β-alkyl-α-allylation of Michael Acceptors through the Palladium-Catalyzed Three-Component Coupling between Allylic Substrate, Trialkylboranes, and Activated Olefins

Yoshinori Yamamoto, et al. *J. Org. Chem*. **2006**, 71(6), 2503-06.

Journal Club Presentation by
Remond Moningka
04/17/2006

Outline

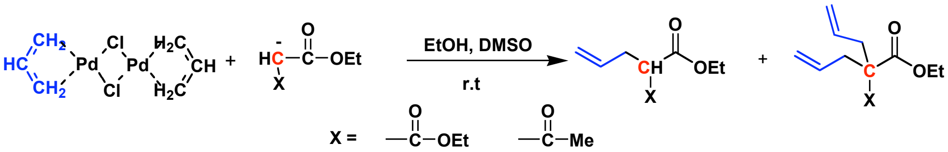
- Background information.
- General Reaction and Mechanism.
- The Scope of π-allylpalladium Chemistry Using Activated Olefins.
- Alkyl-allylation of Activated Olefins through the Palladium-Catalyzed Three-Component Coupling.
- Conclusion.
- Future Direction.
- References.

Background

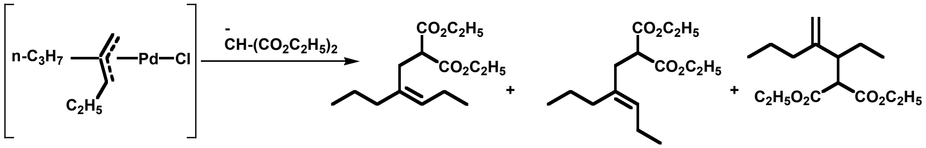
- Discovered by Prof. Jiro Tsuji in 1965. **π-allylpalladium species could be substituted with certain nucleophiles, such as the anion of diethyl malonate and acetoacetate.**
- **Followed by Prof. Barry Trost in 1973. He demonstrated that the allylation prefers the less substituted end of the π-allyl system.**

Professor Barry M. Trost

First Tsuji-type Reaction



Tsuji, J. Takashashi.H. Morikawa, M. *Tetrahedron Lett*. **1965**. *49*. 4387-4388.

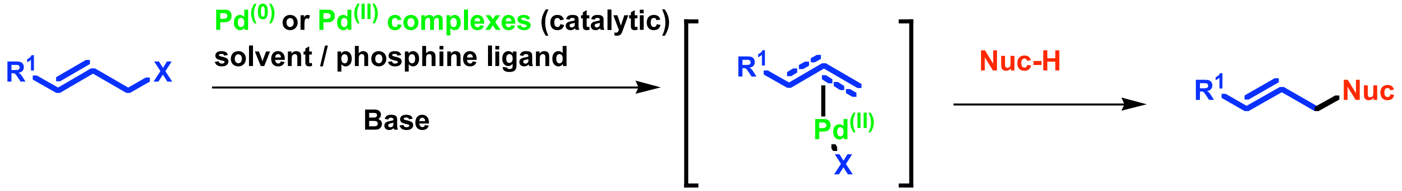


Trost, B.M. Fullerton, T.J. *J. Am. Chem. Soc*. **1973**. 95. 292-294.

Background

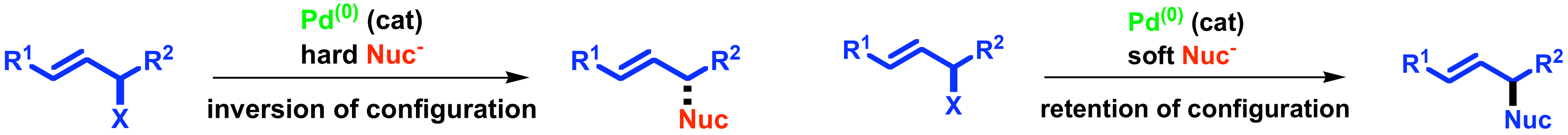
Tsuji-Trost Allylation

- **Pd-catalyzed allylation of carbon nucleophile with allylic compounds via π-allylpalladium complexes.**



