

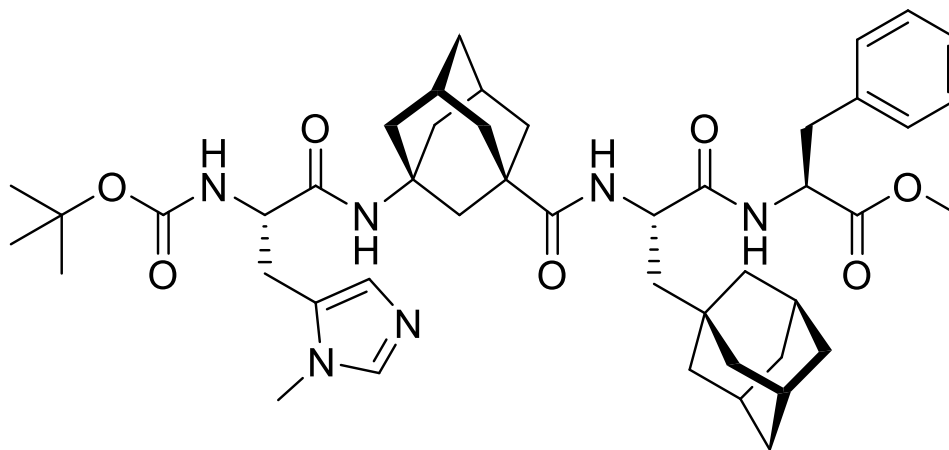
Kinetic Resolutions of *trans*-1,2-Diols Using a Adamantylalanine Containing Peptide Catalyst

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Research Module

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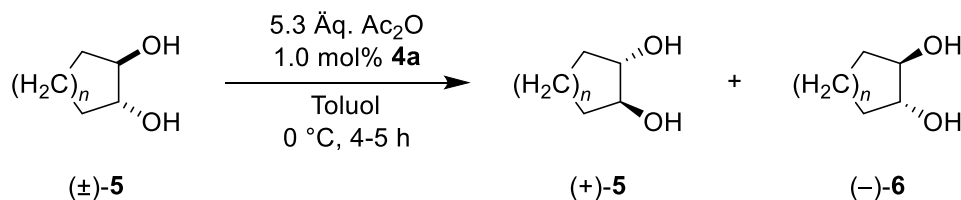
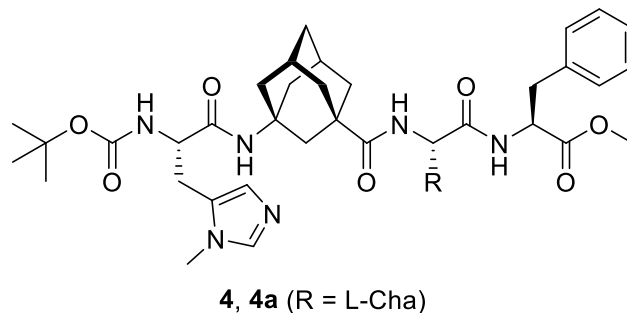




- Acyl transfer reactions important chemistry and biology
 - In biology *via* enzymes
 - Use of enzymes in chemistry labs limited
- Small synthetic peptide catalysts



