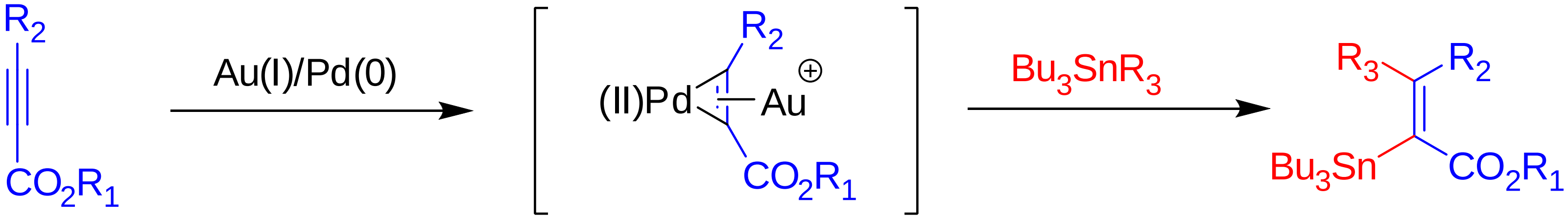
Alkynes as Stille Reaction Pseudohalides: Gold- and Palladium-Cocatalyzed Synthesis of Tri- and Tetra-Substituted Olefins

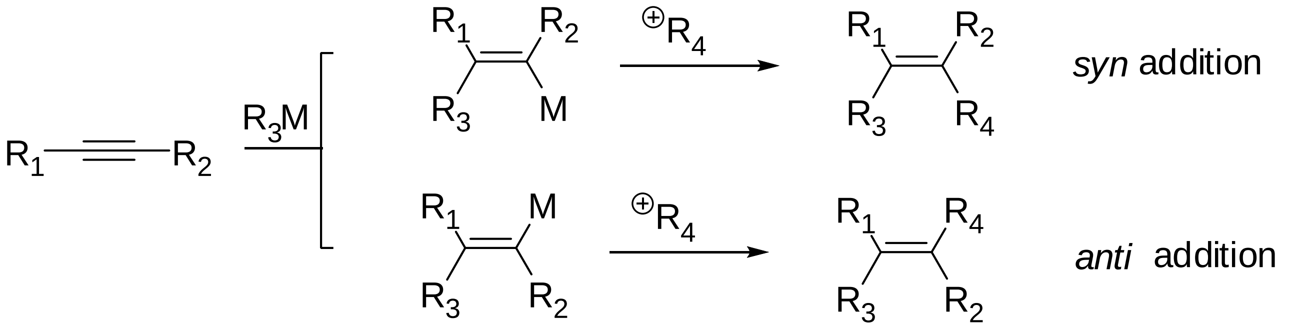


Yili Shi, Sonja M. Peterson, Walter W. Haberaecker III, and
Suzanne A. Blum

J. Am. Chem. Soc., ***130*** *(7), 2168 -2169, 2008*

Current Literature
Chenbo Wang @ Wipf Group
2/16/2008

Carbometallation of Alkynes
-General Concepts

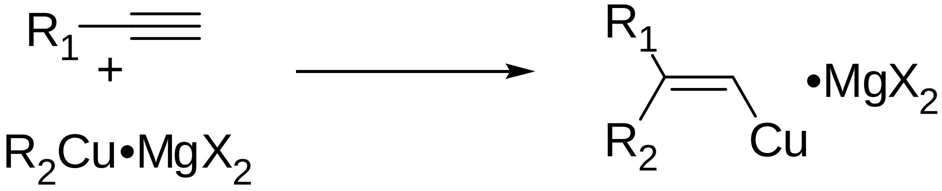


- A powerful way to make stereospecifically substituted alkenes.
- M can be Cu, Al, Zr, Ti, Zn, B, Mg, Li or a combination of two.
- *Syn* or *anti* selectivity depends on the nature of substrate, reagent and reaction conditions.
- Regioselectivity depends on the polarity of the triple bond, steric factor and complexation by the functional groups of the alkyne.
- Polyaddtitions: the product may add to the starting alkyne, resulting polymerization.

