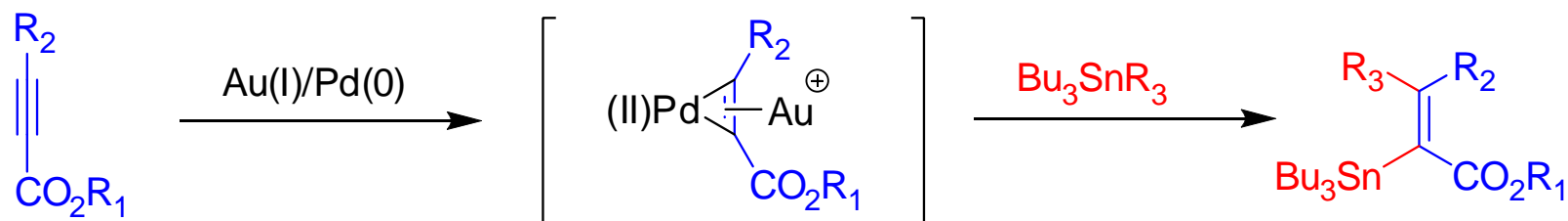


Alkynes as Stille Reaction Pseudohalides: Gold- and Palladium-Cocatalyzed Synthesis of Tri- and Tetra-Substituted Olefins



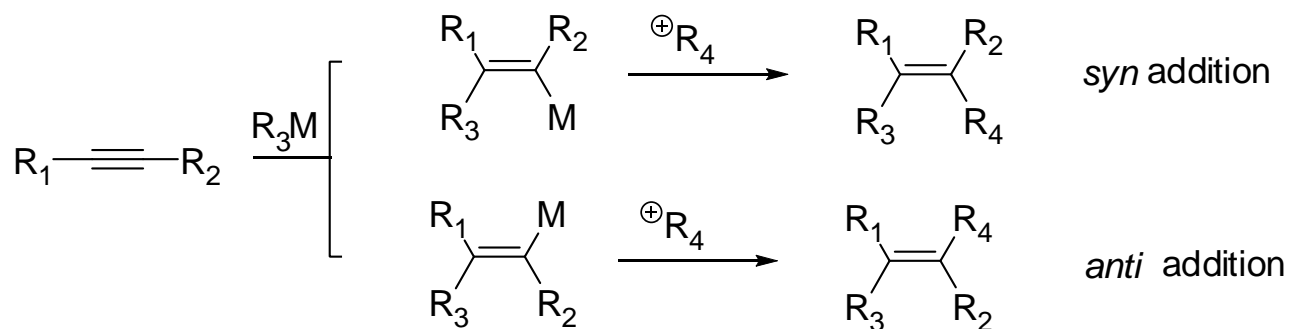
Yili Shi, Sonja M. Peterson, Walter W. Haberaecker III, and
Suzanne A. Blum

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

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

Carbometallation of Alkynes

-General Concepts

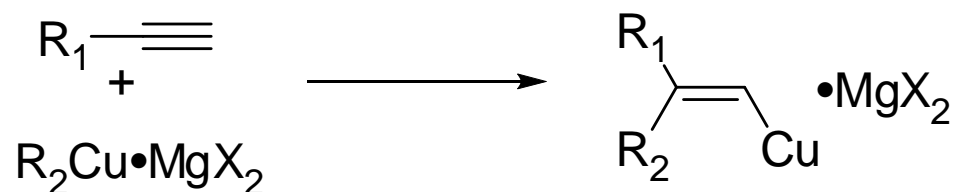


- A powerful way to make stereospecifically substituted alkenes.
- M can be Cu, Al, Zr, Ti, Zn, B, Mg, Li or a combination of two.
- *Syn* or *anti* selectivity depends on the nature of substrate, reagent and reaction conditions.
- Regioselectivity depends on the polarity of the triple bond, steric factor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

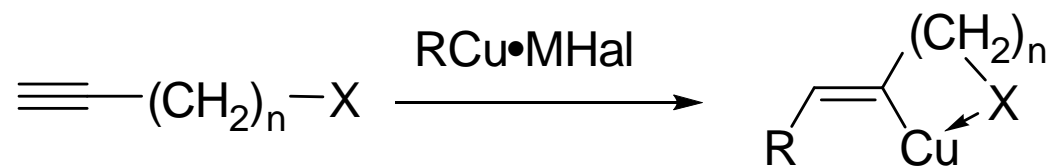
For a review, see: Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841.

