Literature Report X

Ni−Al Catalyzed Enantioselective Cycloaddition of Cyclopropyl Carboxamide with Alkyne

Reporter：Shu-Bo Hu

Checker：Mu-Wang Chen

Date：2018-01-15

Ye, M. *et al. J. Am. Chem. Soc*. **2017**, *139*, 18150.

Contents

CV of Mengchun Ye

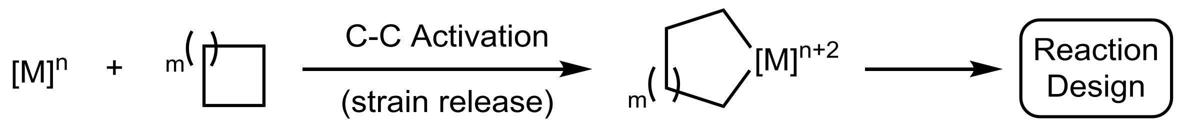
- B.S., Lanzhou University (1997-2001);
- Ph.D., Shanghai Institute of Organic Chemistry, CAS (2001-2006);
- Postdoc., University of North Carolina at Chapel Hill, USA (2006-2009);
- Research Associate, The Scripps Research Institute, USA (2009-2013);
- Professor, Nankai University (2013-now);
- The National Thousand Young Talents Program (2013);
- Nankai University Hundred Young Academic Leaders Program (2014).

Research:

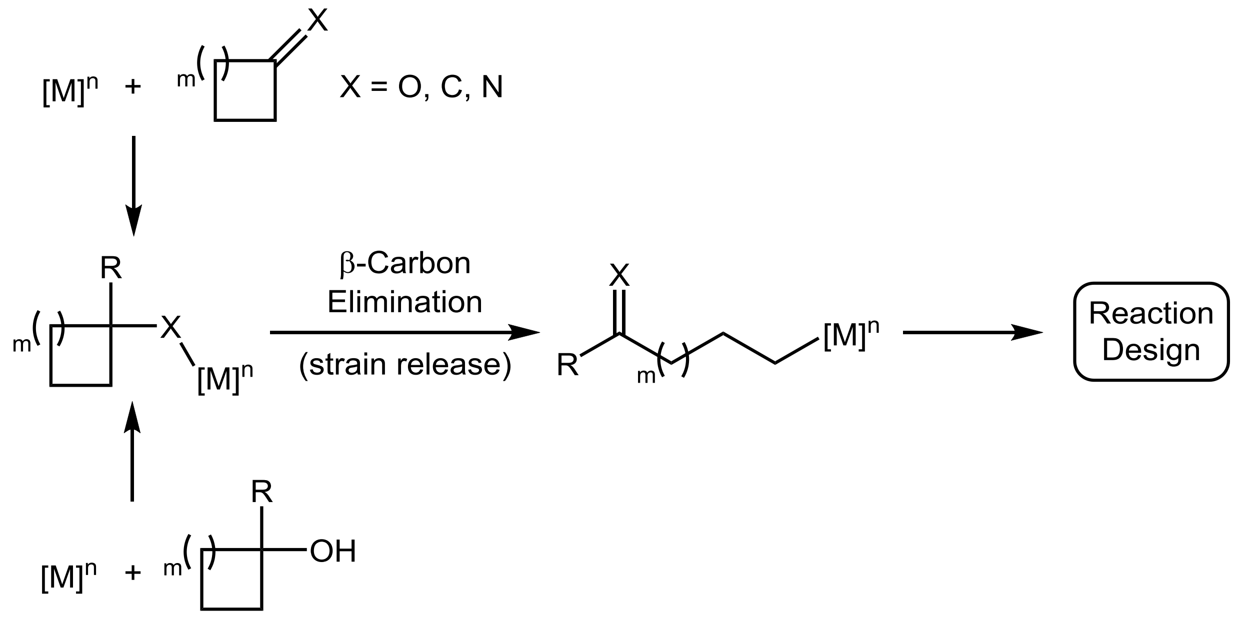
★ Organic Synthesis ★ Organometallic Chemistry ★ Chemical Biology

Introduction

C-C Cleavage of Small Rings by C-C Activation

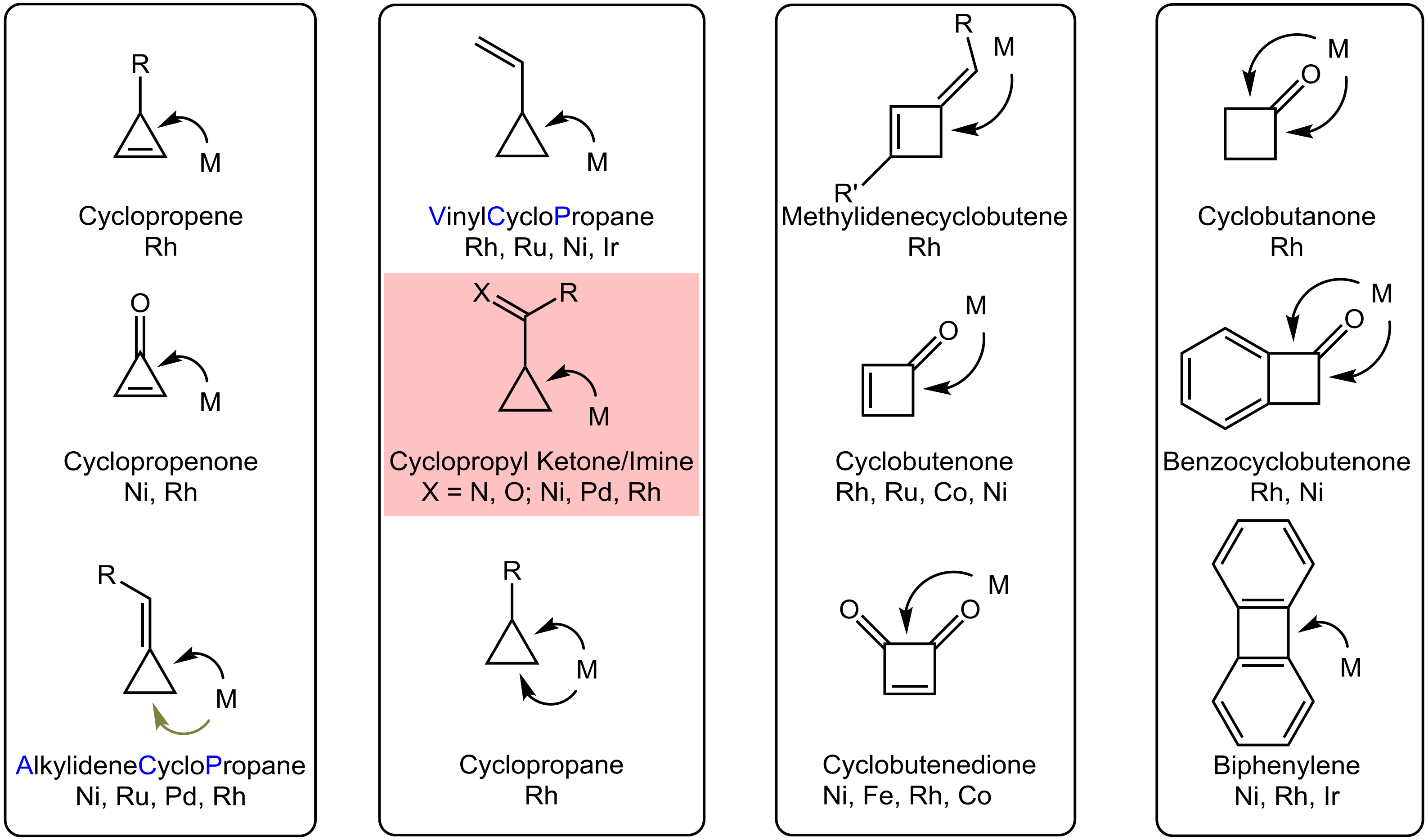


C-C Cleavage of Small Rings by β-Carbon Elimination



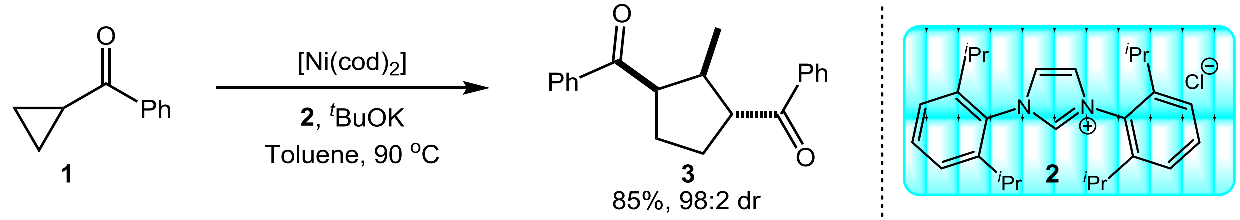
Bower, J. F. *et al*. *Chem. Rev.* **2017**, *117*, 9404.

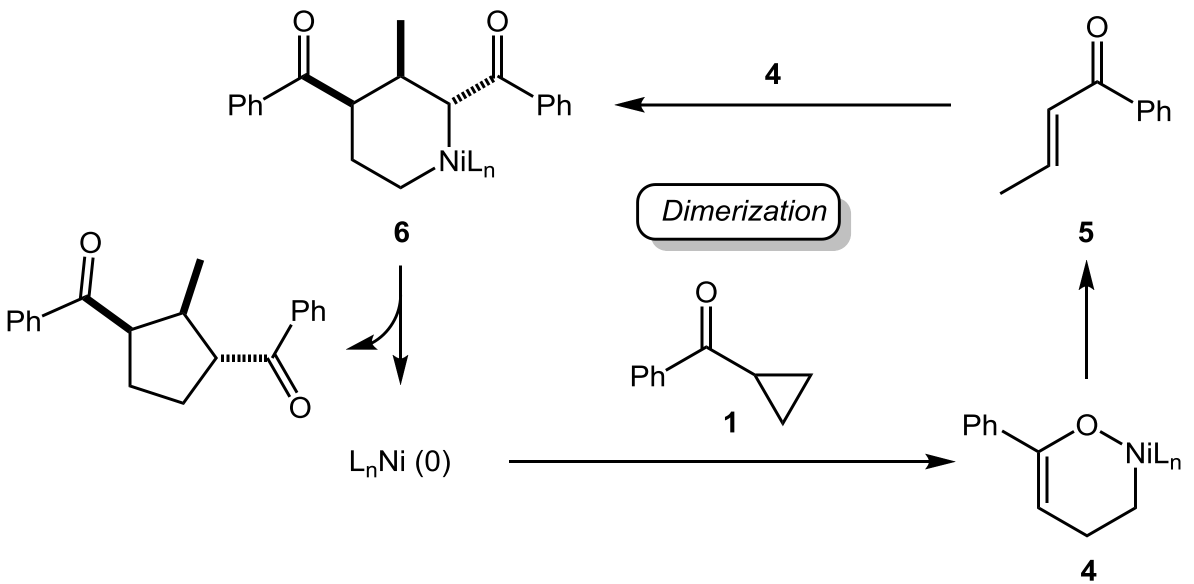
Introduction



Bower, J. F. *et al. Chem. Rev*. **2017**, *117*, 9404; Dong, G. *et al. ACS Catal.* **2017**, *7*, 1340.

