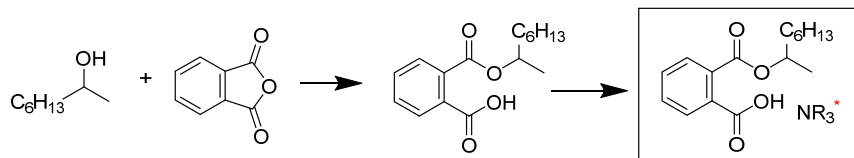


Jak otrzymać związki optycznie czynne ???

Sławomir Jarosz – stereochemia- wykład VII

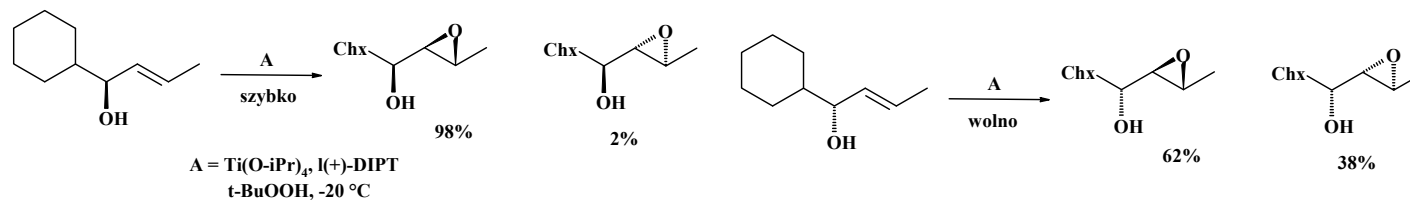
Ze związków chiralnych **1. Rozdział racematu**

a. 'Klasyczny': A (rac) \longrightarrow 50% A(R) + 50%A(S)



b. Rozdział mieszaniny racemicznej na CHIRALNEJ kolumnie (Y. Okamoto, T. Ikai, Chem. Soc. Rev., 2008, 37, 2593-2608)

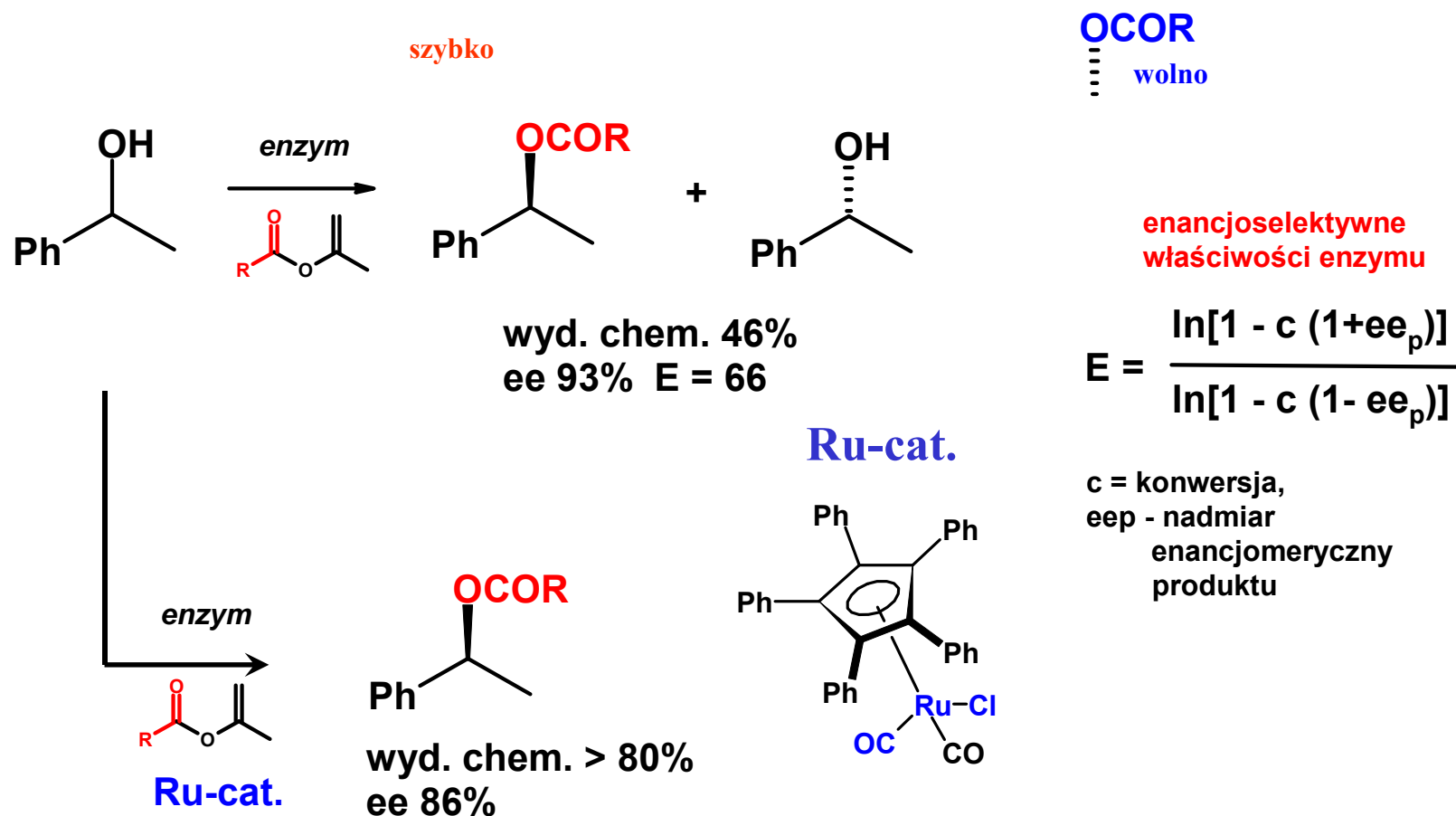
c. 'Kinetyczny': A (rac) \longrightarrow 50% A(R) + 50%B(S)