Carbometallation of Alkynes -Organocopper Reagents

- Unfunctionalized Terminal alkynes: Markownikov rule



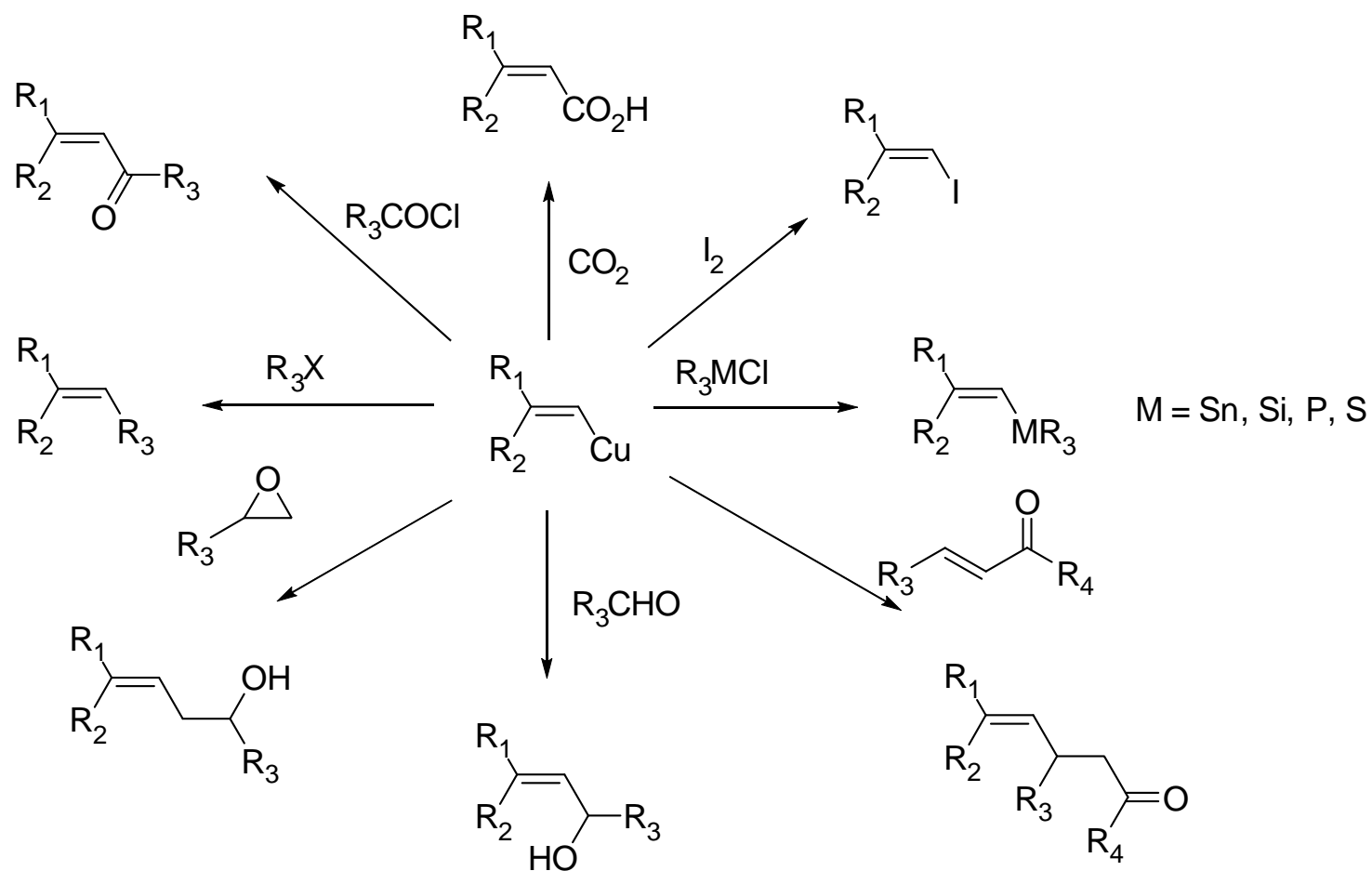
- Functionalized alkynes: directed carbometallation