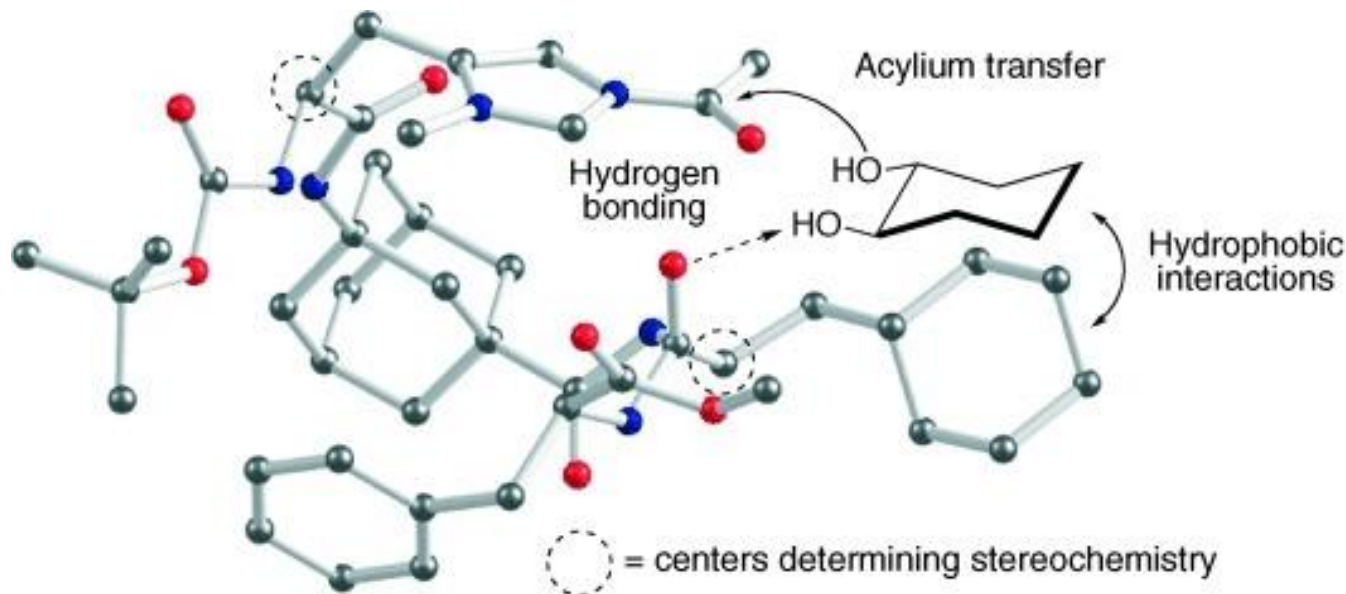
- Schreiner *et al.* different approach to peptide catalyst



- Screening revealed higher selectivity with more lipophilic residues
- Exceptional selectivity for *trans*-cycloalkane-1,2-diols ($2 \leq n \leq 4$)



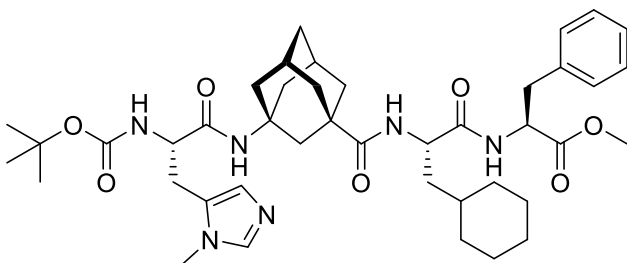
- Proposed transition-state model including dispersive interactions



- Confirmed through modern NMR experiments by Thiele *et al.*
- L-Cyclohexylalanine acts as a Dispersion Energy Donor (DED)

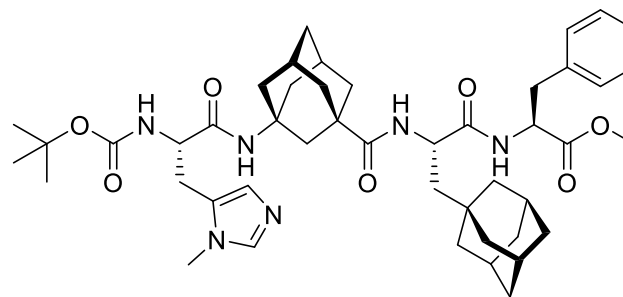


- Does a larger DED lead to a better selectivity?
- L-Adamantylalanine instead of L-cyclohexylalanine



