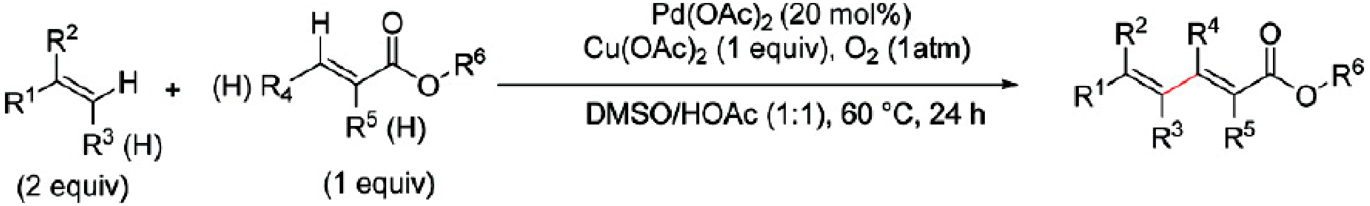
Direct Cross-Coupling Reaction of Simple Alkenes
with Acrylates Catalyzed by Palladium Catalyst



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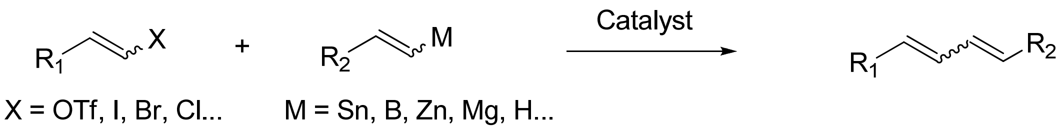
J. Am. Chem. Soc., Article ASAP

Current Literature
Chenbo Wang @ Wipf Group
Jan 17, 2009

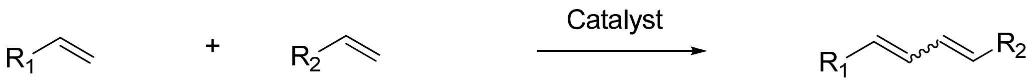
Preparation of Diene Units with Cross-coupling Reactions: Classical Cross-coupling Reactions vs. Direct Cross-Coupling Reaction of Simple Alkenes