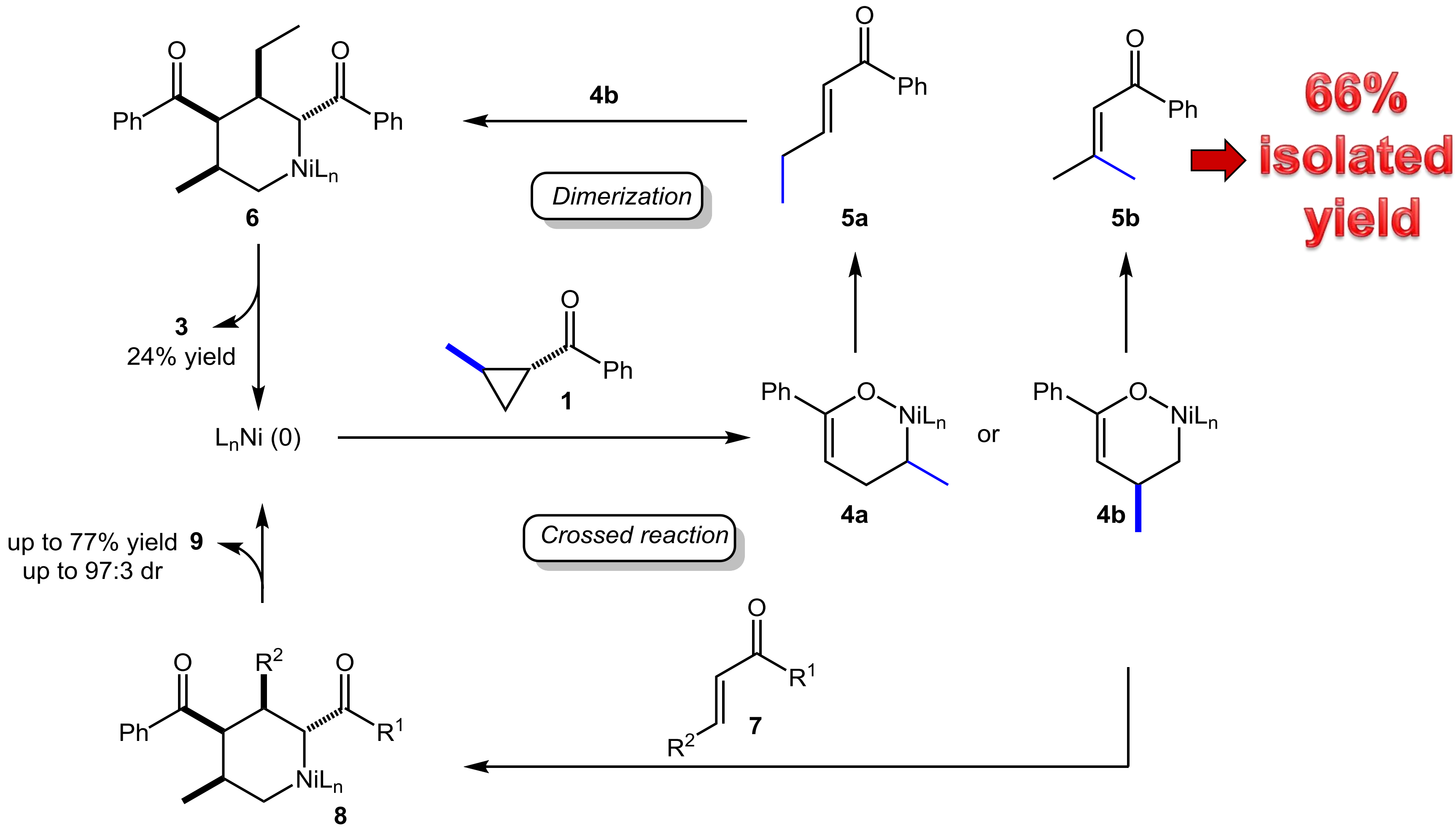
Dimerization of Cyclopropyl Ketones





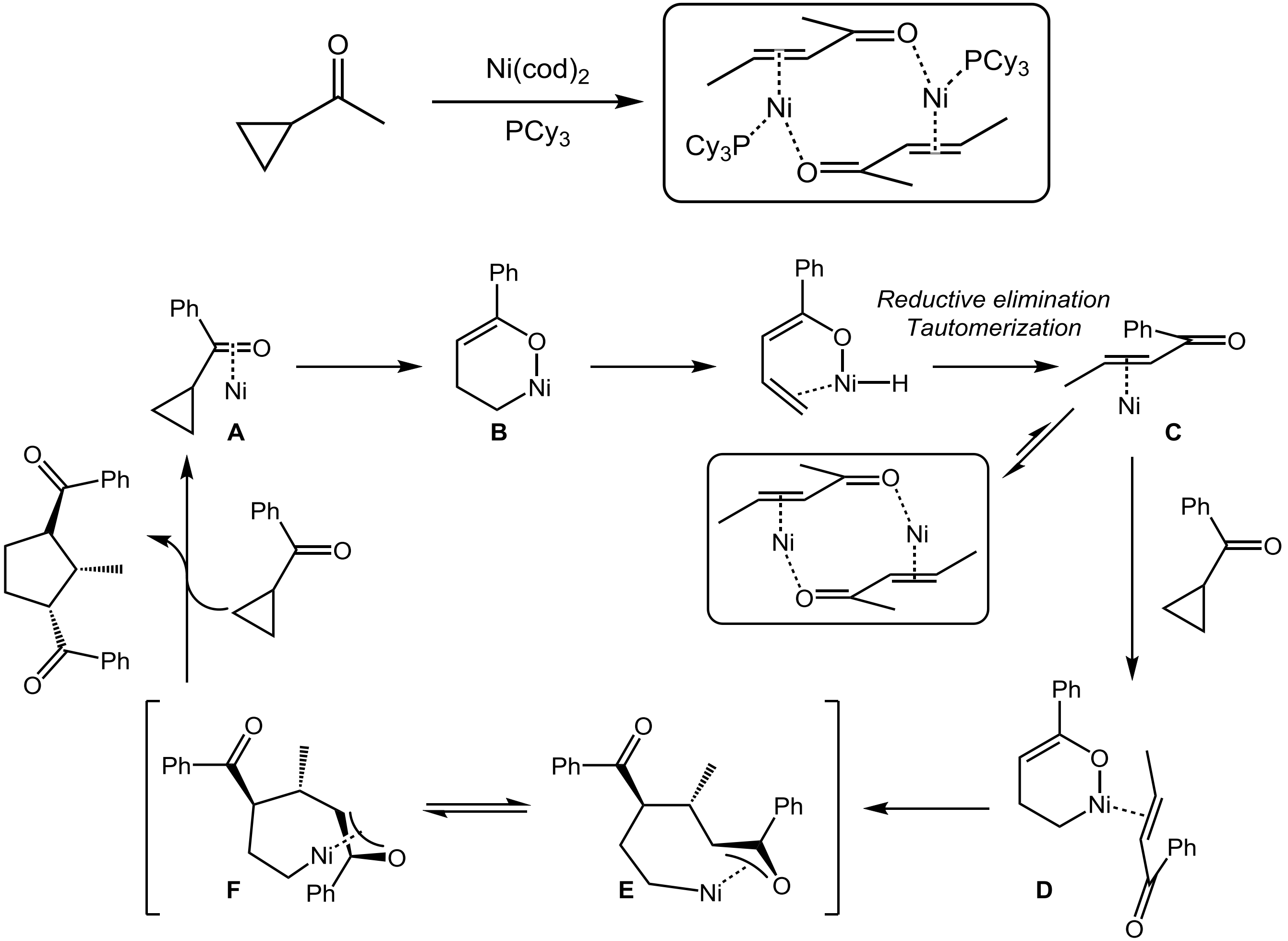
Montgomery, J. *et al*. *J. Am. Chem. Soc*. **2006**, *128*, 5348.

Crossed Reaction of Cyclopropyl Ketones



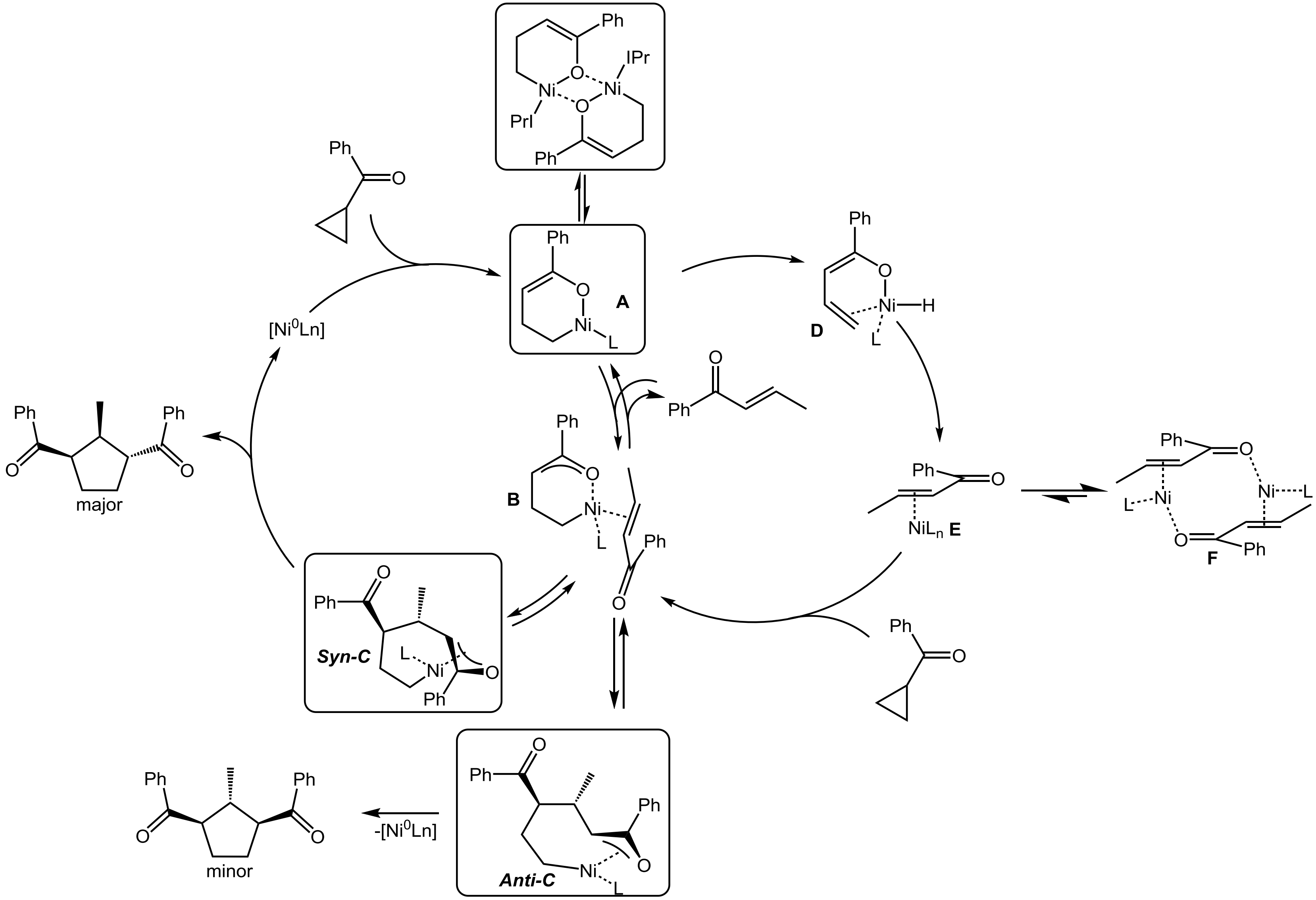
Montgomery, J. *et al*. *J. Am. Chem. Soc*. **2006**, *128*, 5348.

