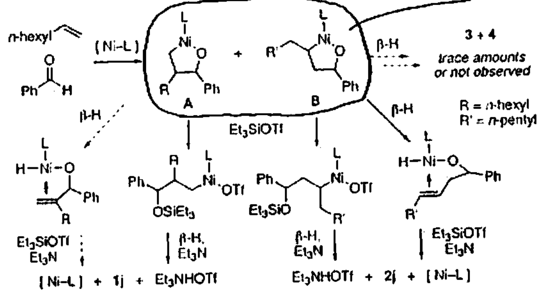


Figure 1. Major and minor products.

Scheme 1. Mechanistic Hypothesis for Product Distribution



oxa nickelacyclopentan

↓

silyltriflate cleavage of Ni-O bond

↓

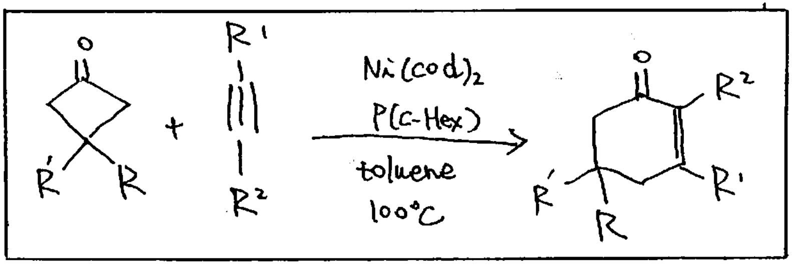
β-H elimination

↓

product

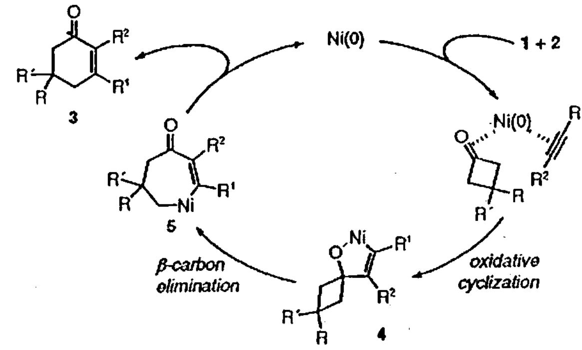
reaction of aldehyde with alkene → Allylic derivative

- return to intermolecular Alkyne insertion cyclobutanone



mechanism.

Scheme 1. Postulated Mechanism for the Nickel-Catalyzed Intermolecular Alkyne Insertion into Cyclobutanones



- Oxanickelacyclopenten (4)

↓

- β-carbon elimination

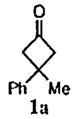
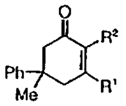
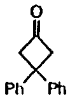
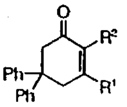
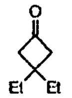
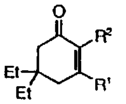
↓

- reductive elimination.

→ The carbonyl group of 1 possess a higher reactivity due to its ring strain.

The carbonyl sp² carbon changes to an sp³ carbon thereby diminishing the ring strain. } → driving force.

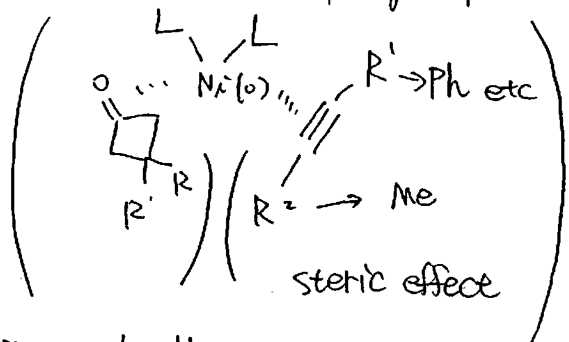
Table 1. Nickel-Catalyzed Reaction of **1** and **2** Forming 2-Cyclohexenone **3**[a]

