

Neuere organisch-chemische Synthesemethoden

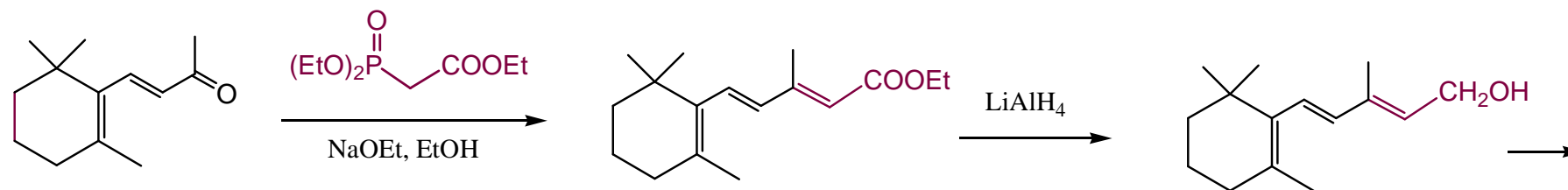
Horst Kunz

Institut für Organische Chemie
Universität Mainz

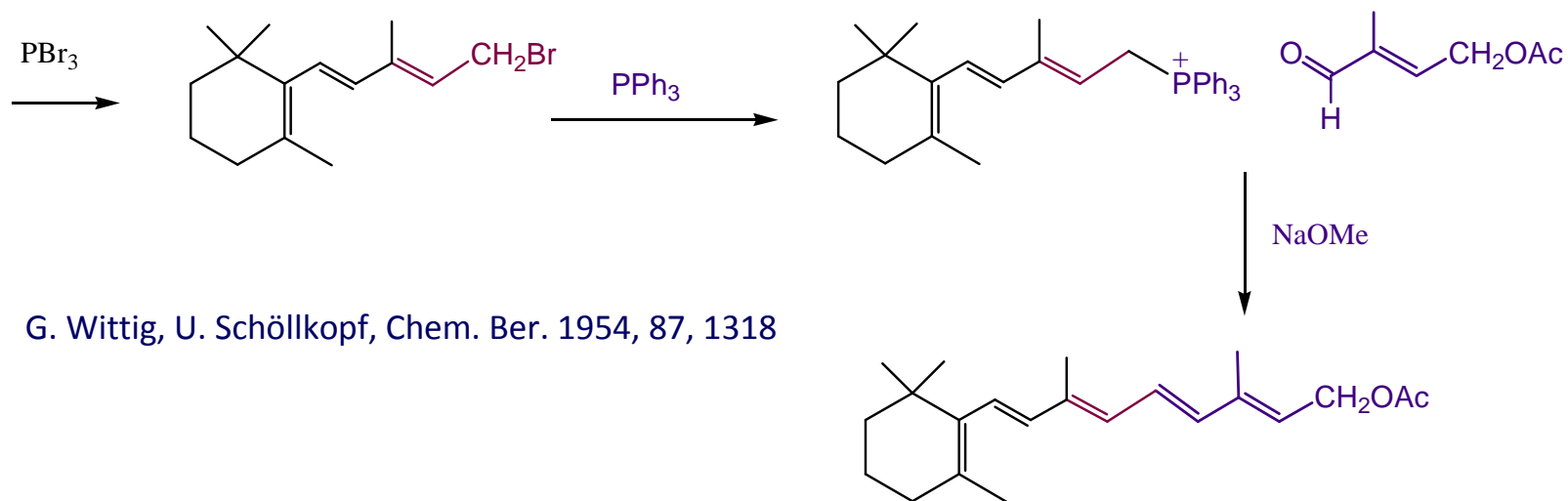


Naturstoffsynthese in den 60/70iger Jahren: Die technische Synthese von Vitamin A der BASF

Horst Pommer, *Angew. Chem.* **1960**, 72, 811-819



L. Horner, H. Hoffmann, H. G. Wippel, *Chem. Ber.* 1958, 91, 61;
Chem. Ber. 1958, 92, 2459

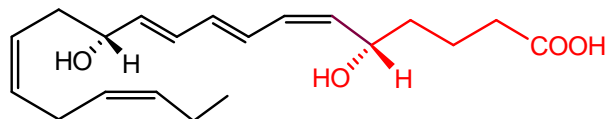


G. Wittig, U. Schöllkopf, *Chem. Ber.* 1954, 87, 1318

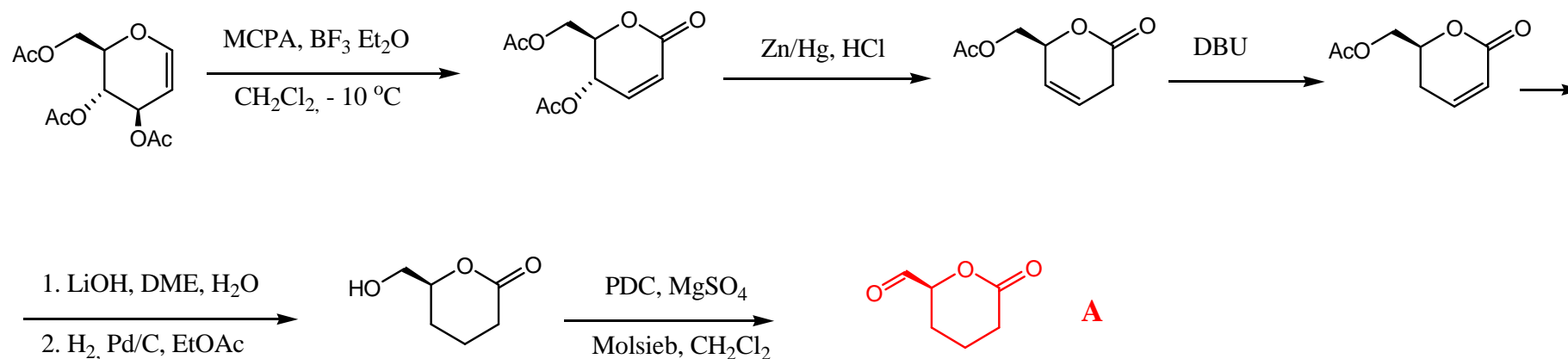
Vitamin A - Acetat

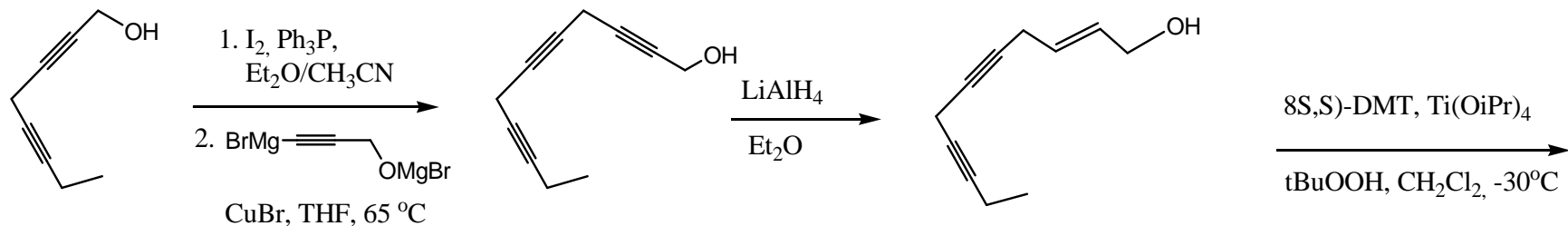
Methodisches Repertoire in der Organischen Chemie: Totalsynthese in den 80er Jahren

Leukotrien B5

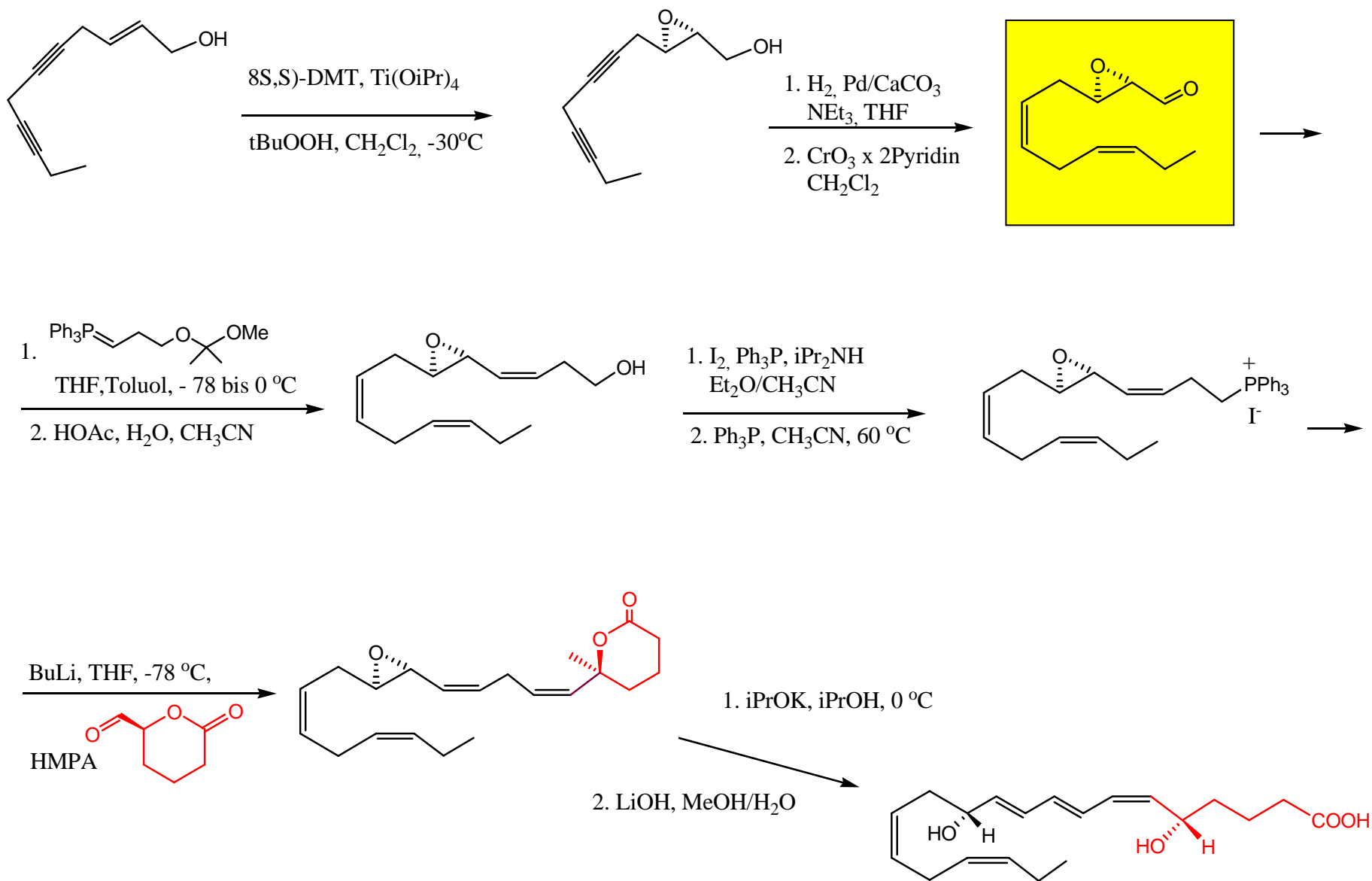


E. J. Corey, S. G. Pyne, W.-G. Su, *Tetrahedron Lett.* **1983**, 24, 4883





Methodisches Repertoire in der Organischen Chemie: Totalsynthese in den 80er Jahren



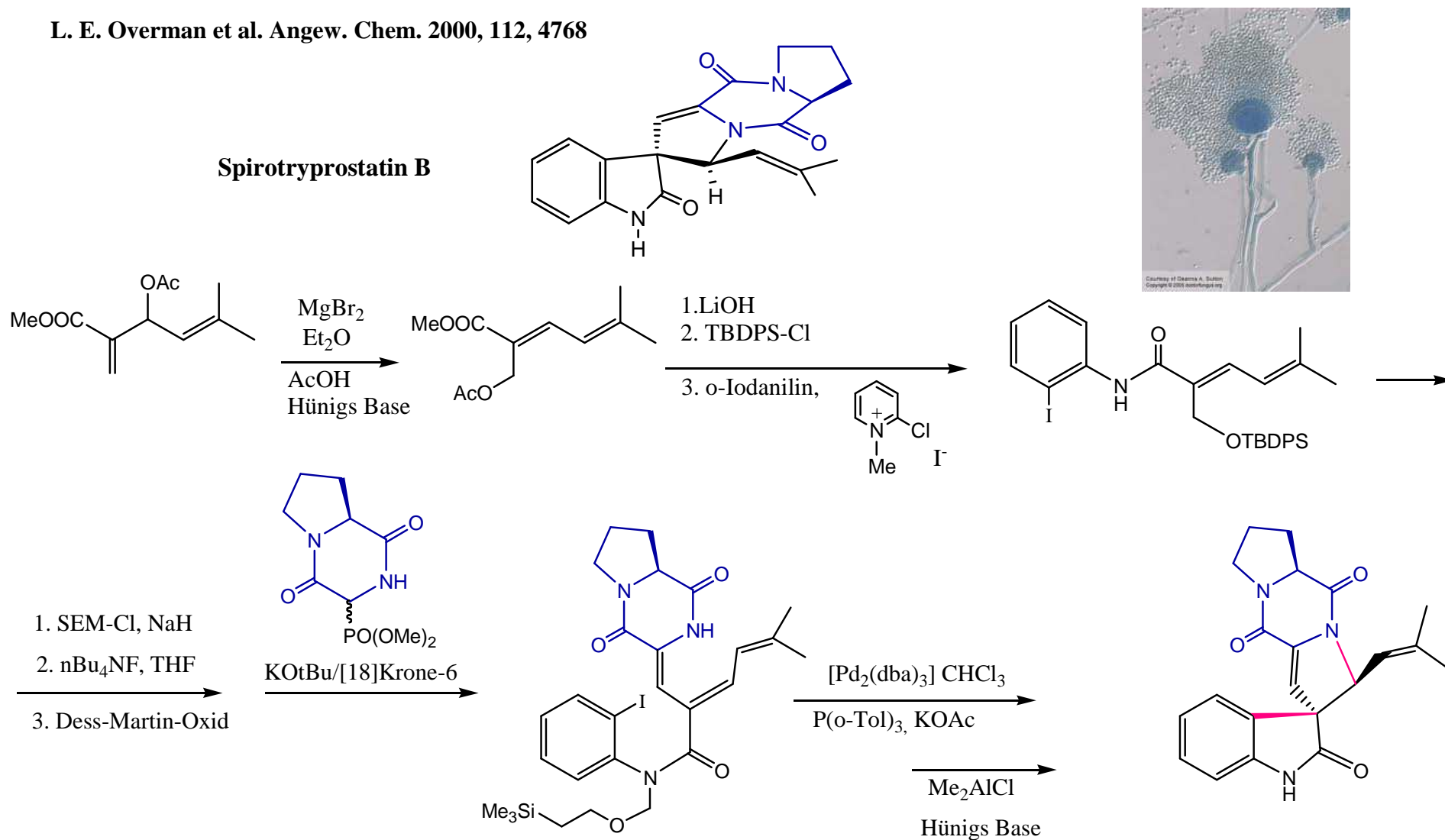
Methodisches Repertoire in der Organischen Chemie: Totalsynthese im neuen Millennium