Mechanism Study



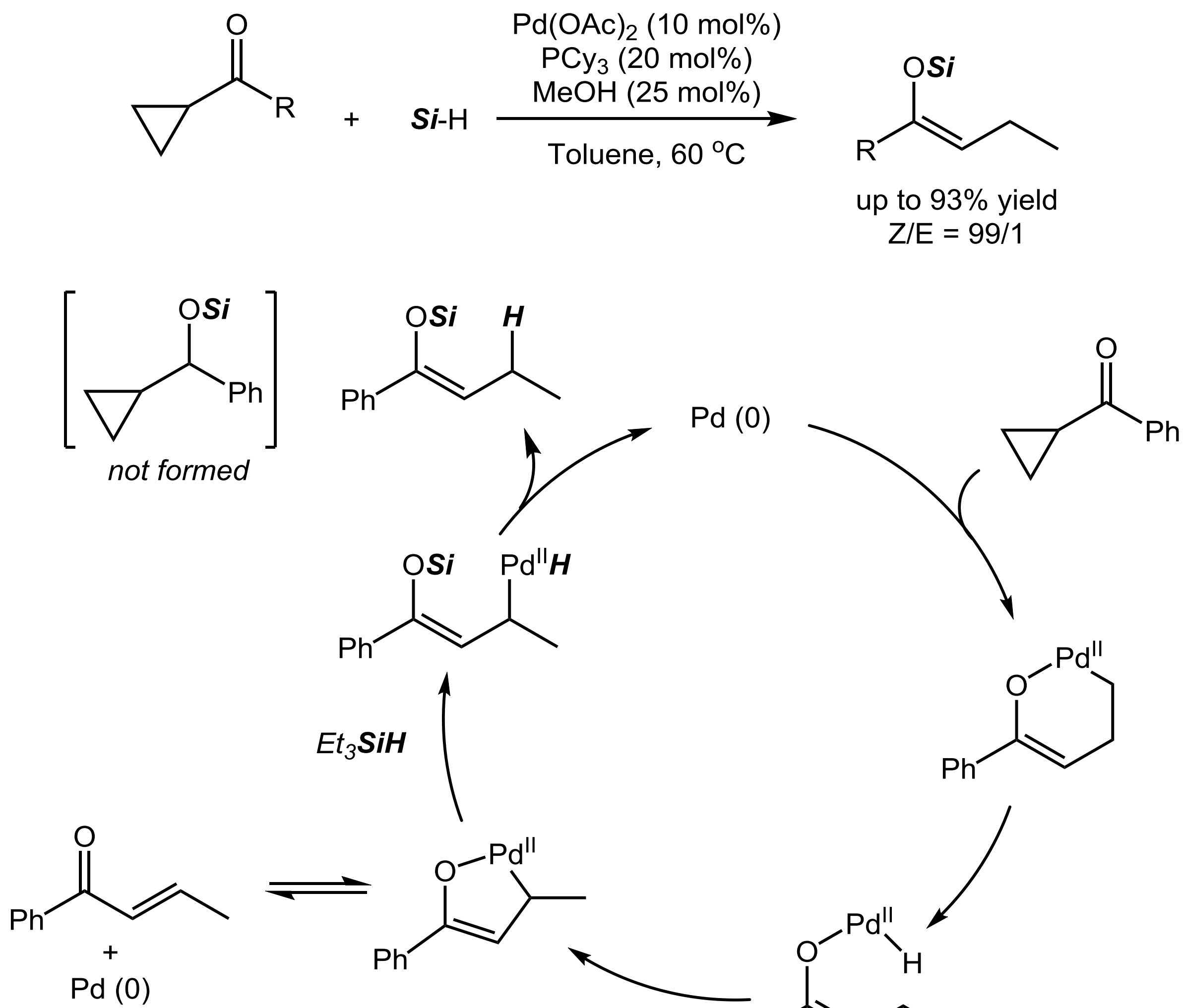
Ogoshi, S.; Kurosawa, H. *et al*. *J. Am. Chem. Soc*. **2006**, *128*, 5350.

Plausible Reaction Mechanism



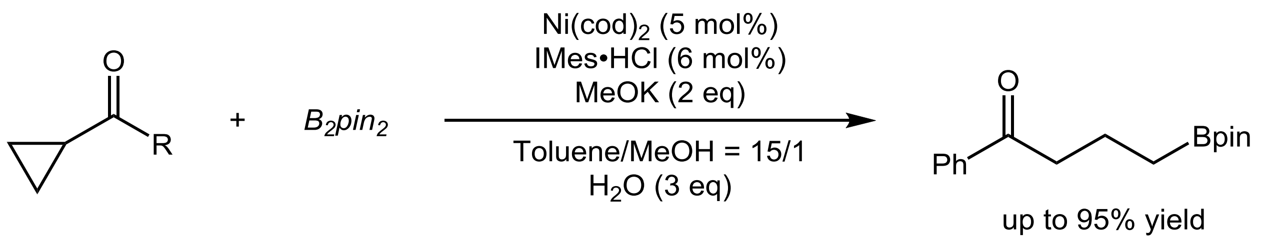
Ogoshi, S. *et al*. *Chem. Eur. J.* **2009**, *15*, 10083.

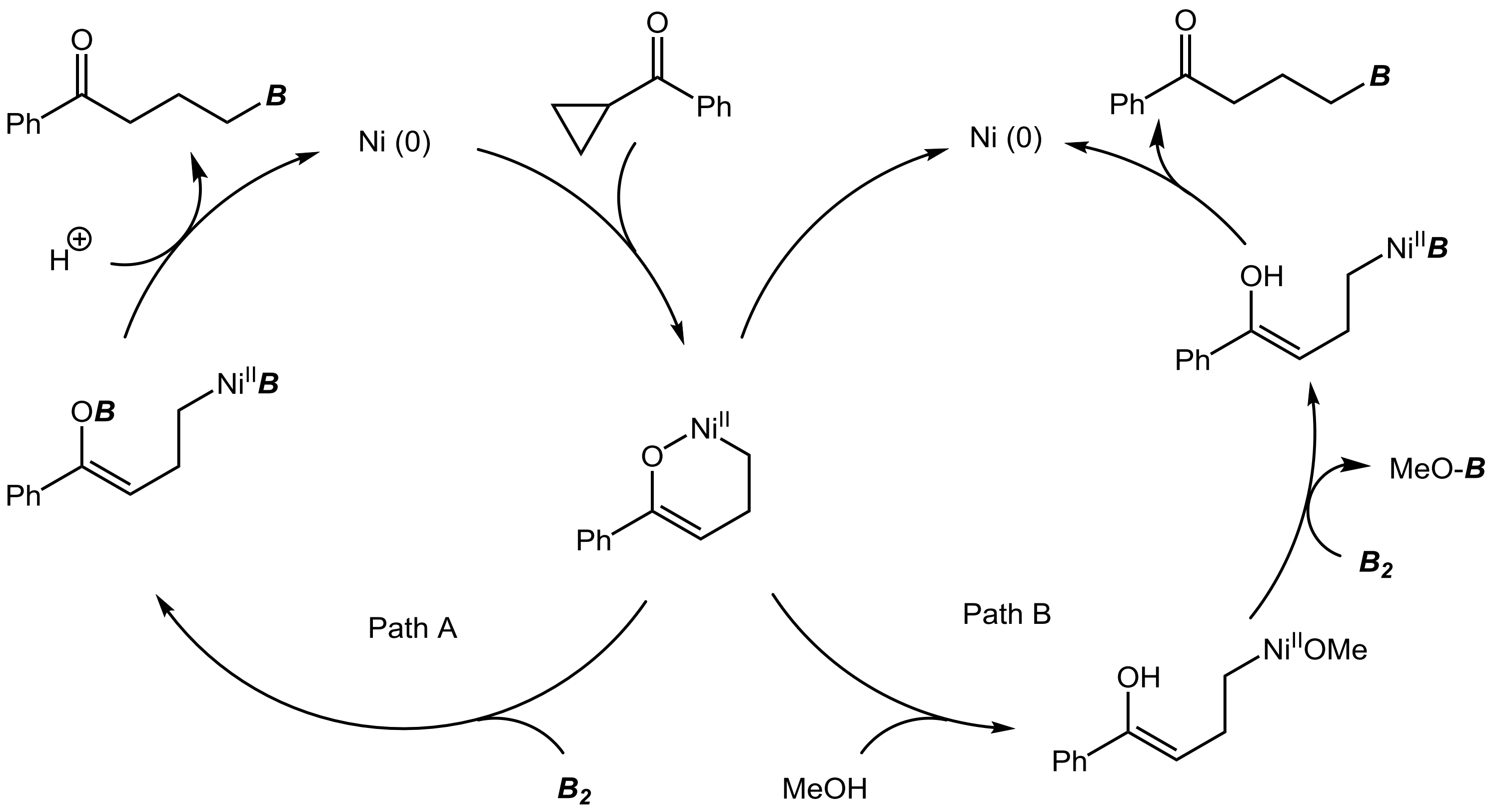
Hydrosilylation of Cyclopropyl Ketones



Yorimitsu, H.; Oshima, K. *J. Org. Chem*. **2009**, *74*, 7986.