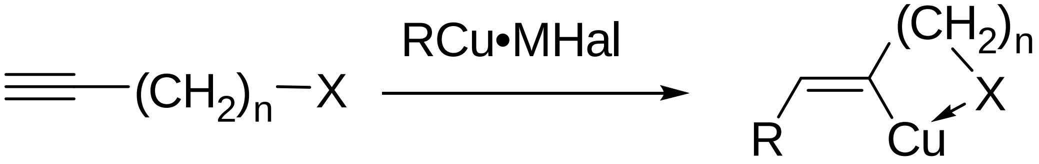
For a review, see: Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841.

Carbometallation of Alkynes
-Organocopper Reagents

- Unfunctionalized Terminal alkynes: Markownikov rule



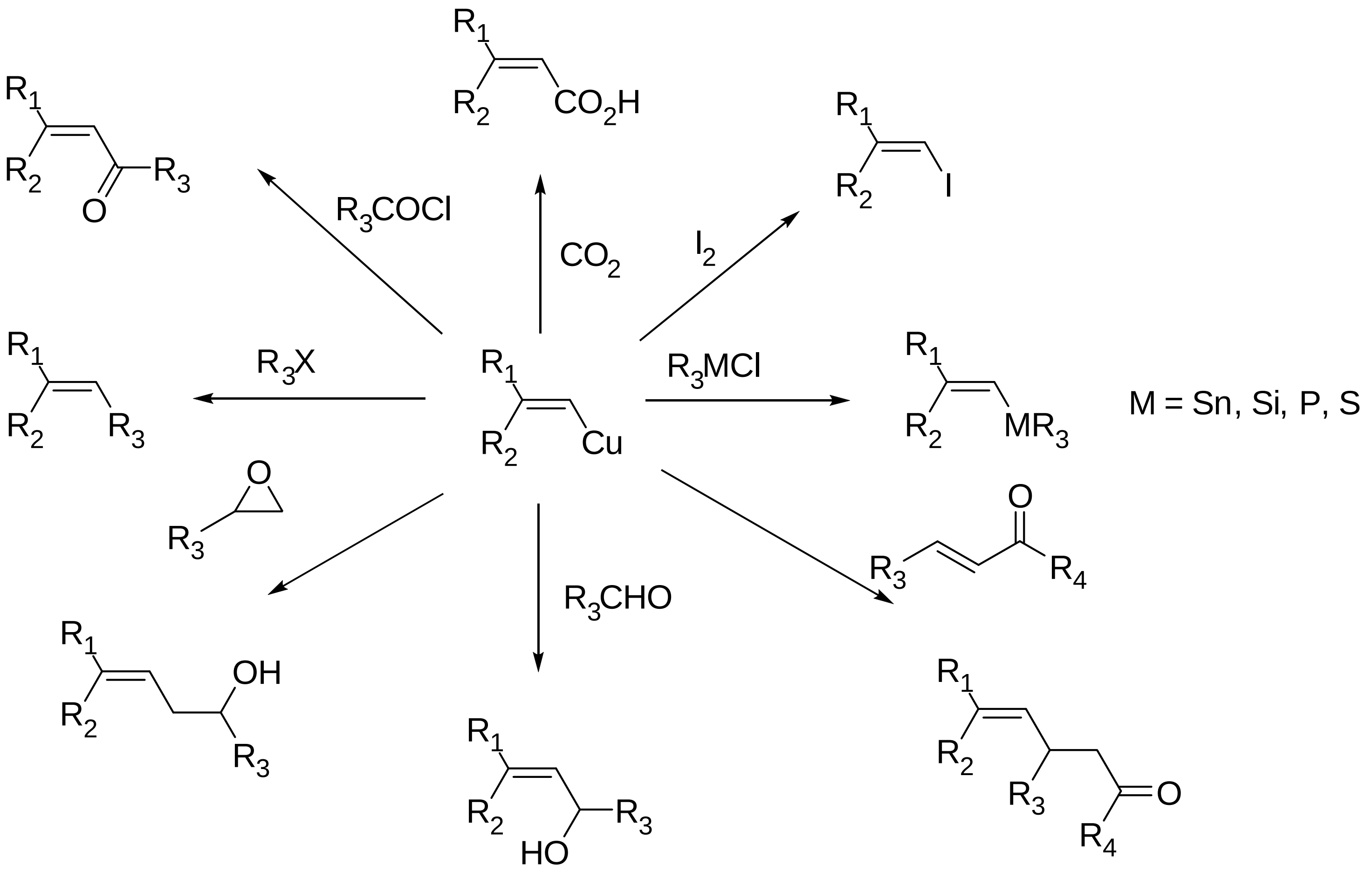
- Functionalized alkynes: directed carbometallation