4a

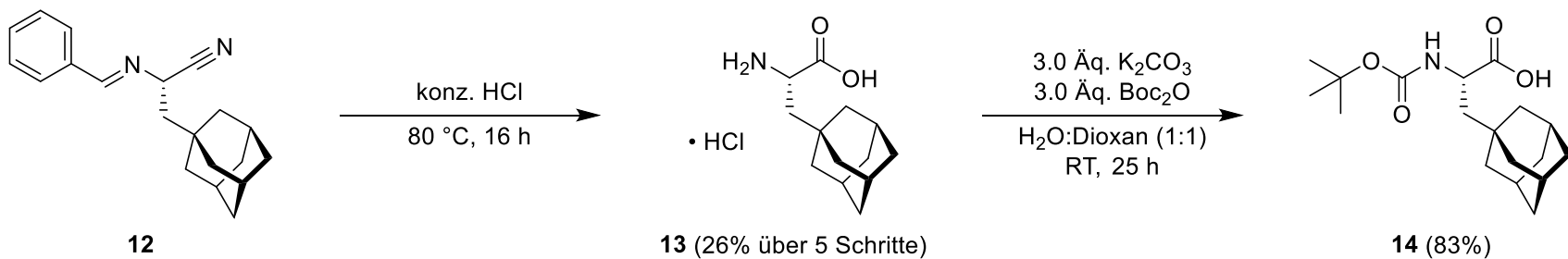
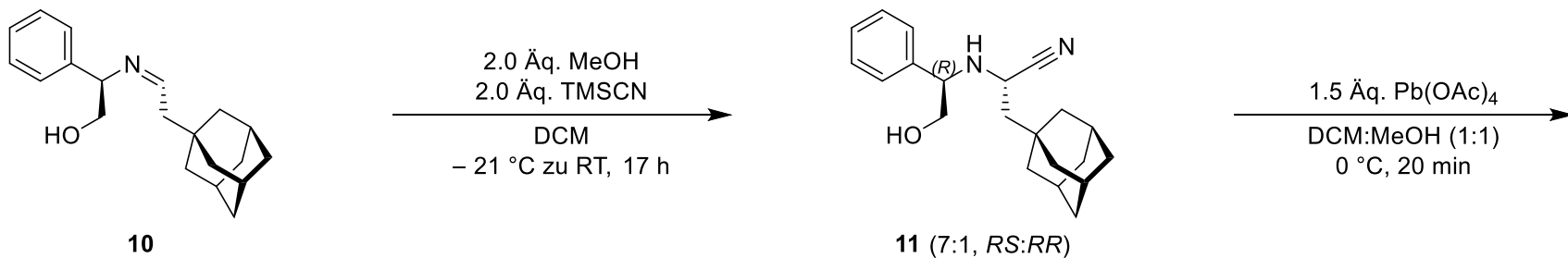
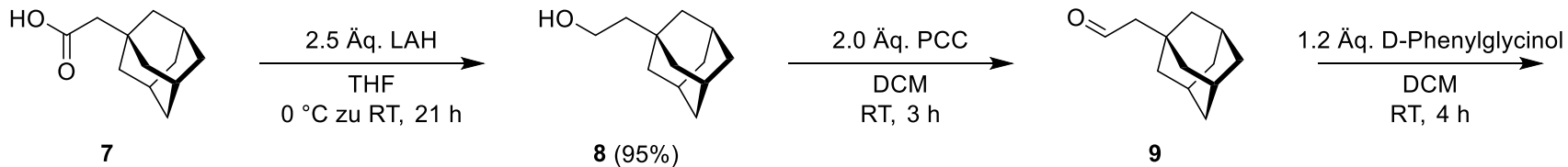
vs.



