Moderne Methoden in der Organischen Chemie

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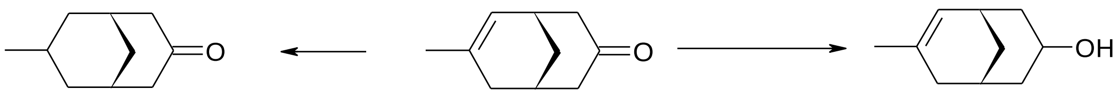
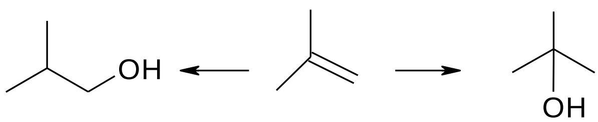
0. Allgemeines:

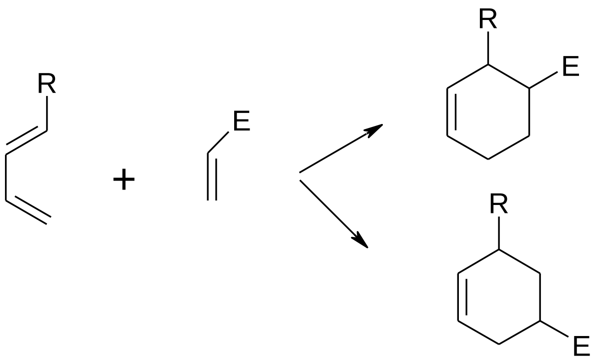
Wichtig für alle chemischen Reaktionen: **Selektivität**

Chemoselektivität:



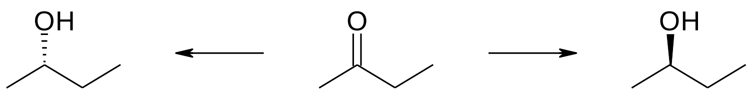
Regioselektivität:



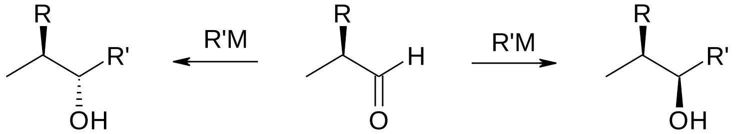


Stereoselektivät:

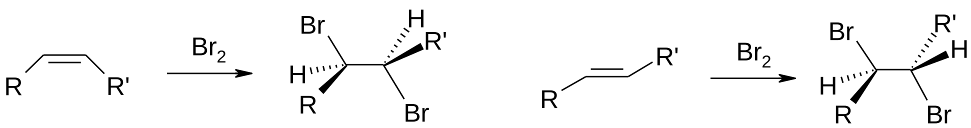
- Enantioselektivität:



-Diastereosektivität:



-Stereospezifität:

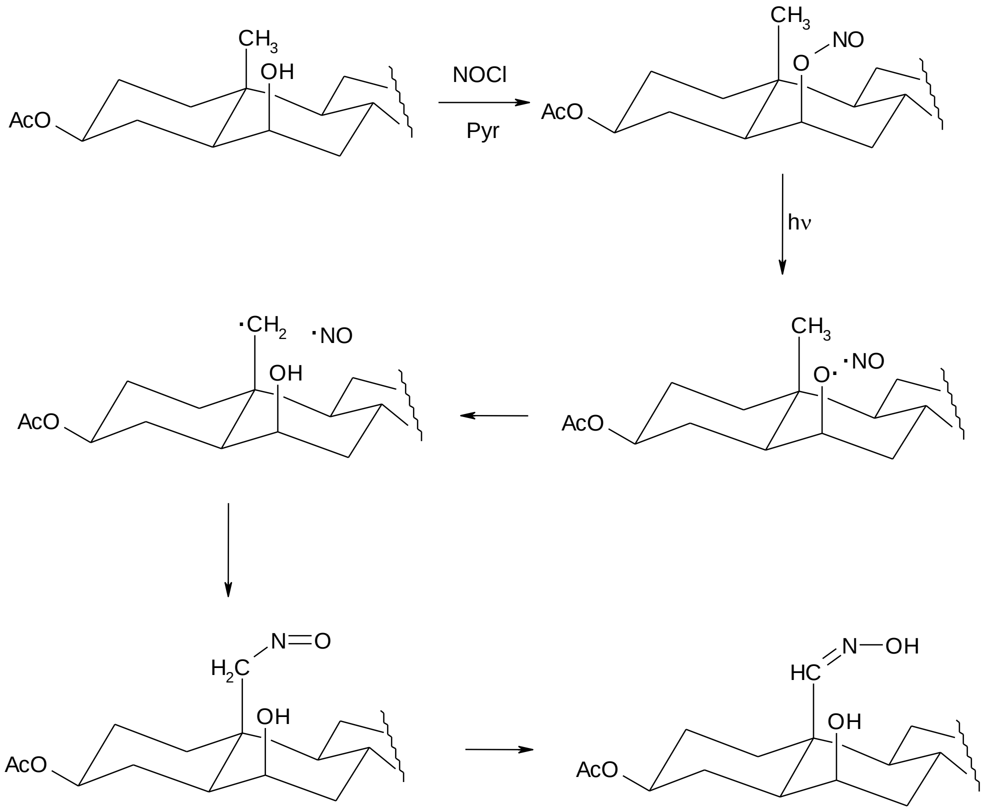


1. Oxidationsreaktionen

1.1 Oxidationen von C–H-Bindungen

1.1.1 Nicht aktivierte C–H-Bindungen

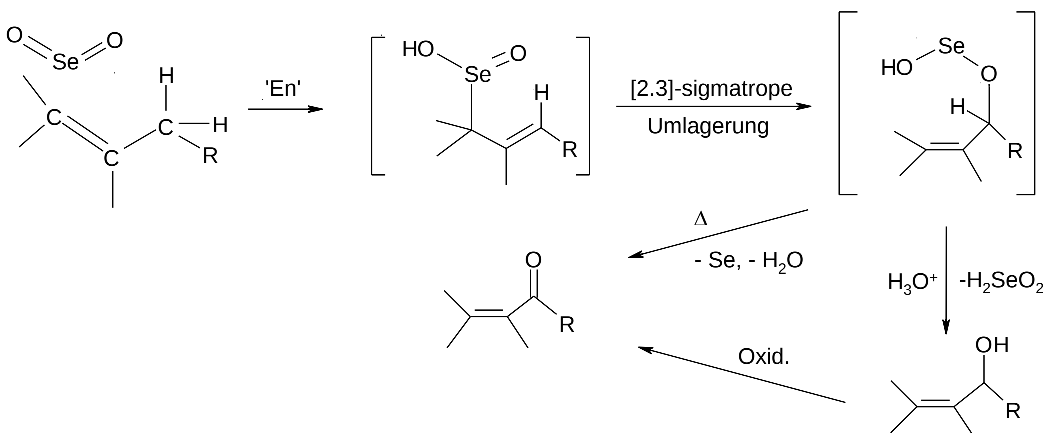
Beispiel: Barton Reaktion



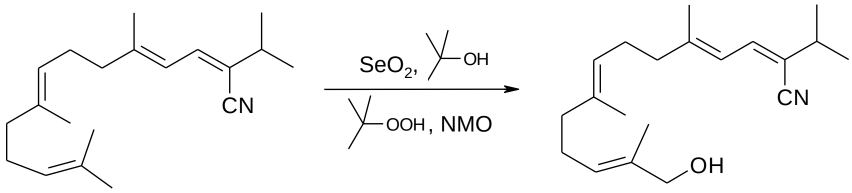
J. Chem. Soc., Perkin I **1979**, 1159.

1.1.2 Allylische/benzylische C–H-Bindungen

- mit Selendioxid



Beispiel:



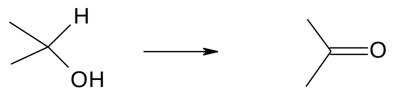
J. Org. Chem. **1978**, 1689

1.1.3 Oxidation α zu C−X-Bindungen

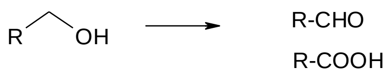
Alkohole

viele Möglichkeiten ⇒ Reagentienwahl sehr wichtig

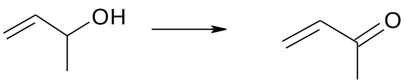
Übersicht:



CrO_3/Pyr; CrO_3/H_2SO_4
$Me_2CO/Al/O\textit{i}Pr)_3$ (Oppenauer, etc.)
DMSO/DCC ($COCl_2$) (Swern, Moffatt)



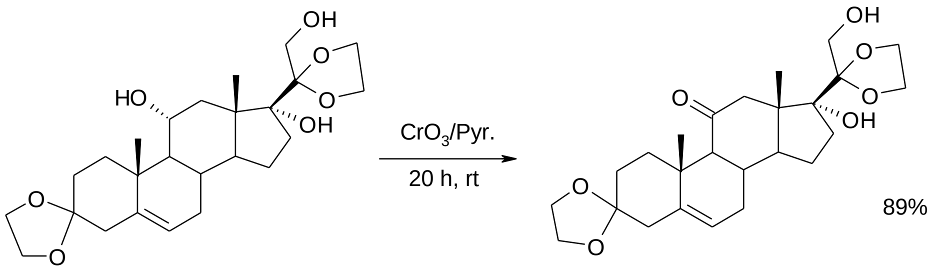
$CrO_2(O\textit{t}Bu)_2$, $Pb(OAc)_4$
starke Ox-Mittel ($KMnO_4$)



