



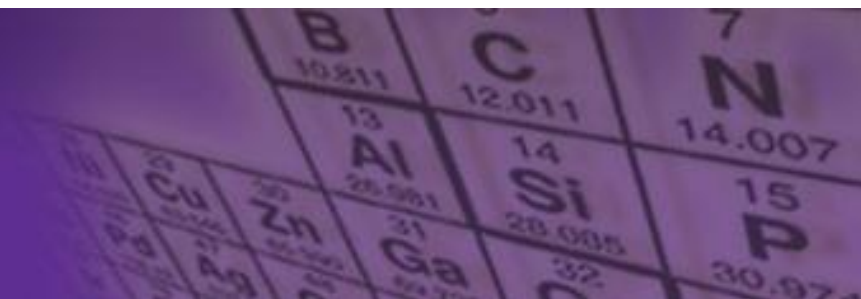
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# Nature Chemistry 2011-2015

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Gaich Group Seminar, Christa Gerlinger, August 3, 2016

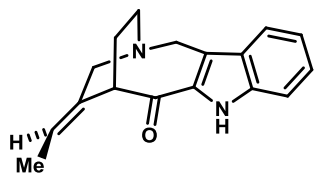
nature  
chemistry



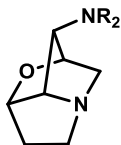


## Total Syntheses and Methodologies

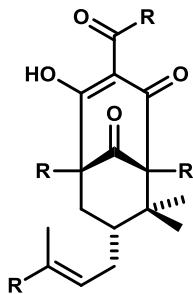
2011



(±)-Conolidine

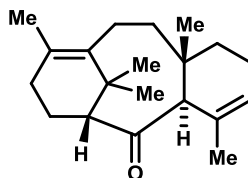


Loline alkaloids

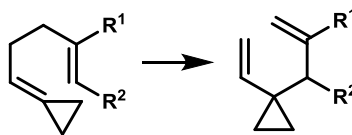


Polyprenylated polycyclic acylphloroglucines

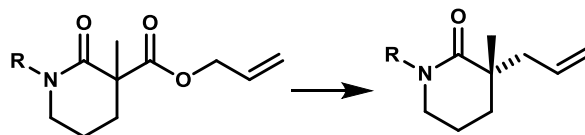
2012



(+)-Taxadienone

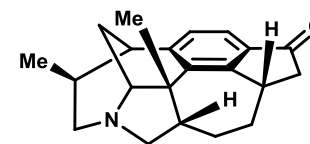


enantioselective cope-rearrangement  
of achiral 1,5-dienes

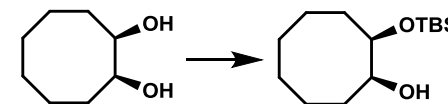


decarboxylative allylic alkylation of lactams

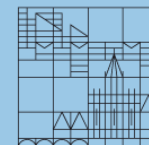
2013



Daphniphyllum

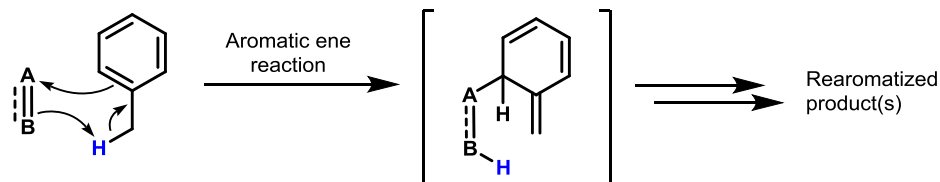


enantioselective silyl-protection

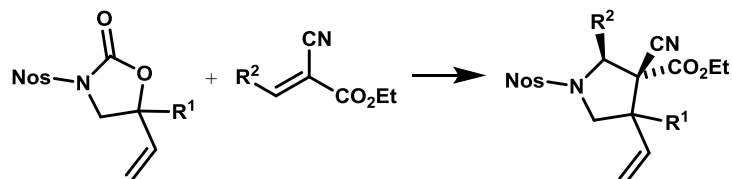


## Total Syntheses and Methodologies

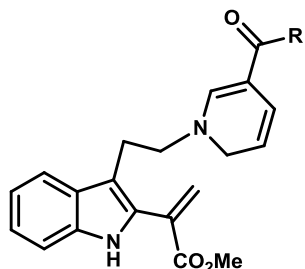
2014



Aromatic ene reaction

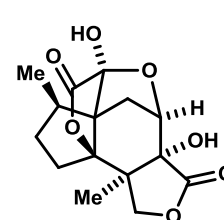


Construction of contiguous all-carbon quaternary stereocentres

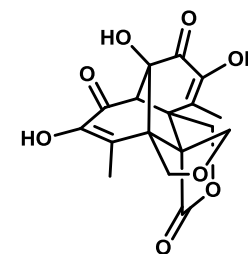


Biogenetically inspired synthesis  
of indole alkaloids

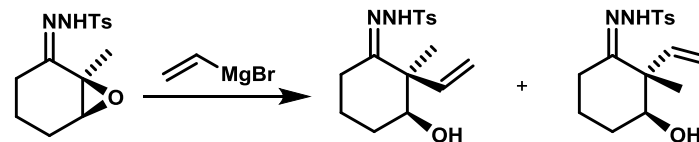
2015



(-)-jiadifenolide



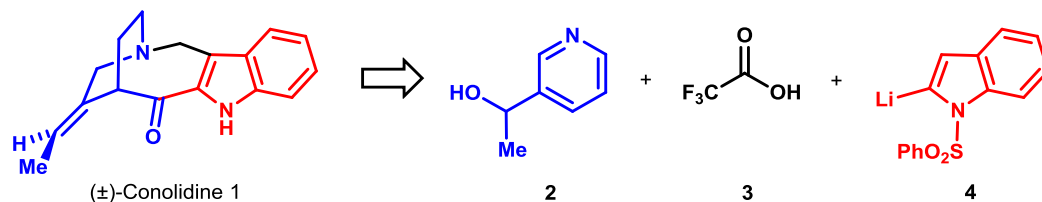
Epicolactone



Diastereoselective addition of Grignard reagents to  
*N*-sulfonyl hydrazones

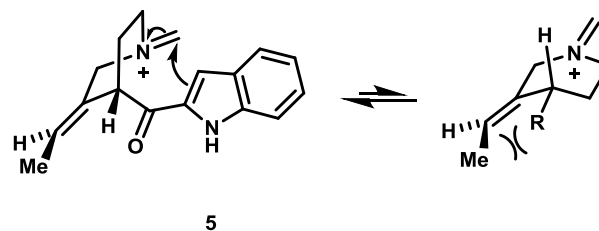


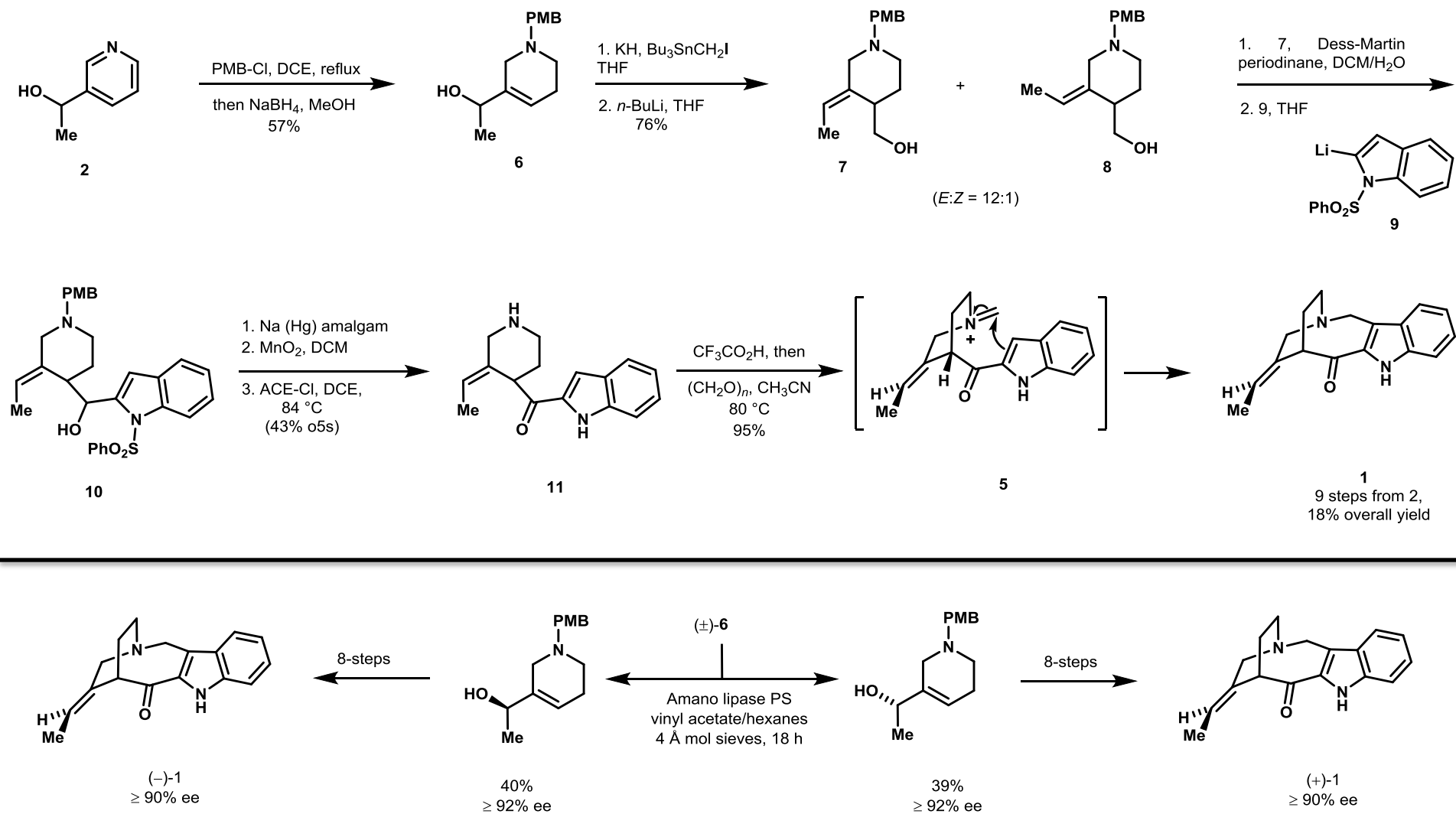
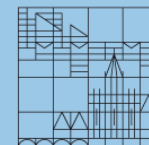
## *(±)*-Conolidine - Micalizio



### Key features:

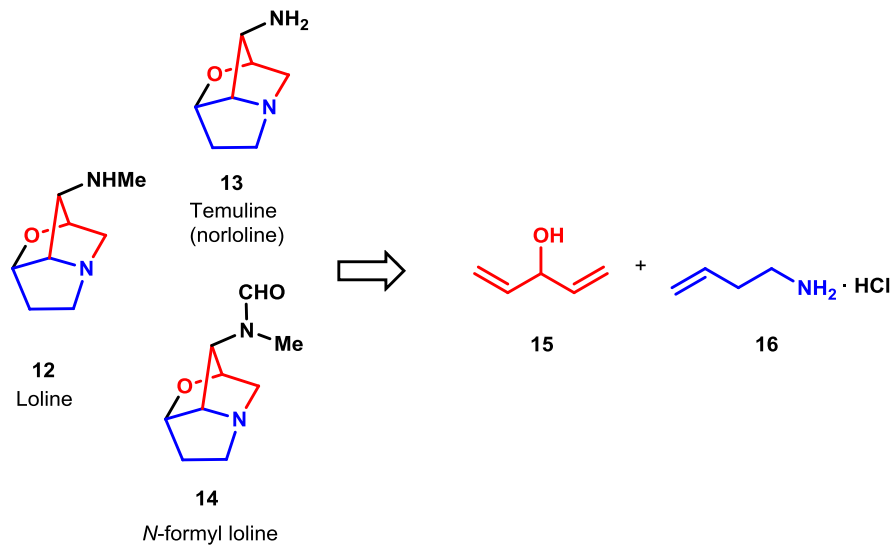
- [2,3]-Wittig rearrangement
- Nucleophilic addition
- Cyclization





