Nickel-Catalyzed Reductive Cyclizations and Couplings

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10/28/2015

Dong Group

Nickel-Catalyzed Reductive Cyclizations and Couplings

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2. General mechanistic considerations
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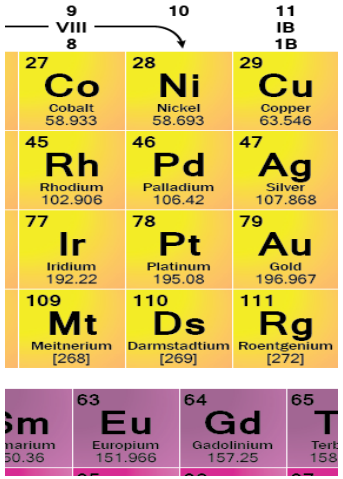
Montgomery, J. *Angew. Chem. Int. Ed*. **2004**, *43*, 3890 – 3908; Louie, J. *Acc. Chem. Res.* **2015**, *48*, 2354-2365; Jamison, T, F. *Acc. Chem. Res.* **2015**, *48*, 1503-1514; Jamison, T, F. *Nature.* **2014**, *300-309*

General introduction of Nickel

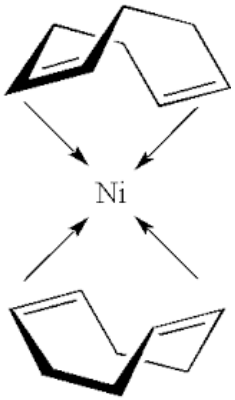


Important event of Nickel:

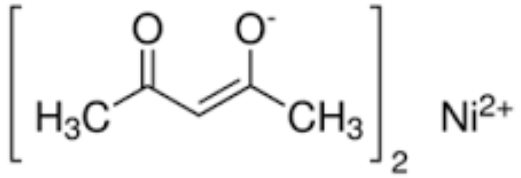
- Nickel was isolated in 1751
- In 1890s, Mond synthesized $Ni(CO)_4$
- Sabatier performed the first hydrogenation of ethylene using Nickel in1912
- Wilke Synthesized $Ni(cod)_2$

Advantage of Nickel:
Ni: $ 1.2/mmol
Pd: $ 1500/mmol

Two major Nickel catalysts:

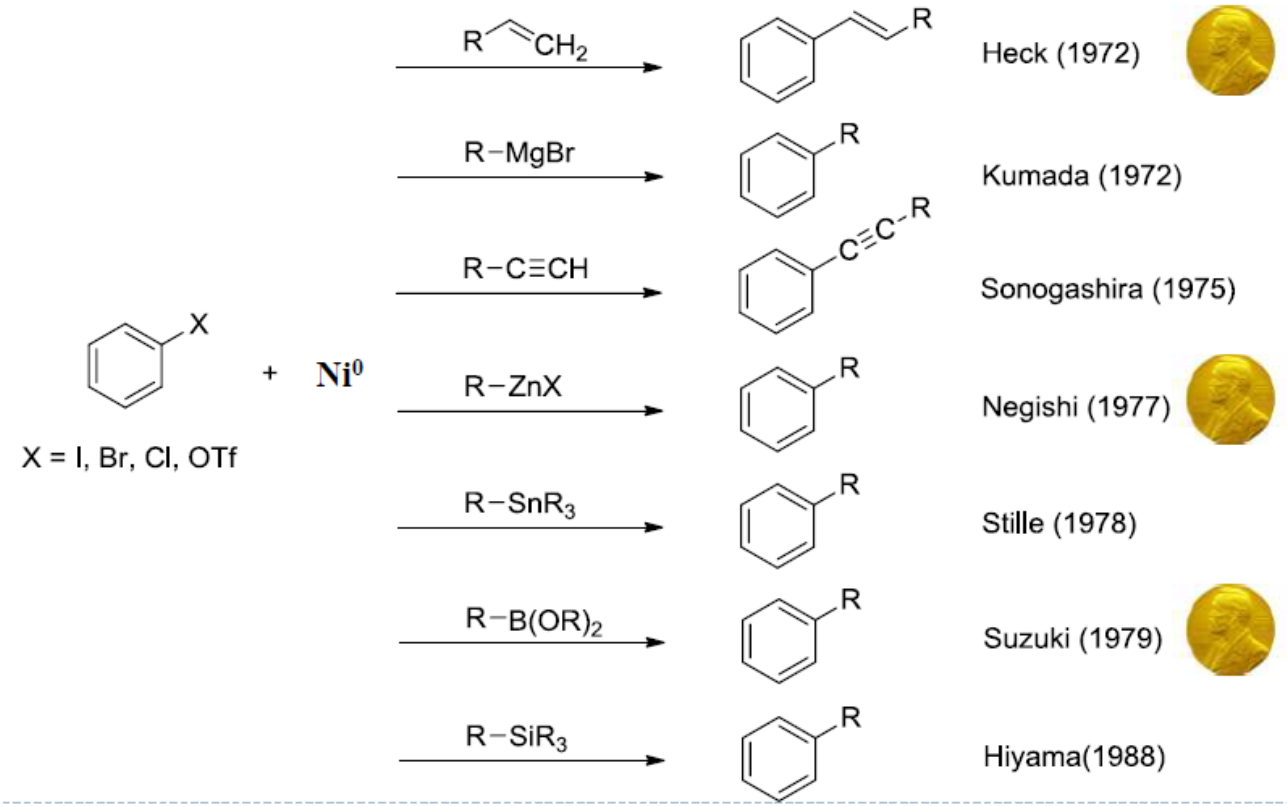


$Ni(cod)_2$



$Ni(acac)_2$

Nickel catalyzed coupling reactions



Nickel vs Palladium

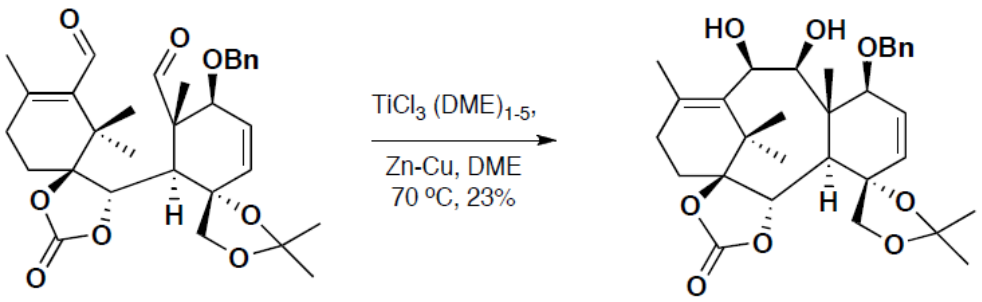
Nickel	Palladium
Smaller atomic radius	Larger atomic radius
Less electronegative	More electronegative
Harder	Softer
Facile oxidative addition	Facile reductive elimination
Facile β-migratory insertion	Facile β-hydride elimination

General introduction of reductive coupling

McMurry type coupling:

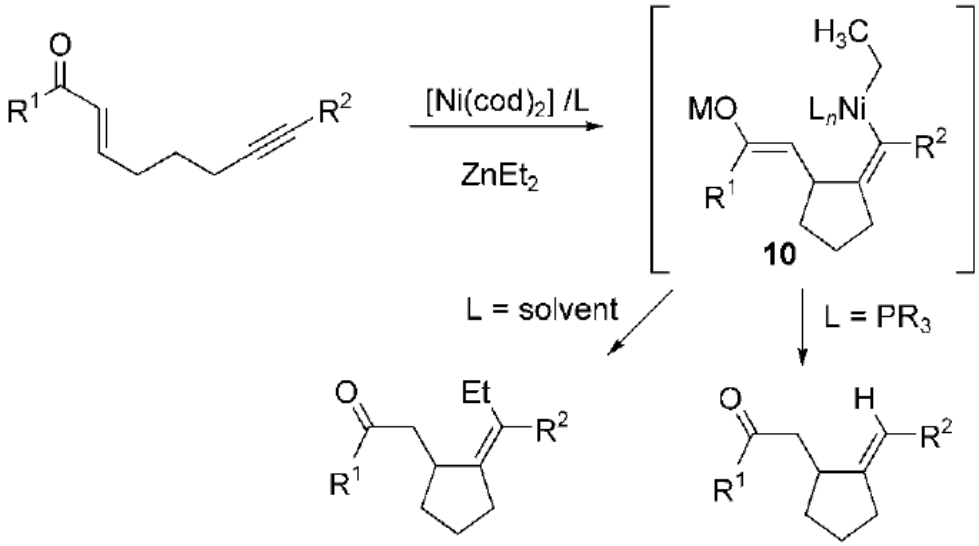
Coupling of two carbonyl-type species to form pinacol type products

Example: McMurry coupling in Nicolau's synthesis of taxol



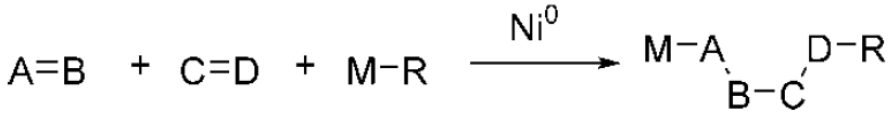
Nicolaou *Nature* **1994**, *367*, 630

Nickel catalyzed reductive coupling

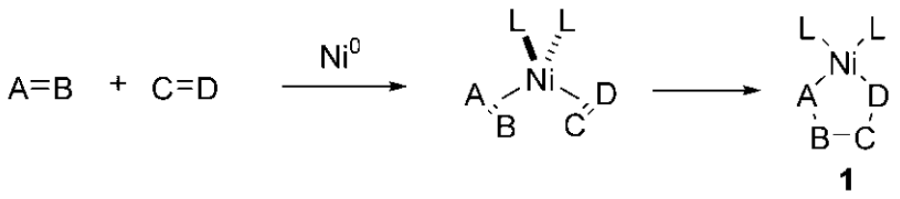


Montgomery, J. *Angew. Chem. Int. Ed*. **2004**, *43*, 3890 – 3908;
Young, I, S. Baran group meeting 3/11/2009

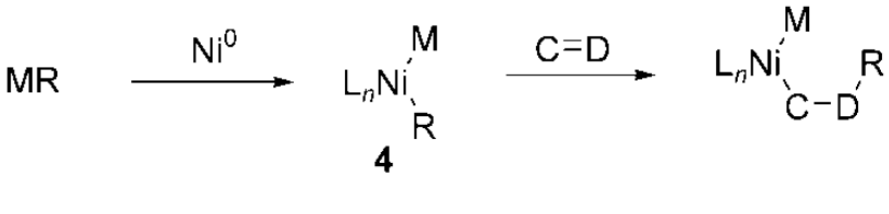
Possible mechanism for reductive coupling

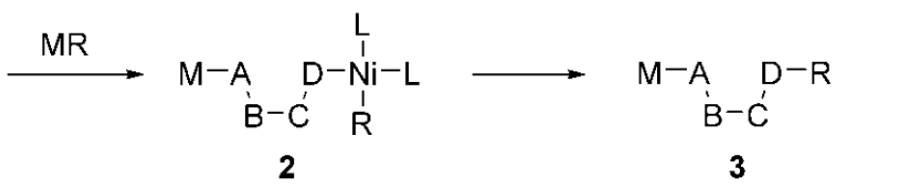


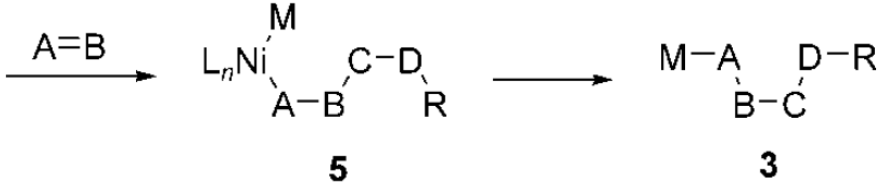
a) Oxidative Cyclization of Two π Components



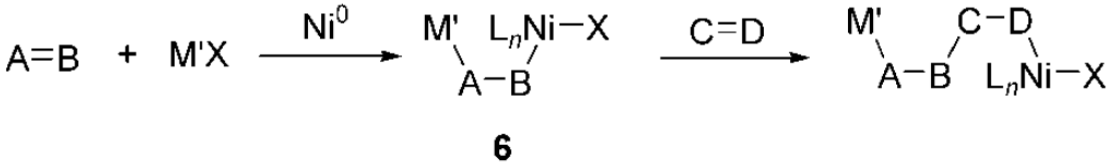
b) Oxidative Addition to Reducing Agent

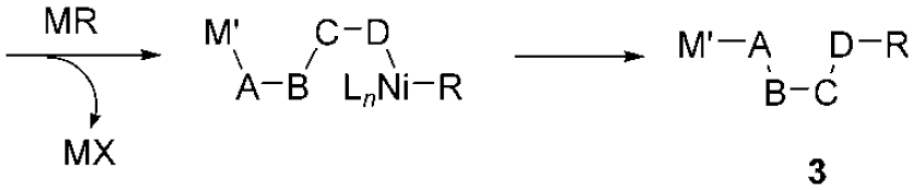






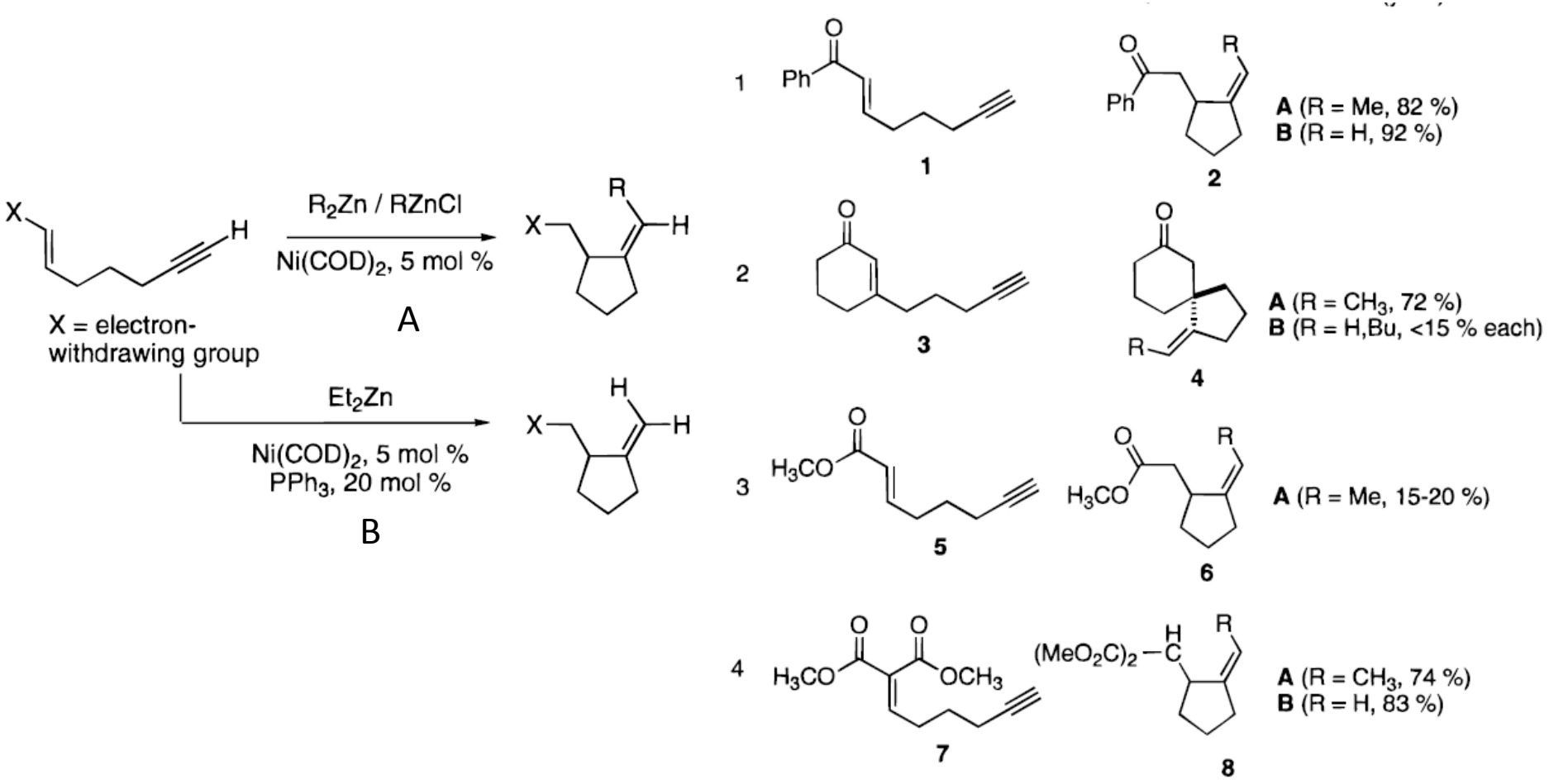
c) Oxidative Addition to One π Component





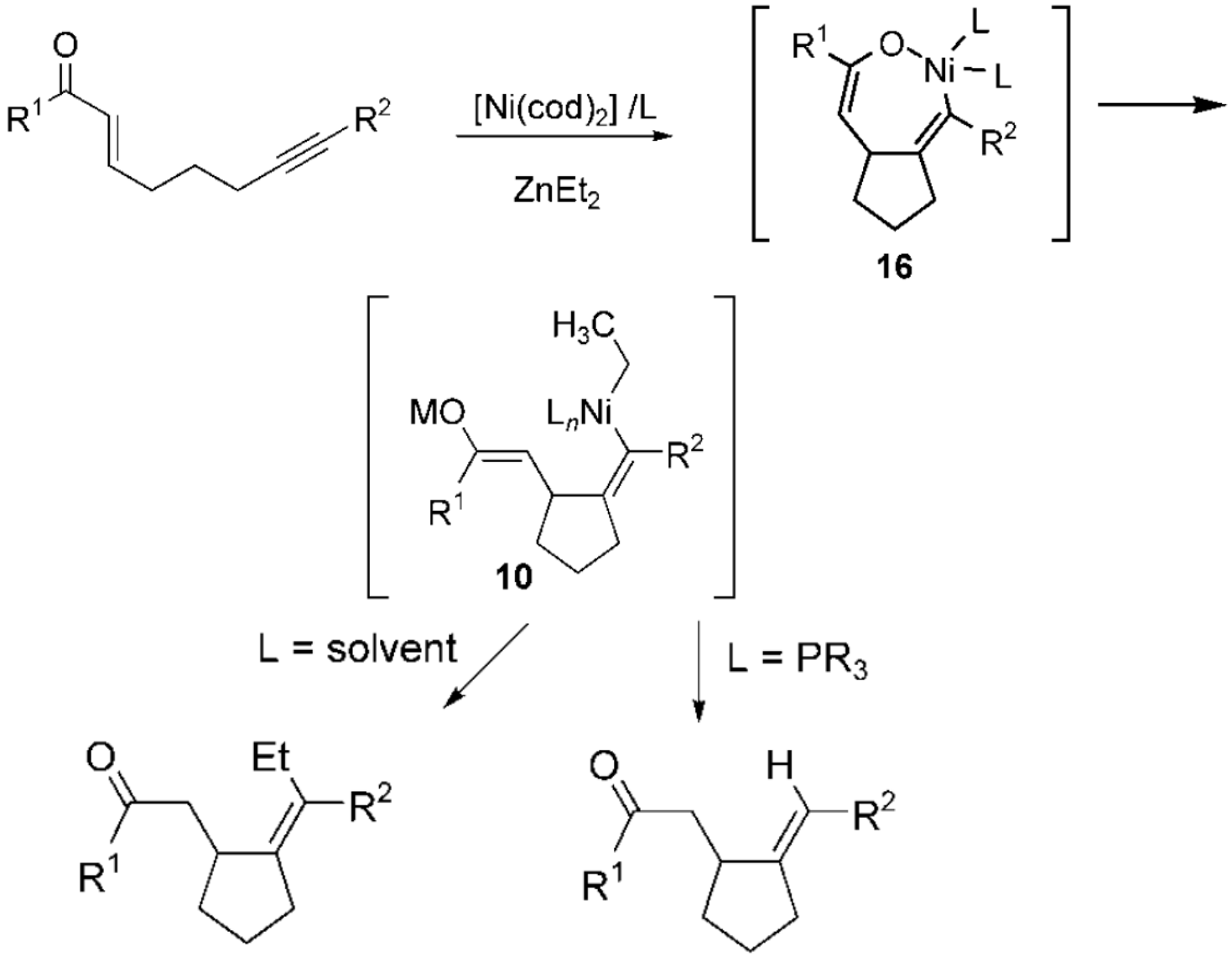
(M'X = Lewis acid)