MnO_2

a) Chromat-Reagentien

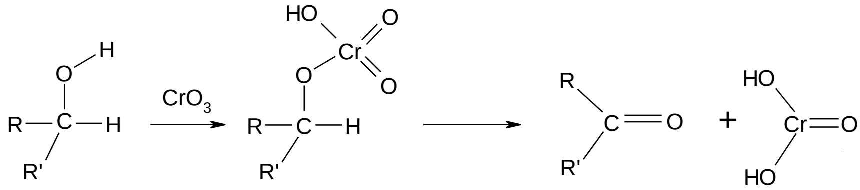
Beispiel:



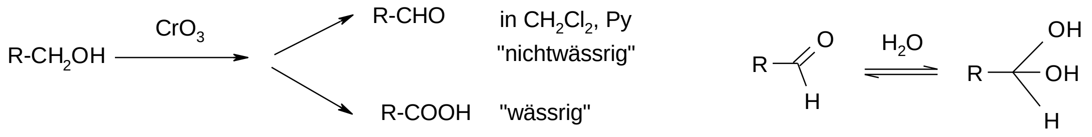
89%

J. Am. Chem. Soc. **1954**, *76*, 6116.

Mechanismus:



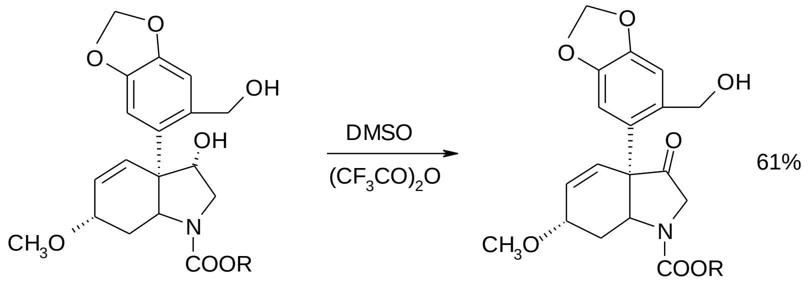
Alkohol → Aldehyd: mit $CrO_2(OtBu)_2$ oder CrO_3



b) Moffatt-Swern-Oxidation (DMSO-Oxidationen)

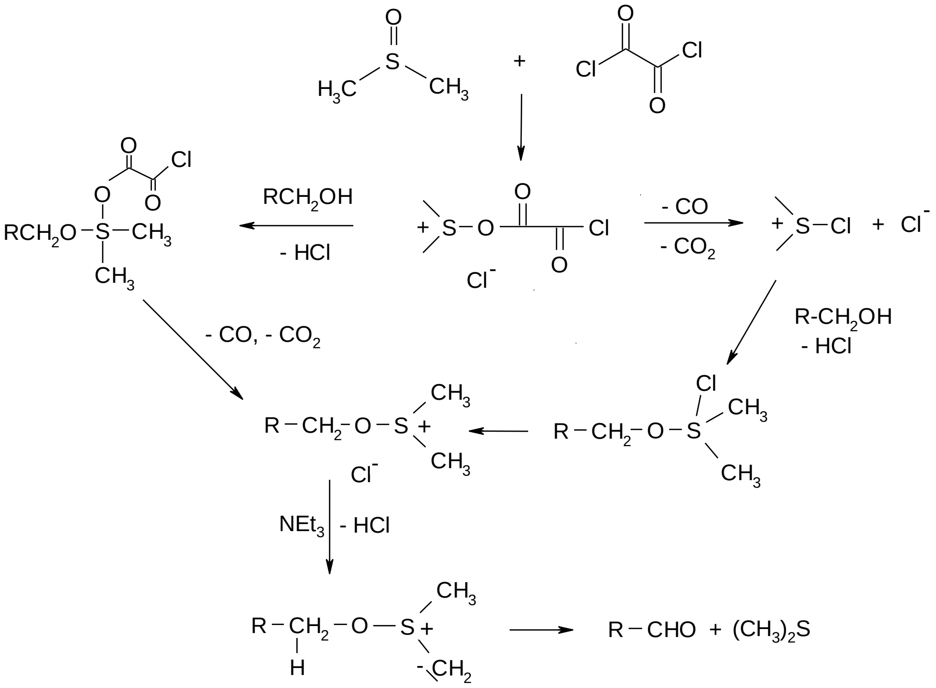
Prinzip: Alkohol + DMSO + $(COCl)_2$ / $COCl_2$ / DCC / Ac_2O / P_4O_{10} (wasserentz. Mittel)

Beispiel:



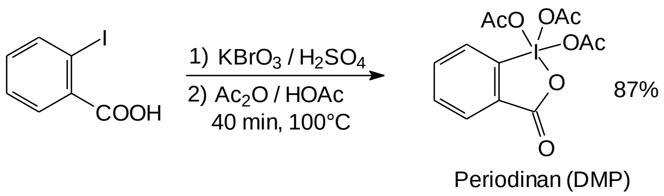
J. Org. Chem. **1978**, *43*, 2480.

Mechanismus: Swern-Oxidation



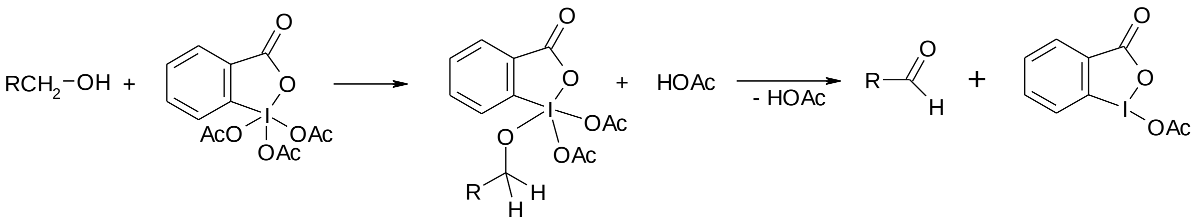
c) Dess-Martin-Oxidation

Herstellung der Reagenzes:

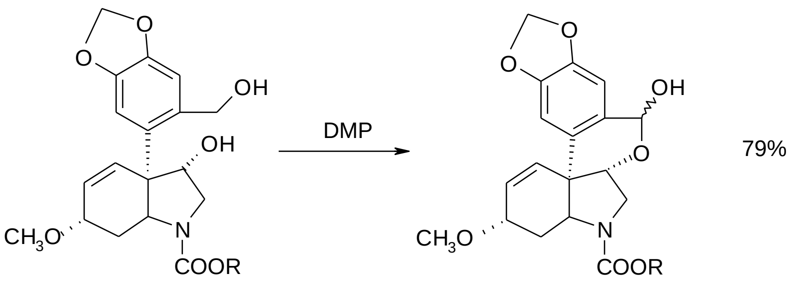


J. Org. Chem. **1983**, *48*, 4155.

Mechanismus:



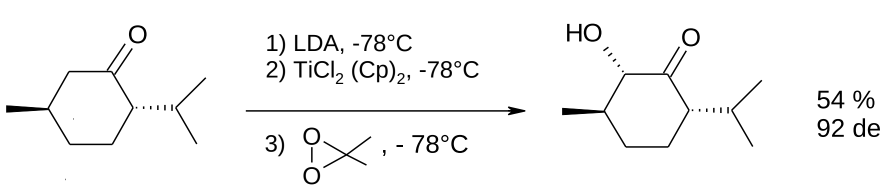
Beispiel:



J. Am. Chem. Soc. **1991**, *113*, 3850.

1.1.4 Oxidationen α zu Carbonylgruppen (Enolat-Oxidationen)

a) Elektrophile α-Hydroxylierung

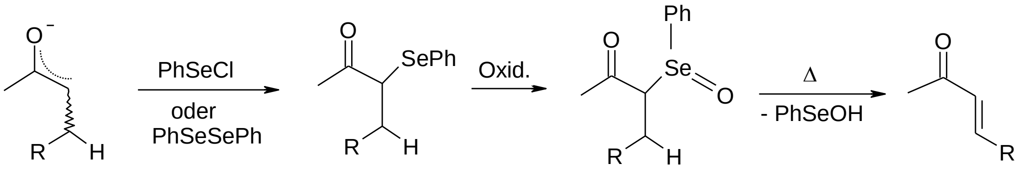


J. Org. Chem. **1984**, *59*, 2358.

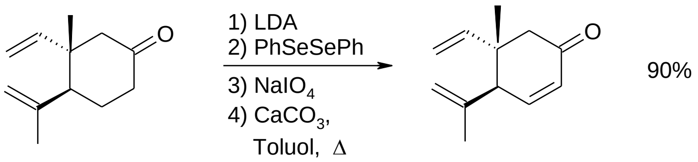
b) α-Selenierung

- mit **LDA und PhSeCl** bzw. PhSeSePh

Prinzip:



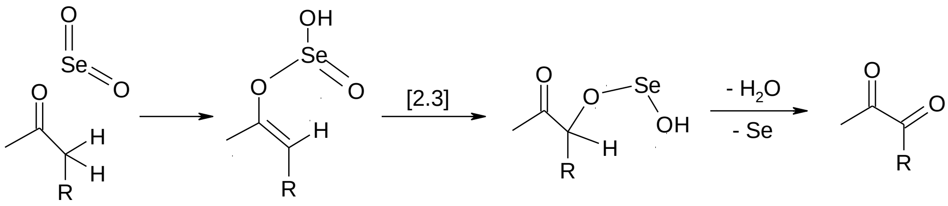
Beispiel:



Tetrahedron Lett. **1989**, *30*, 685.