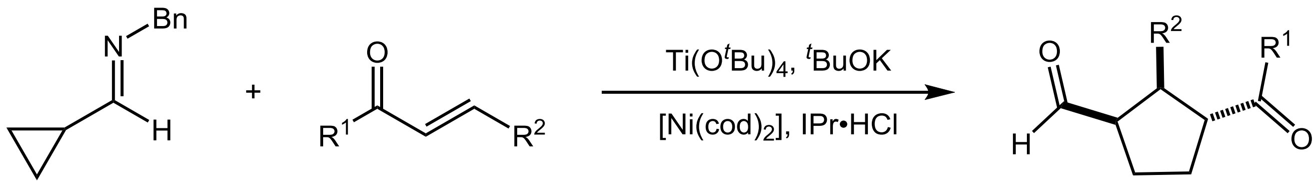
Borylation of Cyclopropyl Ketones



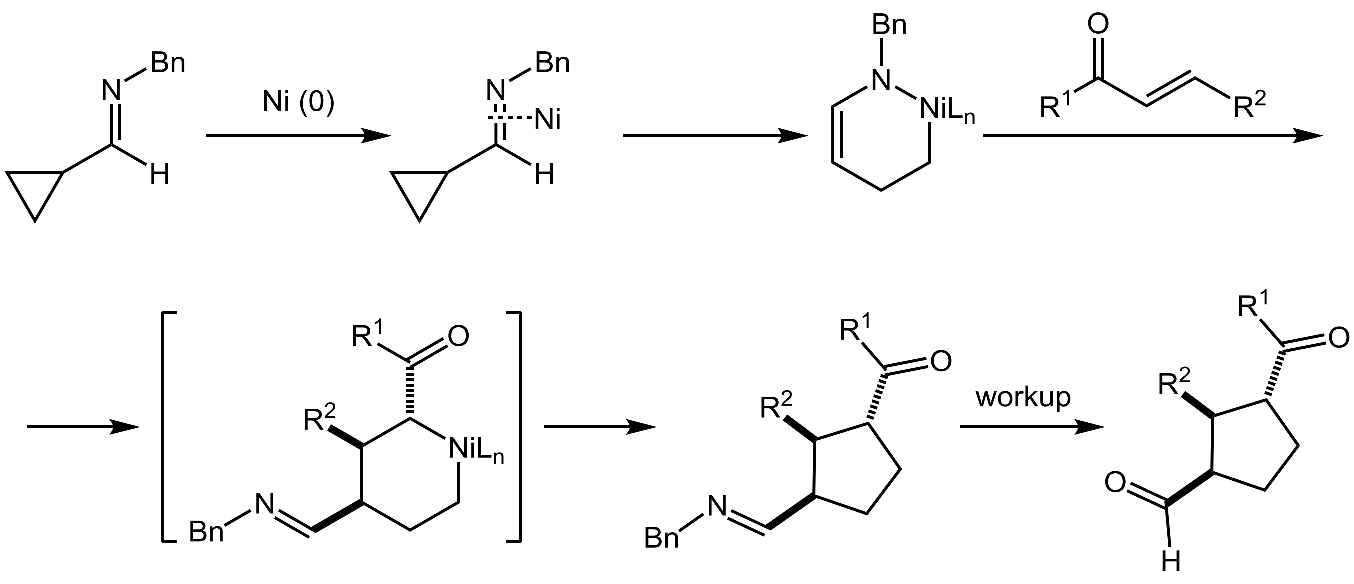


Yorimitsu, H.; Oshima, K. *J. Org. Chem*. **2009**, *74*, 3196.

[3+2] Cycloaddition of Cyclopropyl Imines

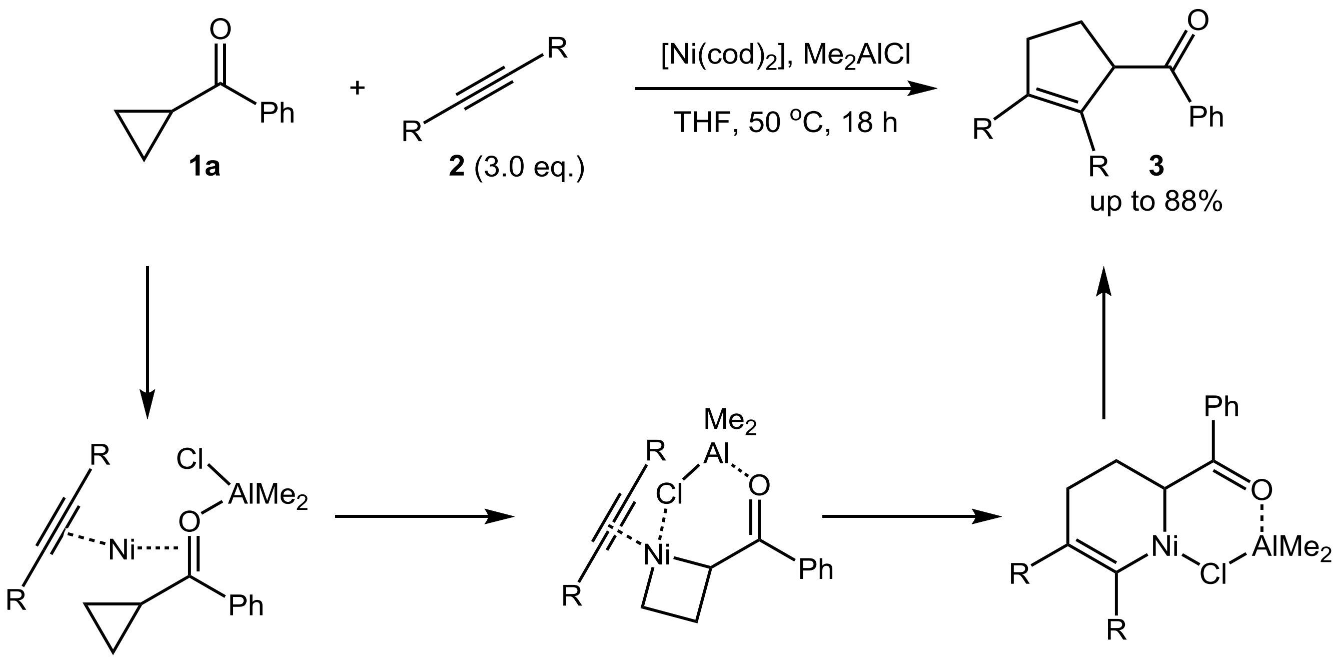


up to 98% (94:6)



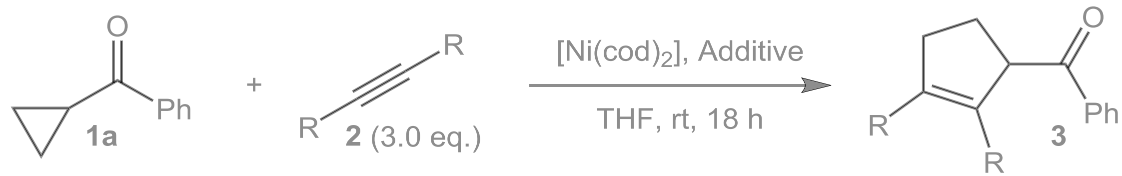
Montgomery, J. *et al*. *Org. Lett*. **2007**, *9*, 3885.

[3+2] Cycloaddition of Cyclopropyl Ketones



Ogoshi, S. *et al*. *Angew. Chem. Int. Ed.* **2011**, *50*, 12067.

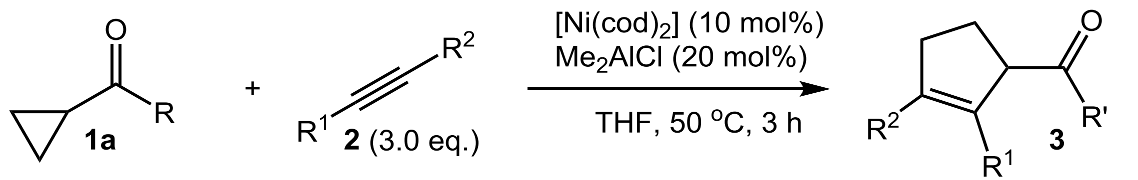
Condition Optimization

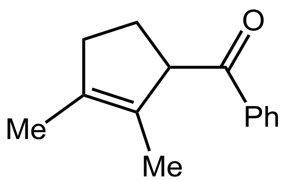


Entry	**2**	Additive	(mol%)	**3**	Yield (**3**) (%)
1	**2a** (R = Me)	$AlMe_3$	100	**3aa**	80
2	**2a**	--	--	**3aa**	0
3	**2a**	Me_2AlOAc	100	**3aa**	99
4	**2a**	Me_2AlOTf	100	**3aa**	84
5	**2a**	Me_2AlCl	100	**3aa**	100 (98)
6	**2a**	Me_2AlCl	20	**3aa**	100
7	**2a**	$AlCl_3$	100	**3aa**	0
8	**2a**	$TiCl_4$	100	**3aa**	0
9	**2a**	$ZnMe_2$	100	**3aa**	0
10	**2a**	PCy_3	20	**3aa**	0
11	**2b** (R = Et)	Me_2AlCl	100	**3ab**	100
12	**2b**	Me_2AlCl	20	**3ab**	29
13[a]	**2b**	**Me_2AlCl**	**20**	**3ab**	**100 (88)**

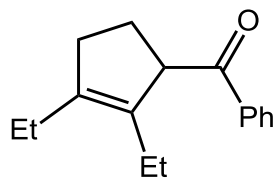
[a] The reaction mixture was stirred at 50 °C for 3 h.