entry	1	2 (R^1, R^2, equiv)	mol % Ni	3 (%yield)[b]
	 **1a**			
1		**2b** (Et, Et, 1.5)	10	**3b** (97)
2		**2c** (Ph, Ph, 3.0)	10	**3c** (84)
3		**2d** (Ph, Me, 3.0)	10	**3d**[c] (78)
4		**2e** (*p*-MeOC$_6$H$_4$, Me, 3.0)	10	**3e**[c] (58)
5		**2f** (*p*-CF$_3$C$_6$H$_4$, Me, 3.0)	10	**3f**[c] (65)
	 **1b**			
6		**2a** (Pr, Pr, 1.5)	10	**3g** (91)
7		**2d** (Ph, Me, 3.0)	10	**3h**[c] (69)
	 **1c**			
8		**2a** (Pr, Pr, 1.5)	20	**3i** (61)
9		**2d** (Ph, Me, 3.0)	20	**3j**[c] (47)

[a] Cyclobutanone **1**, alkyne **2** (1.5−3.0 equiv to **1**), Ni(cod)$_2$ (10 mol %), and P(*c*-Hex)$_3$ (20 mol %) were heated in toluene at 90−110 °C for 3−6 h. [b] Isolated yield. [c] Regioisomeric ratios of the methyl group α:β to the carbonyl group were determined by ^{1}H NMR to be as follows: **3d** (92:8); **3e** (90:10); **3f** (91:9); **3h** (93:7); **3j** (90:10).

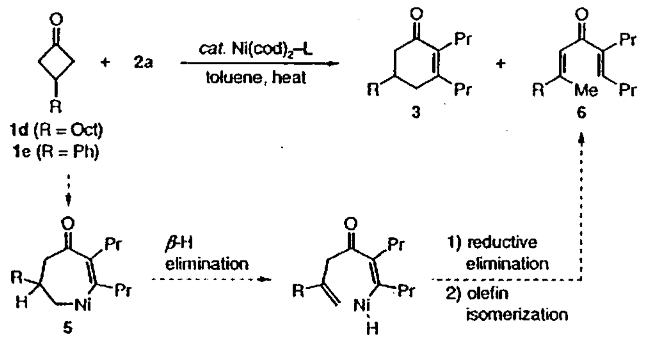
unsymmetrical cyclobutanone. (entry 3-5, 7, 9)

The methyl group was located α to the carbonyl group.



※ Terminal alkyne, such as 1-octyne, failed.

→ oligomerization



entry	1 (R)	mol % Ni	L (mol %)	3 (%)[b]	6 (%)[b]
1	**1d** (Oct)	10	P(*c*-Hex)$_3$ (20)	**3k** (37)	**6a**[c] (37)
2	**1e** (Ph)	10	P(*c*-Hex)$_3$ (20)	**3l** (41)	**6b** (54)
3	**1e** (Ph)	10	PPh$_3$ (20)	**3l** (37)	**6b** (26)
4	**1e** (Ph)	10	IPr (10)	**3l** (61)	–
5	**1e** (Ph)	20	IPr (20)	**3l** (79)	–

[a] Cyclobutanone **1** (0.20 mmol), alkyne **2a** (0.30 mmol), and nickel catalyst were heated in toluene (1.0 mL, 100 °C, 3 h for entries 1−3; 2.0 mL, 110 °C, 18 h for entry 4; 4.0 mL, 110 °C, 15 h for entry 5). [b] Isolated yield. [c] A mixture of *Z*- and *E*-isomers with respect to the 2-methyldec-1-enyl moiety was obtained.

↝ cyclobutanone having a hydrogen at the 3-position

↓

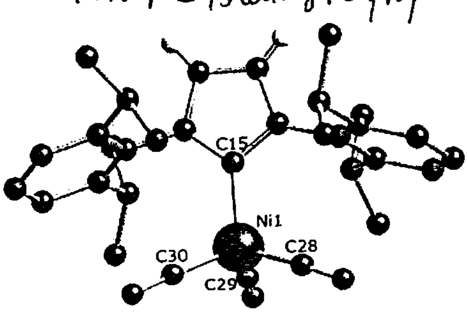
β-H elimination occured from intermediate 5.