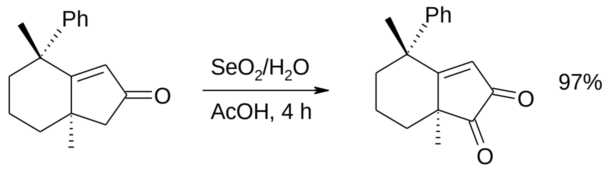
- mit **SeO$_2$** **En-Typ-Oxidation**

Prinzip:



Organic Reactions **1949**, *5*, 331; **1976**, *24*, 261.

Beispiel:



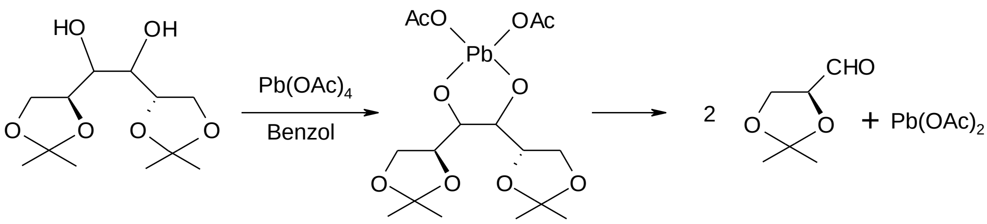
J. Org. Chem. **1970**, *35*, 570.

1.2 Oxidationen von C–C-Bindungen

1.2.1 Oxidative Spaltungen

a) Glykolspaltung

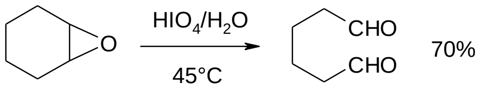
Beispiel:



Helv. Chim. Acta **1936**, *19*, 519ff.

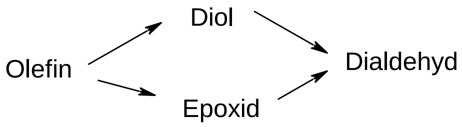
b) Epoxidspaltung

Beispiel:



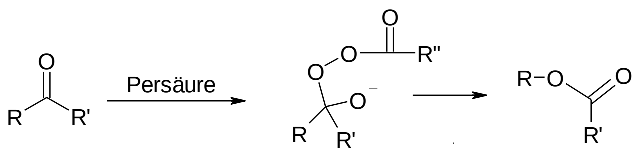
Tetrahedron Lett. **1973**, 4599.

Wichtige Sequenz:



c) Baeyer-Villiger-Oxidation

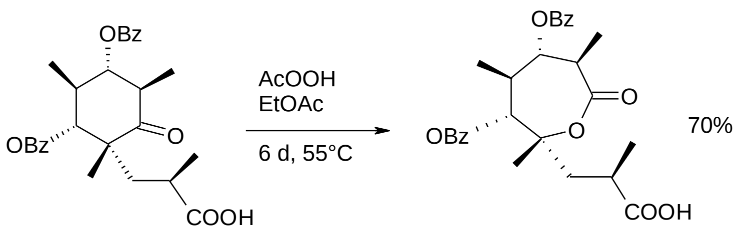
Prinzip:



Wanderungstendenz:

t-alkyl > *s*-alkyl > benzyl > phenyl > *n*-alkyl > methyl

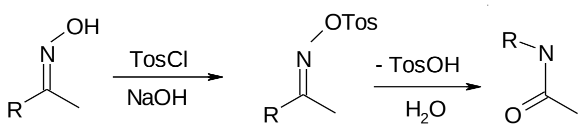
Beispiel:



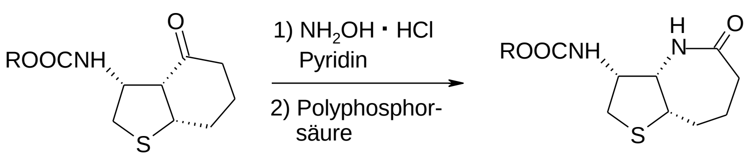
J. Am. Chem. Soc. **1978**, *10*, 4618ff.

d) Beckmann-Umlagerung

Prinzip:



Beispiel:



J. Am. Chem. Soc. **1978**, *100*, 6291.

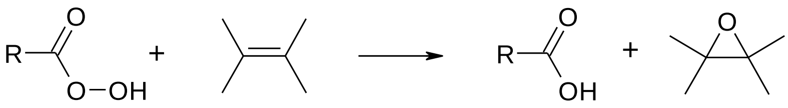
1.3 Oxidationen von C–C-Mehrfachbindungen

1.3.1 Epoxidierung

1.3.1.1 Elektrophile Epoxidierung

a) Persäuren ⇒ Prileshaev-Epoxidierung

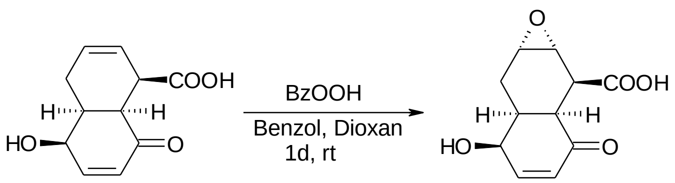
Prinzip:



R =	CH_3	Ph	3-Cl-Ph	4-NO_2-Ph	CF_3
pK_s=	4.8	4.2	3.9	3.4	< 0

Reaktivität der Persäure →

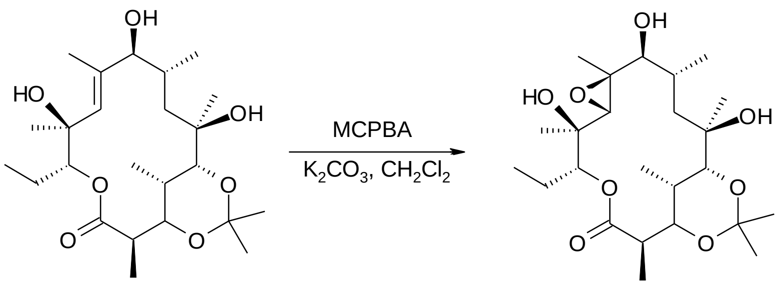
Beispiel:



Tetrahedron **1958**, *2*, 1.

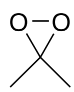
Steuerung über **koordinierende Gruppen** möglich

Beispiel:

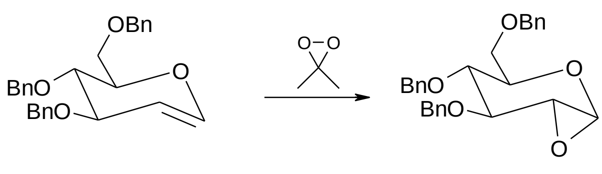


J. Am. Chem. Soc. **1978**, *100*, 4618ff.

b) Dioxiran



Beispiel:



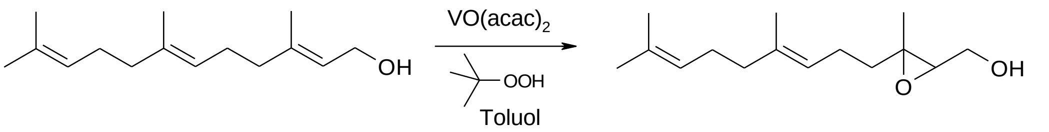
Chem. Ber. **1991**, *124*, 2361.

c) Übergangsmetalle

– Vanadin

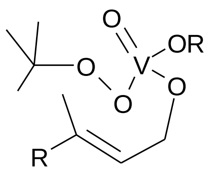
⇒ Selektive Epoxidierung von Allylalkoholen (Sharpless)

Beispiel:



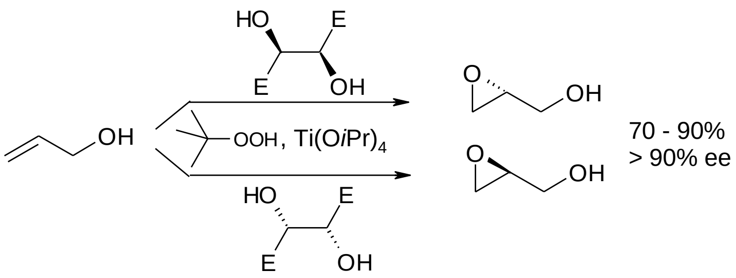
J. Am. Chem. Soc. **1973**, *95*, 6136.

Intermediat:

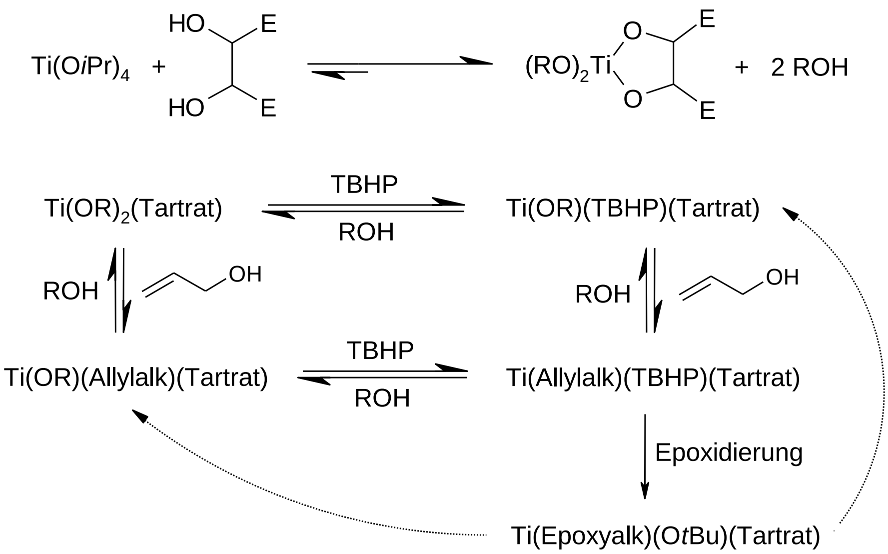


– Titan

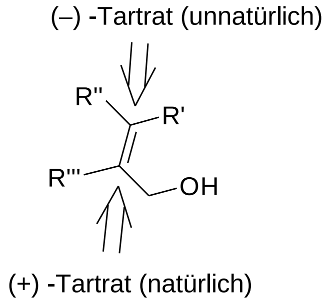
⇒ 1. asymmetrische Epoxidierung (Sharpless Epoxidierung)

