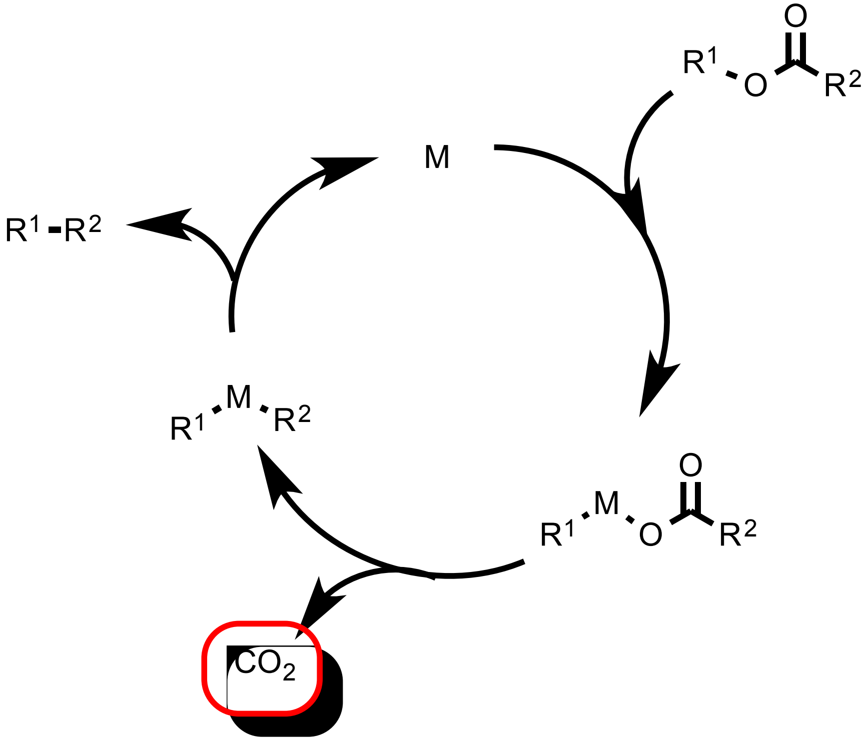
Transition Metal-Catalyzed Decarboxylative allylation and Benzylation reactions

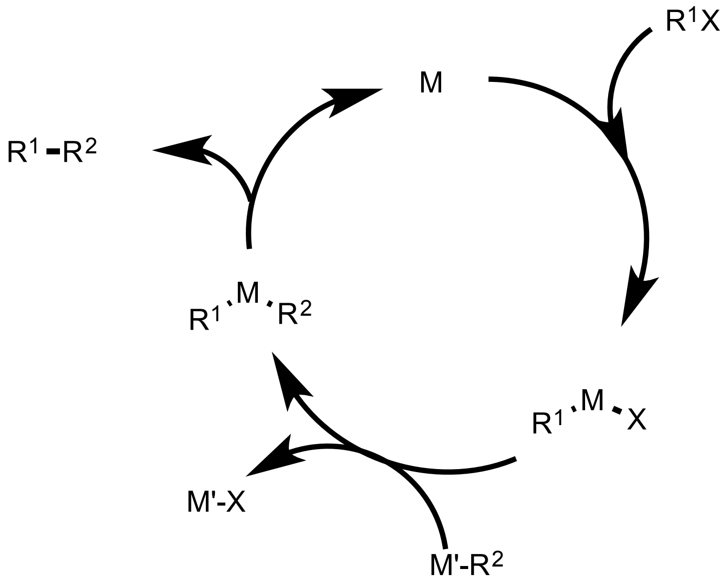


2013. 05. 01
Haye Min Ko

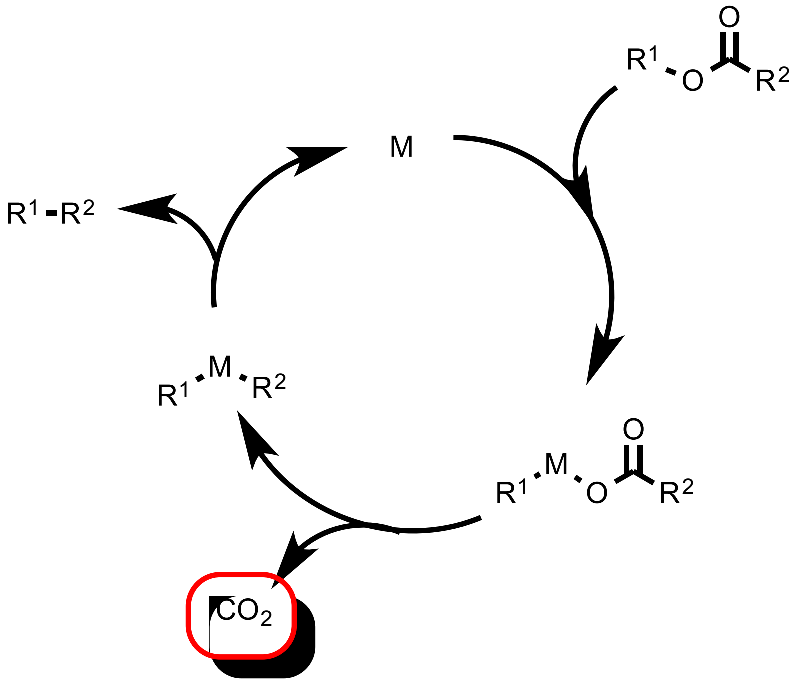
Contents

1. Introduction to Decarboxylative Coupling

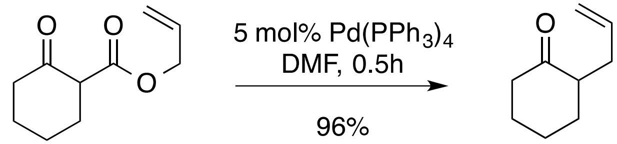
Standard Cross-Coupling vs Decarboxylative Coupling

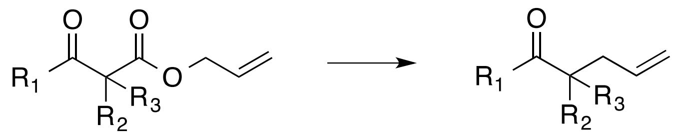


X = Cl, Br, OTf



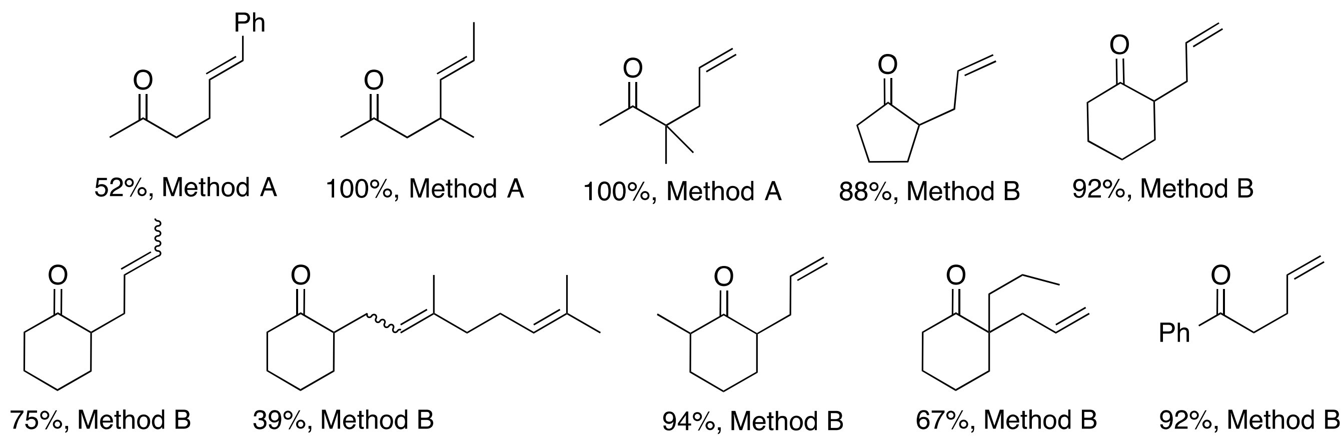
2. Decarboxylative Allylation of Enolates





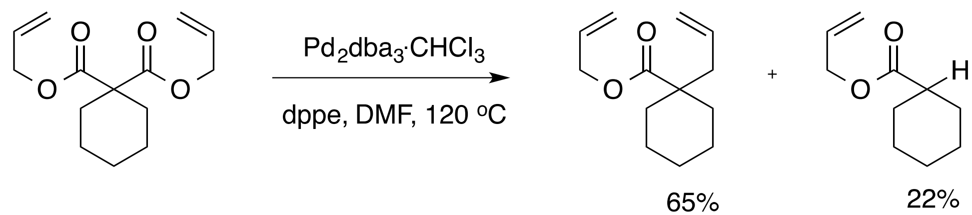
Method A
5 mol% $Pd(OAc)_2$
10 mol% PPh_3
THF, 66 °C

Method B
5 mol% $Pd(PPh_3)_4$
DMF, r.t.

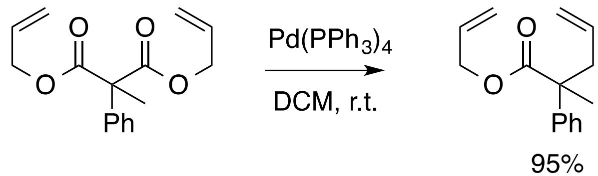


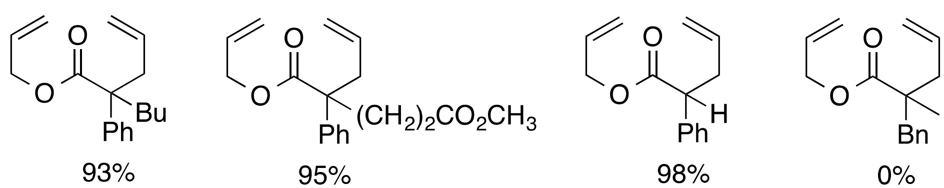
a) Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199.
b) Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381

Ester Enolates



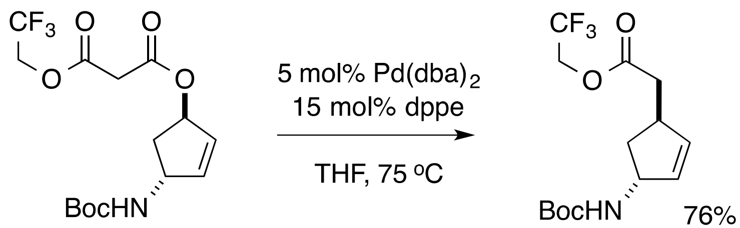
Tsuji, J.; Yamada, T.; Minami, I.; Yuhara, M.; Nisar, M.; Shimizu, I.
J. Org. Chem. **1987**, *52*, 2988.