Übergangsmetall-katalysierte C-C-Bindungen

Die Leistungsfähigkeit Palladium-katalysierter Kupplungen - ein Beispiel:

Aus der Totalsynthese von Spirotryprostatin B (Inhibitor der Zellproliferation [G2/M-Phase] aus *Aspergillus fumigatus*)

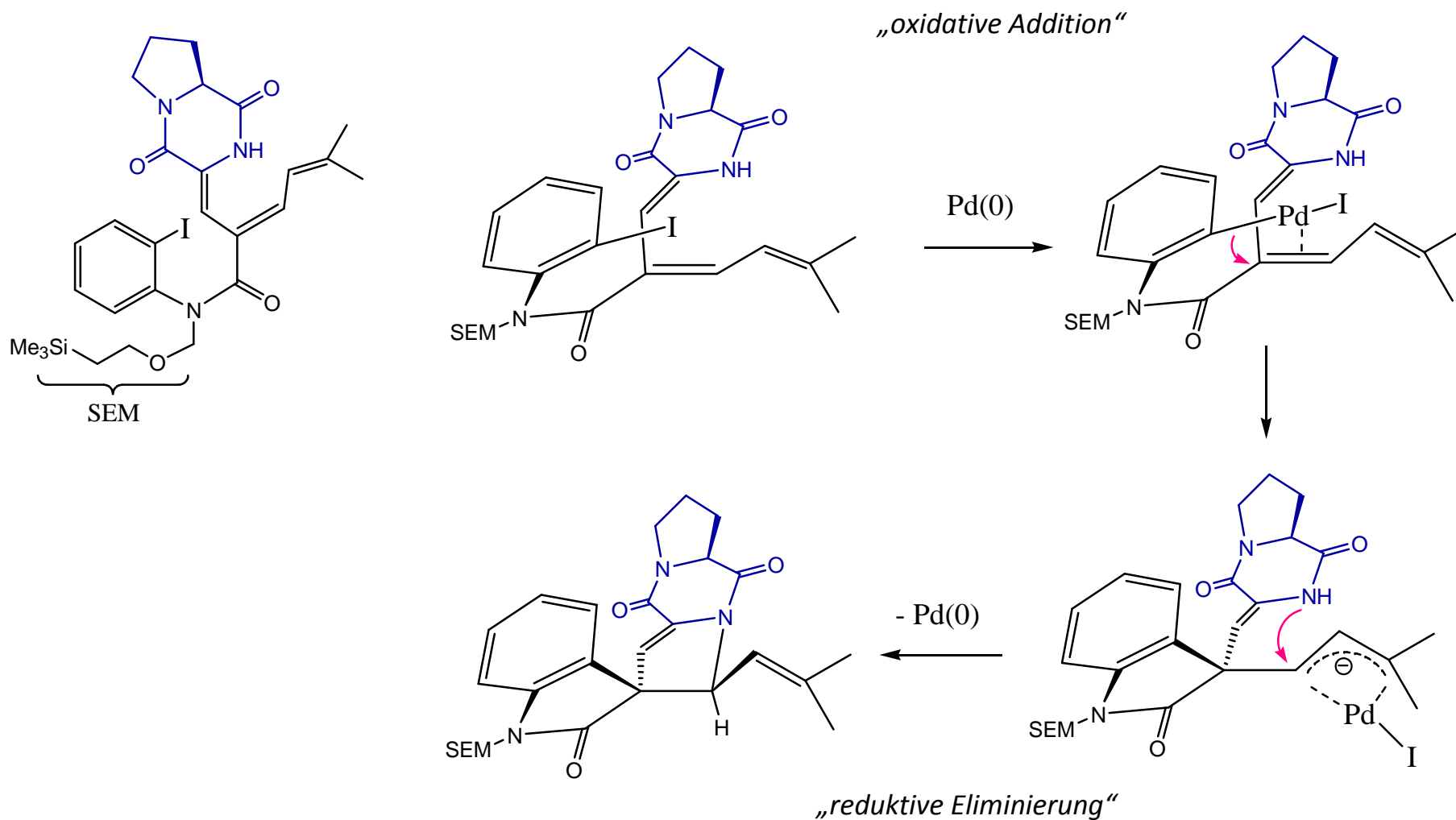
L. E. Overman et al. *Angew. Chem.* 2000, 112, 4768



Methodisches Repertoire in der Organischen Chemie: Totalsynthese im neuen Millennium

Übergangsmetall-katalysierte C-C-Bindungen

Deutung des Reaktionsablaufes der Pd-katalysierten Bildung des Spiropyrostatin-Gerüsts: **Heck-Reaktion**



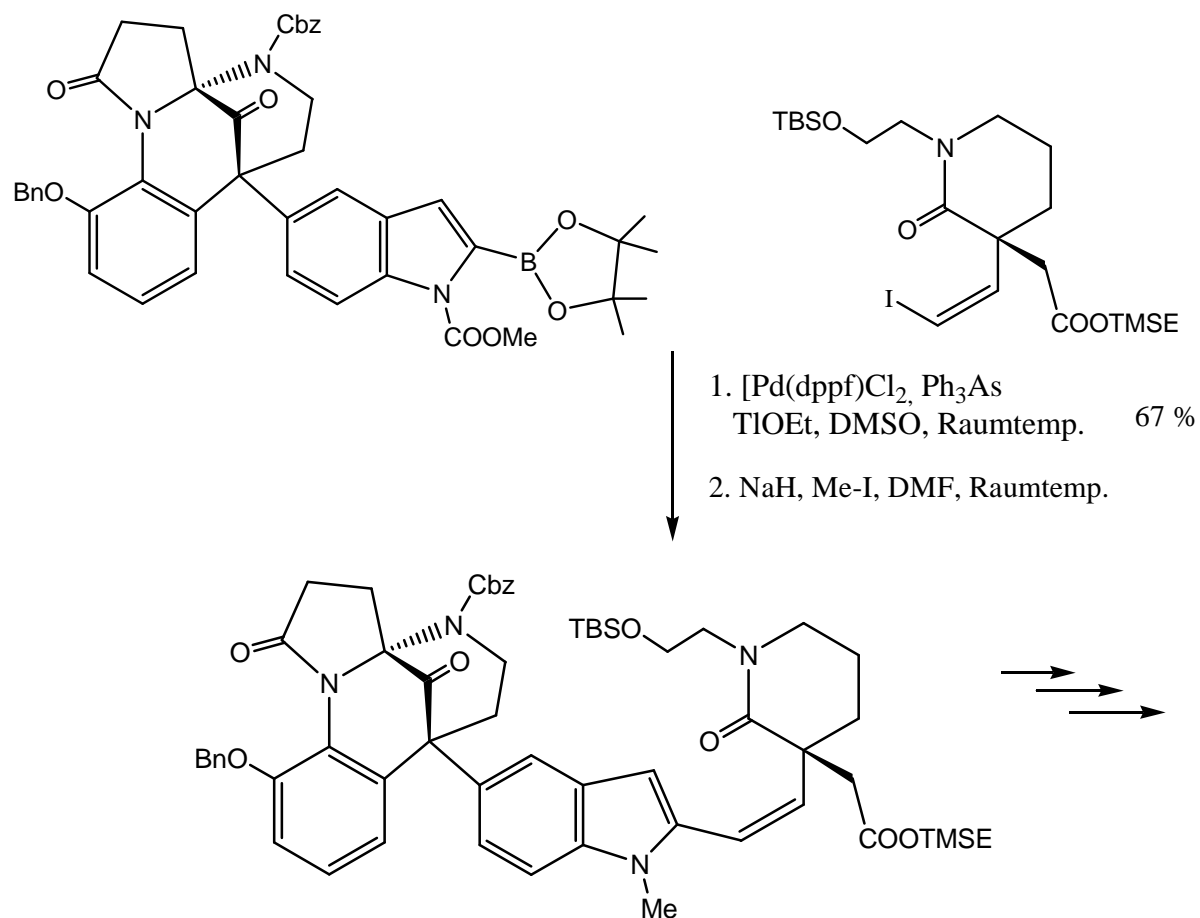
Methodisches Repertoire in der Organischen Chemie: Totalsynthese im neuen Millennium

Übergangsmetall-katalysierte C-C-Bindungen

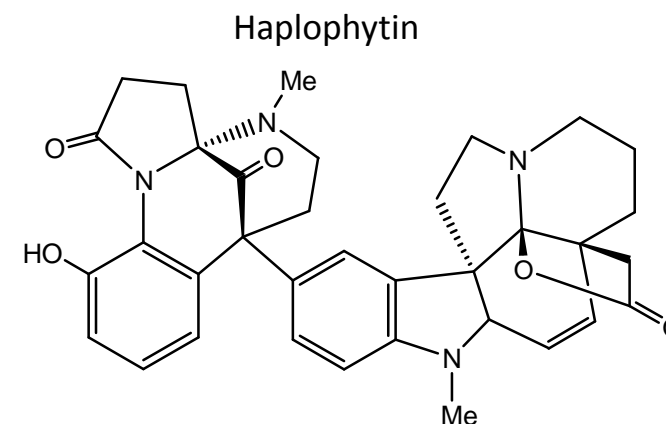
Die Leistungsfähigkeit Palladium-katalysierter Kupplungen - ein weiteres Beispiel:

Aus der Totalsynthese von Haplophytin (Natürliches Insektizid aus einer mexikanischen Wildblume)

K. C. Nicolaou et al. Angew. Chem. 2009, 121, 7752



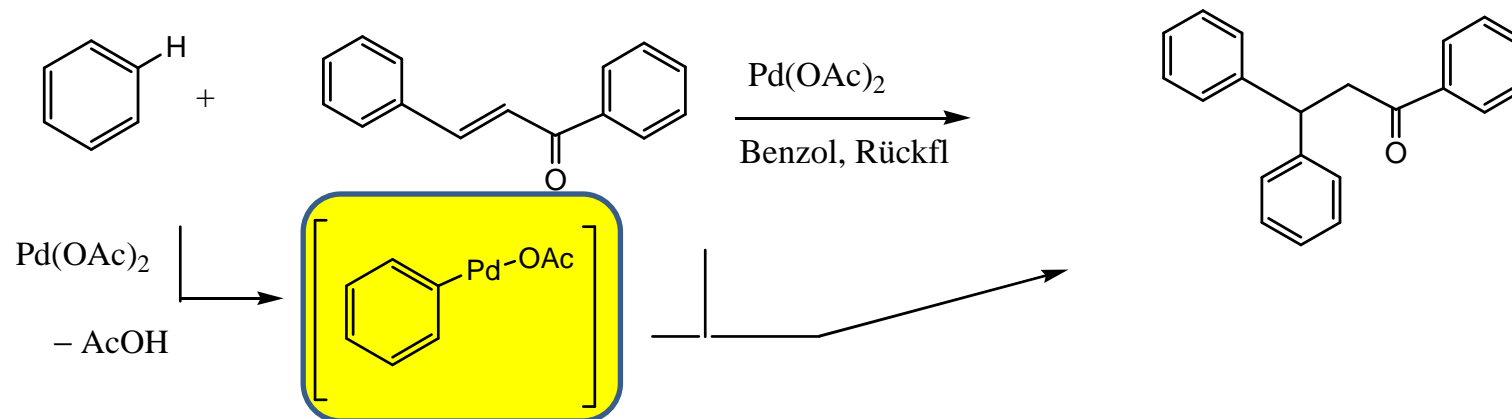
Suzuki-Reaktion



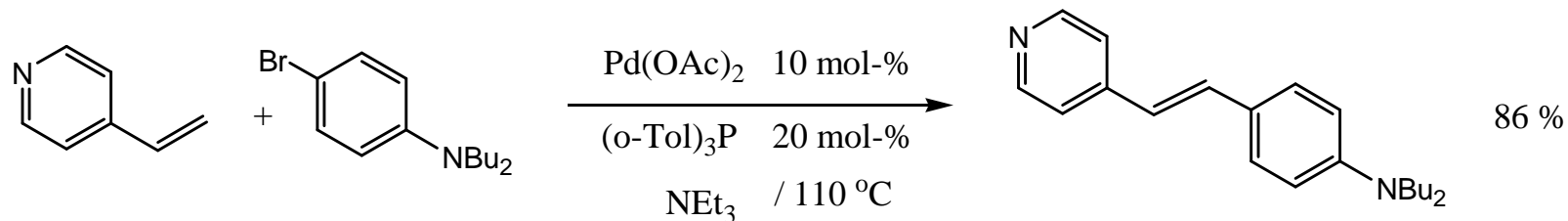
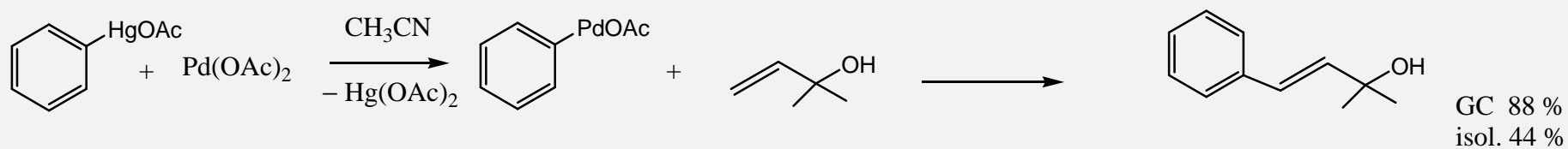
Palladium-katalysierte C-C-Bindungsbildungen - Die Heck-Reaktion