X = leaving groups = epoxides, carbonates, halogens

Optically active substrate

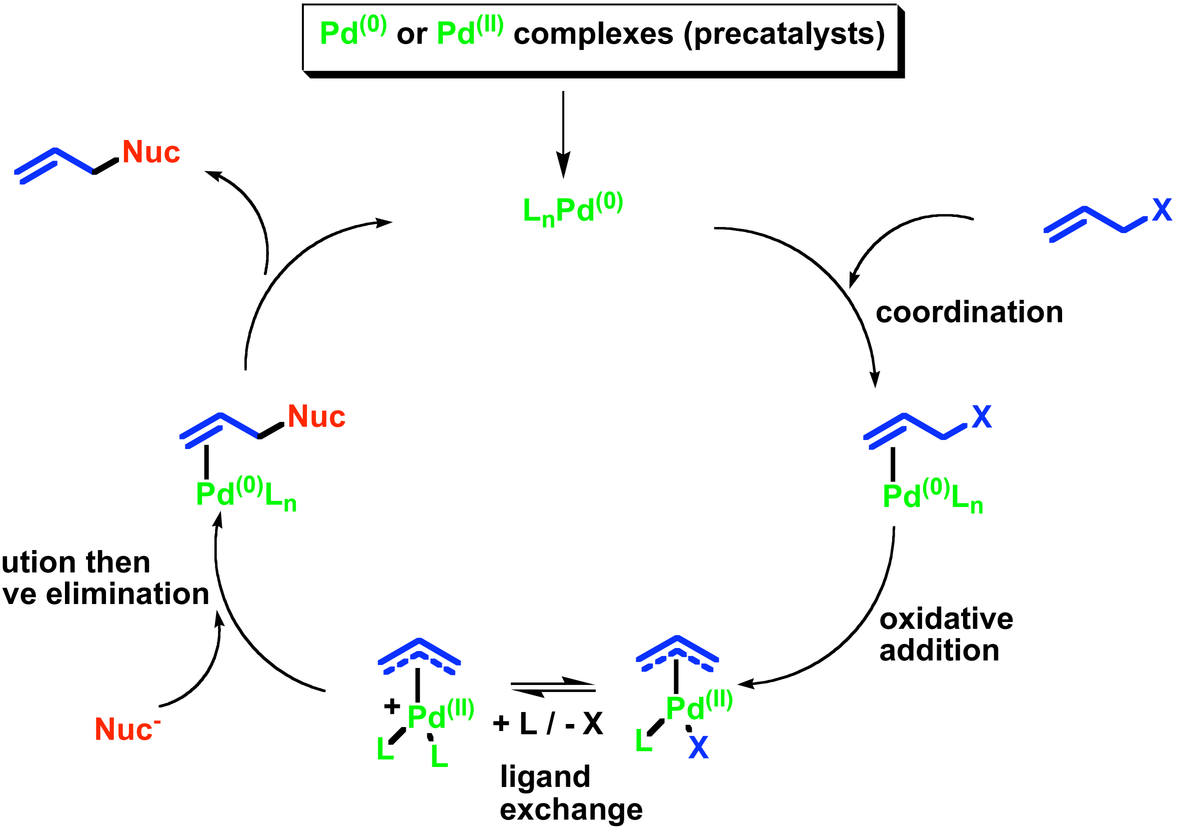


soft Nuc$^-$ = enamines, enolates, CH_2CO_2R, CH_2CN, CH_2SO_2Ph, CH_2SPh.

Laszlo Kurti, Barbara Czako. Strategic Applications of Named Reactions in Organic Synthesis. 2005. Elsevier Inc.