Classical cross-coupling reactions



Pre-functionalized alkene substrates required

Simple alkene cross-coupling reactions

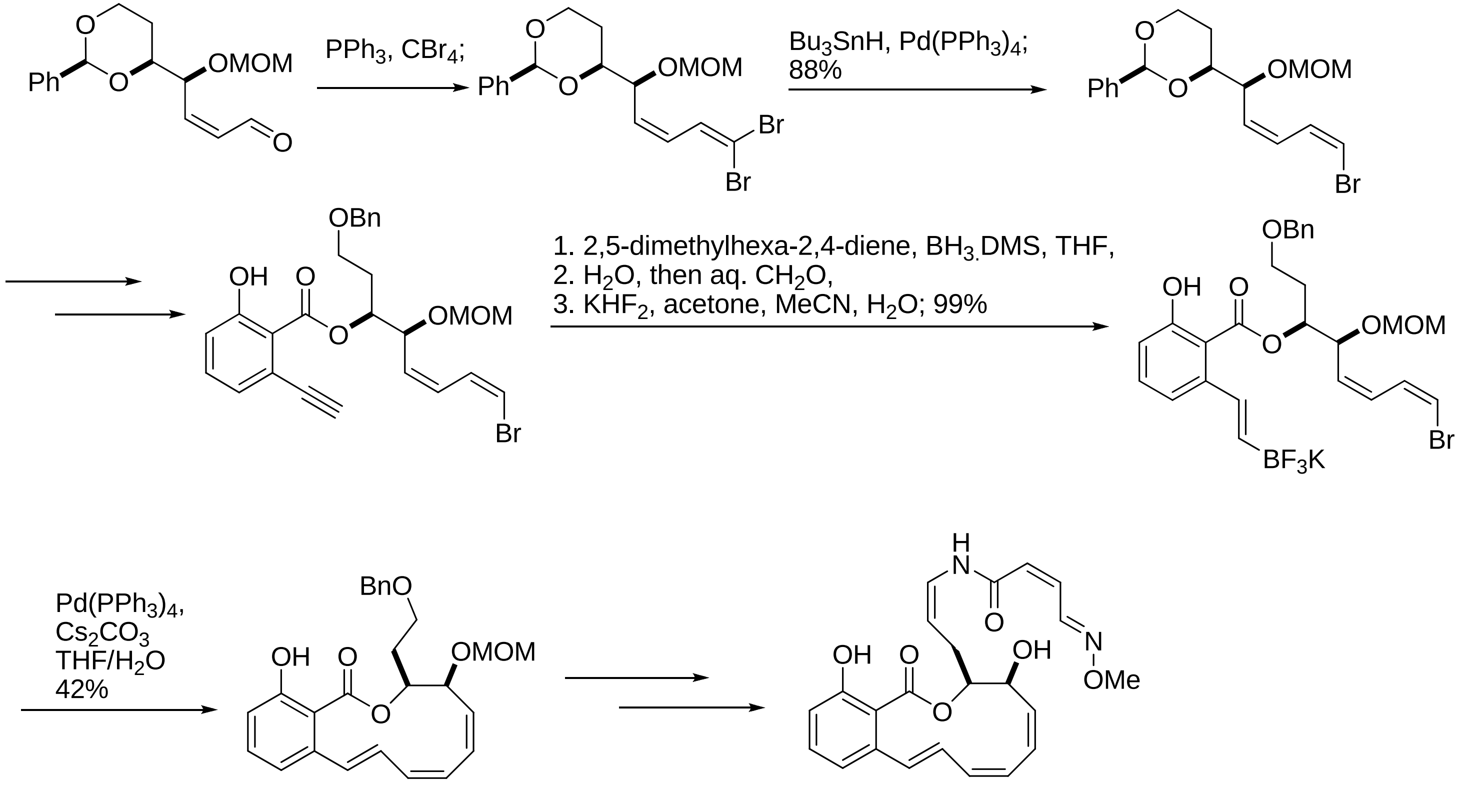


No pre-functionalization needed

The challenge:

- Chemoselectivity: dimerization
- Stereoselectivity: *cis*/*trans*
- Difficulty in activating alkene C-H without a directing group
- Product stability

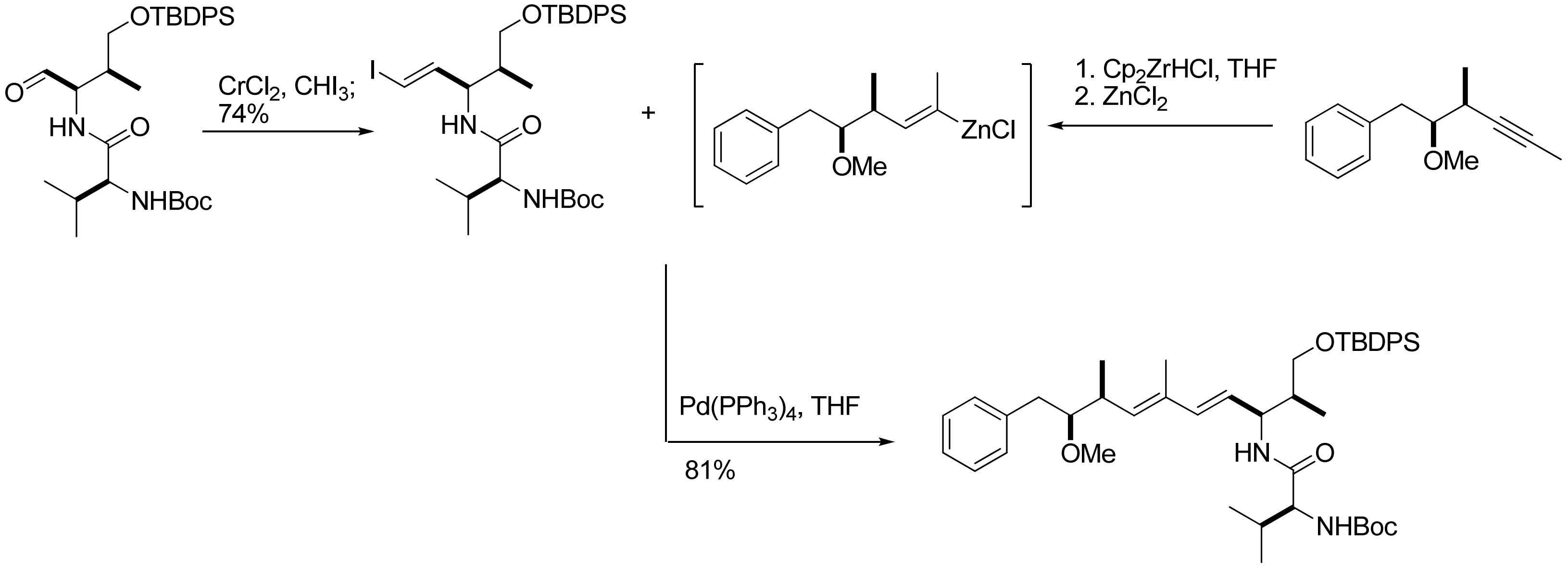
Construction of Diene Units in Natural Product Synthesis: Suzuki Reaction