4b

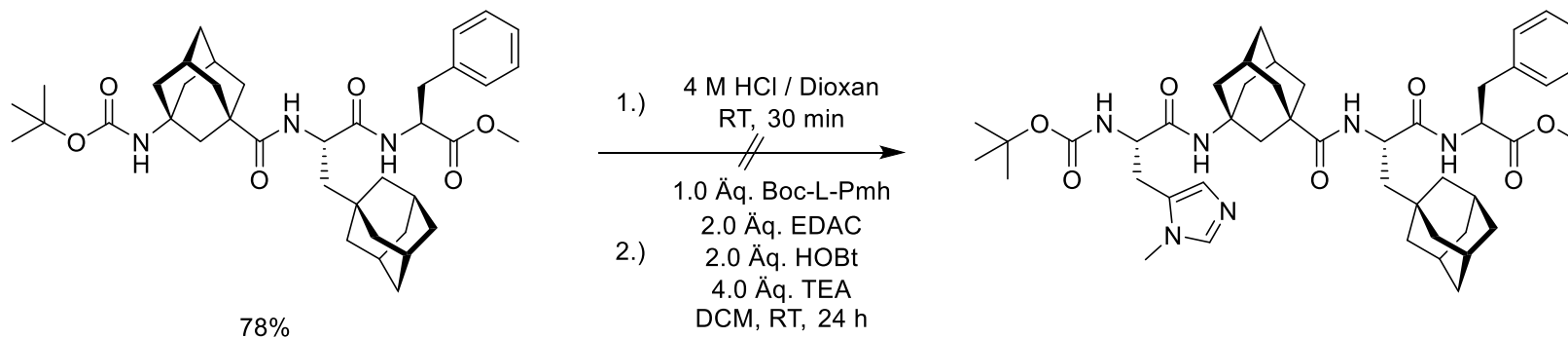
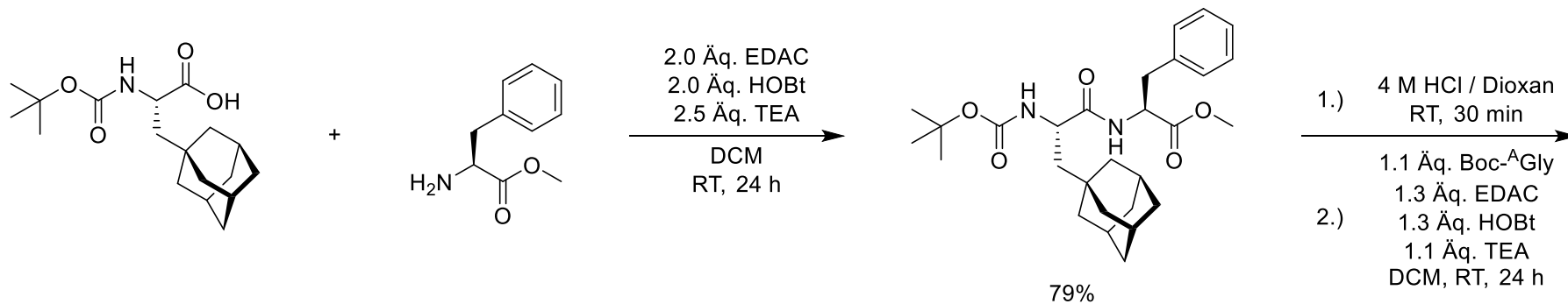
- Perform kinetic resolutions with *trans*-1,2-diols