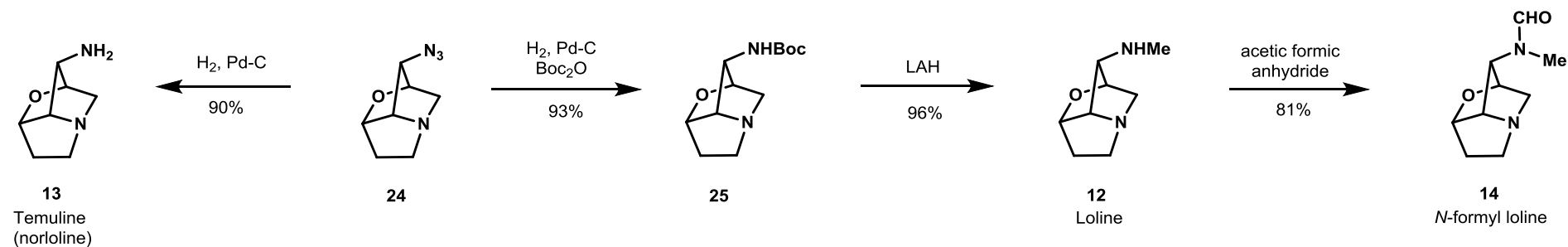
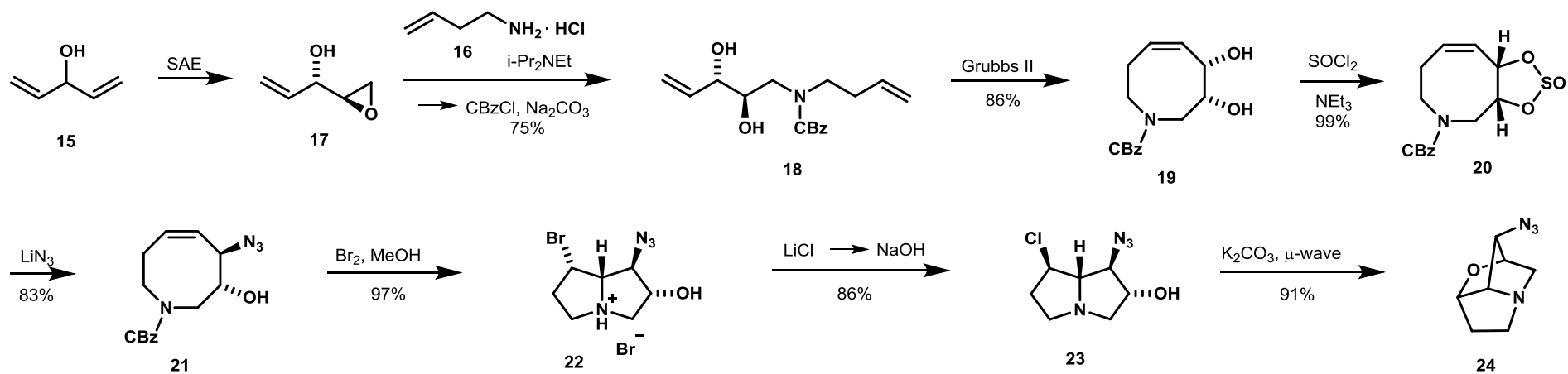
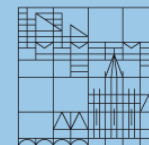


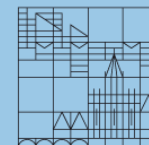
# Loline alkaloids - Trauner



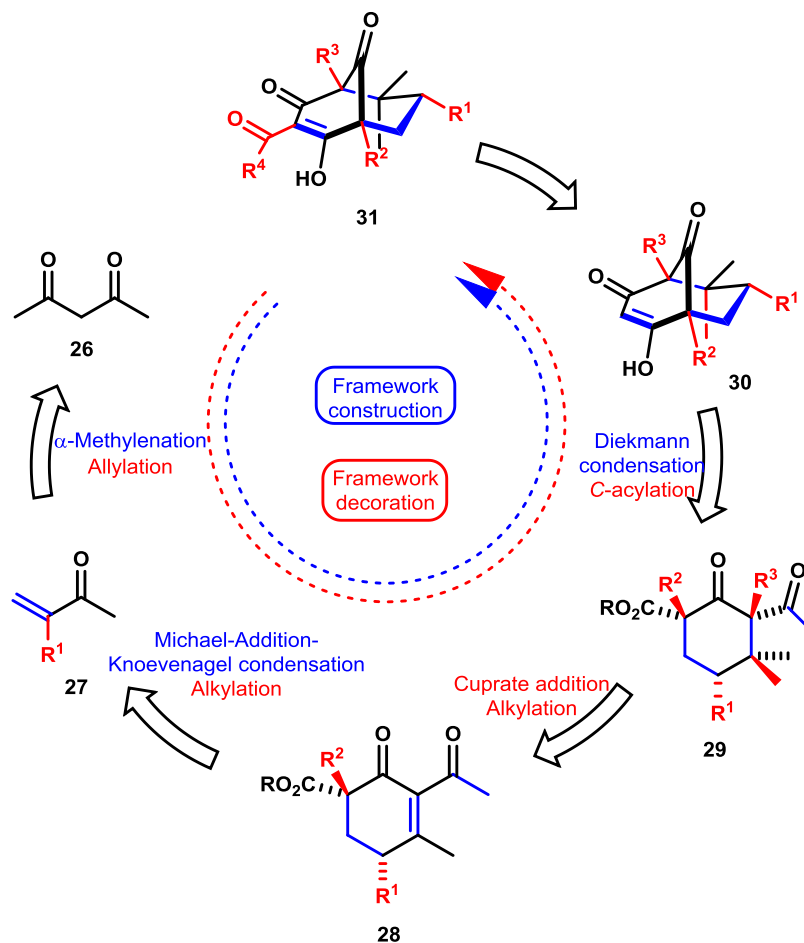
## Key features:

- Sharpless epoxidation
- Grubbs olefin metathesis
- transannular/deoxycarbonylative aminobromination

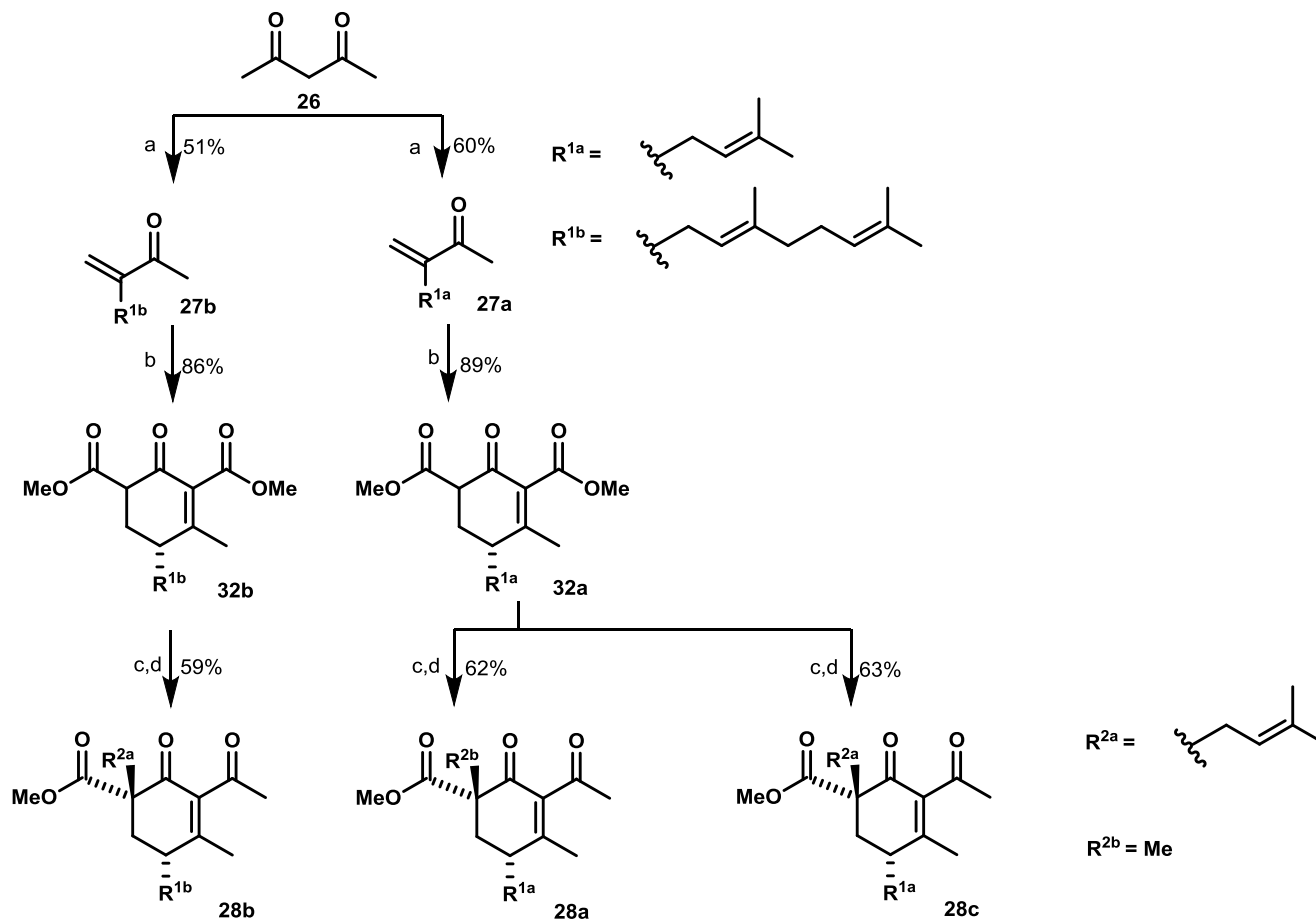
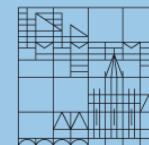