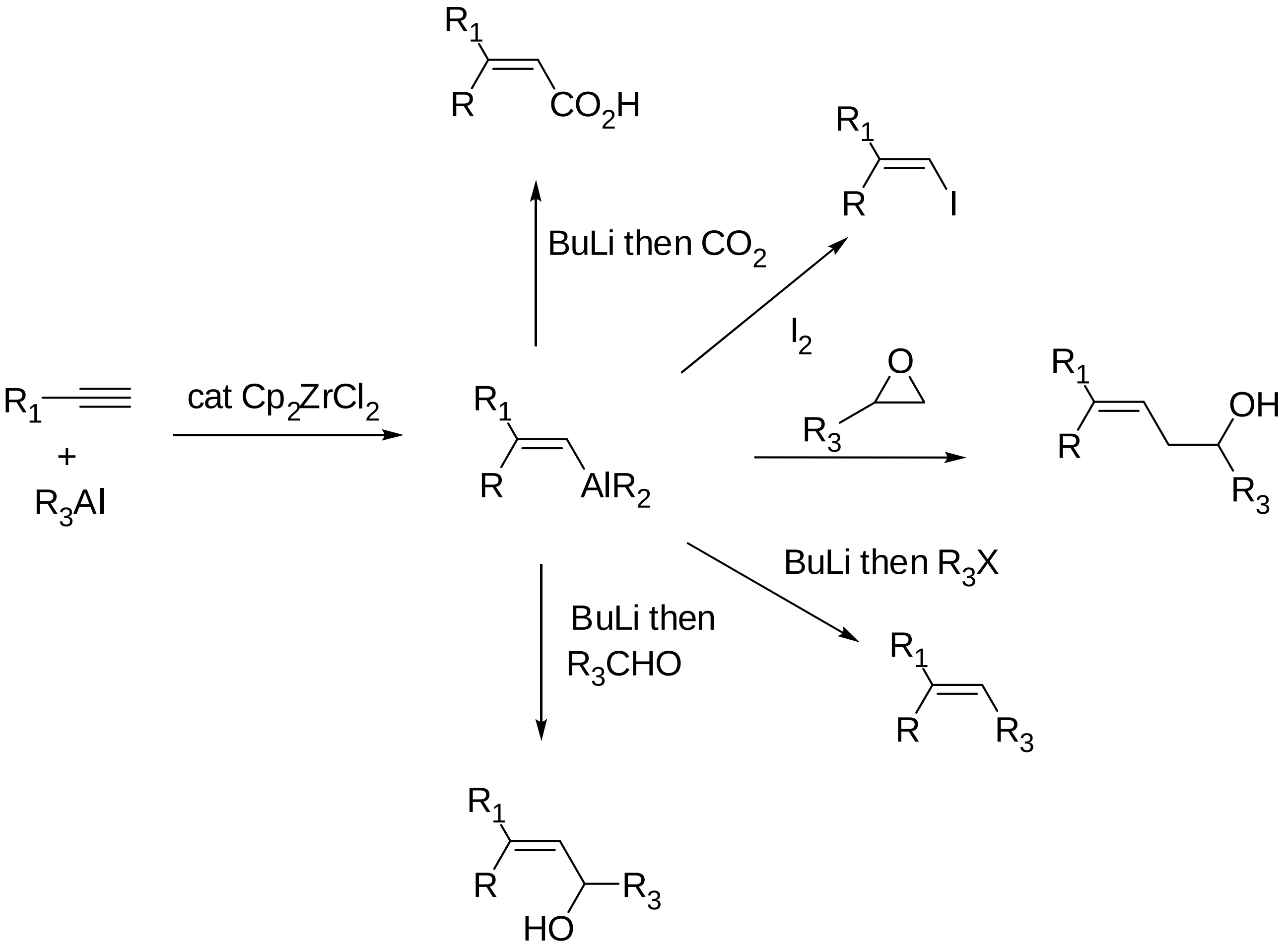
n = 0, 1, 2, 3

X = halogen, SR, OR, O^-, NR_2, OAc

Synthetic Use of Alkenylcopper(I) Derivatives



Carbometallation of Alkynes
-Organoaluminum Reagents

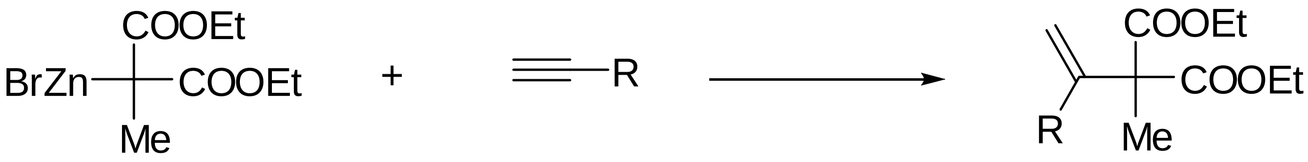


- Complementary to the organocopper reagents

Negishi, E. et al. *Chem. Soc. Rev.* **1996**, *96*, 417

Carbometallation of Alkynes
-Other Metal Reagents

- Organozinc reagents: propagylic, allylic and malonic type organozinc reagents are tolerated