Synthesis of Boc-L-Adamantylalanine



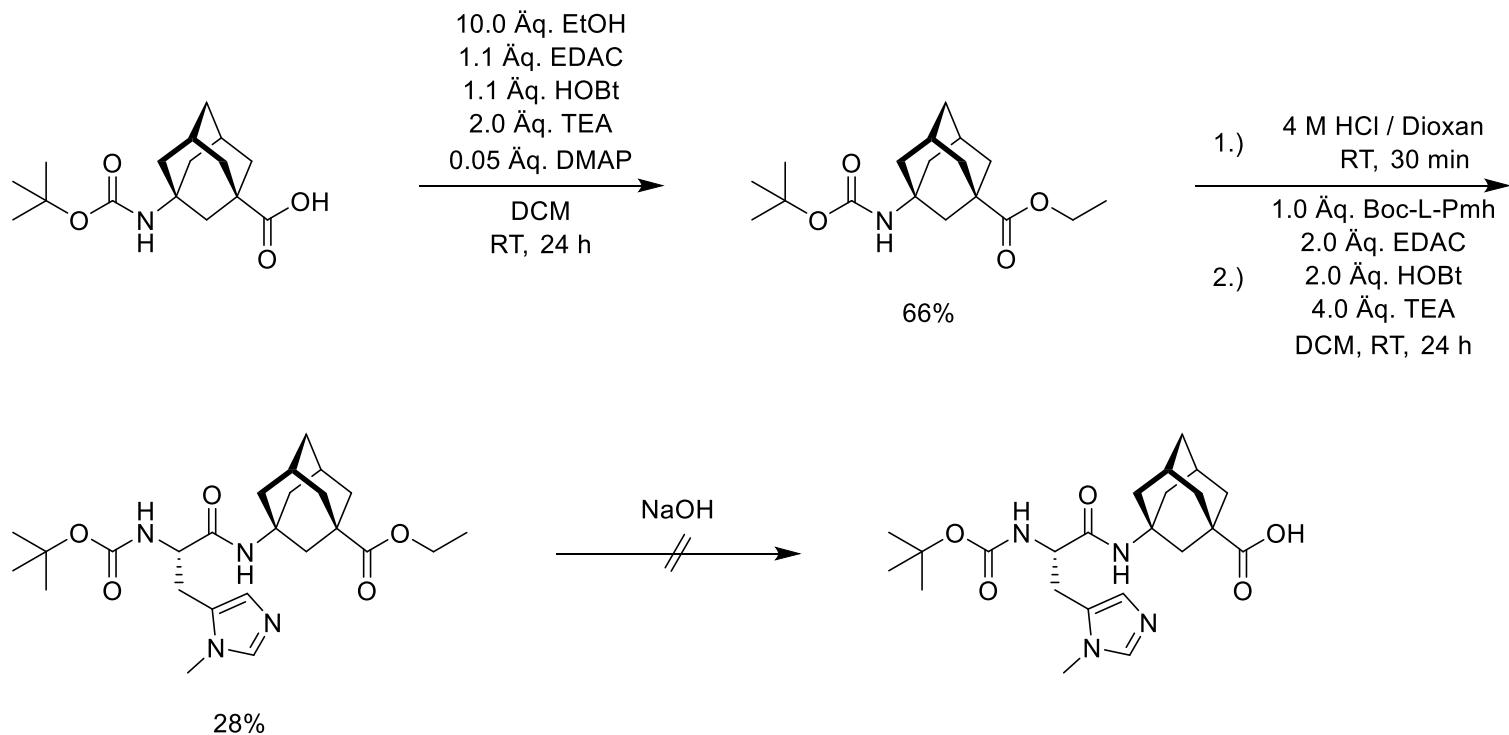


• Regular peptide synthesis failed