d. Dynamiczny: A (rac) \longrightarrow 100% A(R) lub 100%A(S)

A(S) (50%) + A(R)-X (50%)

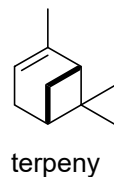
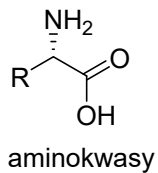
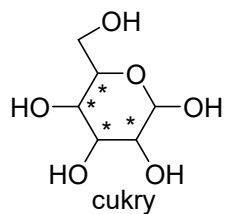
Dynamiczny rozdział racematu



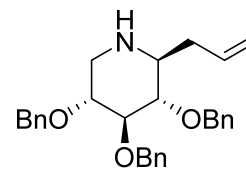
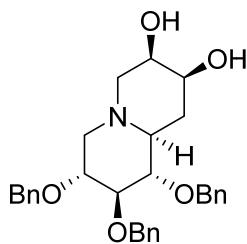
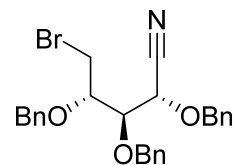
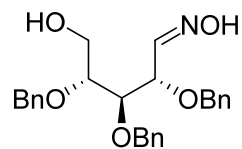
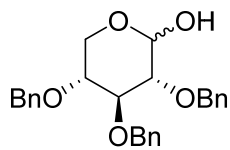
Enzymatyczny rozdział: Bäckvall and co-workers, *Chem. Eur. J.* **2006**, *12*, 225-232

Ogólnie o enzymach w biotransformacjach: K. Faber, .. *Angew.* **2008**, *47*, 8782-8793 (minireview)

Chiron approach: synteza związków optycznie czynnych (czystych) z nieracemicznych substratów



S. Hanessian, *Total Synthesis of Natural Products: The Chiron Approach*;
B. Fraser-Reid, *Acc. Chem. Res.* **1996**, 29(2), 57-66

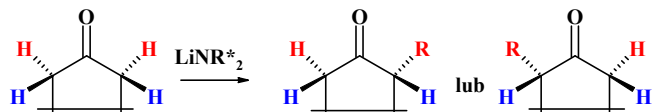


Otrzymywanie związków optycznie czynnych ze związków achiralnych:

Synteza asymetryczna, Kataliza (w tym organokataliza), Reakcje diastereoselektywne z użyciem pomocników

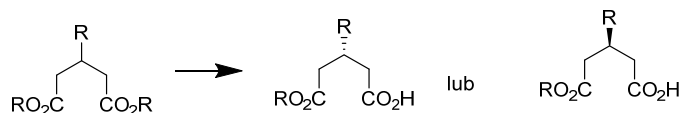
Desymetryzacja związków symetrycznych

1. Chemiczna



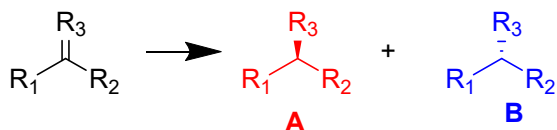
M. Majewski, *Tetrahedron Letters*, **1999**, 40, 8755-8758;
Solid support: P.G. Williard, *Tet: Asymm.* **2006**, 17, 3021-29

2. Enzymatyczna



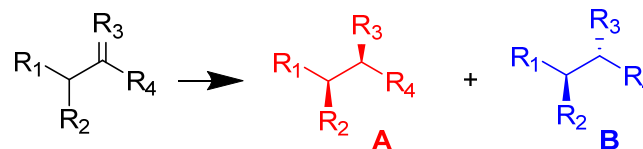
Przykładowo, L.Y. Chen, *et. al.* *JOC*, **1996**, 51, 834;
R. Ostaszewski i wsp. *Tetrahedron: Asymmetry*, **2005**, 16, 2475

Reakcje enancjoróżnicujące



$$ee = \frac{A - B}{A + B} \times 100\%$$

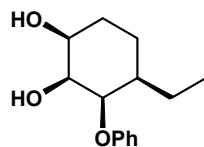
Reakcje diastereoróżnicujące



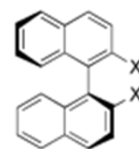
$$de = \frac{A - B}{A + B} \times 100\%$$

Racemat lub związek optycznie czynny

Planowanie syntez związków optycznie czynnych

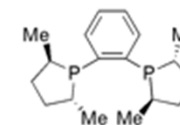


(privileged catalysts)



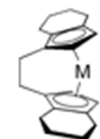
X=OH BINOL
X=PPh₂ BINAP

Diels-Alder
Mukaiyama aldol
aldehyde allylation
hydrogenation
alkene isomerization
Heck reaction



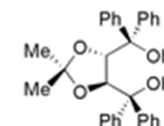
MeDuPhos

hydrogenation
hydrophosphination
hydroacylation
hydrosilylation
Bayer-Villiger oxidation



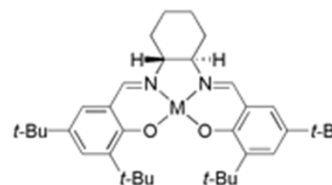
Brintzinger's
ligand

alkene reduction
imine reduction
alkene carbometallation
Ziegler-Natta
polymerization



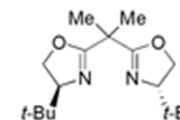
TADDOLate
ligand

Diels-Alder
aldehyde alkylation
ester alcoholysis
iodolactonization



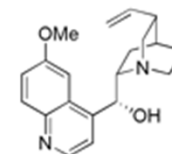
Salen complexes

epoxidation
epoxide ring-opening
Diels-Alder
imine cyanation
conjugate addition



Bis(oxazoline)

Diels-Alder
Mukaiyama aldol
conjugate addition
cyclopropanation
aziridination



Cinchona alkaloid
derivatives

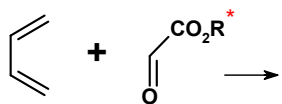
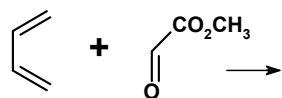
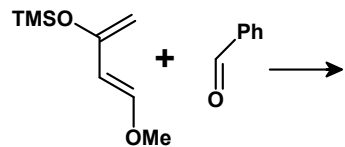
dihydroxylation
acylation
heterogeneous hydrogenation
phase transfer catalysis