Couplings of Alkenes with Alkynes



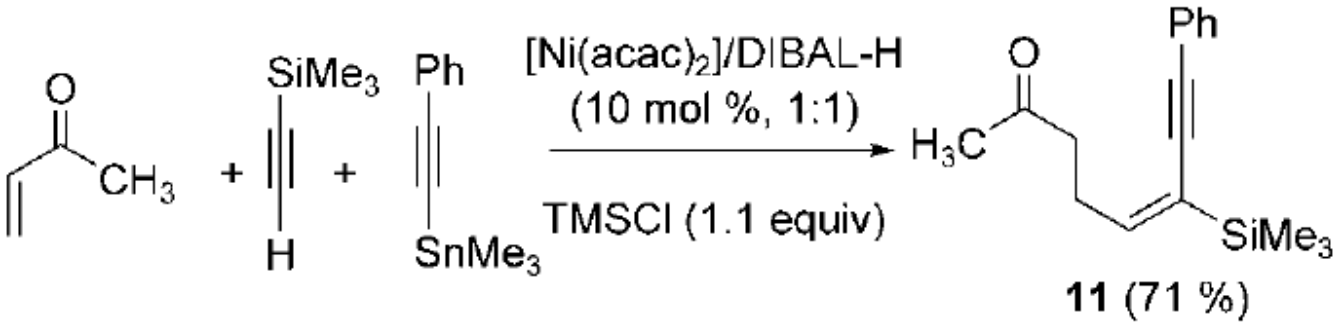
Montgomery, J. *J. Am. Chem.Soc*. **1997**, *119,* 4911

Couplings of Alkenes with Alkynes

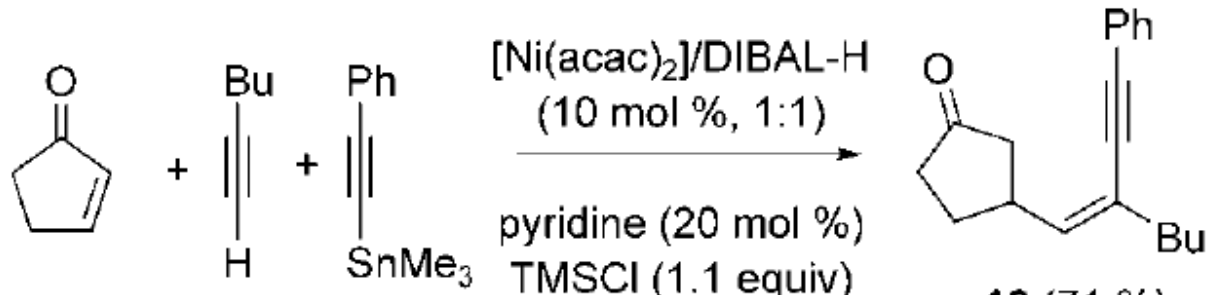


Montgomery, J. *J. Am. Chem.Soc*. **1997**, *119,* 4911

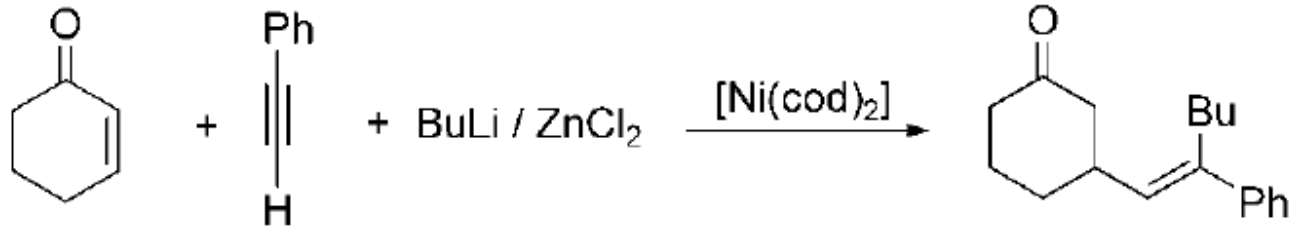
Intermolecular reductive coupling



11 (71 %)



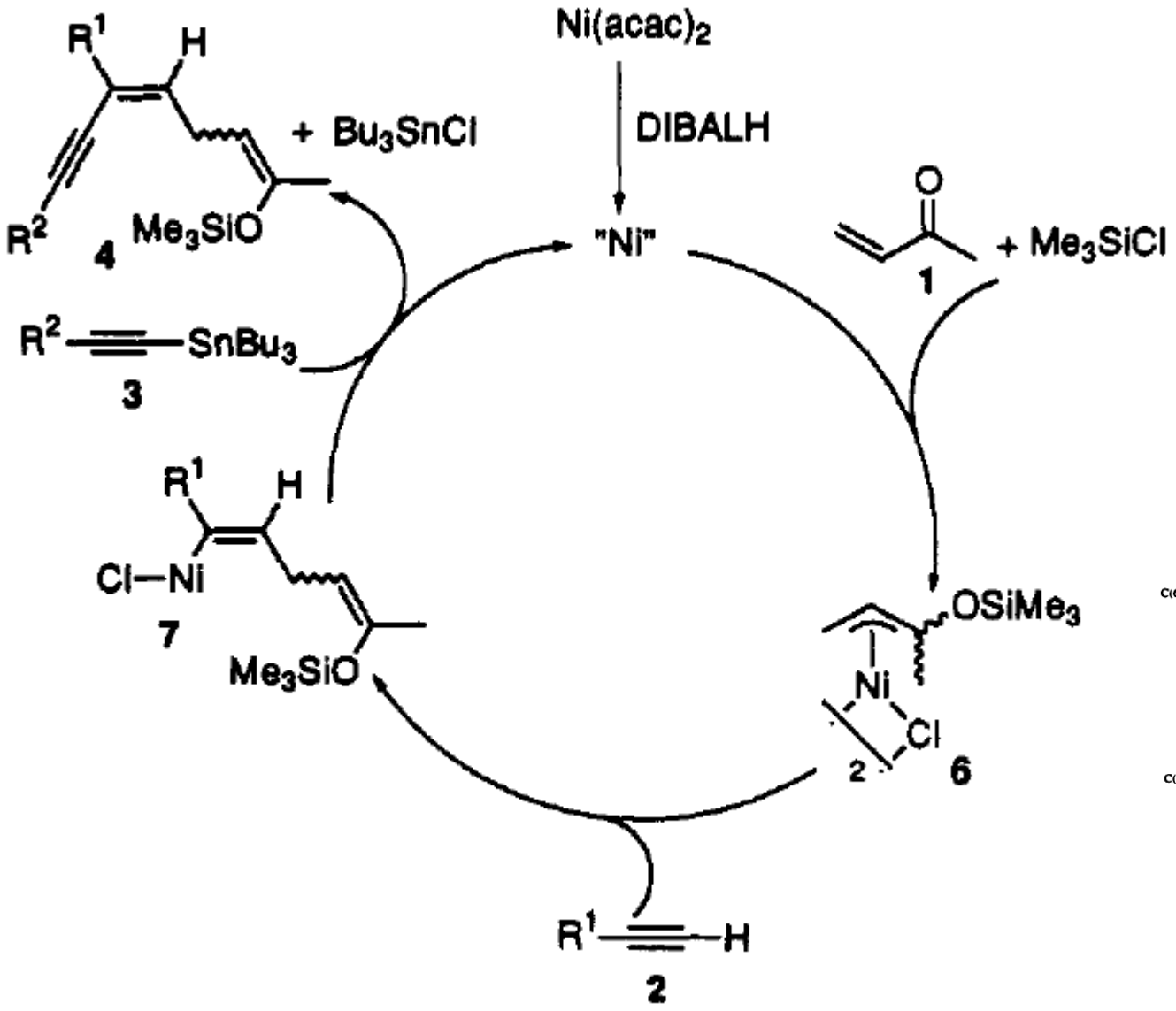
12 (71 %)

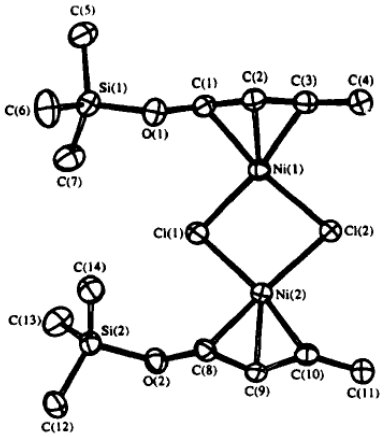


13 (65 %)

Sato, Y. *J. Am. Chem.Soc*. **1994**, *116,* 5975

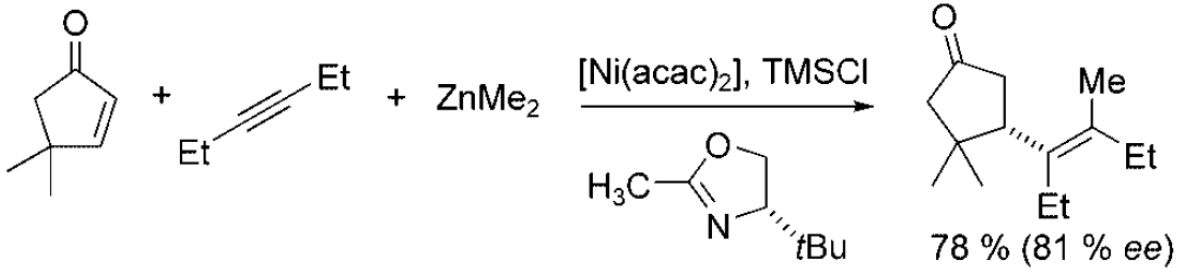
Proposed mechanism for enone-alkyne coupling

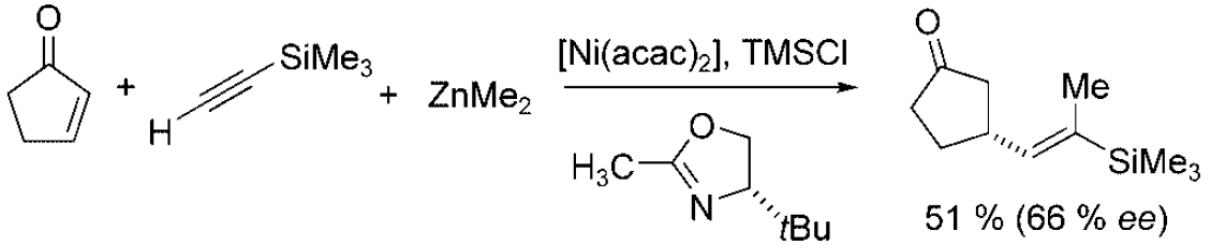


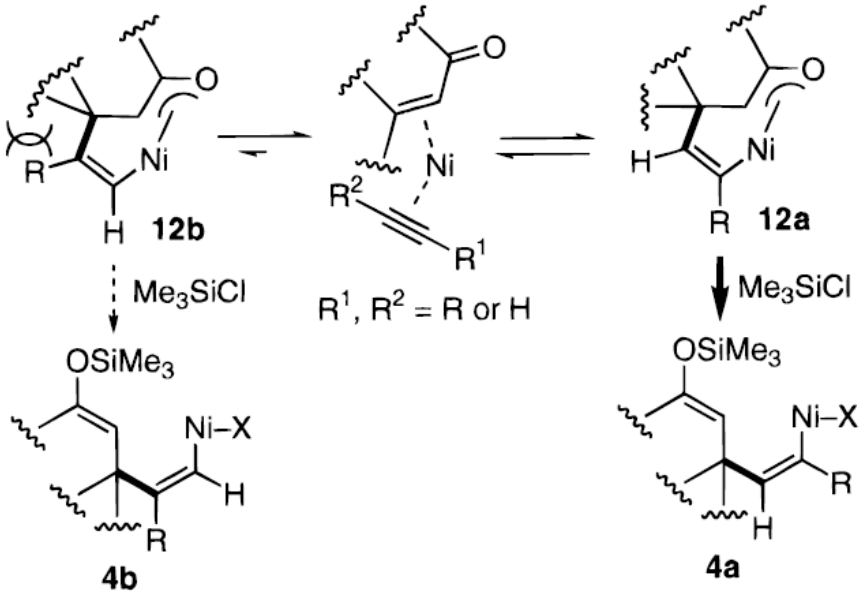


Sato, Y. *J. Am. Chem.Soc*. **1994**, *116,* 5975

Asymmetric intermolecular reductive coupling

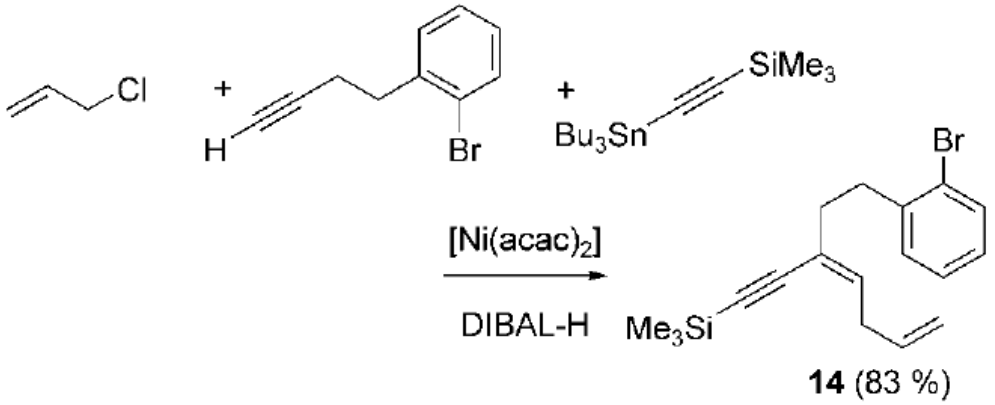


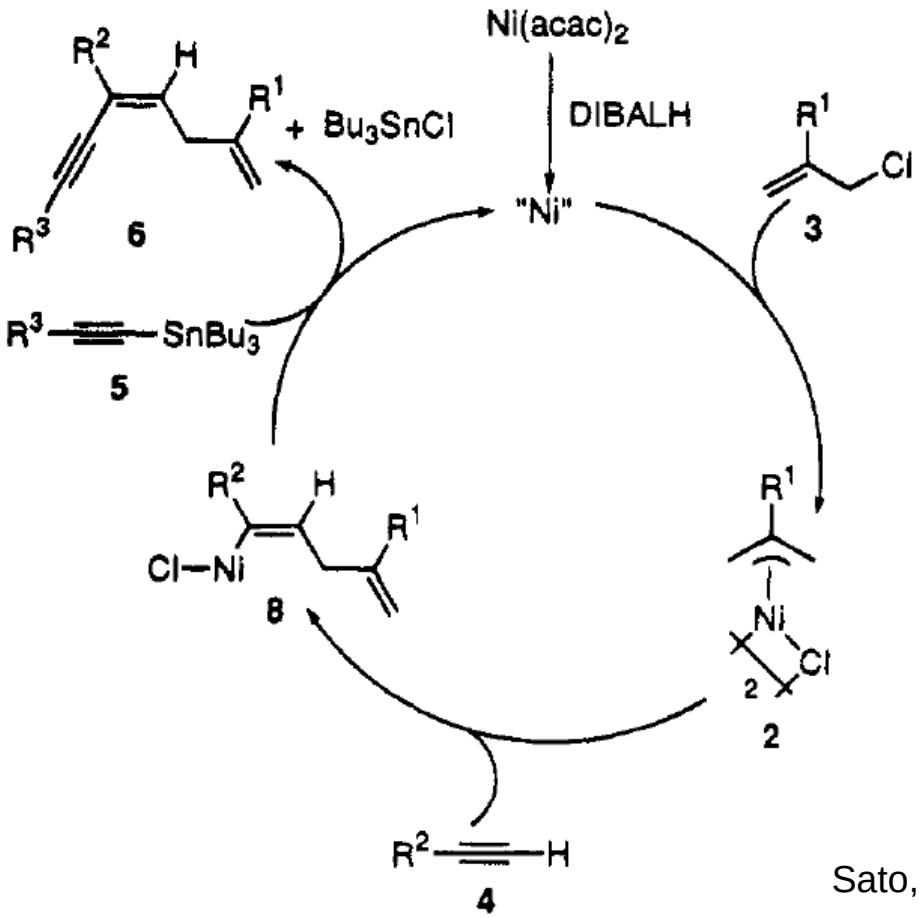




Sato, Y. *J. Org. Chem*. **1996**, *61,* 8248

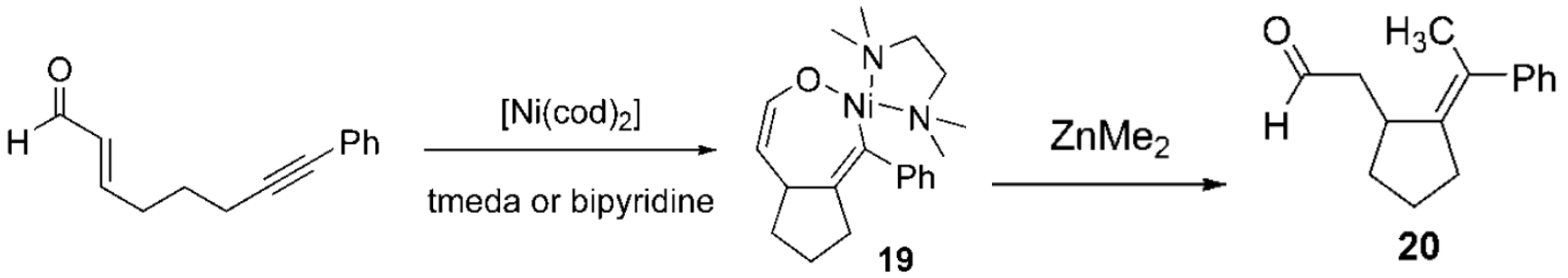
Coupling of allyl halides or acetates

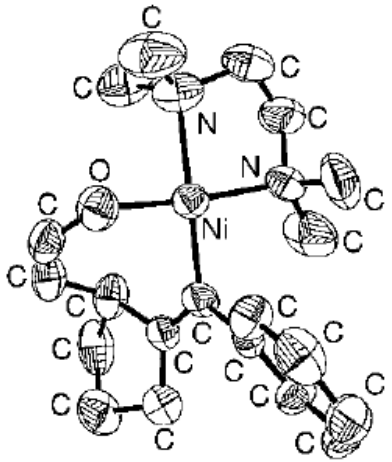




Sato, Y. *J. Org. Chem*. **1994**, *59,* 6877

Mechanism study





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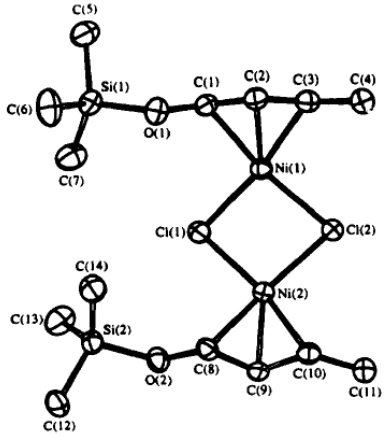