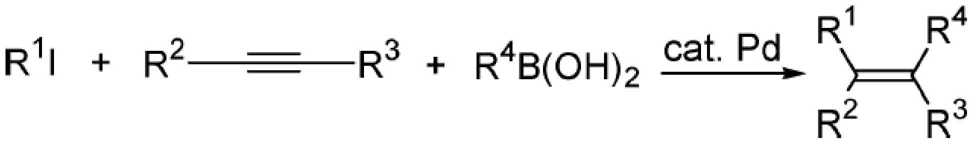
- Organolithium reagents: mostly intramolecular examples

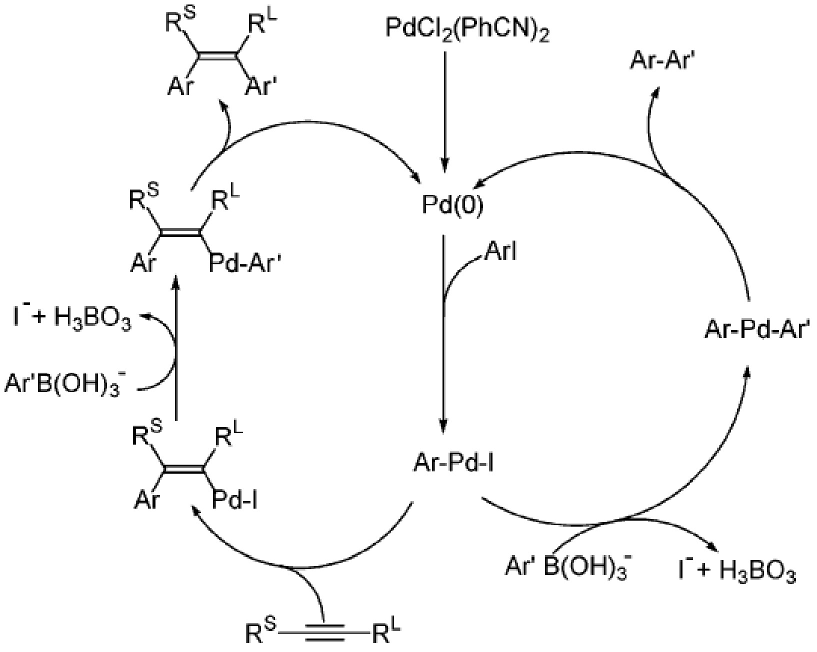
- Organomagnesium reagents: Often used with catalytic Cu salt

- Organoboron reagents: require exceptionally reactive substrates

Bertrand, M. T. et al. *Tetrahedron Lett*. **1974**, 1945

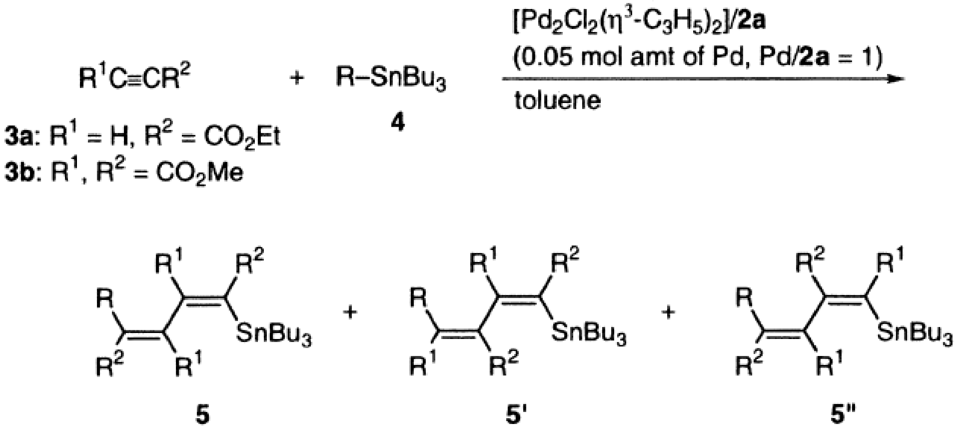
Previous Work on the Carbometallation of Alkynes Catalyzed by Palladium