Background

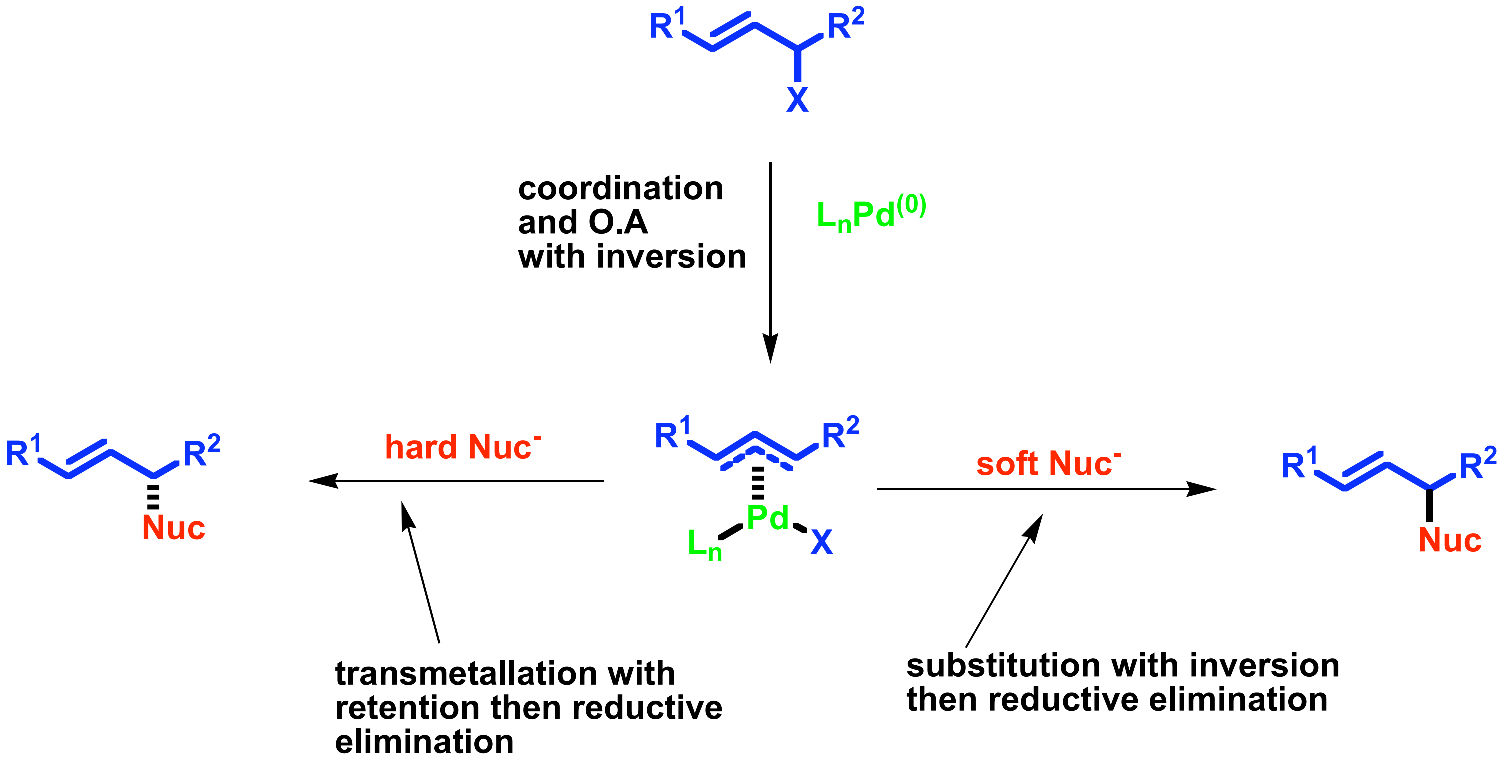
General Tsuji-Trost Mechanism



Laszlo Kurti, Barbara Czako. Strategic Applications of Named Reactions in Organic Synthesis. 2005. Elsevier Inc.

Background

Mechanism with soft and hard Nucleophiles



coordination
and O.A
with inversion

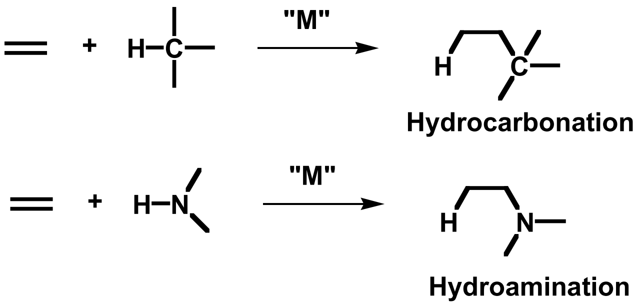
transmetallation with
retention then reductive
elimination

substitution with inversion
then reductive elimination

Laszlo Kurti, Barbara Czako. Strategic Applications of Named Reactions in Organic Synthesis. 2005. Elsevier Inc.

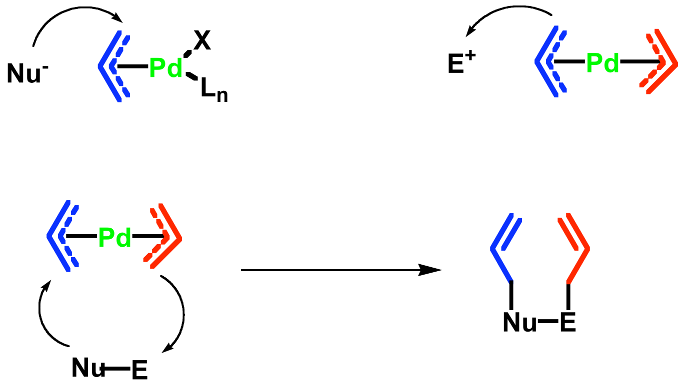
The Scopes of Palladium-catalyzed Activated Olefins

- Early works

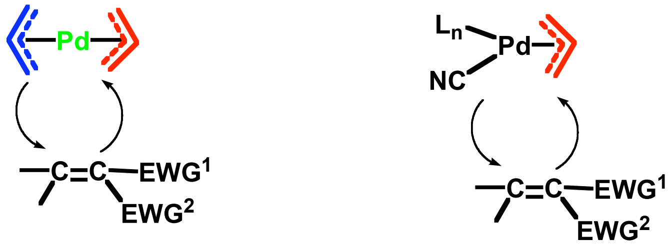


Yamamoto, Y. et. *J. Am. Chem. Soc.* **1998**, *120*, 6838-6839.

- Amphiphilic Catalytic Bis-π-allylpalladium Complex



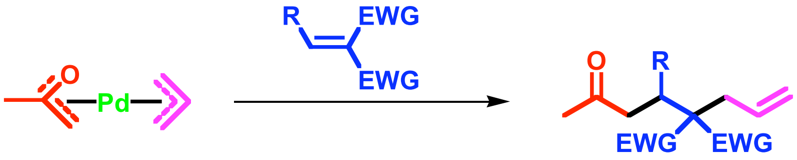
Yamamoto, Y. et. *J. Am. Chem. Soc.* **1997**, *119*, 8113-8114.