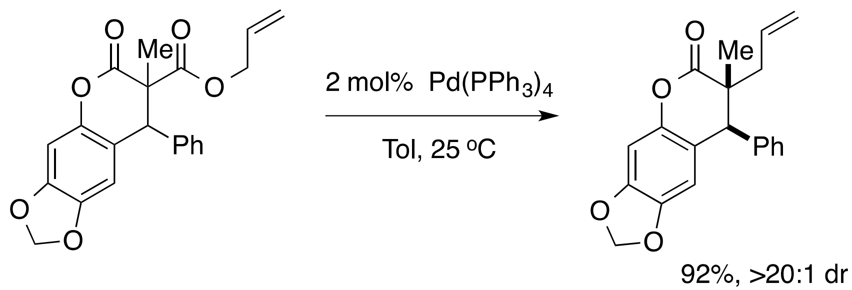




Imao, D.; Itoi, A.; Yamazaki, A.; Shirakura, M.; Ohtoshi, R.;Ogata, K.; Ohmori, Y.; Ohta, T.; Ito, Y.
J. Org. Chem. **2007**, *72*, 1652.

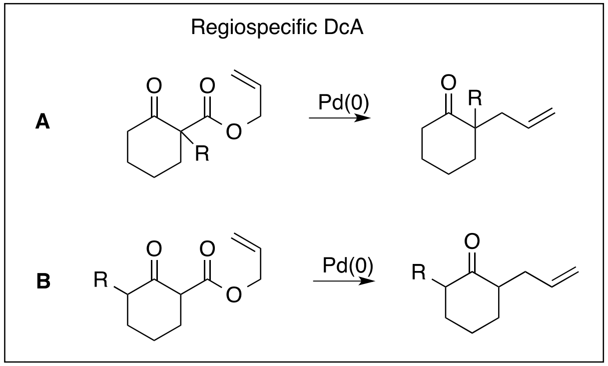
Ester Enolates

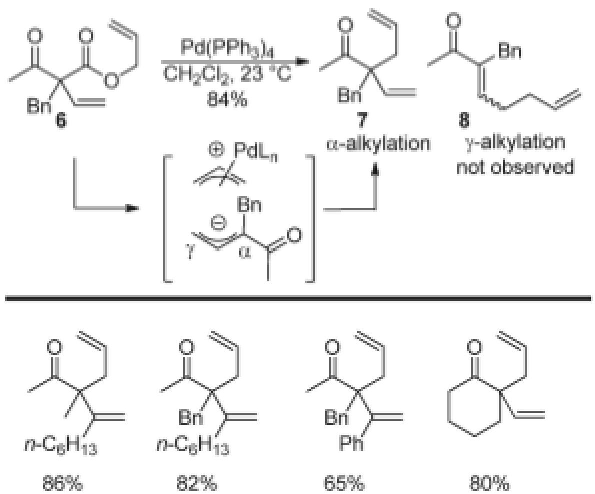


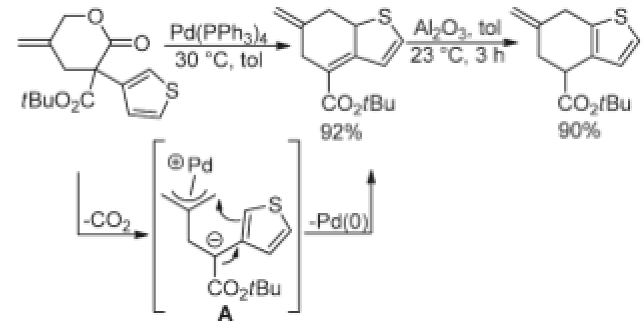


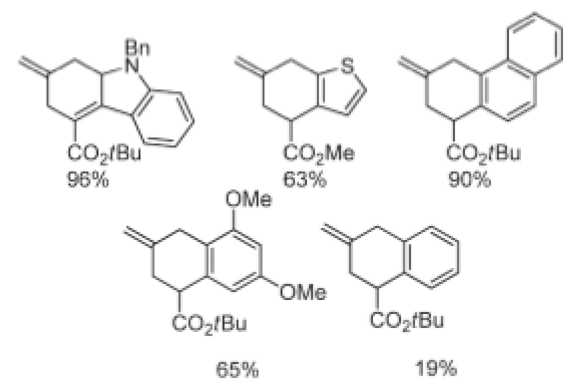
a) Chattopadhyay, K.; Jana, R.; Day, V. W.; Douglas, J. T.; Tunge, J. A. *Org. Lett.* **2010**, *12*, 3042.
b) Tardibono, L. P.; Patzner, J.; Cesario, C.; Miller, M. J. *Org. Lett.*, **2009**, *11*, 4076.

Regioselectivity in Allylation



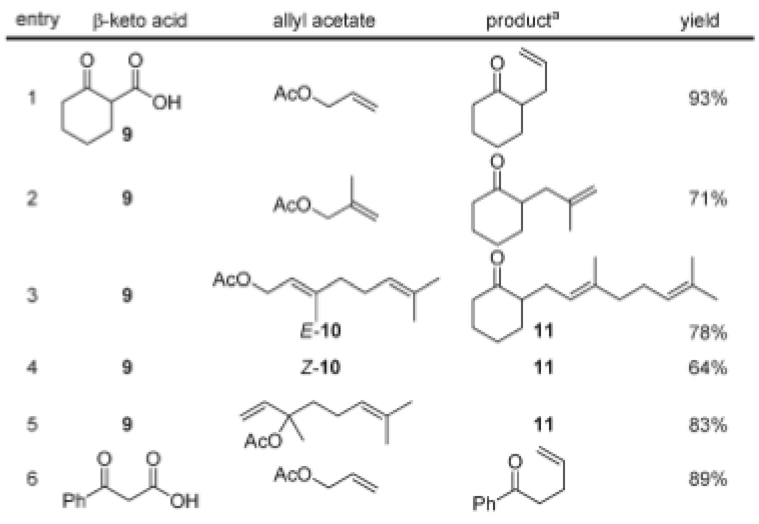




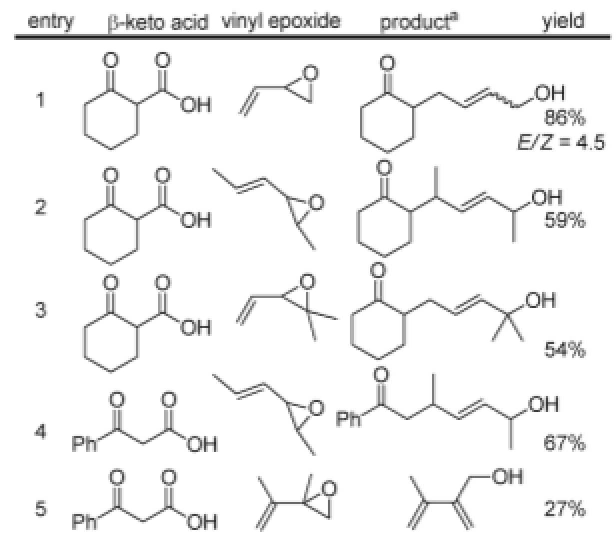


a) Waetzig,S.R.;Rayabharapu,D.K.;Weaver,J.D.;Tunge,J.A. *Angew. Chem., Int. Ed*. **2006**, *45*, 4977.
b) Shintani, R.; Tsuji, T.; Park, S.; Hayashi, T. *Chem. Commun*. **2010**, *46*, 1697.

Intermolecular Coupling of β-Keto Acids



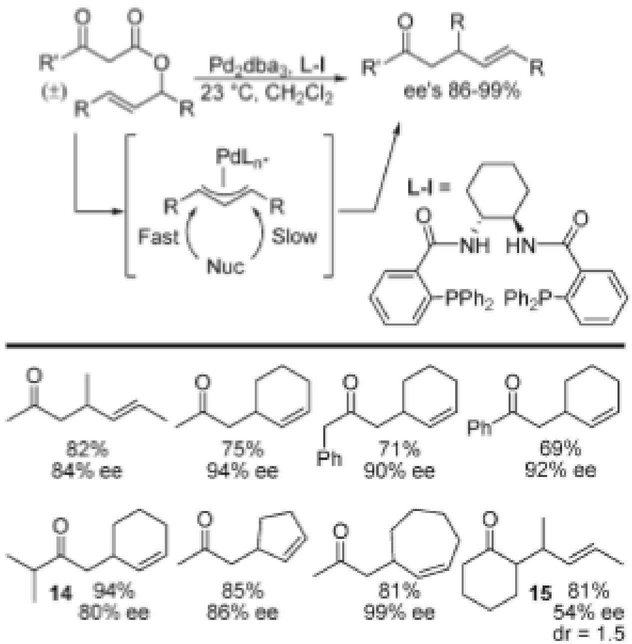
[a] $Pd(PPh_3)_4$, 23 °C, THF or C_6H_6, 0.5-20 h

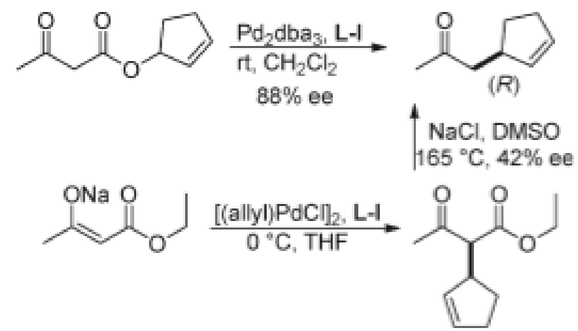


[a] $Pd(PPh_3)_4$, 23 °C, THF or C_6H_6, 0.5-20 h

a) Tsuda,T.;Okada,M.;Nishi,S.;Saegusa,T.*J.Org.Chem.***1986**, *51*, 421.
b) Tsuda,T.;Tokai,M.;Ishida,T.;Saegusa,T.*J.Org.Chem.***1986**, *51*, 5216.

