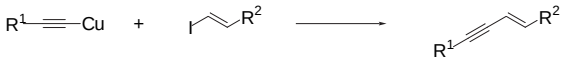
Alkinkupplungen

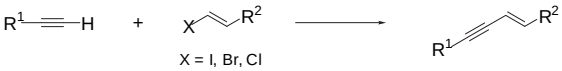
Palladium-katalysierte Alkinkupplungen

Review: R. Rossi *Org. Prep. Proc. Intl.* **1995**, *27*, 127.

A. Castro-Stevens Kupplung



B. The Sonogashira-Hagihara Kupplung

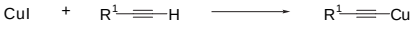


X = I, Br, Cl

$PdCl_2(PPh_3)_2$ (2 mol%)
CuI oder CuOAc(1 mol%)
Amin = Et_2NH, Et_3N oder
25 °C

Lösungsmittel (wichtig!): Amin, THF(!)

Mechanismus: ähnlich wie Suzuki und Stille, aber mit Organokupferverbindung

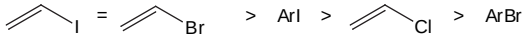


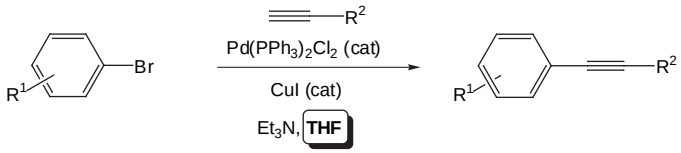
Diese Species wird transmetalliert

A-1

Sonogashira-Hagihara Kupplung

1. Reaktivität der Halogenkomponente





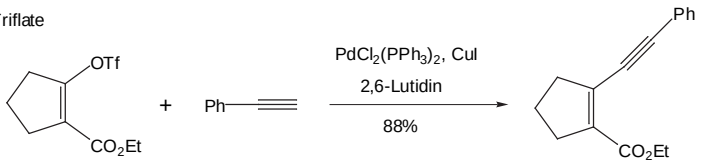
R^1	R^2	Methode*	Bedingungen	Ausbeute [%]
4-CHO	Me_3Si	A	25°C / 1h	99
4-COMe	Me_3Si	A	25°C / 1h	92
2-CO_2Me	Me_3Si	B	25°C / 16h	88
3-CO_2Me	Me_3Si	B	25°C / 16h	87
4-CO_2Me	Me_3Si	B	25°C / 16h	88
4-COMe	n-Bu	B	25°C / 16h	91
4-COMe	Ph	B	25°C / 16h	87
4-CHO	Ph	B	25°C / 16h	82

N. Krause et al, *J. Org. Chem.* **1998**,*63*. 8551

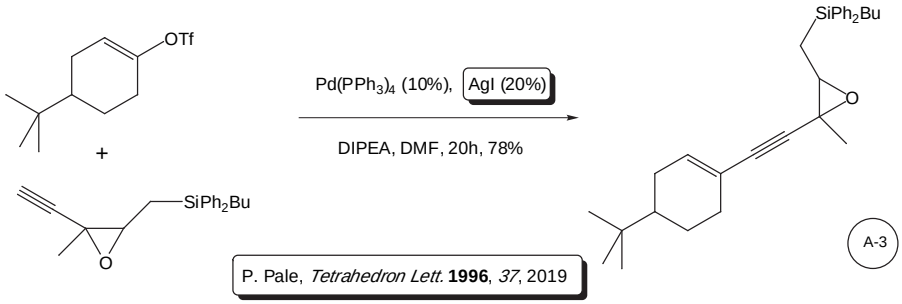
A-2

Sonogashira-Hagihara Kupplung

2. Triflate



I. Saito, *Tetrahedron Lett.* **1996**, *37*, 605

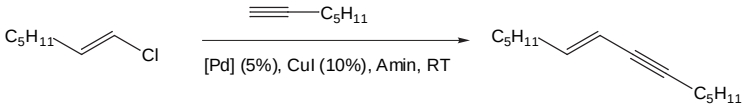


P. Pale, *Tetrahedron Lett.* **1996**, *37*, 2019

A-3

Sonogashira-Hagihara Kupplung

4. Reaktivität Katalysator / Amin

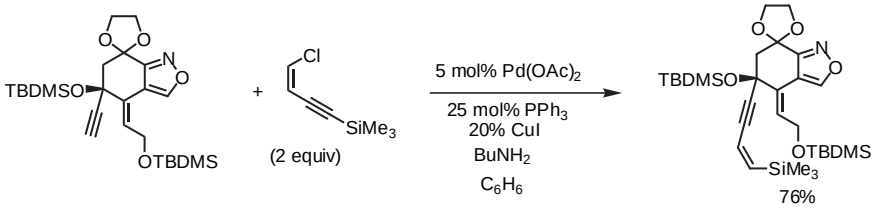


[Pd]	Amin	Zeit [h]	Ausbeute [%]
$PdCl_2(PhCN)_2$	Piperidin	0.5	93
$PdCl_2(PPh_3)_2$	Piperidin	20	93
$Pd(PPh_3)_4$	Piperidin	16	11
$Pd(PPh_3)_4$	*n*-$PrNH_2$	60	62

