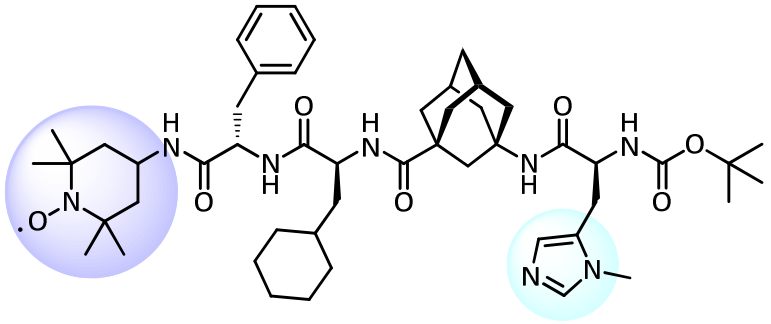
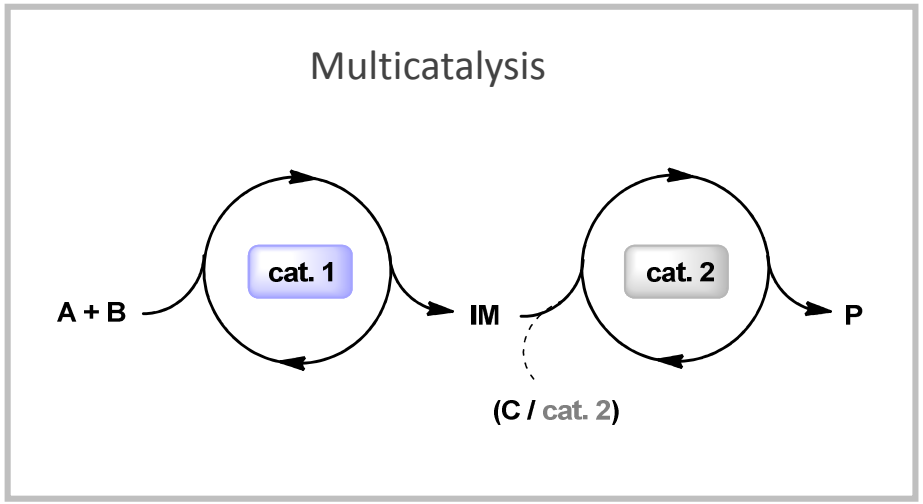
En Route to Multicatalysis:

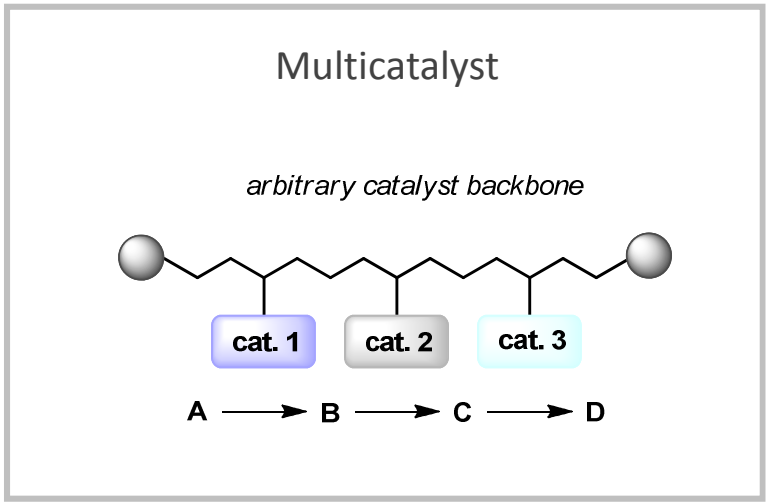
Kinetic Resolution of Diols *via* Oxidative Esterification and an Alcohol-Cross Coupling Strategy