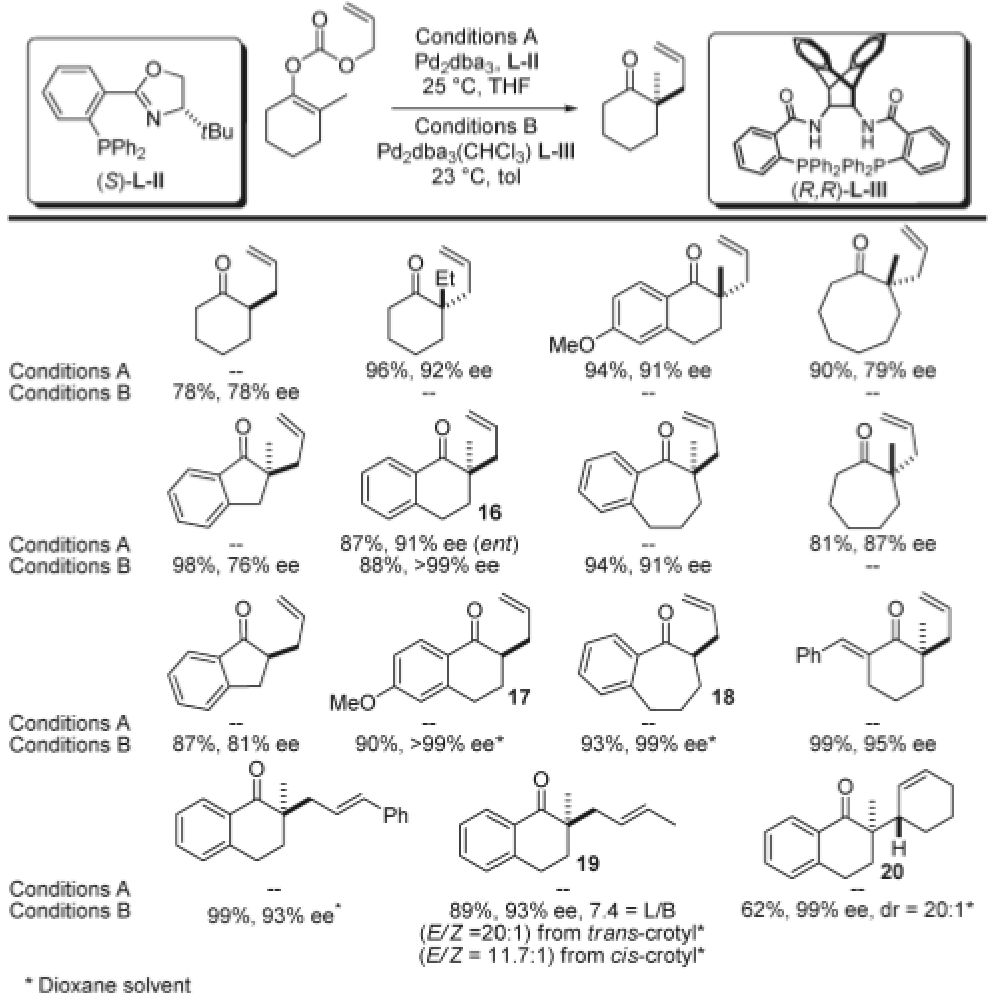
2.1. Asymmetric DcA of Enolates





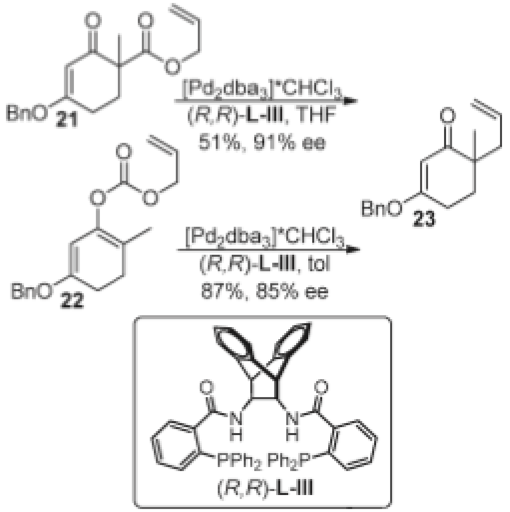
Burger,E.C.;Tunge,J.A. *Org.Lett.* **2004**, *6*, 4113.

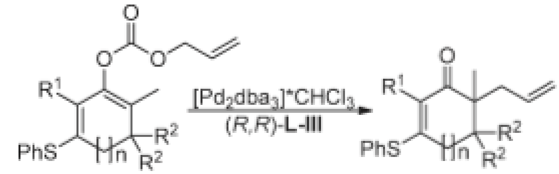
Asymmetric DcA of Allyl Vinyl Carbonates



a) Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 15044
b) Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, *127*, 2846.
c) Trost, B. M.; Xu, J.; Schmidt, T. *J. Am. Chem. Soc.* **2009**, *131*, 18343.

Asymmetric DcA of Allyl Vinylogous Carbonates



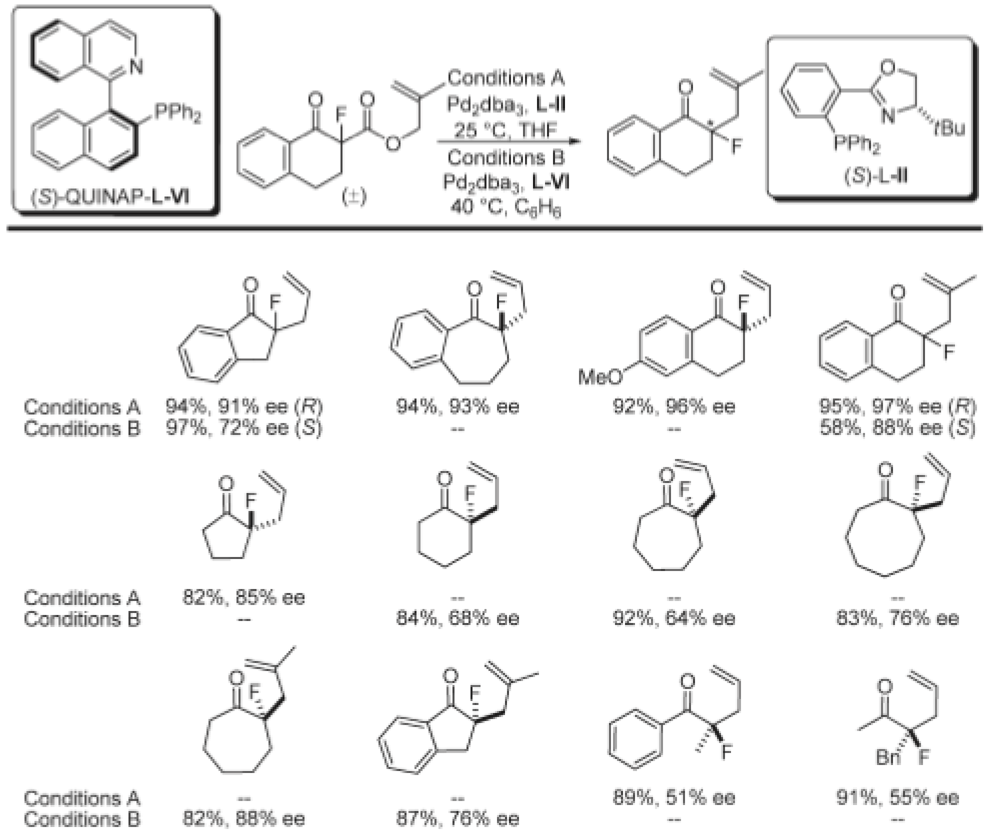


entry	*n*	R[1]	R[2]	solvent	temp (°C)	yield (%)	ee (%)
1	1	H	H	THF	−20	100	98
2	2	H	H	THF	0−4	100	94
3	1	Me	H	THF	0−4	100	99
4	0	Me	H	THF	0−4	96	80
5	1	Ph	H	dioxane	23	100	97
6	1	H	Me	THF	0−4	91	79

entry	R	time (h)	yield (%)	ee (%)
1	Me	16	75	100
2	Bn	16	78	92
3	H_2C–CH=CH–Ph	2	98	95
4	CH_2CO_2Et	1	80	92
5	$CH_2CH_2CO_2Et$	4	90	73
6	$CH_2CH_2CH_2CO_2Et$	2	86	94

a) Trost, B. M.; Bream, R. N.; Xu, J. *Angew. Chem., Int. Ed*. **2006**, *45*, 3109.
b) Levine, S. R.; Krout, M. R.; Stoltz, B. M. *Org. Lett*. **2009**, *11*, 289.