Oximidine **II**

Molander, G. A. et al *J. Am. Chem. Soc.*, **2004**, 126, 10313

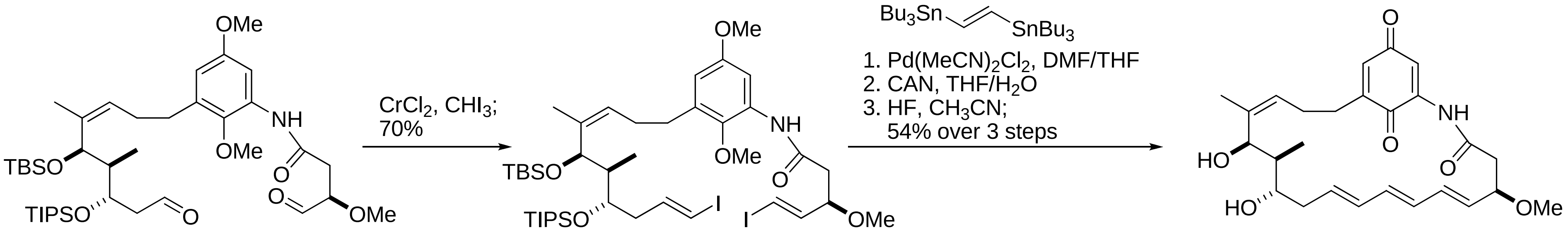
Construction of Diene Units in Natural Product Synthesis: Negishi Reaction



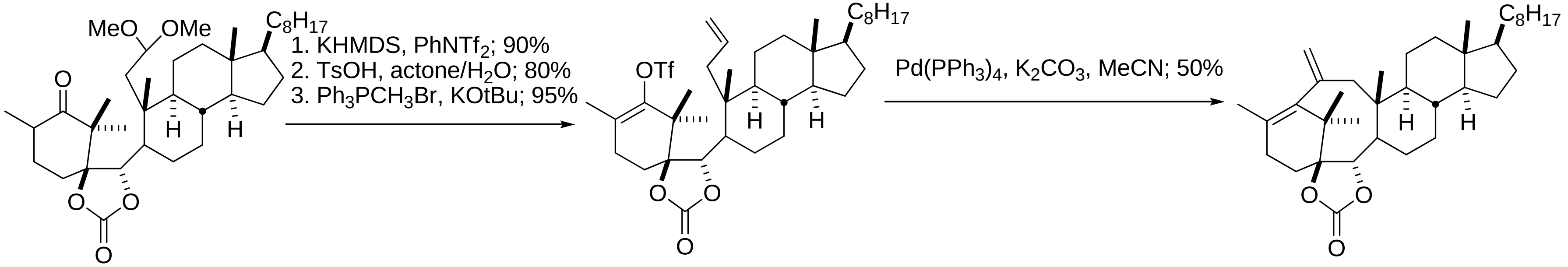
Fragment in the total synthesis of (-)-motuporin

Panek, S. J. et al *J. Am. Chem. Soc*. **2002**, *124*, 11368

Construction of Diene Units in Natural Product Synthesis: Stille and Heck Reaction