Small-Molecule C-H donors in Asymmetric Catalysis;

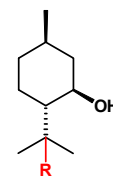
A.G. Doyle, E.N. Jacobsen, *Chem. Rev.* **2007**, 107 (12), 5713-5743

Cały zeszyt 12 Chem. Rev. 2007 rok

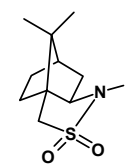
Planowanie syntez związków optycznie czynnych



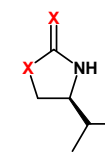
Pomocniki chiralne (chiral auxiliary)



R = H (mentol)
R = Ph 8-fenylomentol (Corey, 1978)

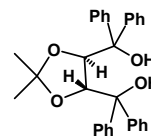


sultam Oppolzera

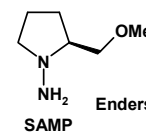


Evans aux.

X = O, S

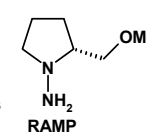


TADDOL
(Seebach)



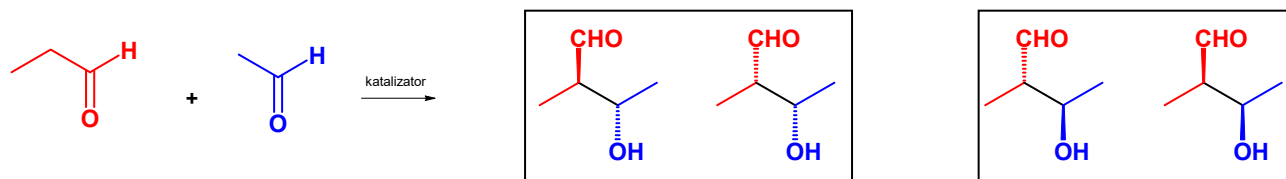
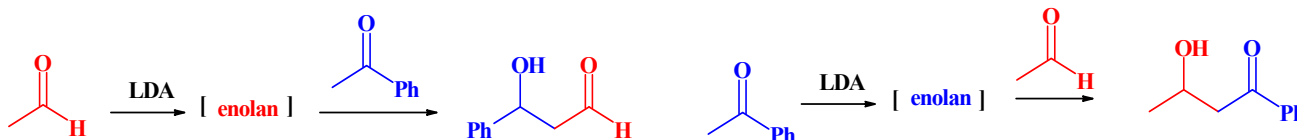
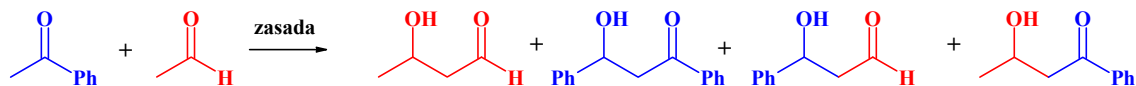
SAMP

Enders



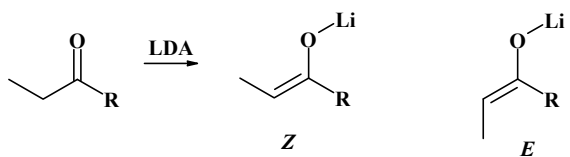
RAMP

Reakcja aldolowa

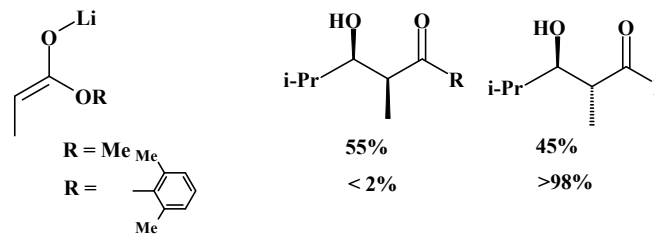
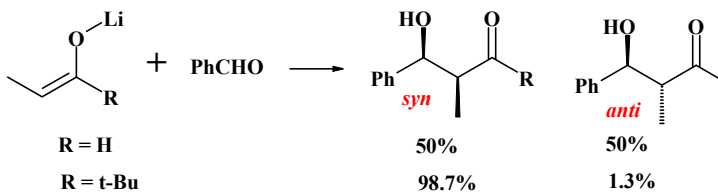