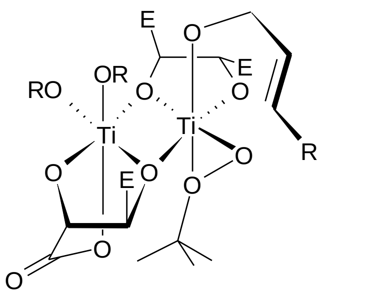


vereinfachter Mechanismus:



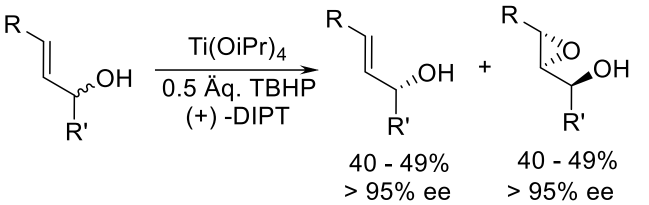
generell gilt: **wahrscheinlicher Übergangszustand:**

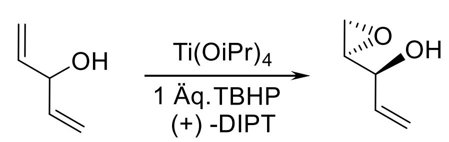




Anwendungen: kinetische Racematspaltungen

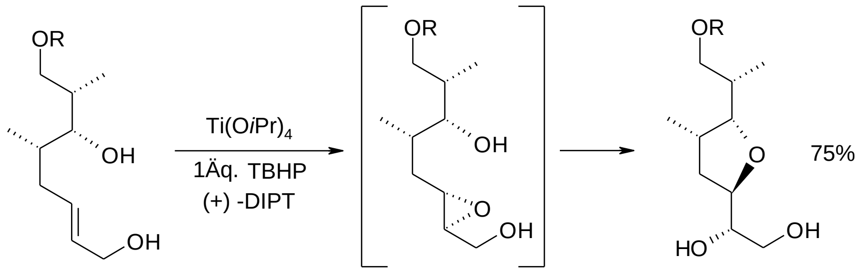
a) racemische Allylalkohole **b**) prochirale Substrate





Angew. Chem **1986**, *98*, 89.

Tandemreaktionen:

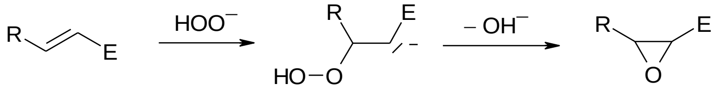


Tetrahedron Lett. **1986**, *27*, 105.

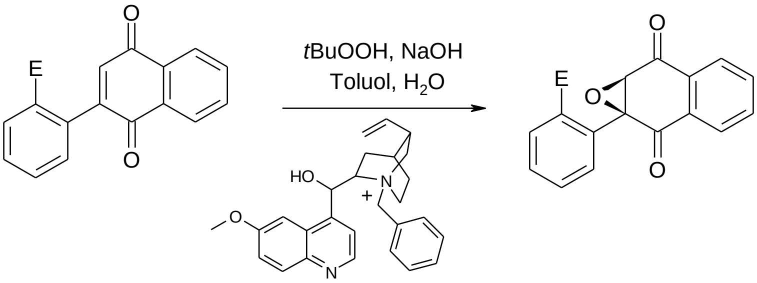
1.3.1.2 Nucleophile Epoxidierung

selektive Epoxidierung e⁻-armer Doppelbind. mit H_2O_2 /OH^- (**Scheffer-Weitz-Epoxid.**)

Prinzip:



Beispiel:

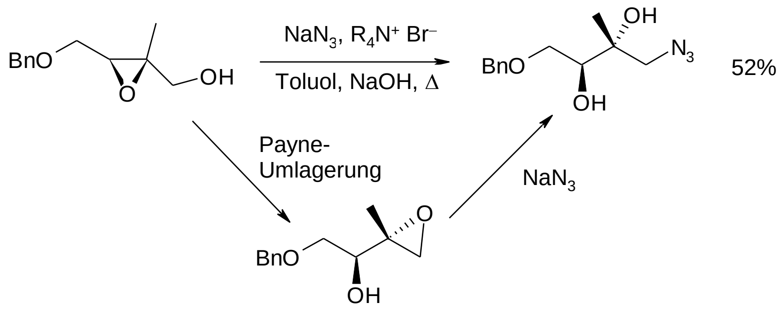


J. Org. Chem. **1980**, *45*, 158.

1.3.2 Dihydroxylierung

1.3.2.1 *trans*-Diole   durch Hydrolyse von Epoxiden

Beispiel:

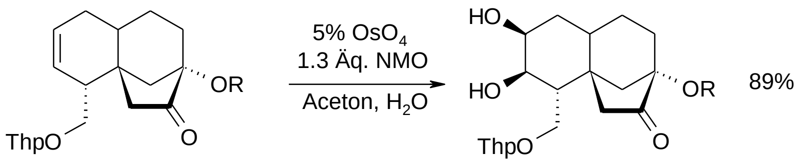


Tetrahedron Lett. **1985**, *26*, 3299.

1.3.2.2 *cis*-Diole

mit OsO_4 Dihydroxylierung bevorzugt von der sterisch weniger gehinderten Seite

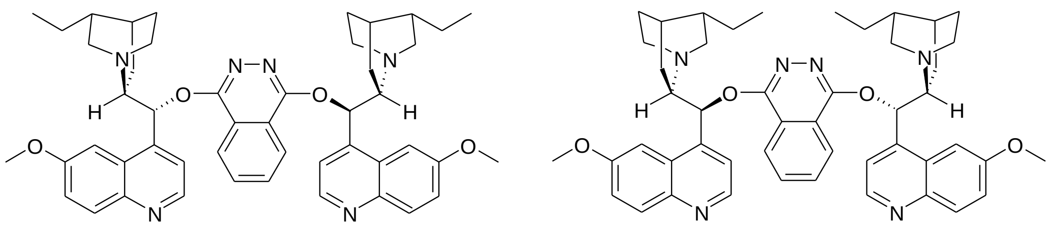
Beispiel :



J. Am. Chem. Soc. **1978**, *100*, 8031ff.

– Sharpless Dihydroxylierung   Chirale Liganden auf Chinin-Basis

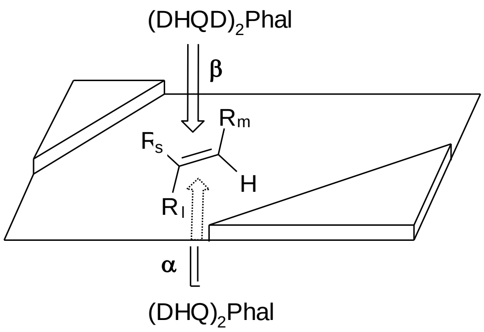
Beispiele:



(DHQ)$_2$Phal (abgeleitet vom Chinin)   (DHQD)$_2$Phal (abgeleitet vom Chinidin)

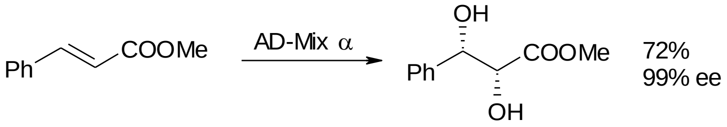
J. Org. Chem. **1992**, *57*, 2768.

Modell:

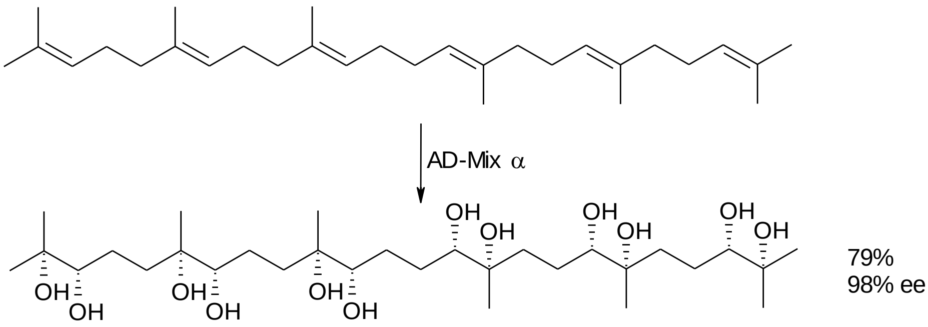


J. Am. Chem. Soc. **1988**, *110*, 1968.

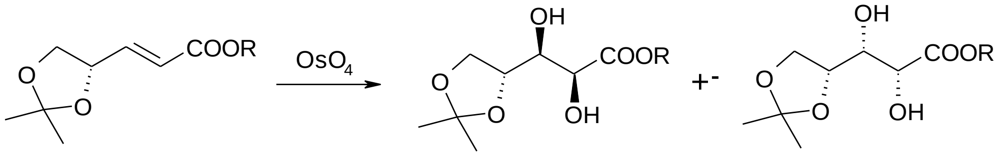
Beispiele:



J. Org. Chem. **1994**, *59*, 5104.



Science **1993**, *259*, 64.



