

# Biocatalytic Synthesis

Examples of reactions investigated at the

University of Graz  
Austrian Centre of Industrial Biotechnology

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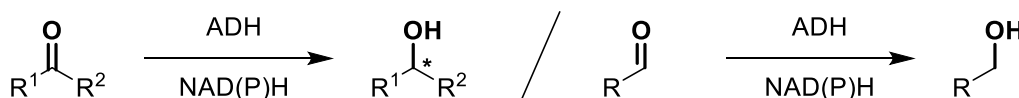
phone: +43 316 380 5332

e-mail: [kurt.faber@uni-graz.at](mailto:kurt.faber@uni-graz.at)

[www.biocatalysis.uni-graz.at](http://www.biocatalysis.uni-graz.at)

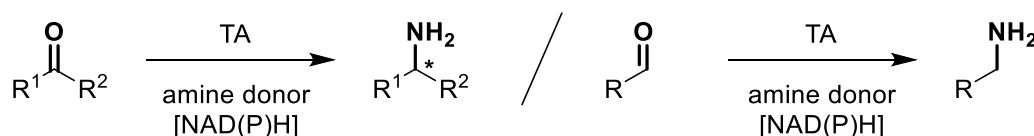
# Reductive Biotransformations

## Reduction of Aldehydes and Ketones



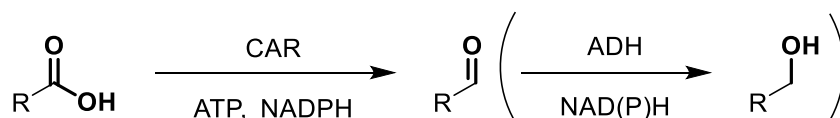
(ADH = alcohol dehydrogenase; *Angew. Chem., Int. Ed.* **2002**, 41, 1014; *Angew. Chem., Int. Ed.* **2008**, 47, 714; *ChemCatChem* **2013**, 5, 1744.)

## Reductive Amination of Aldehydes and Ketones



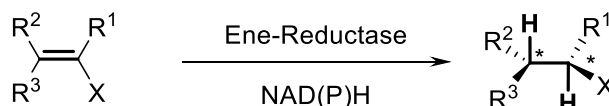
(TA =  $\omega$ -transaminase; *Angew. Chem., Int. Ed.* **2008**, 47, 9337; *Angew. Chem., Int. Ed.* **2012**, 51, 9156; *Org. Proc. Res. Dev.* **2013**, 17, 751; *ACS Catal.* **2014**, 4, 129.)

## Reduction of Carboxylic Acids



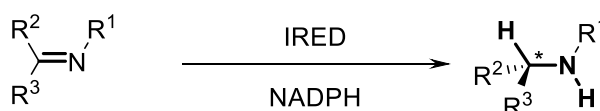
(CAR = carboxylate reductase, ADH = alcohol dehydrogenase; *Chem. Monthly*, **2016**, 147, 575.)

## Reduction of C=C-Bonds



(X = electron-withdrawing group; *Angew. Chem., Int. Ed.* **2007**, 46, 3934; *Chem. Eur. J.* **2012**, 18, 10367; *Curr. Opin. Chem. Biol.* **2007**, 11, 203; *J. Biotechnol.* **2012**, 162, 381; *Nat. Commun.* **2014**, 5, 4150; *Curr. Opin. Chem. Biol.* **2018**, 43, 97)

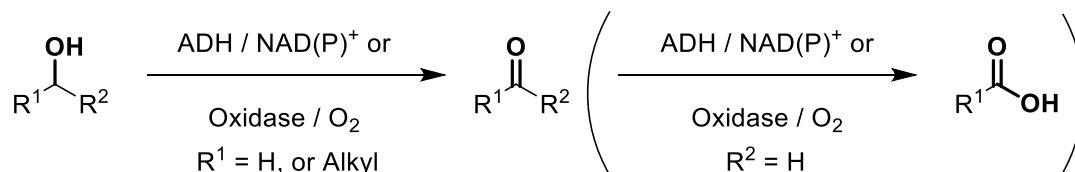
## Reduction of Imines



(IRED = imine reductase; *Adv. Synth. Catal.* **2015**, 357, 1655; *ChemCatChem* **2018**, 10, 3236.)