Yamamoto, Y. et. *Tetrahedron Letters*. **2000**, *41*, 2911-2914.

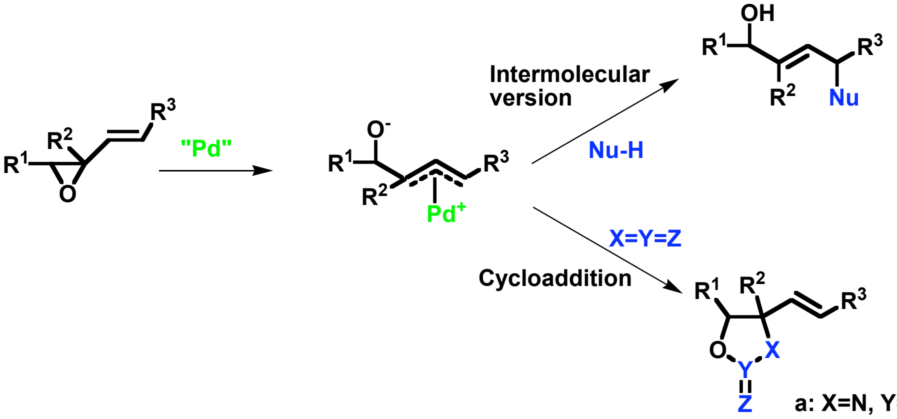
The Scope Continued

- **Oxa-π-allyl-π-allylpalladium**



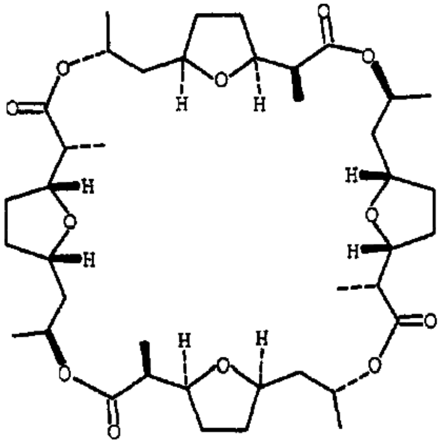
Yamamoto, Y. et. *J. Org. Chem*. **1998**, *63*, 8470-8474.

- **[3+2] Cycloaddition**.



a: X=N, Y=C, Z=O
b: X=O, Y=C, Z=O
c: X=NR, Y=C, Z=NR^1

Yamamoto, Y. et. *J. Org. Chem*. **1998**, *63*, 3067-3071.

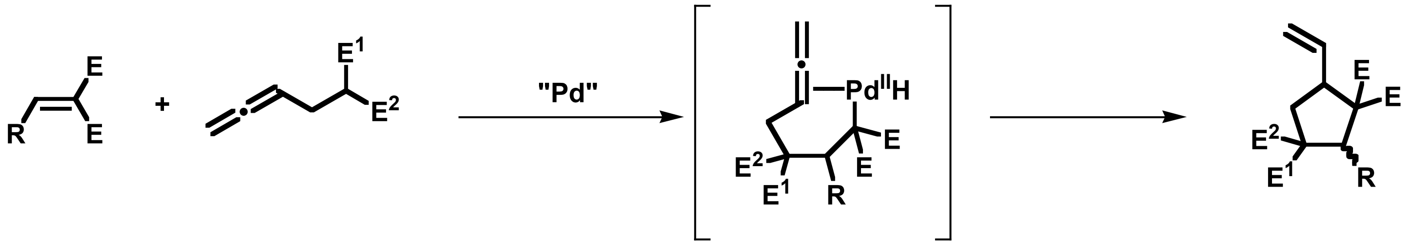


nonactin, 1

Paul A. Bartlett, James D. Meadows, Eckhard Ottow
J. Am. Chem. Soc. **1984**. *106*(18); 5304-5311.

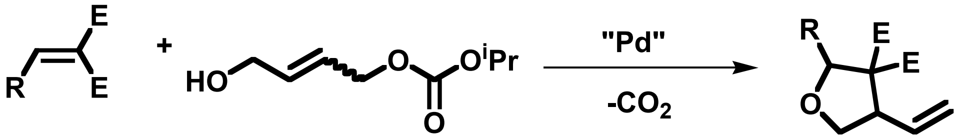
The Scope Continued

- Construction of Cyclopentene rings via [3+2] Cycloaddition.