→ N-heterocyclic carben (NHC) afforded cyclohexenone selectively

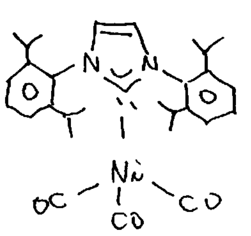
※ IPr = 1,3-bis (2,6-diisopropylphenyl) imidazol-2-ylidene.

IPr

X ray crystallography … J. Am. Chem. Soc 2005, 127, 2485



≡



○ N-heterocyclic carbene ligands are better σ-donors than even the most basic phosphine PtBu$_3$

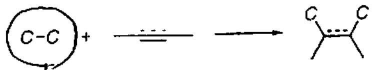
↓

reductive elimination > β-Hydride elimination

Nickel-Catalyzed Arylcyanation of Alkynes

→ J. Am. Chem. Soc. 2004, 126, 13904

Yoshiaki Nakao,* Shinichi Oda, and Tamejiro Hiyama*

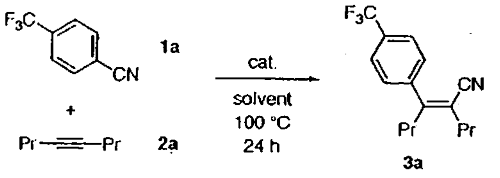


(1)

cleavage of C-C bond rely on the release of strain energy

↓

not rely on the release of strain energy



(2)

(cleavage of C-CN bond
↓
insertion of alkyne)

→ high atom economy.

---

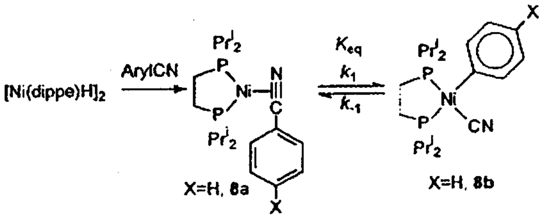
cleavage C-CN bond

Cleavage of Carbon−Carbon Bonds in Aromatic Nitriles Using Nickel(0)

→ J. Am. Chem. Soc. 2002, 124, 9547

Juventino J. Garcia,† Nicole M. Brunkan,‡ and William D. Jones*,‡

The The Nickel dimer [(dippe)NiH]$_2$ cleaved C-CN bond.



(2)

|||

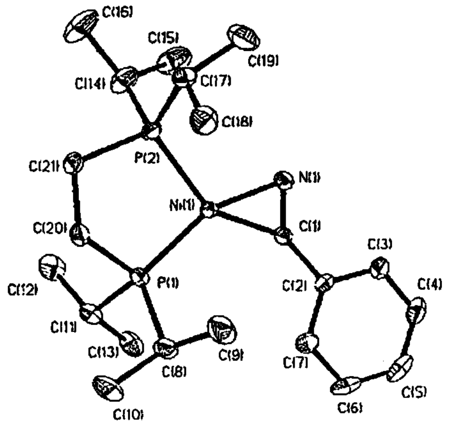
Reaction of [(dippe)NiH]$_2$ with benzonitrile in THF-d_8 solution

↓

formation of the η^2-nitrile complex

(The color of solution turn red to yellow.

The product can be isolated by remaval of solvent and recrystallization at low temperature.



← X-ray

Figure 7. ORTEP drawing of (dippe)Ni(η^2-benzonitrile), 8a. Ellipsoids are shown at the 30% probability level. Selected distances (Å) and angles (deg): Ni(1)−N(1), 1.908(3); Ni(1)−C(1), 1.867(4), C(1)−N(1), 1.225(6); N(1)−C(1)−C(2), 136.1(4); P(1)−Ni(1)−P(2), 91.54(5).