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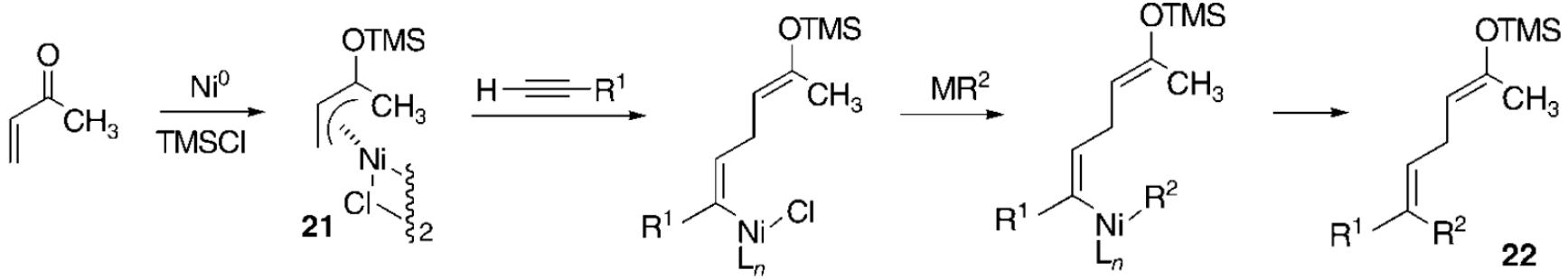
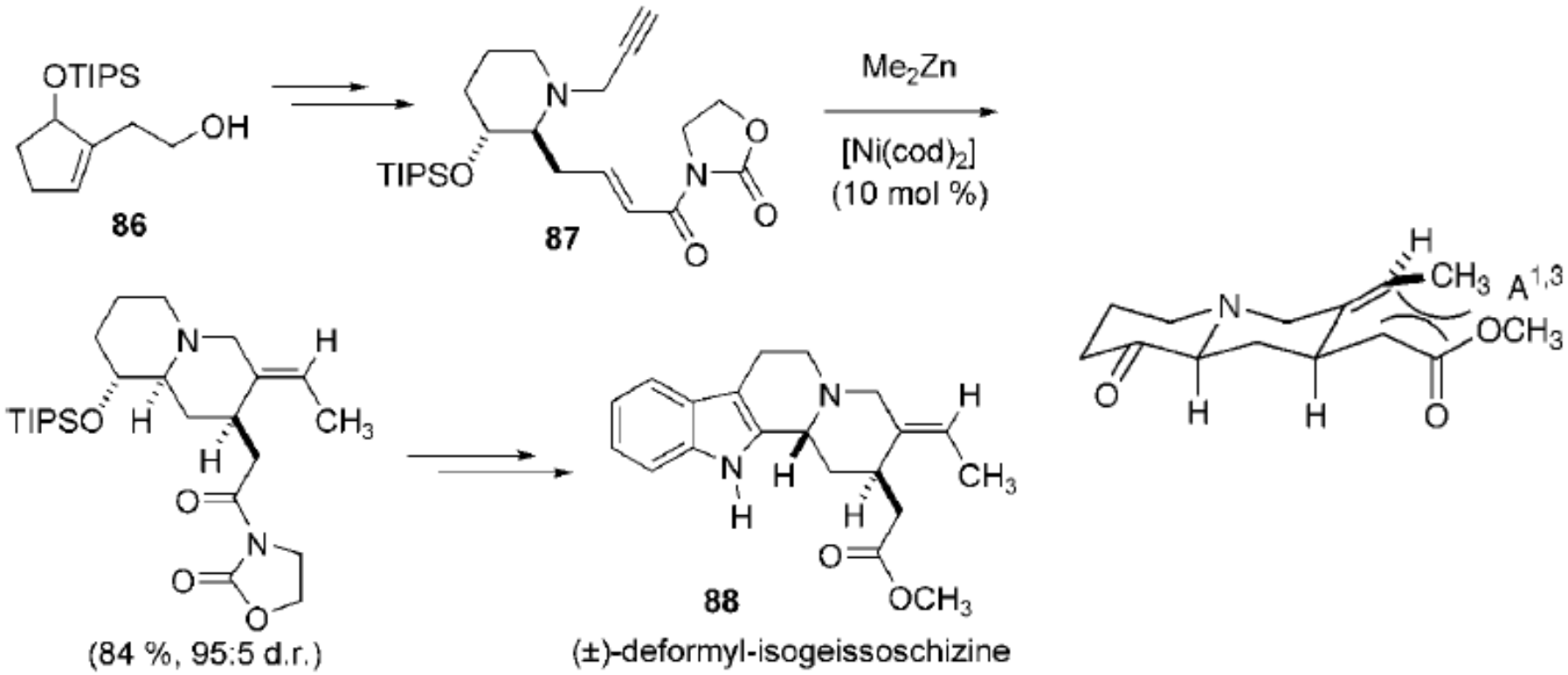
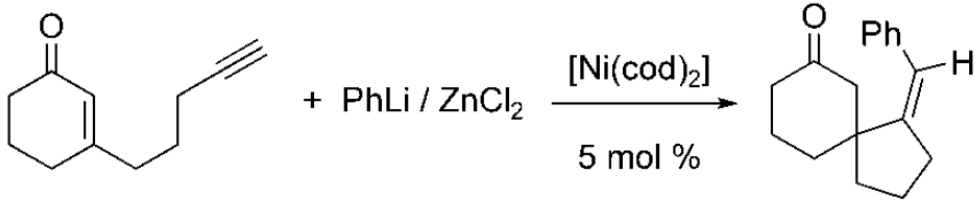


Construction of the framework of isogeissoschizine

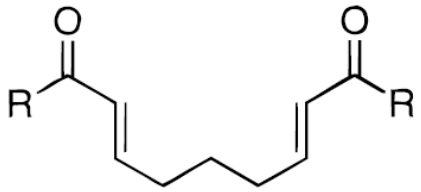


Montgomery, J. *Org. Lett*. **2002**, *4,* 615

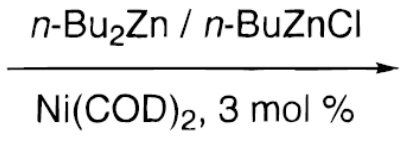
Coupling of Two Alkenes

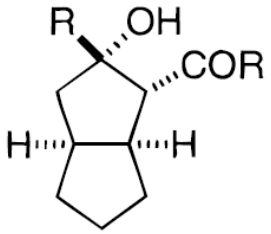


7 (76 %)



1a R = Ph
1b R = Me





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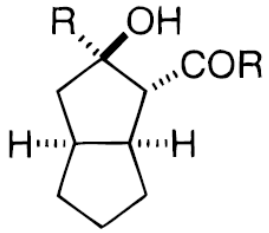
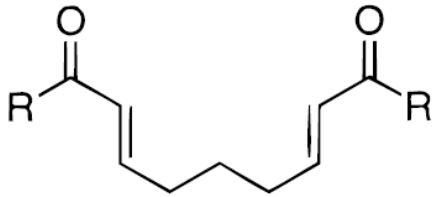
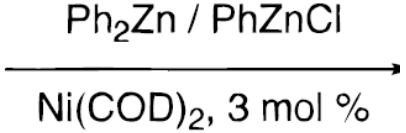


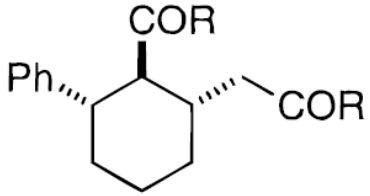
4a R = Ph (60-90 %)
4b R = Me (17 %)

5b R = Me (54 %)

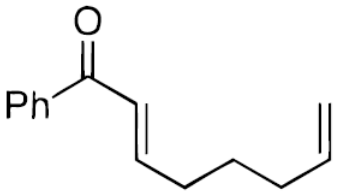


1a R = Ph
1b R = Me





2a R = Ph (65 %)
2b R = Me (58 %)



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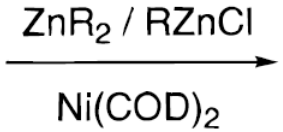
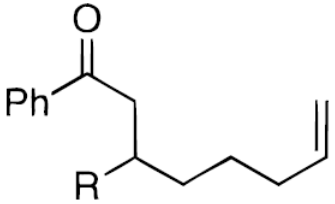
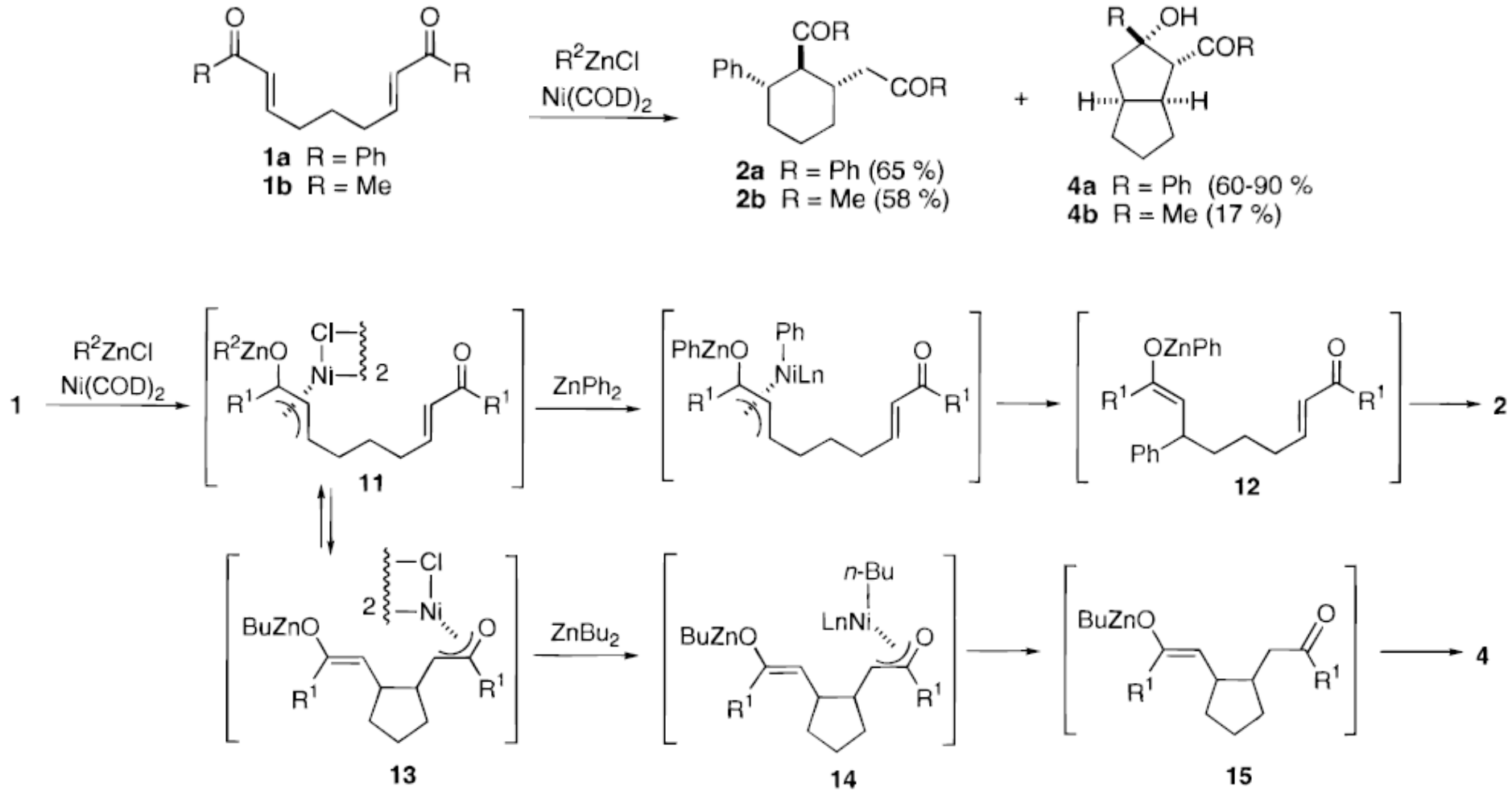




9a R = *n*-Bu (75 %)
9b R = Ph (68 %)

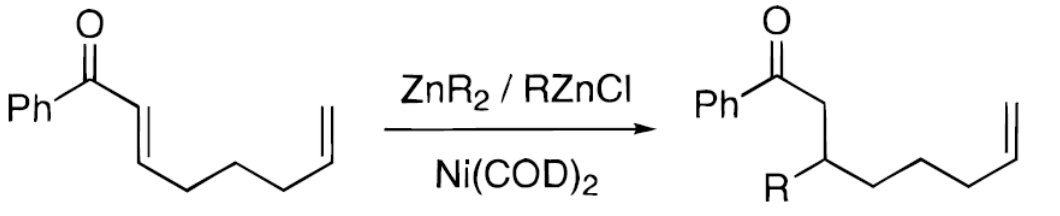
Montgomery, J. *J. Org. Chem*. **1996**, *61*, 1562

Coupling of Two Alkenes



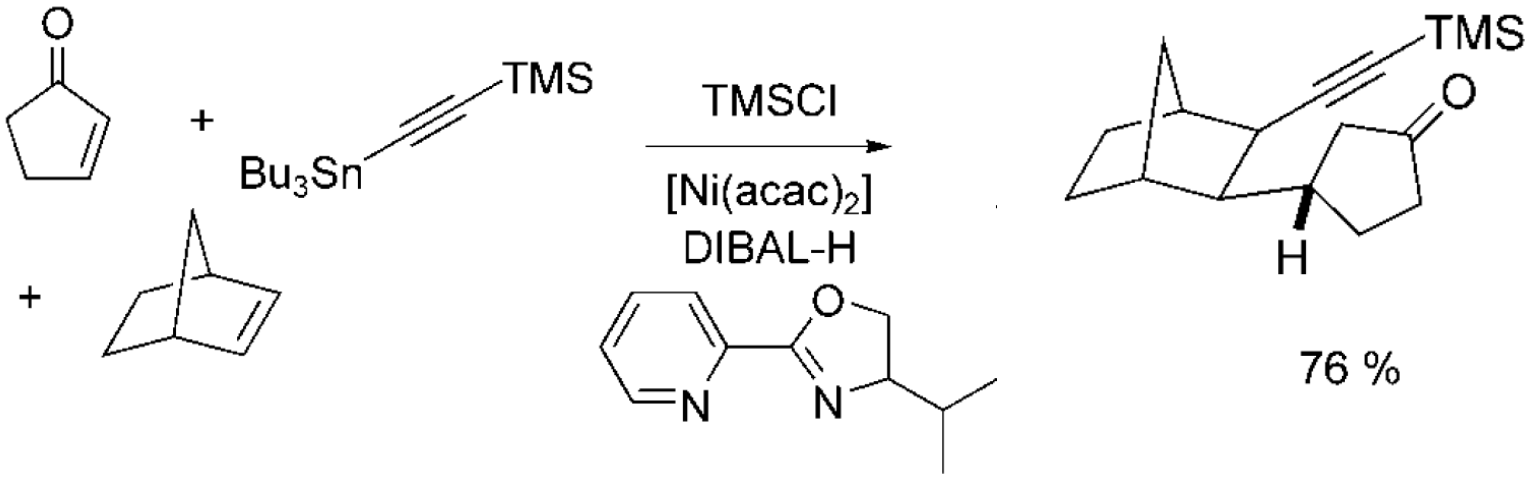
Montgomery, J. *J. Org. Chem*. **1996**, *61,* 1562

Intermolecular coupling of an electron-deficient olefin with a strained olefin



8

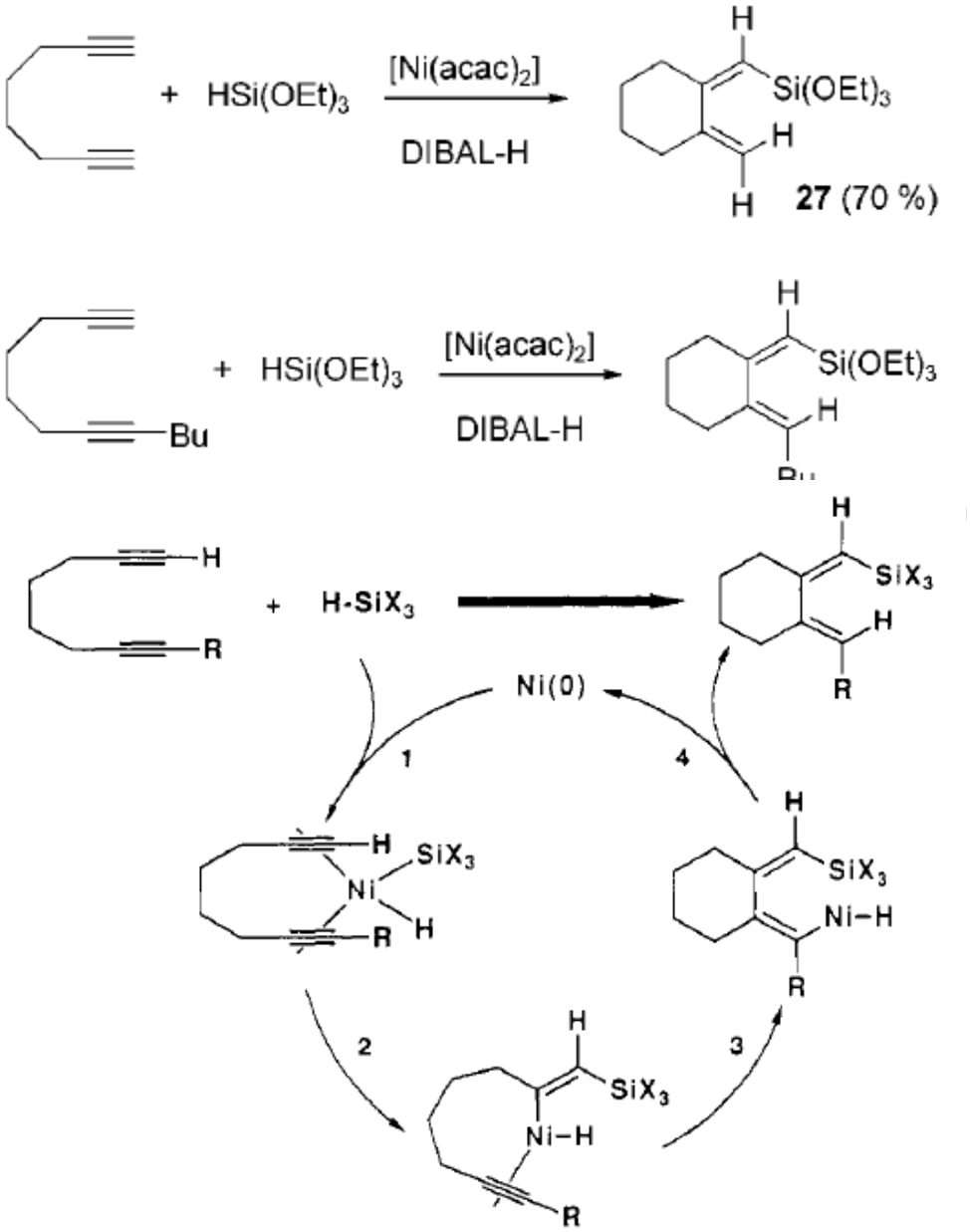
9a R = *n*-Bu (75 %)
9b R = Ph (68 %)