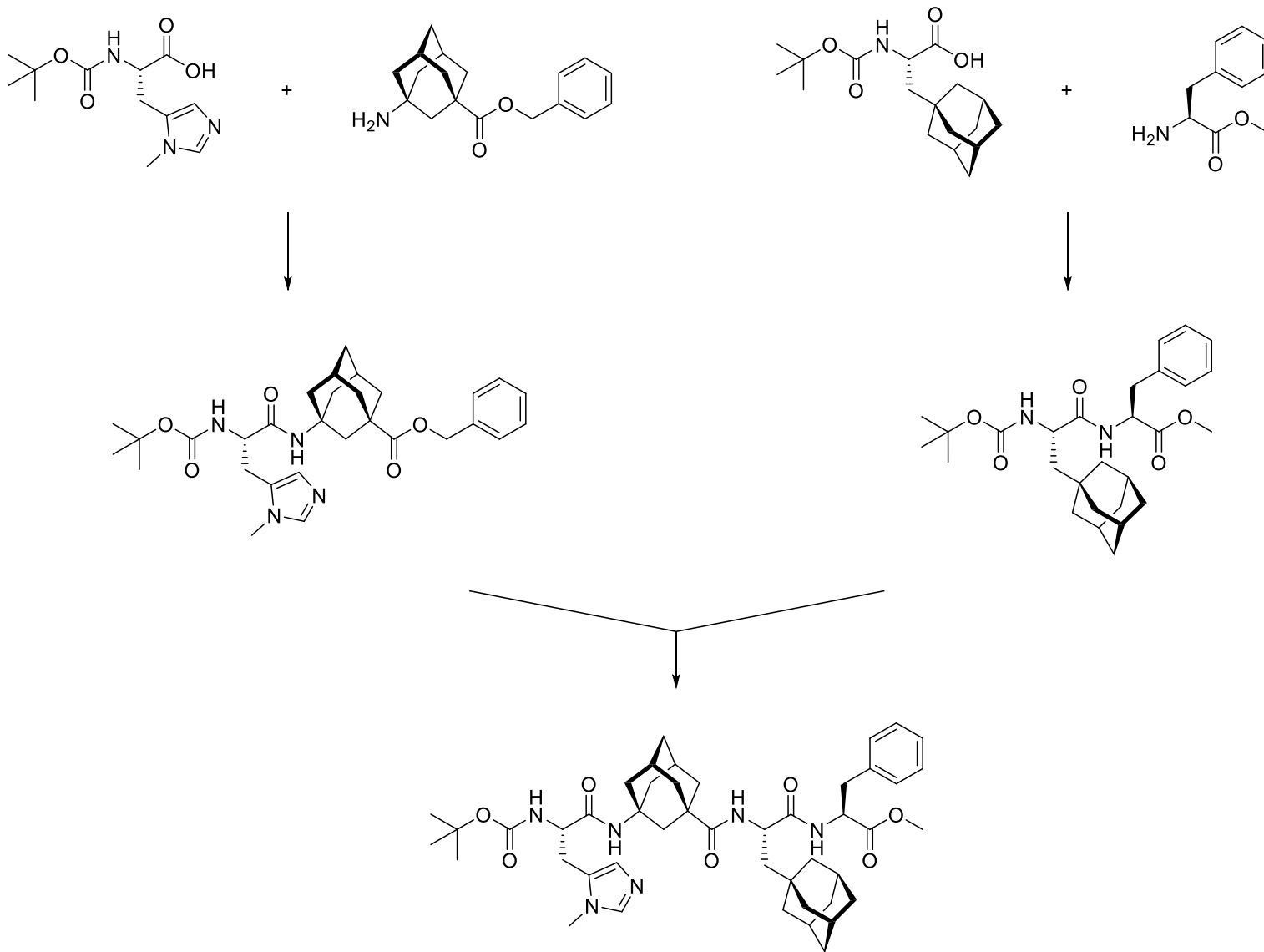


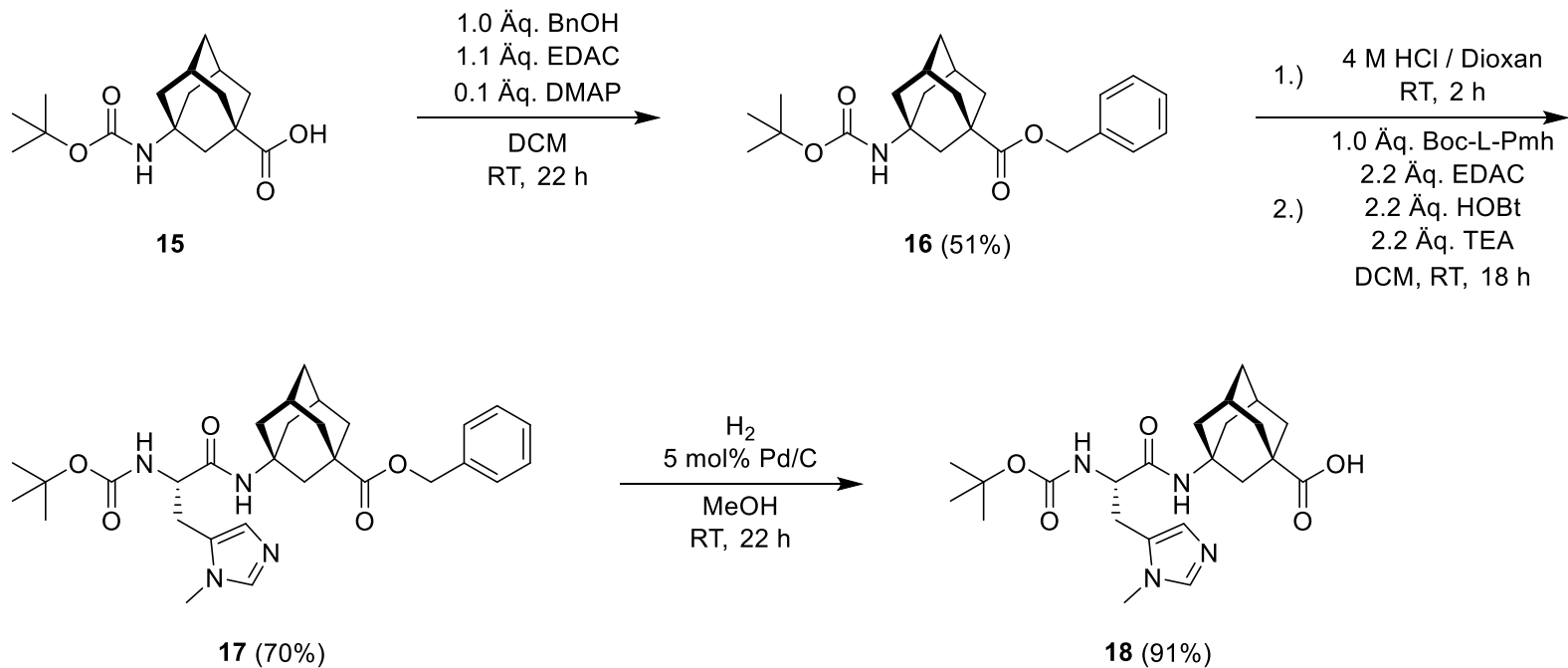


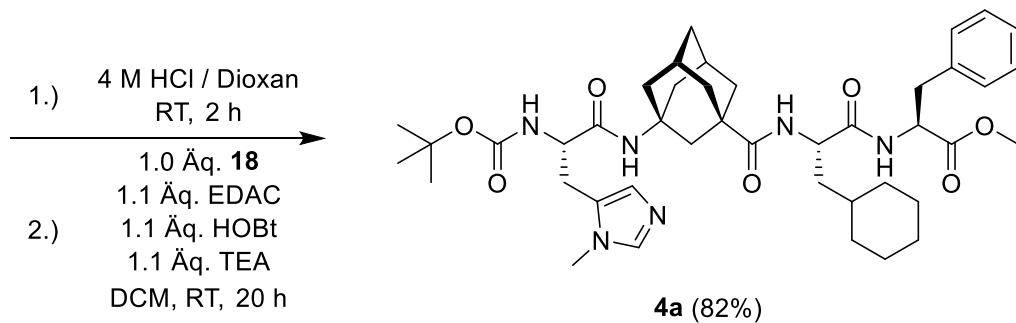
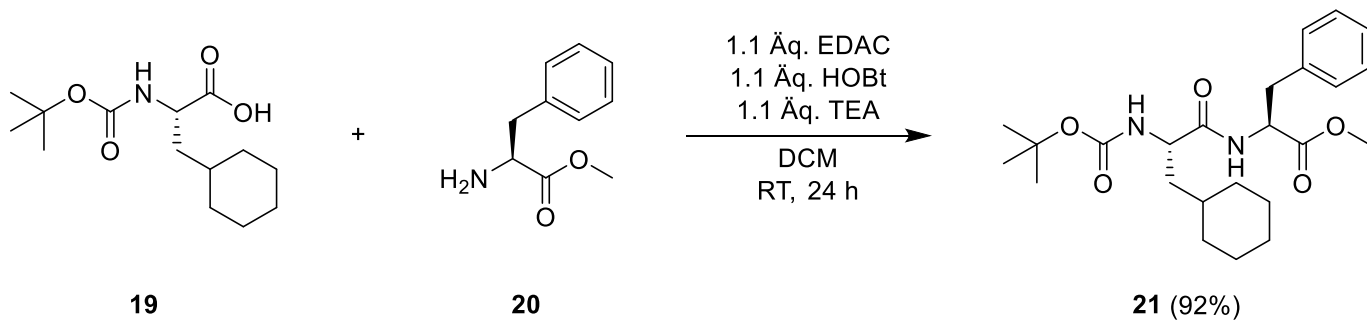