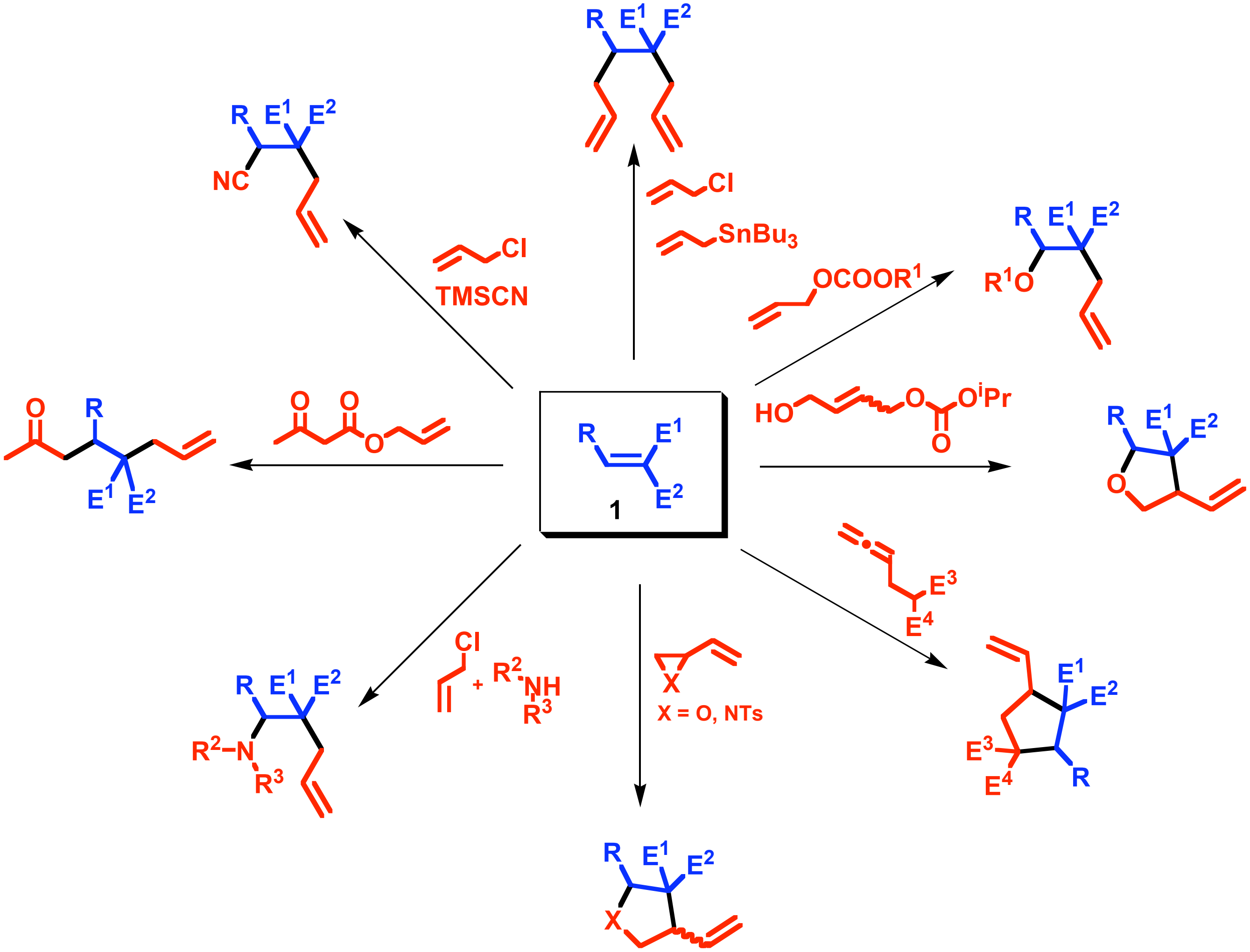
Yamamoto, Y. et. *J. Org. Chem*. **1999**, *64*, 694-695.