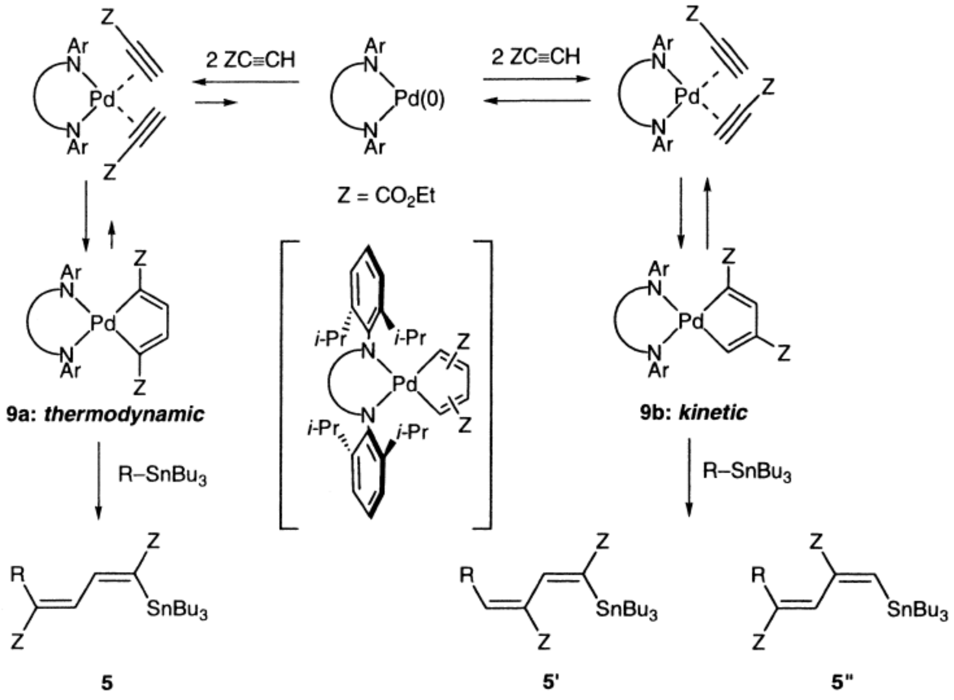


Zhou, C.; Larock, R. C. *J. Org. Chem*. **2005**, *70*, 3765

Previous Work on the Carbostannylation of Alkynes Catalyzed by Palladium

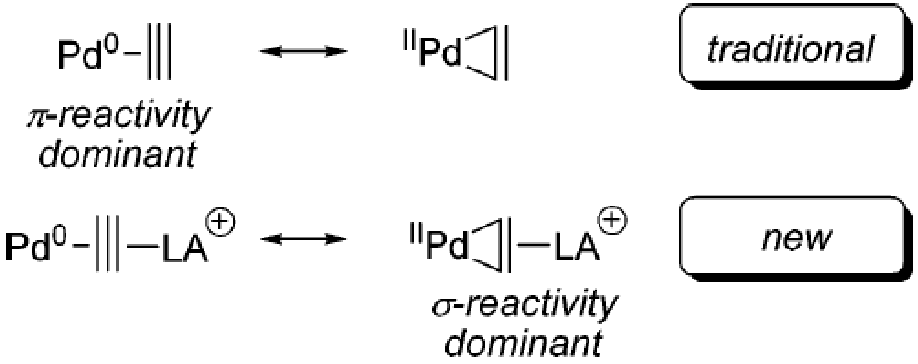


- Dimerization predominates.