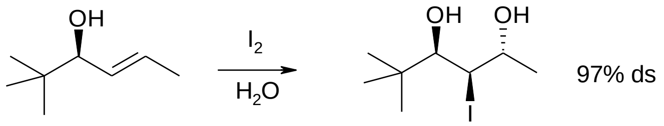
ohne Ligand	2.8	:	1
$(DHQD)_2Phal$	39	:	1
$(DHQ)_2Phal$	1	:	1.3

Tetrahedron Lett. **1993**, *34*, 5375.

1.3.3 Halooxygenierung

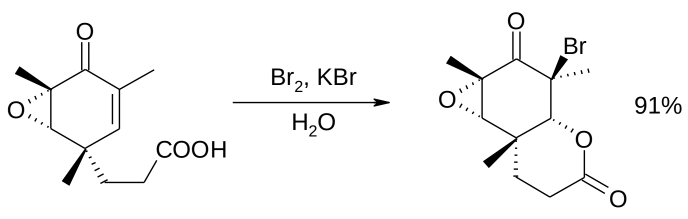
analog Halogenaddition in Gegenwart von O-Nucleophilen

Beispiel:



Tetrahedron **1984**, *40*, 2297.

– Halolactonisierung:

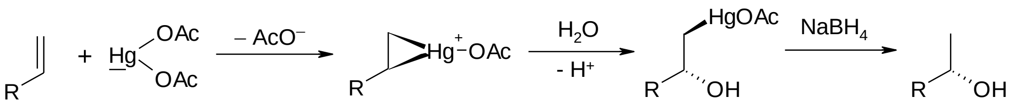


J. Am. Chem. Soc. **1978**, *100*, 4618.

1.3.4 Hydratisierung

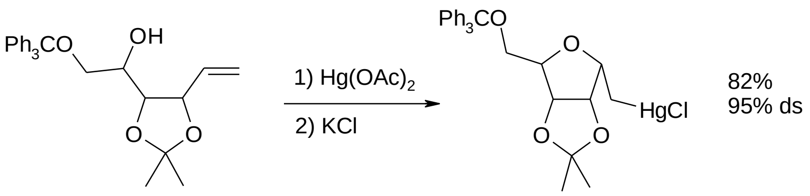
a) Oxymercurierung / Reduktion

Prinzip:



hohe Regioselektivität ⇒ Addition nach **Markownikow**

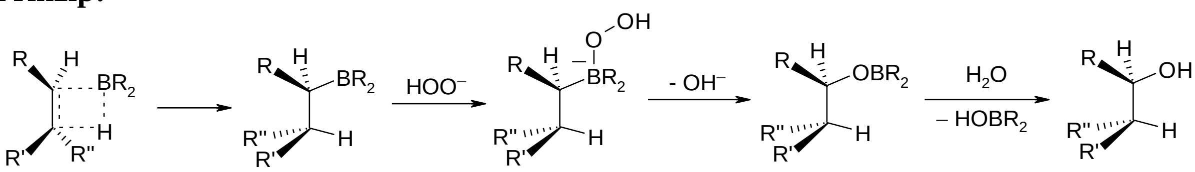
Intramolekulare Variante:



Tetrahedron Lett. **1984**, *25*, 5937.

b) Hydroborierung / Oxidation

Prinzip:



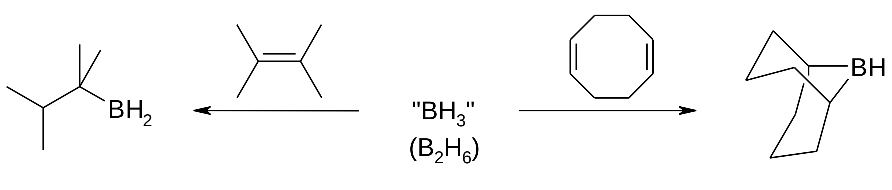
Addition an sterische weniger gehinderte Position ⇒ Addition nach ***anti*-Markownikow**

R_2BH RBH_2 BH_3

Reaktivität →

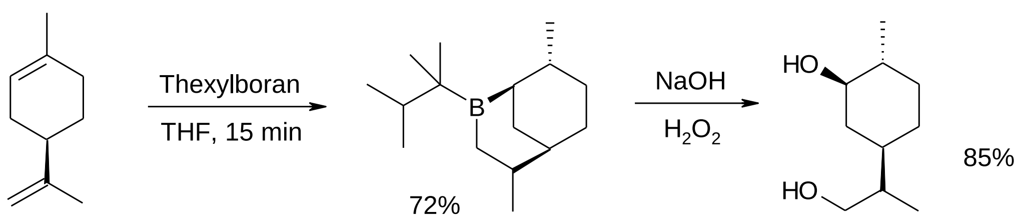
Selektivität ←

Gängige Borane:



Thexylboran **Diboran** **9-BBN**

Beispiele:



J. Am. Chem. Soc. **1972**, *94*, 3567.

2. Reduktionsreaktionen

Übersicht über gängige Reduktionsverfahren

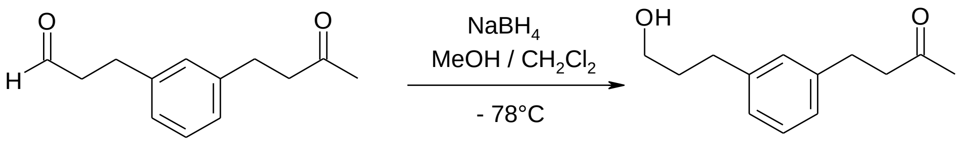
Reaktion	$NaBH_4$ in EtOH	$NaBH_4$ + LiCl	$NaBH_4$ + $AlCl_3$	BH_3 in THF	Disiamylboran in THF	9-BBN	$LiAlH(OtBu)_3$ in THF	$LiAlH(OMe)_3$ in THF	$LiAlH_4$ in Ether	AlH_3 in THF	$LiBEt_3H$	Dibal-H	$NaAlEt_2H_2$	Katalytische Hydrierung
RCHO → RCH_2OH	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RCOR → RCHOHR	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RCOCl → RCHO oder RCH_2OH	+	+	+	–	–	+	+	+	+	+	+	+	+	+
Lacton → Diol	–	+	+	+	+	+	±	+	+	+	+	+	+	±
Epoxid → Alkohol	–	+	+	+	±	±	±	+	+	+	+	+	+	+
RCOOR' → RCH_2OH + R'OH	–	+	+	±	–	±	+	+	+	+	+	+	+	±
RCOOH → RCH_2OH	–	–	+	+	–	±	–	+	+	+	–	+	+	–
$RCOO^-$ → RCH_2OH	–	–	+	–	–	–	–	+	+	+	–	–	–	–
$RCONR'_2$ → $RCH_2NR'_2$ oder RCHO	–	–	–	+	+	+	–	+	+	+	+	+	+	+
RCN → RCH_2NH_2	–	–	–	+	–	±	–	+	+	+	±	+	+	+
RNO_2 → RNH_2 oder RN=NR	–	–	–	–	–	–	–	+	+	–	–	+	+	+
RCH=CHR' → RCH_2CH_2R'	–	–	–	+	+	+	–	–	–	–	+	–	–	+

2.1 Reduktion mit komplexen Hydriden

2.1.1 Aldehyde und Ketone

a) Aldehyde neben Ketonen

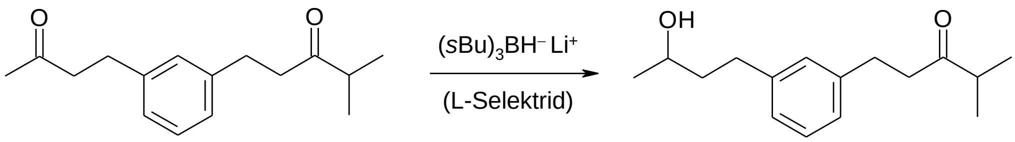
Beispiel:



b) Ketone neben Ketonen

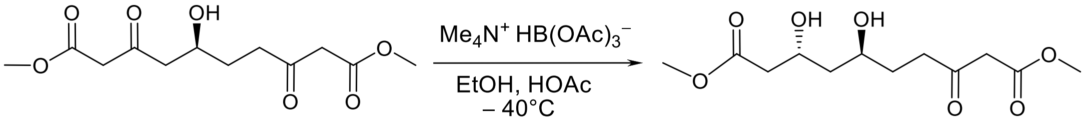
- sterische Differenzierung

Beispiel:

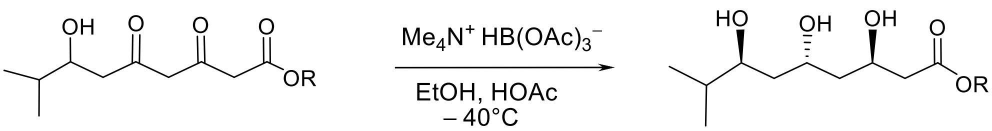


- durch Nachbargruppenbeteiligung

Beispiele:

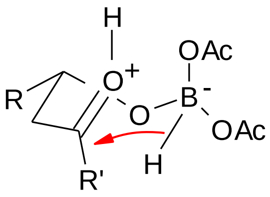


J. Org. Chem. **1991**, *56*, 741.

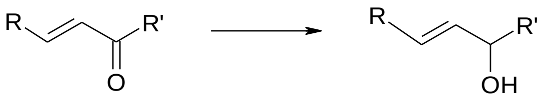


J. Am. Chem. Soc. **1988**, *110*, 3560.

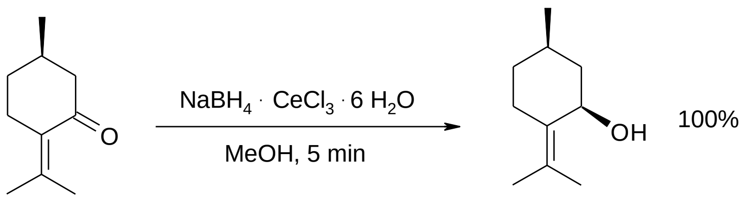
Intermediat:



c) 1,2- neben 1,4-Reduktion



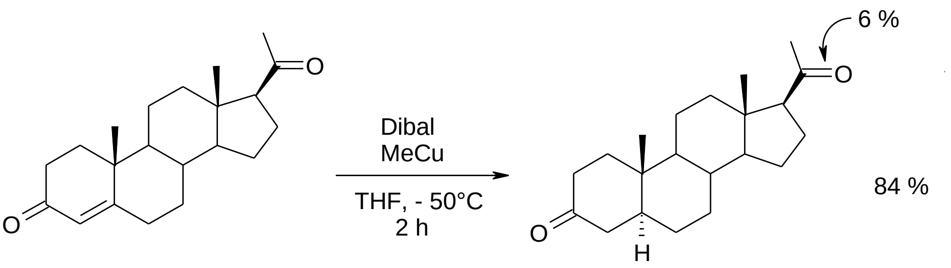
Beispiel: **Luche-Reduktion** mit $NaBH_4$ / $CeCl_3$



Chem. Commun. **1978**, 601.

d) 1,4- neben 1,2-Reduktion

Beispiel:



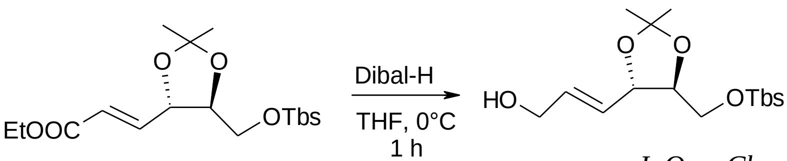
J. Org. Chem. **1986**, *51*, 537.

2.1.2 Carbonsäuren und Derivate

1) zum Alkohol

a) 1,2- neben 1,4-Reduktion

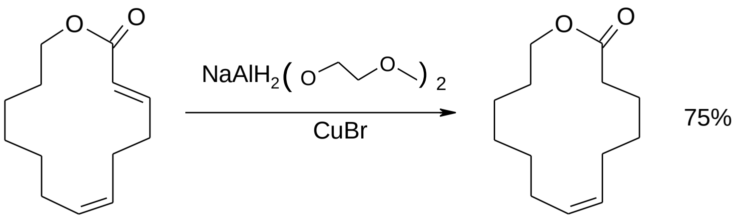
Beispiel:



J. Org. Chem. 1**994**, *5*9, 6614.

b) 1,4- neben 1,2-Reduktion

Beispiel: Cu(I)-Reagentien

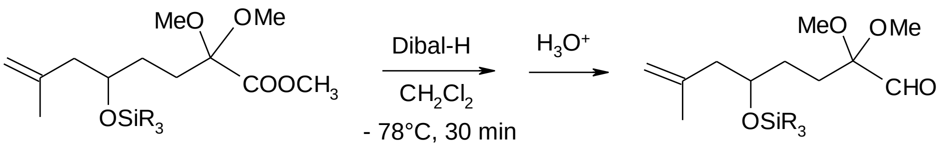


Angew. Chem. **1983**, *95*, 810.

2) zum Aldehyd

a) Ester

Beispiele:

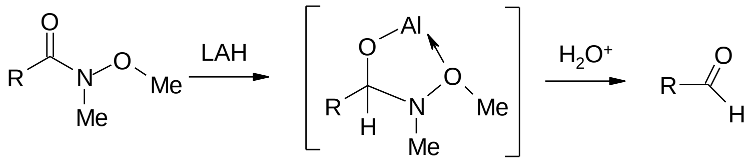


J. Am. Chem. Soc. **1975**, *97*, 2287.

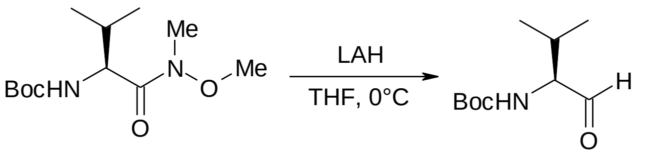
b) Amide

Methode der Wahl: **Weinreb-Amide**

Prinzip:



Beispiel:



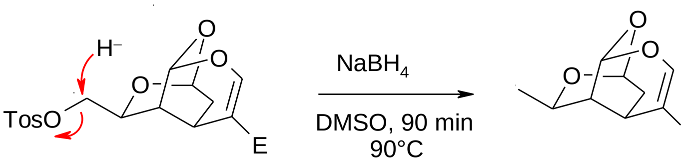
92%

J. Amer. Chem. Soc. **199**2, *114*, 6568.

2.1.3 Desoxygenierung

a) Reduktion von Tosylaten

Beispiel:

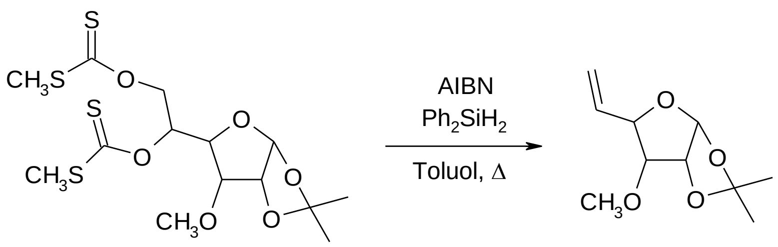


61%

Angew. Chem. **1982**, *96*, 81.

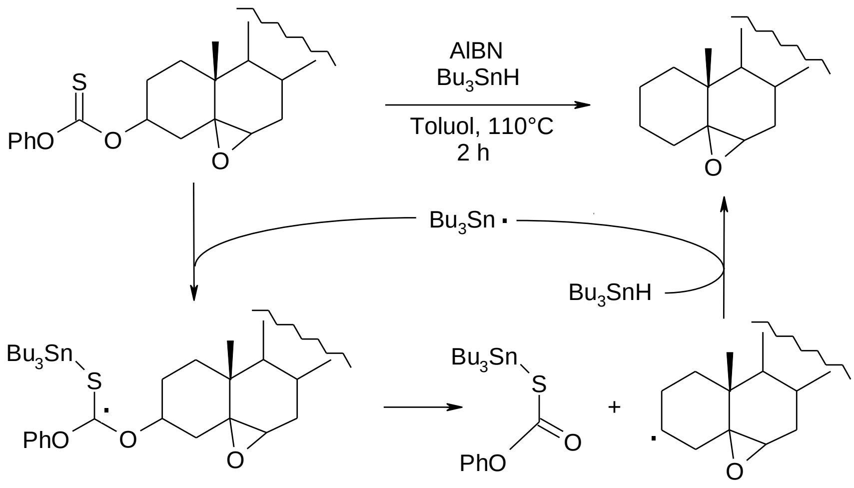
b) Radikalische Desoxygenierung

Beispiele:



100 %

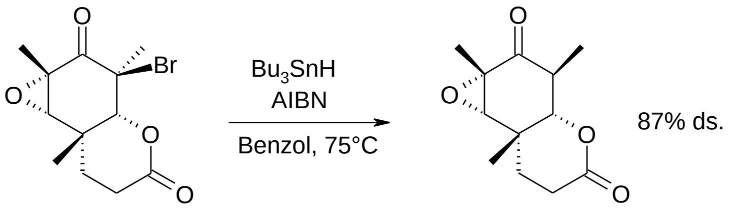
Tetrahedron Lett. **1991**, *32*, 2569.



J. Am. Chem. Soc. **1981**, *103*, 932.

2.1.4 Dehalogenierung

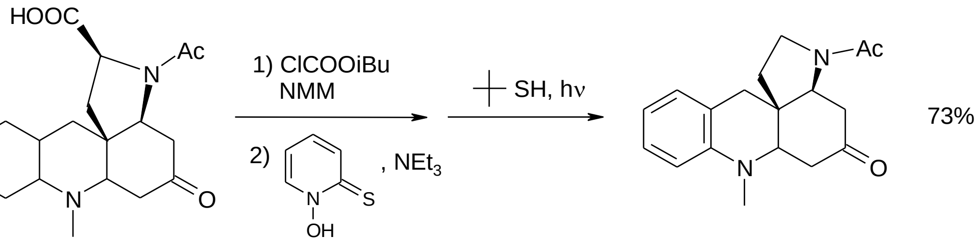
Beispiel: radikalisch



J. Am. Chem. Soc. **1978**, *100*, 4618*ff*.

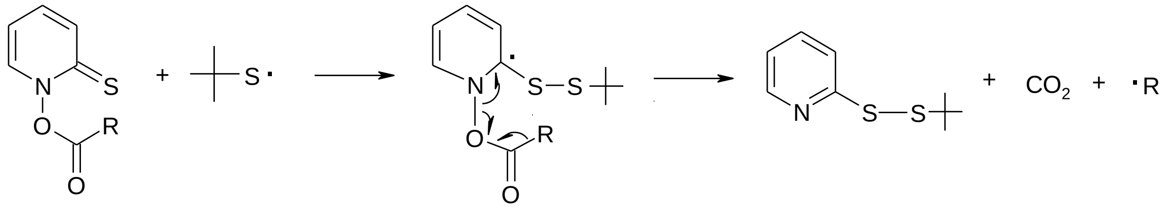
2.1.5 Reduktive Decarboxylierung

Beispiel:



J. Am. Chem. Soc. **1990**, *112*, 8971.

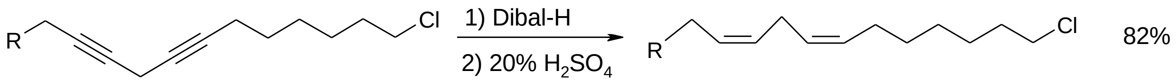
Prinzip:



2.1.6 Reduktion von C–C-Mehrfachbindungen

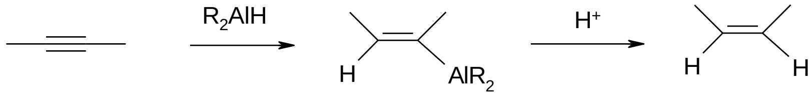
Alkine zu Alkenen

Beispiel: Dibal-Reduktion (Review: *Synthesis* **1975**, 617)

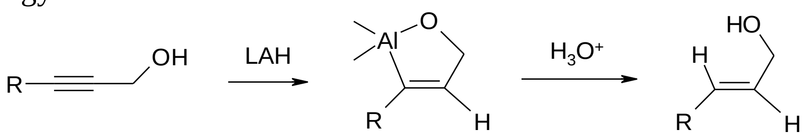


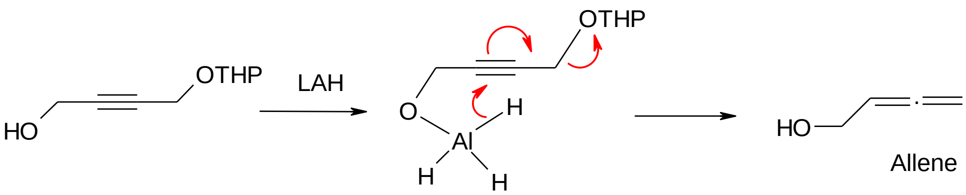
J. Org. Chem. **1963**, *28*, 1254.

Mechanismus:



Beispiele: Propargylakohole



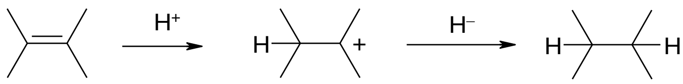


Acta Chem. Scand B **1987**, *41*, 442.

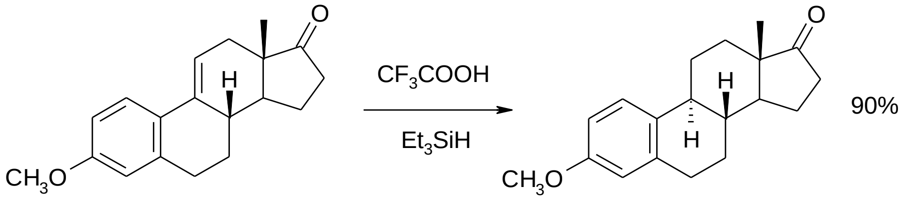
2.1.7 Ionische Hydrierung

Hydrierung durch Übertragung von H^+ und H^- ⇒ Reduktion von C=C, C=X und C–X

Prinzip:



Beispiele:



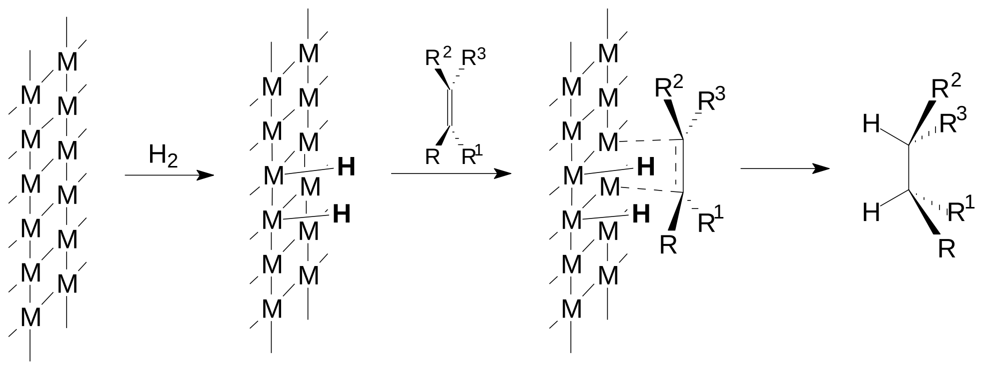
J. Am. Chem. Soc. **1986**, *108*, 1239.

2.2 Reduktion durch katalytische Hydrierung

geeignete Metalle: Ni, Pd, Pt, Ru, Rh, etc.

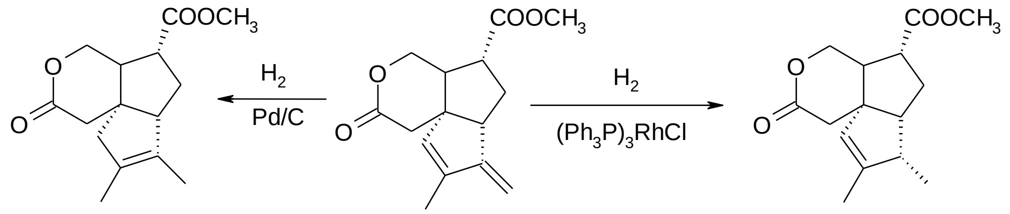
Metallische Katalysatoren: heterogene Hydrierung
Komplexe Katalysatoren: homogene Hydrierung

Mechanismus:



2.2.1 Reduktion von C–C-Doppelbindungen

Beispiel:

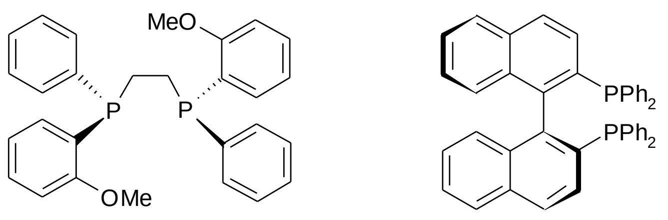


J. Am. Chem. Soc. **1979**, *101*, 7020.

– asymmetrische katalytische Hydrierung

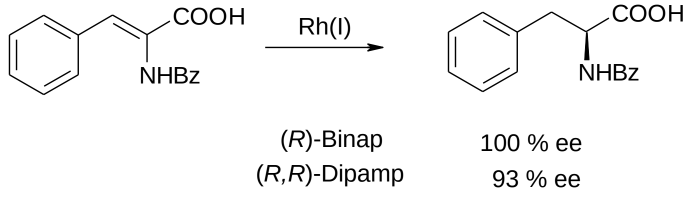
Zusatz chiraler Liganden

Beispiel:



Dipamp (Knowles) **Binap** (Noyori)

Beispiel: Asymmetrische Synthese von Aminosäuren

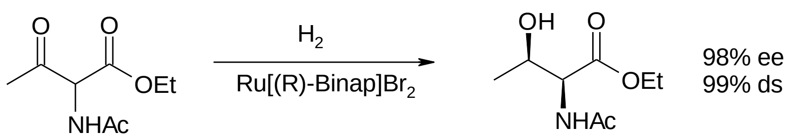


J. Am. Chem. Soc. **1977**, *99*, 5946; *J. Am. Chem. Soc.* **1980**, *102*, 7932.

2.2.2 Reduktion von C-O-Doppelbindungen

besonders gut mit Ru-Komplexen, bevorzugte Substrate: β-Ketoester

Beispiel:

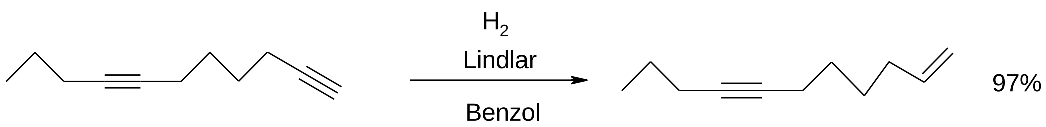


J. Am. Chem. Soc. **1989**, *111*, 9134.

2.2.3 Reduktion von C–C-Dreifachbindungen

Selektive Hydrierung von Dreifachbindung zur Doppelbindung mit **Lindlar-Katalysator** (Pd/$BaSO_4$ oder Pd/$CaCO_3$ mit $Pb(OAc)_2$ oder Chinolin vergiftet)

Beispiel:



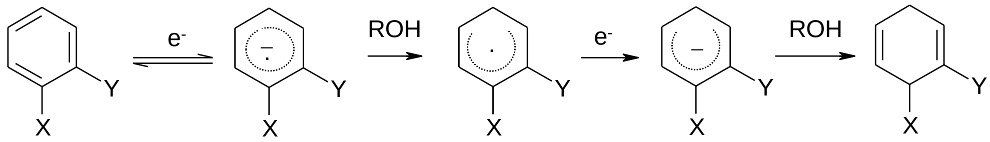
J. Chem. Soc. **1955**, 3358.