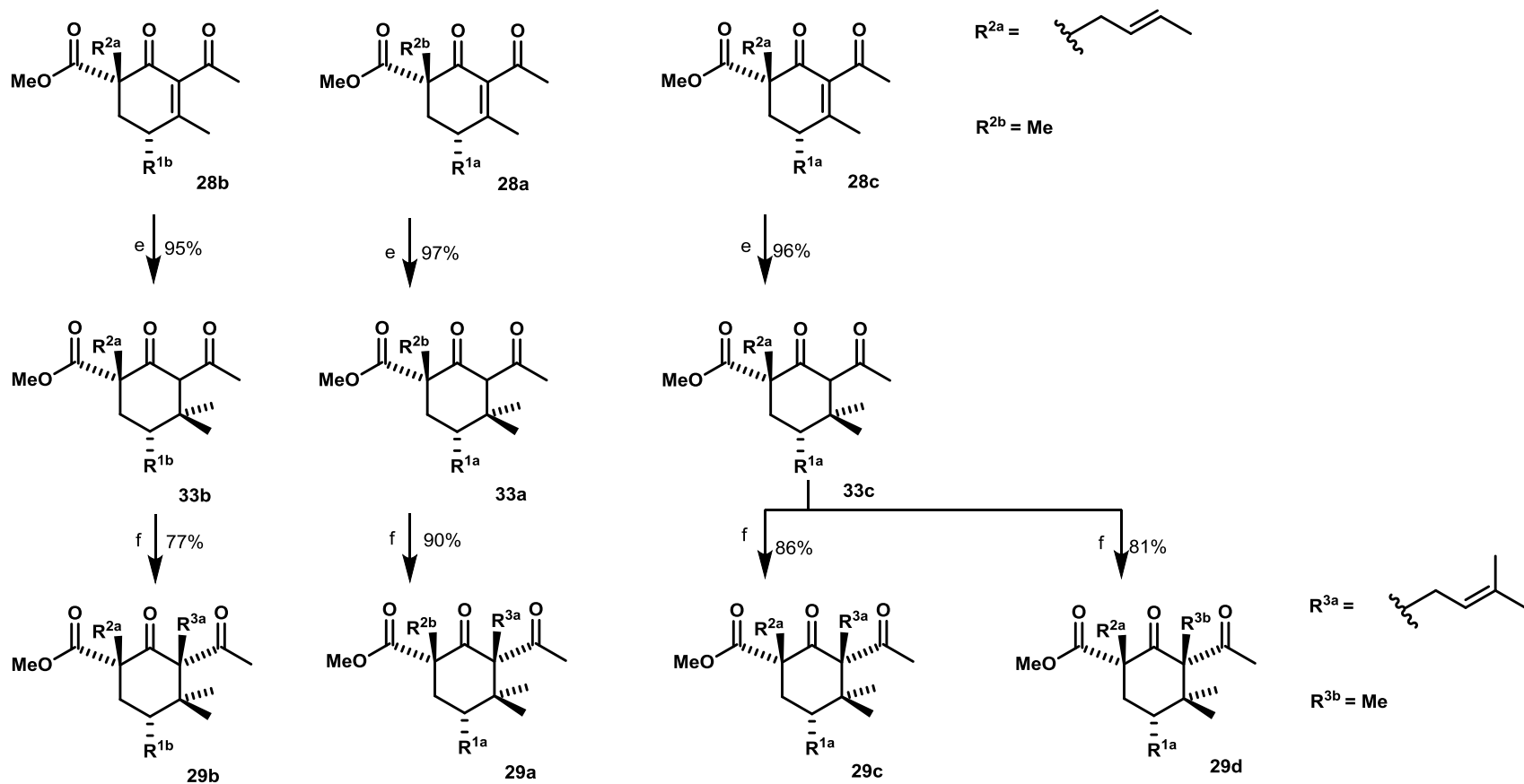
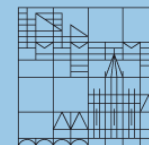
# Hyperpapuanone, Hyperibone L, epi-Clusianone, Oblongifolin A - Plietker



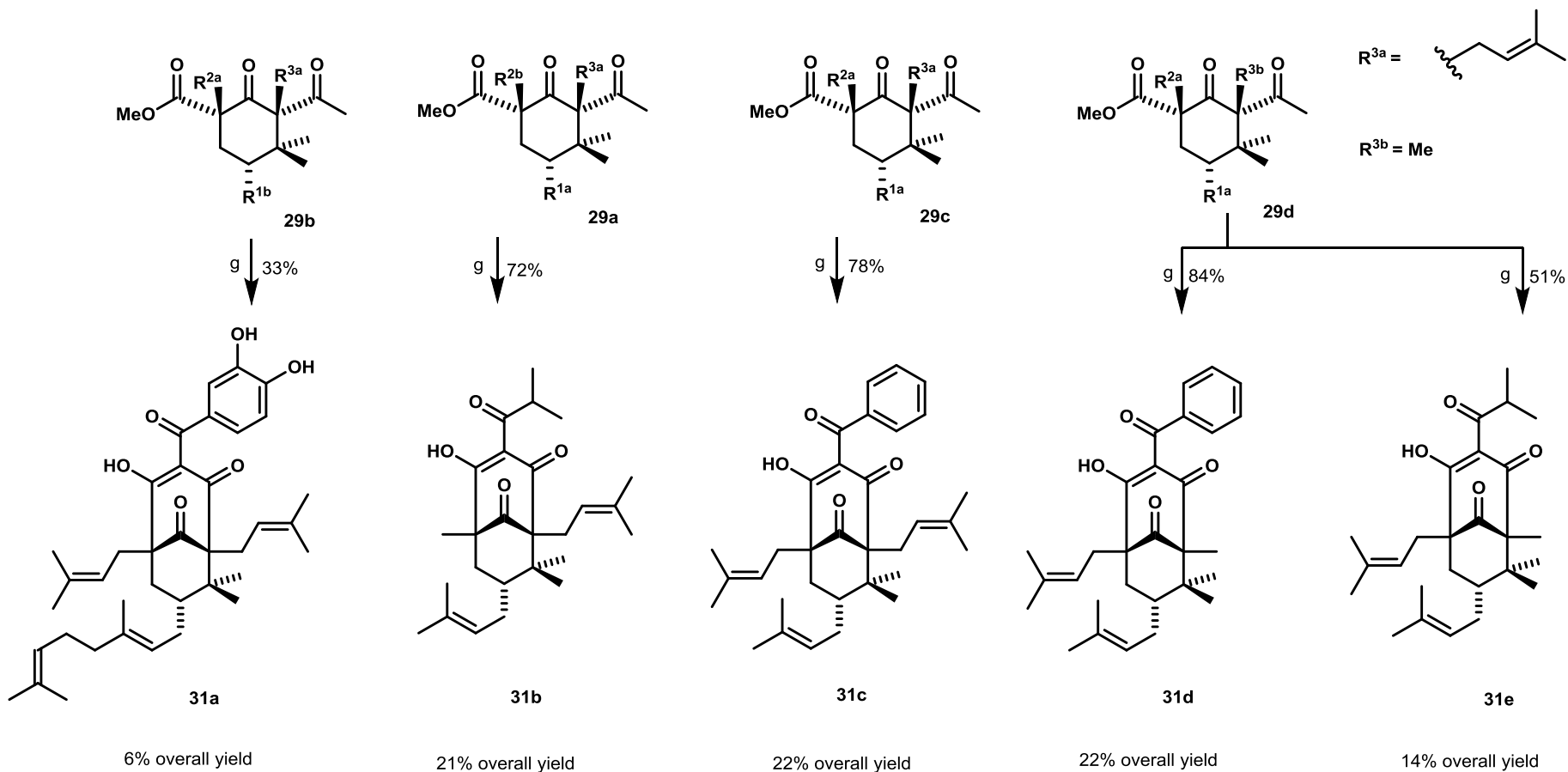
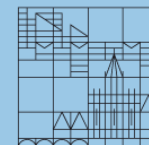




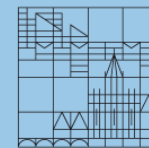
a) NaH (1.1 equiv),  $R^1X$  (1.5 equiv), EtOH, 0 °C to rt, 15 h, then  $K_2CO_3$  formaldehyde, rt b) MeMgCl (2 equiv), dimethyl 1,3-acetonedicarboxylate (1 equiv), MeOH, 0 to 60 °C, 15 h, c) NaH (1.1 equiv), MeLi (2.3 equiv). THF, 0 °C, 5 h, d) NaH (1.1 equiv), 18-crown-6 (0.1 equiv),  $R^2X$  (1.5-2.5 equiv), THF, 0 °C to rt, 15 h,



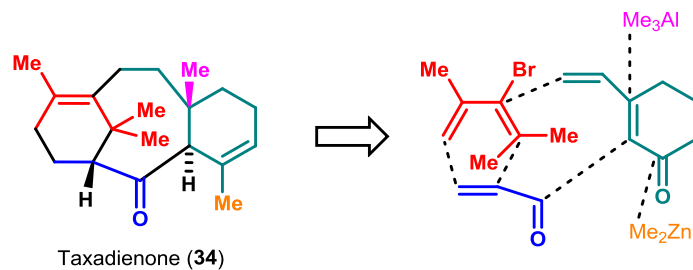
e) LiCl (2.02 equiv), CuI (2 equiv), MeMgBr (2equiv), Me<sub>3</sub>SiCl (2 equiv), THF, -78 °C, 5 h, f) KO-*t*-amylate (2 equiv), 1,3-dimesitylimidazolin-2-ylidene hexafluorophosphat (0.1 equiv), Bu<sub>4</sub>N[Fe(CO)<sub>3</sub>(NO)] (0.1 equiv), 2-methyl-3-butene-2-yl methylcarbonate (2 equiv), THF/MTBE, 0 to 80 °C, 20 h, f) KH (1.1 equiv), 18-crown-6 (0.1 equiv), MeI (2 equiv), dimethoxyethane, 0 °C to rt, 15 h



g) KOtBu (2 equiv), R<sub>4</sub>-C(=CO)CN (3.3 equiv), THF, 0 to 35 °C, 24 h

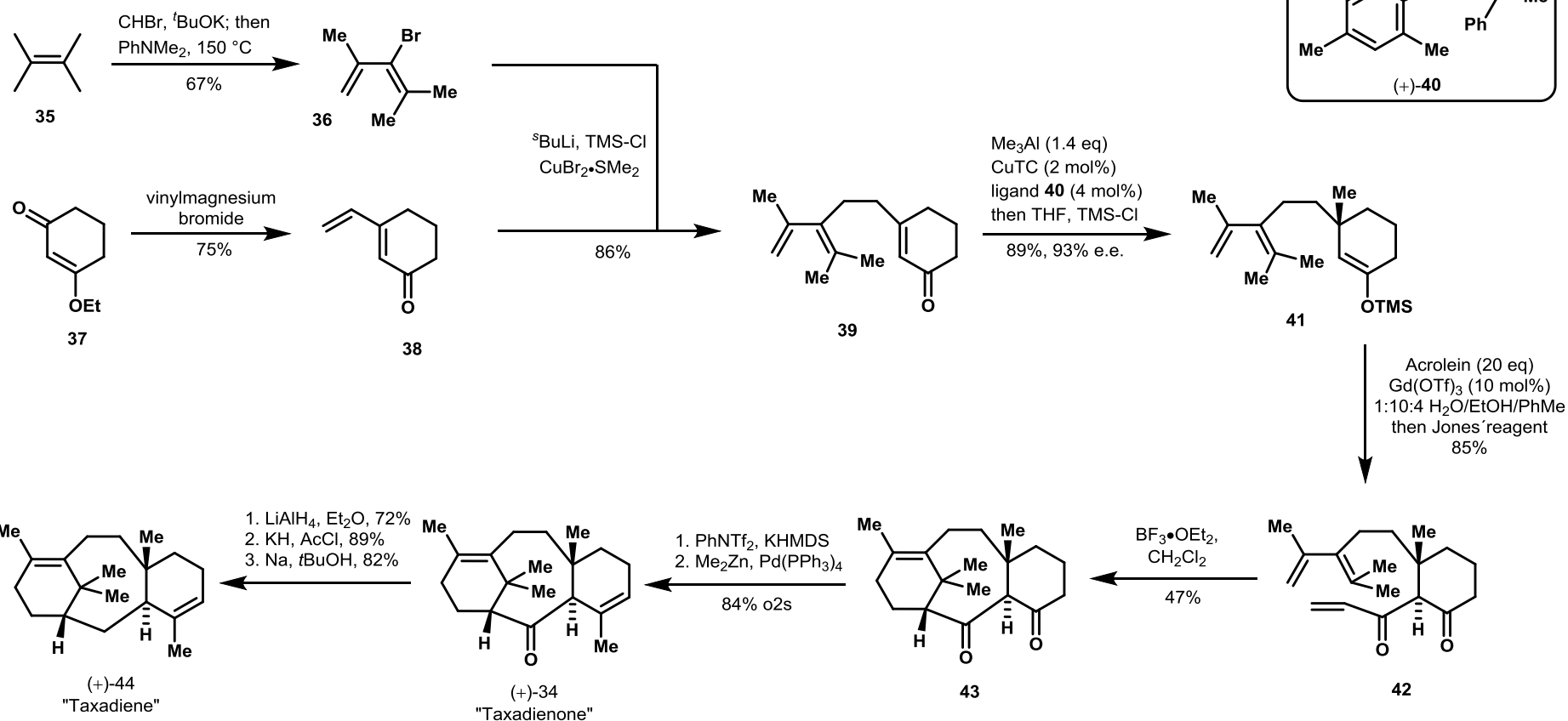
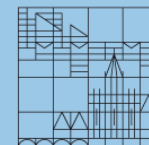