Die Anfänge:

Y. Fujiwara et al., Tetrahedron Lett. 1967, 1119



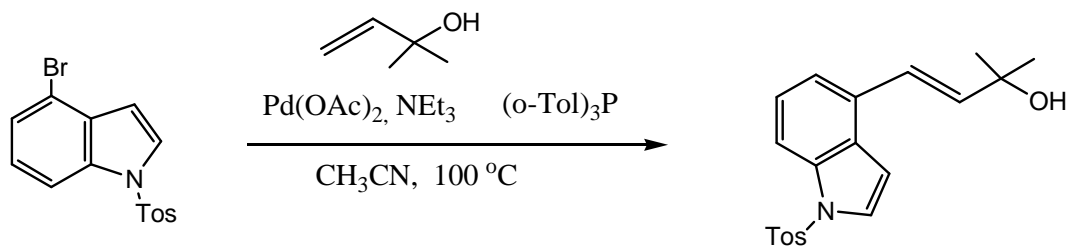
R. F. Heck, J. Am. Chem. Soc. 1968, 90, 5518, 5535, J. Am. Chem. Soc. 1969, 91, 6707



A. Hassner et al. J. Org. Chem. 1984, 49, 2546

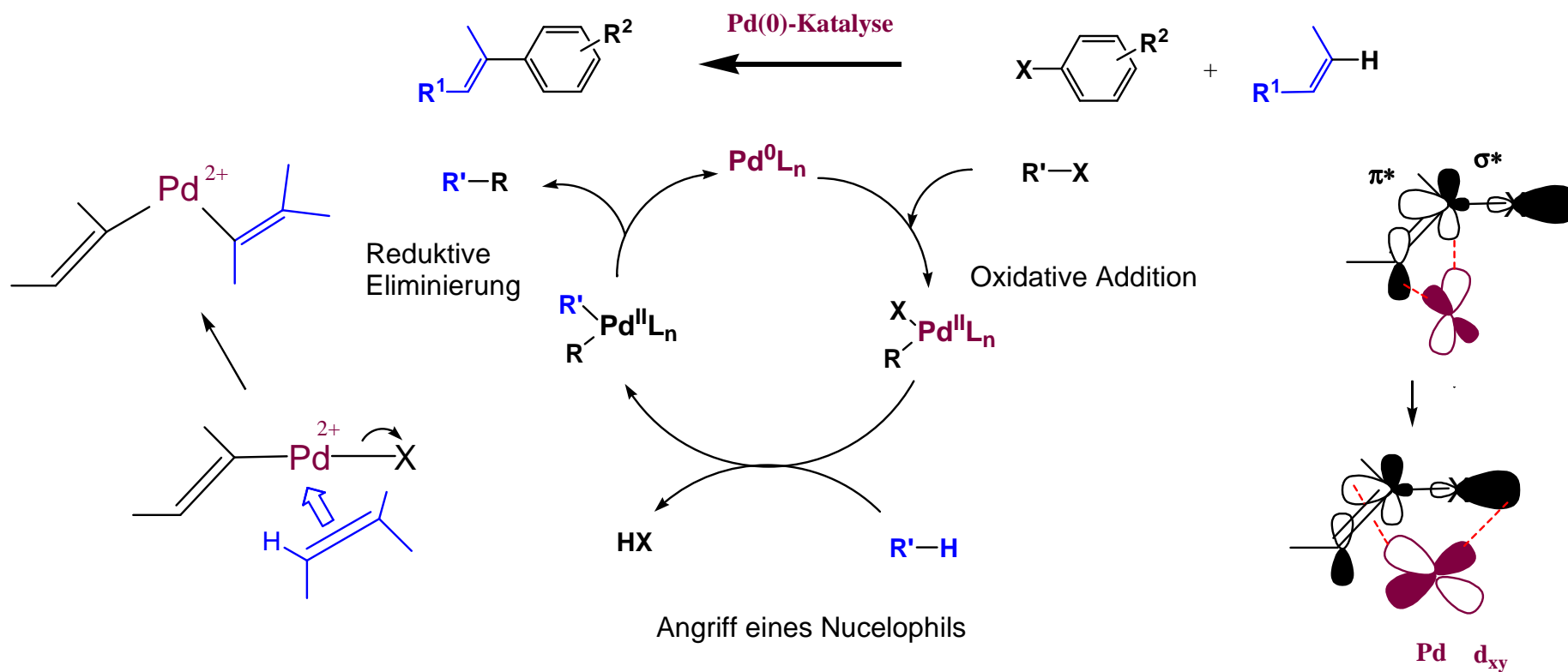
Mechanismus der Heck-Reaktion

Beispiel



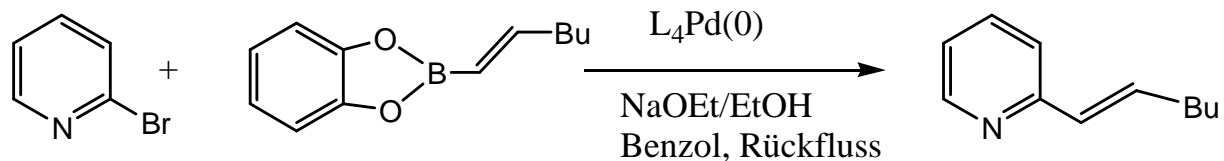
L. S. Hegedus et al.
J. Org. Chem. 1984, 49, 2657

Mechanismus der Pd(0)-katalysierten Kupplungen



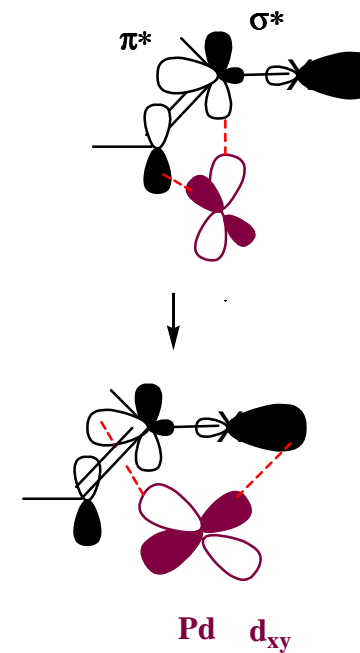
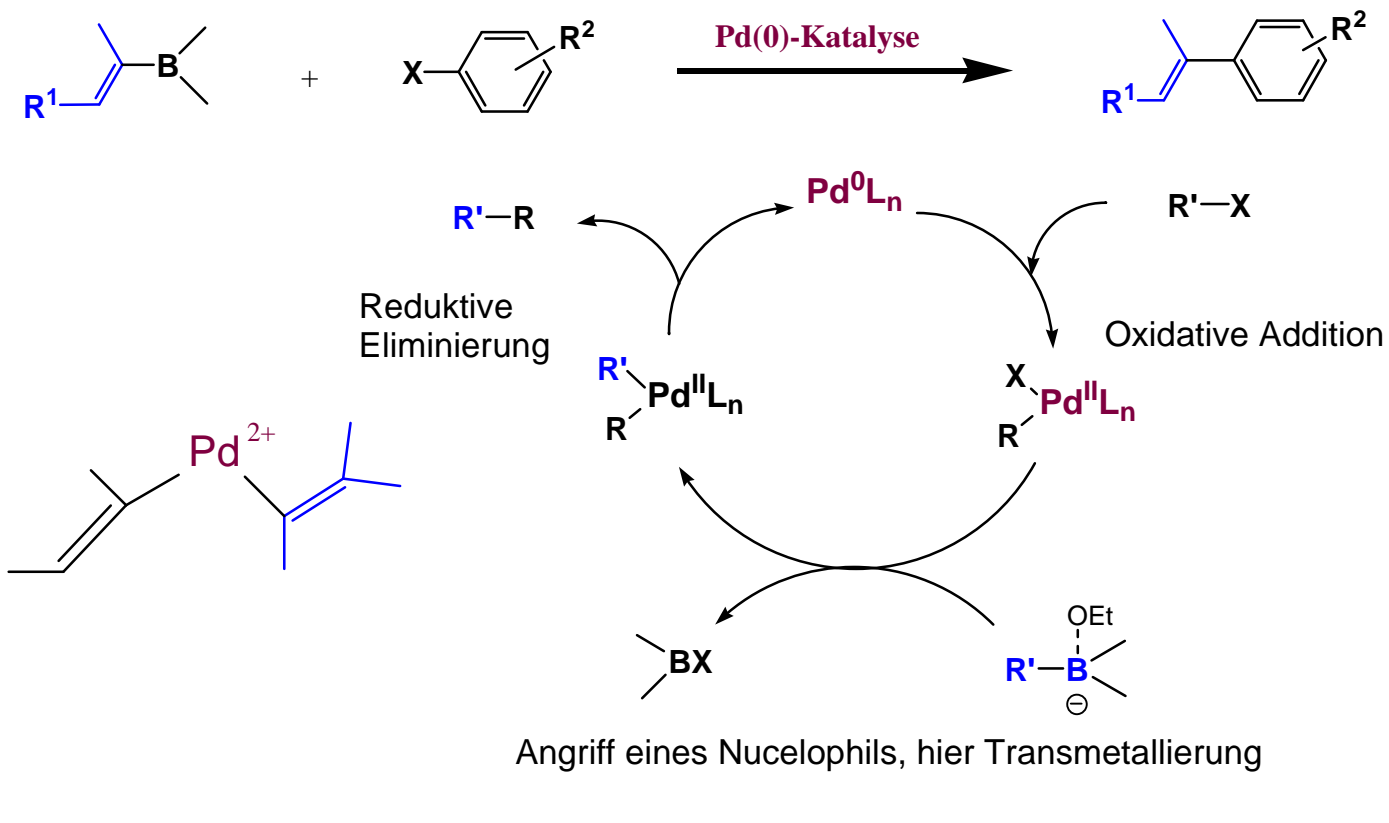
Organometall-Verbindungen als Nucleophil: z. B. die Suzuki-Kupplung

Beispiel

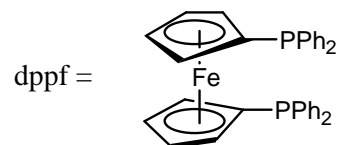
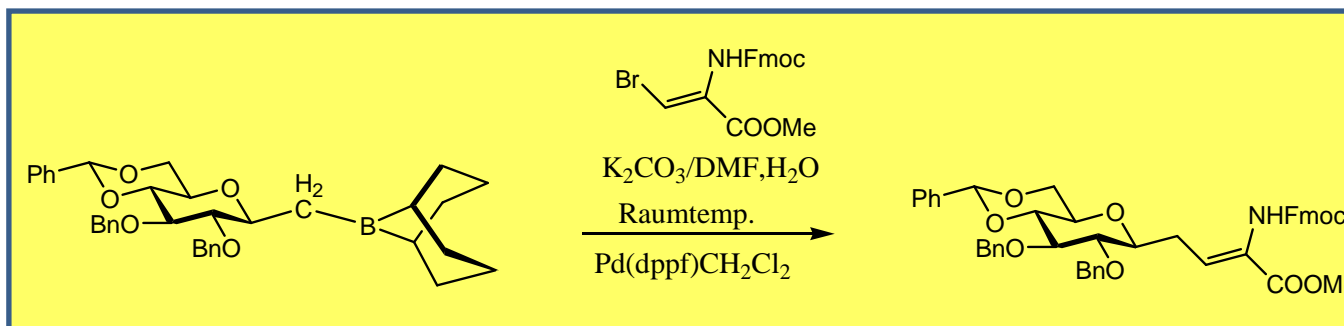
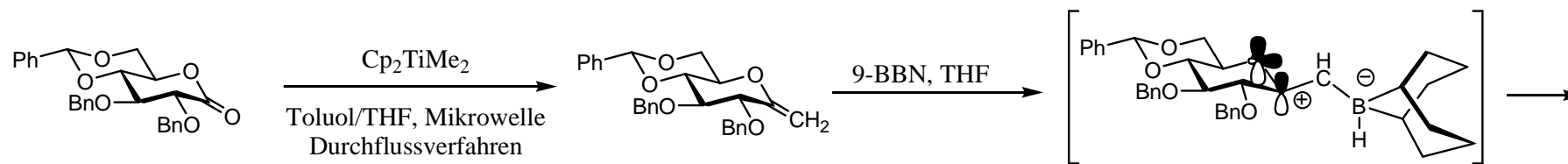