• Coupling of two dipeptides

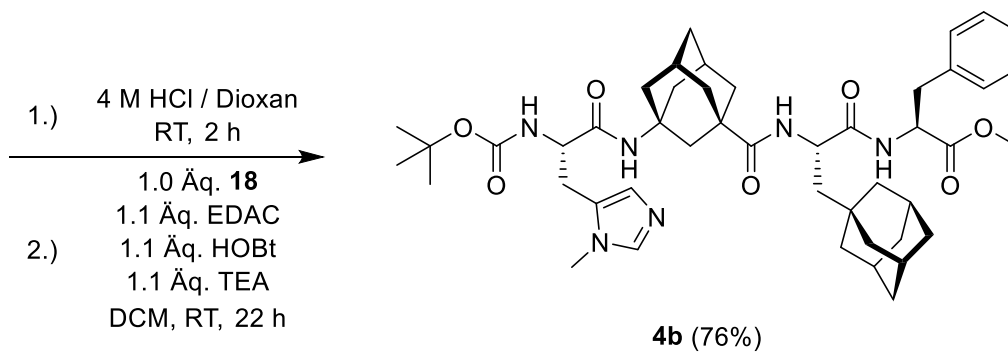
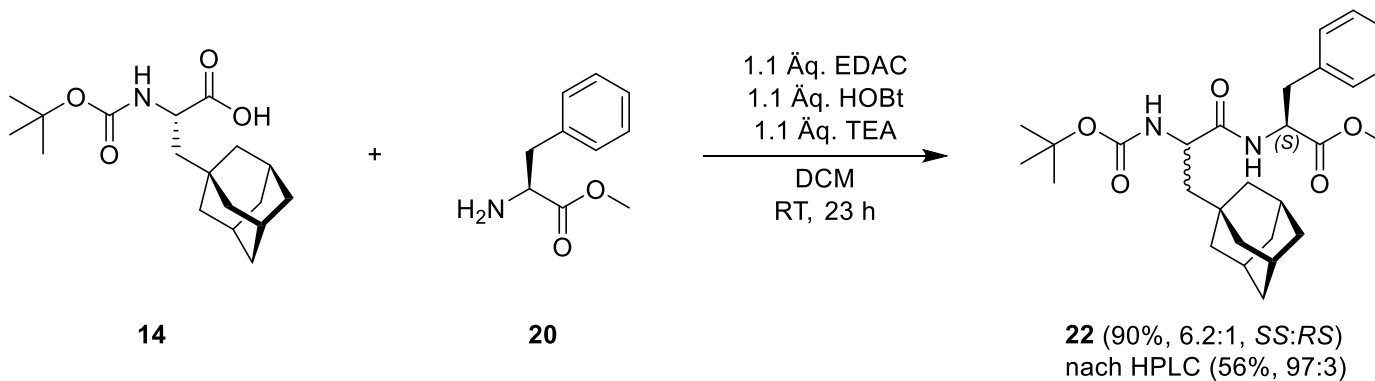