76 %

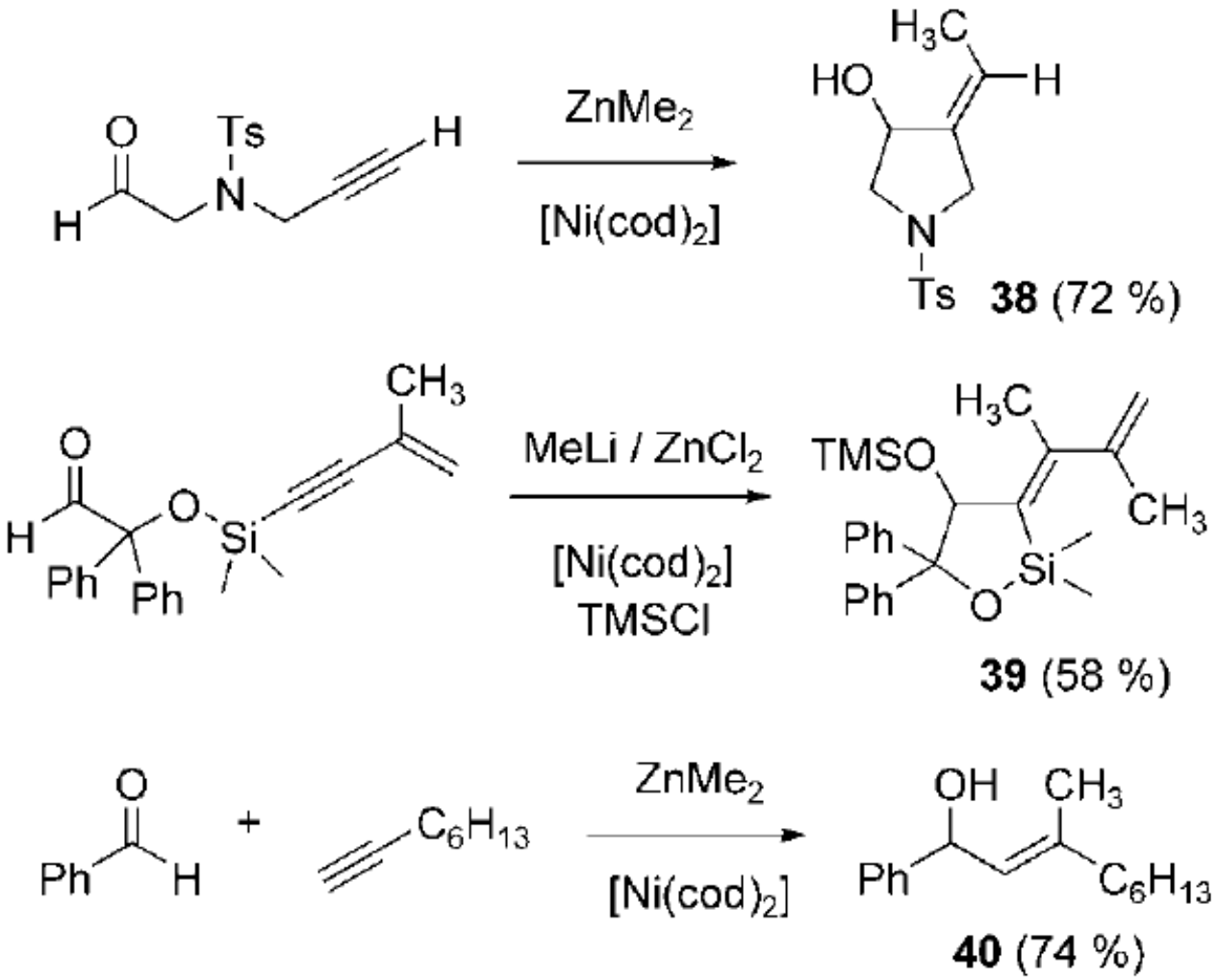
Ikeda, S. *J. Org. Chem*. **1996**, *61,* 1562

Coupling of two alkynes



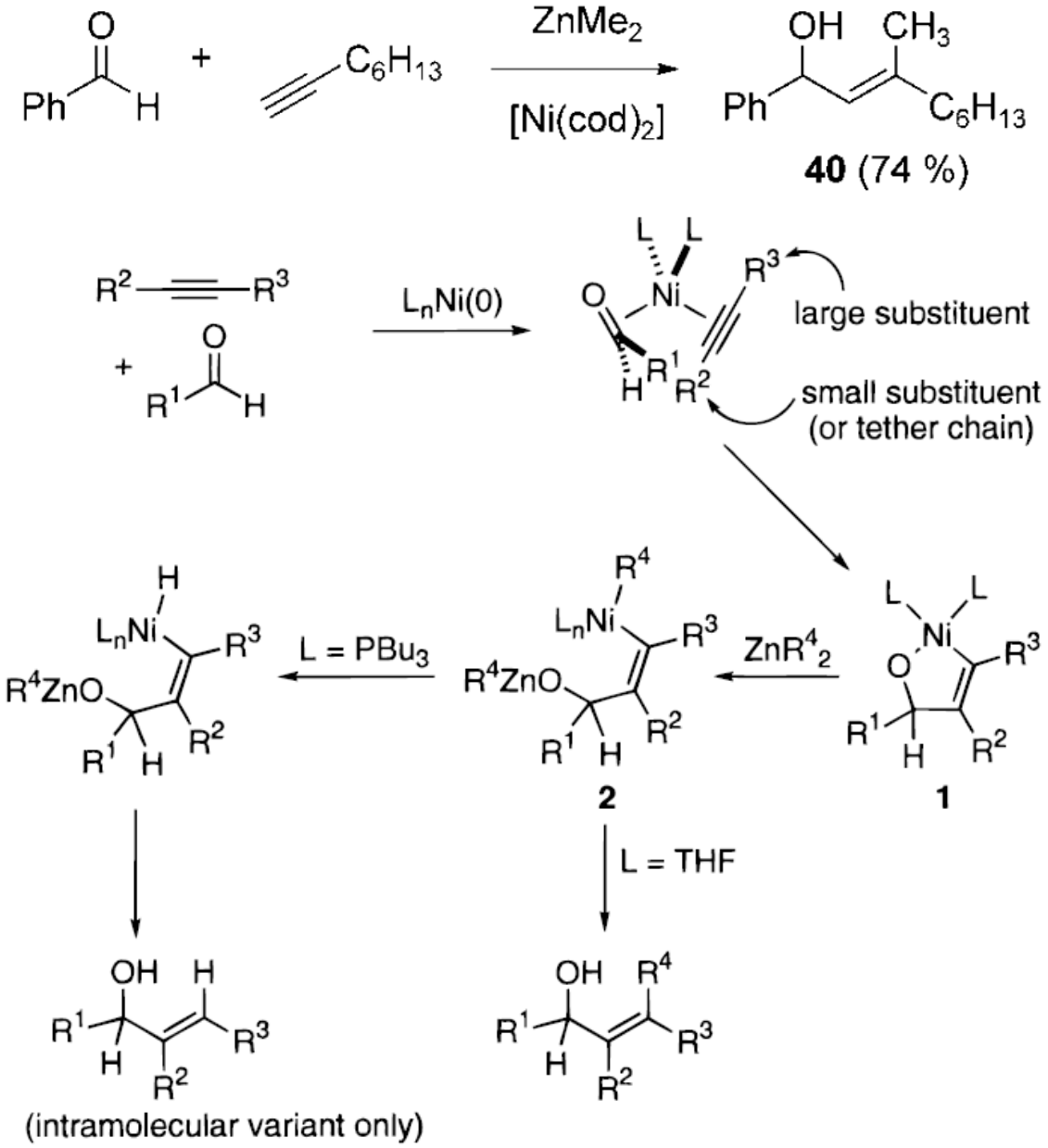
Tamao, K. *J. Am. Chem.Soc*. **1989**, *111,* 6478

Coupling of Carbonyl Compounds with Alkynes



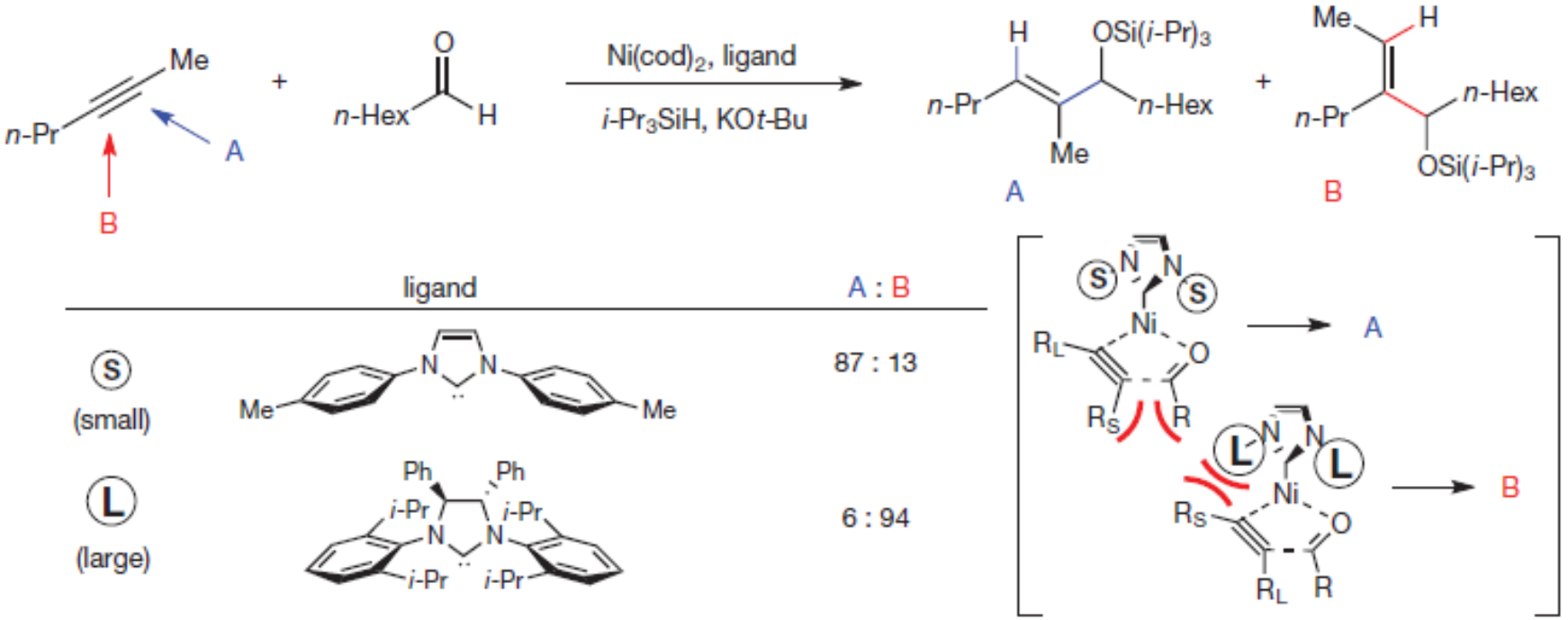
Montgomery, J. *J. Am. Chem. Soc*. **1997**, *119,* 9065

Coupling of Carbonyl Compounds with Alkynes



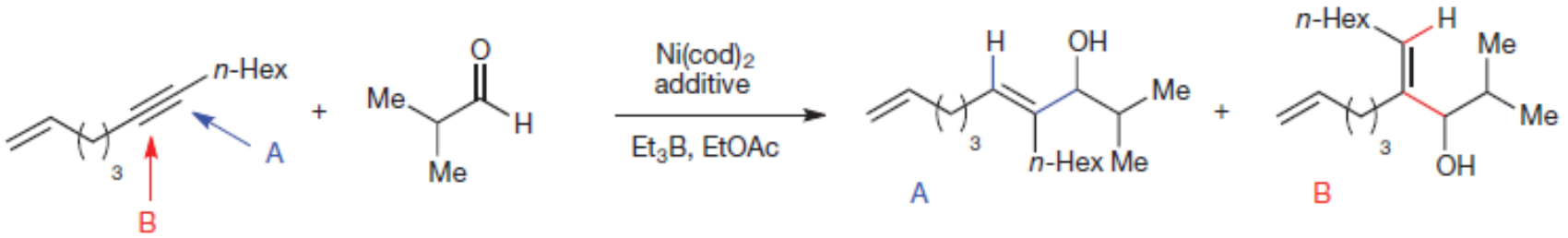
Montgomery, J. *J. Am. Chem. Soc*. **1997**, *119,* 9065

Regiocontrol in reductive coupling reactions

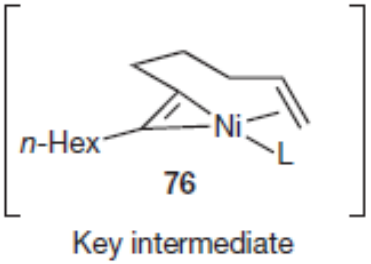


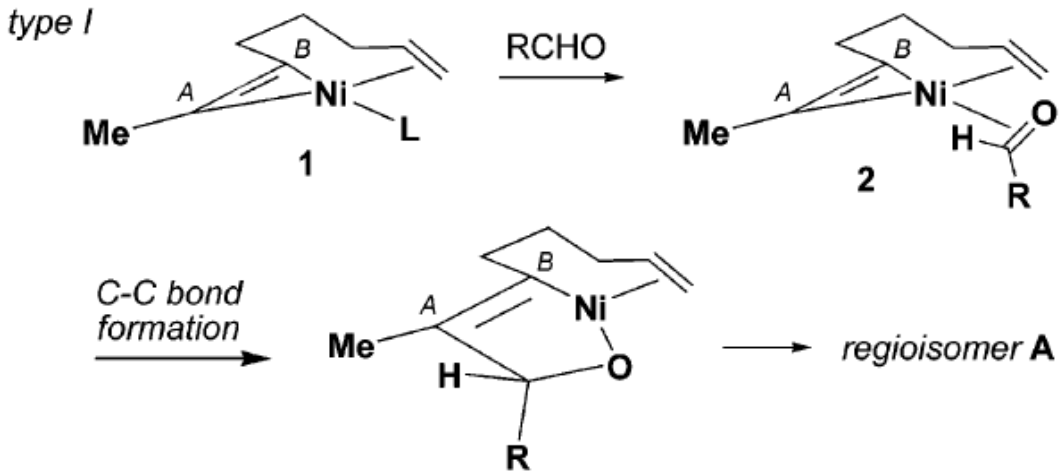
Montgomery, J. *J. Am. Chem. Soc*. **2010**, *132,* 6304

Regiocontrol in reductive coupling reactions

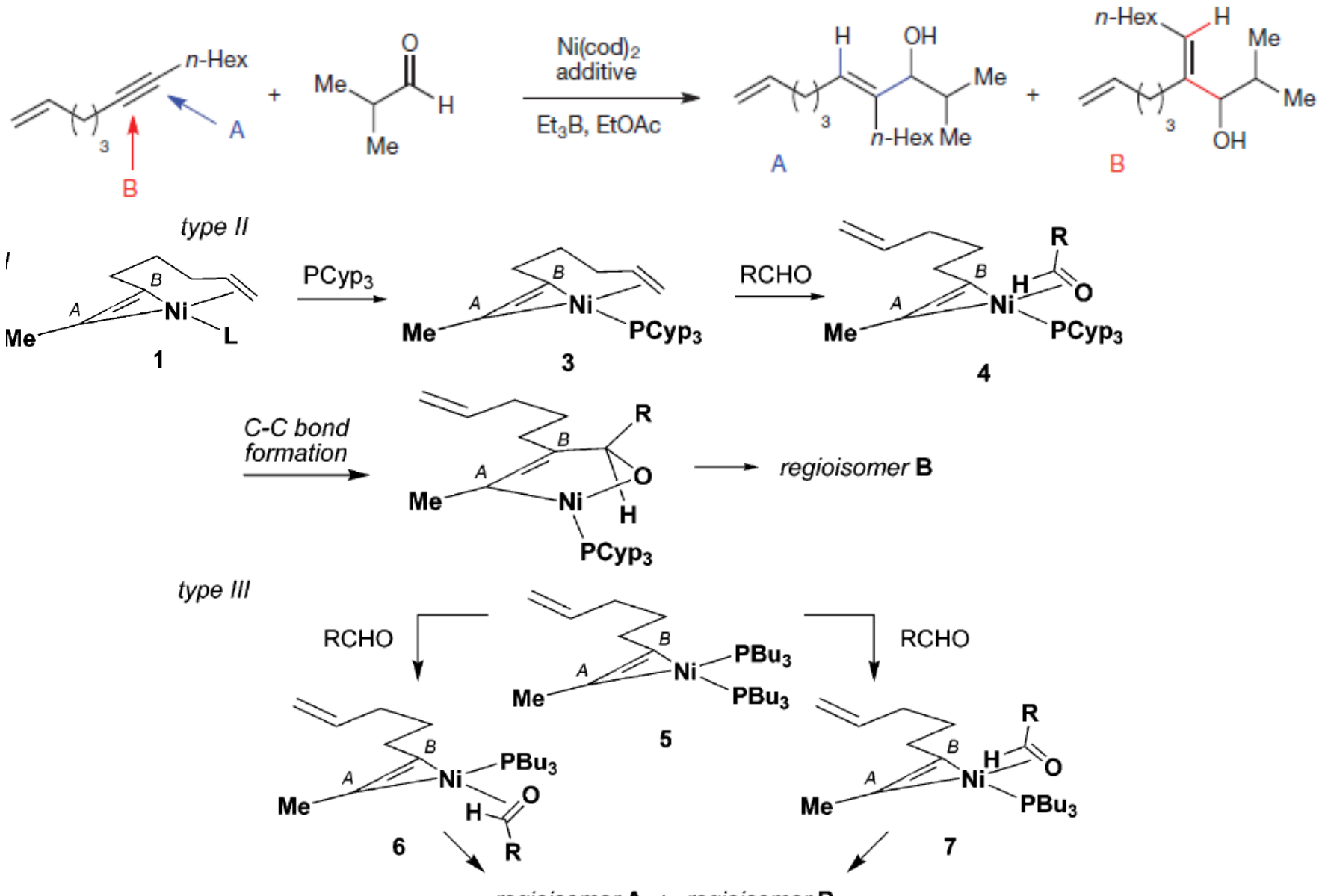


Additive	A : B	Comments
None	> 95 : 5	Alkene stays bound, directs aldehyde to distal position (A)
PBu_3	50 : 50	Two phosphines bind, displacing alkene, aldehyde can displace either
$PCyp_3$	5 : > 95	Aldehyde displaces alkene ligand at proximal position (B) rather than phosphine



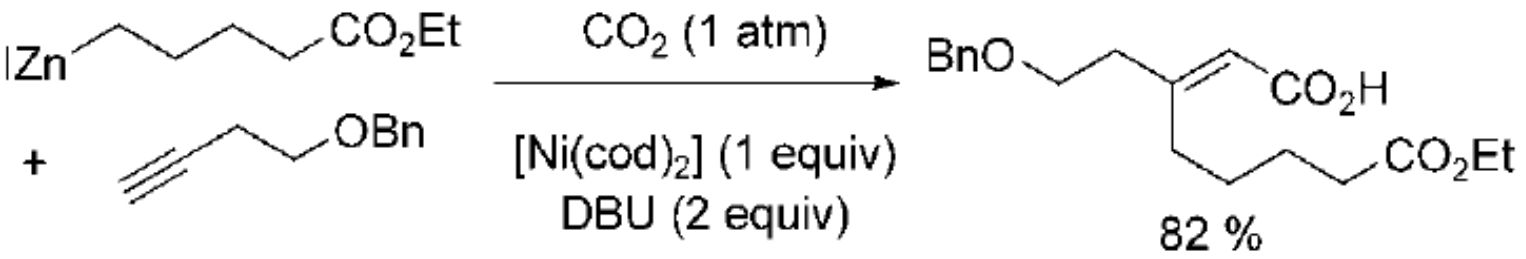


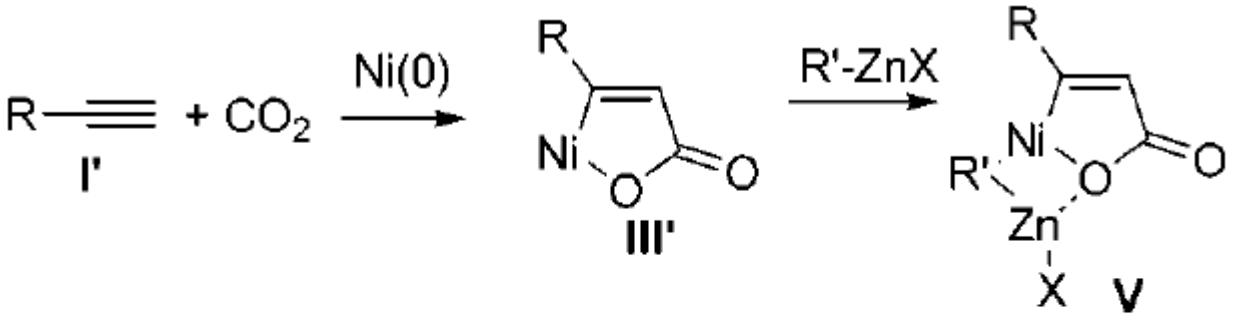
Regiocontrol in reductive coupling reactions