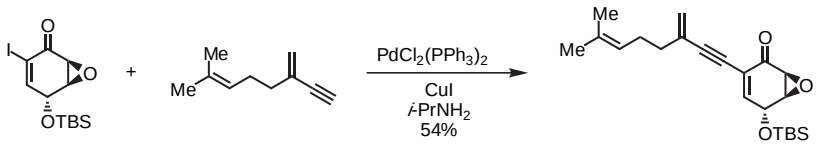
M. Alami, G. Linstrumelle, *Tetrahedron Lett.* **1991**, *32*, 6109

A-4

Palladium-katalysierte Akinkupplungen



K. C. Nicolaou, *J. Am. Chem. Soc.* **1993**, *115*, 7612.

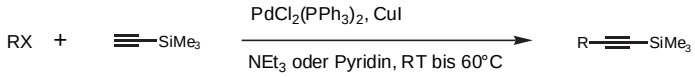


C. R. Johnson *J. Org. Chem.* **1997**, *62*, 1582.

A-5

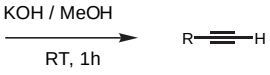
Palladium-katalysierte Akinkupplungen

Terminale Acetylene



70-92%

R = Aryl, Alkenyl



79-94%

[auch Fluorid möglich]

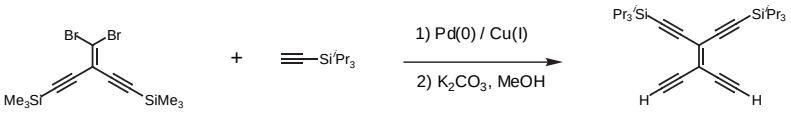
Synthesis **1980**, 627-30
Tetrahedron Lett. **1993**, *34*, 2071-74

Review: K. Sonogashira in *Comprehensive Organic Synthesis* **1990**, Vol. 3 (Pergamon), 521-49

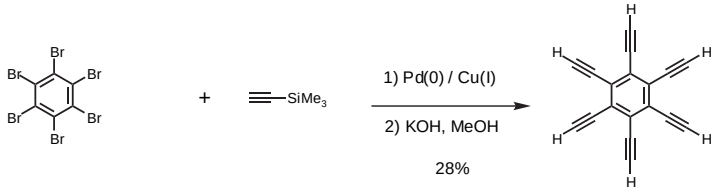
A-6

Palladium-katalysierte Akinkupplungen

Terminale Acetylene



F. Diederich, *Angew. Chem.* **1993**, *105*, 437-40

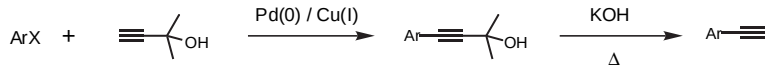


K.P.C. Vollhart, *Angew. Chem.* **1986**, *25*, 268-9.

A-7

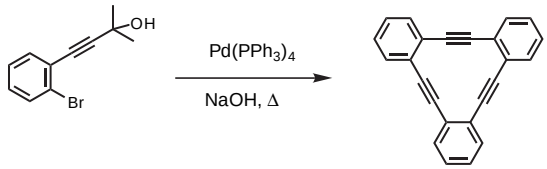
Palladium-katalysierte Akinkupplungen

Terminale Acetylene; andere Schutzgruppen als TMS



2-Methyl-3-butyn-2-ol

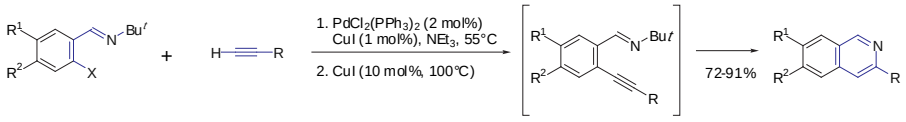
J. Org. Chem. **1985**, *50*, 1763
Synthesis **1996**, 589



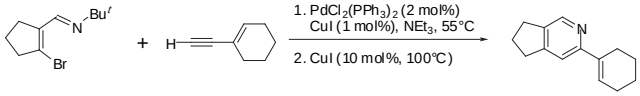
G. Instrumelle, *Tetrahedron* **1988**, *44*, 6337-44.