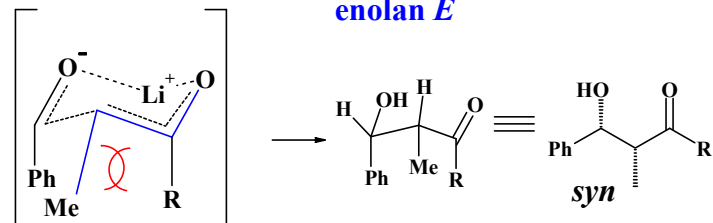
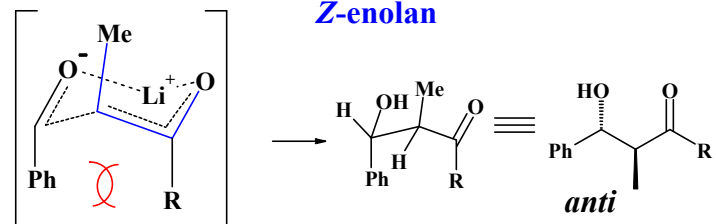
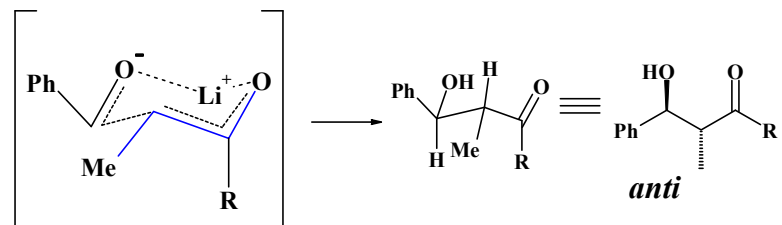
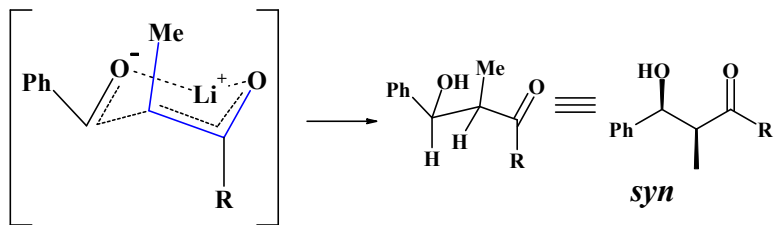
tworzenie enolanów

kontrola kinetyczna szbciej tworzą się izomery Z
szczególnie gdy mamy duże (stosunkowo) podstawniki

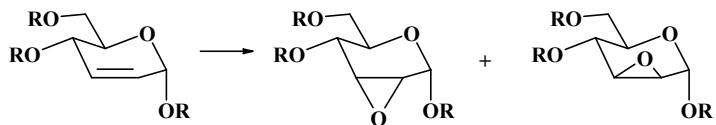
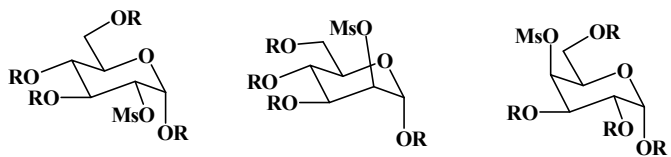


mały R = OMe Z = 3% E = 97%
duży R = Ph Z = 100% E = 0%

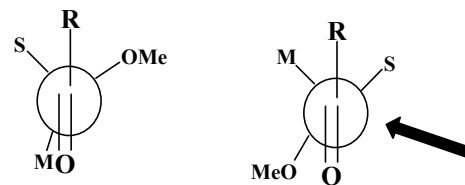
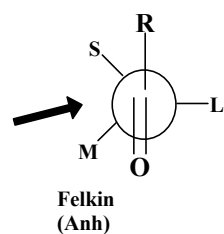
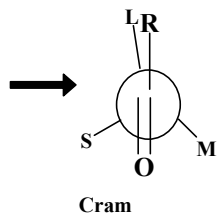
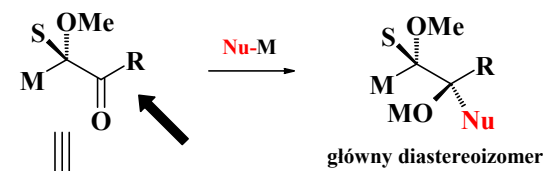
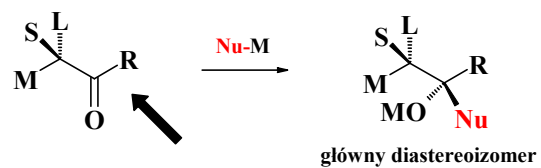