Substrate Scope

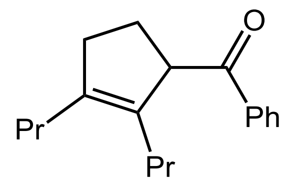




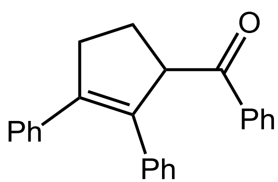
3aa, 81%



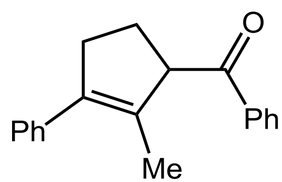
3ab, 88%



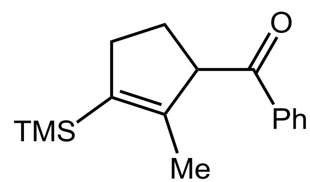
3ac, 88%



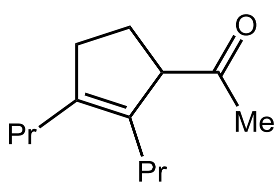
3ad, 59%, 80 °C



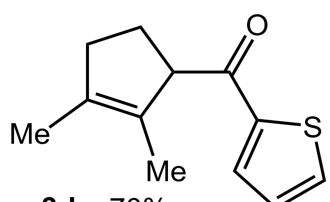
3ae, 76% (95/5)
Me_2AlCl (40 mol%)



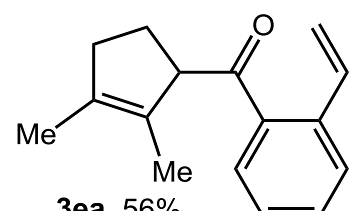
3af, 70% (94/6)
Me_2AlCl (40 mol%)



3cc, 69%
Me_2AlCl (100 mol%)