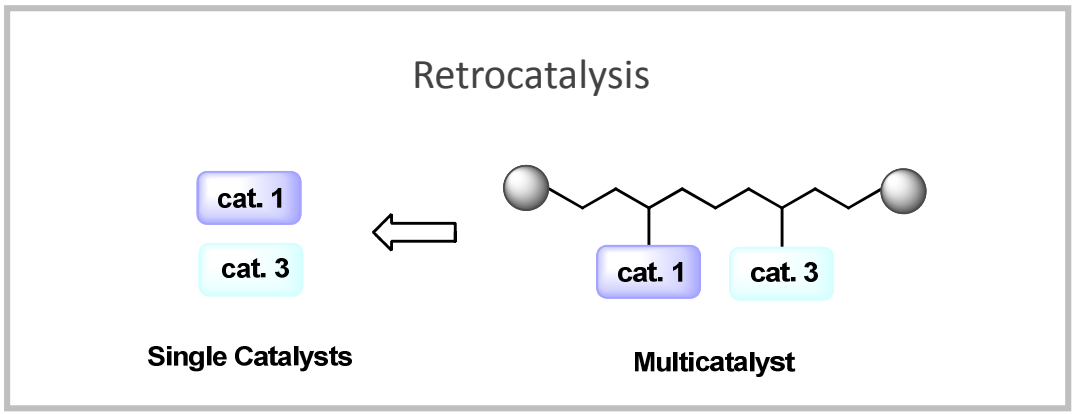
28.11.2014 AG Seminar

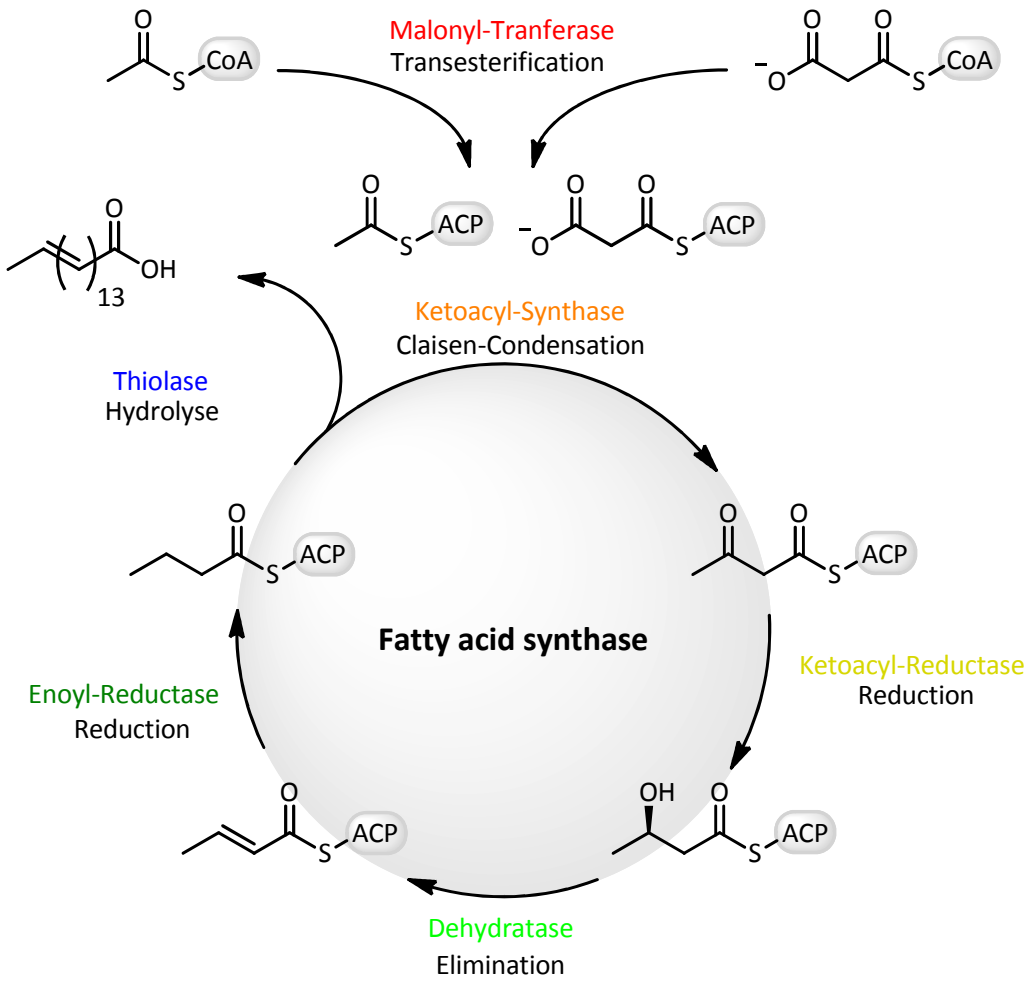
Christine Hofmann
Institute of Organic Chemistry
Justus-Liebig University
35392 Giessen, Germany

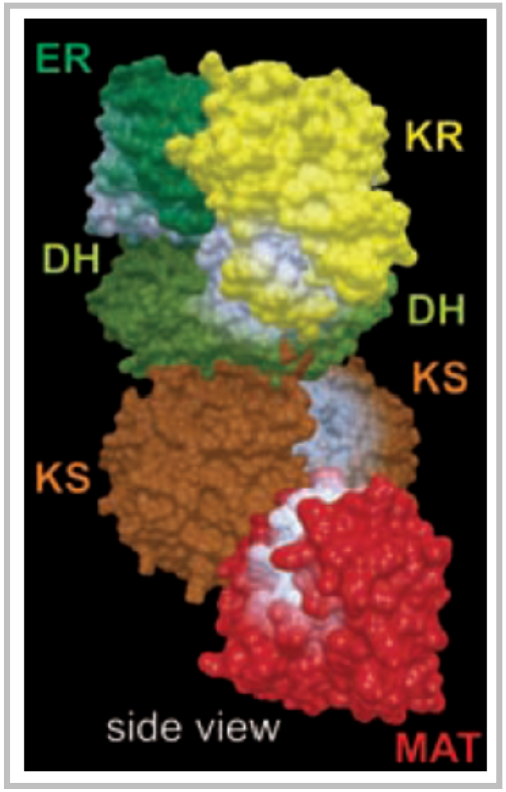



Multicatalysis
A + B
cat. 1
IM
cat. 2
P
(C / cat. 2)