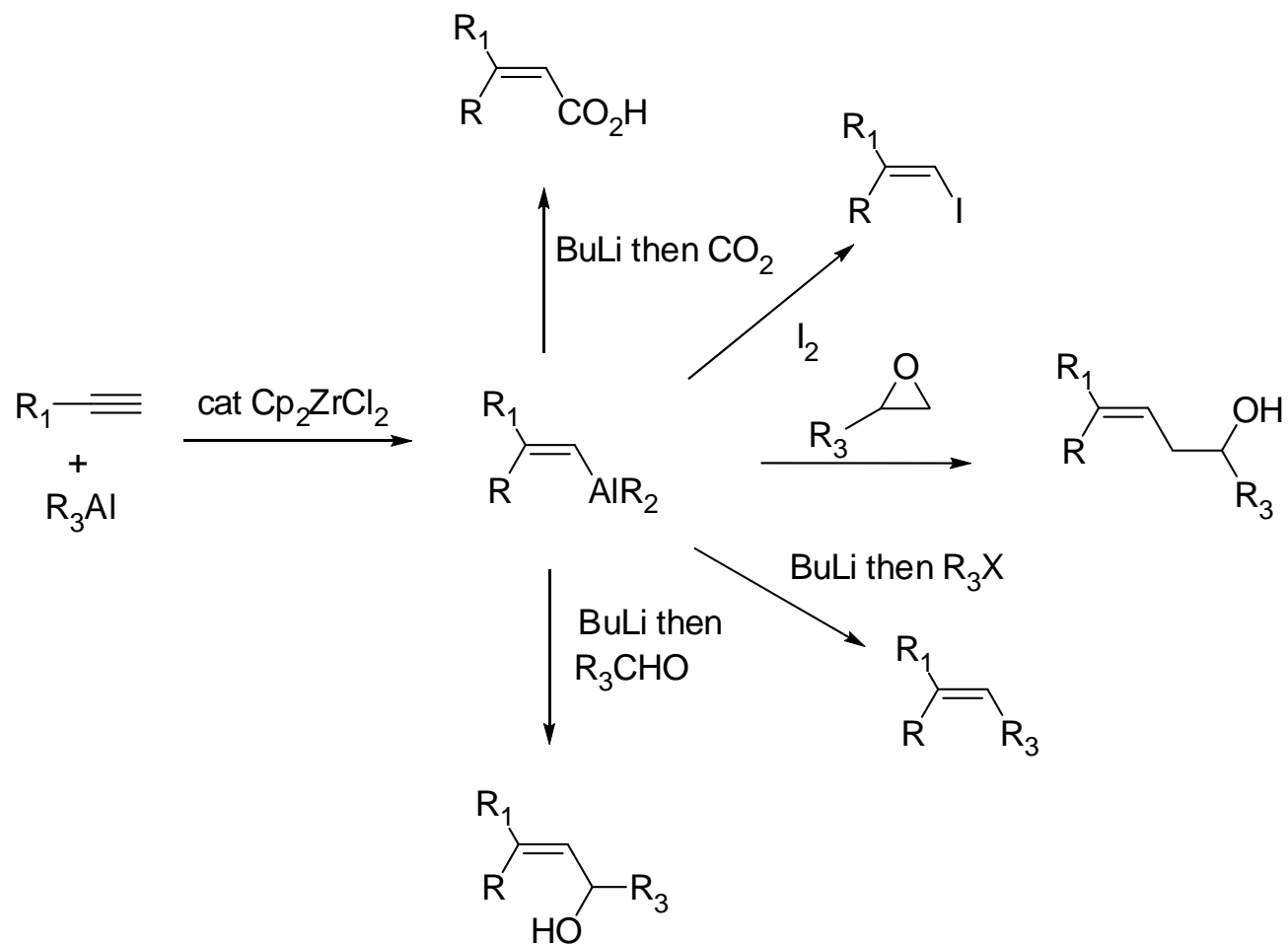
$$n = 0, 1, 2, 3$$

$$X = \text{halogen, SR, OR, O}^-, \text{NR}_2, \text{OAc}$$

Synthetic Use of Alkenylcopper(I) Derivatives



Carbometallation of Alkynes -Organoaluminum Reagents

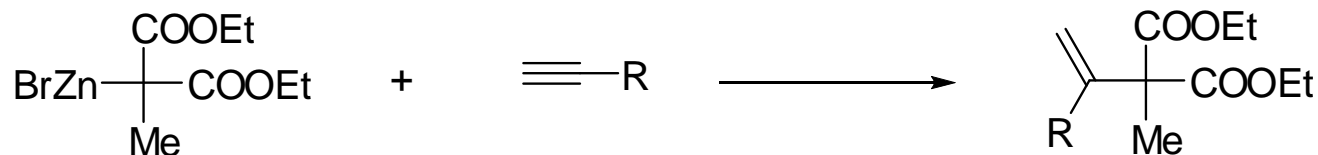


•Complementary to the organocopper reagents

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

Carbometallation of Alkynes -Other Metal Reagents

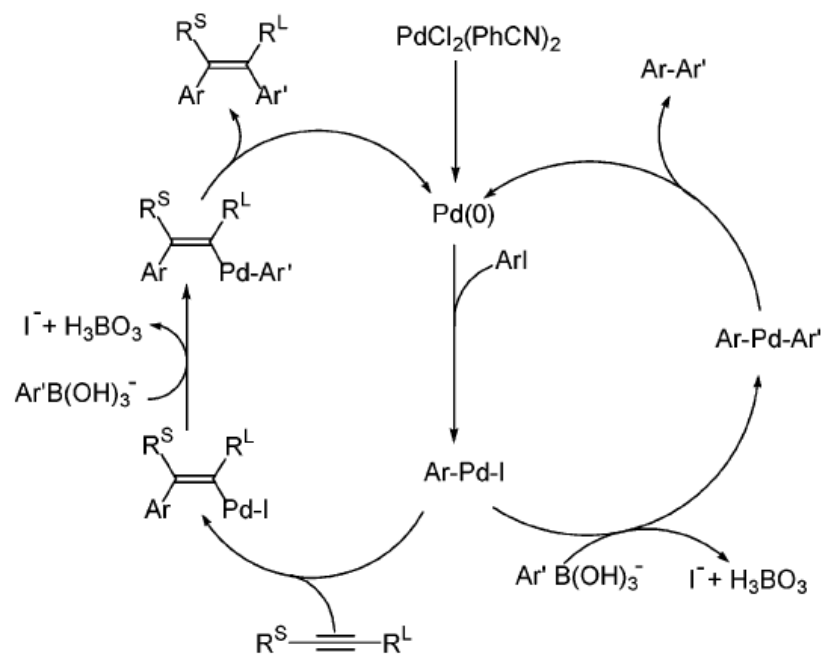