Hiyama, T. et al *Bull. Chem. Soc. Jpn*. **2001,** *74*, 637—647

Title Paper: Carbostannylation Catalyzed by Palladium and Gold



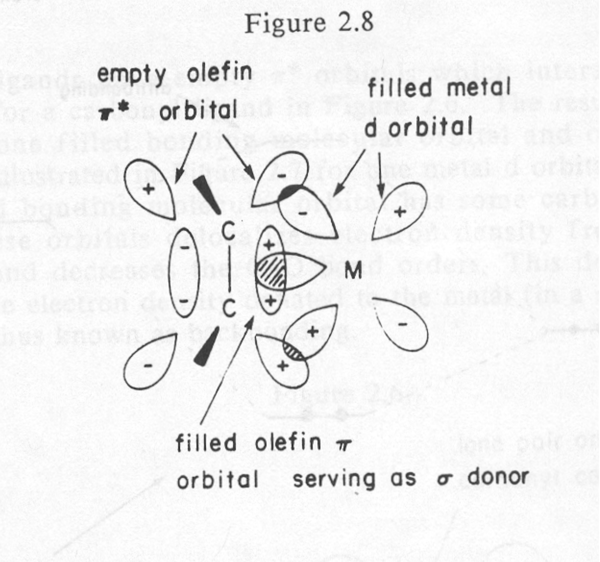
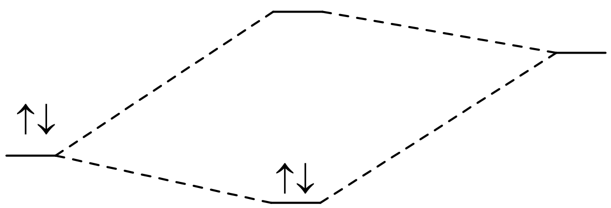


Figure 2.8

Without Au(I)



Filled metal
d orbital

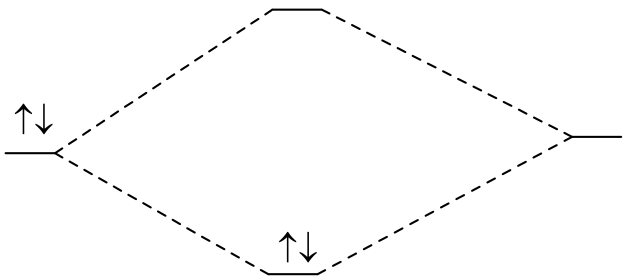
molecular orbitals
of Pd-backbonding
to alkyne

alkyne π*
orbital

↑↓

↑↓

With Au(I)



Filled metal
d orbital

molecular orbitals
of Pd-backbonding
to alkyne

alkyne π*
orbital

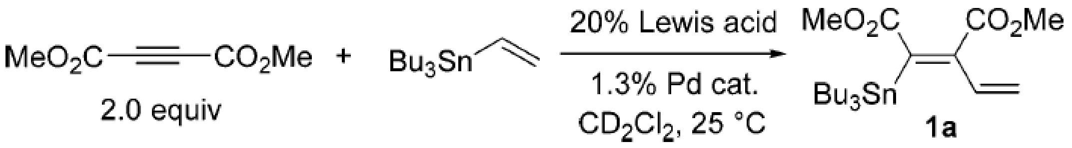
↑↓

↑↓

Collman, J. P. et al Principles and Applications of Organotransition Metal Chemistry; University Science Books: Sausalito, CA, 1987; pp 155, 645-647

Optimization of Reaction Conditions

Table 1. Effect of Catalyst Composition on Product ^{1}H NMR Yield



1a

entry	Lewis acid	Pd cat.	^{1}H NMR yield (%)
1	PPh_3AuCl	$Pd_2(dba)_3$	24
2	$PPh_3AuCl/AgSbF_6$ (1:1)	$Pd_2(dba)_3$	51
3	$PPh_3AuCl/AgSbF_6$ (1:2)	$Pd_2(dba)_3$	33
4	$PPh_3AuSbF_6{\cdot}CH_3CN$	$Pd_2(dba)_3$	62
5	PPh_3AuPF_6	$Pd_2(dba)_3$	73
6	PPh_3AuPF_6	none	0
7	none	$Pd_2(dba)_3$	0
8	$BF_3{\cdot}(OMe_2)$	$Pd_2(dba)_3$	25
9	$AgSbF_6$	$Pd_2(dba)_3$	0
10	$PhCO_2H$	$Pd_2(dba)_3$	0
11	$PPh_3AuCl/AgSbF_6$ (1:1)	$Pd(Pt\text{-}Bu_3)_2$	39
12	$PPh_3AuCl/AgSbF_6$ (1:1)	$(PPh_3)_2PdCl_2$	trace

- Only Au(I) can effect the reaction, other Lewis acids failed.
- Weakly coordinating anions are preferred.
- Ag cation reduces the reaction yield.