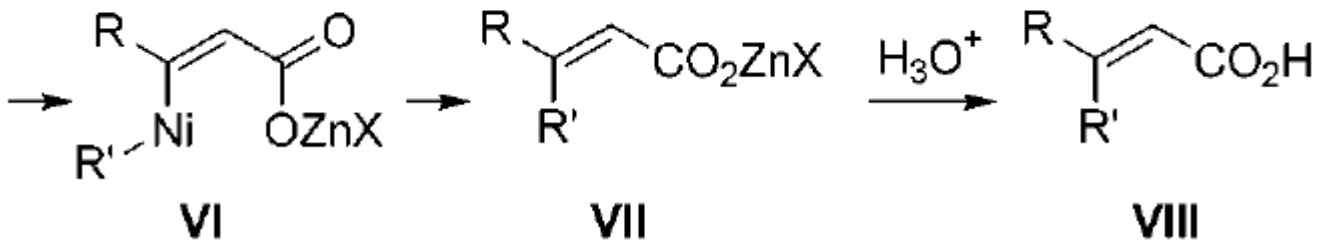


Montgomery, J. *J. Am. Chem. Soc*. **2008**, *130,* 469

Reductive coupling of alkynes and CO_2

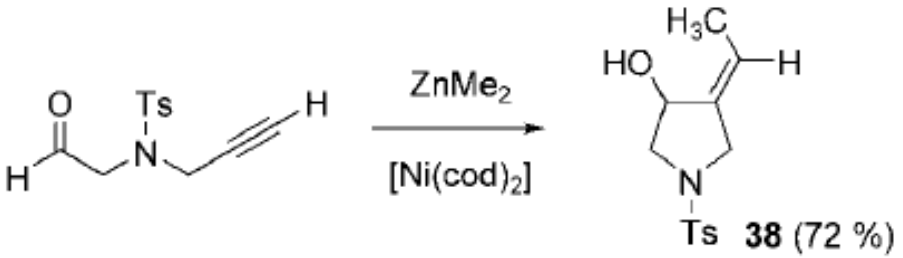


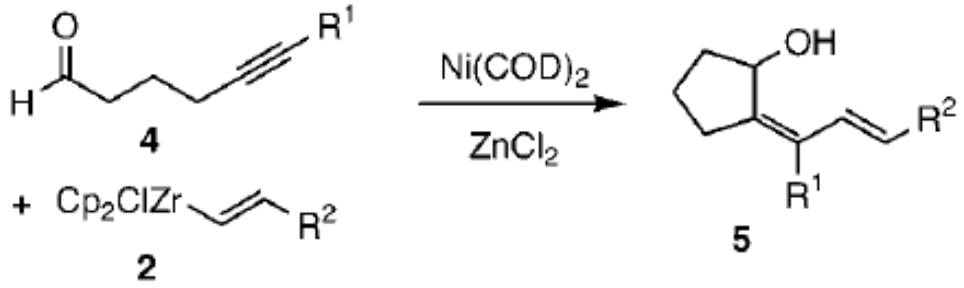




Mori, M. *Org. Lett*. **2001**, *3,* 3345

Addition of Alkenyl zirconium complexes to aldehydes and alkynes

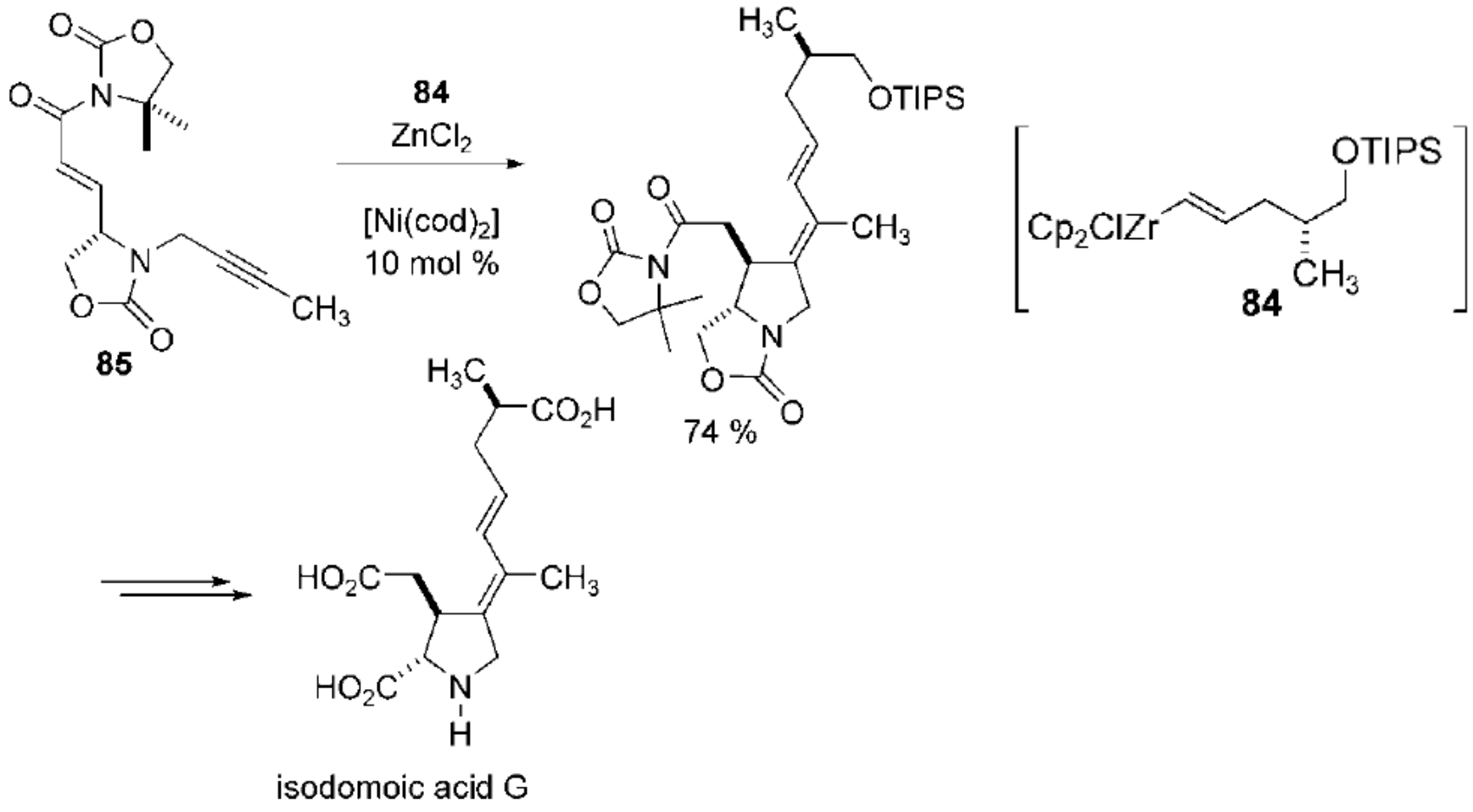




entry	R_1	R_2	yield, %
1	H	C_6H_{13}	56
2	Me	C_6H_{13}	50
3	Ph	C_6H_{13}	68
4	Me	Ph	66

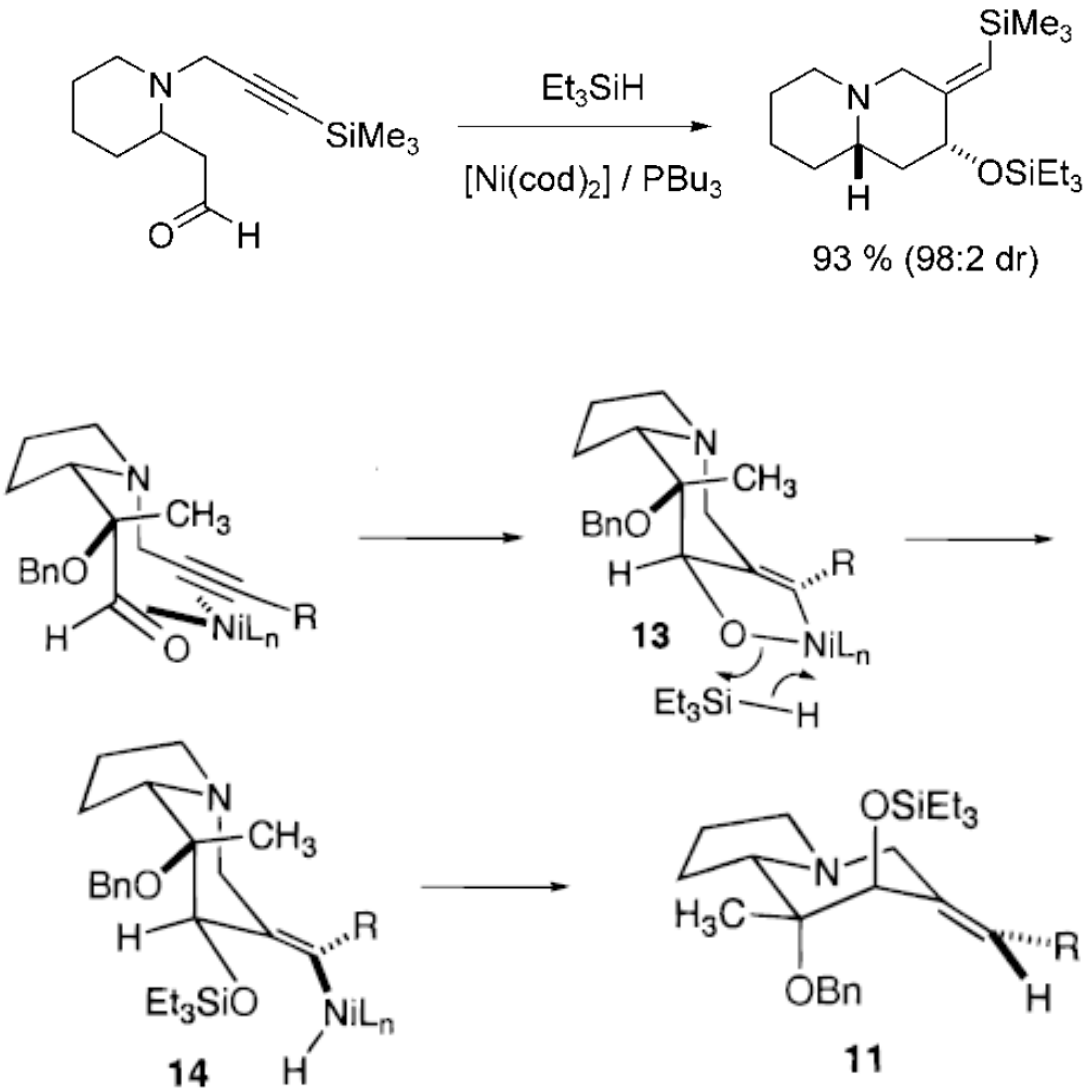
Montgomery, J. *Org. Lett*. **2002**, *4,* 1743

Key step in the total synthesis of isodomoic acid G



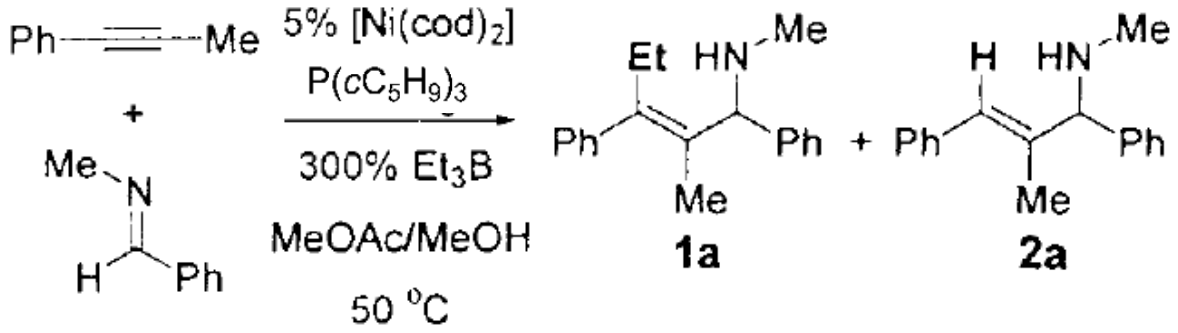
Montgomery, J. *Org. Lett*. **2003**, *5,* 3771

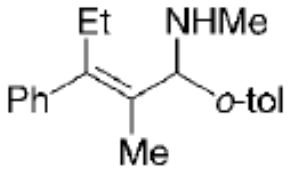
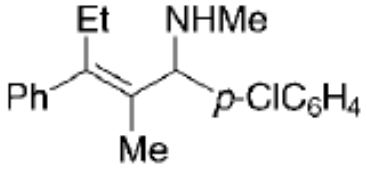
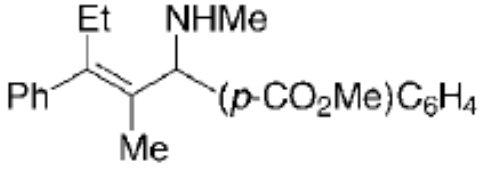
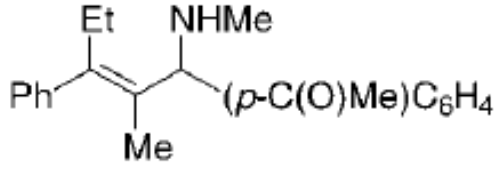
Using triethylsilane as the reductive agent



Montgomery, J. *J. Am. Chem. Soc*. **1999**, *121,* 6098

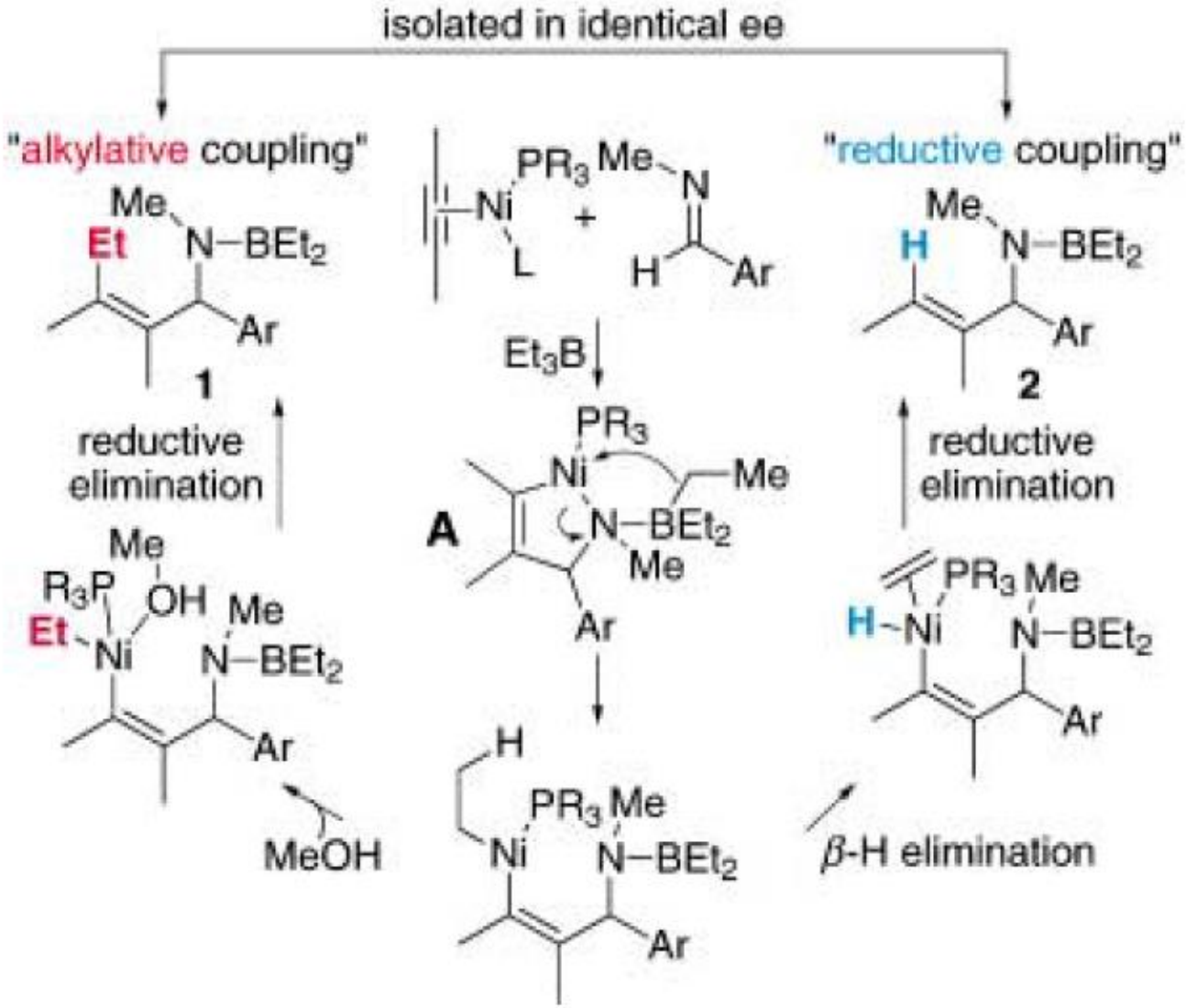
Intermolecular coupling of imines with Alkynes



	Product	Yield [%][b]	1:2[c]	Regio-selectivity[c,d]
1b		85	94:6	90:10
1c		95	96:4	90:10
1d		82	> 96:4	90:10
1e		78	> 96:4	91:9