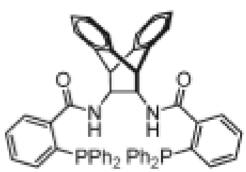
Asymmetric DcA of α-Fluoro- β-Ketoesters



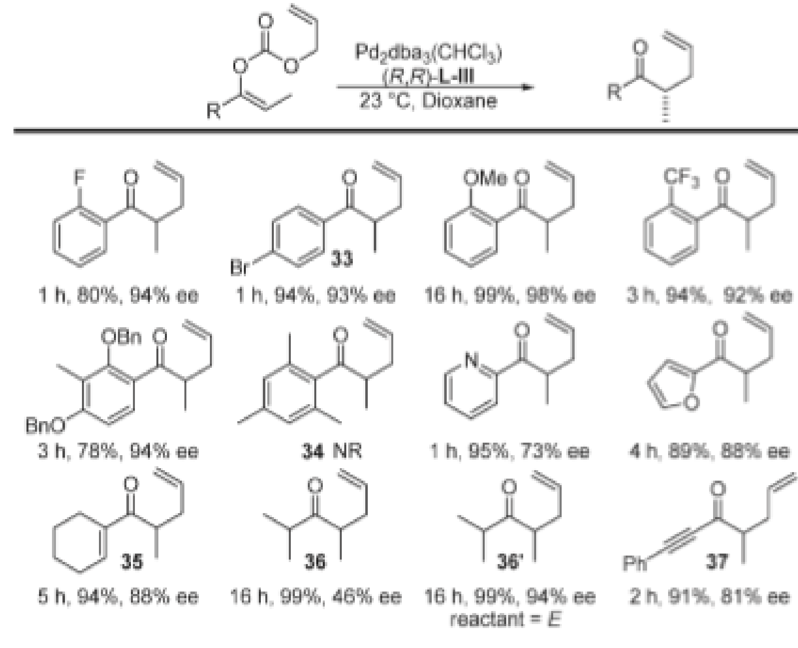
a) Nakamura, M.; Hajra, A.; Endo, K.; Nakamura, E. *Angew. Chem., Int. Ed.* **2005**, *44*, 7248.
b) Burger, E. C.; Barron, B. R.; Tunge, J. A. *Synlett* **2006**, 2824.

Asymmetric DcA of Acyclic Allyl Enol Carbonates

entry	R	time (h)	yield (%)	ee (%)
1	Me	3	96	94
2	Et	2	94	94
3	*n*-Pent	16	93	92
4	Bn	1	75	88
5	*i*-Pr	24	30	32

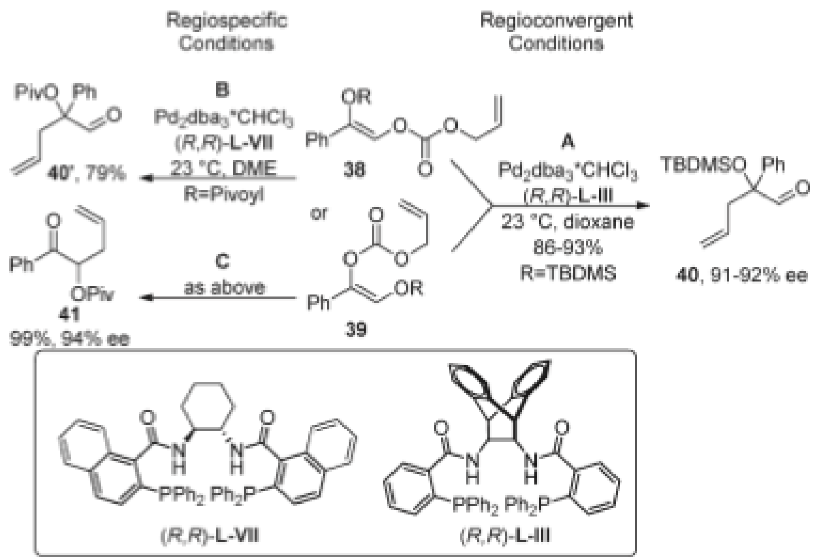


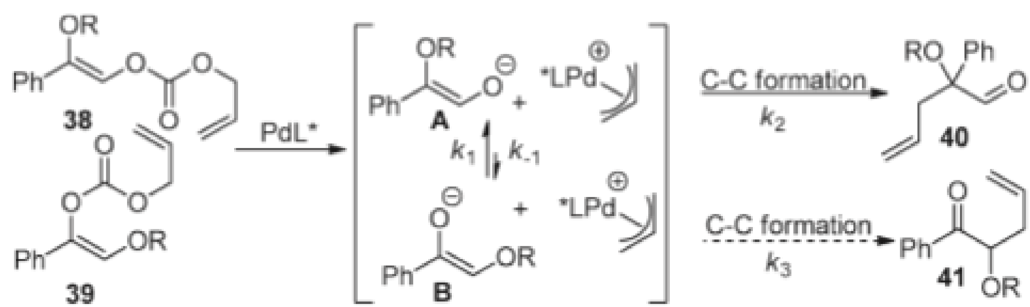
(*R*,*R*)-L-III



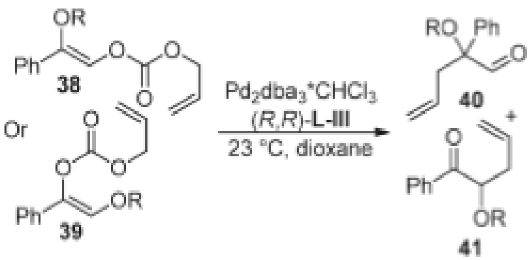
Trost, B. M.; Xu, J.; Schmidt, T. *J. Am. Chem. Soc.* **2009**, *131* , 18343.

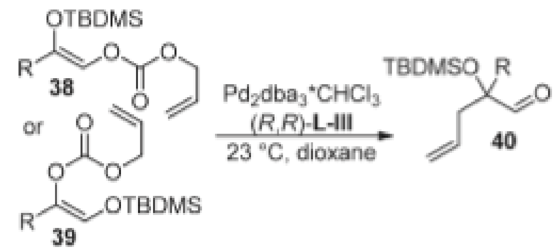
Protected α-Hydroxy Allyl Vinyl Carbonates





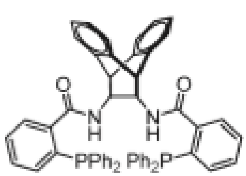
Protected α-Hydroxy Allyl Vinyl Carbonates





entry	SM	R	yield **40**	yield **41**
1	38	TBDMS	93	0
2	39	TBDMS	86	0
3	38	benzoyl	93	0
4	39	benzoyl	11	75 (dppe)
5	38	acetyl	40	60

entry	SM	R	yield (%)	ee (%)
1	38	Ph	93	92
2	39	Ph	89	91
3	38	*p*-$MeOC_6H_4$	94	92
4	39	*p*-$MeOC_6H_4$	86	92
5	38	*o*-$NO_2C_6H_4$	69	79
6	39	*o*-$NO_2C_6H_4$	69	72
7	38	2-furyl	81	93
8	38	1-cyclohexenyl	93	98
9	38	PhCC	76	89

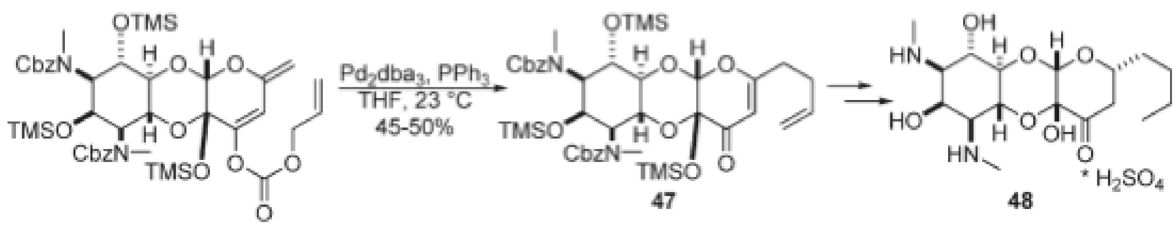


(*R*,*R*)-**L-III**

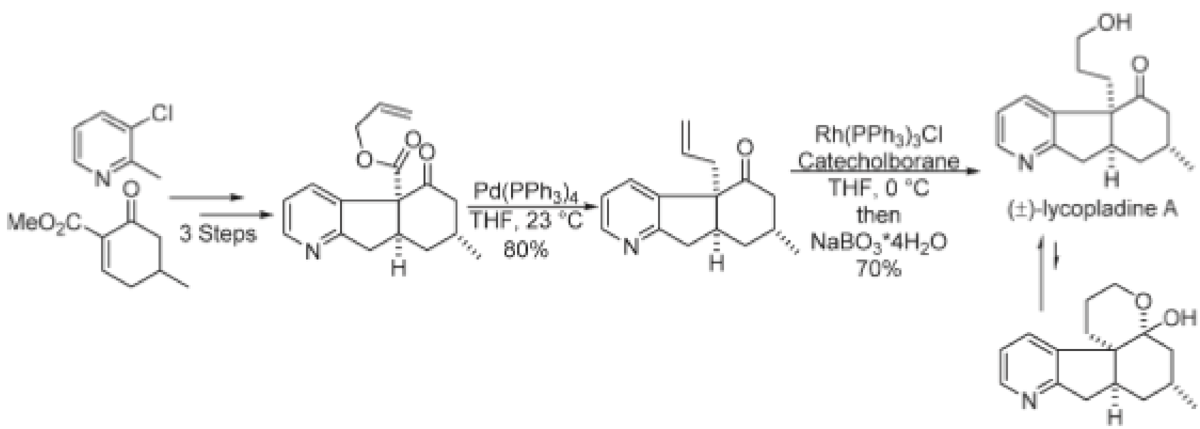
a) Trost, B. M.; Xu, J.; Reichle, M. *J. Am. Chem. Soc.* **2007**, *129*, 282.
b) Trost, B. M.; Xu, J.; Schmidt, T. *J. Am. Chem. Soc.* **2008**, *130*,11852.