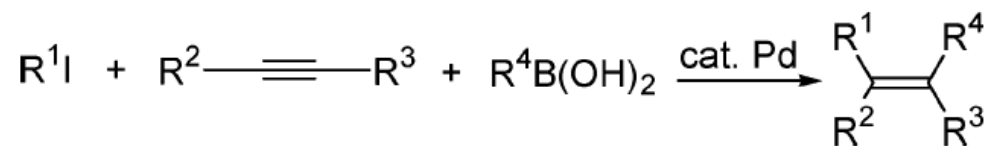
- Organozinc reagents: propargylic, allylic and malonic type organozinc reagents are tolerated



- Organolithium reagents: mostly intramolecular examples
- Organomagnesium reagents: Often used with catalytic Cu salt
- Organoboron reagents: require exceptionally reactive substrates

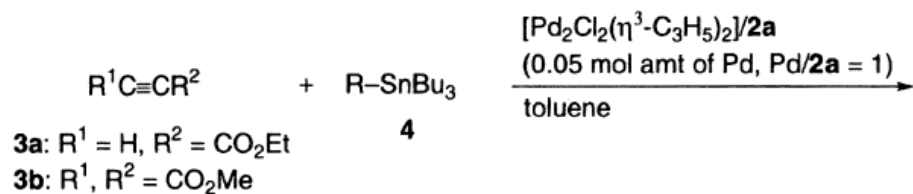
Bertrand, M. T. et al. *Tetrahedron Lett.* **1974**, 1945