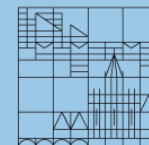
## Taxanes - Baran



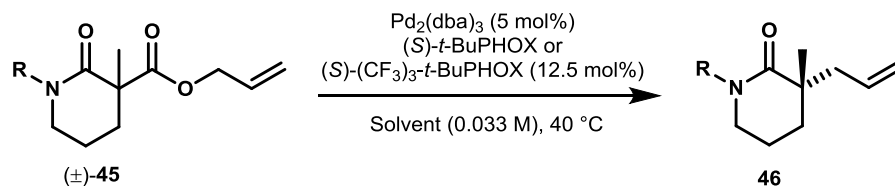
### Key features:

- 1,6-addition
- Mukaiyama aldol reaction
- Diels-Alder reaction



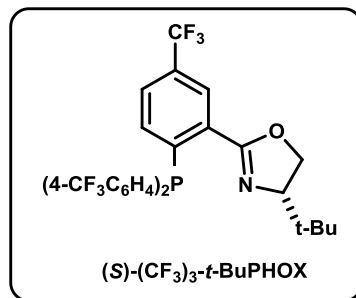


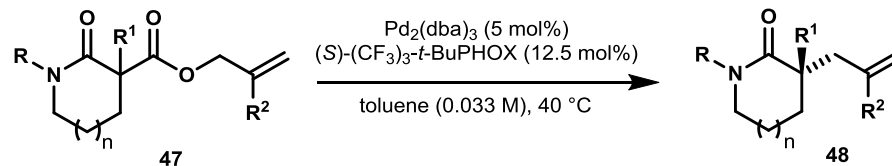
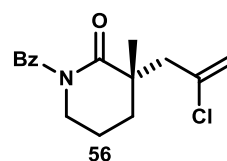
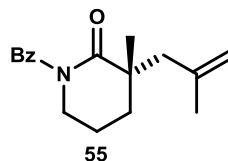
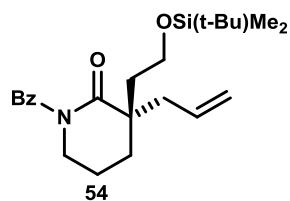
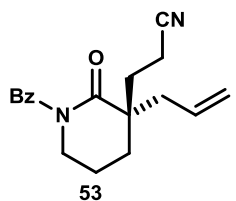
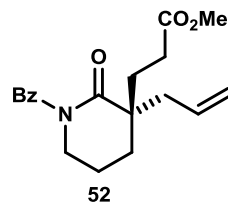
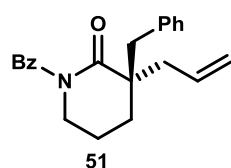
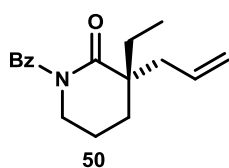
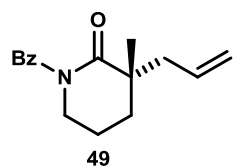
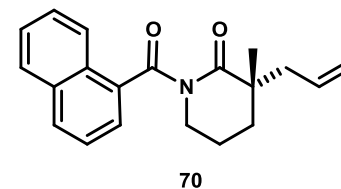
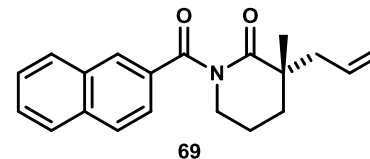
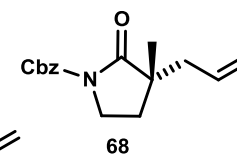
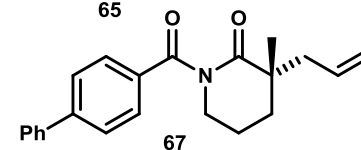
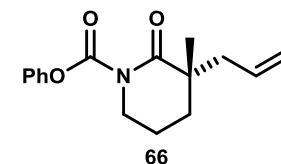
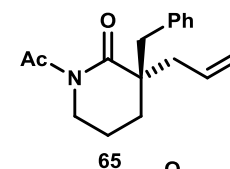
# Decarboxylative allylic alkylations of lactams - Stoltz



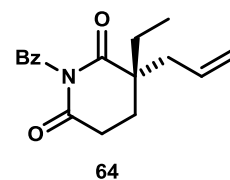
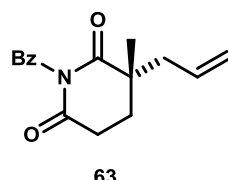
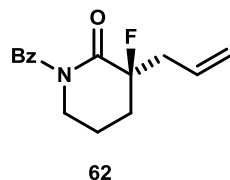
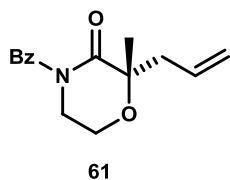
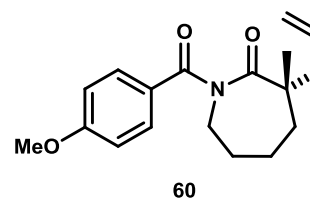
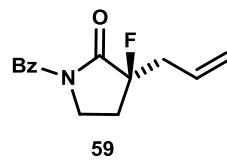
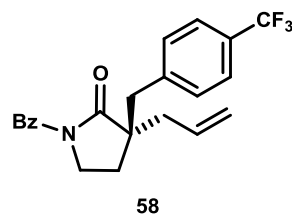
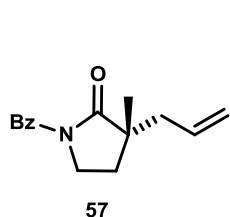
R = Ts, Boc, CBz, Fmoc, Ac, 4-OMe, 4-F-Bz, Bz

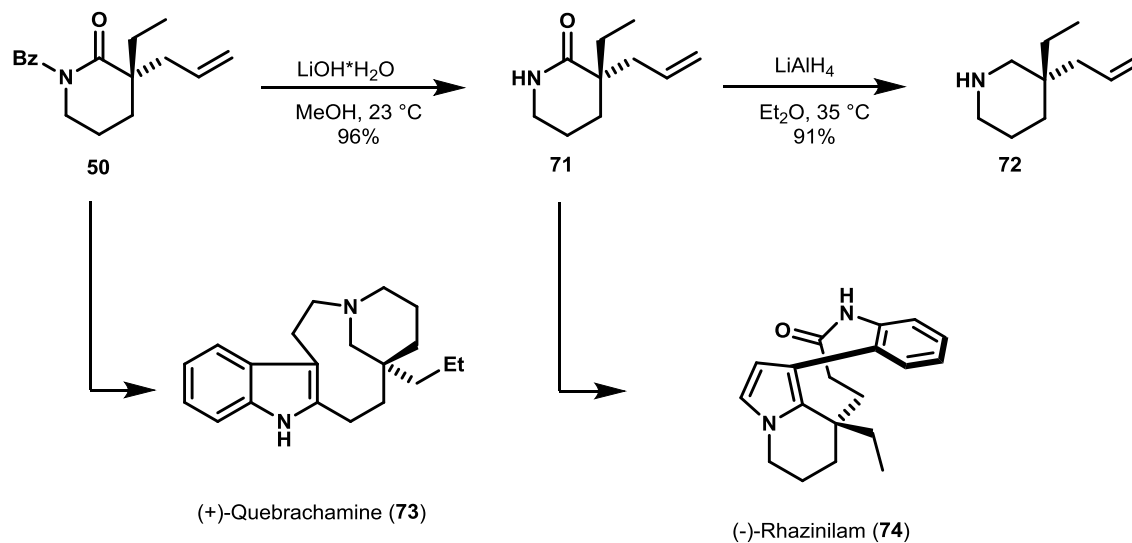
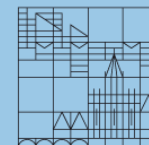
Solvent = THF, MTBE, Tol, Hex:Tol 2:1



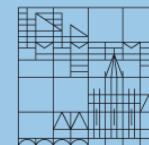

 a)  $\alpha$ -quaternary  $\delta$ -lactams

 c) other *N*-acyl groups


## b) other ring sizes and frameworks

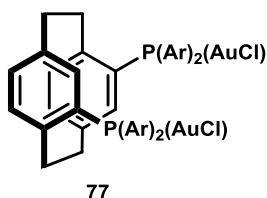
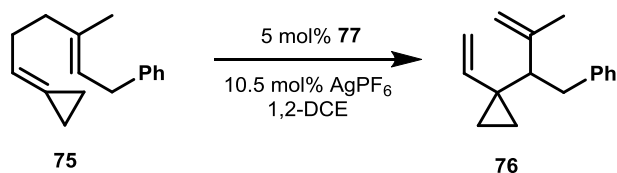




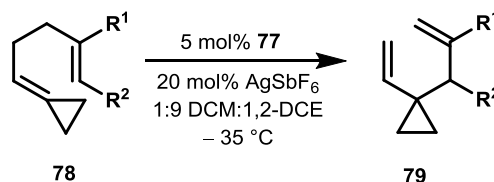




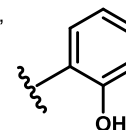
# *Au-catalysed enantioselective cope-rearrangement of achiral 1,5-dienes—Gangé*



(S)-3,5-xylyl-PHANEPHOS(AuCl)<sub>2</sub>  
 (PHANEPHOS = 4,12-bis(diphenylphosphino)-  
 [2.2]-paracyclophane)

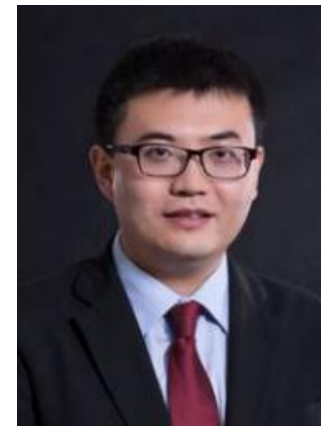
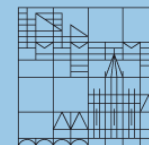


R<sup>1</sup> = alkyl (93% e.e.), aryl (87% e.e.),  
 methoxy (70% e.e.)