(+)-mycotrienol

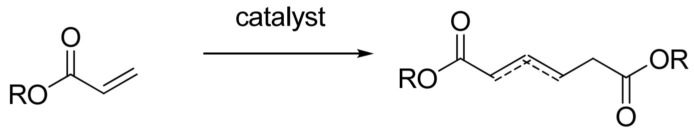


Intermediate in the total synthesis of taxol

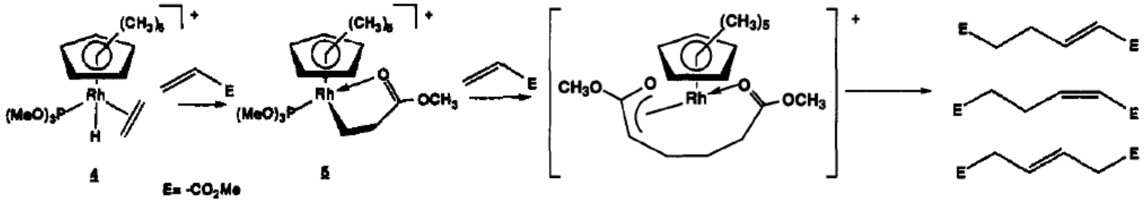
Panek, J. S. et al *J. Am. Chem. Soc.* **1998,** *120,* 4123
Danishefsky, S. J. et al *J. Am. Chem. Soc.*, **1996**, *118*, 2843

Alkene Dimerization Reaction: Previous Work

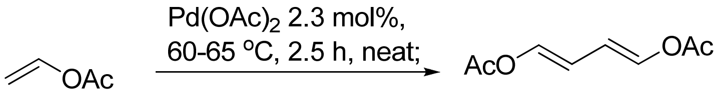
Metal-catalyzed olefin dimerization:



catalyst: Co, Ni, Ru, Rh, Pd



The first example of oxidative alkene-alkene cross-coupling:

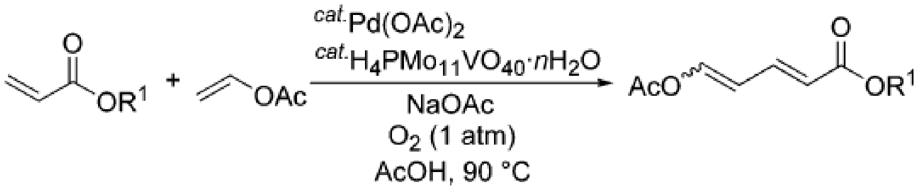


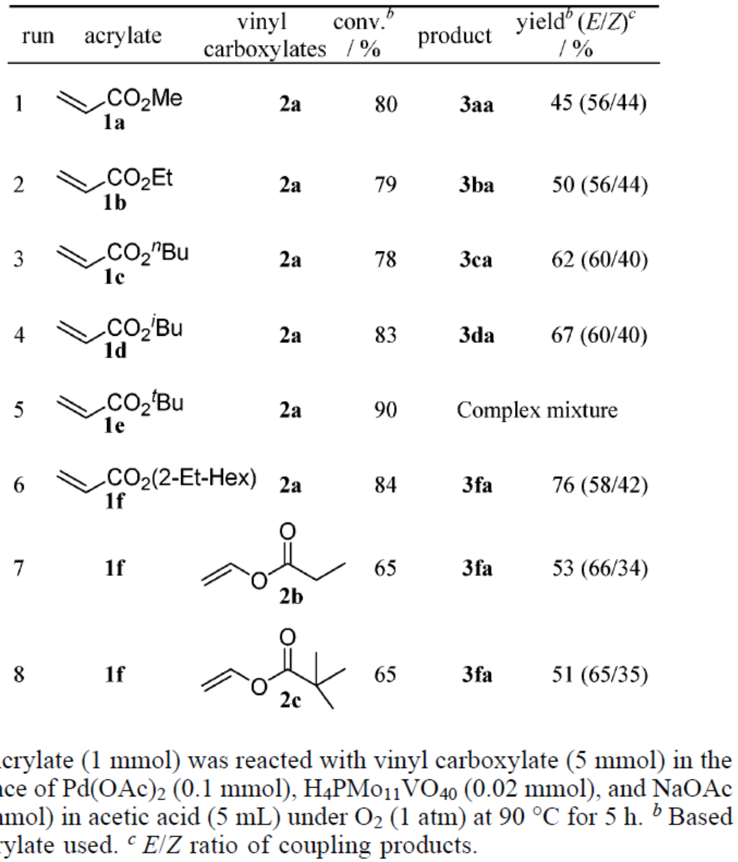
0.64%

Ishii, Y. et al *Org. Lett.* **2004**, *6*, 4623 and references therein

Kohll, C. F. and Van Helden, R. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1930