N. Miyaura, K. Maeda, H. Suginome, A. Suzuki, J. Org. Chem. **1982**, 47, 2117

Mechanismus der Pd(0)-katalysierten Kupplungen mit Organometallverbindungen

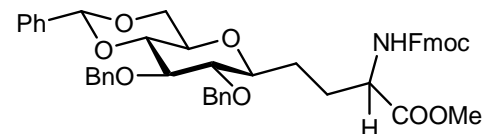


**Pd(0)-katalysierte Kupplung mit Alkylboranen als metallorganischen Komponenten
Suzuki-Miyaura-Reaktion**



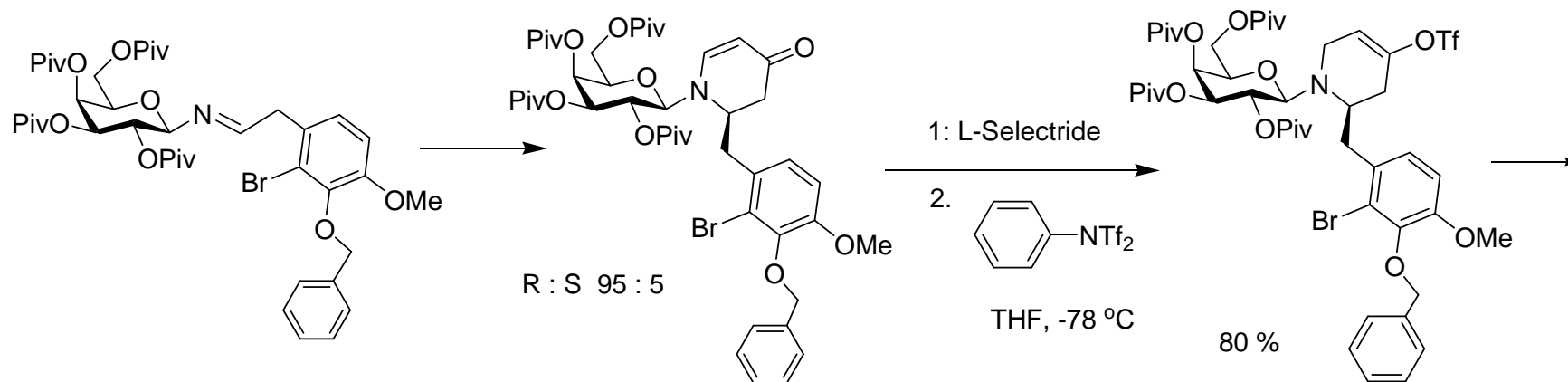
(R)-Tol-BINAP,
[Rh(COD)₂]Cl₂,
H₂ (25 bar), THF

85%, nur ein Diastereomer

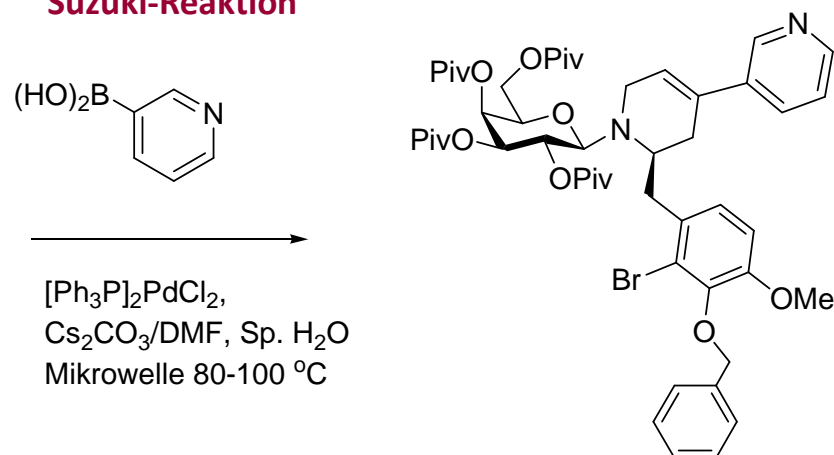


Stereoselektive Synthese von Benzomorphanen

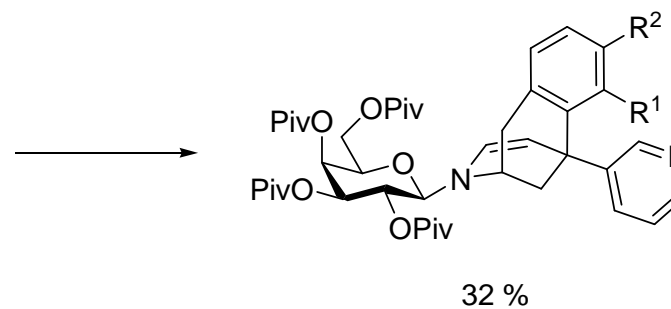
Eine Domino-Sequenz aus Suzuki- und Heck-Kupplung



Suzuki-Reaktion



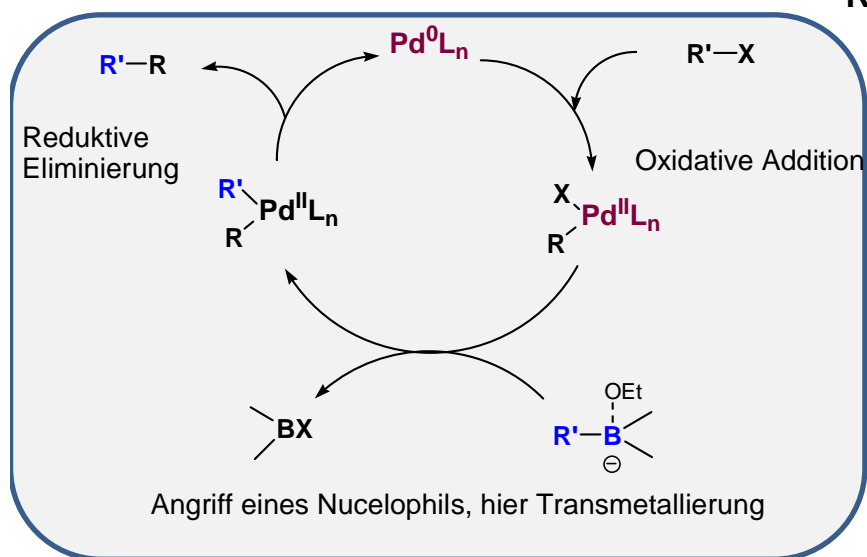
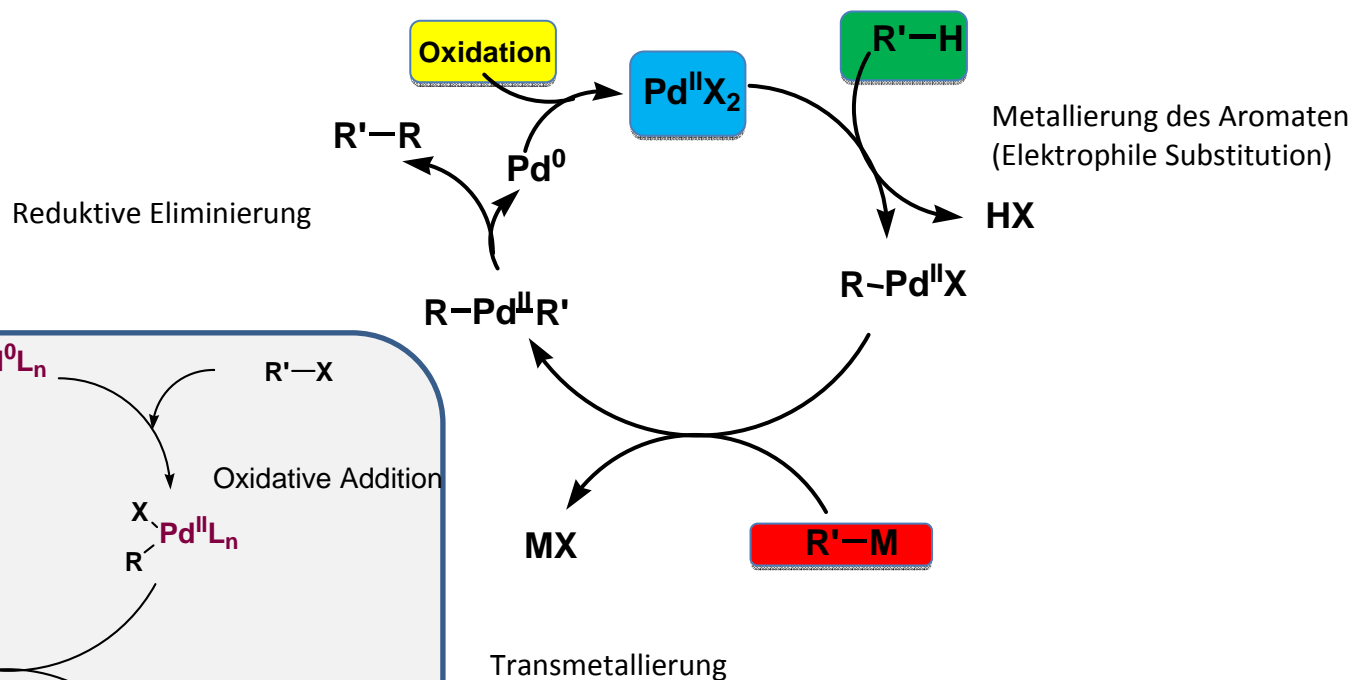
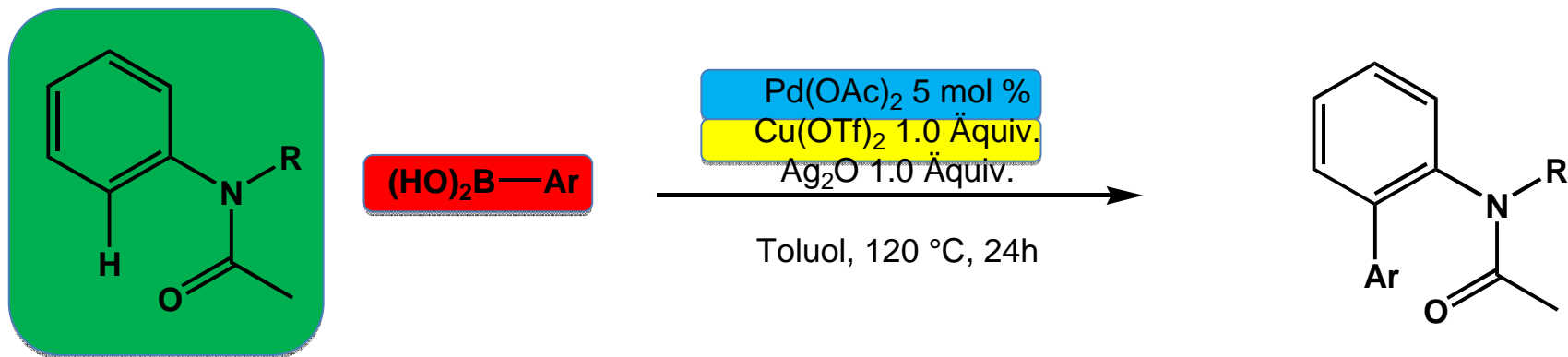
Heck-Reaktion



Stefan Knauer 2005

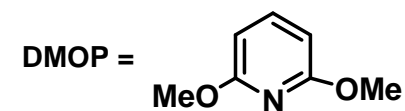
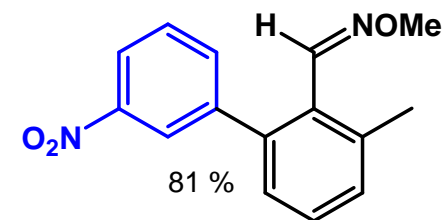
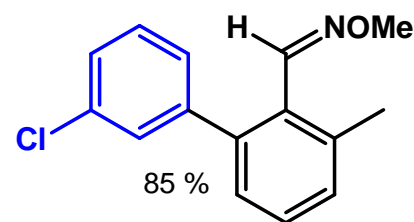
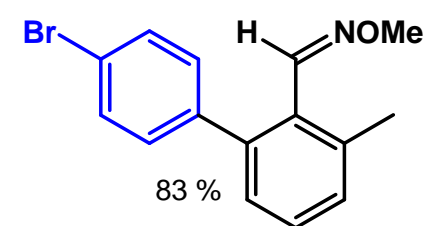
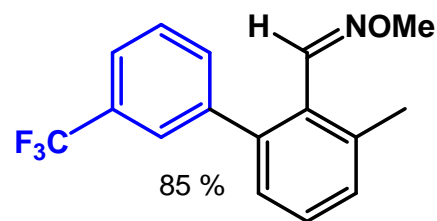
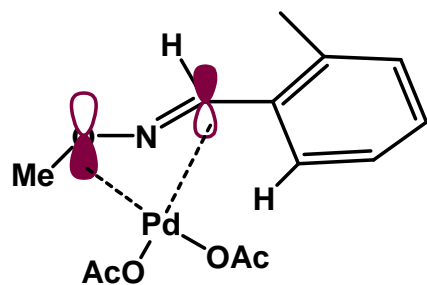
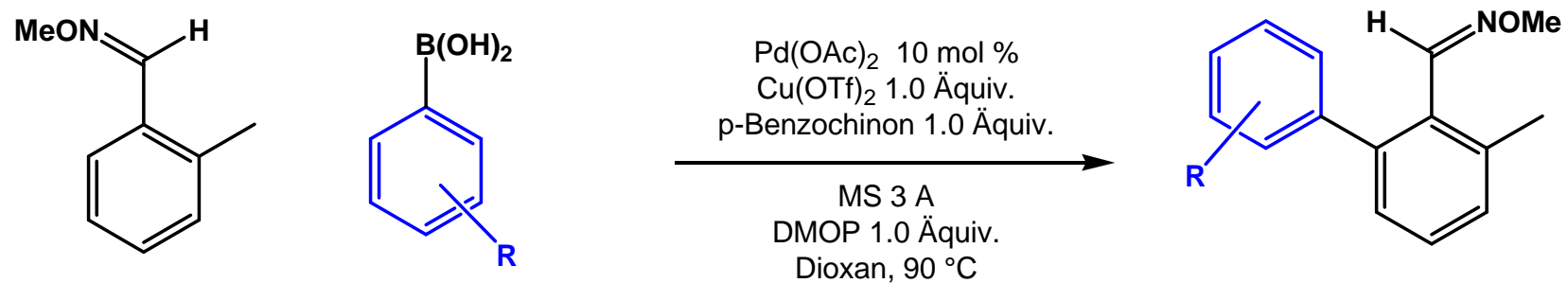
Angew. Chem. **2006**, 118, 2685