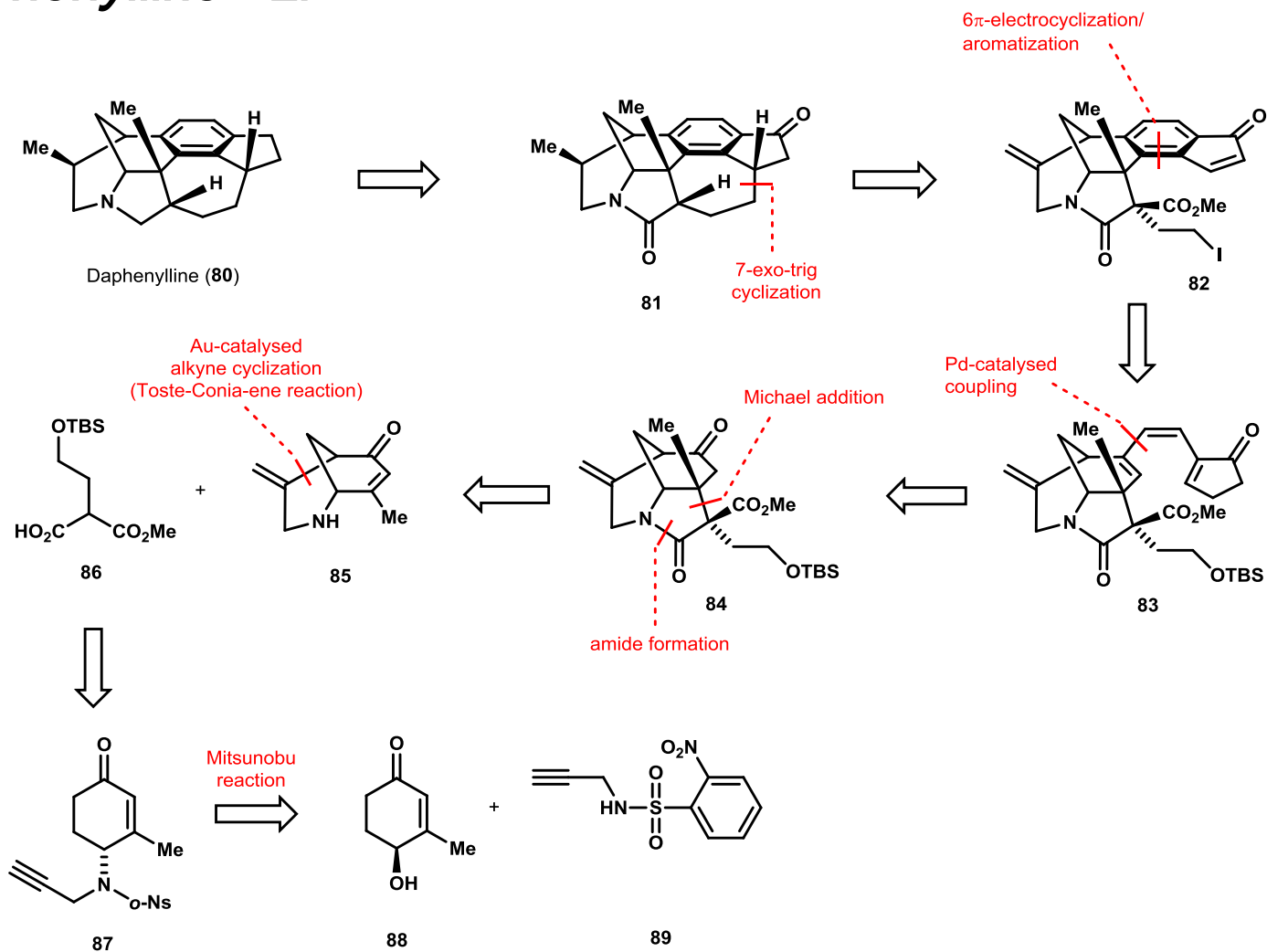


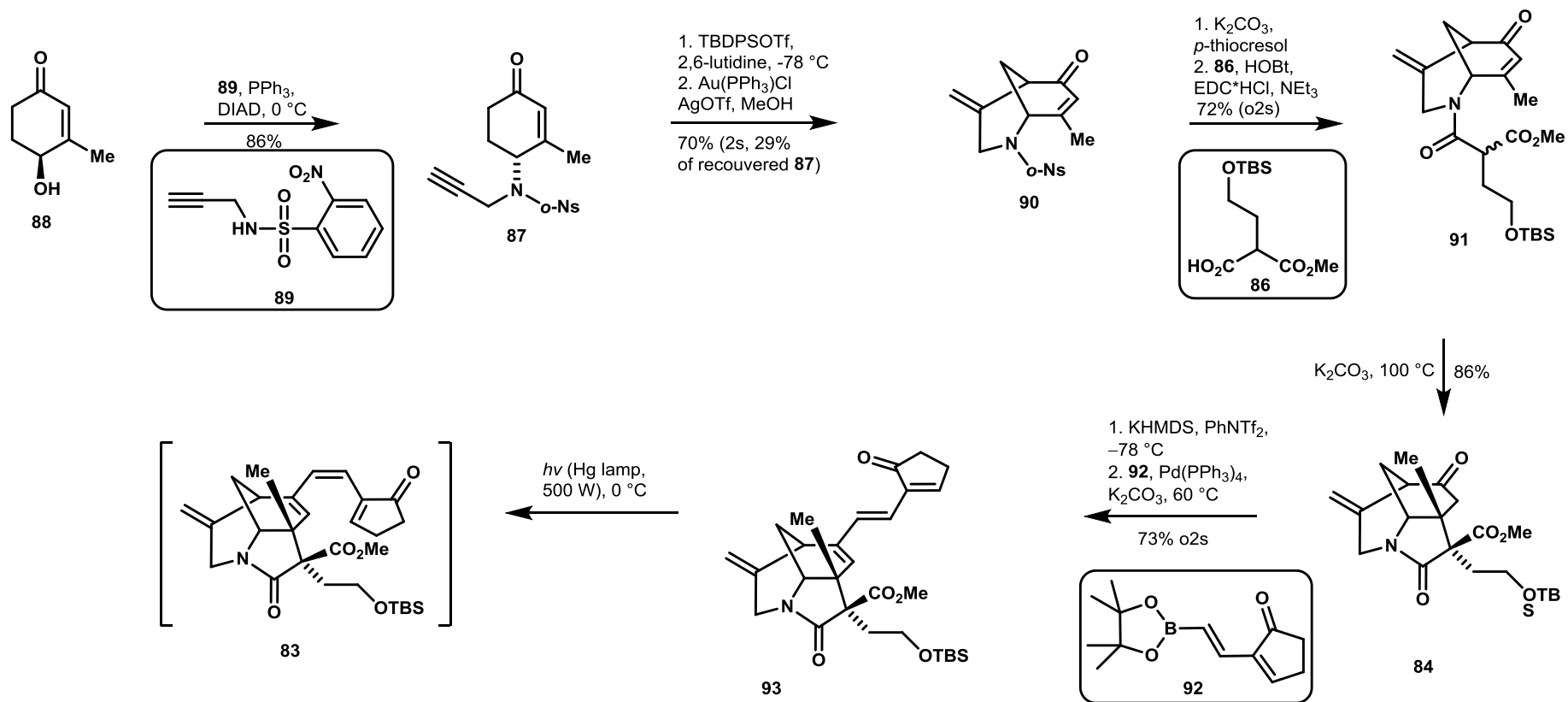
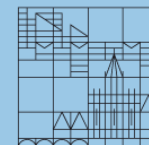
R<sup>2</sup> = -OTHP (73% e.e.), -OAc (82% e.e.),  
 -OH (76% e.e.), -NPth (58% e.e.)

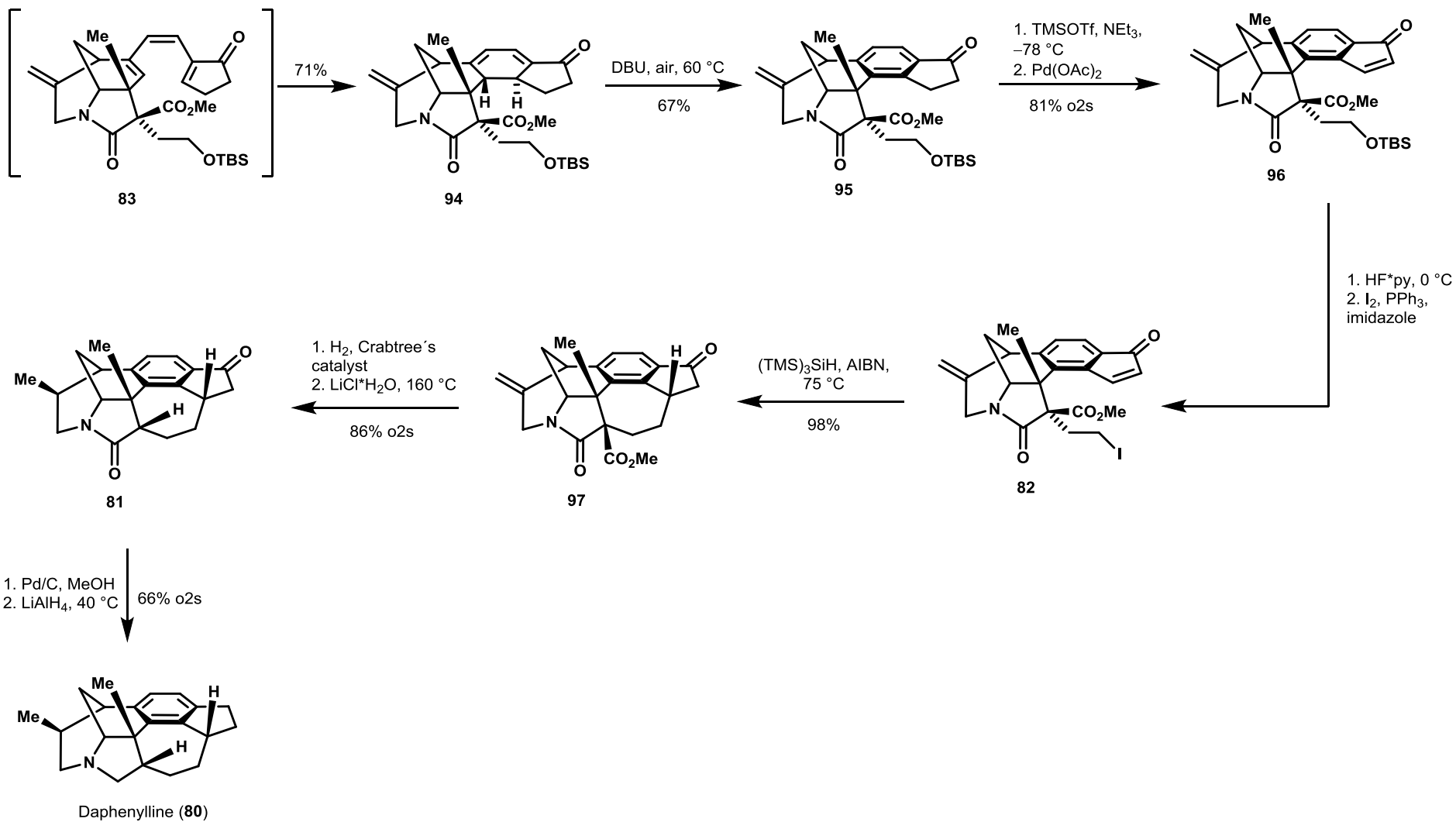
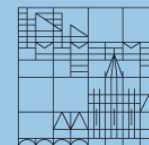