- Formation of Cyclic Ethers

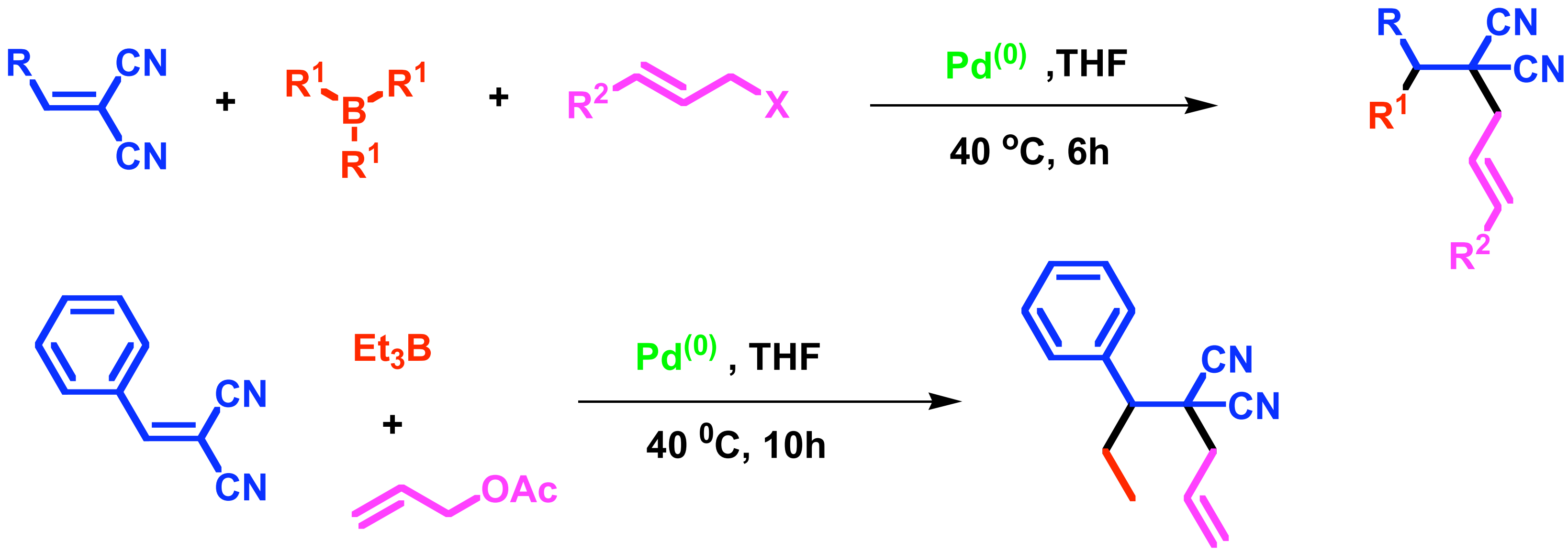


Yamamoto, Y. et. *J. Org. Chem*. **2001,** *66*, 7142-7147.

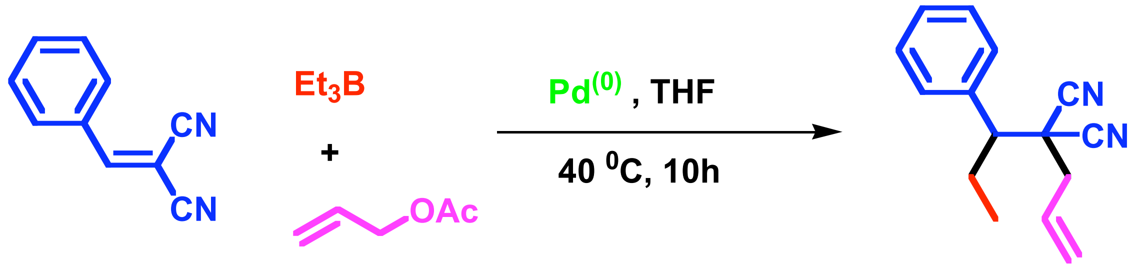
Palladium-Catalyzed Reactions of Highly Activated Olefins



The palladium-catalyzed three component β-alkyl-α-allylation

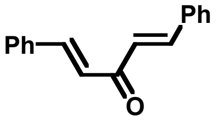


Ligand Screen for the Alkyl-allylation Reaction



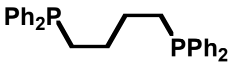
entry	Pd catalyst (5%)	phosphine	NMR yield[b] (%)
1	$Pd(PPh_3)_4$		87 (81)[c]
2	$Pd_2dba_3 \cdot CHCl_3$		0[d]
3	$Pd_2dba_3 \cdot CHCl_3$	PPh_3 (40 mol%)	81
4	$Pd_2dba_3 \cdot CHCl_3$	dppb (20 mol%)	71
5	$Pd_2dba_3 \cdot CHCl_3$	dppf (20 mol%)	82
6	$Pd_2dba_3 \cdot CHCl_3$	dppp (20 mol%)	60
7	$Pd_2dba_3 \cdot CHCl_3$	dppm (20 mol%)	78
8	$Pd_2dba_3 \cdot CHCl_3$	dppe (20 mol%)	10[d]

dba = dibenzylideneacetone

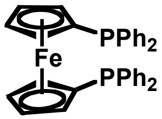


dppm = bis(diphenylphosphino)methane

dppb = 1,4-bis(diphenylphosphino)butane



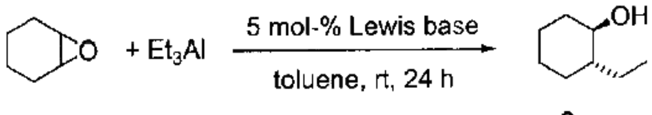
dppf = 1,1'-bis(diphenylphosphino) ferrocene



dppp = 1,3-bis(diphenylphosphino)propane

The role of Phosphine Ligands?