A-8

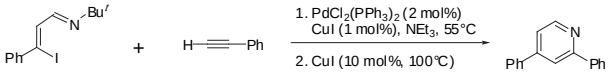
Isoquinoline



X = I, Br



55%



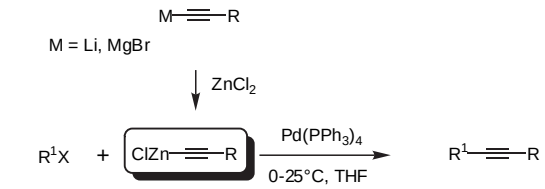
57%

R. Larock, *Org. Lett*. **1999**, *1*, 553

A-8a

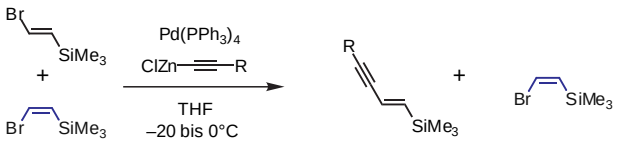
Palladium-katalysierte Akinkupplungen

Alkynylzinkverbindungen



R^1 = Aryl, Vinyl X = Br, I

E. Negishi, *J. Chem. Soc. Chem. Commun.* **1977**, 683-4
E. Negishi, *J. Org. Chem.* **1978**, *43*, 358-60

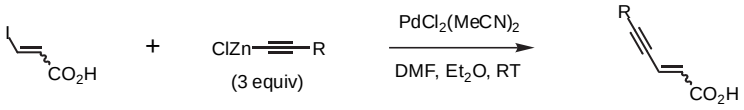


R. Rosshi, *Tetrahedron Lett.* **1988**, *29*, 2239

A-9

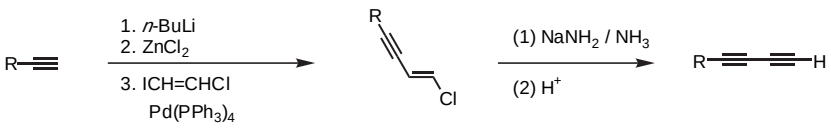
Palladium-katalysierte Akinkupplungen

Alkynylzinkverbindungen



(*E*) oder (*Z*), Reaktion ist stereospezifisch

A. Duchene, *Synthesis* **1996**, 82-6.

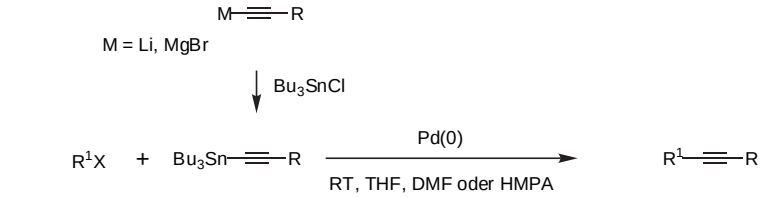


E. Negishi, *J. Org. Chem.* **1984**, *49*, 2629

A-10

Palladium-katalysierte Akinkupplungen

Alkynylzinnverbindungen



R^1 = Aryl, Vinyl X = I > Br > OTf >> Cl

bei Zusatz von LiCl: I > OTf >Br >> Cl *Kein Amin und kein Cu(I) nötig!*

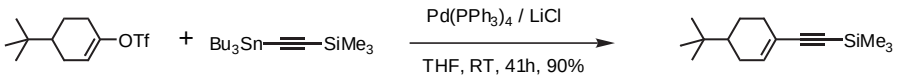
Ligandenfreie Katalyatoren wie $PdCl_2(CH_3CN)_2$ oftmals reaktiver als $Pd(PPh_3)_4$

I. Beletskaya, *Doke. Akad. Nauk. SSSR* **1983**, *272*, 1384
J. K. Stille, *Tetrahedron Lett.* **1988**, *29*, 1509

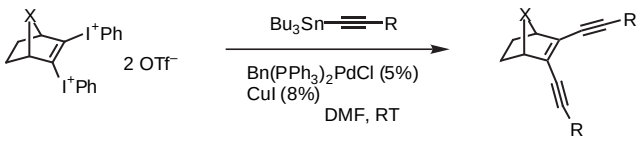
A-11

Palladium-katalysierte Akinkupplungen

Alkynylzinnverbindungen



J. K. Stille, *J. Am. Chem. Soc.* **1984**, *106*, 4630.



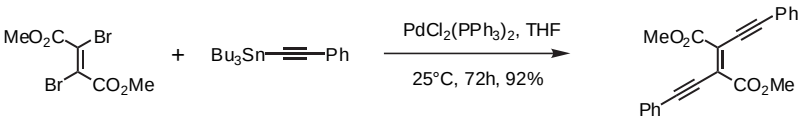
P. Stang, *J. Org. Chem.* **1996**, *61*, 6162

A-12

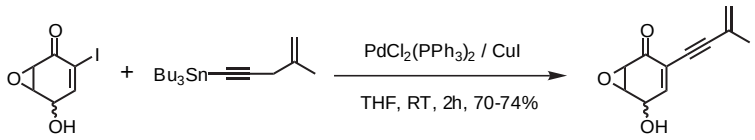
Palladium-katalysierte Akinkupplungen

Alkynylzinnverbindungen

Latent basenempfindliche Substrate - Sonogashira Kupplung nicht möglich!