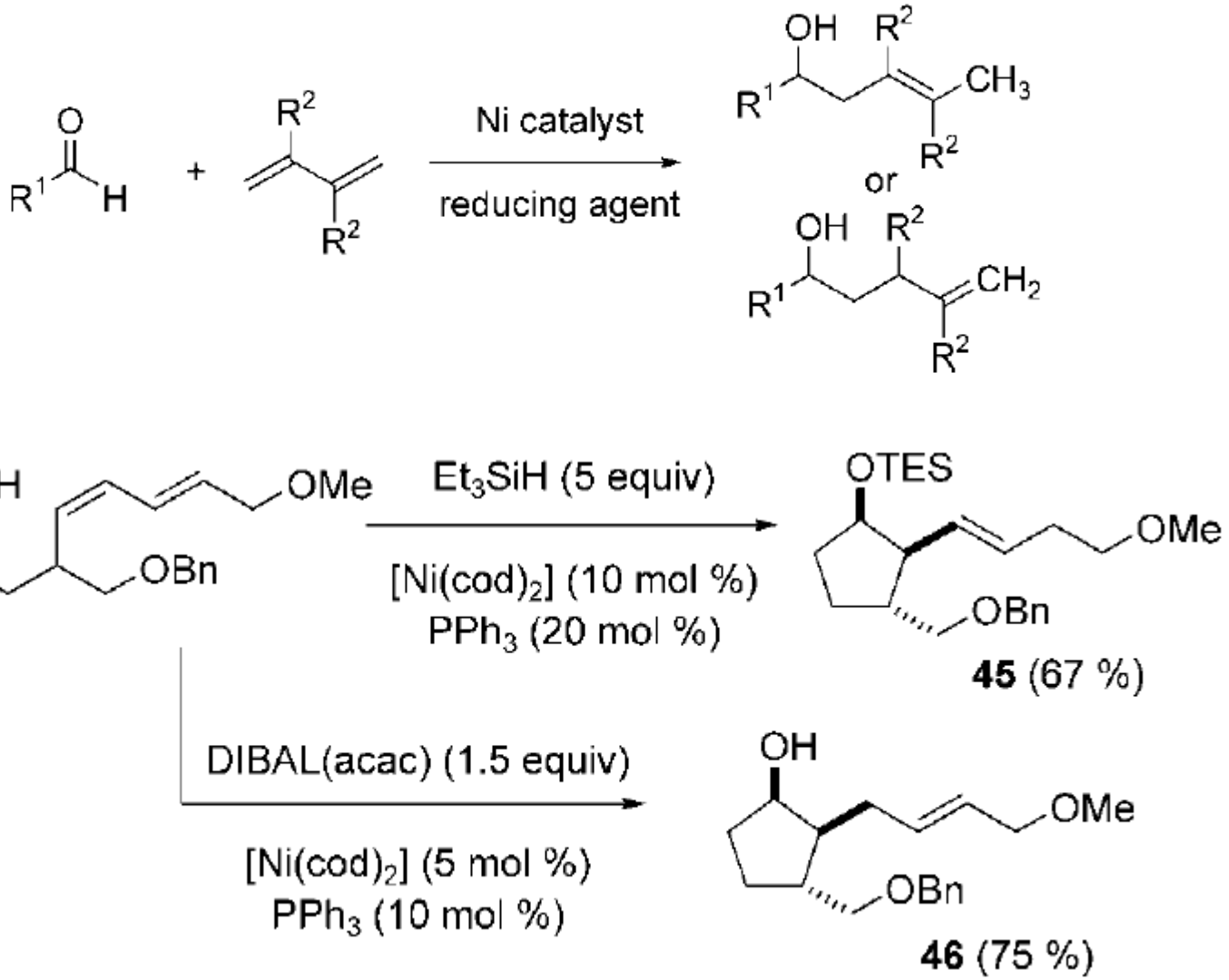
Jamison, F. *Angew. Chem. Int. Ed*. **2003**, *42,* 1364

Intermolecular coupling of imines with Alkynes



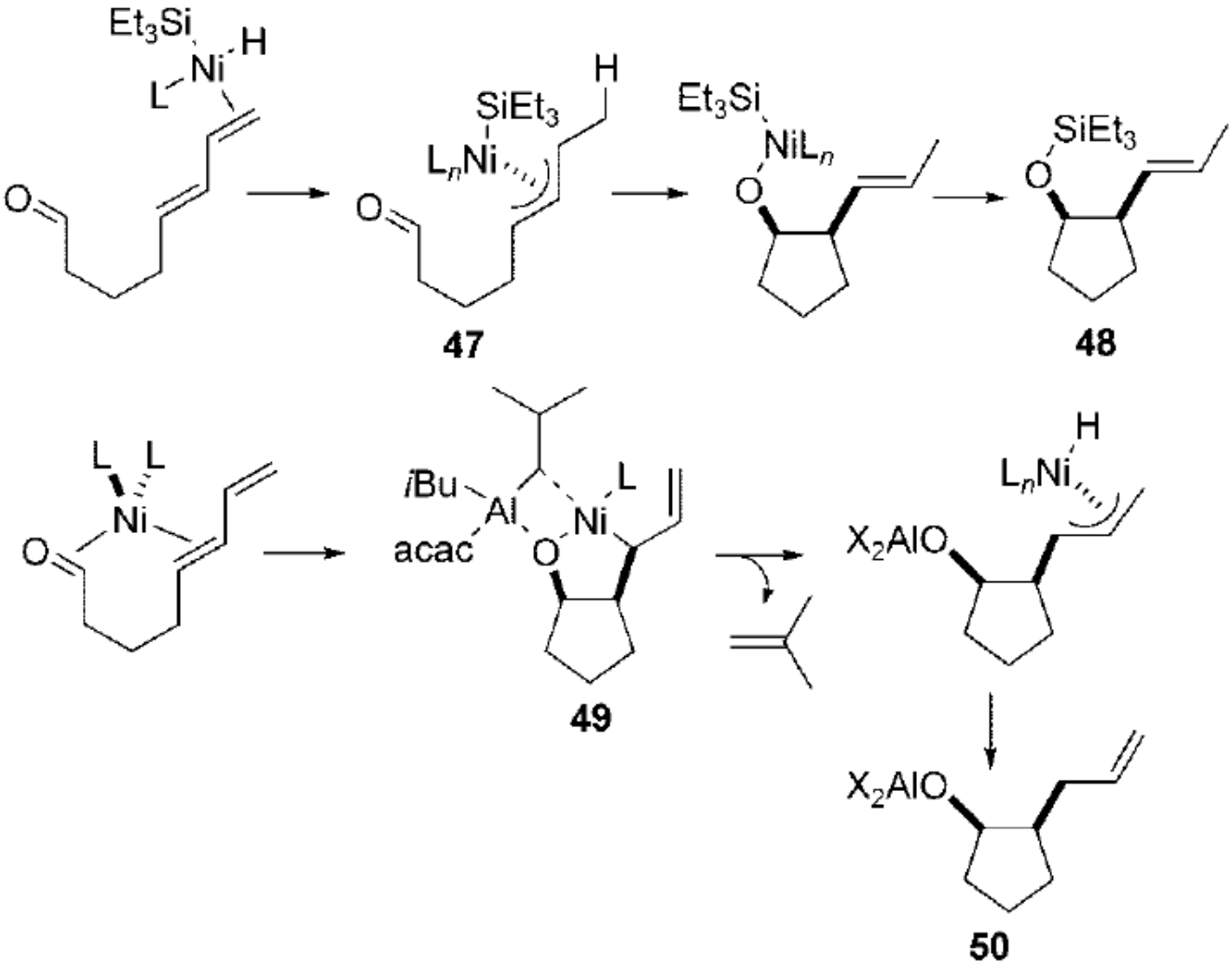
Jamison, F. *Angew. Chem. Int. Ed*. **2003**, *42,* 1364

Couplings of Carbonyls with Dienes



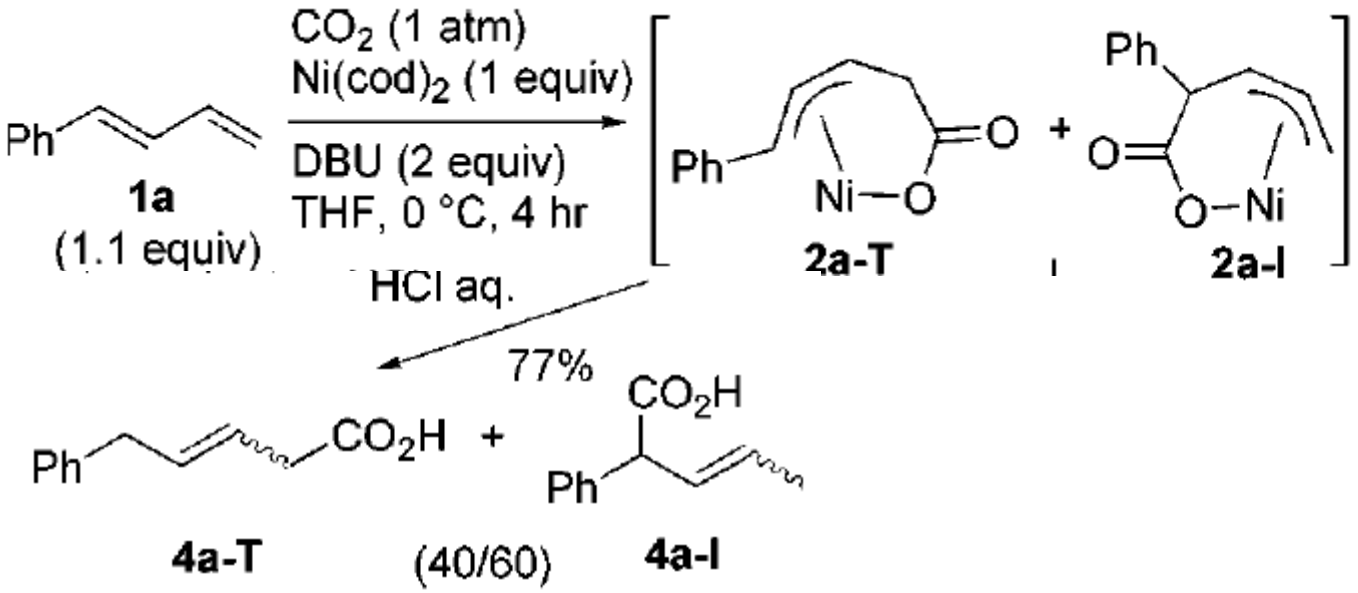
Mori, M. *J. Am. Chem. Soc*. **2000**, *122,* 1264

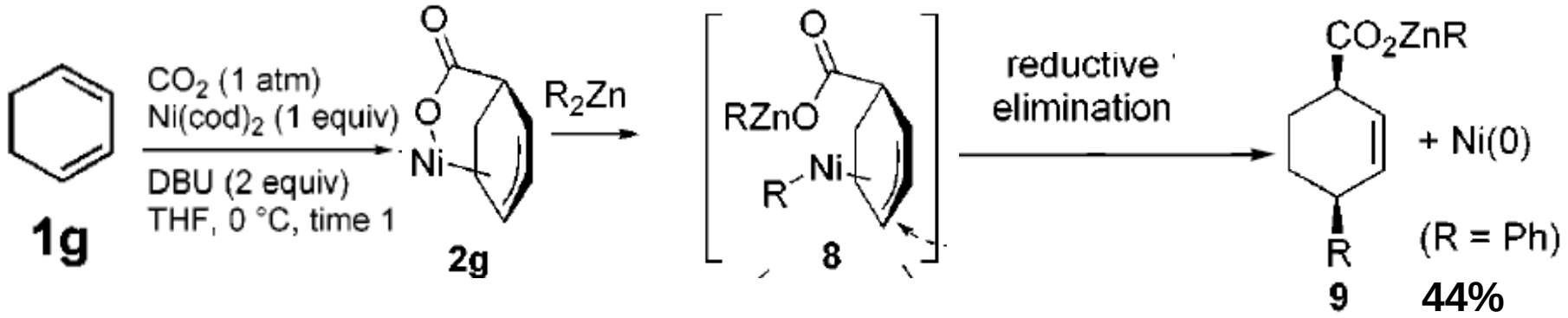
Couplings of Carbonyls with Dienes



Mori, M. *J. Am. Chem. Soc*. **2000**, *122,* 1264

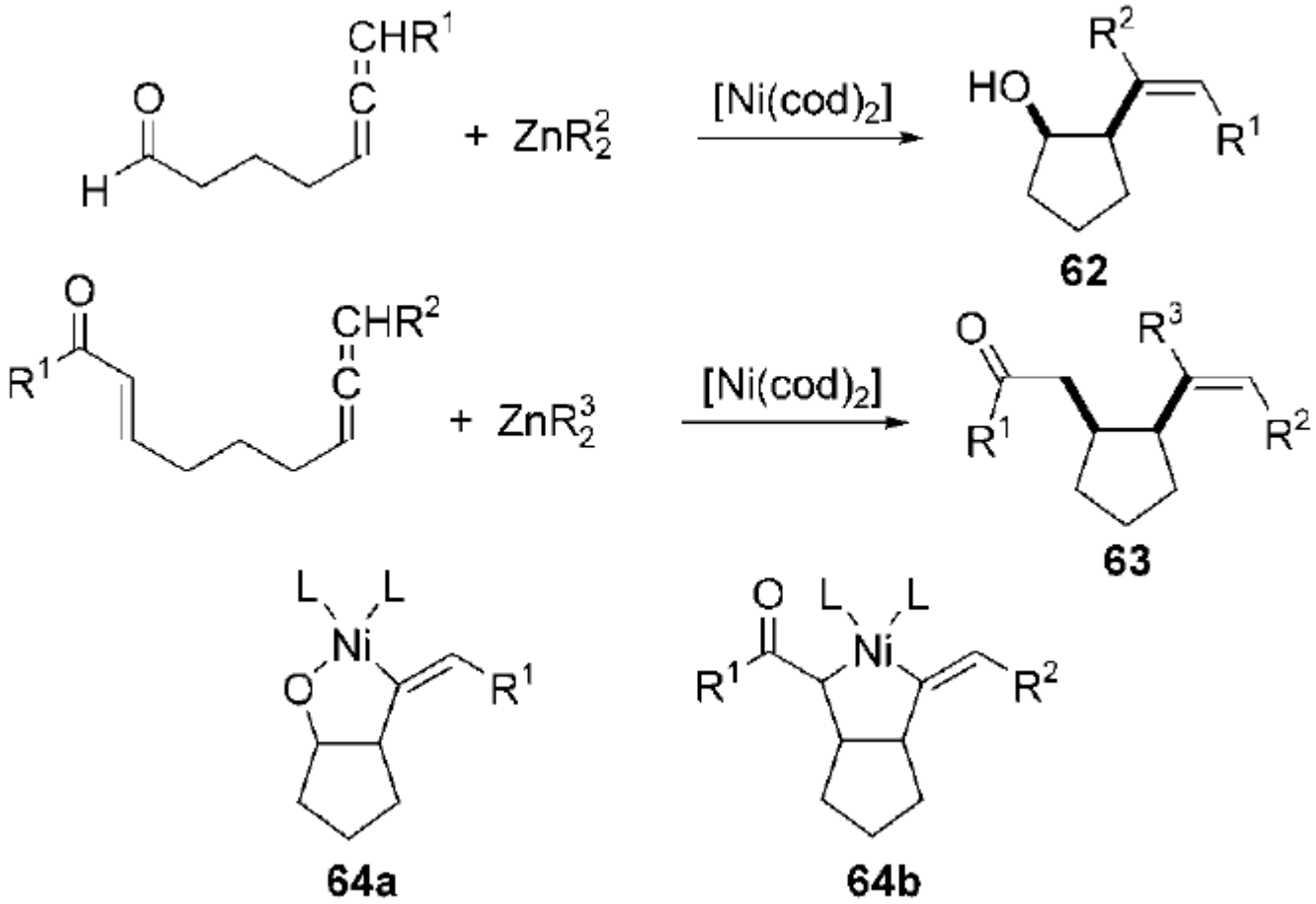
Diene-CO_2 coupling





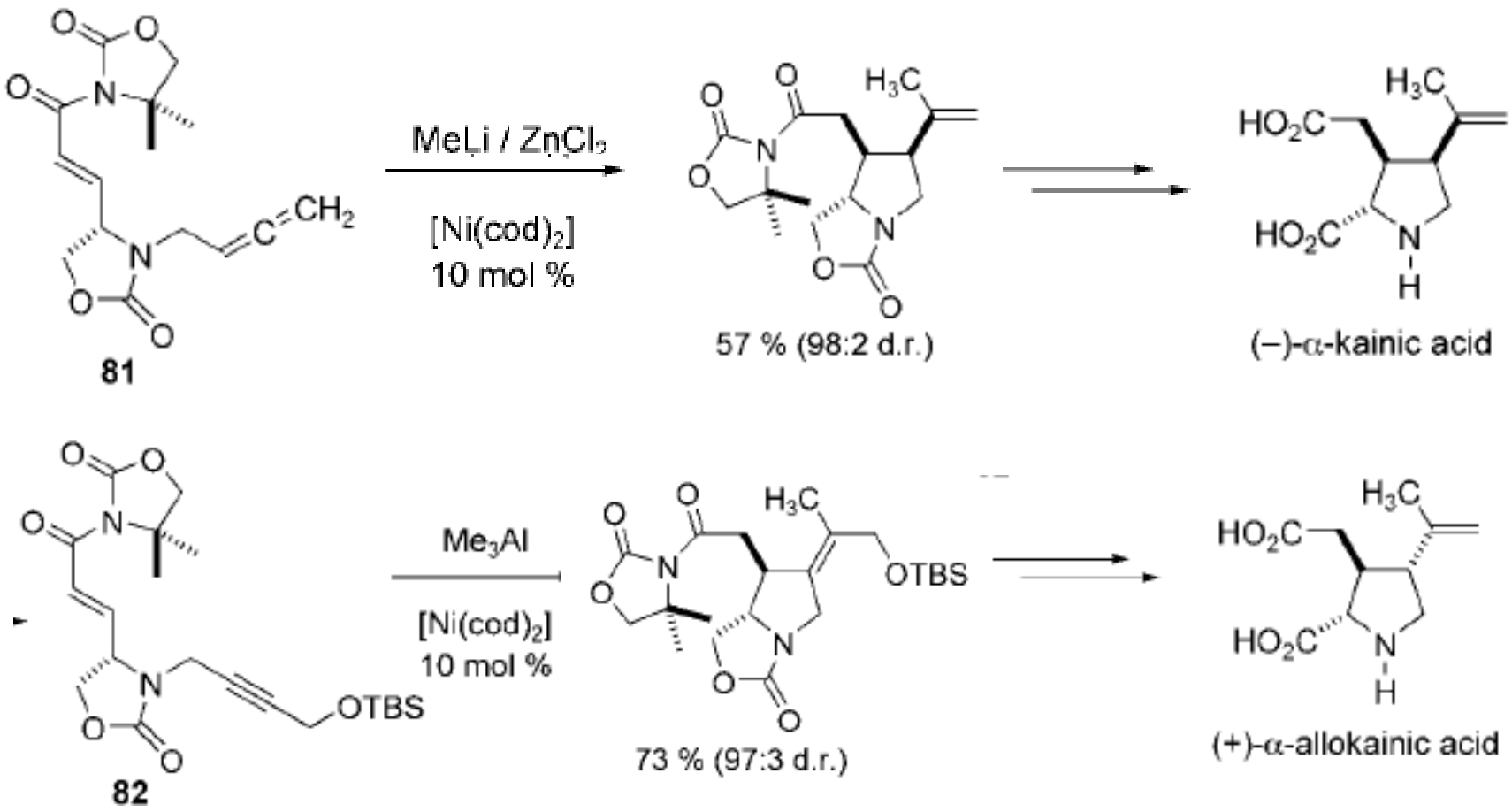
Mori, M. *J. Am. Chem. Soc*. **2001**, *123,* 2895

Coupling of Alkenes or Carbonyl Compounds with Allenes



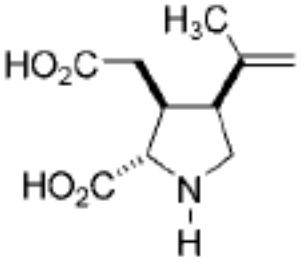
Montgomery, J. *Angew. Chem. Int. Ed*. **2004**, *43*, 3890 – 3908