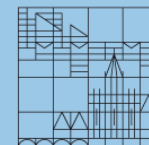


# Daphenylline - Li

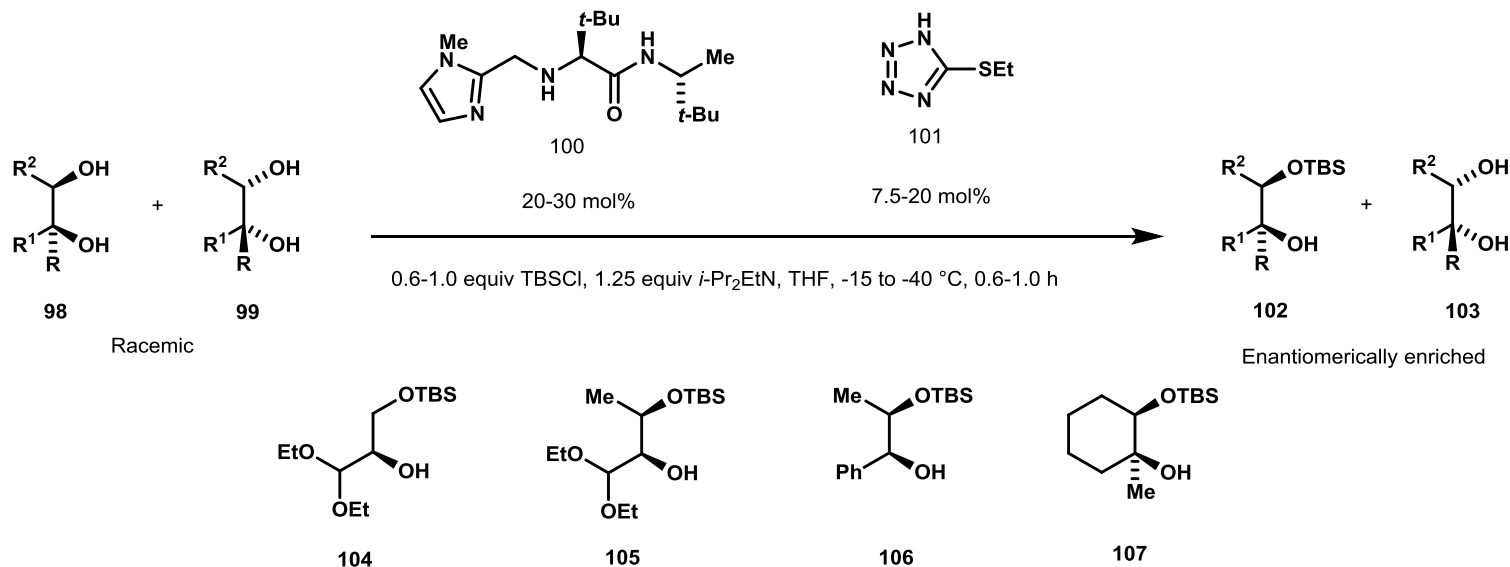






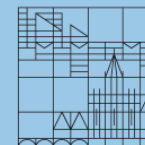


# Enantioselective silyl protection of alcohols - Snapper

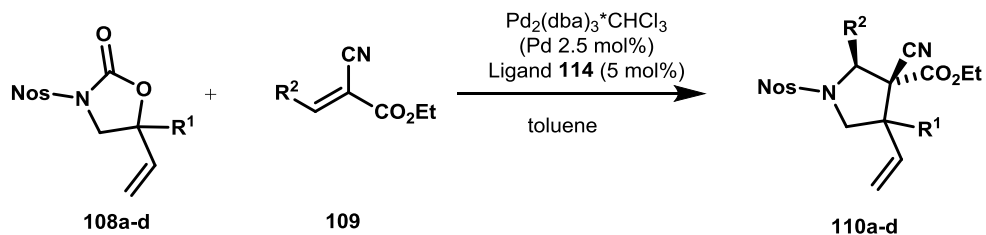


## Features:

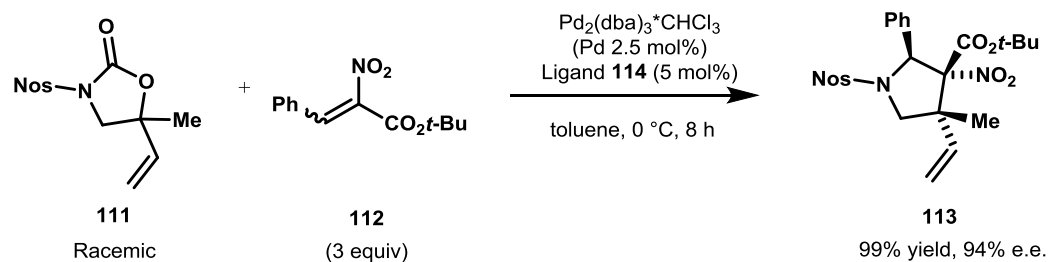
- lower catalyst loadings and reaction temperatures
- shorter reaction times



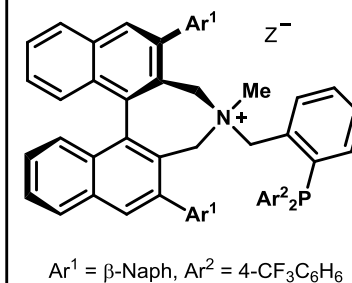
# Construction of contiguous all-carbon *qc* stereocentres - Ooi

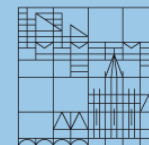


$R^1$  = alkyl, aryl, 4-Cl-C<sub>6</sub>H<sub>4</sub>, 4-MeO-C<sub>6</sub>H<sub>4</sub>  
 $R^2$  = alkyl, aryl, 4-Br-C<sub>6</sub>H<sub>4</sub>, 4-MeO-C<sub>6</sub>H<sub>4</sub>,



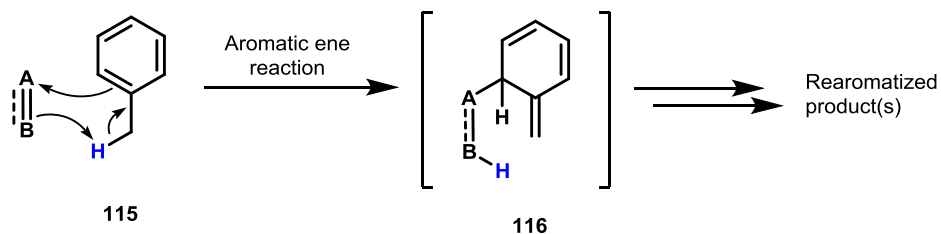
## Ligand (114)



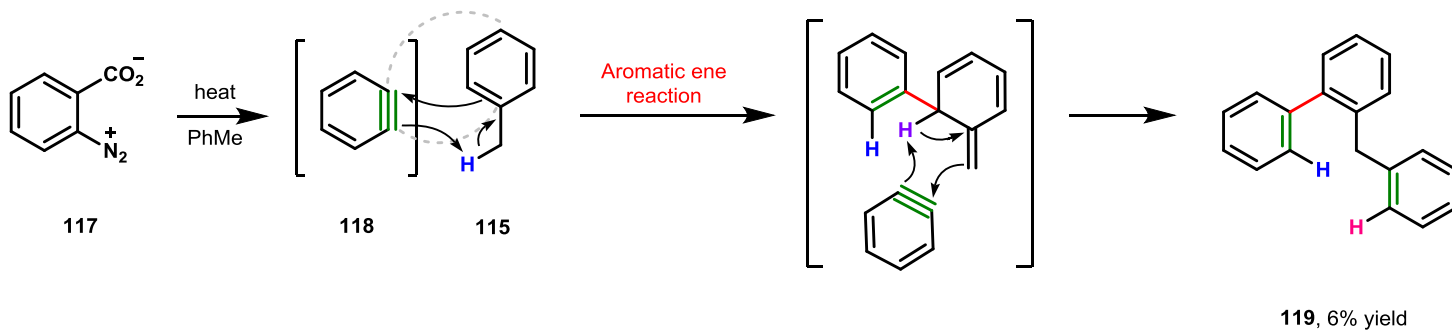


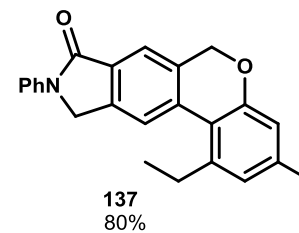
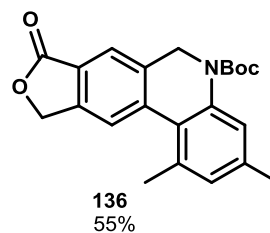
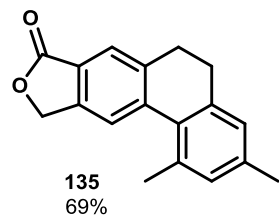
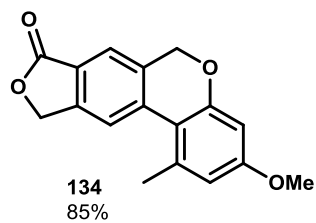
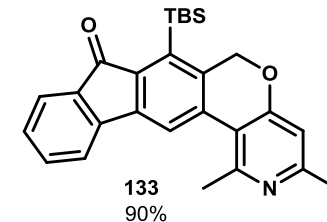
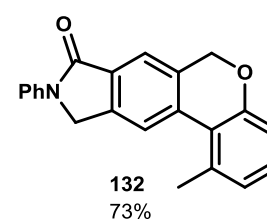
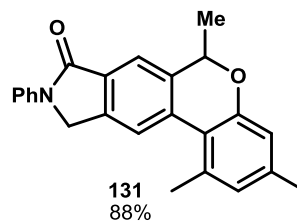
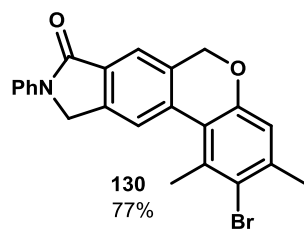
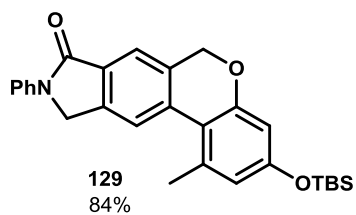
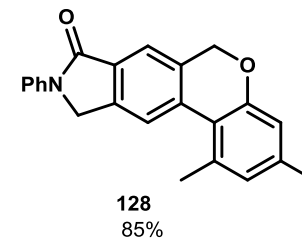
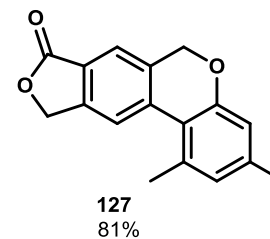
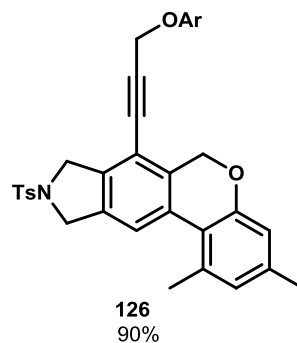
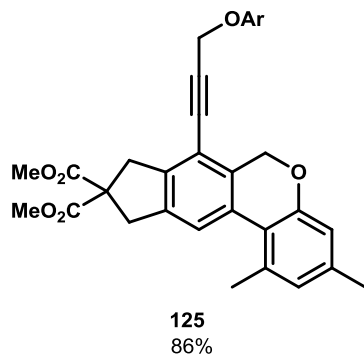
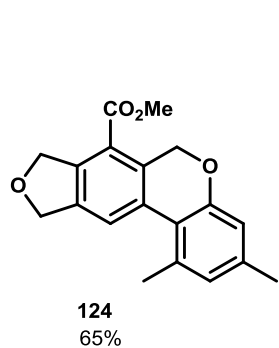
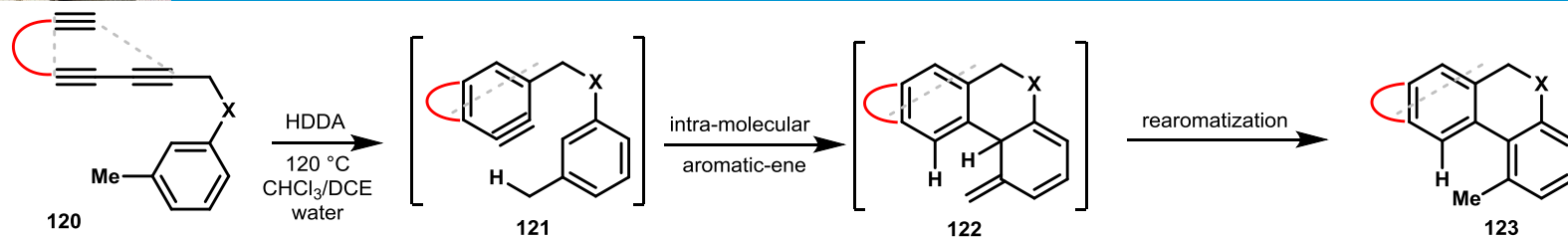
# Aromatic ene reaction - Hoye

Minimal structural elements for an aromatic ene reaction:

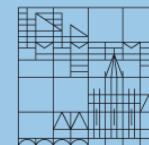


The only reported aromatic ene reaction(s):