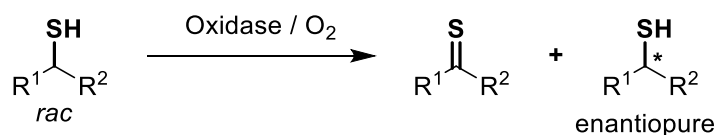
# Oxidative Biotransformations

## Oxidation of Alcohols / Aldehydes



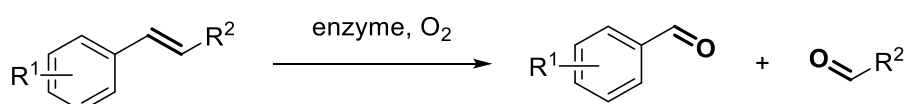
(ADH = alcohol dehydrogenase; *Angew. Chem., Int. Ed.* **2002**, 41, 1014; *Angew. Chem., Int. Ed.* **2008**, 47, 714; *J. Am. Chem. Soc.* **2008**, 130, 13969; *ChemCatChem* **2013**, 5, 1744.)

## Oxidation of Thiols



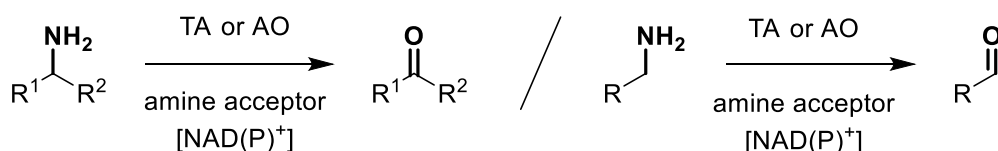
(*Angew. Chem., Int. Ed.* **2018**, 57, 2864.)

## C=C-Bond Cleavage



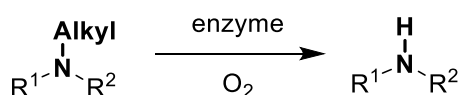
(*Angew. Chem., Int. Ed.* **2006**, 45, 5201; *J. Am. Chem. Soc.* **2009**, 131, 5368; *Chem. Commun.* **2012**, 48, 3303; *Adv. Synth. Catal.* **2015**, 357, 3309; *Front. Microbiol.* **2016**, 7, 1511.)

## De-Amination



(TA =  $\omega$ -transaminase; AO =  $\alpha$ -amino oxidase; *Angew. Chem., Int. Ed.* **2008**, 47, 9337; *Org. Proc. Res. Dev.* **2013**, 17, 751; *ACS Catal.* **2014**, 4, 129.)

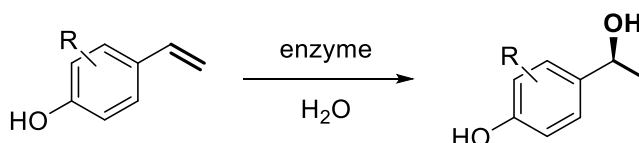
## N-De-Alkylation



(*Angew. Chem., Int. Ed.* **2015**, 54, 15051.)

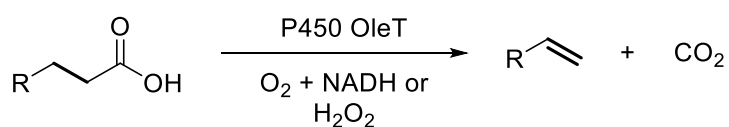
# Oxidative Biotransformations

## Hydration of Styrenes



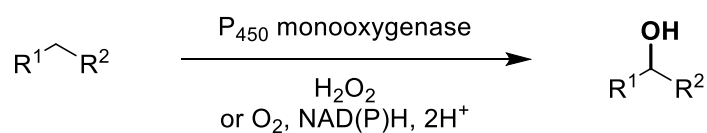
(*Angew. Chem., Int. Ed.* **2013**, *52*, 2293; *ACS Catal.* **2018**, *8*, 2438.)