- **Trialkylborane is usually not an alkylating agent unless if it coordinates to a Lewis base prior to the reaction.**
- **Coordination of borane species to a Lewis base (PPh_3) should result in the formation more reactive tetracoordinate boron “ate” complex I.**
- **Proven by ^{31}P NMR spectroscopy, and is proposed to form a more nucleophilic alkylating agent.**
- **The formation of an aluminum “ate” complex II from trialkylaluminum is known.**

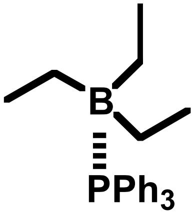


1

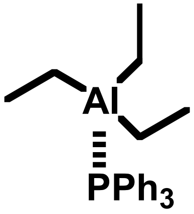
2

Entry	Lewis base	Yield (%)[a]
1	–	0
2	NEt_3	0
3	Et_2O	0
4	PBu_3	89
5	PPh_3	99
6	$P(NMe_2)_3$	97
7	$AsPh_3$	100
8	$SbPh_3$	89
9	Me_2S	100

[a] Determined by GC.



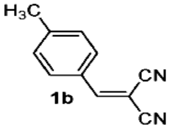
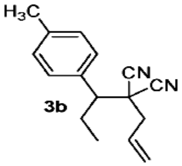
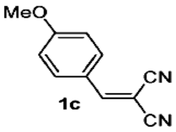
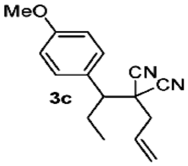
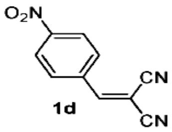
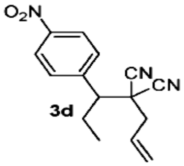
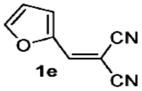
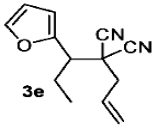
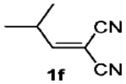
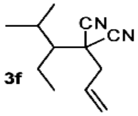
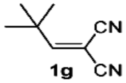
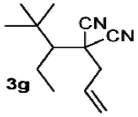
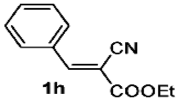
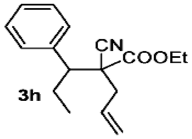
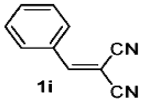
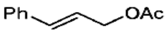
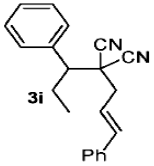
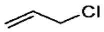
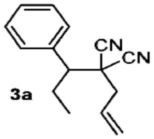
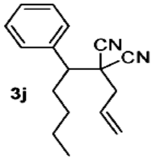
I



II

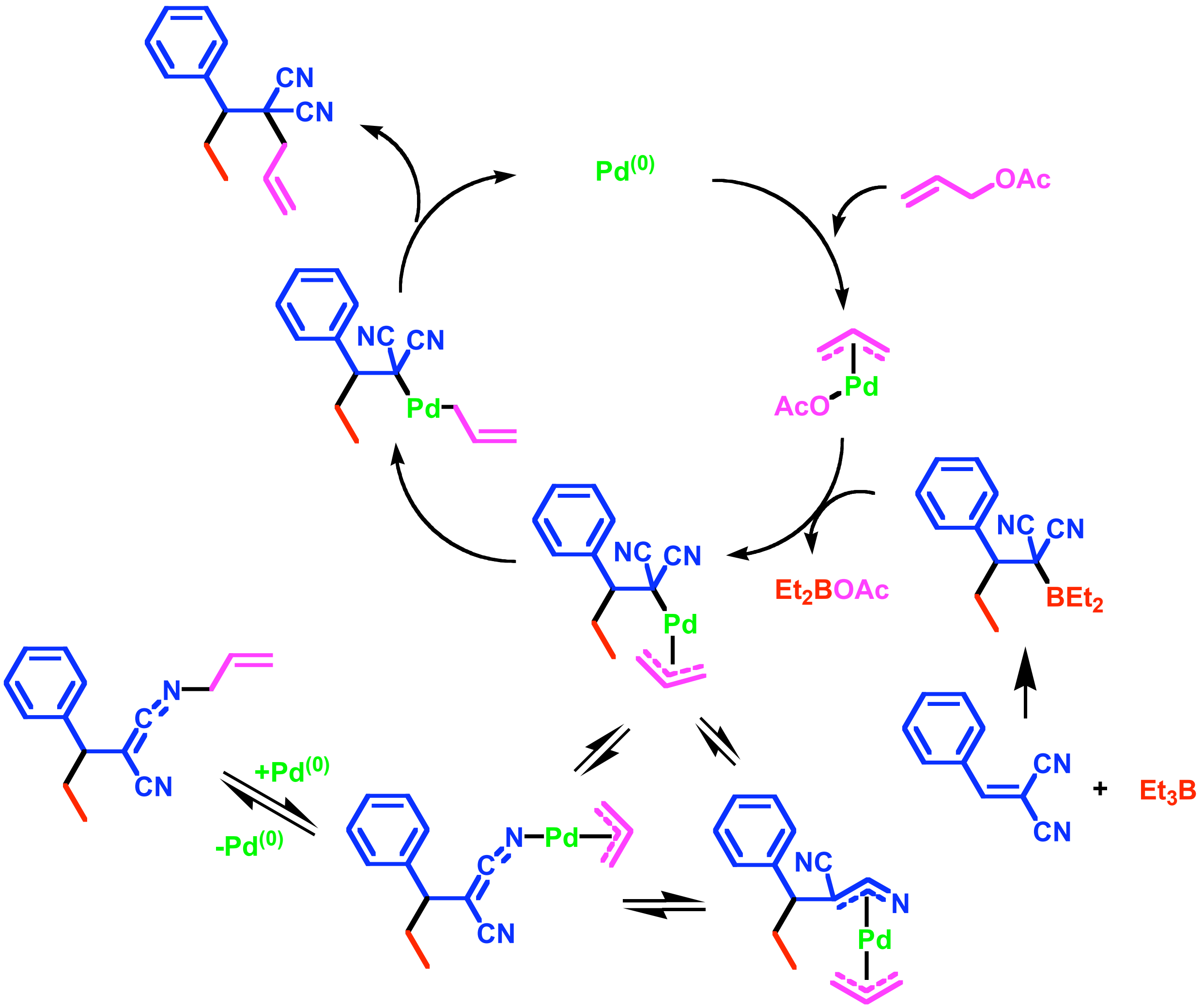
Schneider, C. Brauner, *J. Eur. J. Org. Chem*. **2001**, 4445-4450.