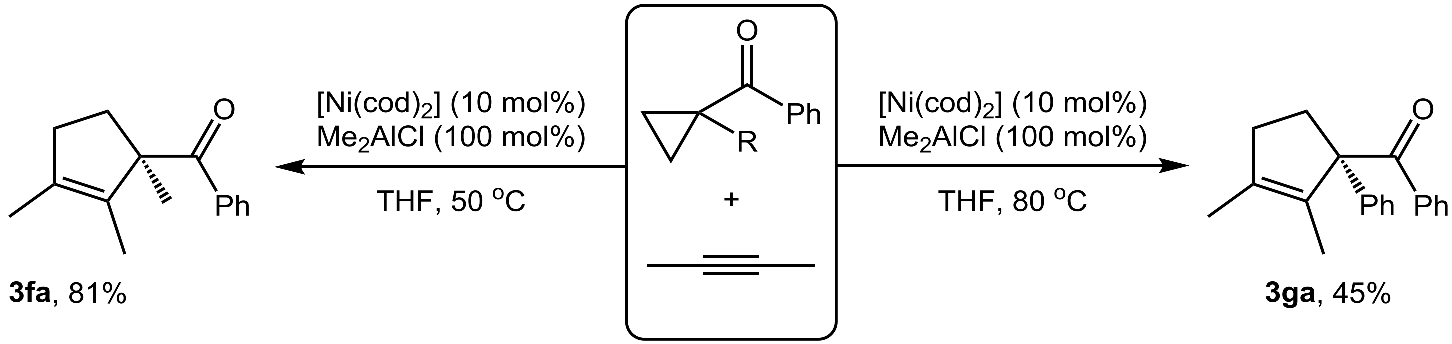


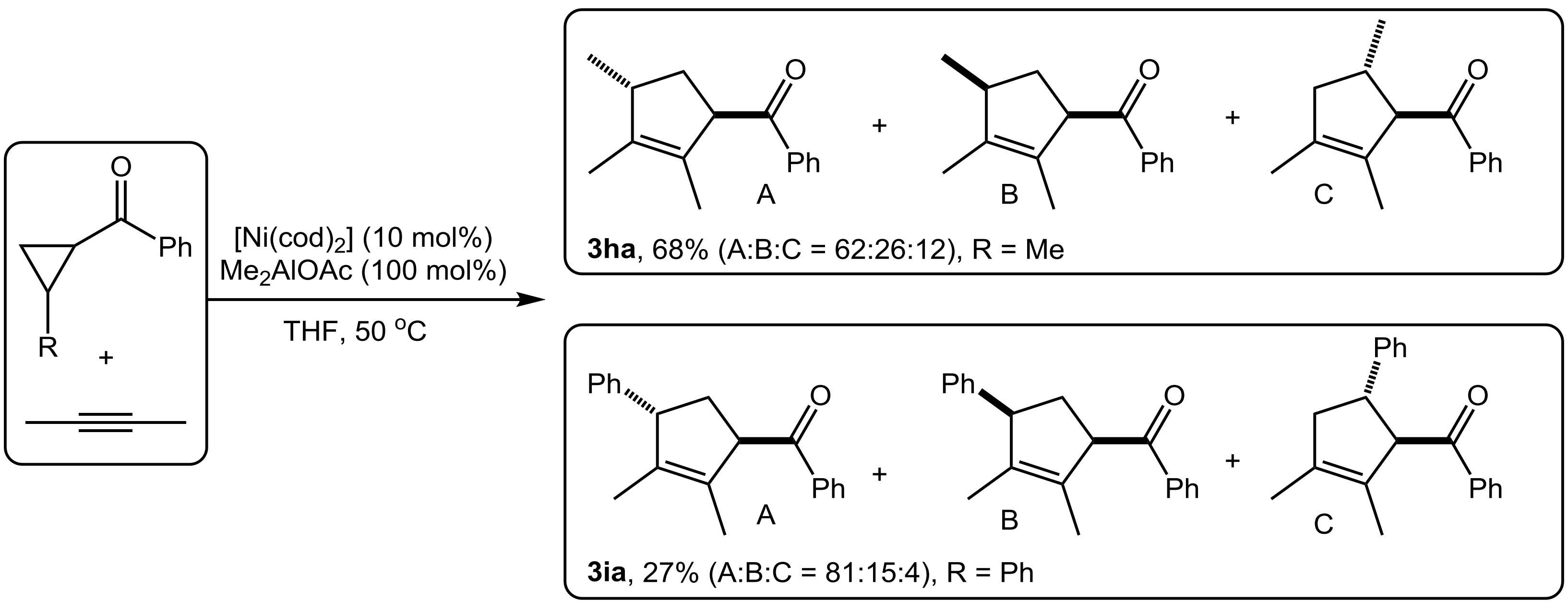
3da, 70%



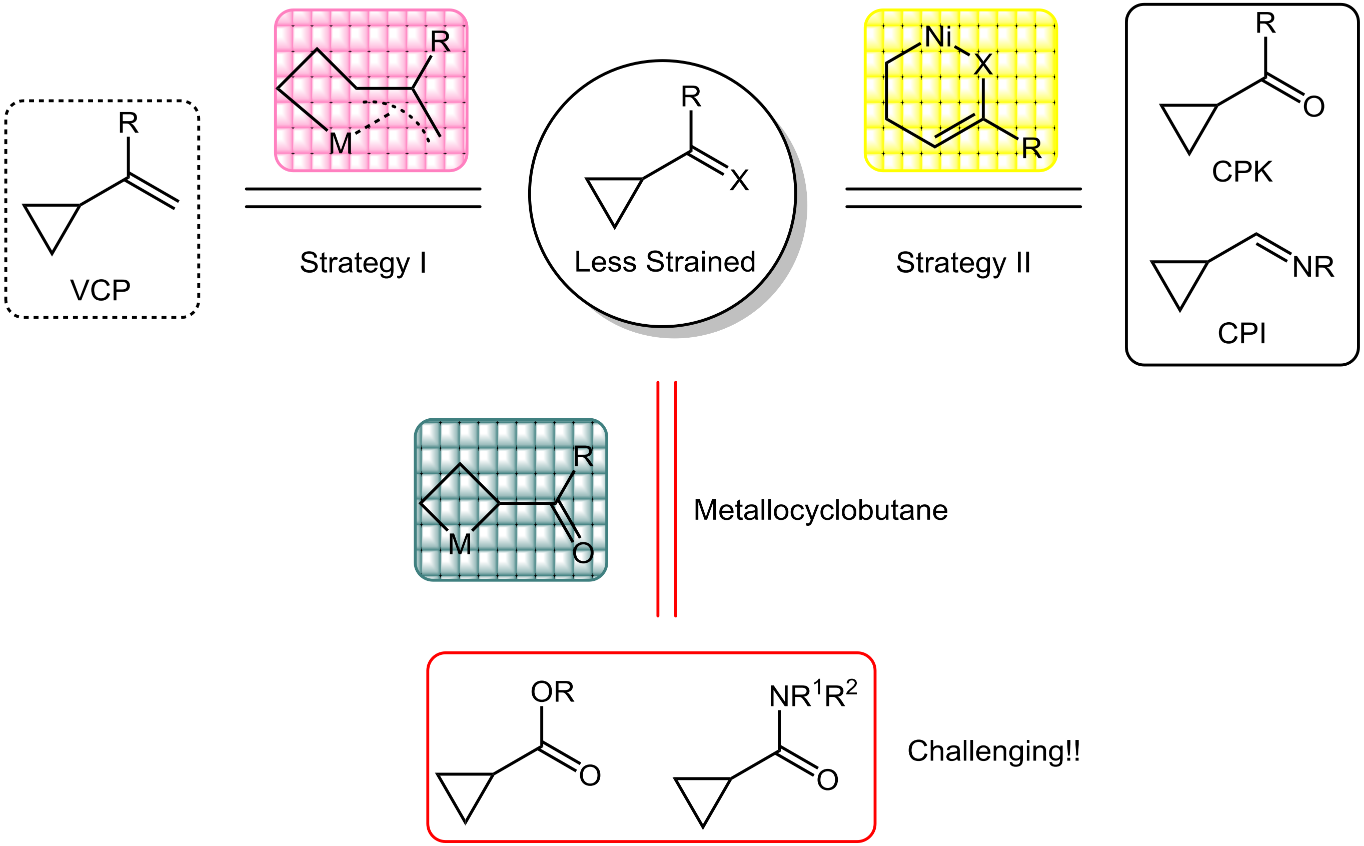
3ea, 56%

Substrate Scope





[3+2] Cycloaddition of Cyclopropyl Carboxamide



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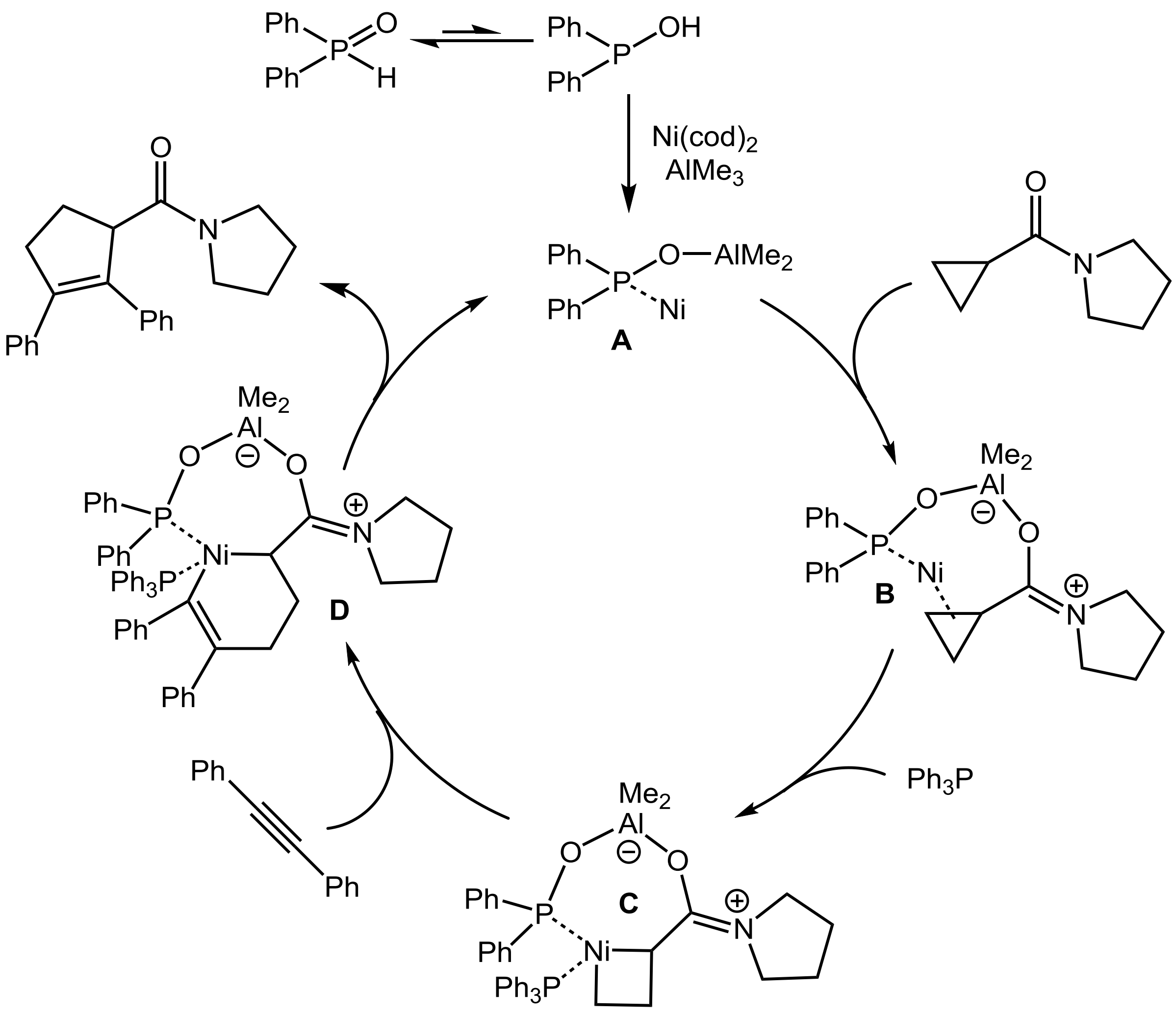
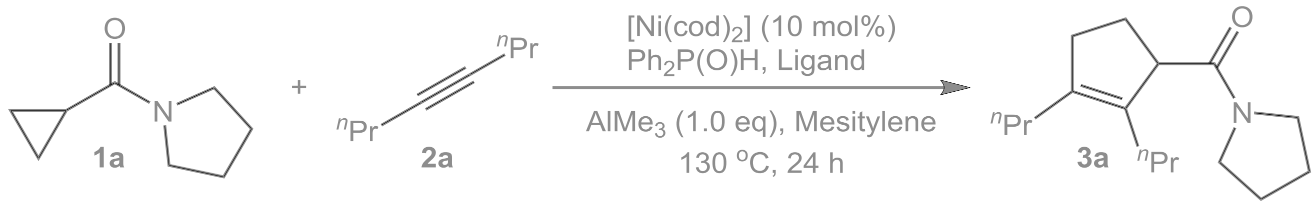
Plausible Mechanism

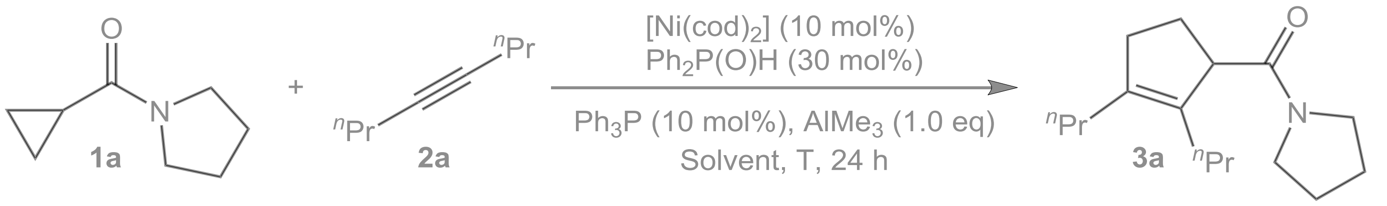


Condition Optimization



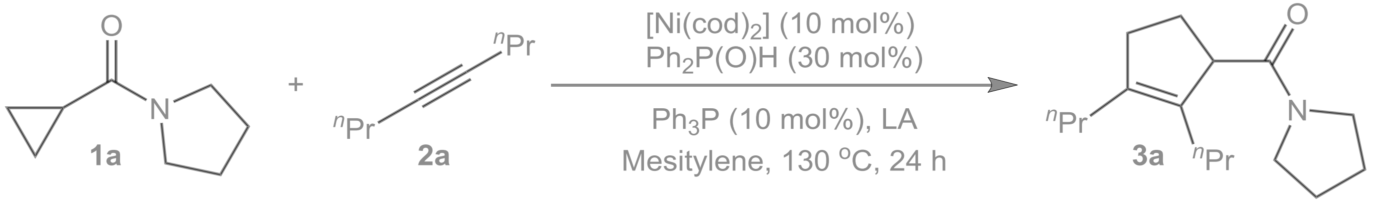
Entry	$Ph_2P(O)H$ (mol%)	Ligand (mol%)	Yield (**3a**, %)
1	0	0	NR
2	10	0	44
3	20	0	74
4	30	0	81
5	**30**	**Ph_3P (10)**	**86**
6	30	Ph_3P (20)	77
7	30	Ph_3P (30)	75
8	30	Ph_3P (40)	72
9	30	$^tBu_3P$ (10)	59
10	30	Cy_3P (10)	67
11	30	BINAP (10)	40
12	30	IPr-HCl (10)	50
13	30	IMes-HCl (10)	29

Condition Optimization



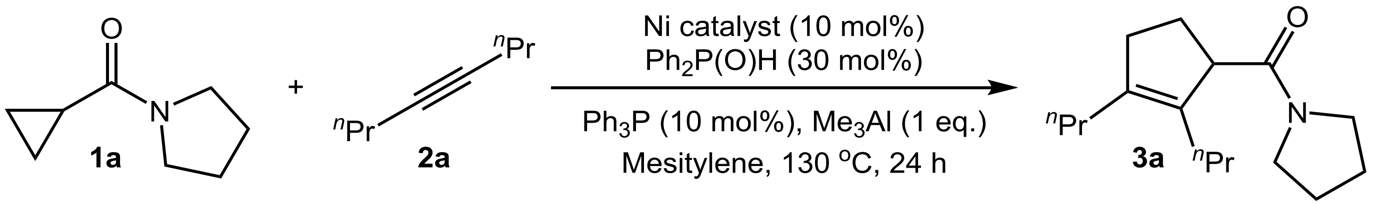
Entry	T (ºC)	Solvent	Yield (**3a**, %)
1	140	Mesitylene	64
2	**130**	**Mesitylene**	**86**
3	120	Mesitylene	76
4	110	Mesitylene	48
5	100	Mesitylene	46
6	130	Toluene	73
7	130	Xylene	61
8	130	Hexane	43
9	130	DME	36
10	130	CH_3CN	NR
11	130	Dioxane	9
12	130	$PhNO_2$	NR
13	130	^{i}PrOH	NR

Condition Optimization



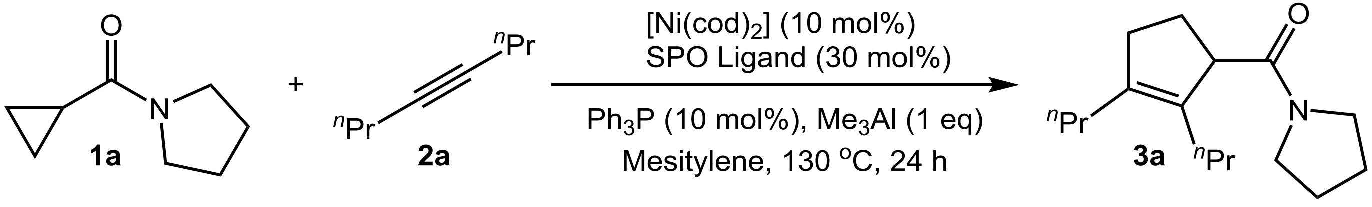
Entry	LA	(eq)	Yield (**3a**, %)
1	**$AlMe_3$**	**1.0**	**86**
2	$AlMe_3$	1.5	84
3	$AlMe_3$	0.9	76
4	$AlMe_3$	0.8	70
5	$AlMe_3$	0.7	58
6	$AlMe_3$	0.6	52
7	$AlMe_3$	0.5	49
8	$AlMe_3$	0.4	46
9	$AlMe_2Cl$	1.0	39
10	$TiCl_4$	1.0	NR
11	$Ti(O^iPr)_4$	1.0	Trace
12	$B(OMe)_3$	1.0	NR
13	$B(C_6F_5)_3$	1.0	NR