## Oxidative Decarboxylation



(*Angew. Chem., Int. Ed.* **2015**, *54*, 8819; *Chem. Commun.*, **2016**, *51*, 1918; *Eur. J. Org. Chem.*, **2016**, 2473; *Eur. J. Org. Chem.* **2016**, 3473.)

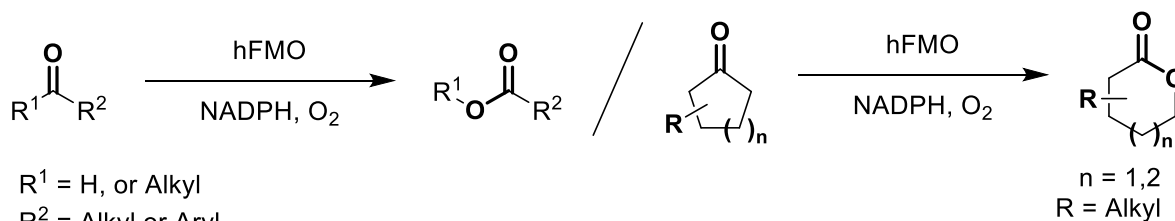
## C-H Hydroxylation



terpenoid, steroid, APIs

(*Angew. Chem., Int. Ed.* **2006**, *45*, 5201; *J. Am. Chem. Soc.* **2009**, *131*, 5368; *Chem. Commun.* **2012**, *48*, 3303; *Adv. Synth. Catal.* **2013**, *355*, 3321; *Angew. Chem. Int. Ed.* **2018**, *57*, 427; *Catal. Lett.* **2018**, *148*, 787)

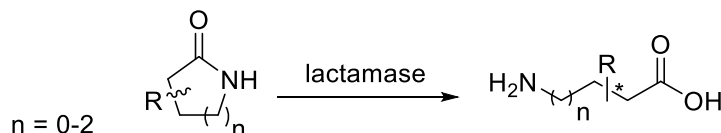
## Baeyer-Villiger Oxidation



(hFMO = human flavin containing monooxygenase; *ACS Chem. Biol.*, **2016**, *11*, 1039; *ACS Chem. Biol.* **2017**, *12*, 2379.)

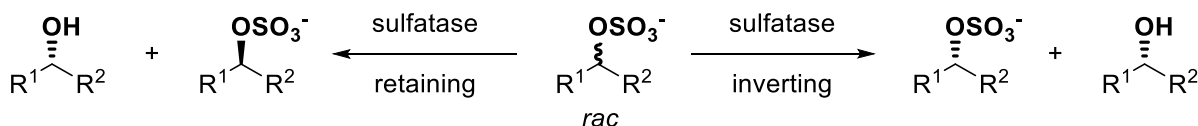
# Hydrolysis / Esterification

## Hydrolysis of Lactams



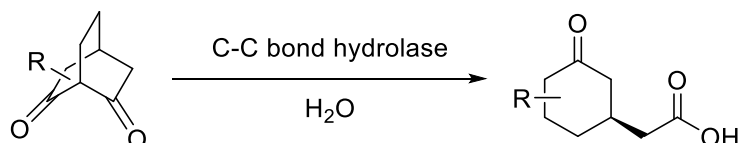
(*ChemCatChem* **2014**, 6, 2517.)

## Bio-Mitsunobu-Inversion



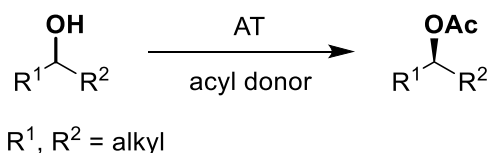
(*Angew. Chem., Int. Ed.* **2002**, 41, 1014; *Angew. Chem., Int. Ed.* **2005**, 44, 6381; *Angew. Chem., Int. Ed.* **2013**, 52, 3277; *Eur. J. Org. Chem.* **2013**, 356; *Trends Biotechnol.* **2013**, 31, 468; *Appl. Microbiol. Biotechnol.* **2014**, 4, 1485.)