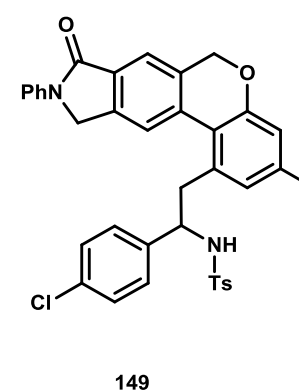
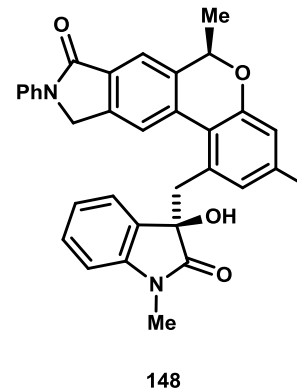
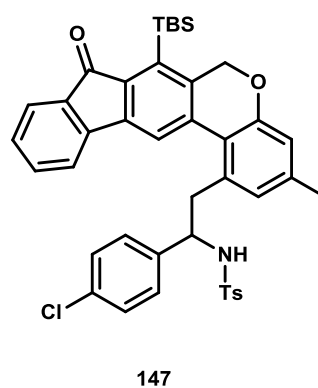
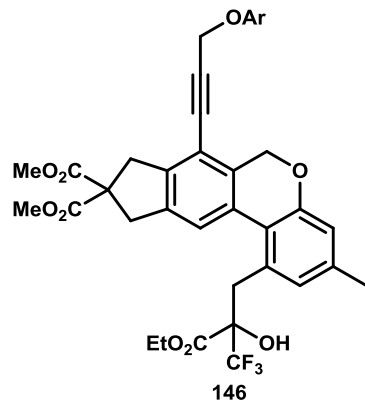
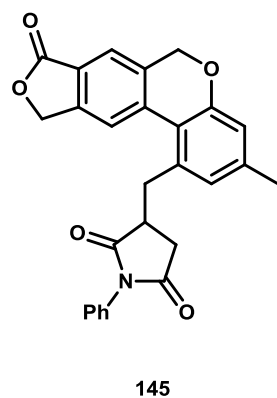
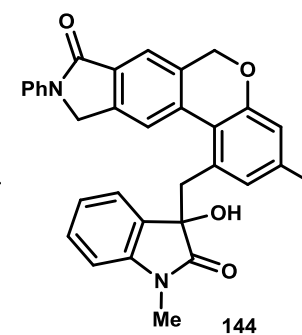
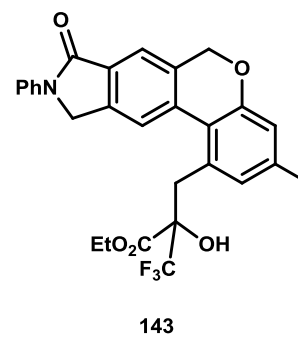
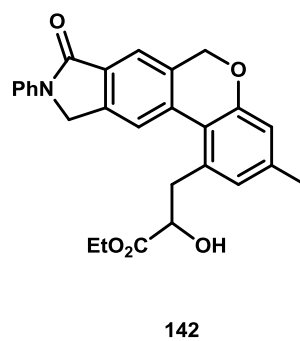
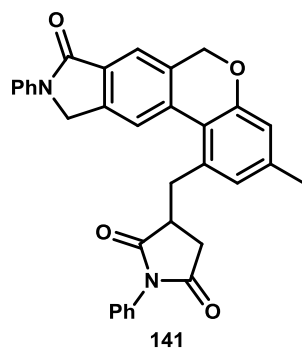
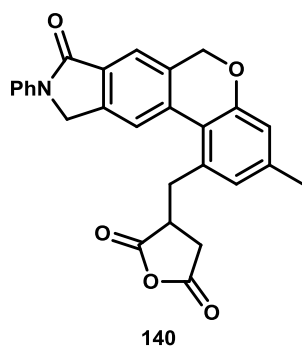
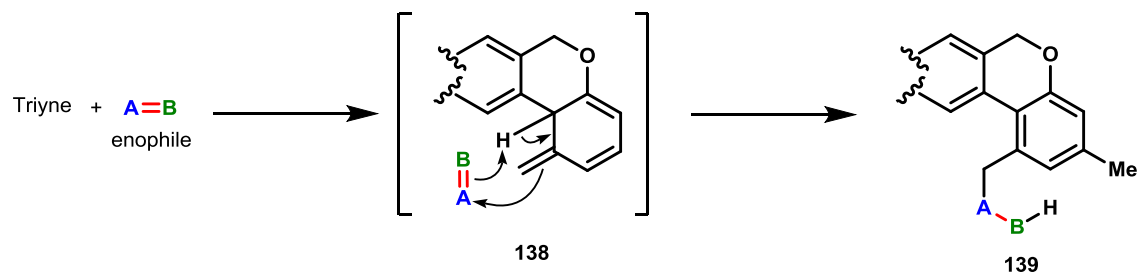






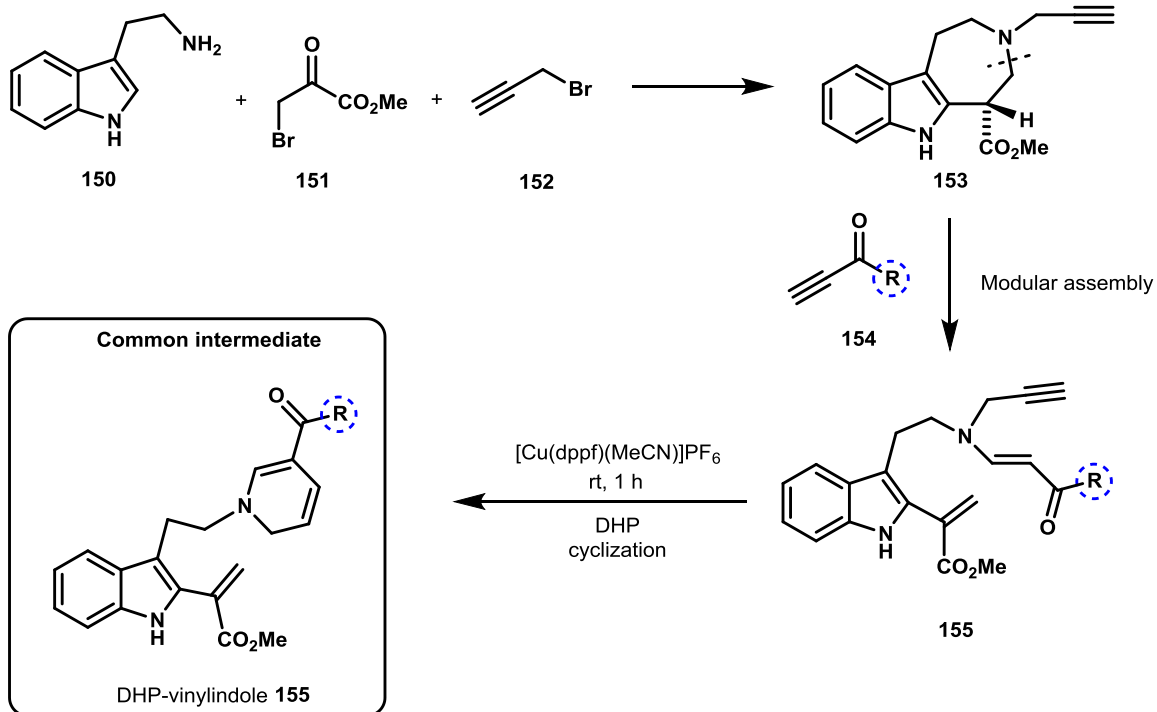


Examples of the HDDA / aromatic ene / Alder ene cascade:

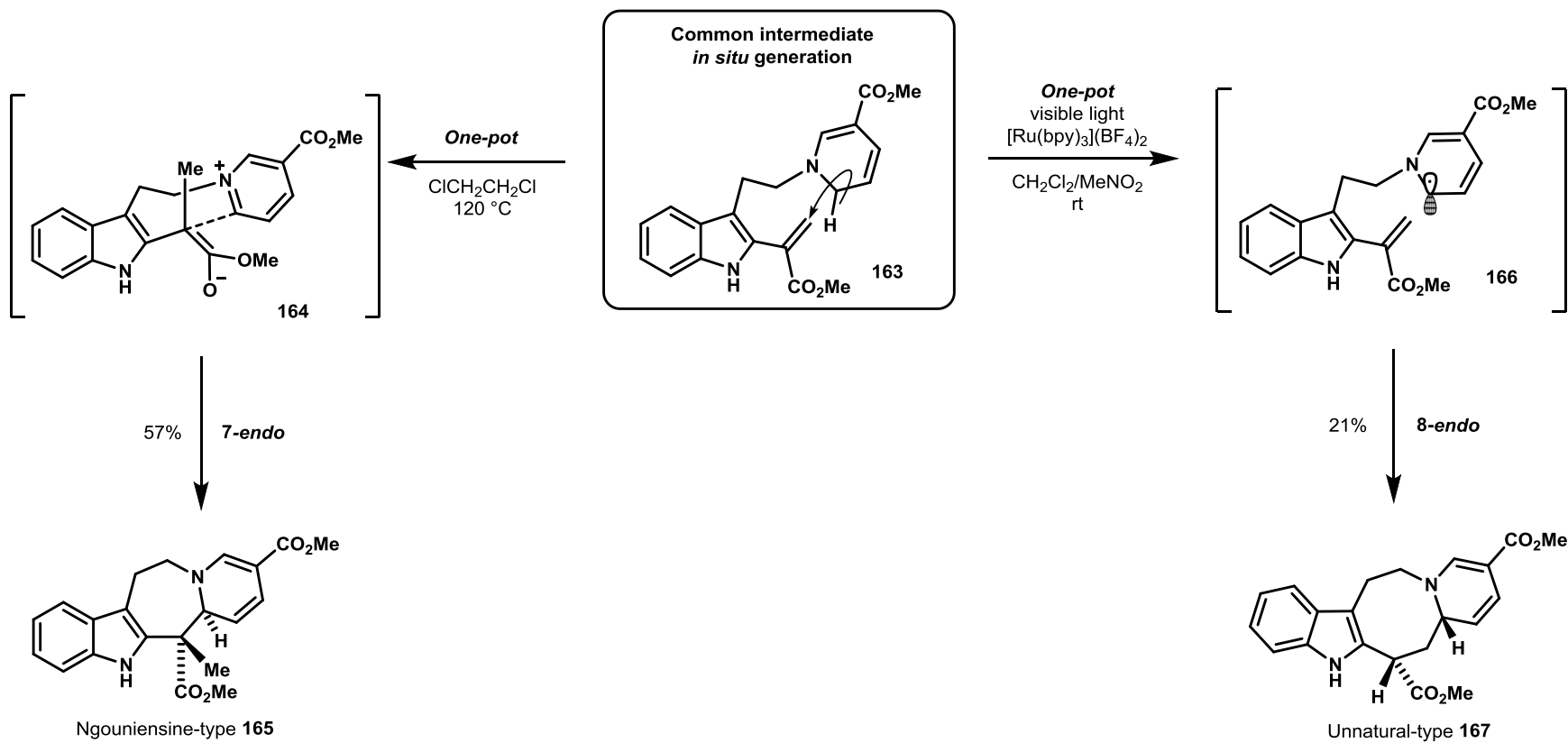
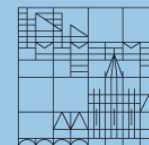