F. Diederich, *Angew. Chem.* **1992**, *104*, 1270.

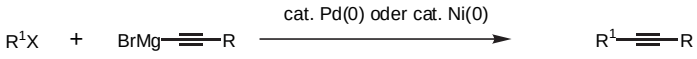


R. J. K. Taylor, *Tetrahedron Lett.* **1996**, *37*, 7445.
K. Ogasahara, *J. Chem. Soc. Chem. Commun.* **1996**, 1679.

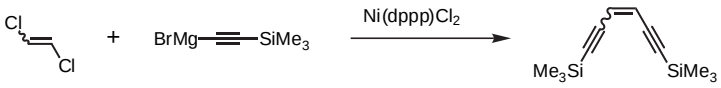
A-13

Palladium-katalysierte Akinkupplungen

Alkynylmagnesiumverbindungen



G. Linstrumelle, *Tetrahedron Lett.* **1978**, 191
R. Rossi, *Tetrahedron* **1984**, *40*, 2773



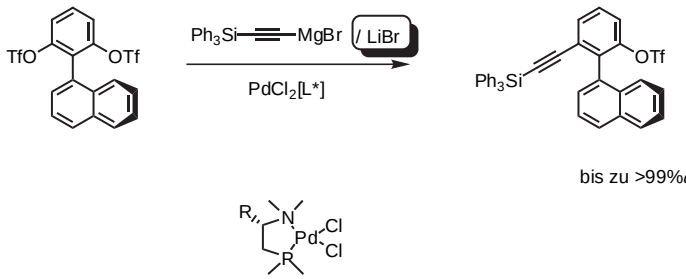
(*E*) oder (*Z*), Reaktion ist stereospezifisch

F. Wudl, *J. Org. Chem.* **1984**, *49*, 4733

A-14

Palladium-katalysierte Akinkupplungen

Alkynylmagnesiumverbindungen



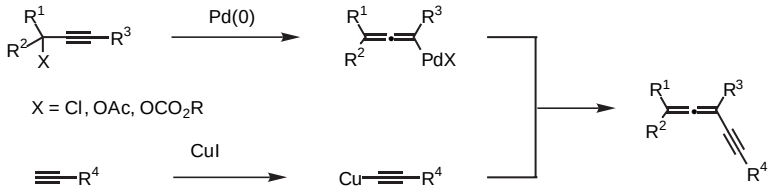
bis zu >99%*ee*

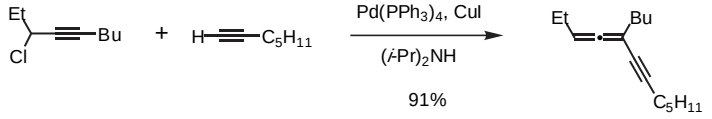
T. Hayashi, *Tetrahedron Lett.* **1996**, *37*, 3161

A-15

Palladium-katalysierte Akinkupplungen

2-Alkynylverbindungen (Propargyl)





J. Tsuji, *Tetrahedron Lett.* **1990**, *31*, 7179
J. Tsuji, *J. Organomet. Chem.* **1991**, *417*, 305

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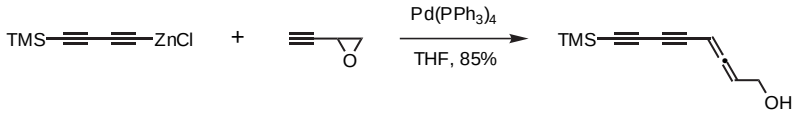
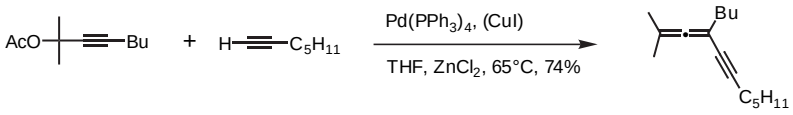
Palladium-katalysierte Akinkupplungen

2-Alkynylverbindungen (Propargyl)

- Zink



H. Kleijn, *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 97



G. Linstrumelle, *Tetrahedron Lett.* **1993**, *34*, 3853

A-17