Metallorganyl und CH-Bindung

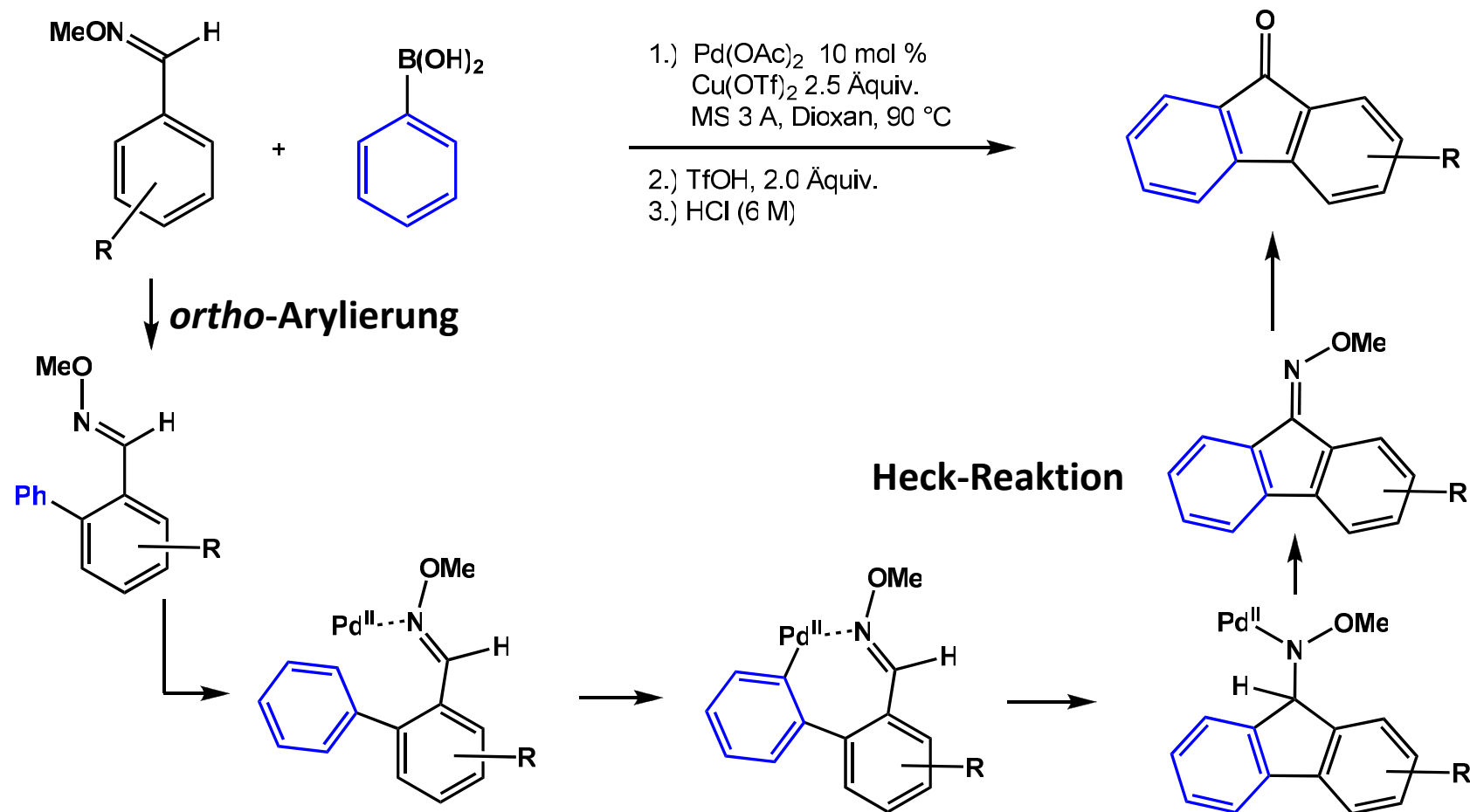


Z. Shi et al. J. Am. Chem. Soc. 2006, 128, 7416

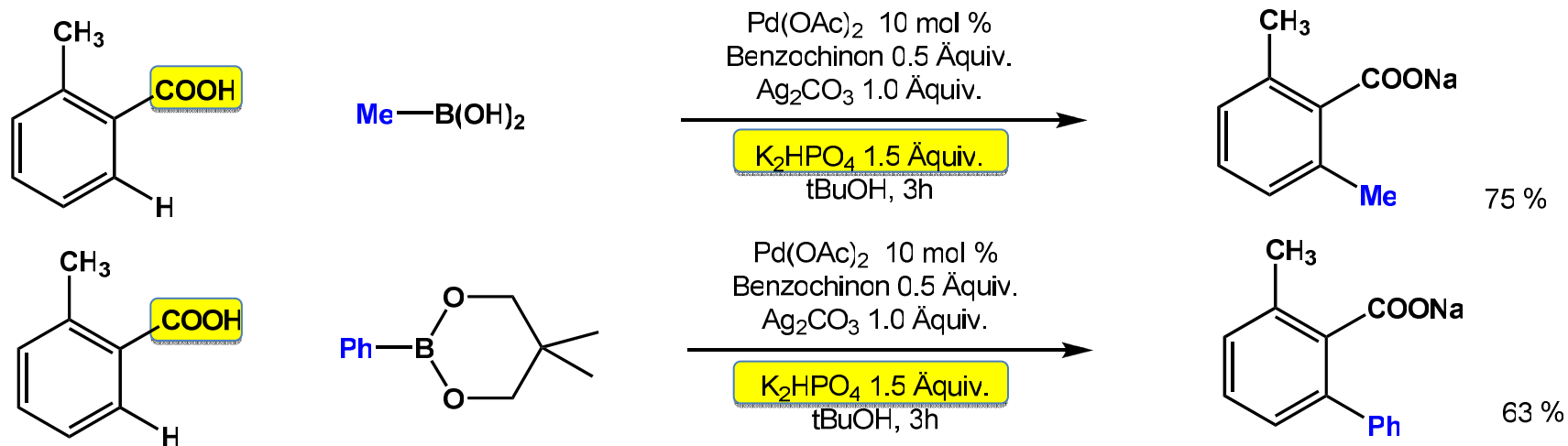
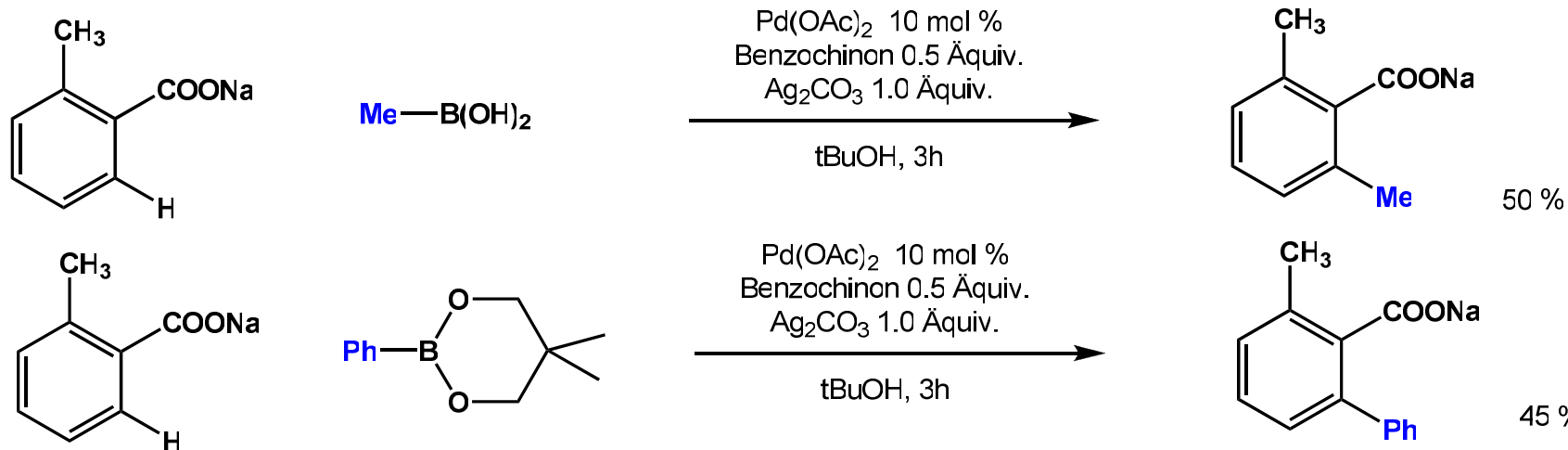
ortho-Arylierung von O-Methyl-Oximen



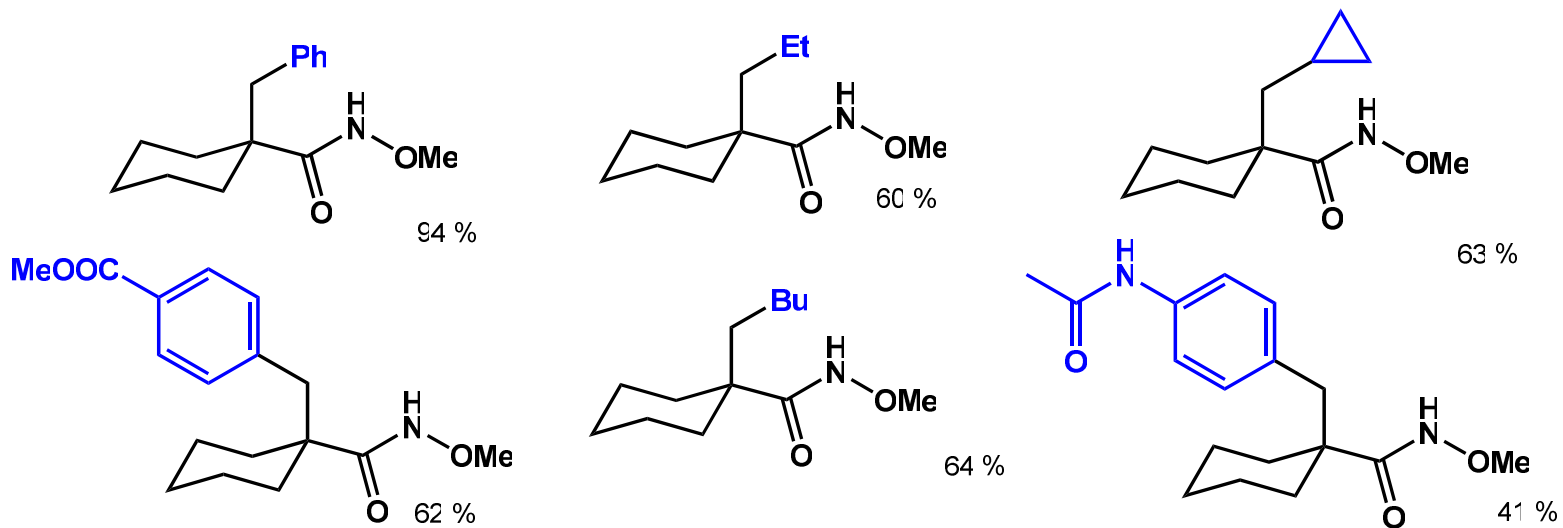
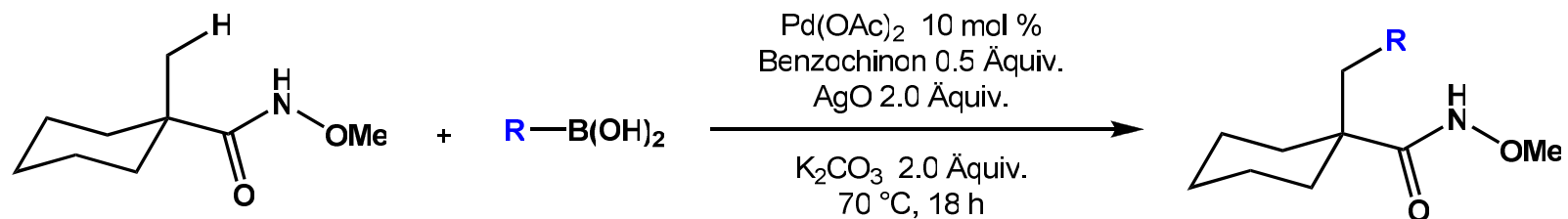
Eintopfreaktion zu substituierten Fluorenonen



Dirigierende Säurefunktion

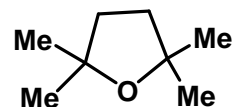


Alkylierung und Arylierung von aliphatischen O-Methyl-Hydroxamsäuren



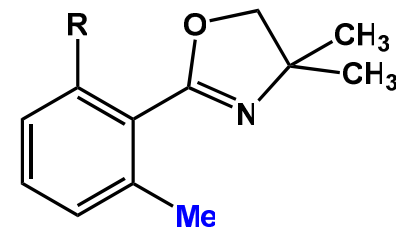
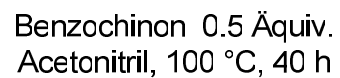
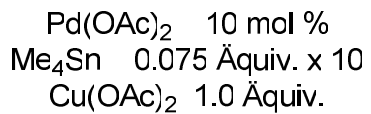
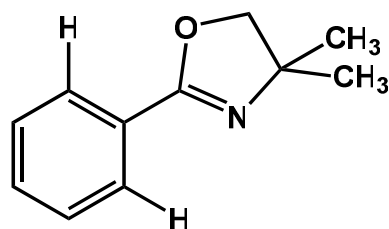
Lösungsmittel für die Kupplung der Arylboronsäuren: tBuOH

für die Kupplung der Alkylboronsäuren:

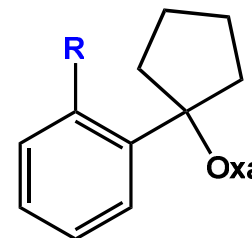
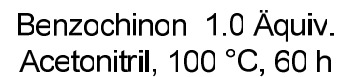
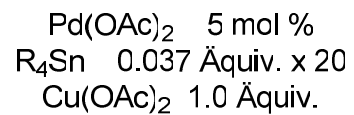
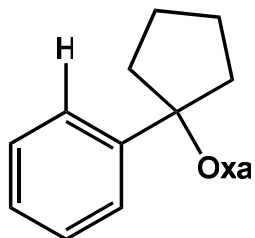


J.-Q. Yu, J. Am. Chem. Soc. 2008, 130, 7190

Zinnorganyle als Kupplungspartner



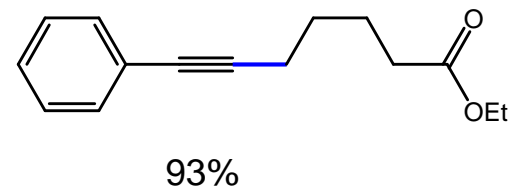
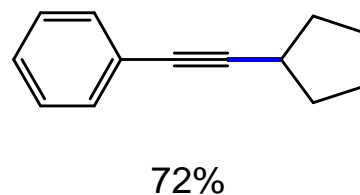
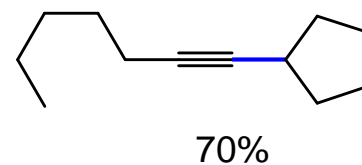
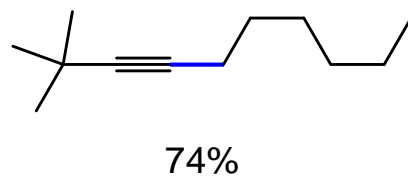
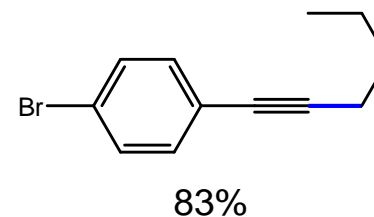
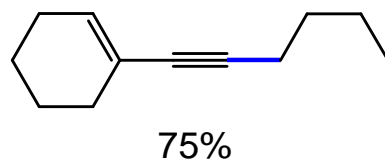
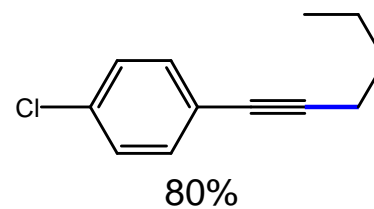
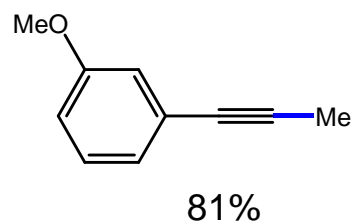
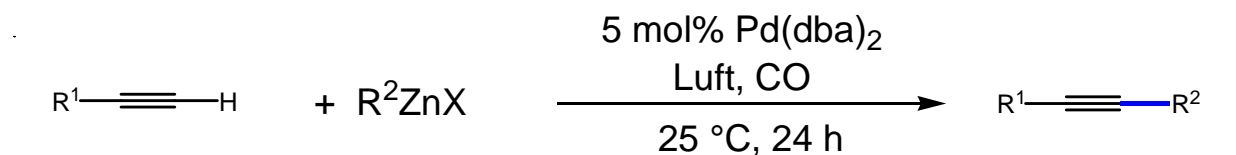
R = H, 20 % + R = Me, 64 %



R = Me, 71 %
Et, 79 %
Pr, 82 %
Bu, 75 %
Oct, 83 %

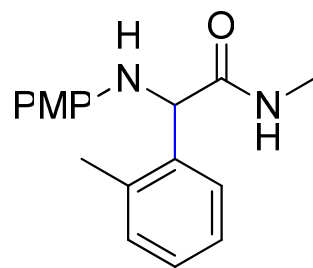
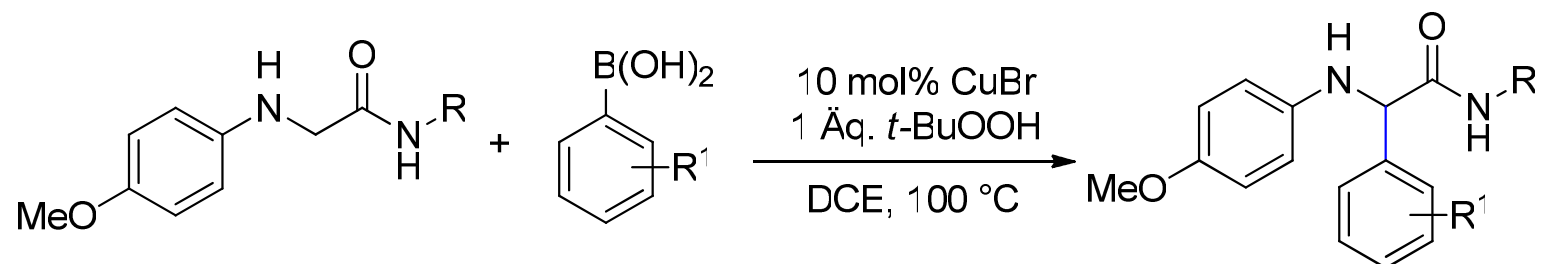
C-C-Bindungsknüpfung zwischen Metallorganyl und CH-Verbindungen

Kupplung von terminalen Alkinen mit Alkyl-Metall-Verbindungen (Zinkorganyle)

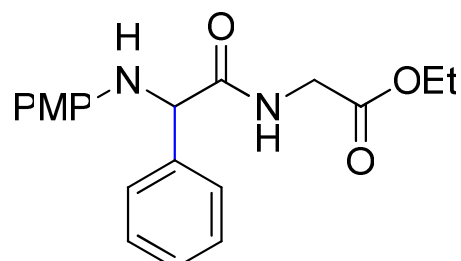


Kreuzkupplungen: C-C-Bindungsknüpfung: Metallorganyl mit CH-Verbindungen

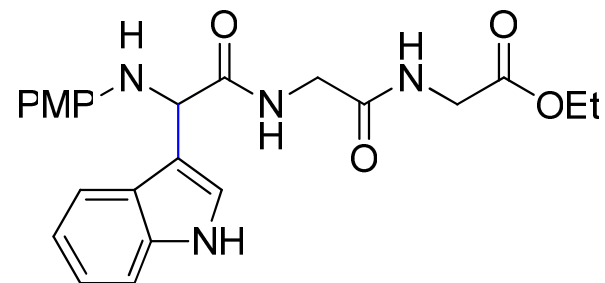
Kupplung von Alkylaminen mit Bororganyle



82 %



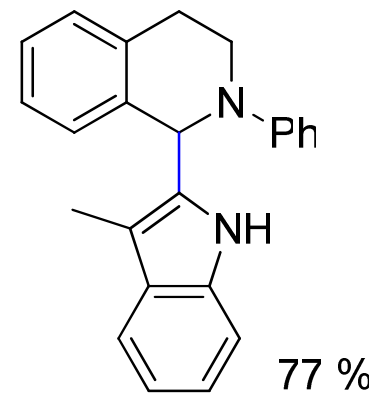
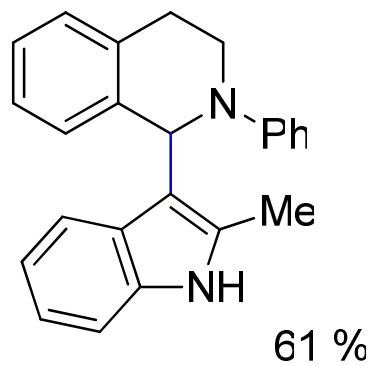
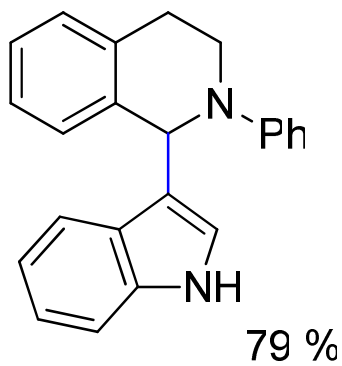
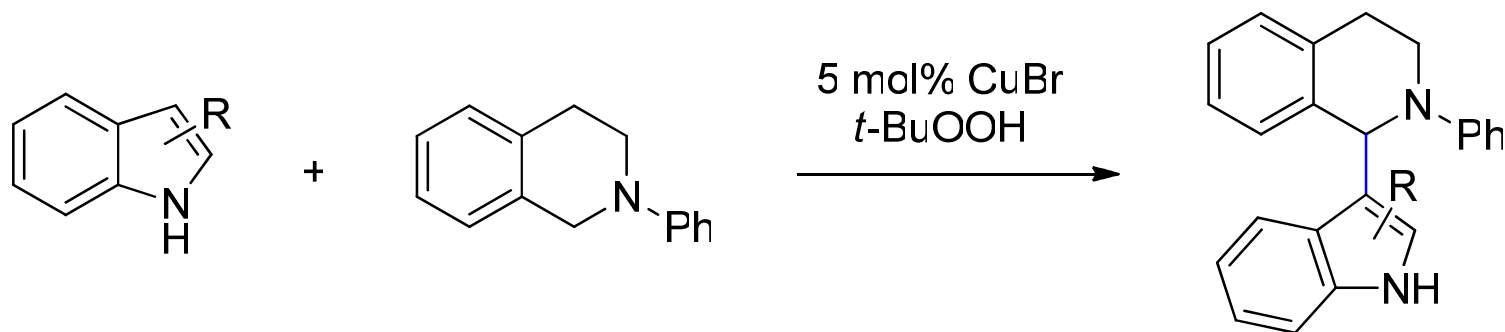
94 %



89 %

Kreuzkupplungen: C-C-Bindungsknüpfung: Kupplung zweier CH-Verbindungen

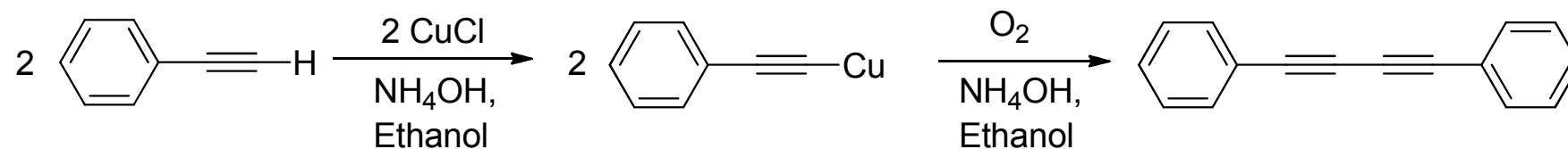
Kupplung von Alkylaminen mit elektronenreichen Aromaten



C-C-Bindungsknüpfung zwischen zwei Alkinen - Glaser-Kupplung

Die Kupplung zweier terminale Alkine:

Die Kupplung nach Glaser (1869) liefert symmetrische konjugierte Bis-acetylene

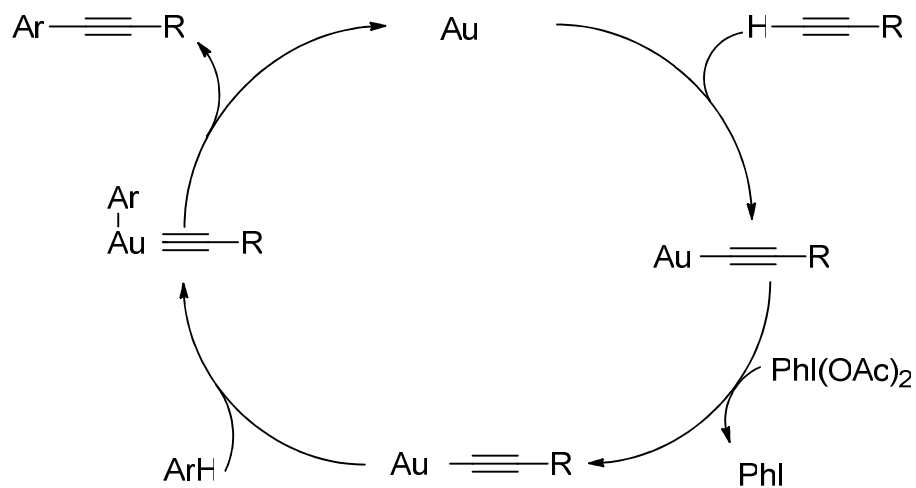
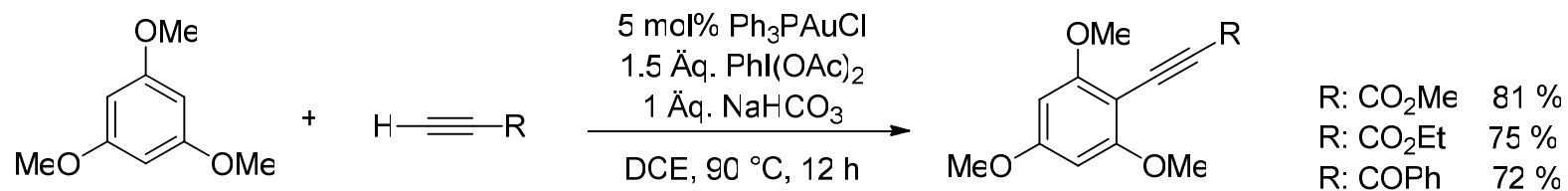