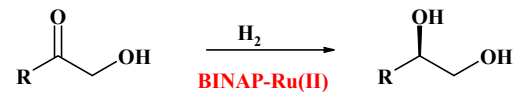
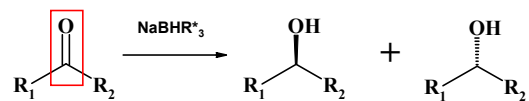
Reakcije substitucije – eliminacije



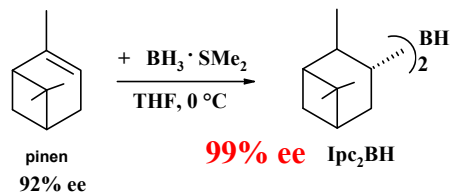
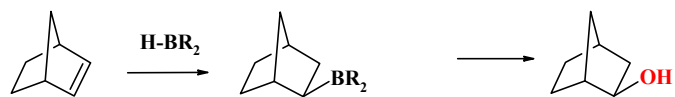
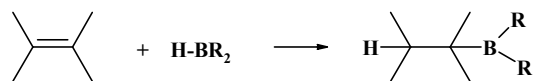
Addycja do grupy karbonylowej



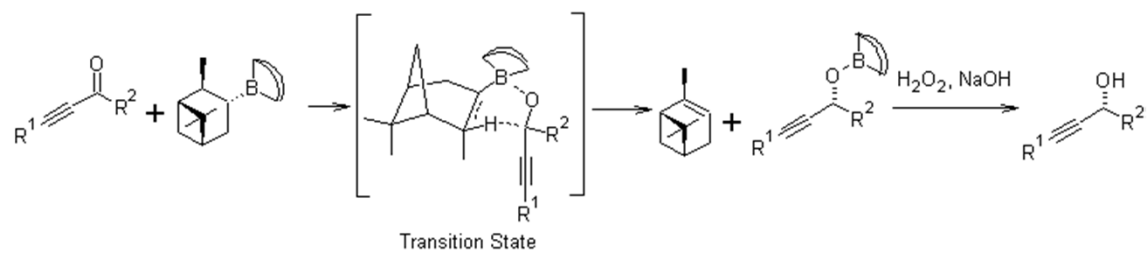
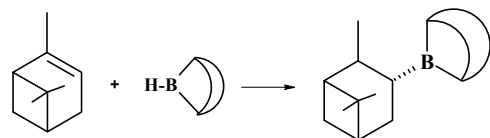
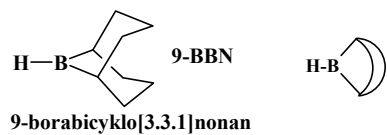
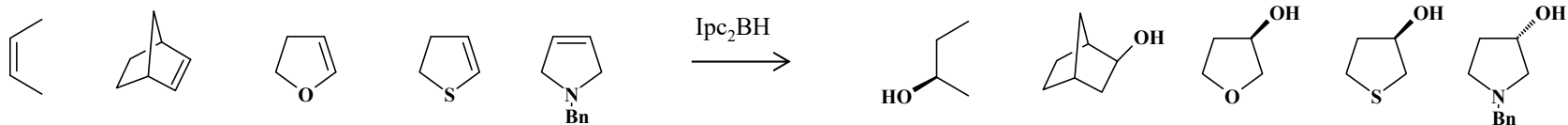
Jak dokonać asymetrycznej redukcji grupy karbonylowej ????