2.2. Applications

Synthesis of Trospectomycin Sulfate



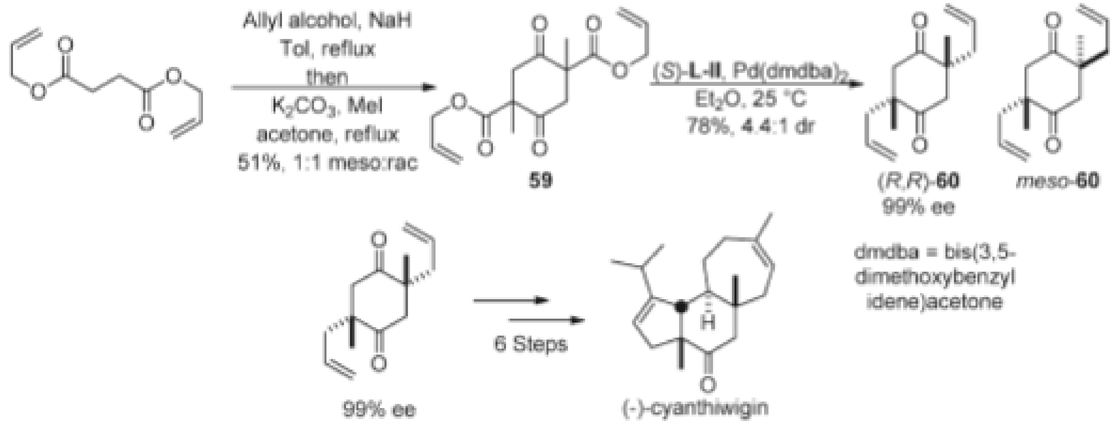
Synthesis of (±)-Lycopladine A



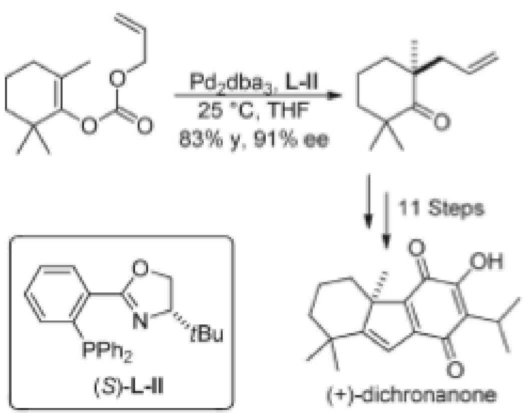
a) Herrinton, P. M.; Klotz, K. L.; Hartley, W. M. *J. Org. Chem*. **1993**, *58*, 678.
b) DeLorbe, J. E.;Lotz, M. D.;Martin, S. F. *Org.Lett*. **2010**, *12*, 1576.

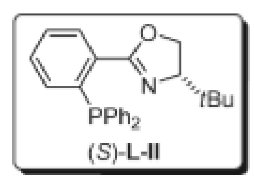
2.2. Applications

Synthesis of (−)-Cyanthiwigin



Synthesis of (+)-*R*-Dichronanone

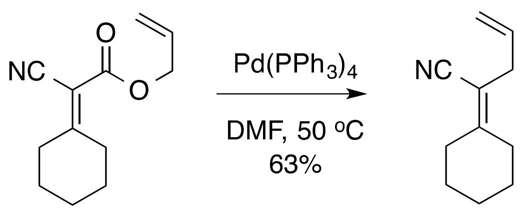




a) McFadden, R. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2006**, *128*,7738.
b) Enquist, J. A., Jr.; Stoltz, B. M. *Nature* **2008**, *453*, 1228.

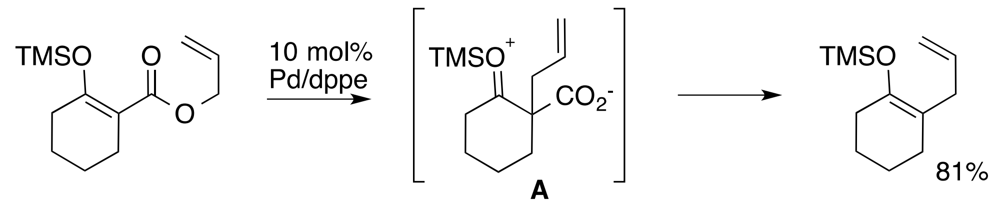
3. Sp²-Hybridized Carbon Nucleophiles

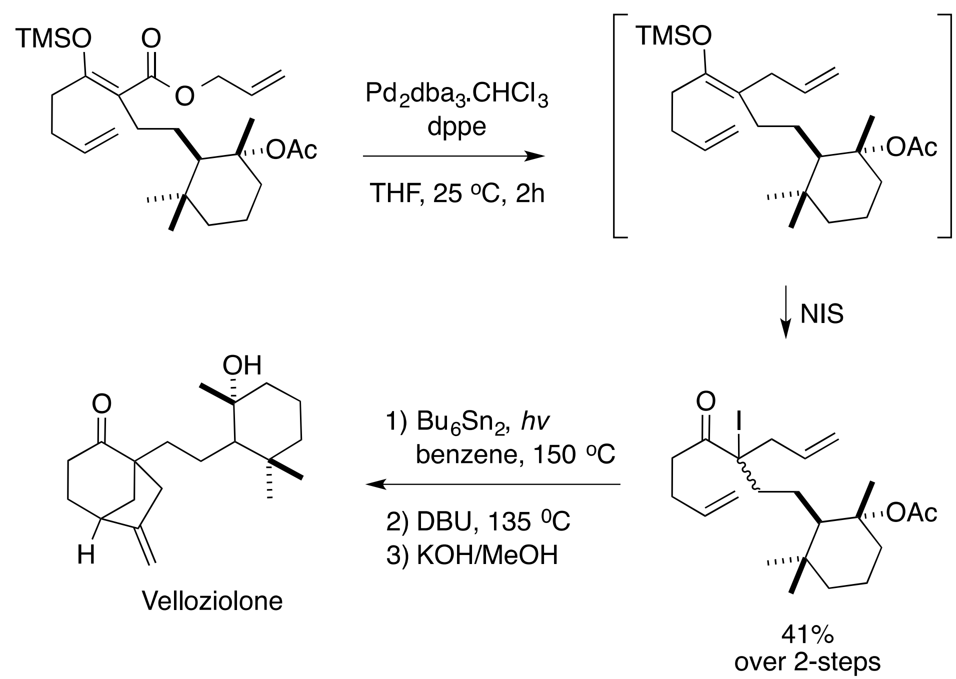
α-allylation of Acrylonitriles



Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381.

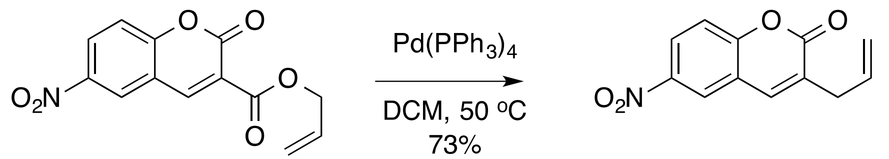
Silyl Enol Ethers



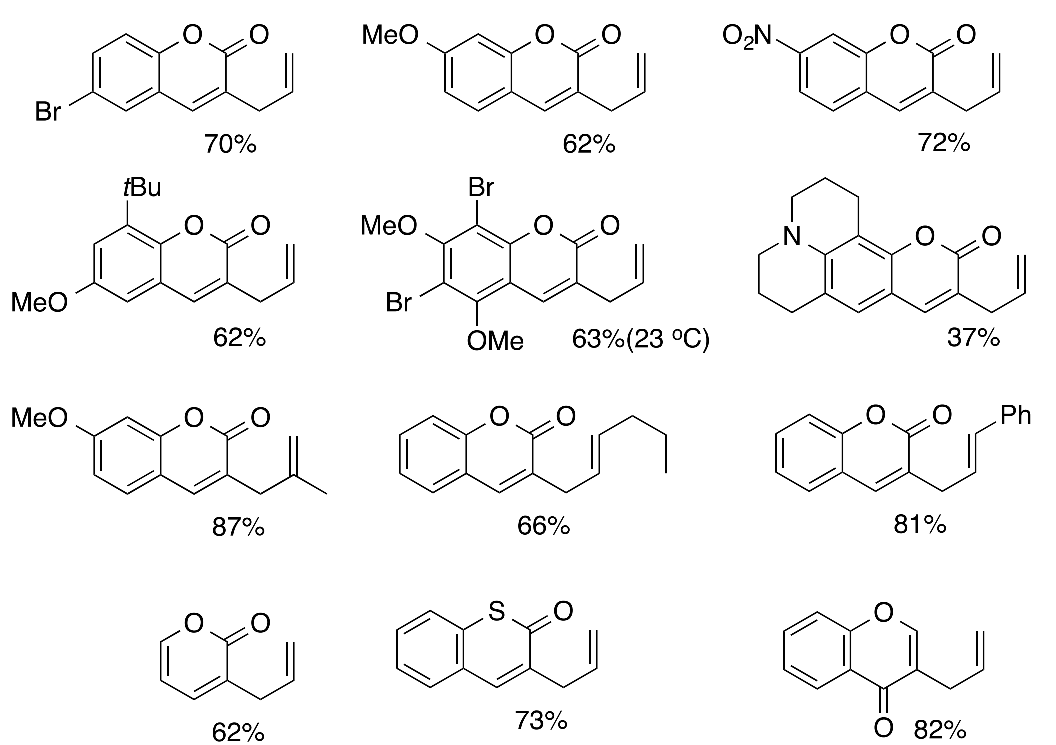


Snider, B. B.; Buckman, B. O. *J. Org. Chem.* **1992**, *57*, 4883

α-allylation of Coumarins

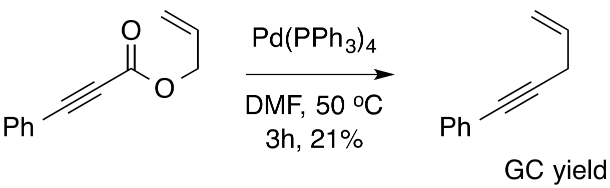


Jana, R.; Trivedi, R.; Tunge, J. A. *Org. Lett.* **2009**, *11* , 3434.