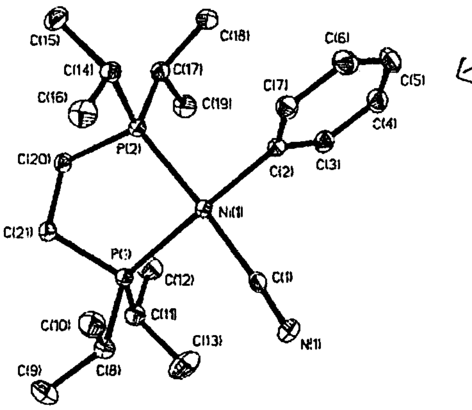
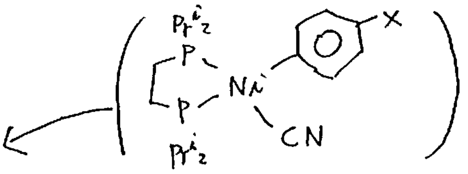


Figure 8. ORTEP drawing of (dippe)Ni(Ph)(CN). 8b. Ellipsoids are shown at the 30% probability level. Selected distances (Å) and angles (deg): Ni(1)–C(2), 1.935(2); Ni(1)–C(1), 1.877(3); C(1)–N(1), 1.148(3), P(1)–Ni(1)–P(2), 88.56(3).



At room temperature, 8a converts to 8b slowly.
the solution turn to yellow.
Crystal of 8b were isolated at room temperature.

← X-ray

→ The rate of approach to equilibrium was also monitored.

p-XC_6H_4CN … electrone with drawing subsetuent's Keq. were large than electrone donating substituents.

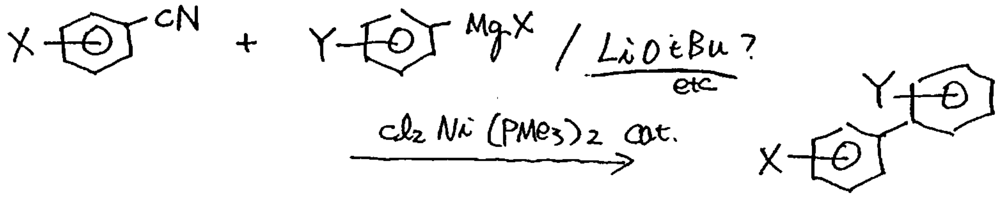
Other reaction using C-CN bond cleavage. $MgCN^X$?

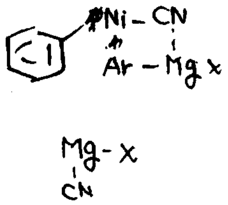
→ Miller et al … Cross-Coupling reaction.

C–C Bond activation with selective functionalization: preparation of unsymmetrical biaryls from benzonitriles

Tetrahedron Lett 2001, 42, 6991

Joseph A. Miller*



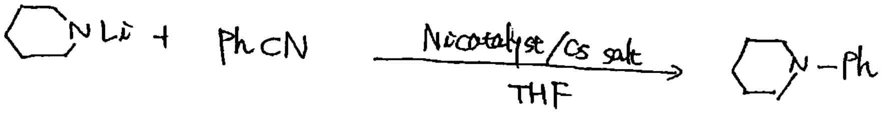


Nickel Catalyzed Cross-Coupling and Amination Reactions of Aryl Nitriles

Synthesis, 2003, 1643

Joseph A. Miller,* John W. Dankwardt, Jonathan M. Penney

$$ArCN + RMgZ \xrightarrow[THF]{Cl_2Ni(PMe_3)_2\ cat.} Ar-R$$

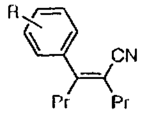
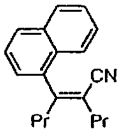
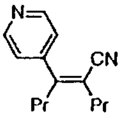
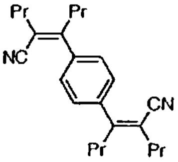
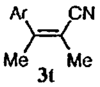
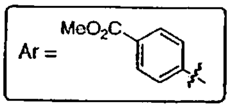
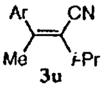
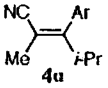
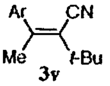
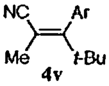
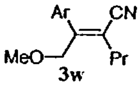
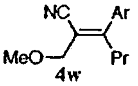