Multicatalyst
arbitrary catalyst backbone
cat. 1
cat. 2
cat. 3
A
B
C
D

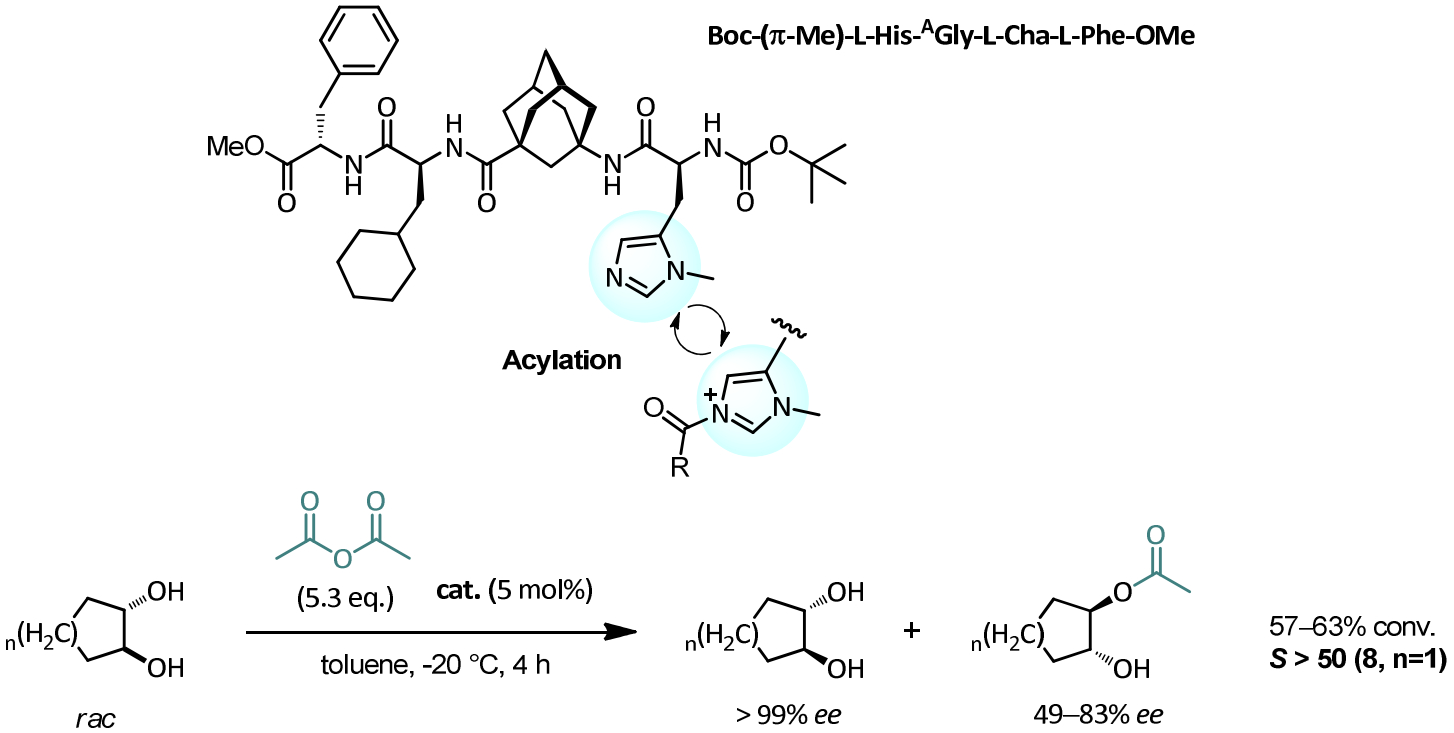

Retrocatalysis
cat. 1
cat. 3
Single Catalysts
cat. 1
cat. 3
Multicatalyst

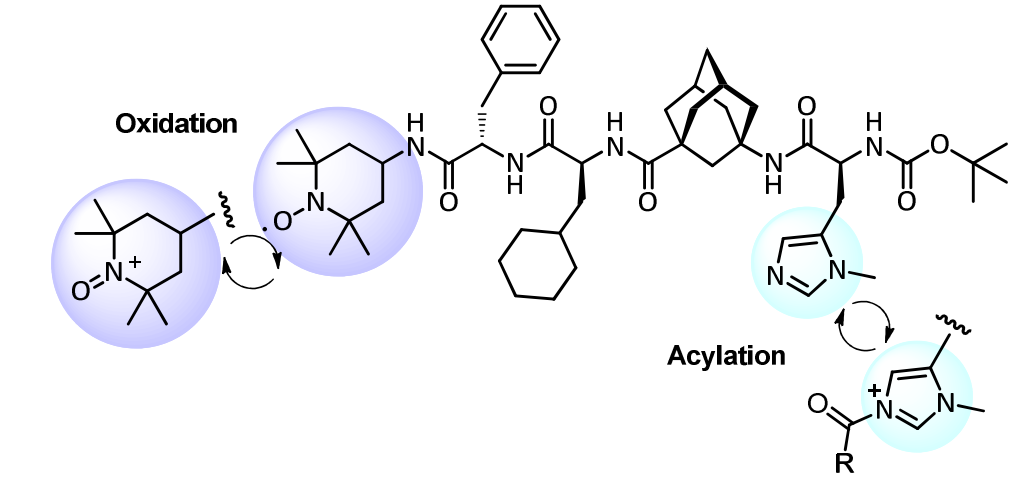


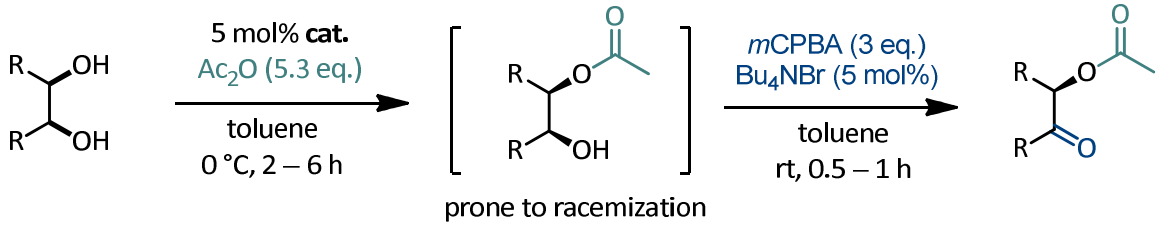


M. Leibundgut, T. Maier, S. Jenni, N. Ban, *Curr. Opin. Struct. Biol.* **2008**, *18*, 714; T. Maier, S. Jenni, N. Ban, *Science* **2006**, *311*, 1258.