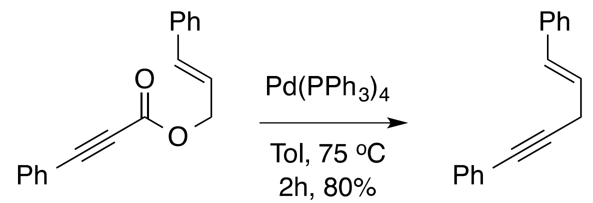


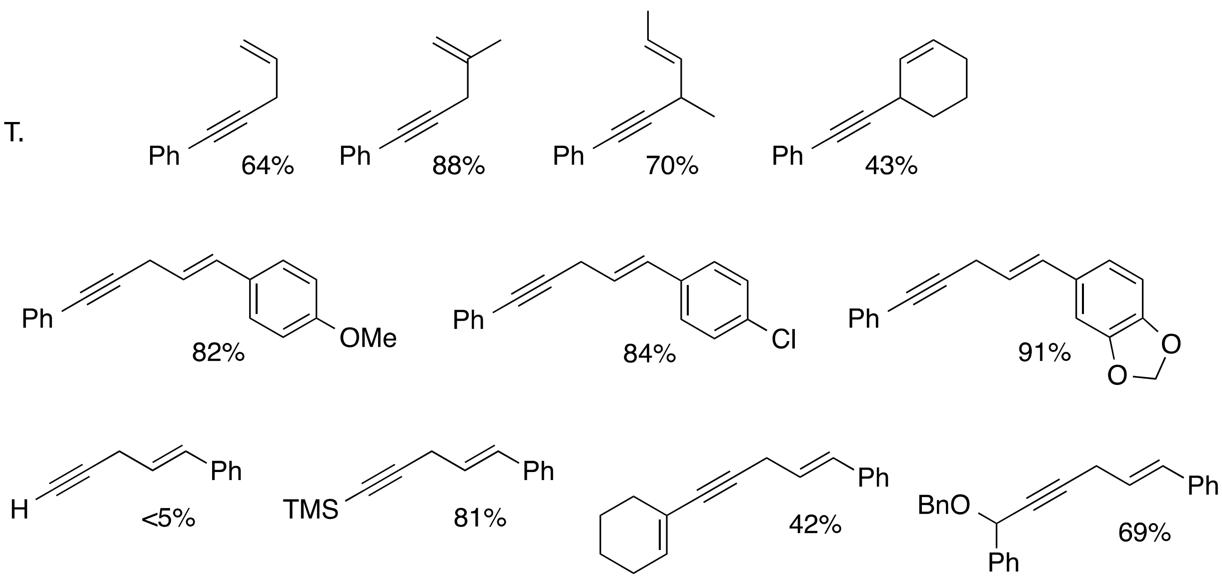
4. SP-Hydridized Carbon Nucleophiles

DcA of Acetylides

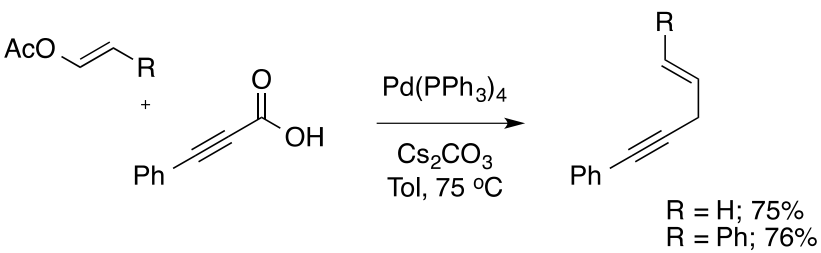


Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T.
J. Am. Chem. Soc. **1980**, *102*, 6381.

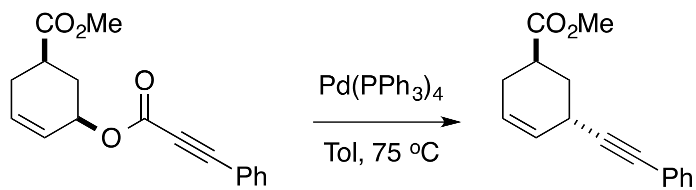


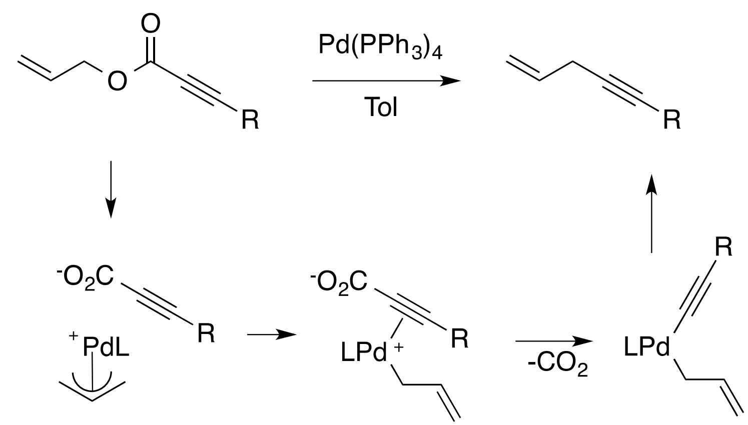


Intermolecular reaciton



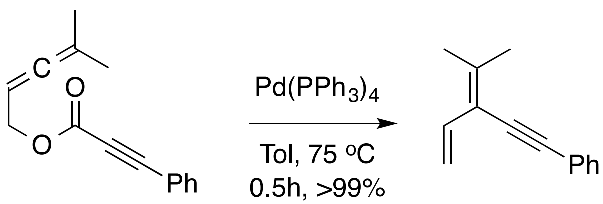
Inner-sphere process



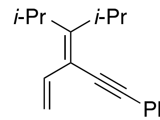
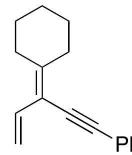
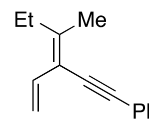
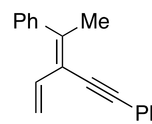
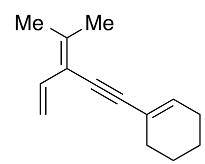
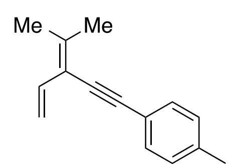
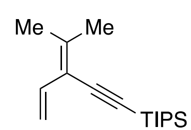


Rayabarapu, D. K.; Tunge, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 13510.

Decarboxylative coupling of Allenes with Acetylides

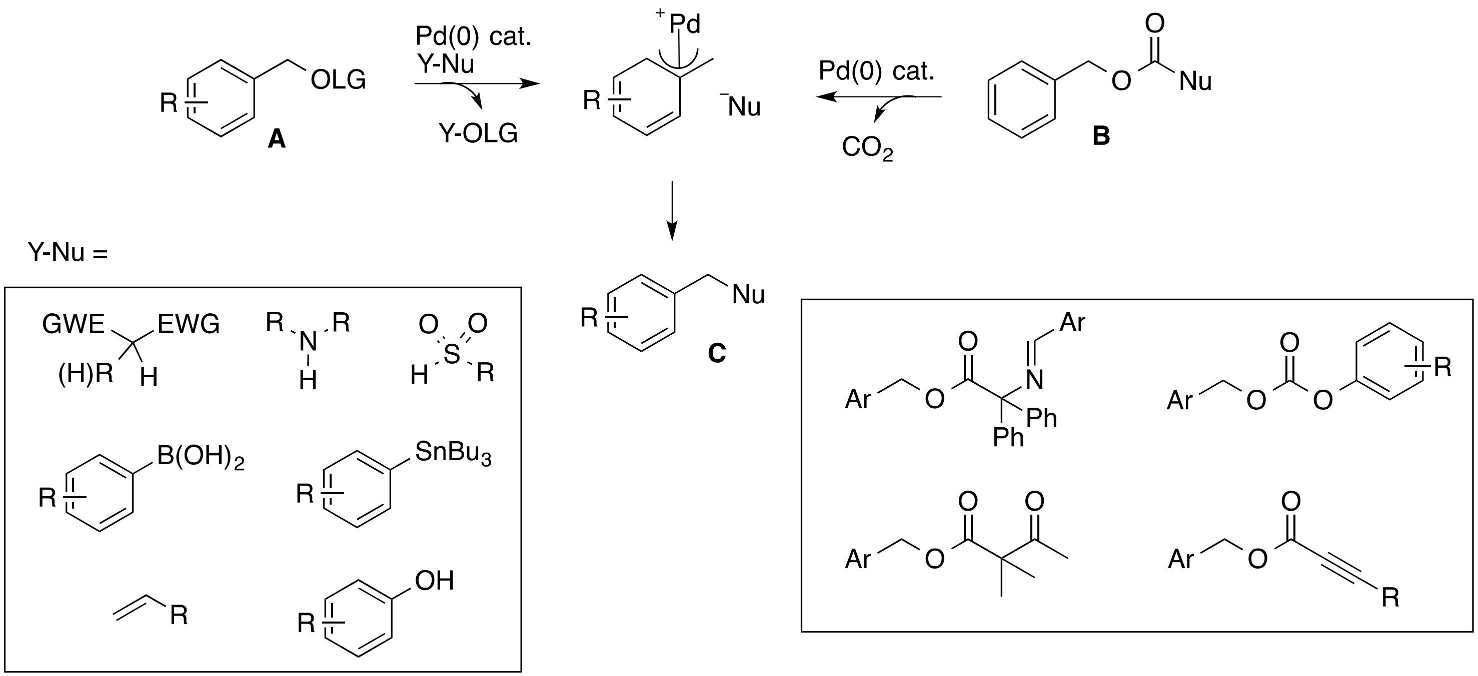


Sim, S. H.; Park, H.-J.; Lee, S. I.; Chung, Y. K.
Org. Lett. **2008**, *10*, 433.