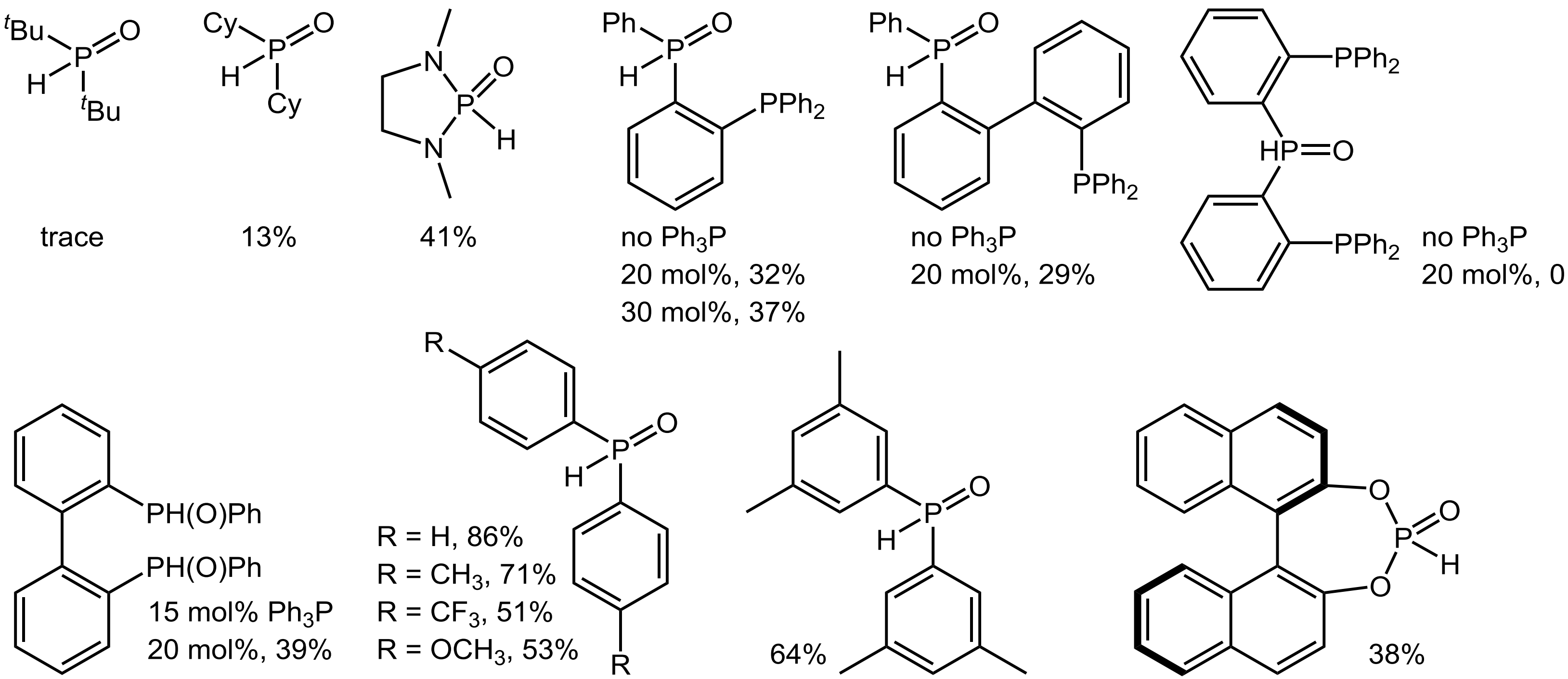
Condition Optimization



Entry	Ni catalyst	Yield (**3a**, %)
1	$Ni(cod)_2$	86
2	$NiCl_2(Ph_3P)_2$	45
3	$NiBr_2$	4
4	$NiCl_2(Ph_3P)_2$	73
5	$Ni(OAc)_2$	21
6	$NiCl_2$·DPPP	23
7	$NiCl_2$(1,1’-di-PPh_2-Ferrocene)	28
8	$NiCl_2 \cdot H_2O$	28
9	$NiBr_2$·Diglyme	8
10	$Ni(CF_3SO_3)_2$	39
11	NiI_2	5
12	$Ni(acac)_2$	38
13	$NiBr_2$·DME	18

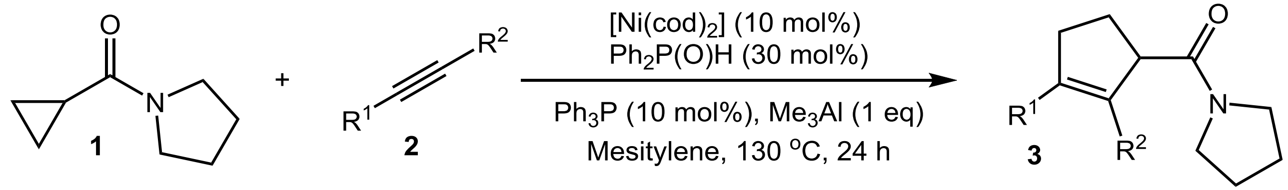
Condition Optimization

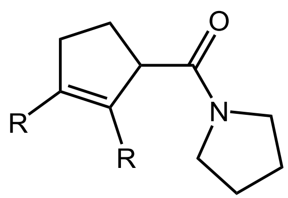




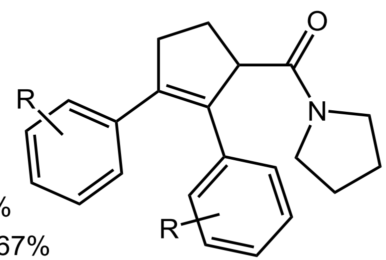
Secondary-Phosphine-Oxide (SPO)

Substrate Scope

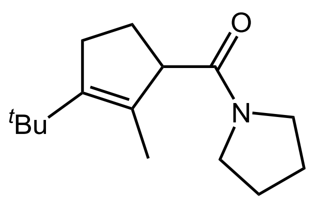




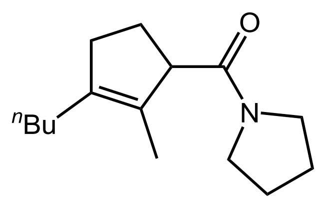
3a, R = Me, 84%
3b, R = Et, 80%
3c, R = ^{n}Pr, 85%
3d, R = ^{n}Bu, 78%
3e, R = 2-Np, 67%
3f, R = 2-thienyl, 67%
3g, R = 3-thienyl, 74%
3h, R = TMS, 52%



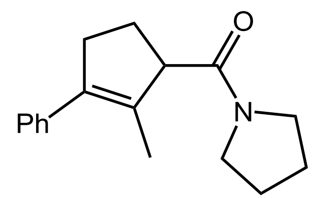
3i, R = H, 93%
3j, R = *o*-OMe, 79%
3k, R = *m*-OMe, 81%
3l, R = *p*-OMe, 86%
3m, R = *p*-F, 86%
3n, R = *p*-CF_3, 44%



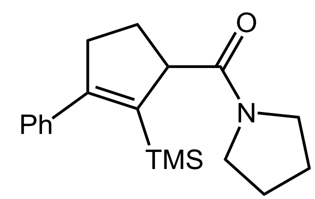
3o, 71% (86:14)



3p, 71% (53:47)

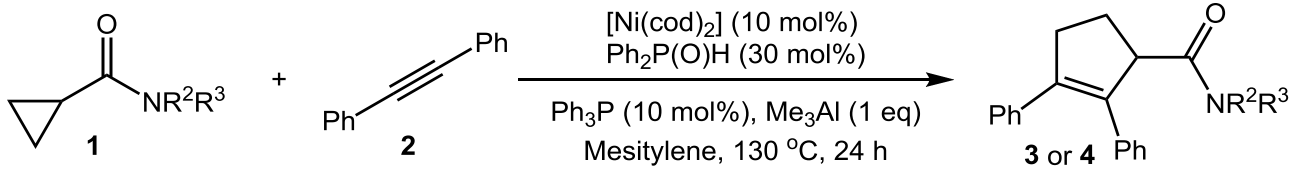


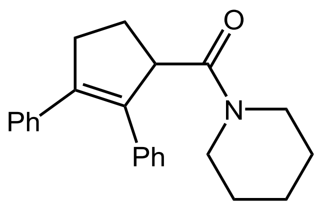
3q, 79% (65:35)



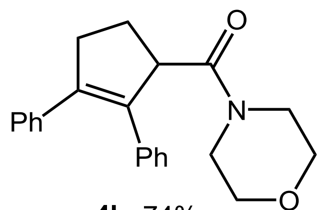
3r, 73% (80:20)

Substrate Scope

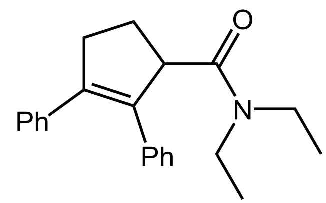




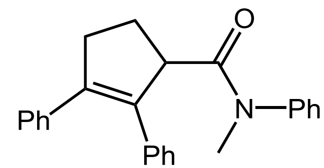
4a, 83%



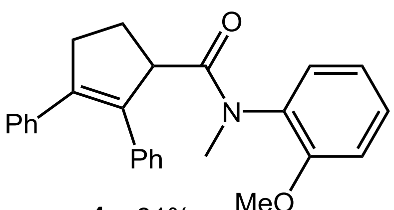
4b, 74%



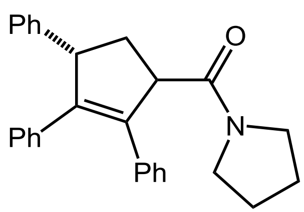
4c, 97%



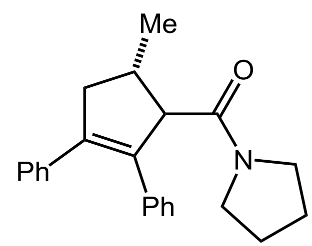
4d, 82%



4e, 81%

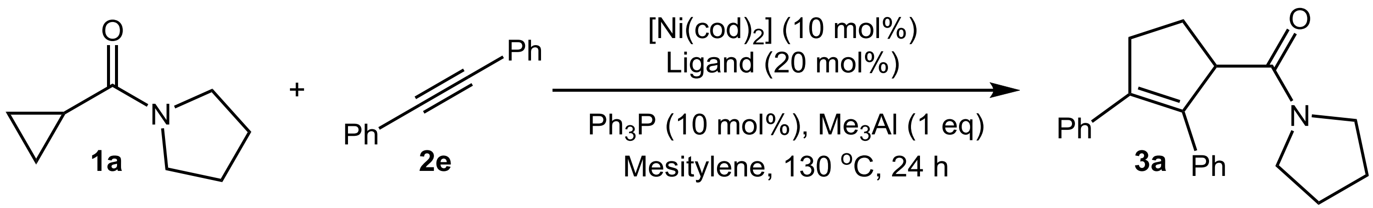


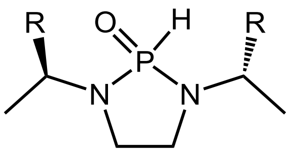
4f, 28% (81:9:10)
$[Ni(cod)_2]$ (15 mol%)
Me_3Al(2 eq)



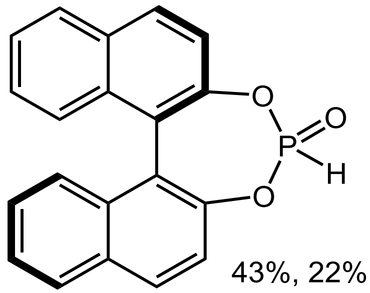
4g, 61%
$[Ni(cod)_2]$ (15 mol%)
Me_3Al(2 eq)