The First Practical Example of Oxidative Alkene-alkene Oxidative Coupling



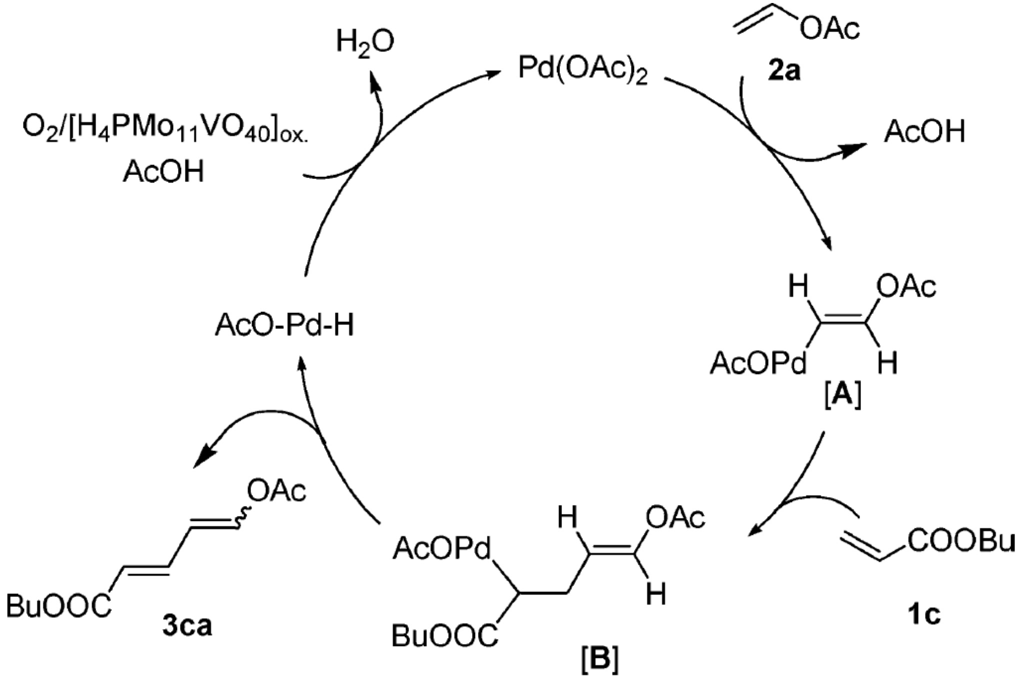


run	acrylate	vinyl carboxylates	conv.[b] / %	product	yield[b] (E/Z)[c] / %
1	CO_2Me **1a**	**2a**	80	**3aa**	45 (56/44)
2	CO_2Et **1b**	**2a**	79	**3ba**	50 (56/44)
3	$CO_2{}^nBu$ **1c**	**2a**	78	**3ca**	62 (60/40)
4	$CO_2{}^iBu$ **1d**	**2a**	83	**3da**	67 (60/40)
5	$CO_2{}^tBu$ **1e**	**2a**	90	Complex mixture	
6	CO_2(2-Et-Hex) **1f**	**2a**	84	**3fa**	76 (58/42)
7	**1f**	**2b**	65	**3fa**	53 (66/34)
8	**1f**	**2c**	65	**3fa**	51 (65/35)

[a] Acrylate (1 mmol) was reacted with vinyl carboxylate (5 mmol) in the presence of $Pd(OAc)_2$ (0.1 mmol), $H_4PMo_{11}VO_{40}$ (0.02 mmol), and NaOAc (0.1 mmol) in acetic acid (5 mL) under O_2 (1 atm) at 90 °C for 5 h. [b] Based on acrylate used. [c] E/Z ratio of coupling products.