Key step in the total synthesis of kainic acid and allokainic acid

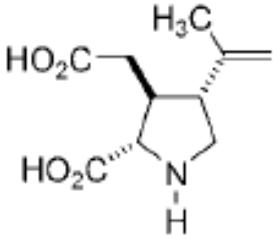


Montgomery, J. *J. Am. Chem. Soc*. **1999**, *121,* 11139

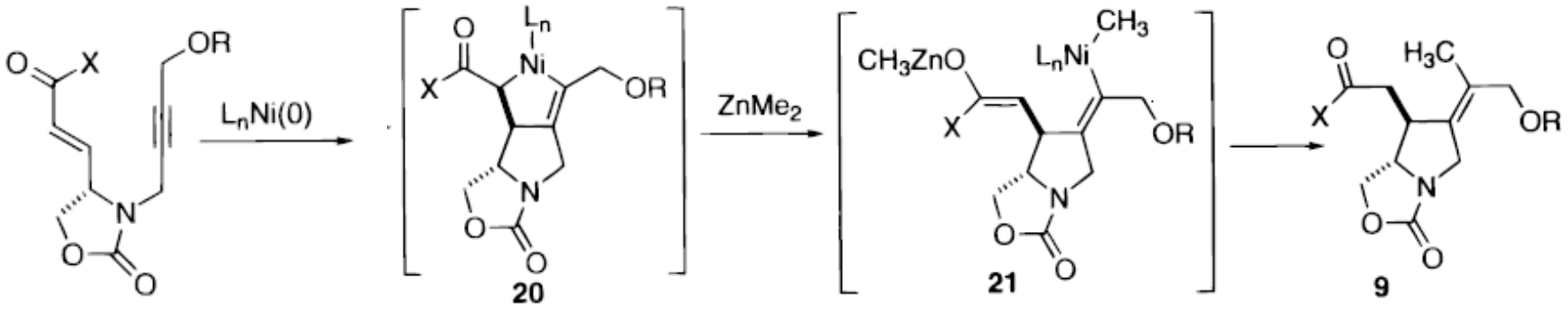
Key step in the total synthesis of kainic acid and allokainic acid

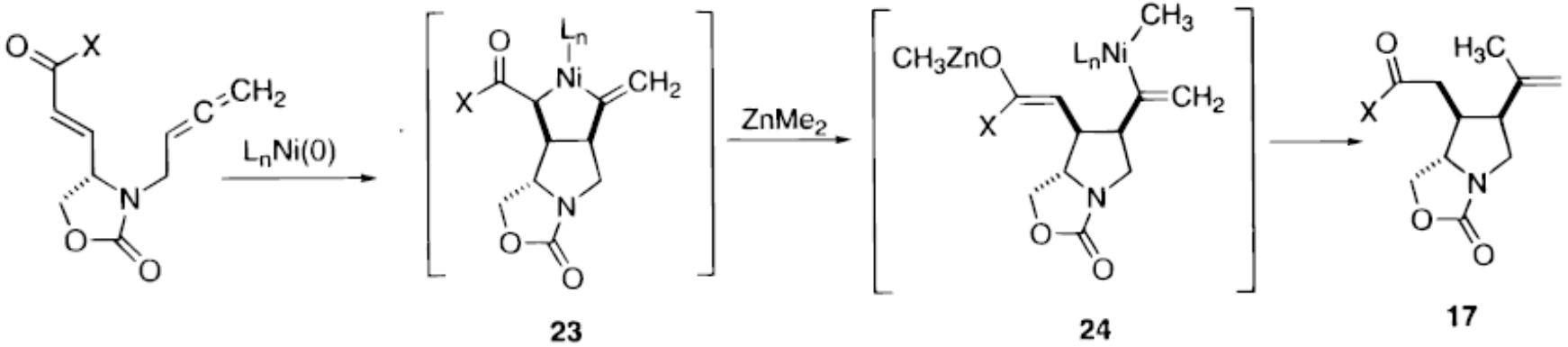


(−)-α-kainic acid



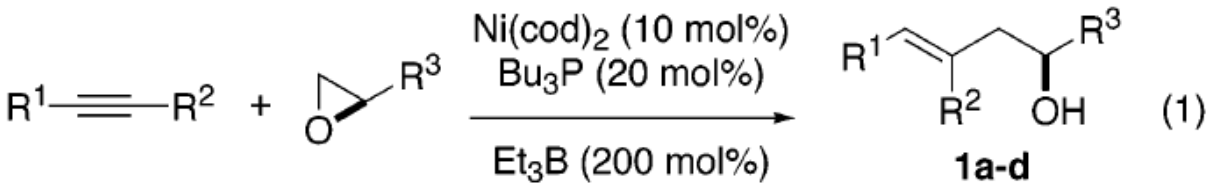
(+)-α-allokainic acid



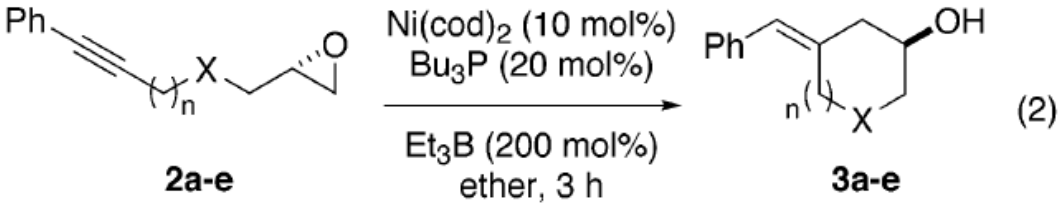


Montgomery, J. *J. Am. Chem. Soc*. **1999**, *121,* 11139

Nickel-Catalyzed Reductive Coupling of Alkynes and Epoxides



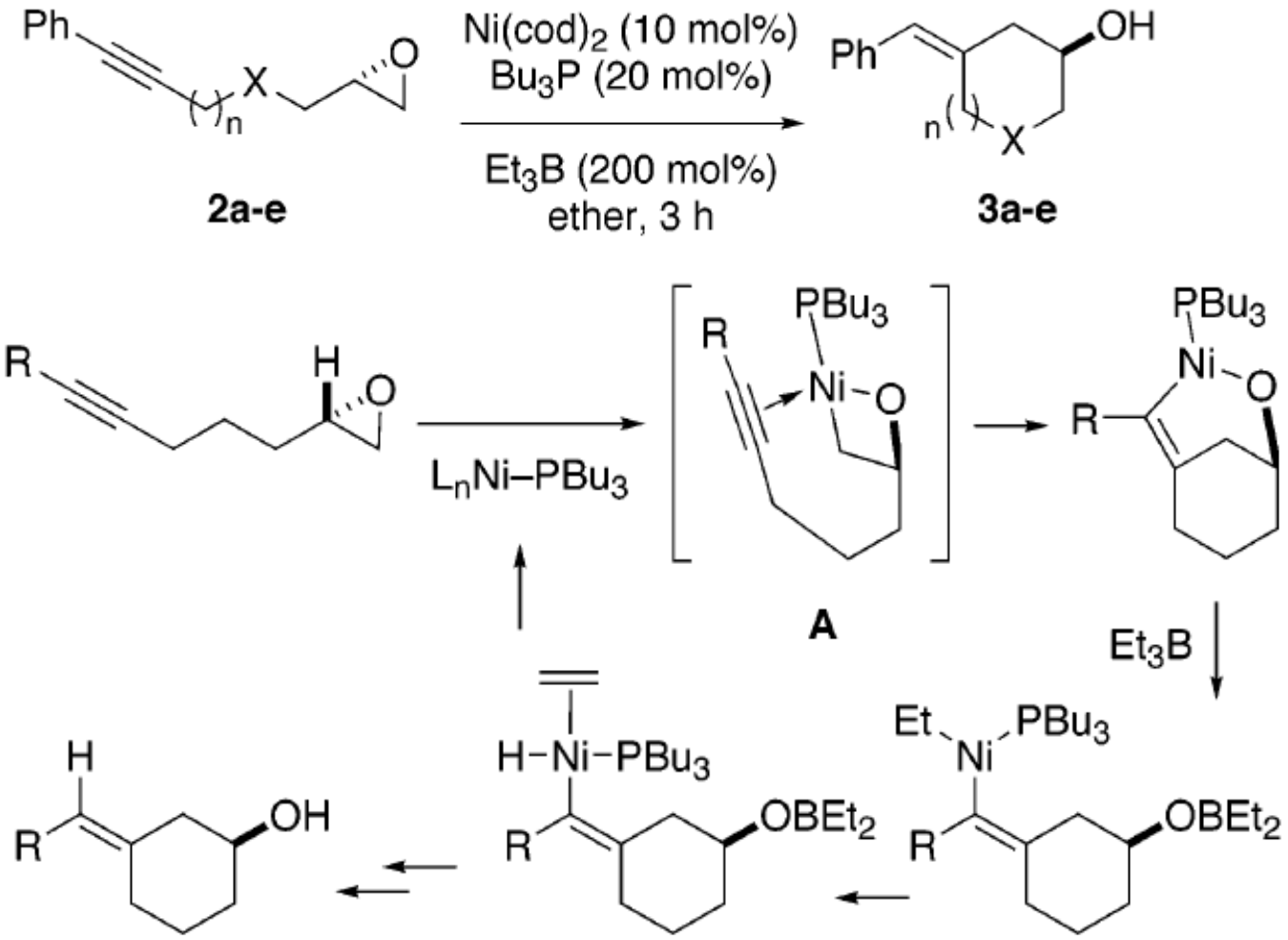
entry	R^1	R^2	R^3	additive	product	yield (%)	regioselectivity alkyne	regioselectivity epoxide
6	Ph	Me	Me	Bu_3P	**1a**	71	>95:5	>95:5
7	Ph	Me	*n*-Hex	Bu_3P	**1b**	68	>95:5	>95:5
8	Ph	Me	Ph	Bu_3P	**1c**	50[e]	88:12	83:17
9	*n*-Pr	*n*-Pr	Et	Bu_3P	**1d**	35[e]	na	>95:5



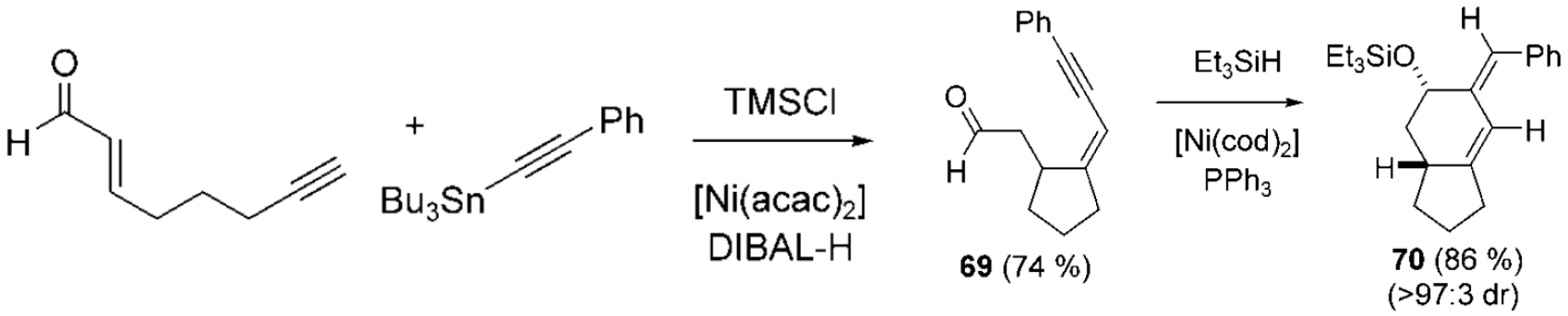
entry	X	*n*	product	yield (%)	regioselectivity (endo:exo)
1[b]	CH_2	1	**3a**	45	>95:5
2	O	1	**3b**	50	>95:5
3	NBn	1	**3c**	65	>95:5
4	$C(CO_2Me)_2$	1	**3d**	88[c]	>95:5
5	CH_2	0	**3e**	54	>95:5

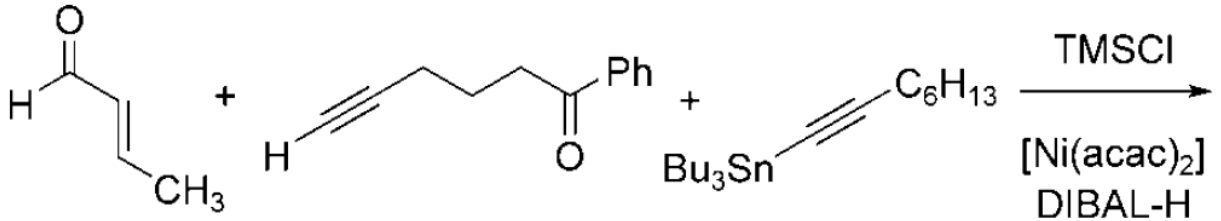
Jamison, F. *J. Am. Chem. Soc*. **2003**, *125,* 8076

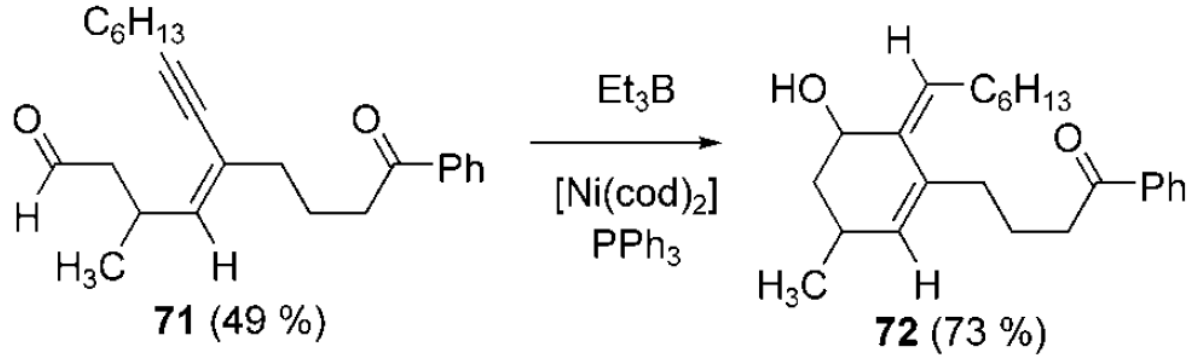
Nickel-Catalyzed Reductive Coupling of Alkynes and Epoxides



Combinations and Domino Reactions

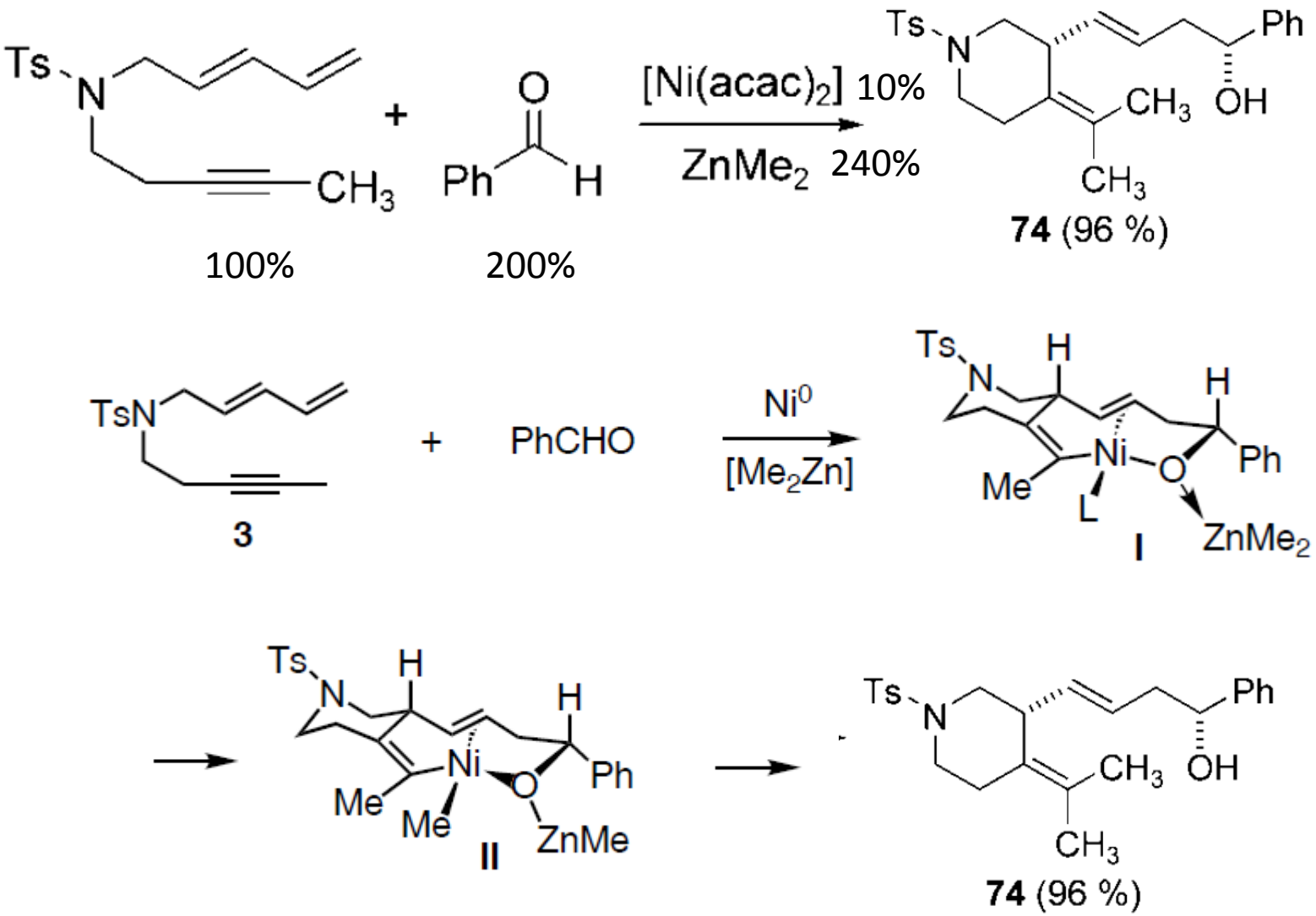






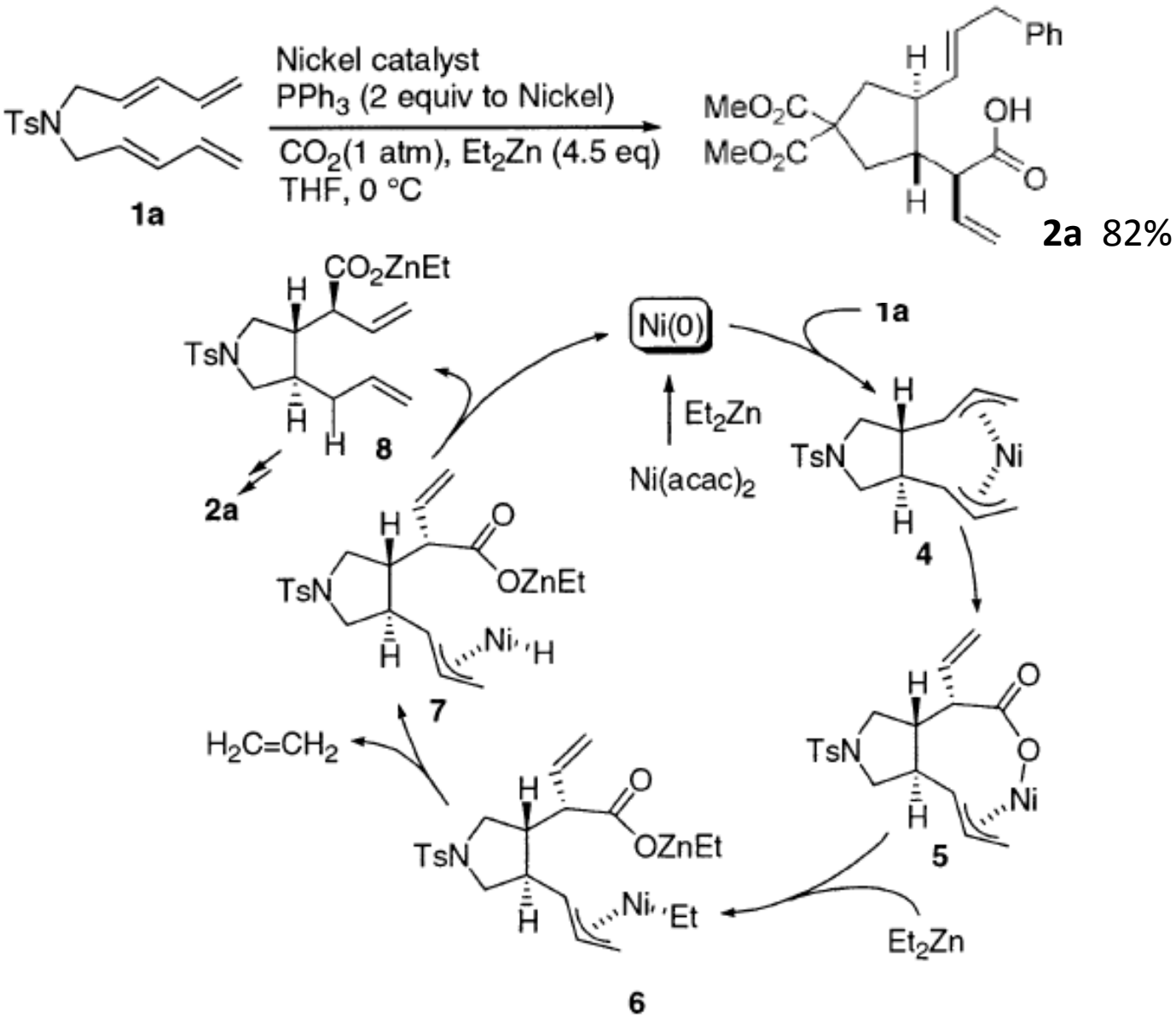
Montgomery, J. *J. Am. Chem. Soc*. **2002**, *124,* 2106