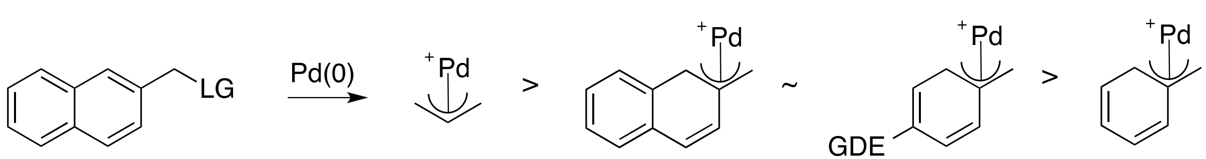
Entry	Product	Temp. (^{o}C)	Time (h)	Yield (%)	*E* : *Z*
1		100	1	38	
		70	3	68	
2		100	4	97	
3		100	1	77	1.2 : 1
4		70	3	62	19 : 1
5		100	0.5	80	
6		100	0.5	87	
7		100	0.25	86	

5. Decarboxylative Benzylation

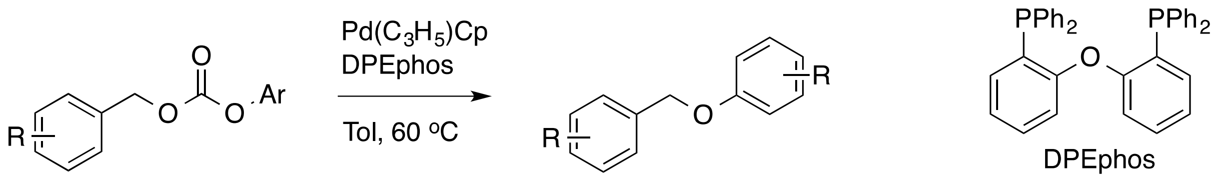
Introduction to Decarboxylative Benzylations

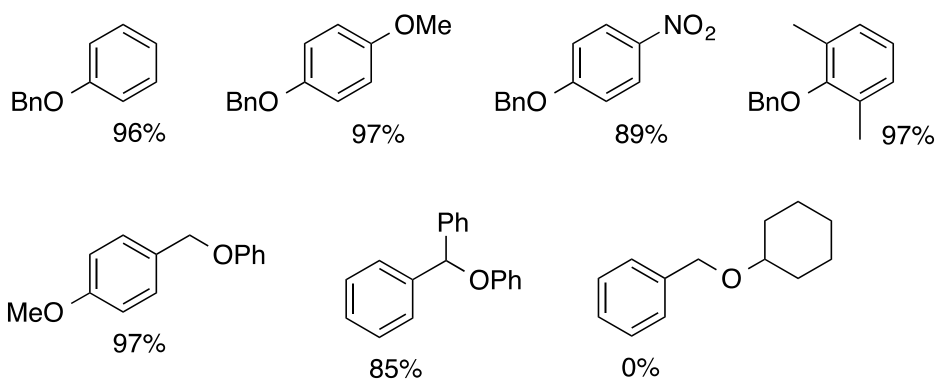


Relative Rates



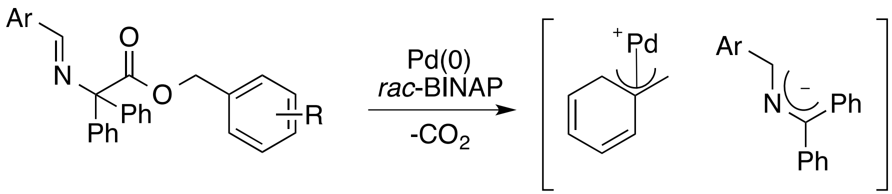
Decarboxylative Benzyl Ether Synthesis

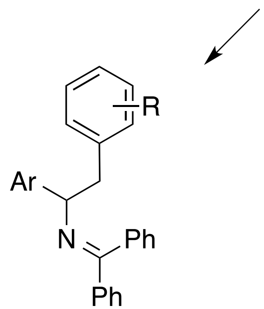




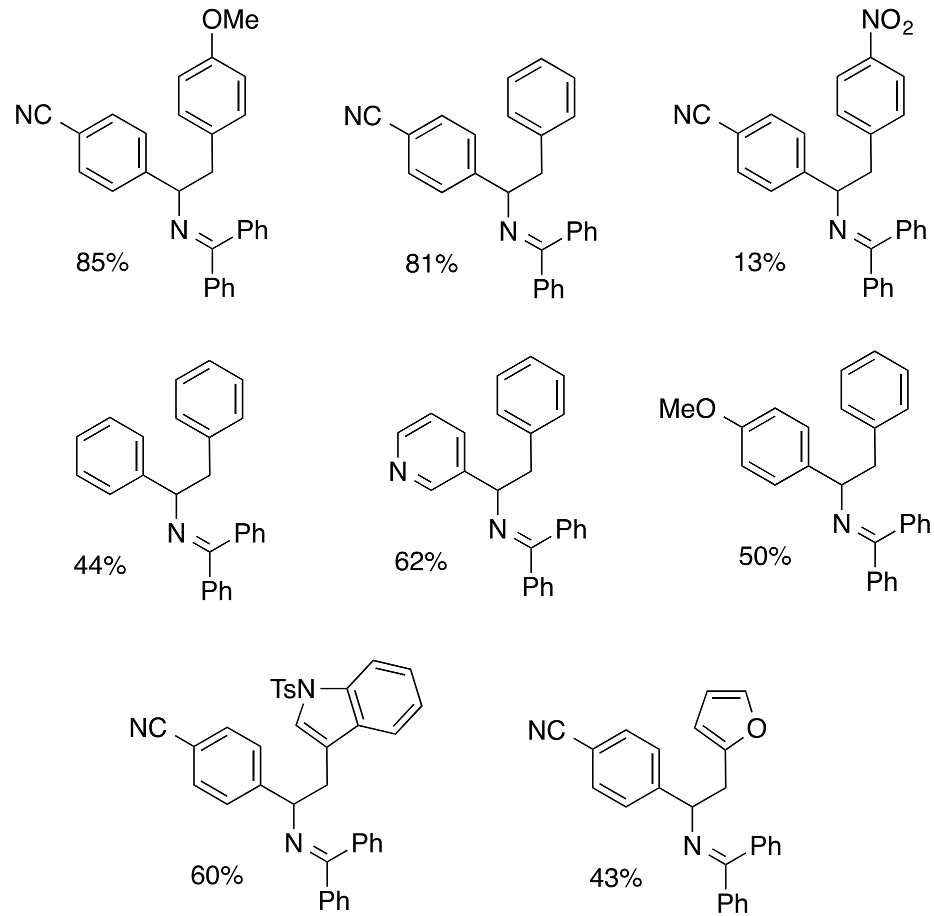
Kuwano, R.; Kusano, H. *Org. Lett.* **2008**, *10*, 1979

Decarboxylative Benzylation of Diphenylglycinate imines



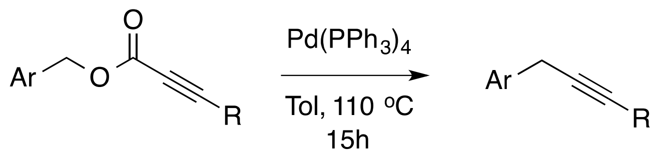


Typical reaction conditions:
3 mol% Pd(OAc)2
20 mol% *rac*-BINAP
DMA, microwave 150ºC/15min

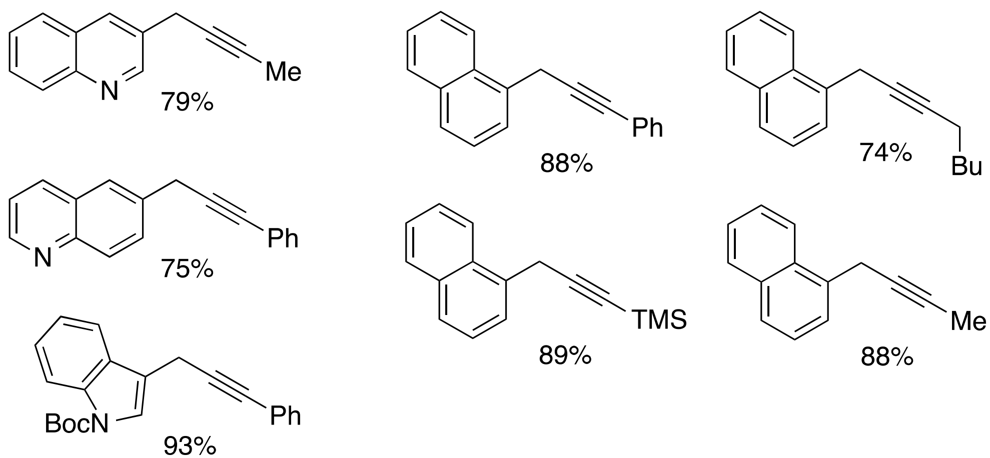


Fields, W. H.; Chruma, J. J. *Org. Lett.* **2010**, *12*, 316.