Asymetryczne borowodorowanie wiązań C=C



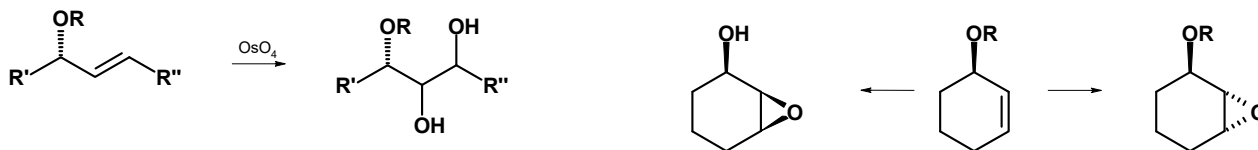
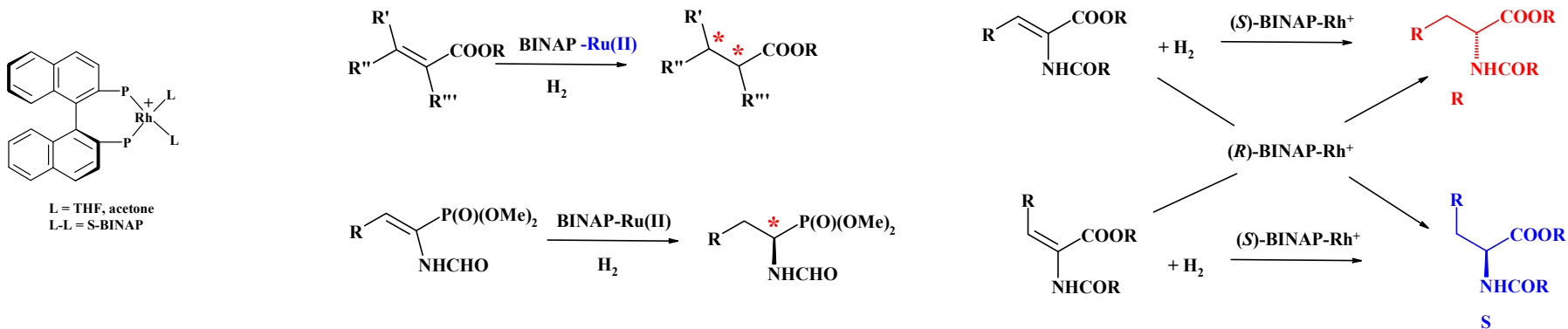
H.C. Brown, P.V. Ramachandran, *Pure Appl. Chem.*, 1994, 66, 201-212



Katalityczna enancjoselektywna redukcja wiązań C=C

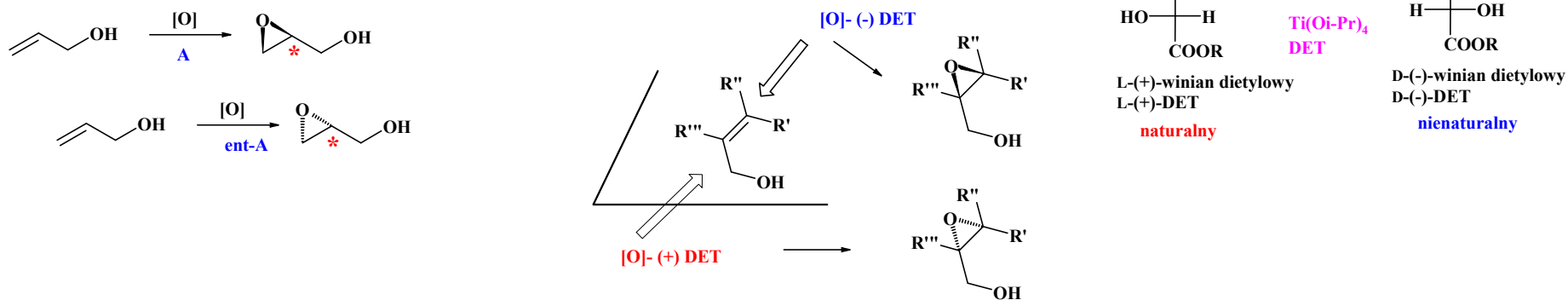
Kompleksy BINAP'u do **ENANCJOSELEKTYWNEJ** redukcji wiązań podwójnych