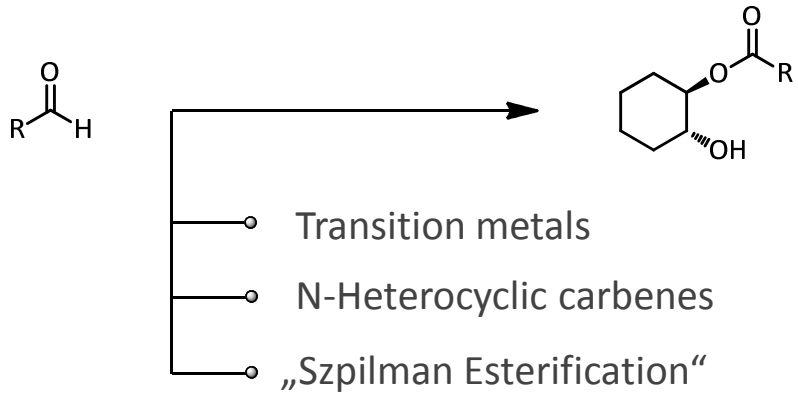
Introduction: Kinetic Resolution of *trans*-Cycloalkane-1,2-diols

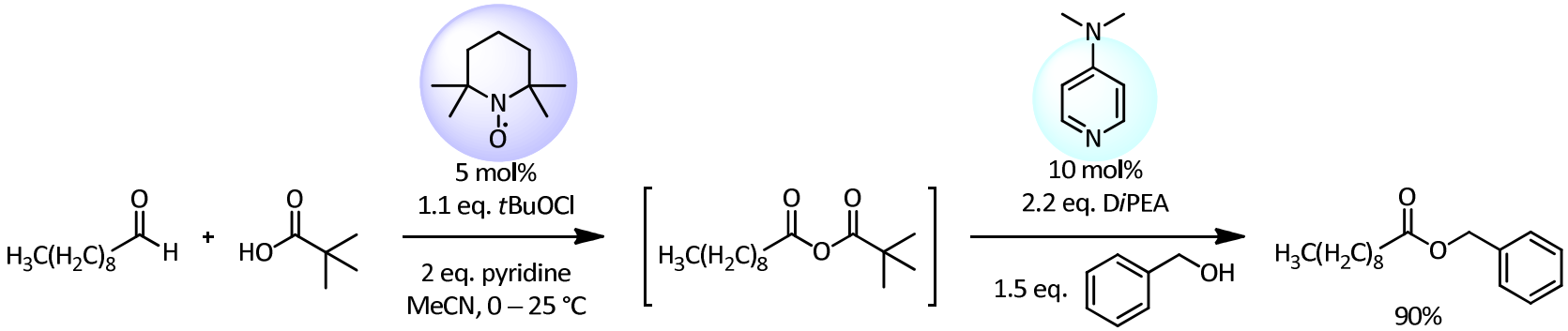






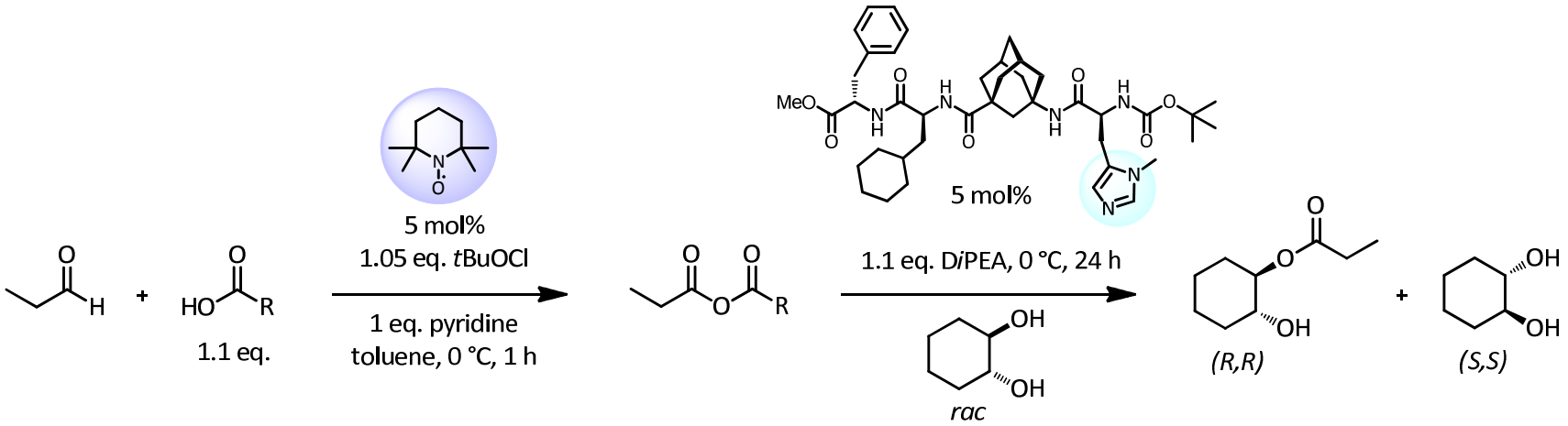
1. Oxidation, 2. Esterification **?**

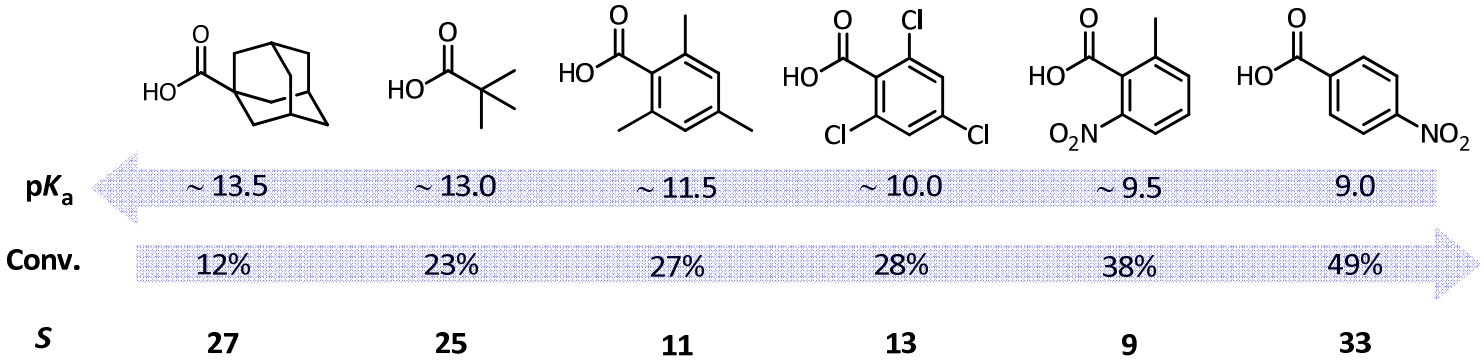




B. E. Maki, K. A. Scheidt, *Org. Lett.* **2008**, *10*, 4331-4334; J. Guin, S. De Sakar, S. Grimme, A. Studer, *Angew. Chem. Int. Ed.* **2008**, *47*, 8727-8730; H. Toledo, E. Pisarevsky, A. Abramovich, A. Szpilman, *Chem. Commun.* **2013**, *49*, 4367-4369.