# Biogenetically inspired synthesis of indole alkaloids - Oguri

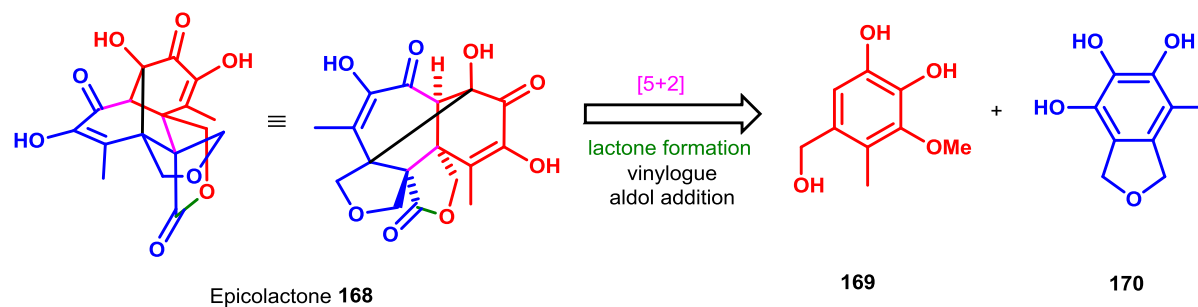






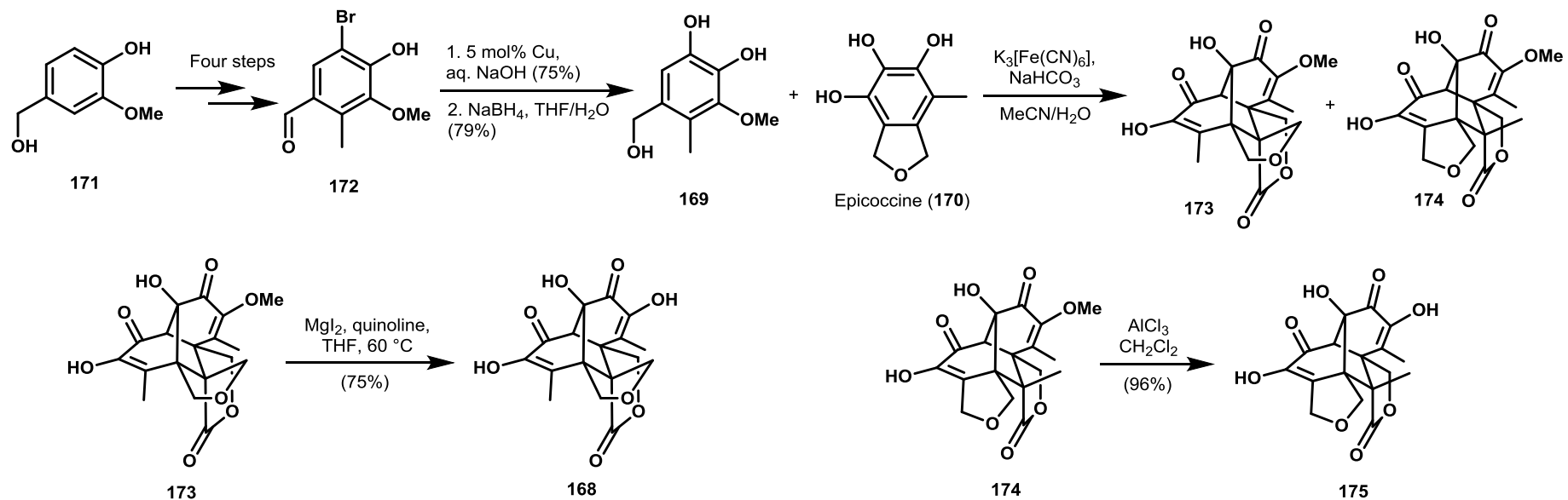
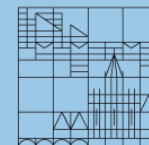


# Epicolactone - Trauner

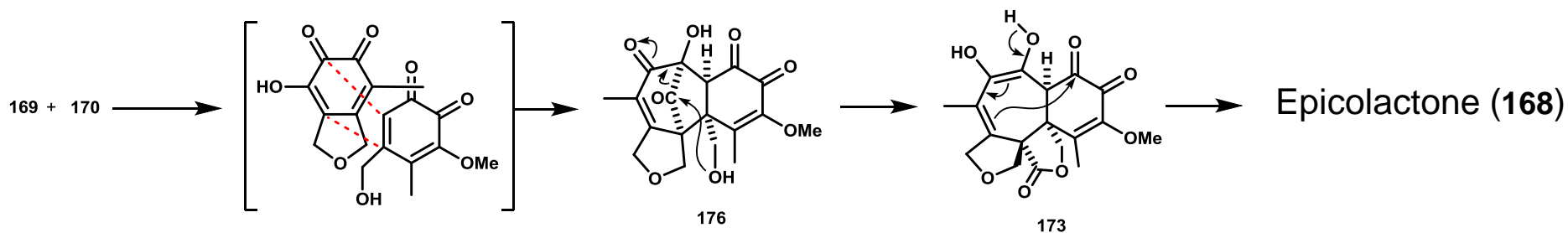


## Key features:

- [5+2] cyclo-addition
- lactone formation
- vinylogue aldol addition

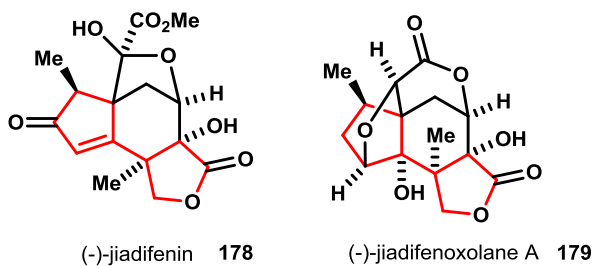
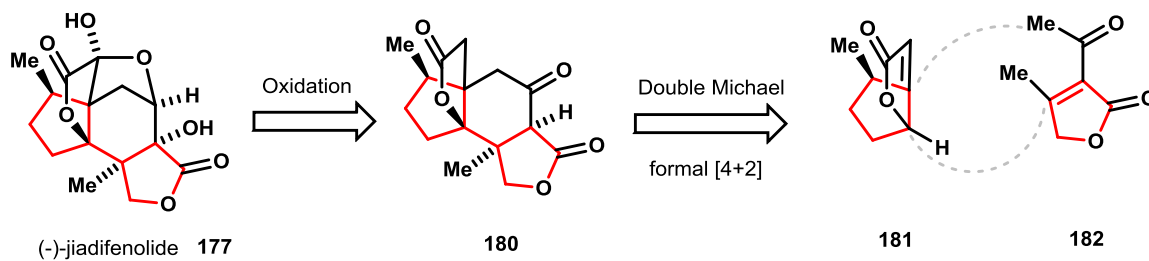


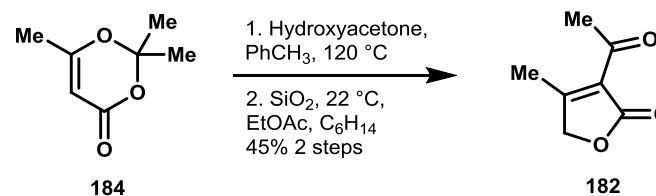
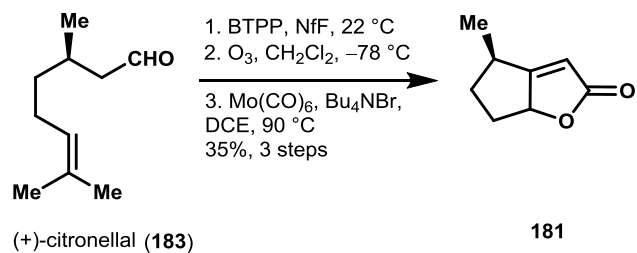
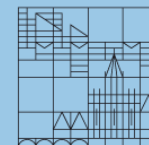
## Possible mechanism



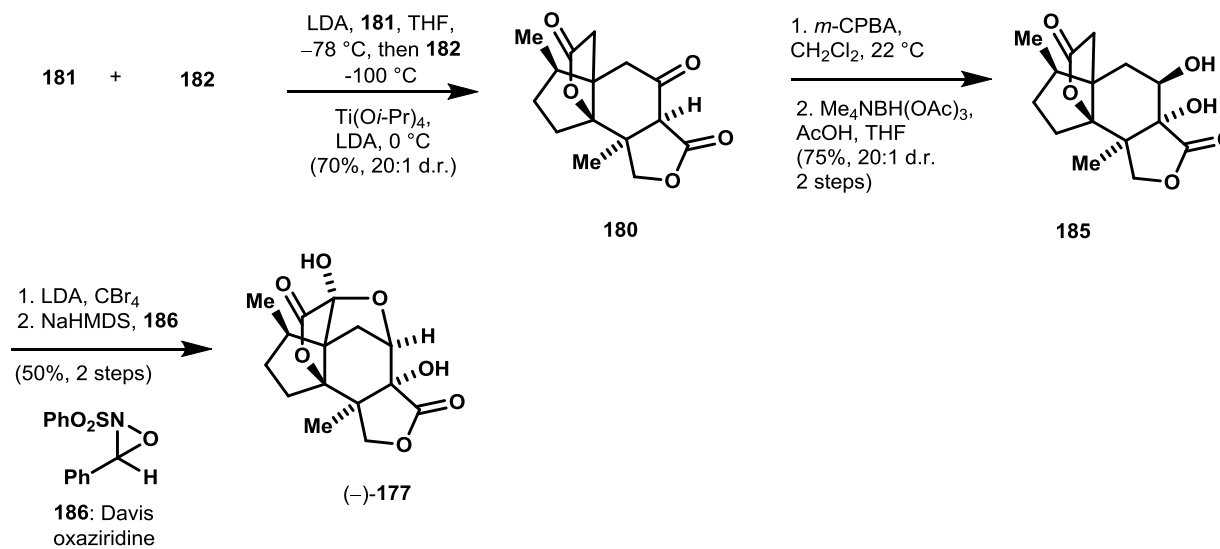


## (-)-jiadifenolide - Shenvi

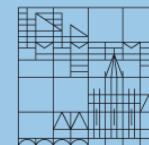




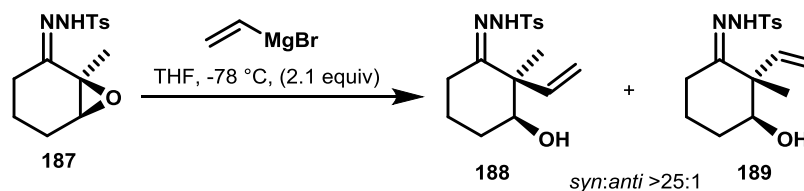
Five step route to (–)-**177** from simple building blocks **181** and **182**



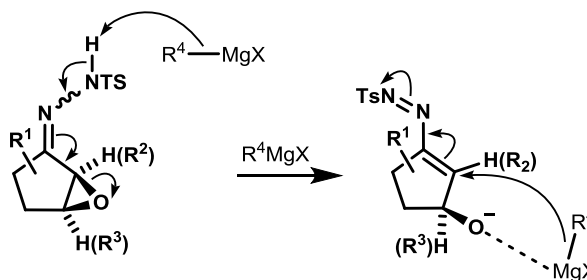


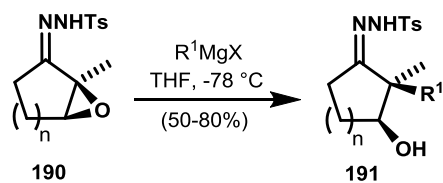


# Addition of Gignard reagents to $\alpha$ -epoxy *N*-sulfonyl hydrazones - Coltart

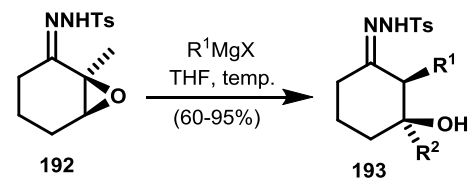


Proposed mechanism:

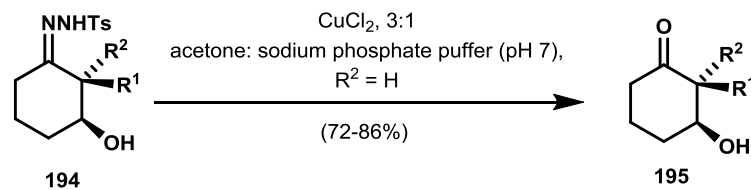


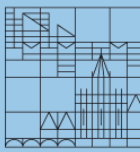


$\text{R}^1$  = ethyl, isopropyl, vinyl, phenyl, *tert*-butyl (*syn:anti*, 3:1)



$\text{R}^1$  = ethyl ( $\text{R}^2$  = H), isopropyl, vinyl ( $\text{R}^2$  = Me), phenyl





Thank you!