Combinations and Domino Reactions



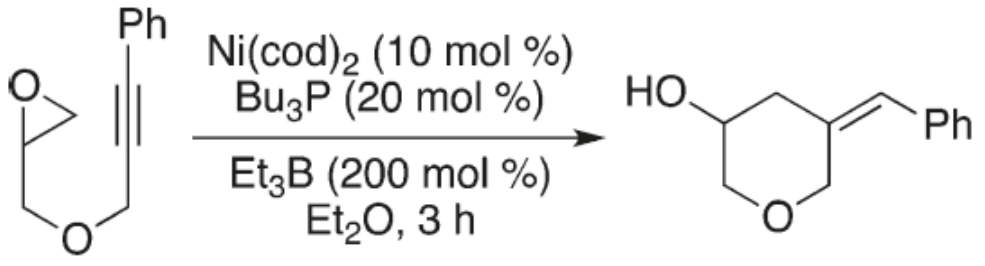
Tamaru, Y. *Angew. Chem. Int. Ed*. **2002**, *41*, 2784

Combinations and Domino Reactions

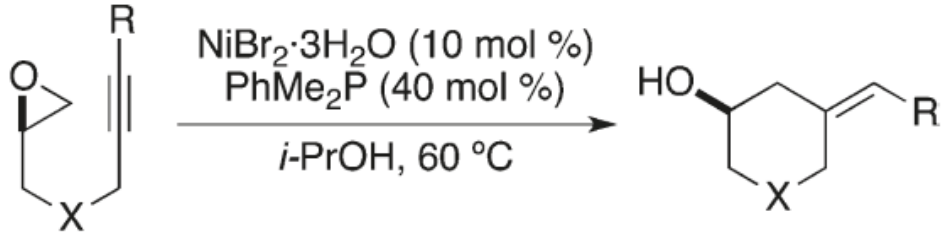


Mori, M. *J. Am. Chem. Soc*. **2002**, *124,* 10008

$NiBr_2$ Catalyzed Reductive Coupling



1 **2** (50% yield)

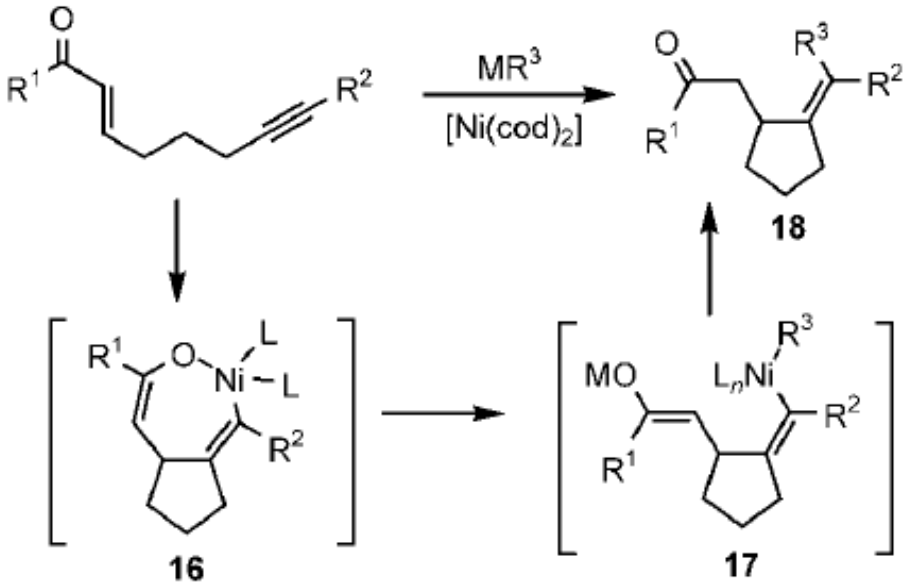


1b-g (*Z*)-**2b-g**

entry	X	R	product	yield (%)[a]	*Z*/*E*[b]
1	CH_2	Ph	**2b**	70	88:12
2	$C(CO_2Me)_2$	Ph	**2c**	76	>95:5
3	NBn	Ph	**2d**	74	88:12
4	O	*n*-C_5H_{11}	**2e**	75	>95:5
5	O	CO_2Me	**2f**	<5[c]	---
6	O	H	**2g**	55[d]	---

Jamison, F. *Org. Lett*. **2011**, *13,* 4140

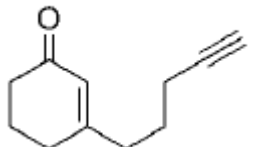
Summary



Ni: $Ni(cod)_2$, $Ni(acac)_2$, $NiBr_2$

Reducing agent: R_2Zn, R_3Al, $HSiR_3$, BR_3..

a



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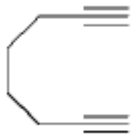

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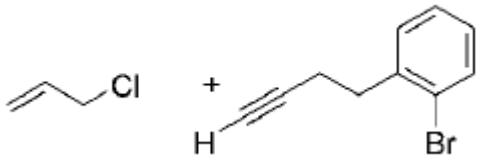

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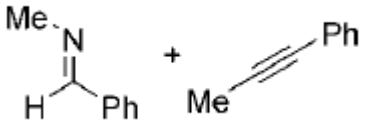

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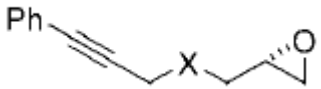

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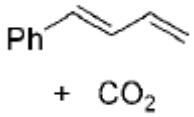

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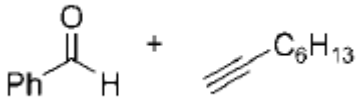

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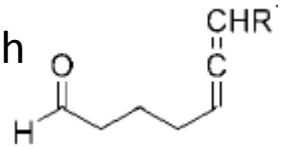

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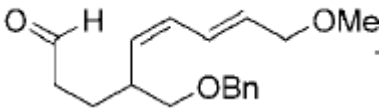

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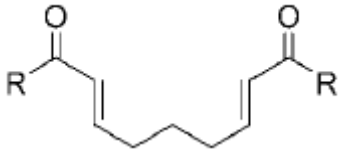
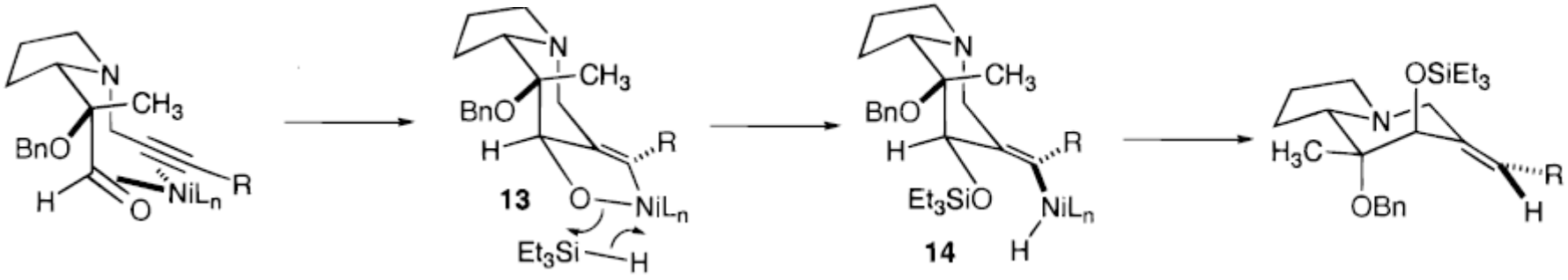
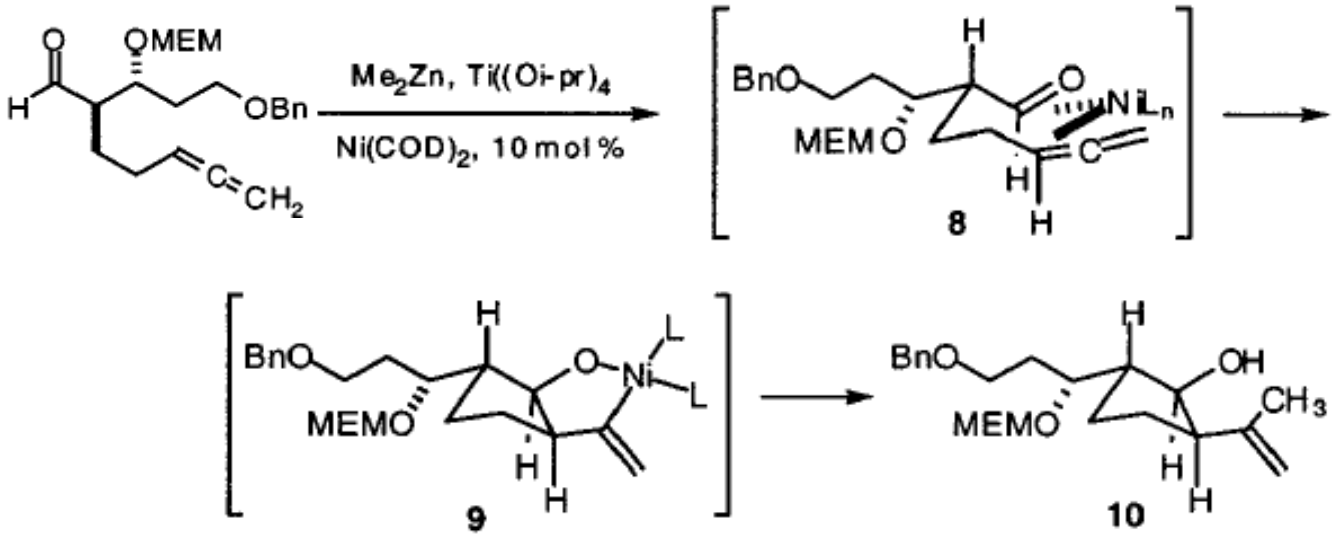
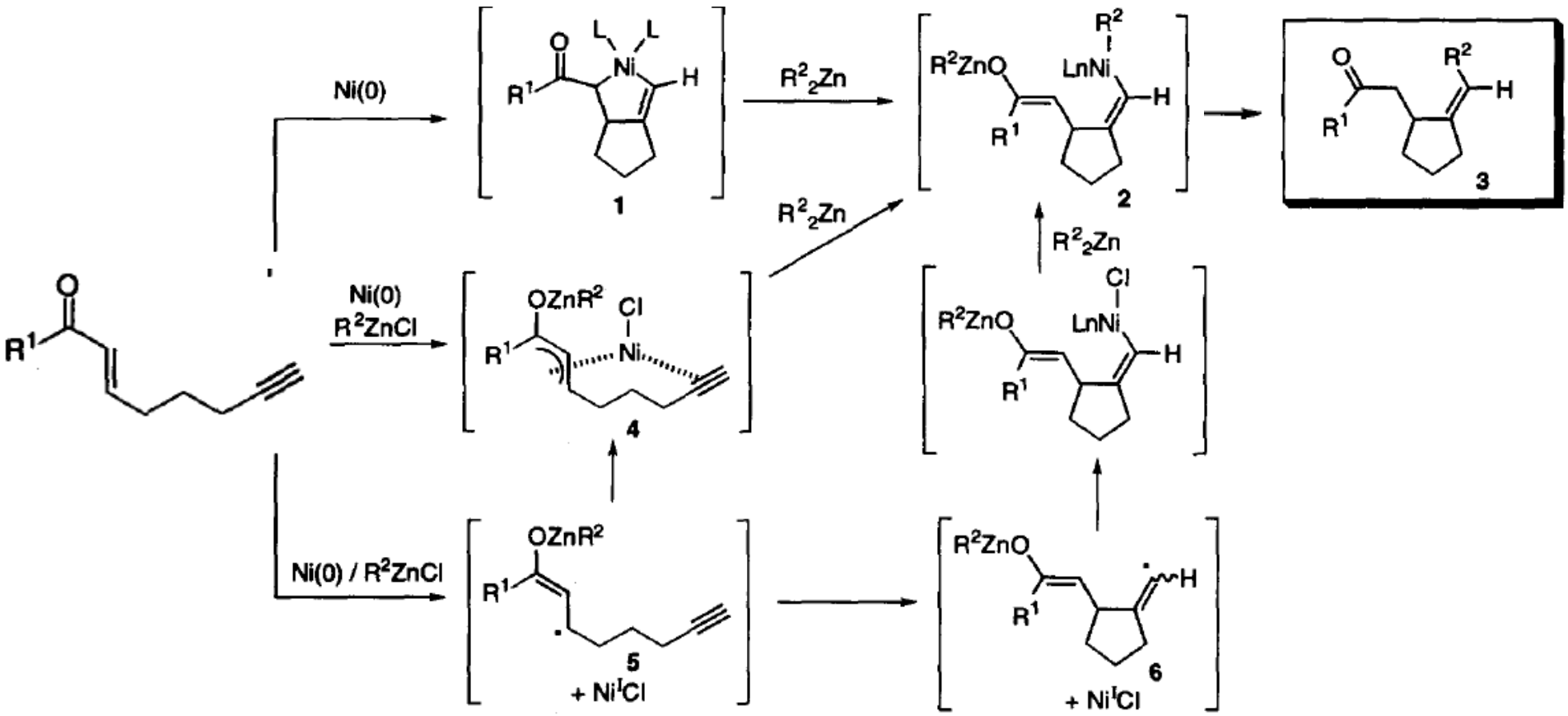
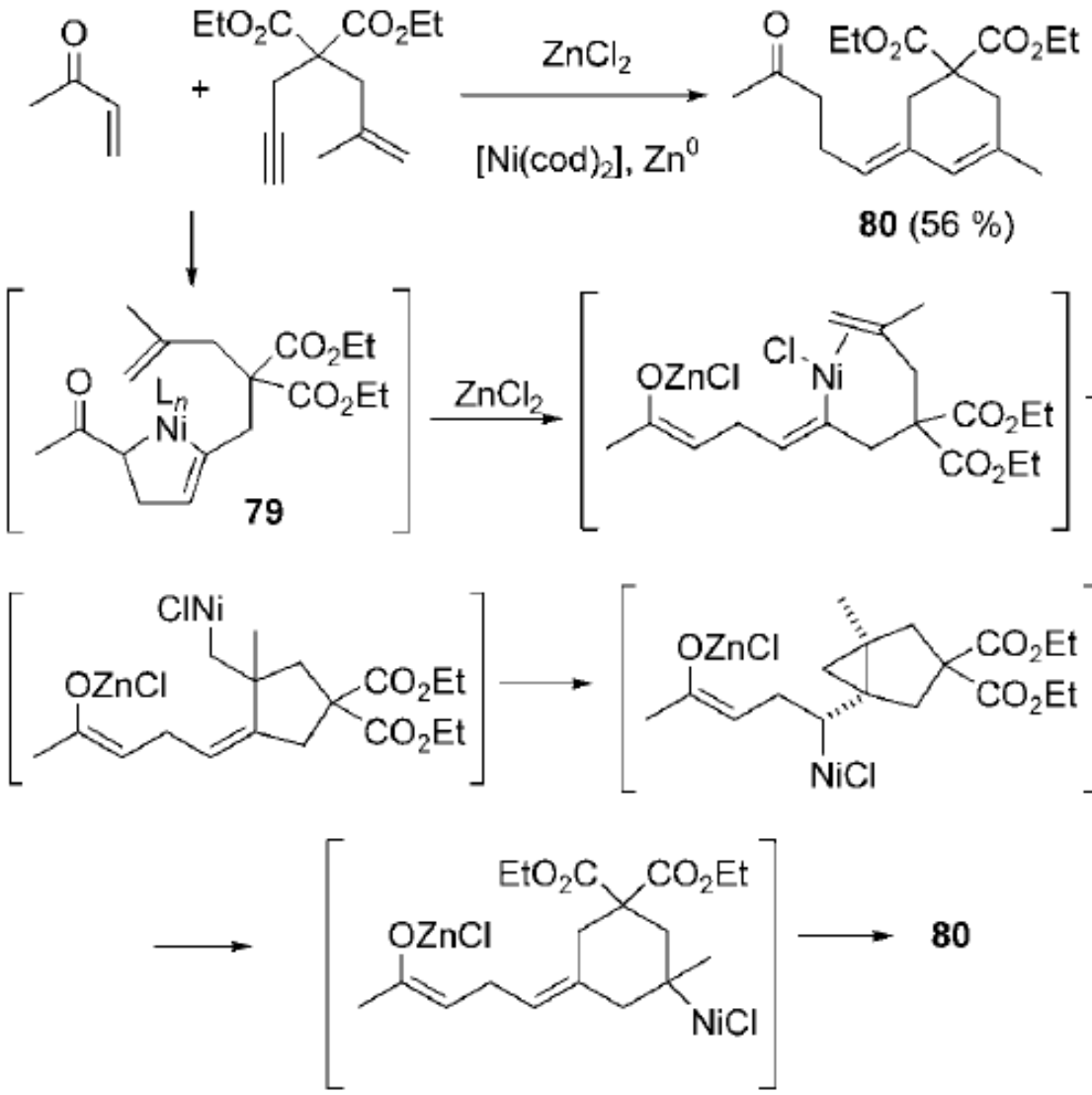


Thanks!


N
CH3
BnO
H
O
NiLn
R
13
Et3Si
H
14
Et3SiO
OSiEt3
H3C
OBn


OMEM
H
OBn
C=CH2
Me2Zn, Ti((Oi-pr)4
Ni(COD)2, 10 mol %
BnO
MEMO
NiLn
8
L
Ni
9
OH
CH3
10


Ni(0)
Ni(0)
R2ZnCl
Ni(0) / R2ZnCl
R2ZnO
LnNi
OZnR2
Cl
+ NiICl
+ NiICl
R2 2Zn
R2 2Zn
R2 2Zn
1
2
3
4
5
6


EtO2C
CO2Et
ZnCl2
[Ni(cod)2], Zn0
80 (56 %)
Ln
Ni
79
OZnCl
Cl
ClNi
NiCl