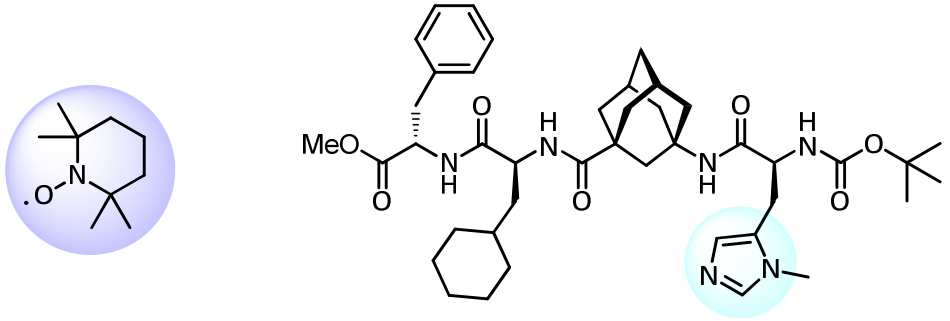
Optimization Studies: Acid Screening

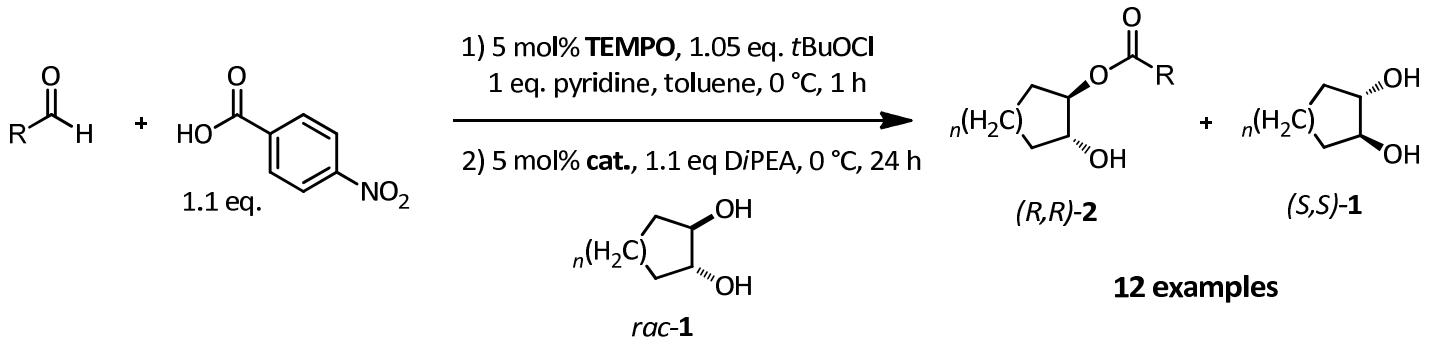


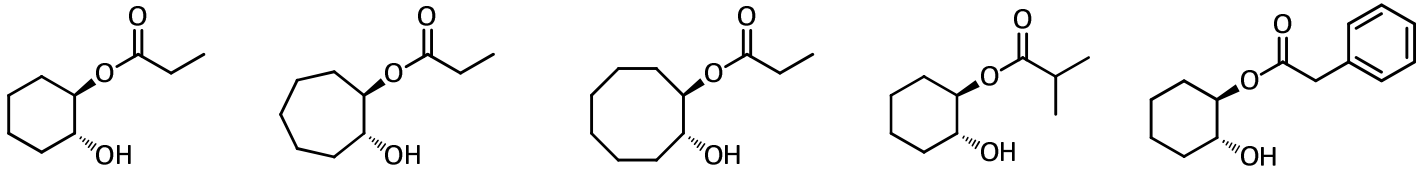


F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456-463; C. Hofmann, S. M. M. Schuler, R. C. Wende, P. R. Schreiner, *Chem. Commun.* **2014**, *50*, 1221-1223.