Ishii, Y. et al *Org. Lett.* **2004**, *6*, 4623

Proposed Mechanism for Oxidative Alkene-alkene Oxidative Coupling



Direct Cross-Coupling Reaction of Simple Alkenes with Acrylates: Optimization of Reaction Conditions

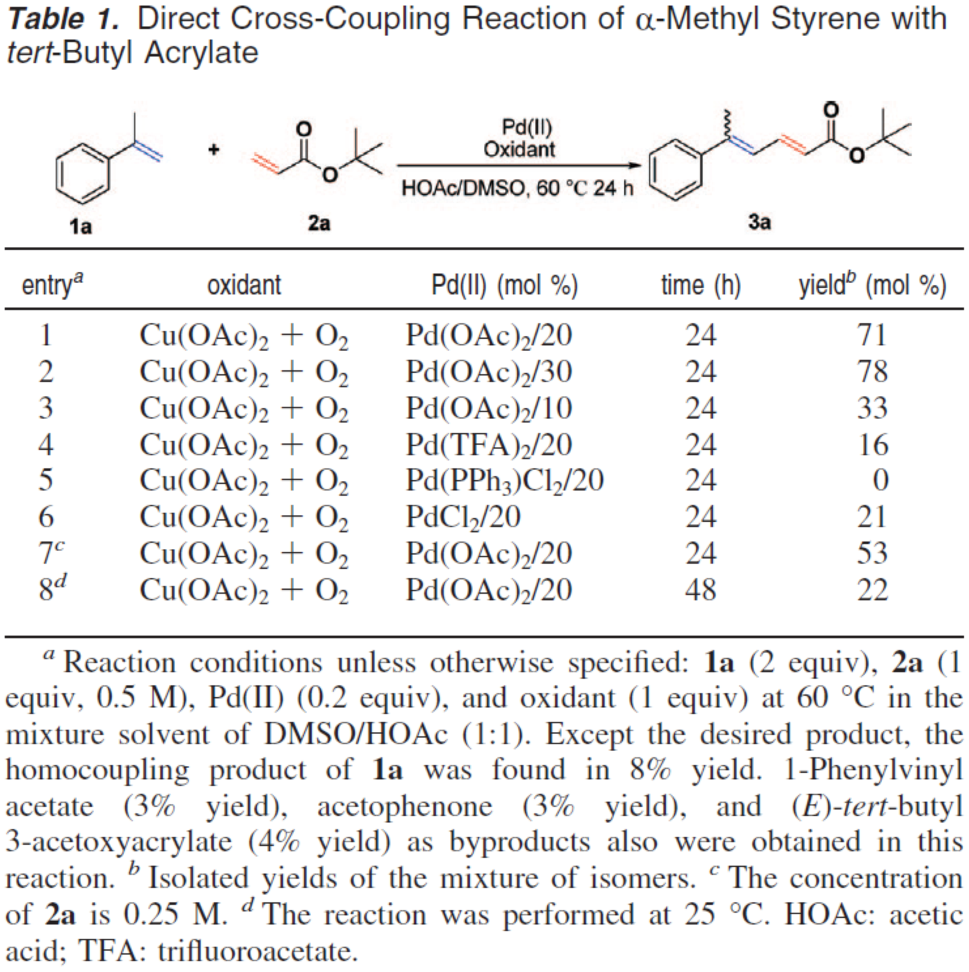
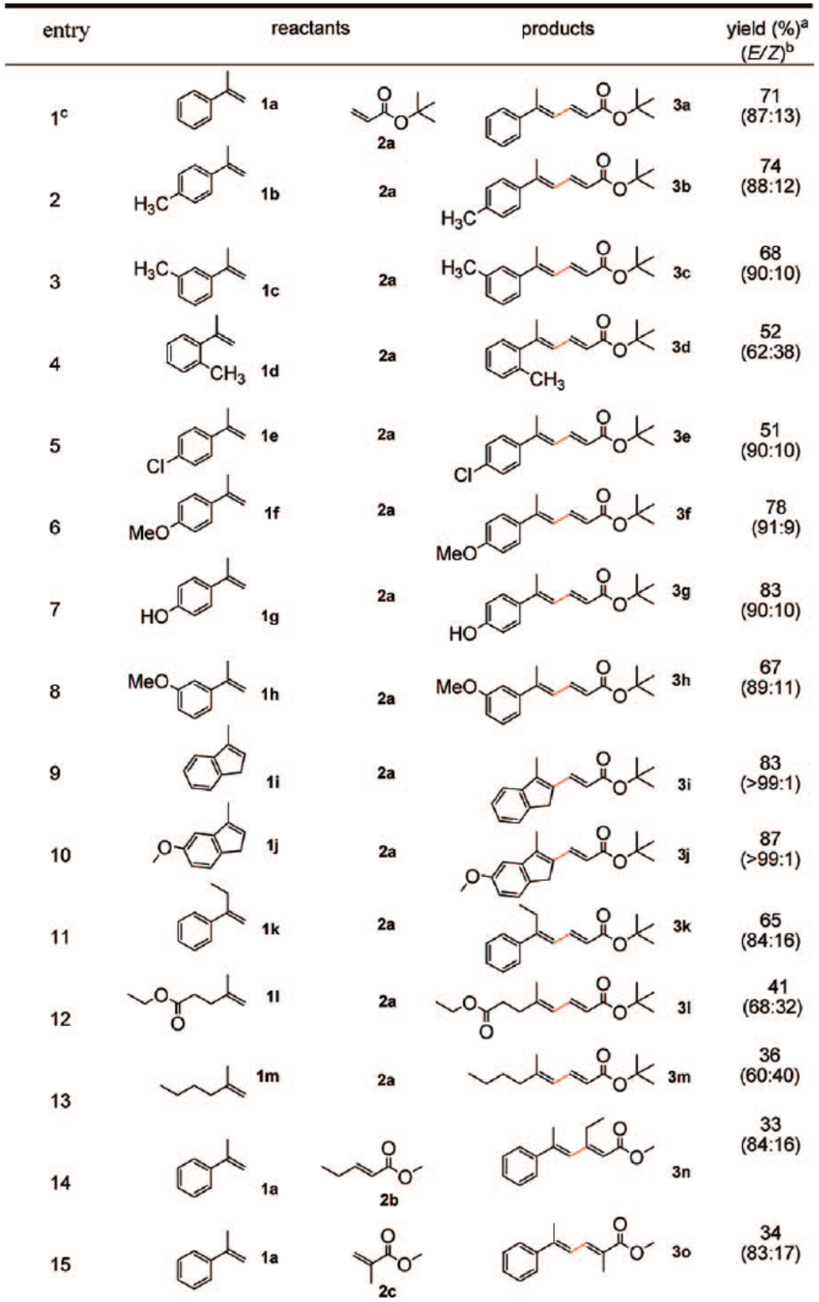