Condition Optimization

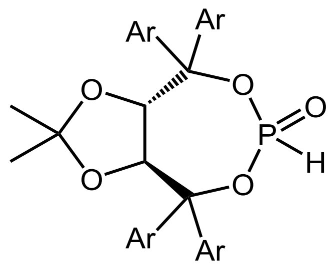




R = Ph, 70%, 4% ee
R = 1-Np, 72%, 11% ee



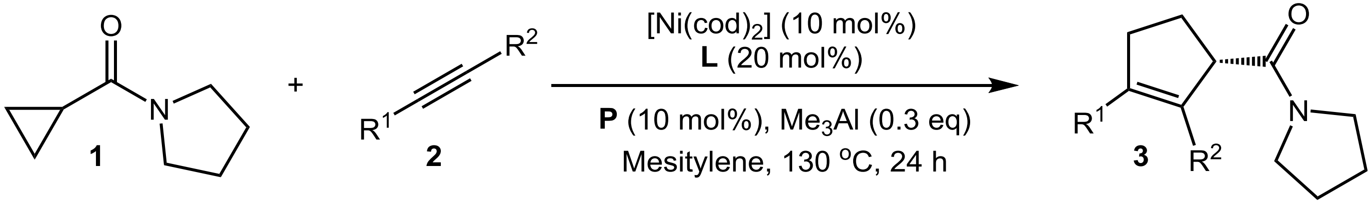
43%, 22% ee

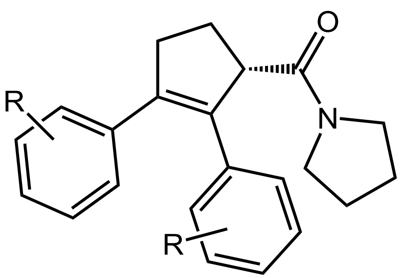


Ar = Ph, 95%, 8% ee
Ar = *p*-PhC_6H_4, 92%, 50% ee
Ar = *p*-$F_3CC_6H_4$, 77%, 2% ee
Ar = 3,5-$Ph_2C_6H_3$, 90%, 47% ee
Ar = 3,5-$^{t}Bu_2C_6H_3$, 36%, 32% ee
Ar = 2-Np, 91%, 79% ee, **L**

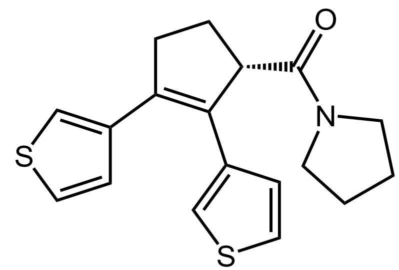
Entry	**P**	$AlMe_3$ (eq.)	Yield (**3a**, %)	ee (**3a**, %)
1	Ph_3P	1.0	91	79
2	Ph_3P	0.6	78	88
3	Ph_3P	0.3	40	90
4	(*o*-Tol)$_3$P	0.3	99	93
5	Cy_2PTipp	0.3	99	79
6	Cy_2PPh	0.3	65	57
7	CyPPh_2	0.3	37	88
8	Cy_3P	0.3	46	40

Substrate Scope

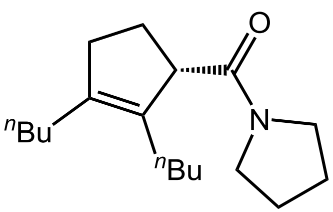




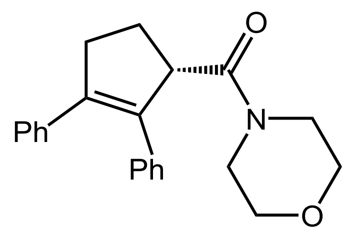
R = H, *(o-Tol)$_3$P,* 99%, 93% ee
R = 4-Me, *Cy$_2$PTipp,* 94%, 89% ee
R = 4-MeO, *(o-Tol)$_3$P,* 99%, 90% ee
R = 4-MeO, *Cy$_2$PTipp,* 59%, 94% ee
R = 4-F_3CO, *Cy$_2$PTipp,* 60%, 90% ee
R = 4-F, *Cy$_2$PPh,* 66%, 92% ee
R = 3-MeO, *(o-Tol)$_3$P,* 82%, 86% ee



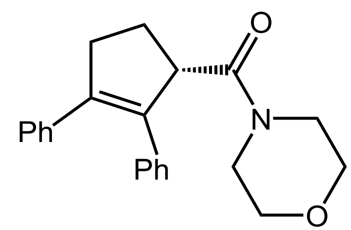
(o-Tol)$_3$P, 71%, 86% ee



(o-Tol)$_3$P, 43%, 59% ee
Me_3Al (1.0 eq)

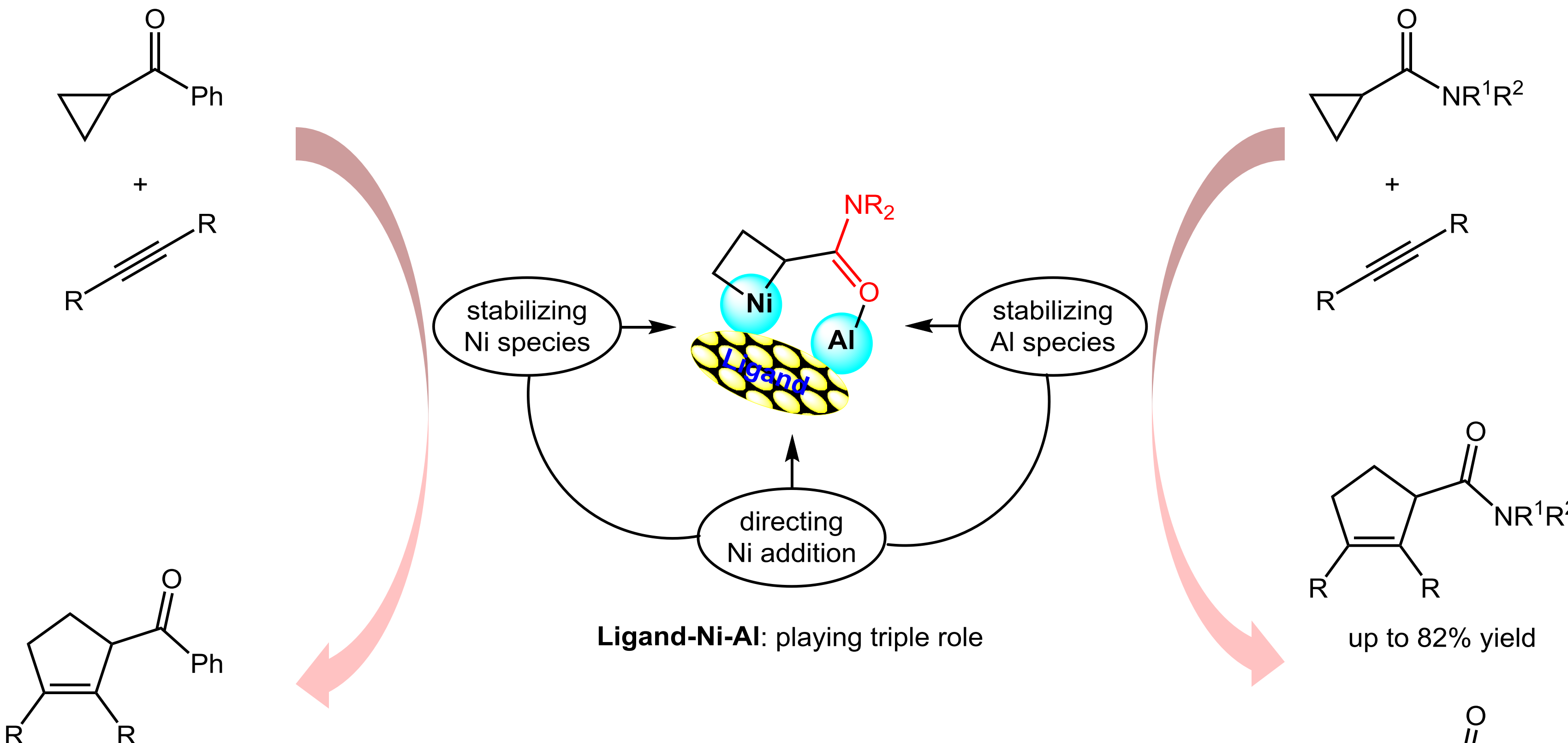


(o-Tol)$_3$P, >99%, 65% ee

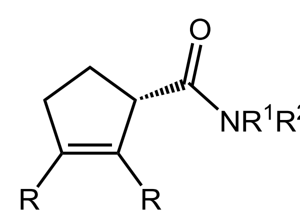


Cy$_2$PTipp, >99%, 75% ee

Summary



up to 88% yield



up to 94% ee

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2011, *50*, 12067.

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J. Am. Chem. Soc.
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The First Paragraph

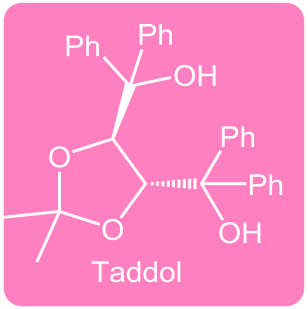
Transition-metal-catalyzed cycloaddition of cyclopropane with π-unsaturated compound has emerged as a powerful tool for the construction of cyclic structural units during the past decades. Among various functionalized cyclopropanes used in cycloaddition reactions, cyclopropyl carboxylates, including carboxylic acids, esters and amides, are one of the most attractive classes of substrates because carboxylate groups are not only readily available but also participate in versatile transformations in organic synthesis. However, their cycloaddition reaction still remains an elusive challenge. Different from highly strained cyclopropanes bearing fused π-unsaturation (cyclopropene and alkylidenecyclopropane), less strained cyclopropanes bearing adjacent π-unsaturation (vinylcyclopropane and cyclopropanes containing polar π-bonds) prove quite inert in transition metal-catalyzed cloaddition reactions. Wender and co-workers in 1995 revealed for the first time that a [5+2] cycloaddition reaction was facilitated through formation of an allyl-metal intermediate (Scheme 1a, strategy (i)).

The First Paragraph

Later, Montgomery group and Ogoshi group independently found that the formation of an oxa(aza)-nickelacycle intermediate also greatly improved the oxidative addition and the subsequent cycloaddition with an activated π-compound (strategy (ii)). However, in sharp contrast, cyclopropyl carboxylates could generate neither allyl-metal nor oxa(aza)nickelacycle intermediates, so that a high activation energy barrier has to be overcome for the formation of unstable metallocyclobutane species. Herein, we report a Ni−Al bimetallic synergism to facilitate the cycloaddition reaction of cyclopropyl carboxamide with alkyne for the first time, in which the ligand−Ni−Al combination probably played a triple role: activating cyclopropane substrate, directing nickel oxidative addition and stabilizing the in situ formed nickellacycle (Scheme 1b). In addition, a successful enantioselective control of this reaction was also achieved by the use of taddol-derived chiral phosphine oxide ligand with up to 94% ee.

The Last Paragraph

In summary, we have developed the first example of nickel-catalyzed enantioselective cycloaddition reaction of unreactive cyclopropyl carboxamide with alkyne. A series of synthetically useful cyclopentenyl carboxamides are obtained in up to 99% yield and 94% ee. The cooperation of ligand with Ni and Al may provide new insights into the C−C bond activation of unreactive substrates.



Acknowledgement

Thanks

for your attention