Substrate Scope







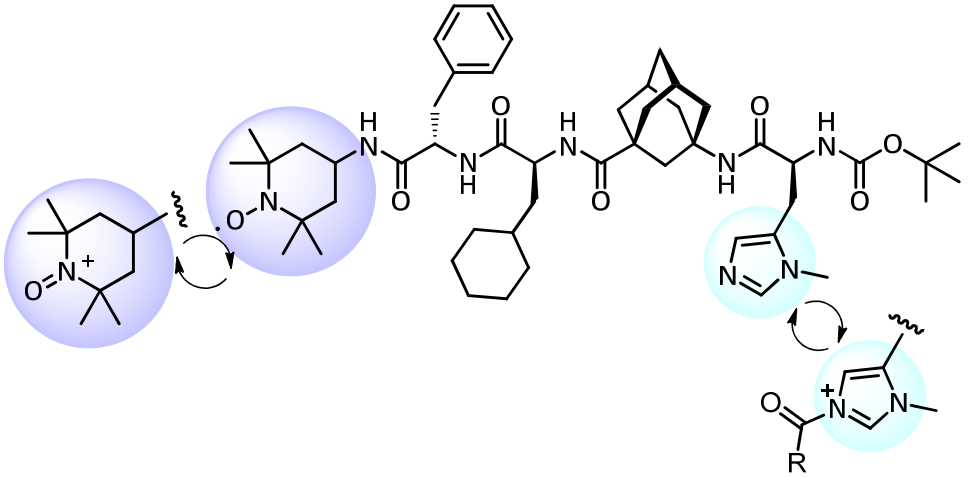
47% conv., 88% *ee*
S = 39

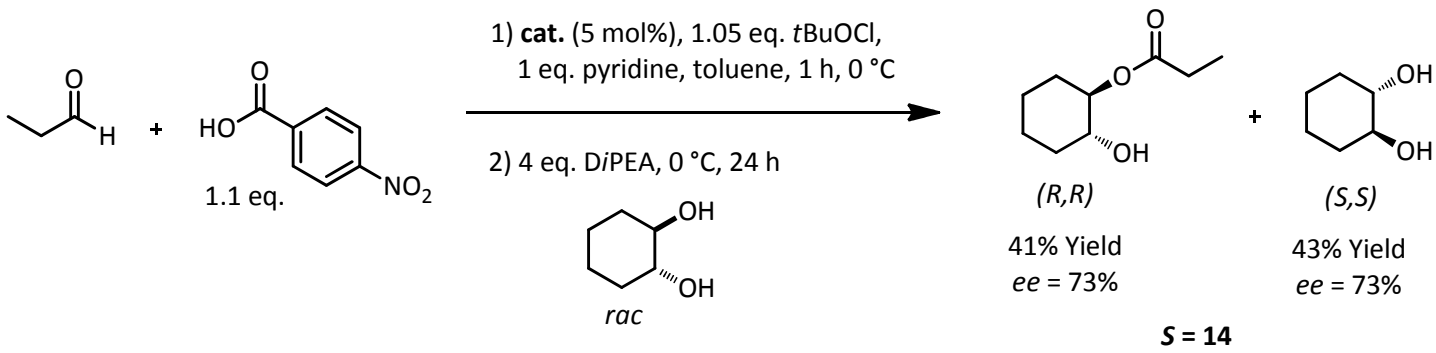
49% conv., 88% *ee*
S = 43

50% conv., 93% *ee*
S > 50

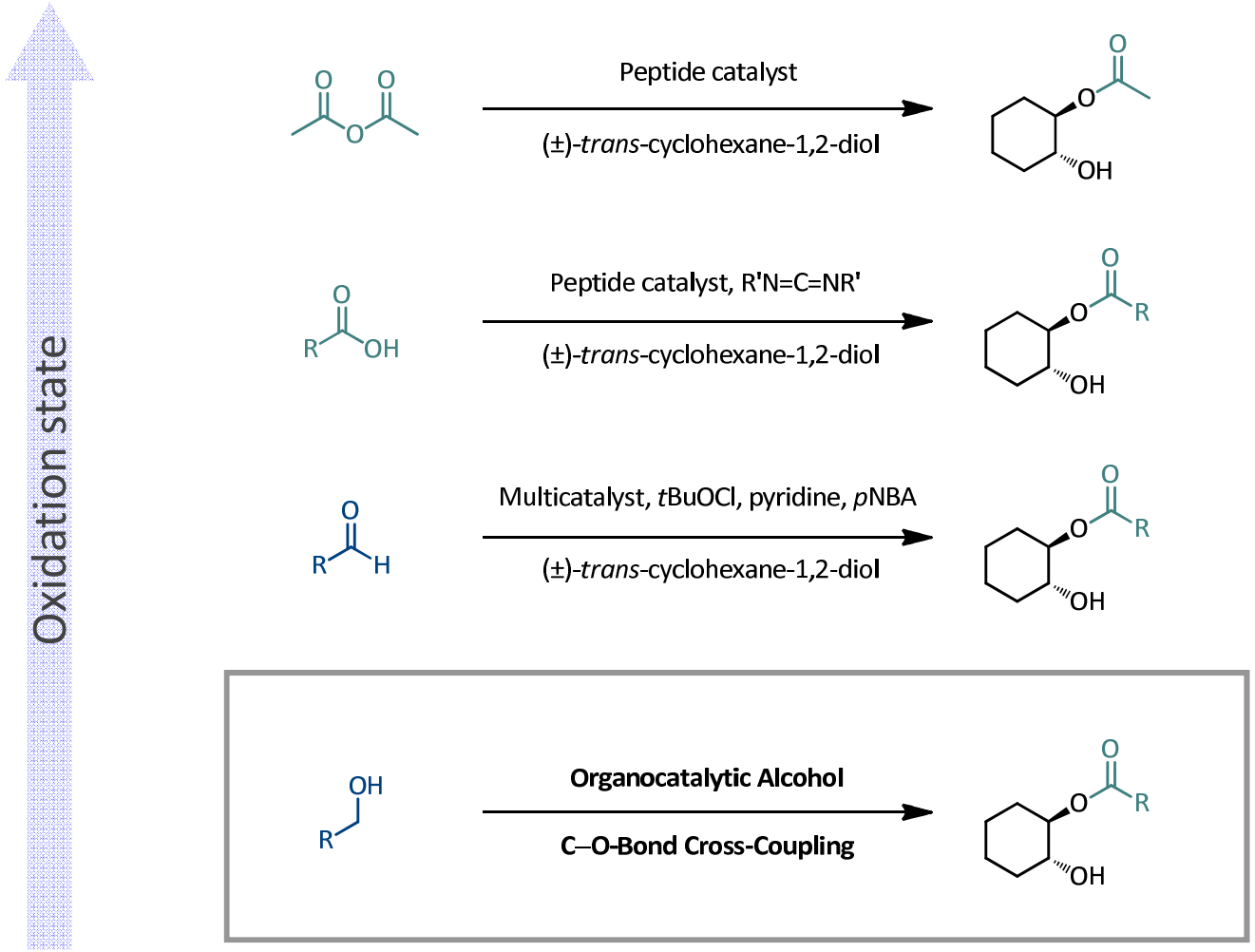
44% conv., 90% *ee*