## C-C-Bond Hydrolysis



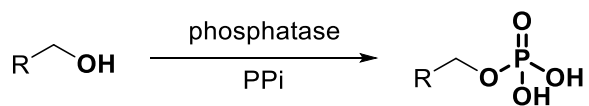
(*Adv. Synth. Catal.* **2013**, 355, 1677; *Adv. Synth. Catal.* **2013**, 355, 1703; *Top. Catal.* **2014**, 57, 376.)

## Ester-Formation in Aqueous Systems



(AT = acyl transferase; *ACS Catal.* **2018**, 8, 10698.)

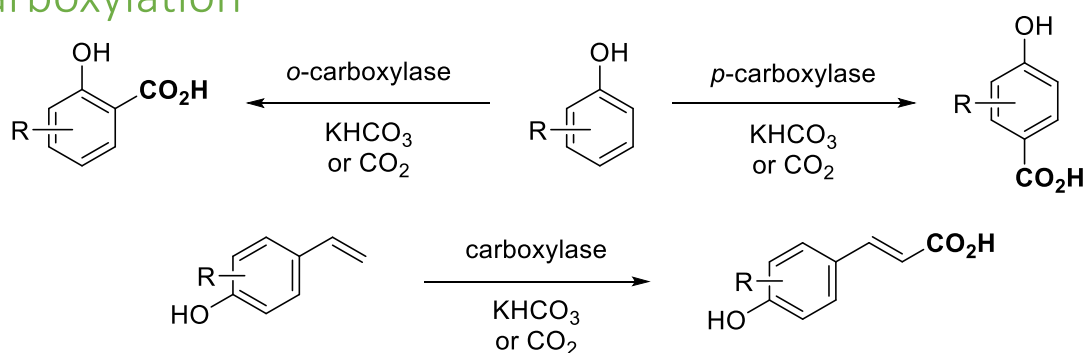
## Phosphorylation



(PPi = pyrophosphate; *Eur. J. Org. Chem.*, **2016**, 45; *J. Biotechnol.* **2016**, 233, 219; *Adv. Synth. Catal.* **2018**, 360, 2394.)

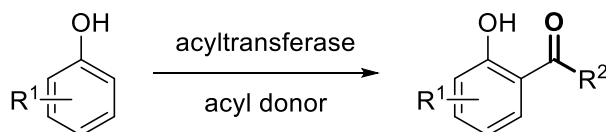
# Biocatalytic C-C-Bond Formation

## Carboxylation



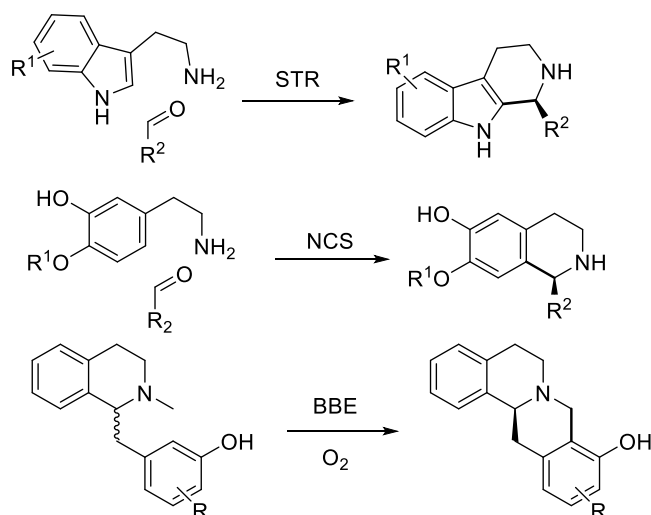
(*Chem. Soc. Rev.* **2010**, 39, 313; *Org. Lett.* **2012**, 14, 1974; *J. Biotechnol.* **2013**, 168, 264; *RSC Adv.* **2014**, 4, 9673; *Angew. Chem. Int. Ed.* **2017**, 56, 13893.)