Scope of the Reaction

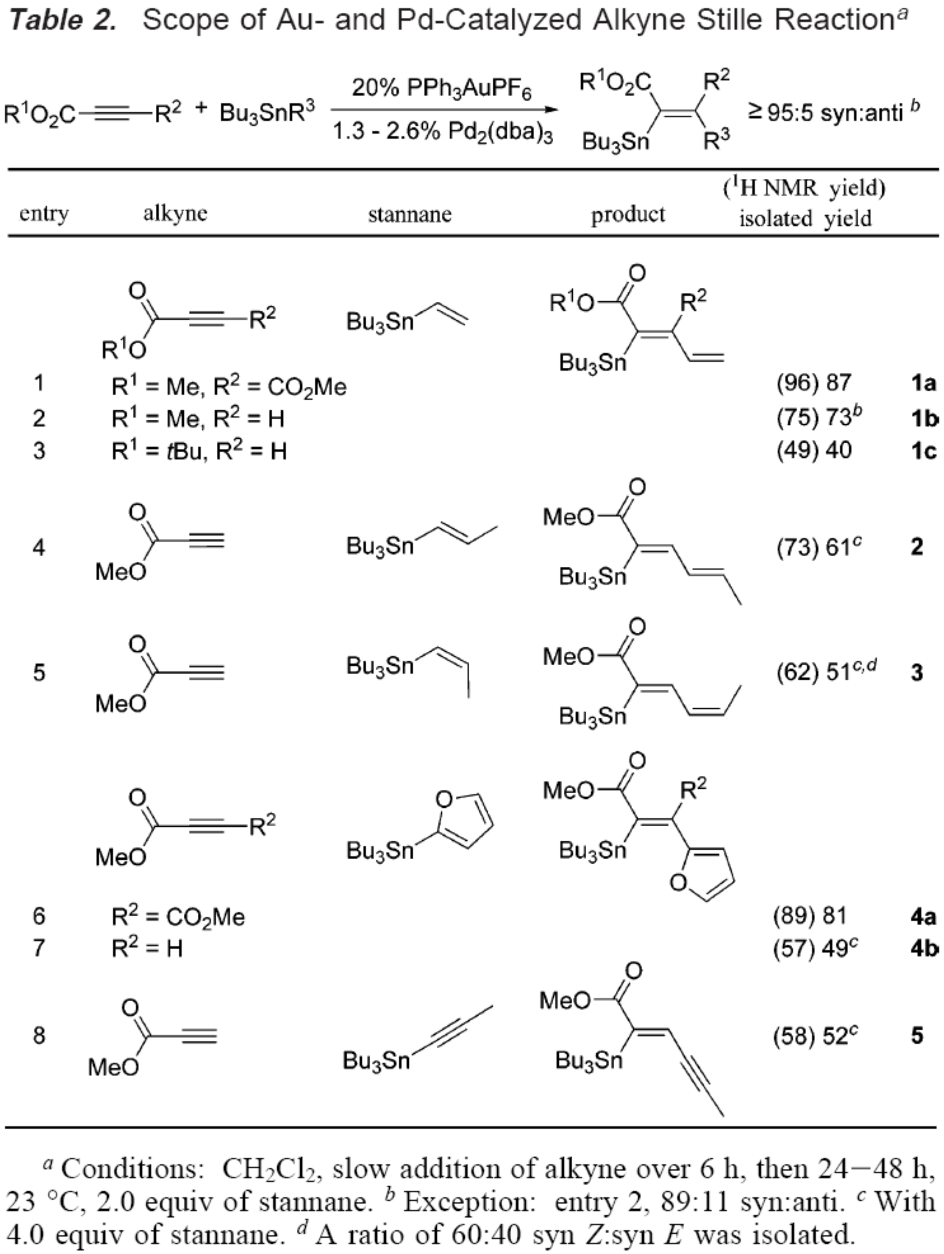


Table 2. Scope of Au- and Pd-Catalyzed Alkyne Stille Reaction[a]