2.3 Reduktion durch ‚auflösende Metalle'

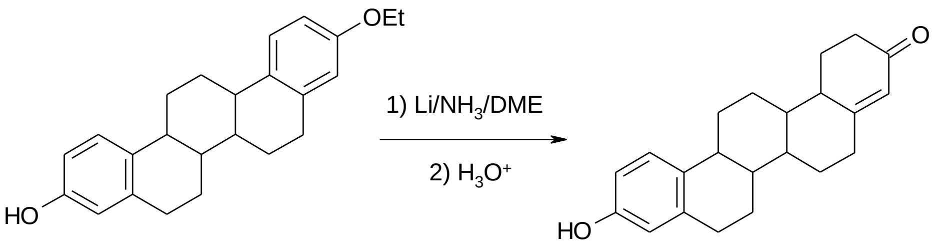
Anwendung: Reduktion von Aromaten, Enonen, Alkinen → *trans*-Alkenen

2.3.1 Reduktion von Aromaten

Mechanismus:



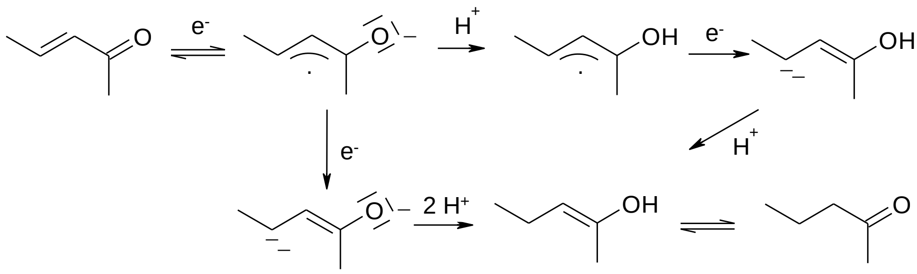
Beispiel:



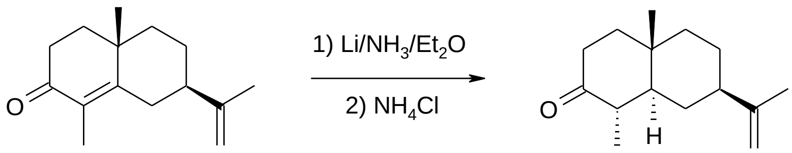
J. Am. Chem. Soc. 1**973**, *95*, 7829.

2.3.2 Reduktion von Enonen

Mechanismus:



Beispiele:



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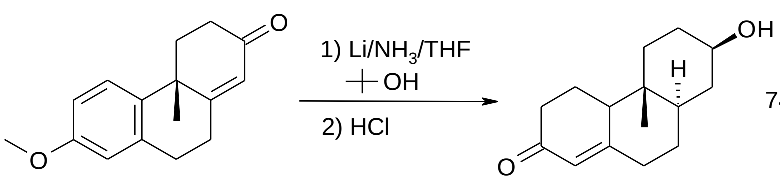
95% ds

J. Chem. Soc. **1956**, 2670.

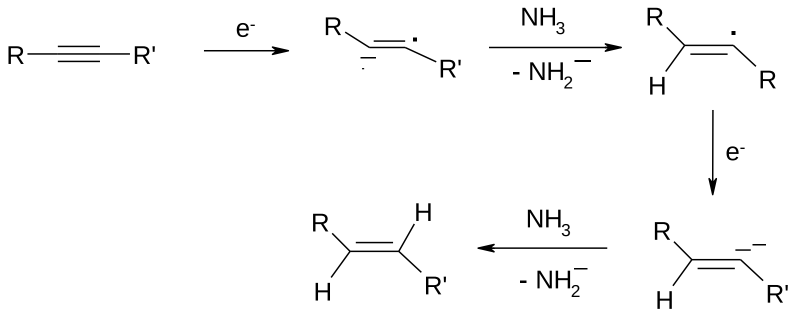


74%

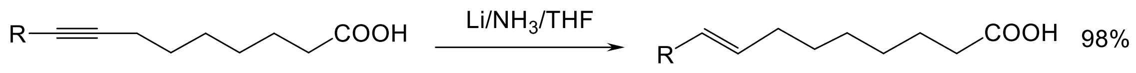
J. Org. Chem. **1967**, *32*, 689.

2.3.2 Reduktion von Dreifachbindungen

Mechanismus:



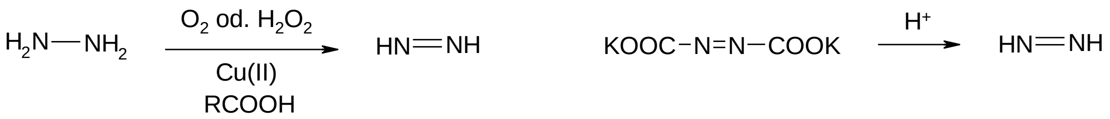
Beispiele:



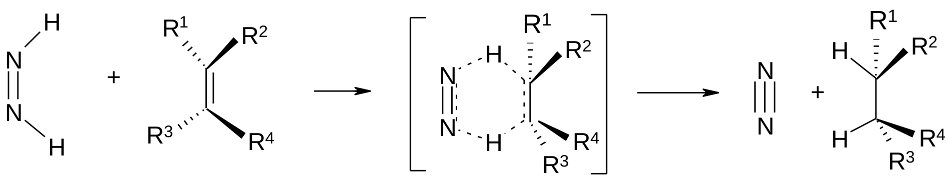
J. Am. Chem. Soc. **1963**, *85*, 622.

2.4 Reduktion mit Diimid (HN=NH)

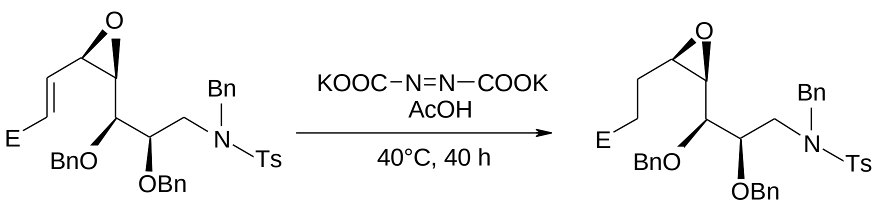
Erzeugung:



Mechanismus:



Beispiel:



J. Org. Chem. **1985**, *50*, 470.

LITERATUR

Oxidationen

Allgemeine Lehrbücher:

F. A. Carey, R. J. Sundberg: *Organische Chemie; Einweiterführendes Lehrbuch*, Wiley-VCH

J. March: *Advanced Organic Chemistry*, Wiley

R. Brückner: *Reaktionsmechanismen*, Spektrum

J. Fuhrhop, G. Penzlin: *Organic Synthesis*, Wiley-VCH

Aktuelle Reviews zum Thema **Oxidationen:**

Recent advances in the asymmetric dihydroxylation of alkenes; *Tetrahedron Asym.* **1992**, *3*, 1317.

The Baeyer-Villiger oxidation of ketones and aldehydes; *Org. Reactions* **1993**, *43*, 251.

Catalytic asymmetric dihydroxylations; *Chem. Rev.* **1994**, 2483.

Chemical and biological synthesis of chiral epoxides; *Tetrahedron* **1994**, *50*, 8885.

Dioxiranes – highly reactive oxidants for stereoselective oxyfunctionalizations; *J. Prakt. Chem. / Chem. Ztg.* **1995**, *337*, 162; *J. Prakt. Chem. / Chem. Ztg.* **1997**, *339*, 298.

Asymmetric epoxidation of allylic alcohols: The Katsuki-Sharpless epoxidation reaction; *Org. Reactions* **1996**, *48*, 1.

Chemical transformations induced by hypervalent iodine reagents; *Tetrahedron* **1997**, *53*, 1179.

Polymer supported catalytic asymmetric Sharpless dihydroxylation of olefins; *Eur. J. Org. Chem.* **1998**, 21.

100 Years of Baeyer-Villiger-oxidations; *Eur. J. Org. Chem.* **1999**, 737.

Iodocarbocyclization and iodoaminocyclization reactions mediated by a metallic reagent; *Synlett* **1999**, 1191.

Asymmetric epoxidation of electron-deficient olefins; *Chem. Commun.* **2000**, 1215.

Recent Advances in Immobilized Metal Catalysts for Environmentally Benign Oxidation of Alcohols; *Chem. Asian J.* **2008**, p 196.

Reduktionen

Allgemeine Lehrbücher:

F. A. Carey, R. J. Sundberg: *Organische Chemie; Einweiterführendes Lehrbuch*, Wiley-VCH

J. March: *Advanced Organic Chemistry*, Wiley

R. Brückner: *Reaktionsmechanismen*, Spektrum

J. Fuhrhop, G. Penzlin: *Organic Synthesis*, Wiley-VCH

Aktuelle Reviews zum Thema **Reduktionen:**

The use of chiral organoboranes in organic synthesis; *Synthesis* **1986**, 973.

Enantioselective Ru-mediated hydrogensations; developments and applications; *J. Organomet. Chem.* **1989**, *567*, 163.

Boranes in Organic Synthesis; *J. Organomet. Chem.* **1993**, *457*, 1.

Enantioselective transition metal catalyzed hydrogenations concerning the asymmetric amine synthesis; *Angew. Chem.* **1993**, *105*, 245.

Zinc borohydride, a reducing agent with high potential; *Synlett* **1993**, 885.

Recent advances in the boron route to asymmetric synthesis; *Pure & Appl. Chem.* **1994**, *66*, 201.

Low valent titanium – a versatile reagent for deoxygenation and carbonyl coupling; *J. Prakt. Chem. / Chem. Ztg.* **1995**, *337*, 250.

New reagents for the ‚old' pinacol coupling reaction; *Angew. Chem.* **1996**, *108*, 65.

Enantioselective catalytic hydrogenation; *Angew. Chem.* **1996**, *108*, 444.

Weinreb amides in modern organic synthesis; *J. Prakt. Chem. / Chem. Ztg.* **1997**, *339*, 517.

Hydroboration catalyzed by transition metal complexes; *Tetrahedron* **1997**, *53*, 4957.

Enantioselective reduction of ketones; *Organic Reactions* **1998**, *52*, 395-576.

Asym. transfer hydrogenation of C=O and C=N bonds; *Tetrahedron Asym.* **1999**, *10*, 2045.

Boron Reagents in Process Chemistry - Excellent Tools for Selective Reductions; *Chem. Rev.* **2006**, *106*, 2617.