***S* = 40**

35% conv., 93% *ee*
***S* = 47**

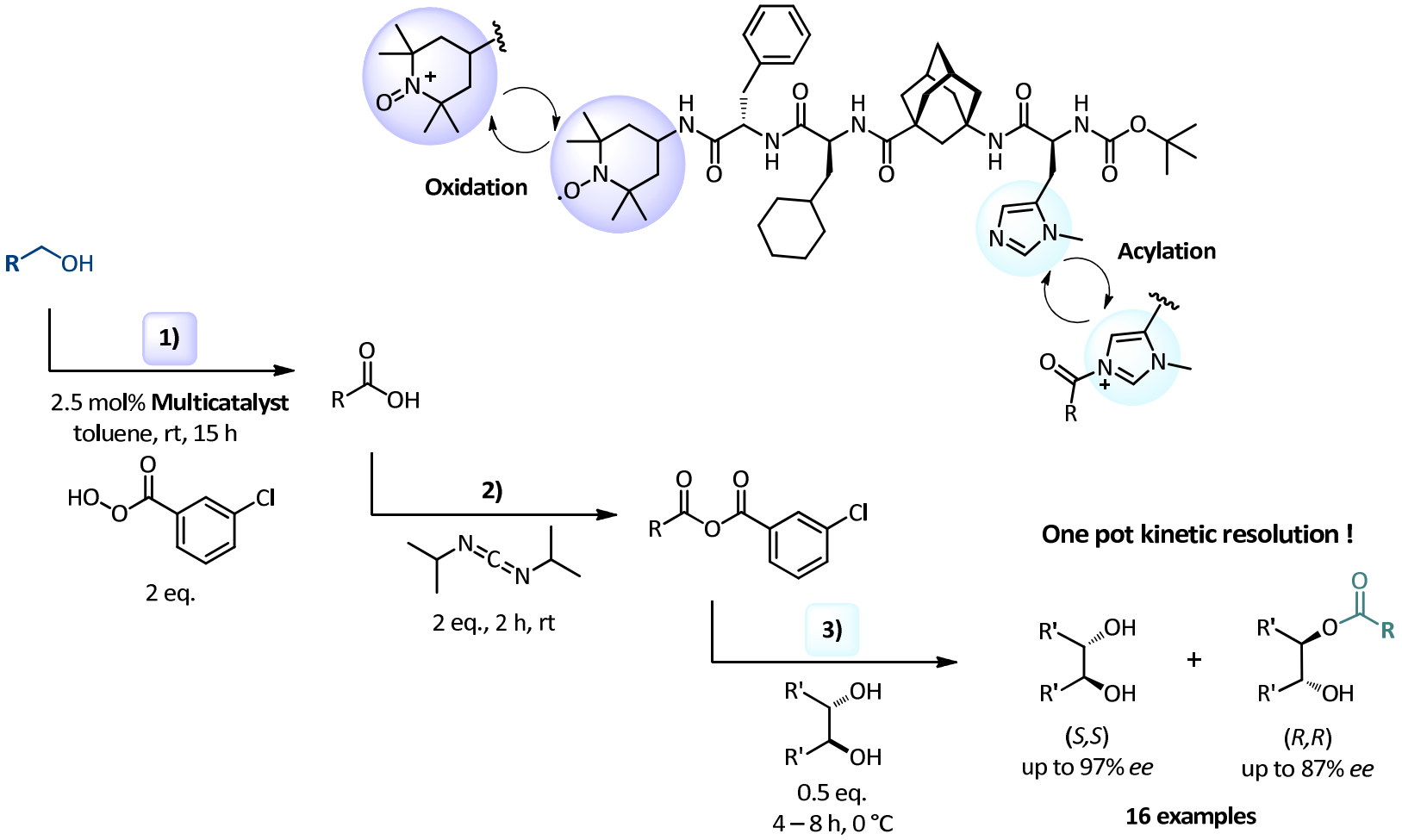



1) **cat.** (5 mol%), 1.05 eq. *t*BuOCl,
1 eq. pyridine, toluene, 1 h, 0 °C
2) 4 eq. D*i*PEA, 0 °C, 24 h
1.1 eq.
rac
(R,R)
41% Yield
ee = 73%
(S,S)
43% Yield
ee = 73%
***S* = 14**