Table 1. Direct Cross-Coupling Reaction of α-Methyl Styrene with *tert*-Butyl Acrylate

entry[a]	oxidant	Pd(II) (mol %)	time (h)	yield[b] (mol %)
1	$Cu(OAc)_2 + O_2$	$Pd(OAc)_2$/20	24	71
2	$Cu(OAc)_2 + O_2$	$Pd(OAc)_2$/30	24	78
3	$Cu(OAc)_2 + O_2$	$Pd(OAc)_2$/10	24	33
4	$Cu(OAc)_2 + O_2$	$Pd(TFA)_2$/20	24	16
5	$Cu(OAc)_2 + O_2$	$Pd(PPh_3)Cl_2$/20	24	0
6	$Cu(OAc)_2 + O_2$	$PdCl_2$/20	24	21
7[c]	$Cu(OAc)_2 + O_2$	$Pd(OAc)_2$/20	24	53
8[d]	$Cu(OAc)_2 + O_2$	$Pd(OAc)_2$/20	48	22

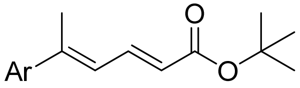
[a] Reaction conditions unless otherwise specified: **1a** (2 equiv), **2a** (1 equiv, 0.5 M), Pd(II) (0.2 equiv), and oxidant (1 equiv) at 60 °C in the mixture solvent of DMSO/HOAc (1:1). Except the desired product, the homocoupling product of **1a** was found in 8% yield. 1-Phenylvinyl acetate (3% yield), acetophenone (3% yield), and (*E*)-*tert*-butyl 3-acetoxyacrylate (4% yield) as byproducts also were obtained in this reaction. [b] Isolated yields of the mixture of isomers. [c] The concentration of **2a** is 0.25 M. [d] The reaction was performed at 25 °C. HOAc: acetic acid; TFA: trifluoroacetate.