BINAP tworzy kompleksy z metalami przejściowymi, przenosząc na nie chiralność

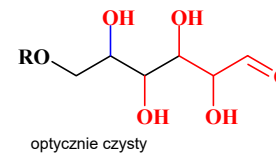
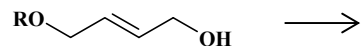


Kishi, et. al. Tetrahedron Lett. 1983, 3943; Tetrahedron, 1984, 2247

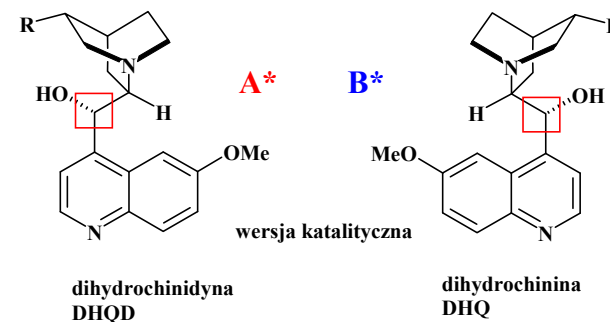
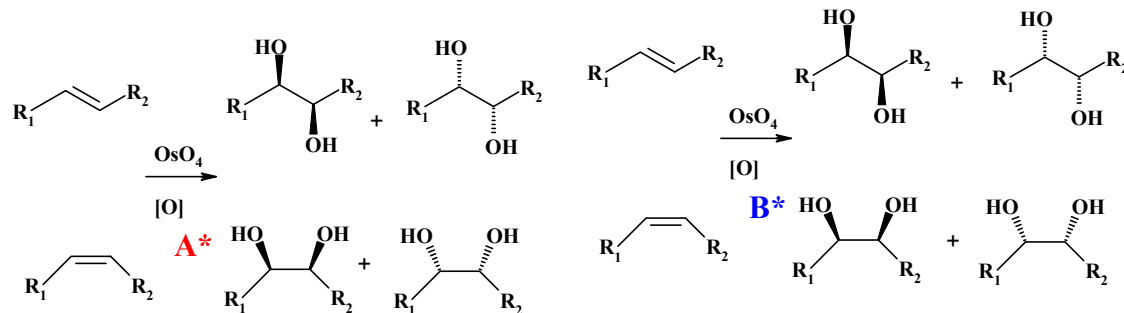
Asymetryczne epoksydowanie alkoholi allilowych



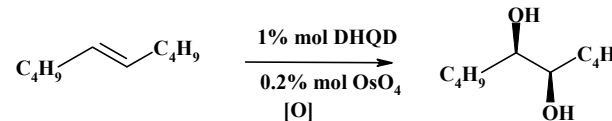
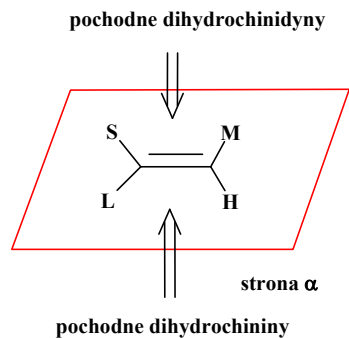
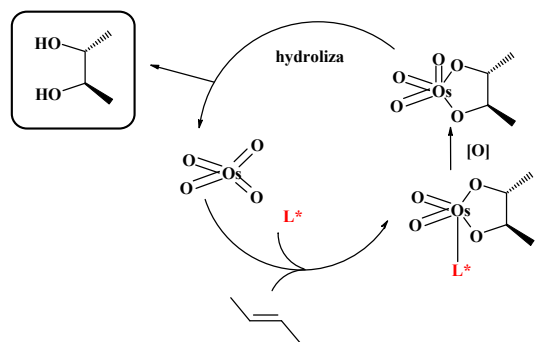
Synteza nienaturalnych cukrów (Sharpless Masamune)



Asymetryczna *cis*-hydroksylacja. Sharpless et al. Chem. Rev. 1994 2483-2547



wersja enancjoselektywna





Przyjemnej nauki !!!!!!!

Do zobaczenia na egzaminie