Overview of various Acyl Sources

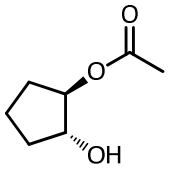


Results: Kinetic Resolution of Diols by an Alcohol Cross-Coupling Strategy

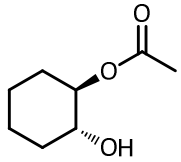


C. Hofmann, J. M. Schümann, P. R. Schreiner, *manuscript submitted.*

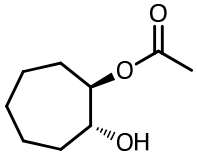
Results: Substrate Scope



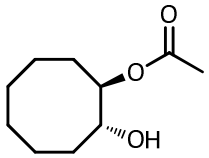
44% *ee*



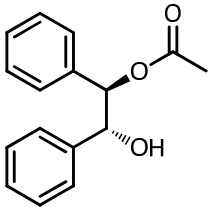
42%, 84% *ee*



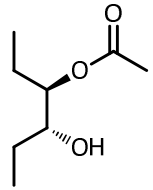
43%, 84% *ee*



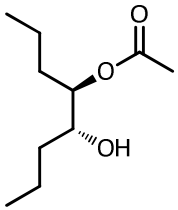
39%, 81% *ee*



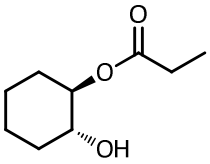
38% *ee*



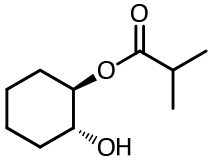
43%, 73% *ee*



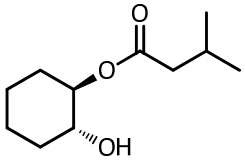
23%, 76% *ee*



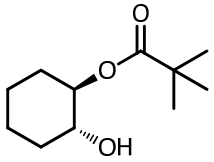
45%, 82% *ee*



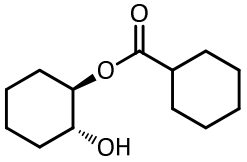
35%, 74% *ee*



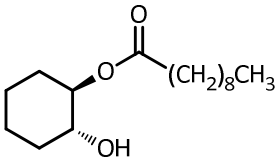
40%, 87% *ee*



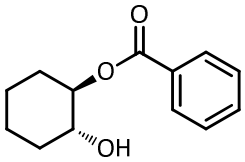
traces, 50% *ee*



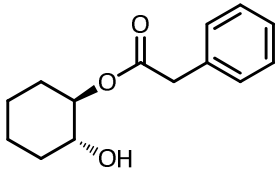
41%, 52% *ee*



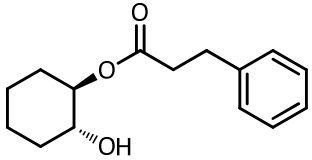
43%, 80% *ee*



traces, 48% *ee*



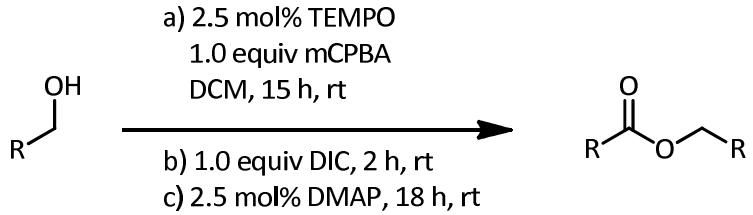
40%, 67% *ee*

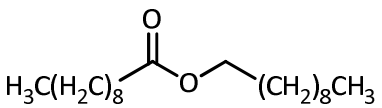


46%, 60% *ee*

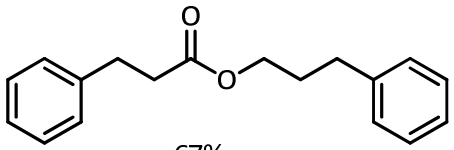
C. Hofmann, J. M. Schümann, P. R. Schreiner, *manuscript submitted.*

Results: Dimerization of Alcohols





59%

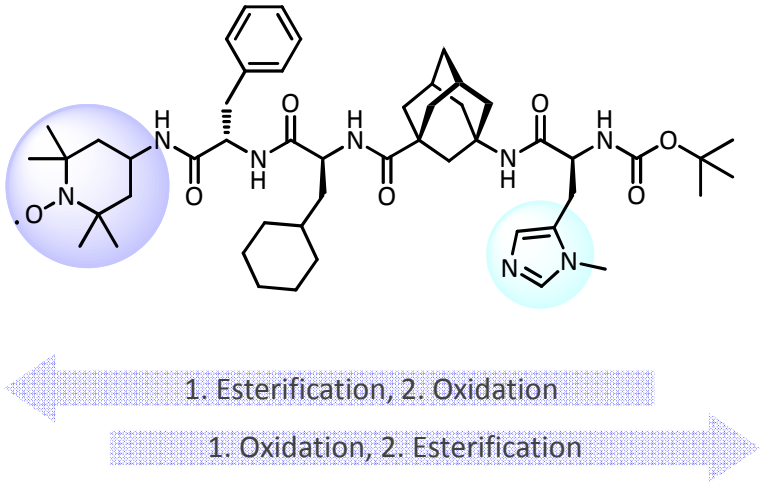


67%

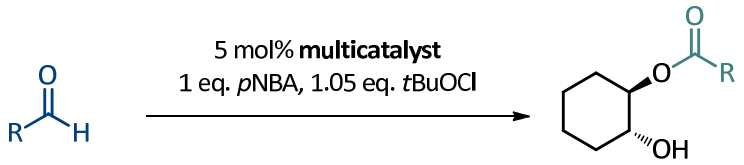
C. Hofmann, J. M. Schümann, P. R. Schreiner, *manuscript submitted.*

Summary / Outlook

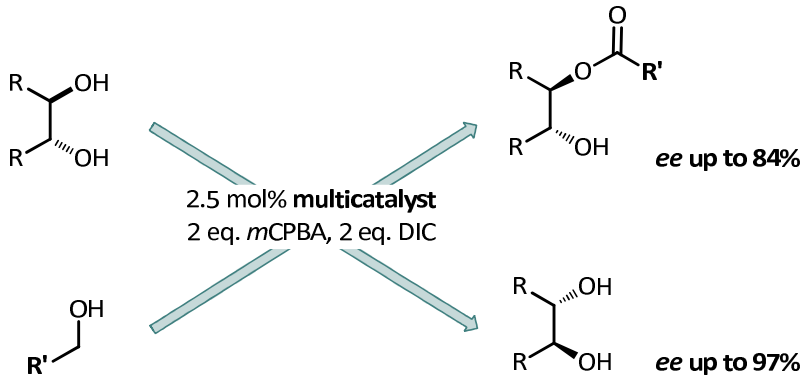
Multicatalytic System



Enantioselective Oxidative Esterification



C–O Alcohol Cross-Coupling



Outlook

- Immobilization of the catalyst
- Expanding the substrate scope
- Enantioselective oxidation reactions
- Further catalytic moieties and reaction sequences

orca
organocatalysis cost action

JUSTUS-LIEBIG-
UNIVERSITÄT
GIESSEN

DFG Deutsche Forschungsgemeinschaft