Decarboxylative Benzylation of Acetylides



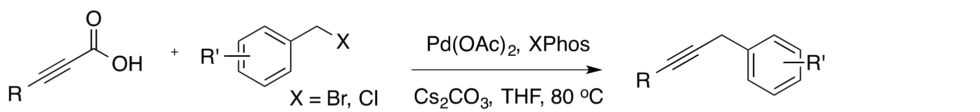
R = Ph, Alkyl, TMS
R = H; no decarboxylative coupling

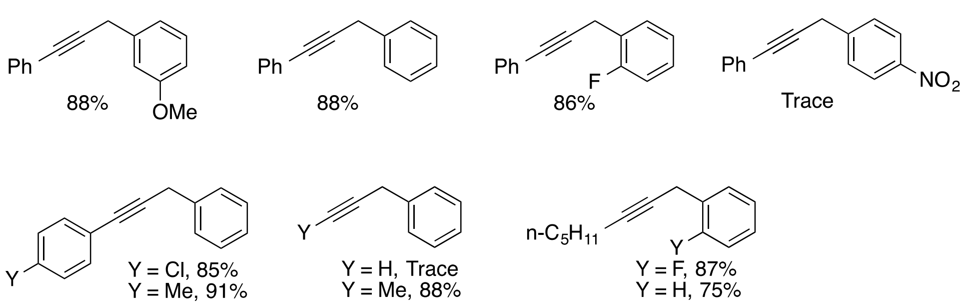


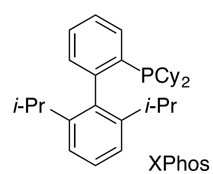
a) Rayabarapu, D. K.; Tunge, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 13510.
b) Pi, S.-F.; Tang, B.-X.; Li, J.-H.; Liu, Y.-L.; Liang, Y. *Org. Lett.* **2009**, *11*, 2309

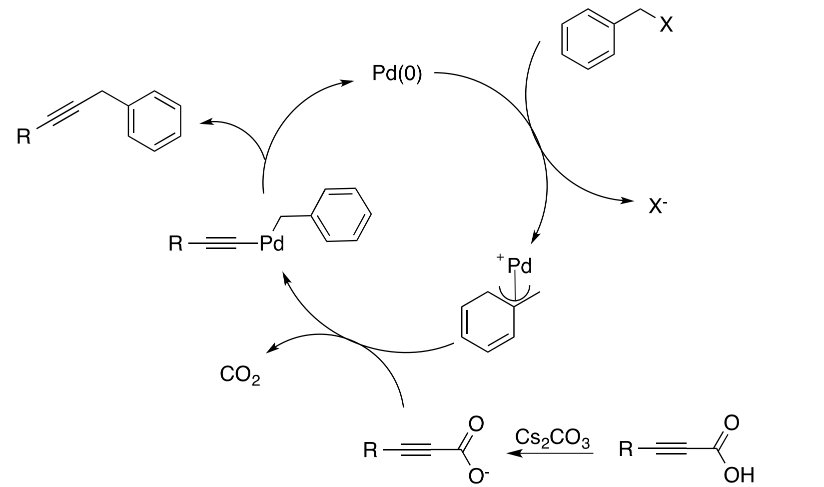
Decarboxylative Benzylation of Acetylides

Intermolecular Decarboxylative Benzylation



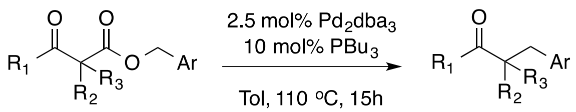


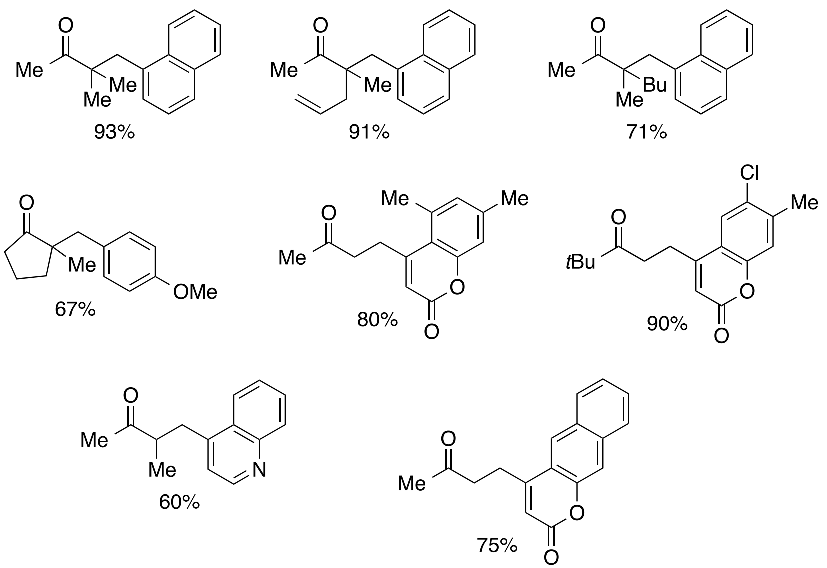




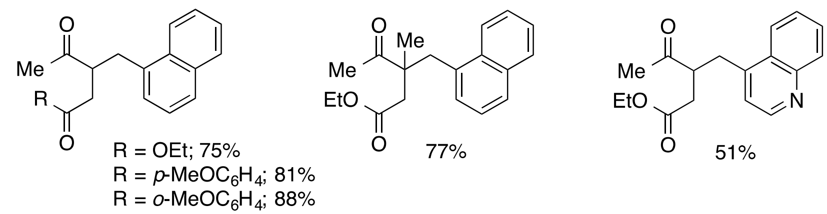
Zhang, W.-W.; Zhang, X.-G.; Li, J.-H. *J. Org. Chem.* **2010**, *75*, 5259.

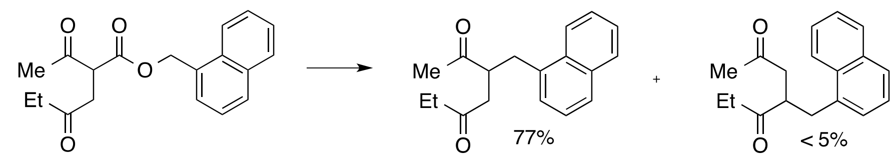
Decarboxylative Benzylation of Enolates





Regiospecific Decarboxylative benzylation





Torregrosa, R. R. P.; Ariyarathna, Y.; Chattopadhyay, K.; Tunge, J. A. *J. Am. Chem. Soc.* **2010**, *132*, 9280.

6. Conclusion

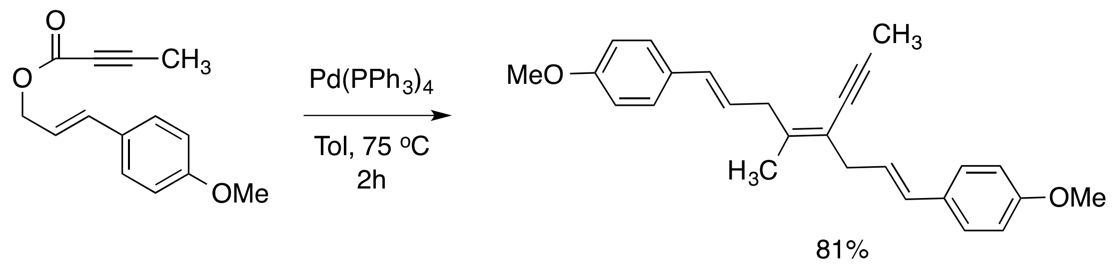
1. Decarboxylative coupling reactions offer a “greener” alternative to standard allylation and benzylation reaction.

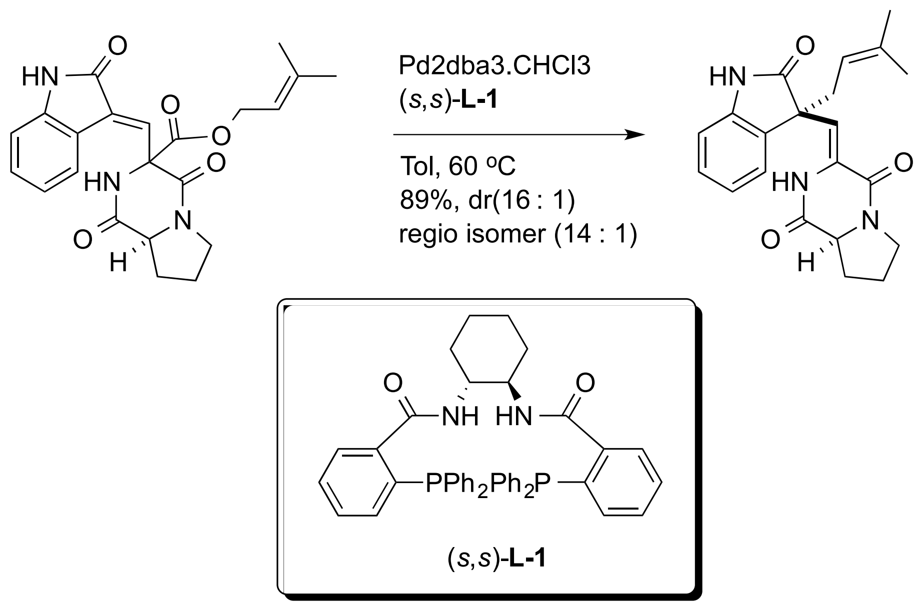
2. Developing interceptive decarboxylations of less activated pronucleophiles would allow the synthsis of many relevant chemical building blocks.

Thank you

Quiz !

Quiz





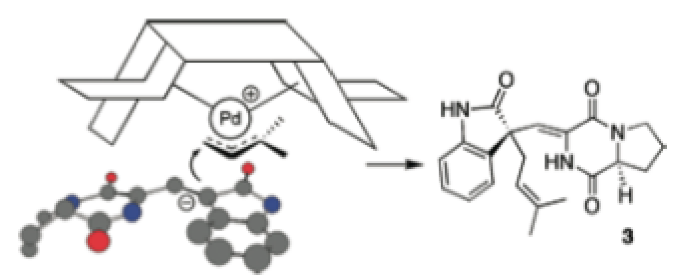
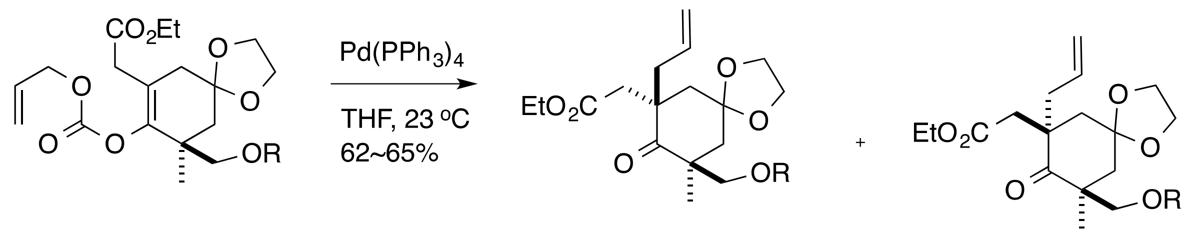


Figure 3. Model for observed selectivity.

Quiz !



a **b**

R = TBS **a** : **b** = 1 : 5.6
R = TBDPS **a** : **b** = 1 : 8.7