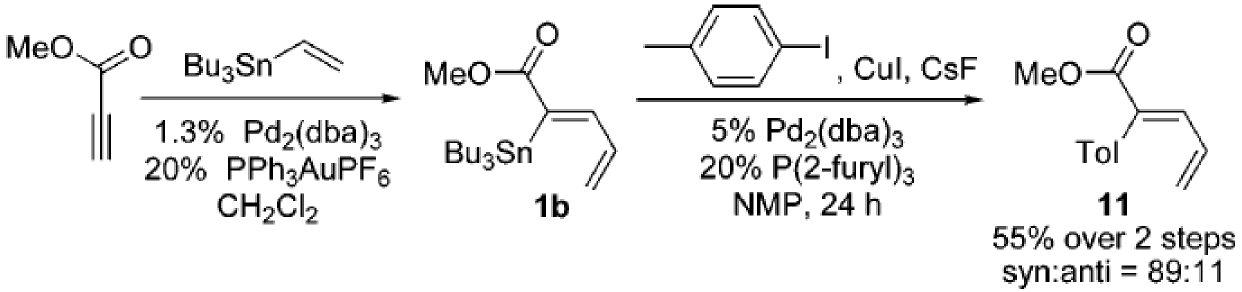
$R^1O_2C-\equiv-R^2 + Bu_3SnR^3 \xrightarrow[1.3-2.6\%\ Pd_2(dba)_3]{20\%\ PPh_3AuPF_6}$ ≥ 95:5 syn:anti [b]

entry	alkyne	stannane	product	(^1H NMR yield) isolated yield	
1	R^1 = Me, R^2 = CO_2Me			(96) 87	**1a**
2	R^1 = Me, R^2 = H			(75) 73[b]	**1b**
3	R^1 = *t*Bu, R^2 = H			(49) 40	**1c**
4				(73) 61[c]	**2**
5				(62) 51[c,d]	**3**
6	R^2 = CO_2Me			(89) 81	**4a**
7	R^2 = H			(57) 49[c]	**4b**
8				(58) 52[c]	**5**

[a] Conditions: CH_2Cl_2, slow addition of alkyne over 6 h, then 24−48 h, 23 °C, 2.0 equiv of stannane. [b] Exception: entry 2, 89:11 syn:anti. [c] With 4.0 equiv of stannane. [d] A ratio of 60:40 syn *Z*:syn *E* was isolated.

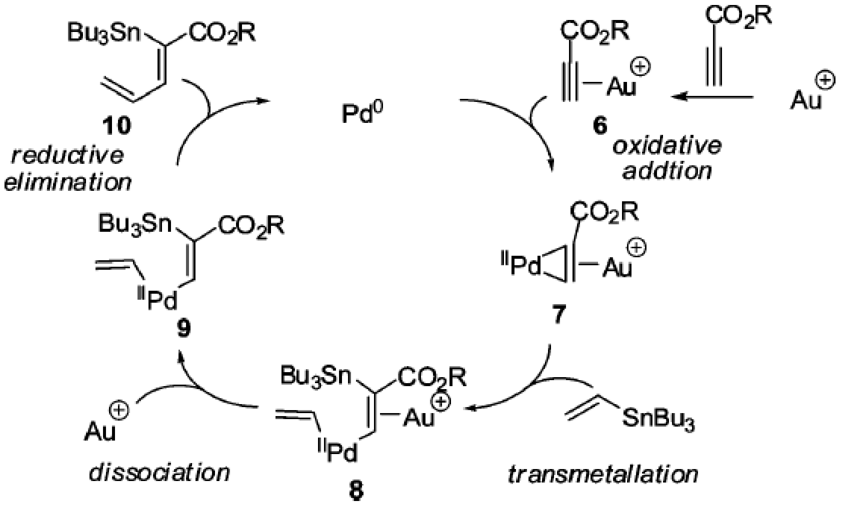
- Alkynes were added slowly to the reaction mixture to prevent polymerization.
- Reactions proceeded with high *syn*-addition selectivity.
- Complete regioselectivity is maintained even with *t*-Bu ester.
- Vinylstannanes reacted with retention of configuration (except Entry 5).

Further Transformation of the Product



Proposed Mechanism

Scheme 1. Proposed Catalytic Mechanism, Showing Analogy to the Traditional Stille Reaction



Summary

- Carbostannylation of alkynes was realized with palladium-gold catalysis.
- The reaction proceeded with high regio- and stereo-selectivity.
- The products are synthetically highly versatile.
- Future work: other alkyne substrates?