## Friedel-Crafts Acylation



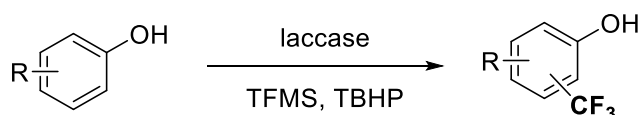
(*Angew. Chem. Int. Ed.* **2017**, 56, 7615.)

## Alkaloid Synthesis



(BBE = berberine bridge enzyme; STR = strictosidine synthase; NCS = norcochlorine synthase; *Angew. Chem., Int. Ed.* **2011**, 50, 1068; *Org. Proc. Res. Dev.* **2013**, 17, 751; *Angew. Chem., Int. Ed.* **2014**, 53, 3731; *ACS Catal.* **2016**, 6, 23; *Angew. Chem. Int. Ed.* **2018**, 57, 10683.)

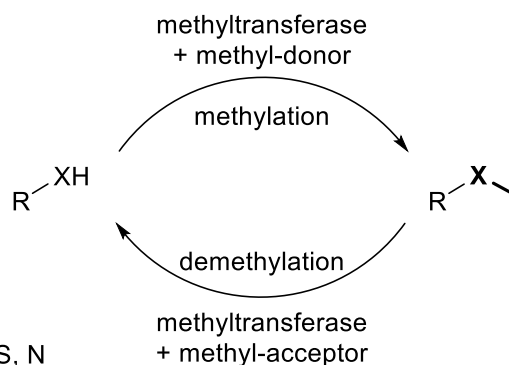
## Trifluoromethylation



(TFMS = trifluoromethylsulfonic acid; TBHP = t-butylhydroperoxide; *Nat. Commun.* **2016**, 7, 13323.)

## Biocatalytic C-O-Bond Formation and Cleavage

### Methylation and De-Methylation

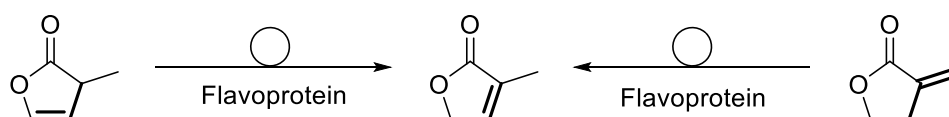


X = O, S, N

(*Communs. Chem.*, **2018**, *1*, 82.)

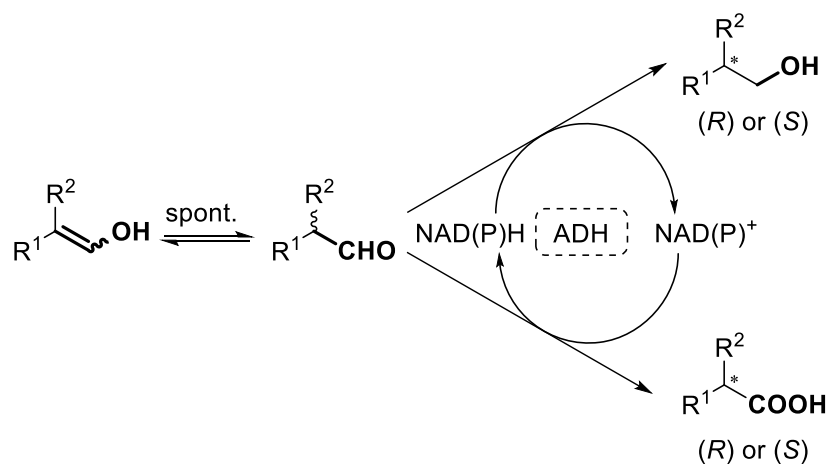
## Enzymatic Isomerisation

### Isomerisation of C=C-Bonds



(*ChemBioChem*, **2012**, *13*, 2346; *ChemSusChem* **2016**, *9*, 3393.)

### Disproportionation: Biocatalytic Cannizzaro Reaction

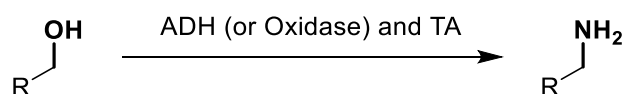


(*ADH = alcohol dehydrogenase; ChemCatChem*, **2013**, *5*, 1744; *Adv. Synth. Catal.* **2018**, *360*, 2742.)