Alkyl-allylation of Various Activated Olefins

entry	olefins (**1**)	allylic substrate (**2**)	product (**3**)	yield (%)^b
1	 **1b**	 **2a**	 **3b**	78
2	 **1c**	**2a**	 **3c**	79
3	 **1d**	**2a**	 **3d**	61
4	 **1e**	**2a**	 **3e**	68
5	 **1f**	**2a**	 **3f**	70
6	 **1g**	**2a**	 **3g**	66
7	 **1h**	**2a**	 **3h**	81^c
8	 **1i**	 **2b**	 **3i**	82
9	**1a**	 **2c**	 **3a**	80
10^d	**1a**	**2a**	 **3j**	62

[a] The reactions of **1** (0.3285 mmol) with Et_3B (1.2 equiv) and allylic substrates **2** (1.2 equiv) in the presence of $Pd(PPh_3)_4$ (5 mol %) were carried out at 40 °C in THF for 6 h. [b] Isolated yields. [c] A mixture of diastereomers in a ratio of 6:4 was obtained. [d] Bu_3B was used, instead of Et_3B.

Mechanism



CN
CN
Pd$^{(0)}$
OAc
AcO
Pd
NC
CN
Pd
NC
CN
Pd
Et$_2$BOAc
NC
CN
BEt$_2$
C
N
CN
+Pd$^{(0)}$
-Pd$^{(0)}$
C
N
Pd
CN
NC
N
Pd
CN
CN
+
Et$_3$B

Conclusion

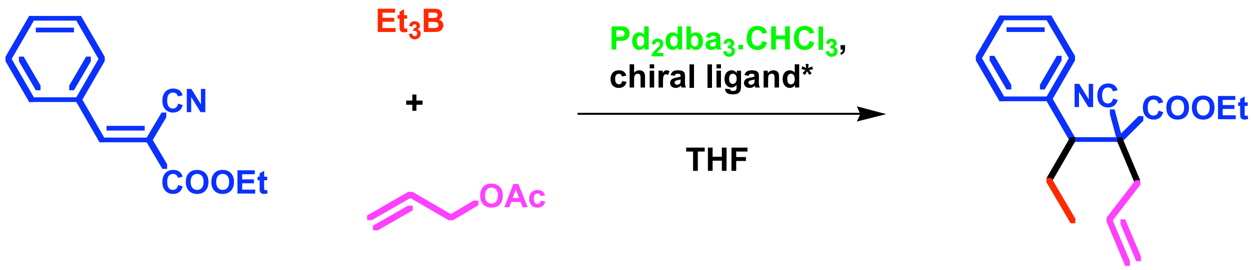
- A new procedure for the alkyl-allylation of activated olefins via the three-component coupling reaction has been established.

- The reaction generally proceeds under milder conditions (40^0 C) and with a high atom economy (catalytic amount of Palladium).

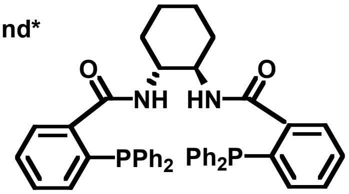
- $Pd(PPh_3)_4$ is required for the reaction to proceed presumably that phosphine ligands are necessary to activate the boron species.

Future Work

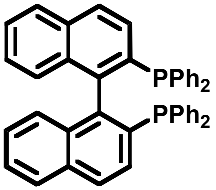
- **Catalytic Asymmetric Synthesis. Instead of using achiral phosphine ligands, various chiral phosphine ligands can be examined.**



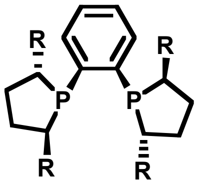
chiral ligand*



Trost ligand



BINAP



DuPHOS

References

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Thank you