Previous Work on the Carbometallation of Alkynes Catalyzed by Palladium

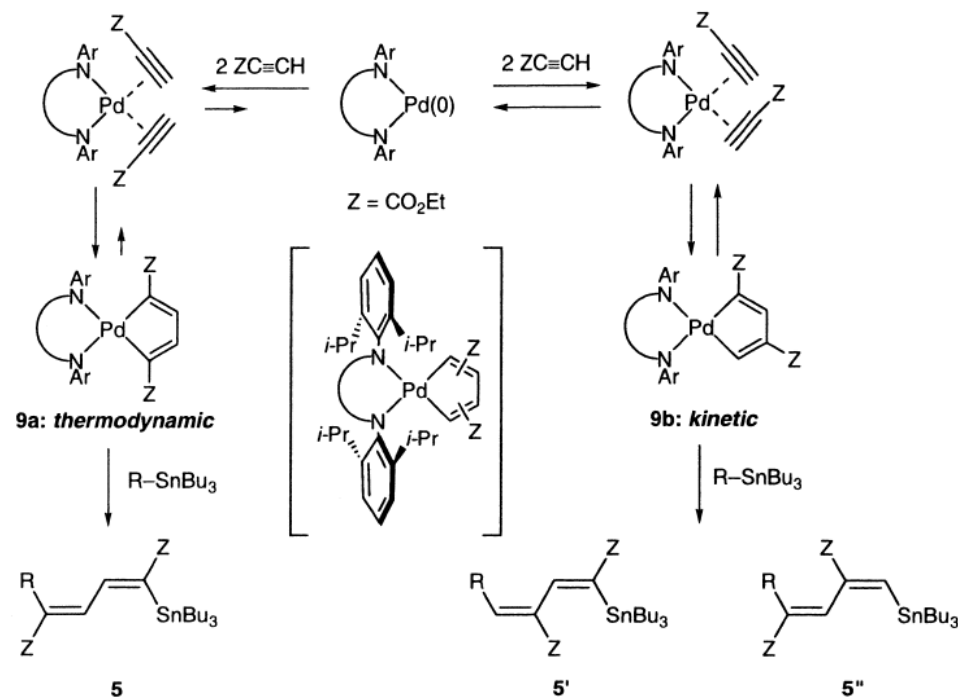
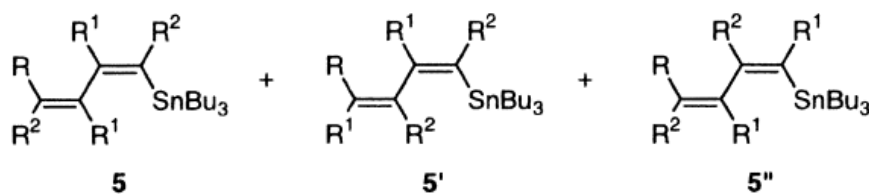


Zhou, C.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 3765

Previous Work on the Carbostannylation of Alkynes Catalyzed by Palladium

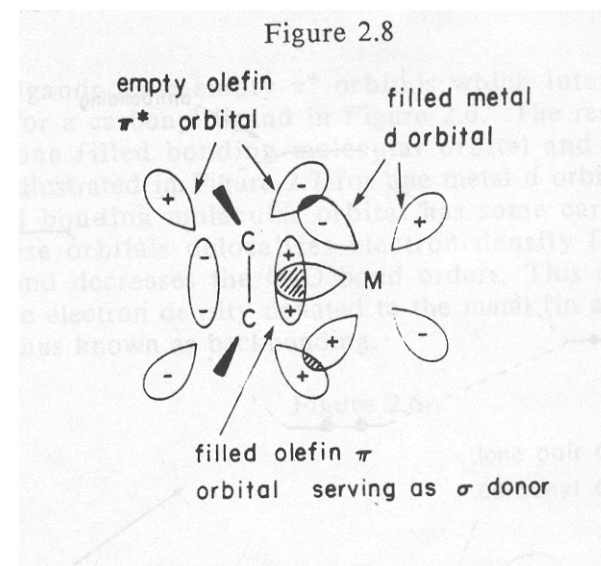
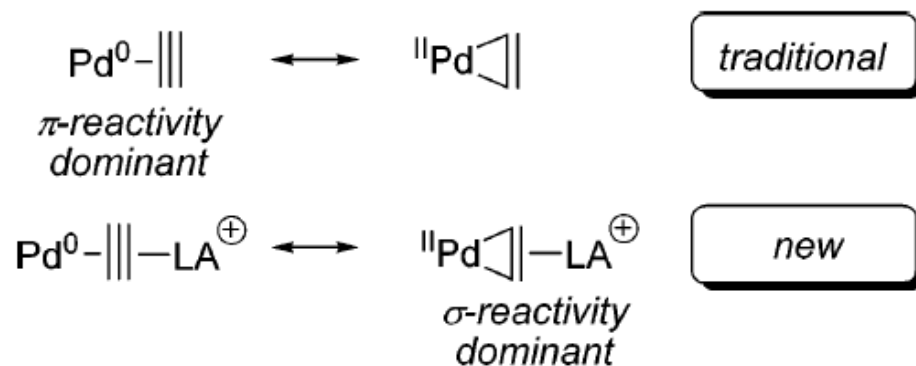