Alkynylation of benzonitriles via nickel catalyzed C–C bond activation

Tetrahedron Lett 2004, 45, 4989

$$ArCN + R-\equiv-ZnX \xrightarrow[THF]{Cl_2Ni(PMe_3)_2\ Cat.} Ar-\equiv-R$$

Table 2. Ni(cod)$_2$–PMe$_3$-Catalyzed Arylcyanation of Alkynes[a]

entry	product(s)	time (h)	yield (%)
1	 R = 4-F (3b)	30	81
2	4-C(O)Me (3c)	30	73
3	4-CO$_2$Me (3d)	24	96
4	4-CHO (3e)	25	67
5	4-CN (3f)	19	67
6	H (3g)	45	64
7	4-Me (3h)	40	70
8	4-Ph (3i)	45	78
9	4-MeO (3j)	111	54
10	4-B(pin) (3k)	30	61
11	3-MeO (3l)	38	70
12	3,5-(MeO)$_2$ (3m)	92	76
13	3,4,5-(MeO)$_3$ (3n)	47	67
14	2-CF$_3$ (3o)	159	76
15	4-F-2-Me (3p)	26	62
16	 3q	48	61
17	 3r	24	85
18[b]	 3s	22	80
19	 3t 	20	70
20[c]	 3u +  4u 62:38	26	84
21[c]	 3v +  4v >99:1	86	59
22[c]	 3w +  4w 63:37	67	59

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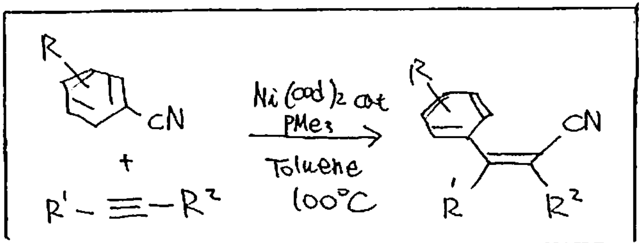
[a] Reactions were carried out using an aryl cyanide (1.0 mmol), an alkyne (1.0 mmol), Ni(cod)$_2$ (0.10 mmol), and PMe$_3$ (0.20 mmol) in toluene at 100 °C. [b] Performed with 2.0 mmol of 2a. [c] Ratio of isomers was determined by GC analysis.



- ligand effect

  → PMe$_3$ was optimum

  PBu$_3$, PCy$_3$, P(t-Bu)$_3$, yield was lower

  Bidentate ligand or other metal complexes completely retarded.

- Substituent effect

  → electronwithdrawing substituent reacted effectively in good to excellent yield.

  (Because oxidative addition of a C-CN bond rapidly occured.)

- Terminal alkynes

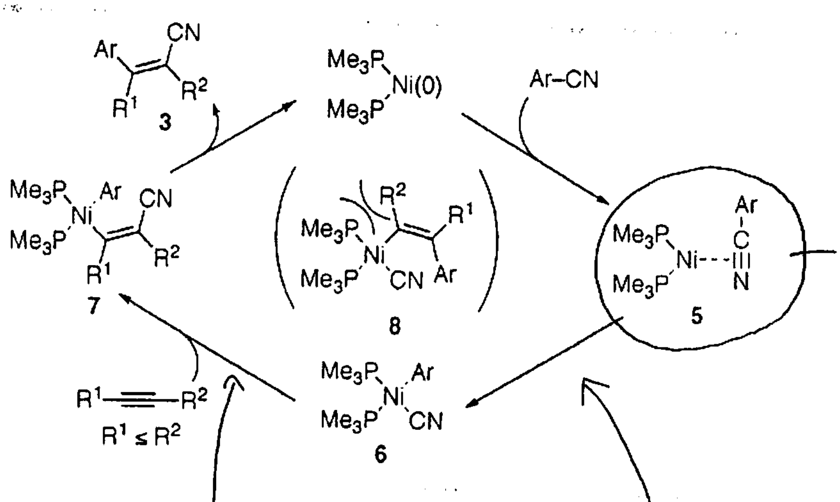
  → oligomerization

- Regioselectivity

  Me – ≡ – tBu

  → complete regioselectivity.

mechanism



π-coordinating intermediate

rate determing step, oxidative addition

insertion of alkyne

insertion of an alkyne take place at the Ni-CN bond.

insertion of an alkyne take place at the Ni-Ar bond

→ steric reason (regioselection) .