C. Glaser, *Ber. Dtsch. Chem. Ges.* **1869**, 2, 422–424.

C. Glaser, *Ann. Chem. Pharm.* **1870**, 154, 137–171.

C-C-Bindungsknüpfung zwischen zwei CH-Verbindungen

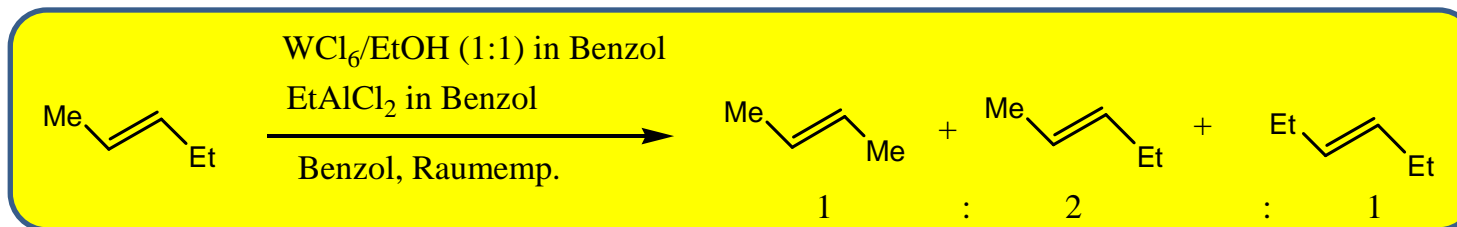
Kupplung von Aromaten mit terminalen Alkinen unter Gold-Katalyse und oxidativen Bedingungen



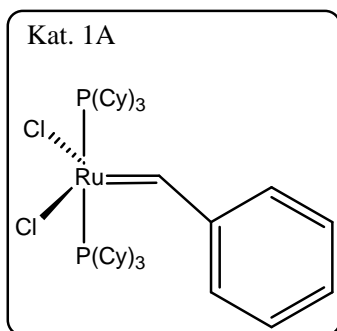
Metathese: Eine sanfte Umwandlung von stabilen Alkenen

Die Anfänge: S. E. Bresler, J. I. Mosevitskii, I. Ya. Poddubnyi Shi Guan-I, Dokl. Akad. Nauk USSR 1960, 134, 117

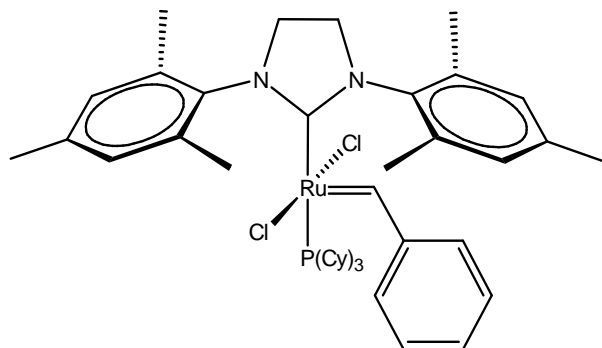
N. Calderon, H. Y. Chen, K. W. Scott, Tetrahedron Lett. 1967, 3327



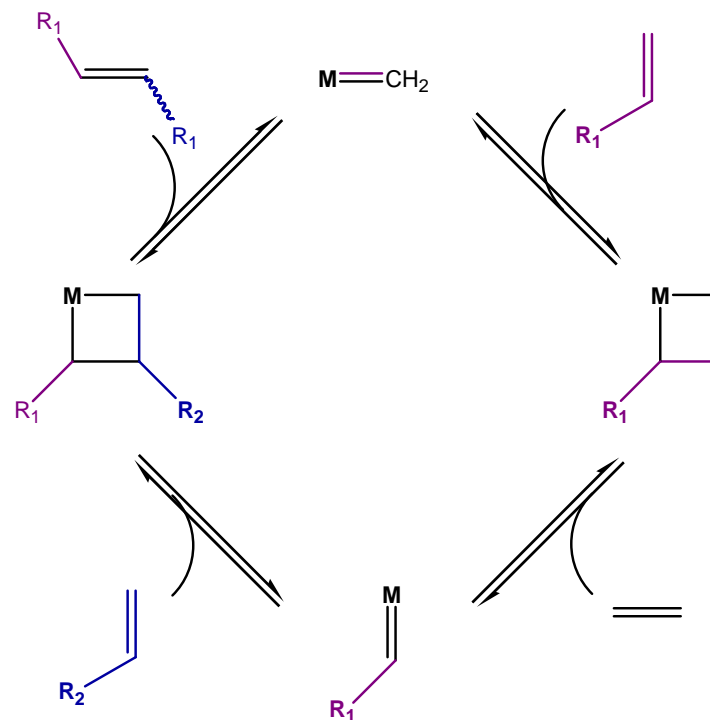
Grubbs I



Grubbs II



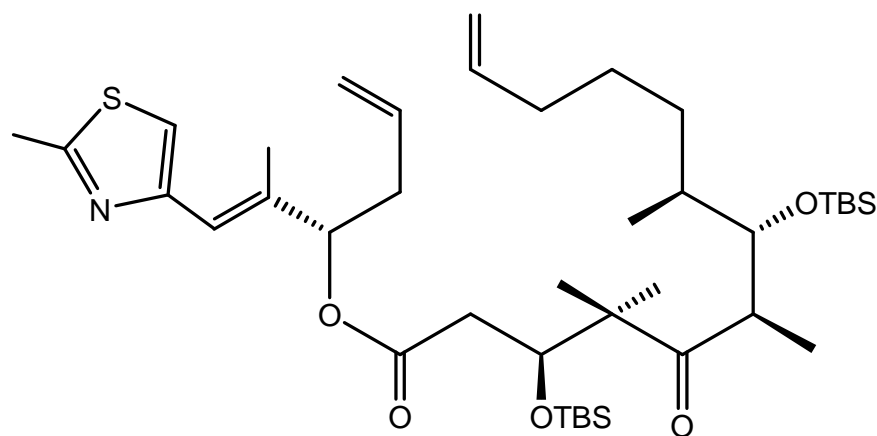
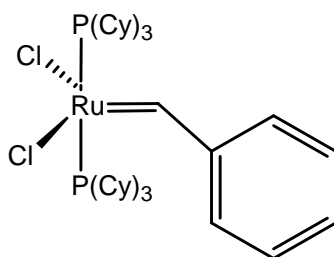
Der Mechanismus nach Chauvin



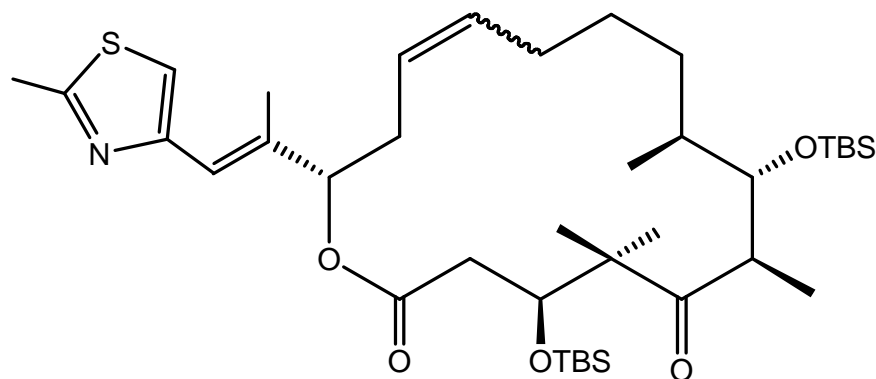
Ringschluss-Metathese in der Naturstoff-Totalsynthese: Epothilon A

D. Schinzer, A. Limberg, A. Bauer, O. M. Boehm, M. Cordes
Angew. Chem. **1997**, *109*, 543

Grubbs I



Grubbs I
CH₂Cl₂
Raumtemp., 12 h
94 %

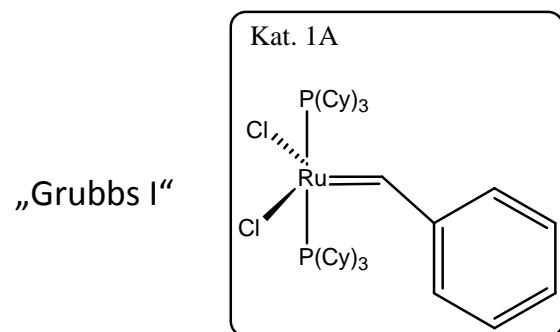
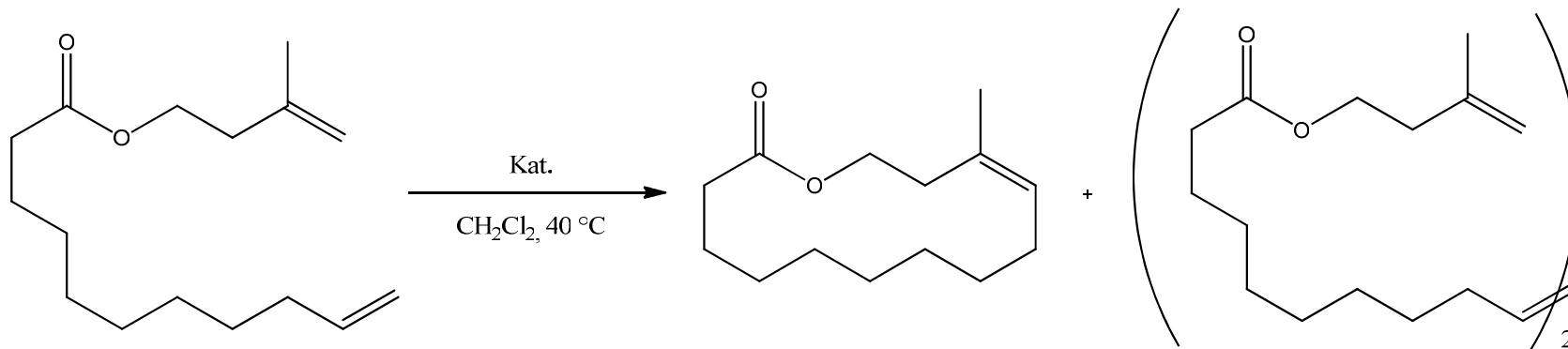


geschützte Form von
Epothilon C

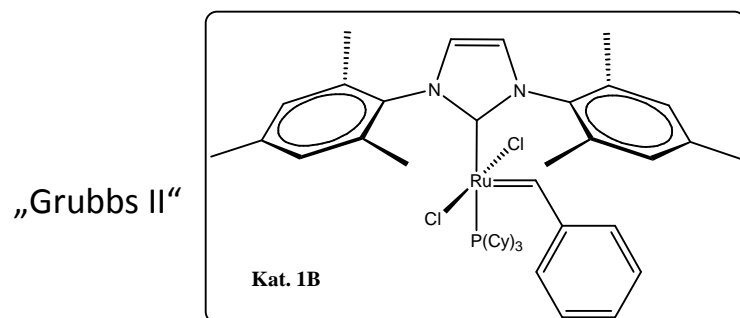
Dimethyldioxiran

Epothilon A

Ringschluss-Metathese: Einfluss des Katalysators auf Cyclisierung vs. Dimerisierung