•Dimerization predominates.

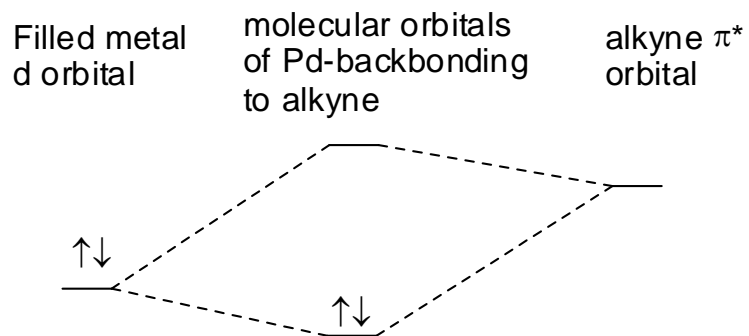


Hiyama, T. et al *Bull. Chem. Soc. Jpn.* **2001**, *74*, 637–647

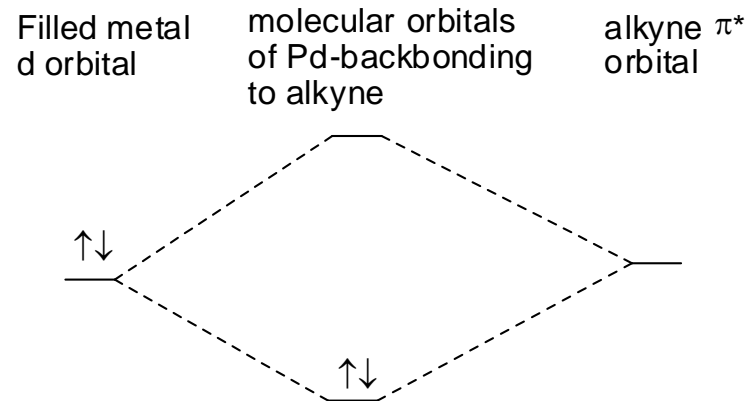
Title Paper: Carbostannylation Catalyzed by Palladium and Gold



Without Au(I)



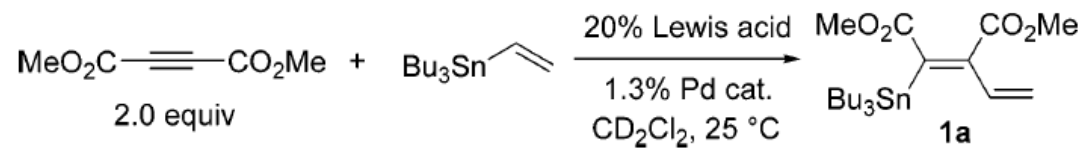
With Au(I)



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 ¹H NMR Yield



entry	Lewis acid	Pd cat.	¹ H NMR yield (%)
1	PPh ₃ AuCl	Pd ₂ (dba) ₃	24
2	PPh ₃ AuCl/AgSbF ₆ (1:1)	Pd ₂ (dba) ₃	51
3	PPh ₃ AuCl/AgSbF ₆ (1:2)	Pd ₂ (dba) ₃	33
4	PPh ₃ AuSbF ₆ ·CH ₃ CN	Pd ₂ (dba) ₃	62
5	PPh ₃ AuPF ₆	Pd ₂ (dba) ₃	73
6	PPh ₃ AuPF ₆	none	0
7	none	Pd ₂ (dba) ₃	0
8	BF ₃ ·(OMe) ₂	Pd ₂ (dba) ₃	25
9	AgSbF ₆	Pd ₂ (dba) ₃	0
10	PhCO ₂ H	Pd ₂ (dba) ₃	0
11	PPh ₃ AuCl/AgSbF ₆ (1:1)	Pd(<i>Pt</i> -Bu ₃) ₂	39
12	PPh ₃ AuCl/AgSbF ₆ (1:1)	(PPh ₃) ₂ PdCl 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