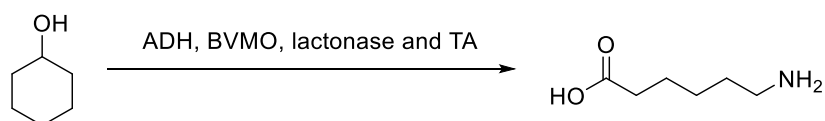
# Enzymatic Cascades

## Direct Amination of Alcohols



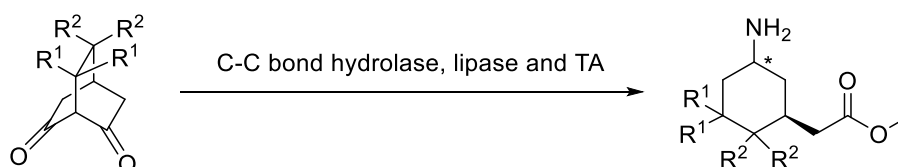
(ADH = alcohol dehydrogenase; TA = transaminase; *ChemCatChem* **2015**, *7*, 3121; *Angew. Chem., Int. Ed.* **2012**, *51*, 9156; *ACS Catal.* **2014**, *4*, 129.)

## 6-Aminohexanoic Acid from Cyclohexanol



(ADH = alcohol dehydrogenase; BVMO = Baeyer-Villiger monoxygenase, TA = transaminase; *Angew. Chem., Int. Ed.* **2014**, *53*, 14153; *ACS Catal.* **2014**, *4*, 129.)

## Cyclohexylamines from Diketones

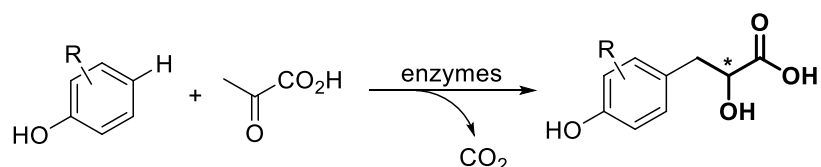


(TA =  $\omega$ -transaminase; *Adv. Synth. Catal.* **2013**, *355*, 1703.)



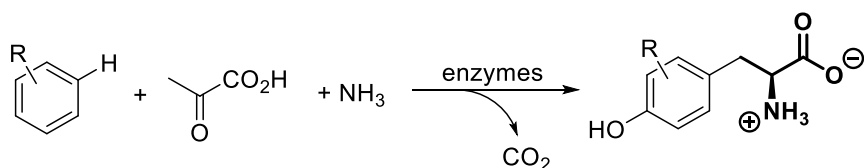
# Enzymatic Cascades

## Enantio-Pure Lactic Acids from Phenols



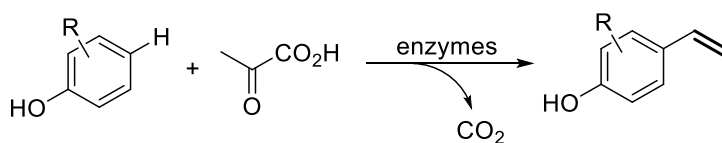
(*ACS Catal.* **2016**, *6*, 2393.)

## L-Tyrosine Derivatives from Benzenes



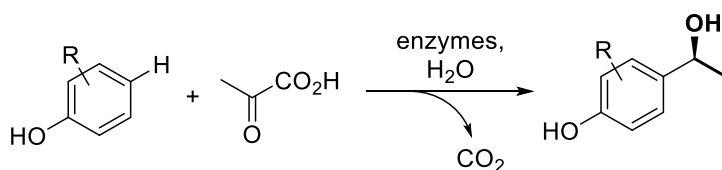
(*ACS Catal.* **2015**, *5*, 7503.)

## Vinylation of Phenols



(*Angew. Chem., Int. Ed.* **2015**, *45*, 10899.)

## Hydroxyethylation of Phenols



(*Org. Lett.* **2018**, *20*, 5139.)