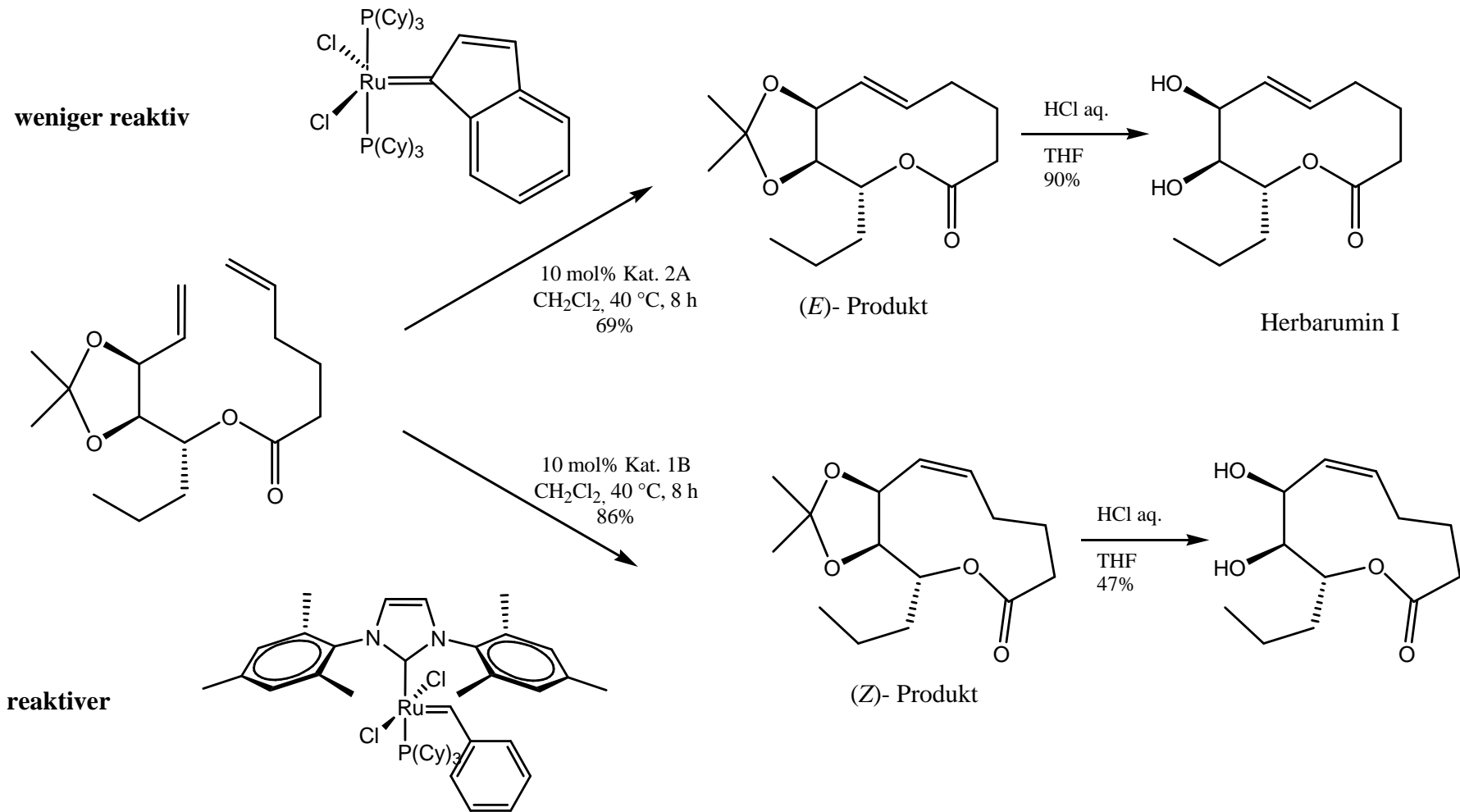


Katal.	Makrolacton	Dimer
10 mol%	--	79 %

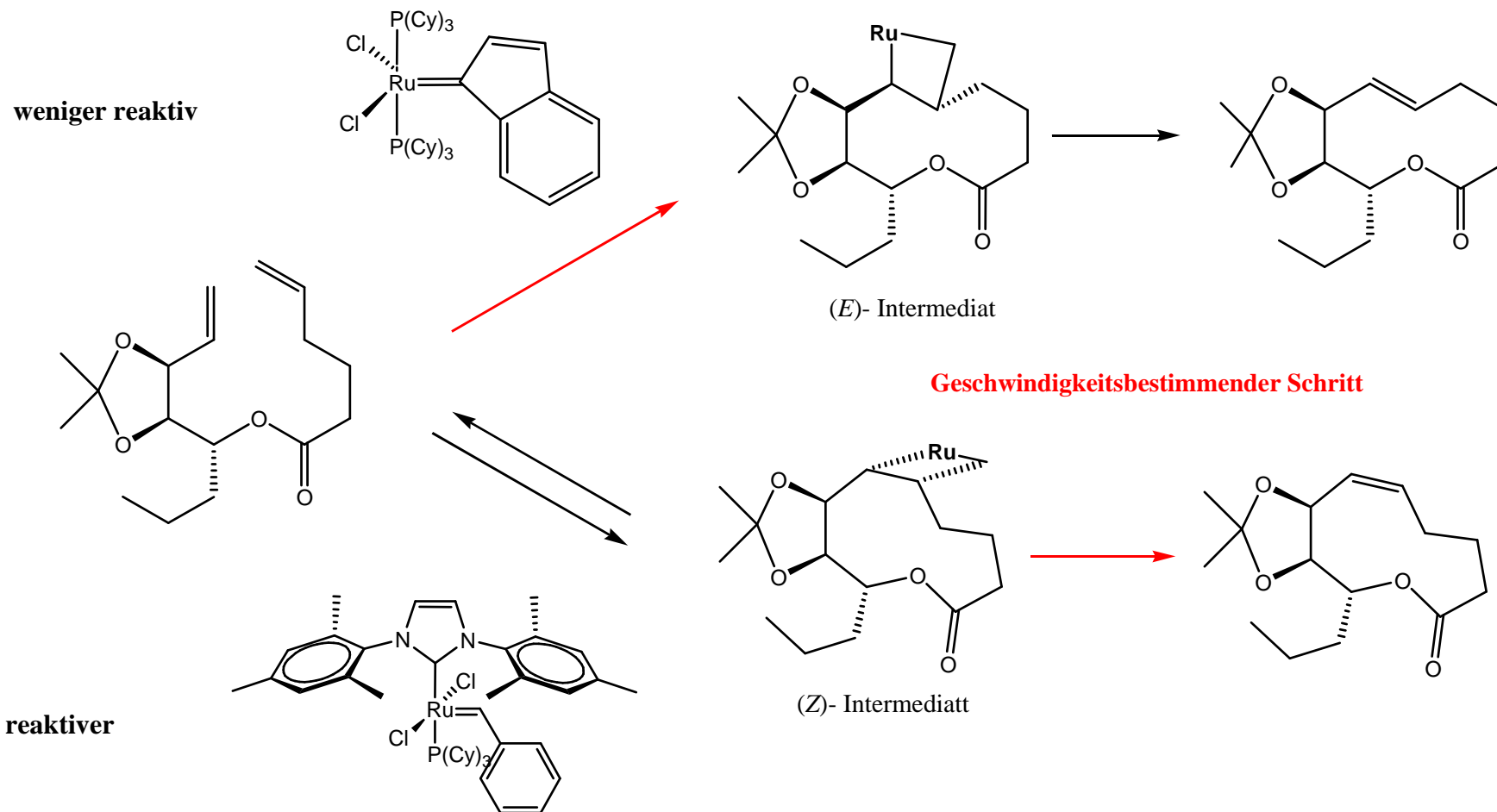


10 mol%	65 %	--
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Ringschluss-Metathese: Einfluss des Katalysators auf cis/trans-Diastereoselektivität

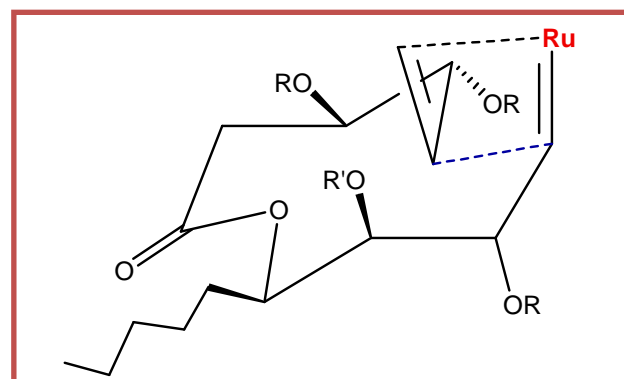
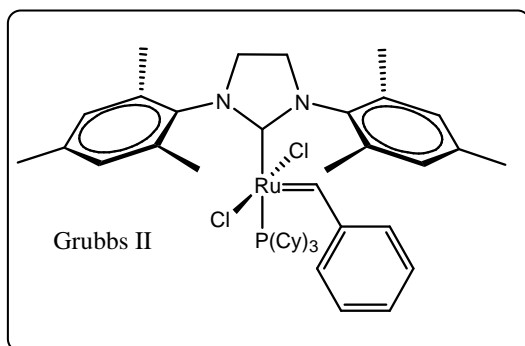
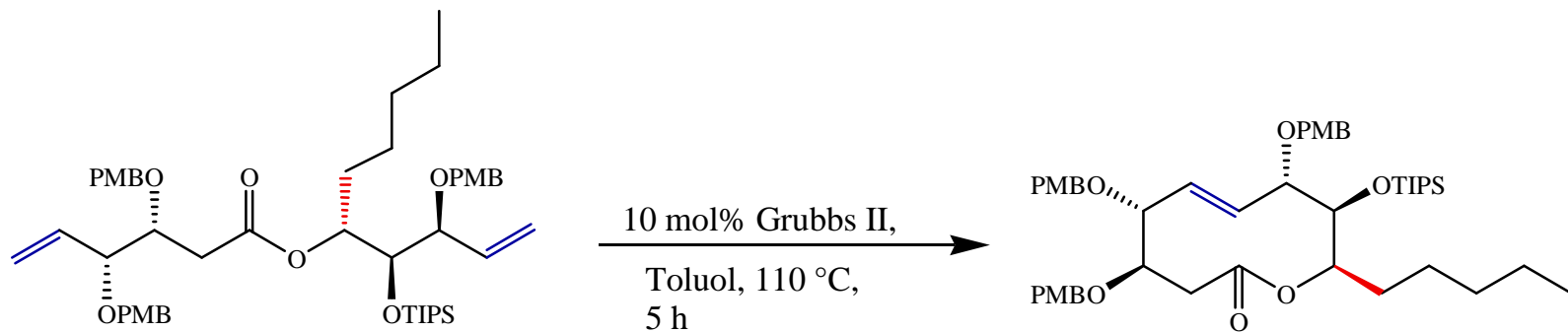
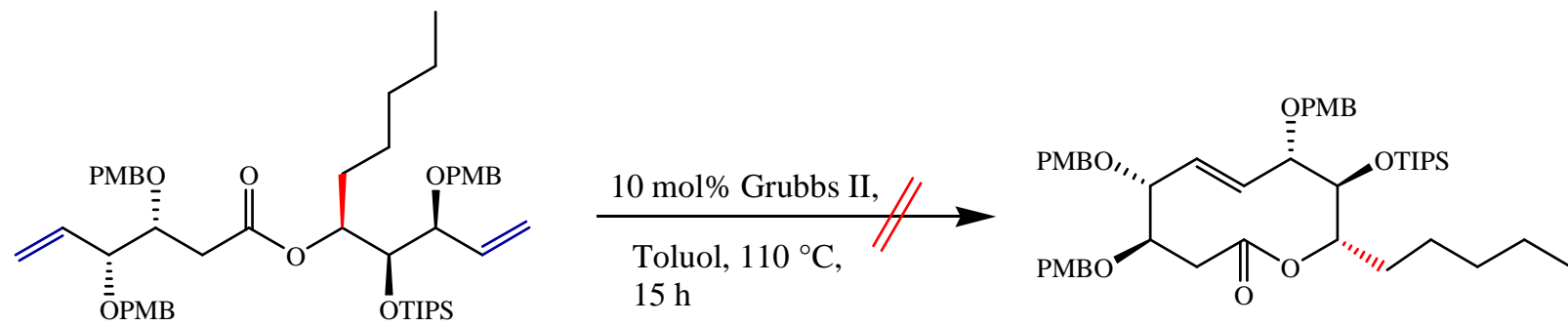


Ringschluss-Metathese: Bicyclische Intermediate



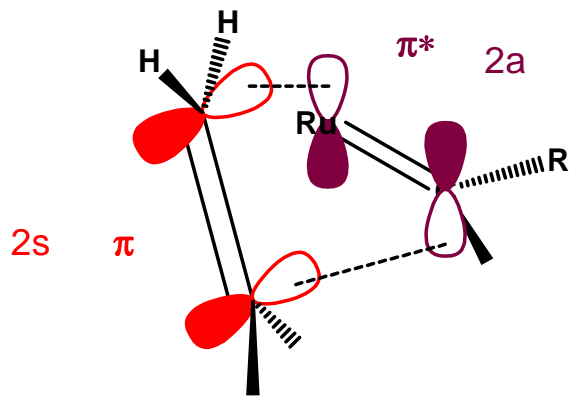
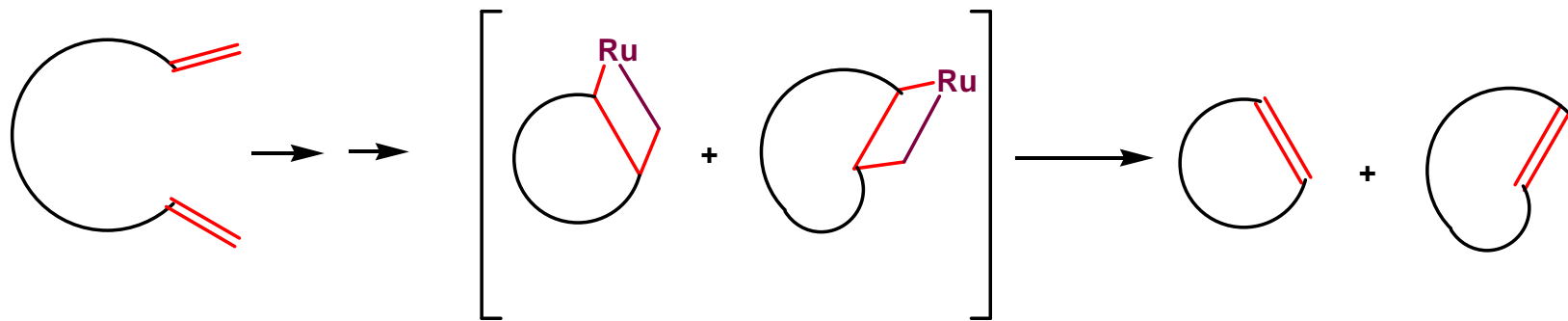
Ringschluss-Metathese bei mittleren Ringen ist stark abhängig von der Stereochemie

Beispiel: Bildung des Zehnringlactons von Phomol (aus Dissertation von Denise Schmidt, Uni. Mainz 2011)

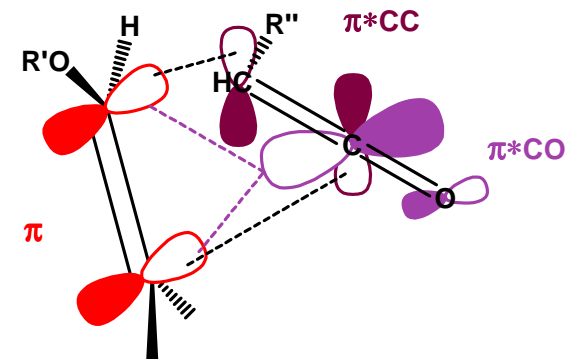


Ringschluss-Metathese als Folge von [2a+2s]-Cycloadditionen

Die Ringschlussmetathese läuft über bicyclische Zwischenprodukte ab:



Keten + Enolether



Neue Reaktionen im Spiegel bekannter Reaktionen

Das Döbereinersche Feuerzeug 1823