Direct Cross-Coupling Reaction of Simple Alkenes with Acrylates: Substrate Scope

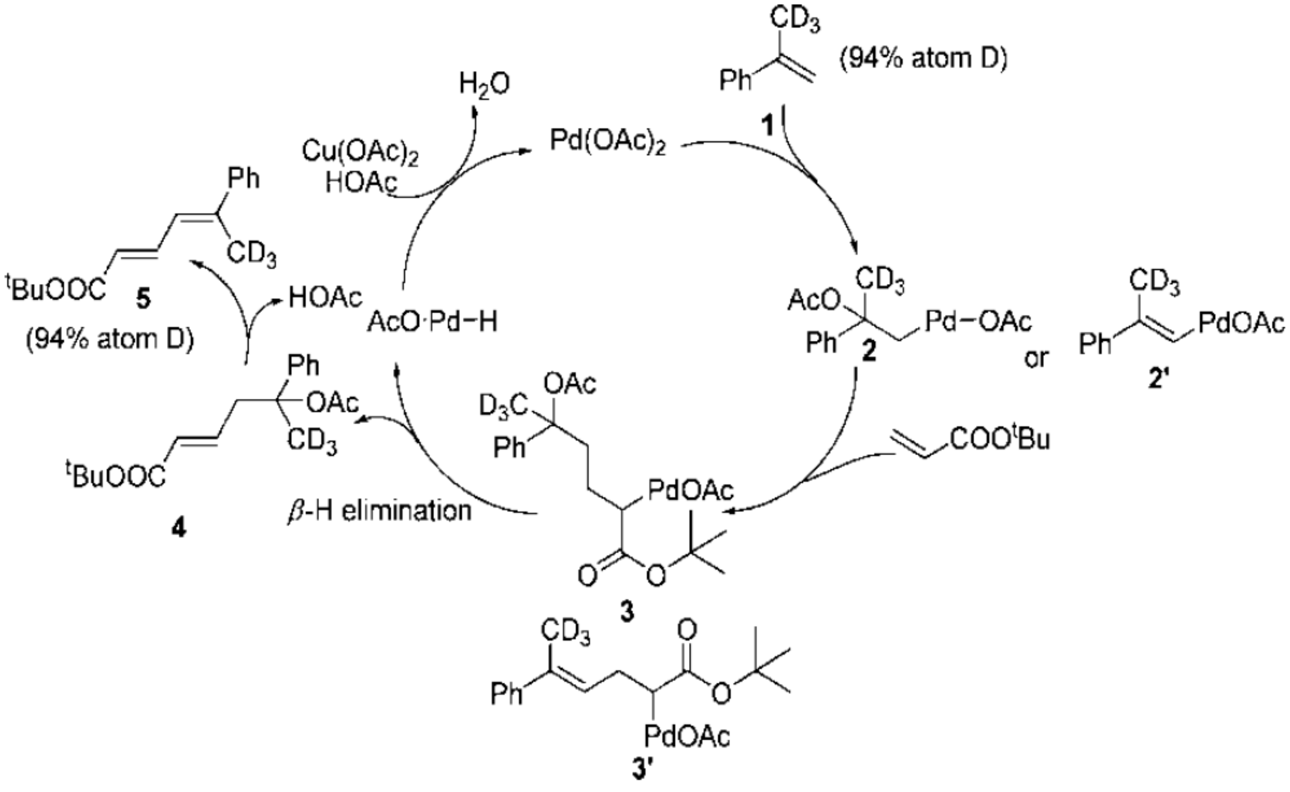


entry	reactants		products	yield (%)[a] (E/Z)[b]
1[c]	1a	2a	3a	71 (87:13)
2	1b	2a	3b	74 (88:12)
3	1c	2a	3c	68 (90:10)
4	1d	2a	3d	52 (62:38)
5	1e	2a	3e	51 (90:10)
6	1f	2a	3f	78 (91:9)
7	1g	2a	3g	83 (90:10)
8	1h	2a	3h	67 (89:11)
9	1i	2a	3i	83 (>99:1)
10	1j	2a	3j	87 (>99:1)
11	1k	2a	3k	65 (84:16)
12	1l	2a	3l	41 (68:32)
13	1m	2a	3m	36 (60:40)
14	1a	2b	3n	33 (84:16)
15	1a	2c	3o	34 (83:17)

Suitable substrate for this methodology:



Direct Cross-Coupling Reaction of Simple Alkenes with Acrylates: Proposed Mechanism



Summary

- First example of direct cross-coupling reaction of simple alkenes with acrylates was reported.
- This methodology is still at early exploratory stage. Substrate scope is very limited.
- Future work: mechanistic study, a directing group for alkene C-H activation, milder conditions.