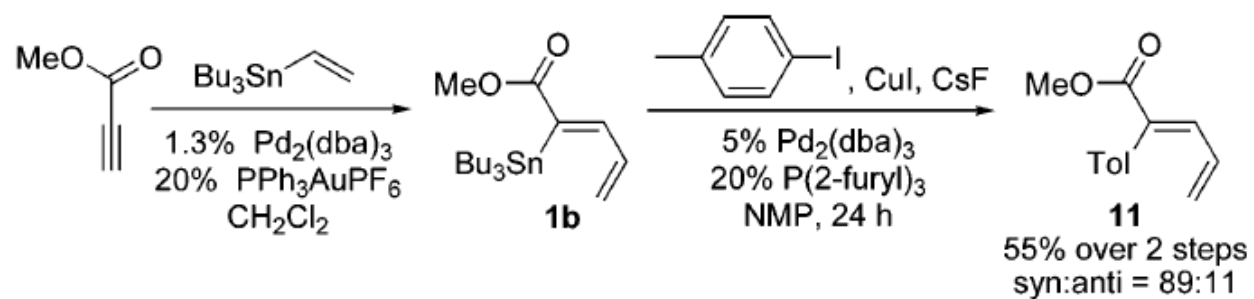
$$R^1O_2C-C\equiv C-R^2 + Bu_3SnR^3 \xrightarrow[1.3 - 2.6\% Pd_2(dba)_3]{20\% PPh_3AuPF_6} R^1O_2C-C(R^2)=C(R^3)-Bu_3Sn \quad \geq 95:5 \text{ syn:anti}^b$$

entry	alkyne	stannane	product	(¹ H NMR yield) isolated yield
1				(96) 87
2	R ¹ = Me, R ² = CO ₂ Me			(75) 73 ^b
3	R ¹ = <i>t</i> Bu, R ² = H			(49) 40
4				(73) 61 ^c
5				(62) 51 ^{c,d}
6				(89) 81
7	R ² = CO ₂ Me			(57) 49 ^c
8				(58) 52 ^c

^a Conditions: CH₂Cl₂, 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.

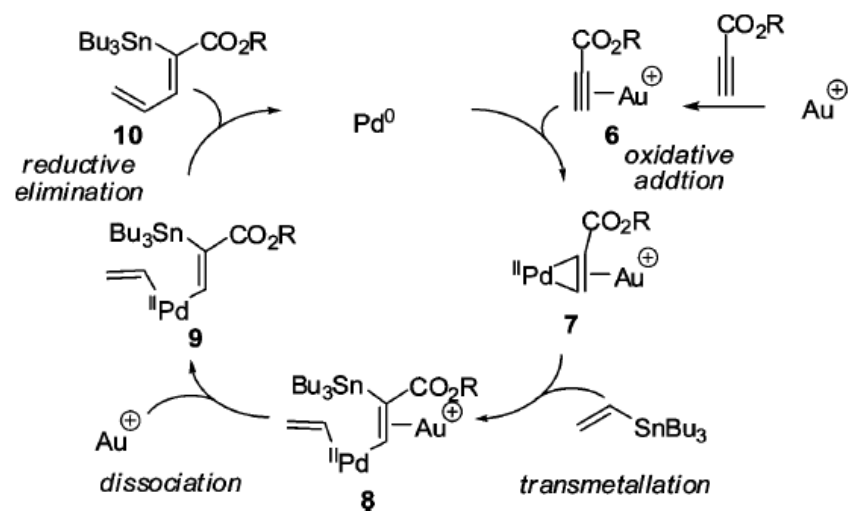
- Alkynes were added slowly to the reaction mixture to prevent polymerization.
- Reactions proceeded with high *syn*-addition selectivity.
- Complete regioselectivity is maintained even with *t*-Bu ester.
- Vinylstannanes reacted with retention of configuration (except Entry 5).

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?