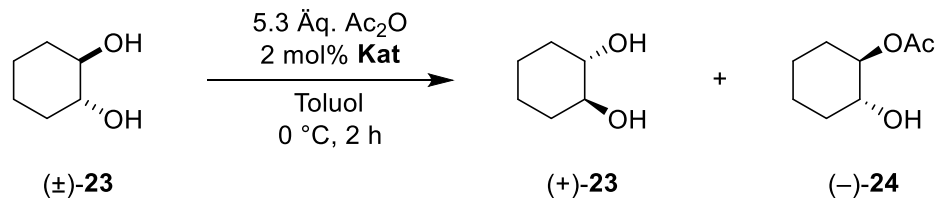
General Synthetic Approach



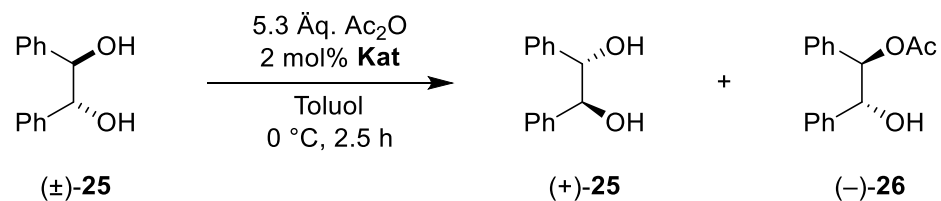








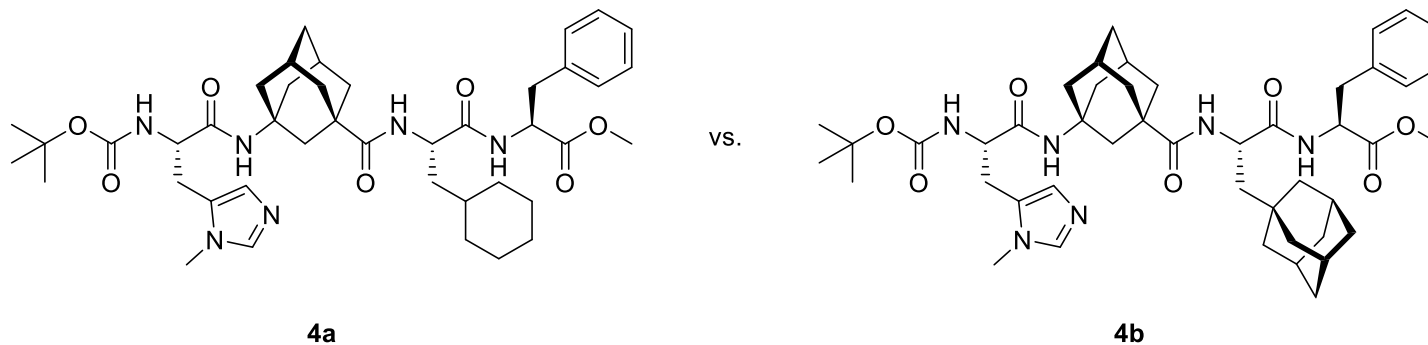
Katalysator	C / % ^[b]	(+)-23 ee / % ^[a]	(-)-24 ee / % ^[a]	S ^[b]
	65.2 (2 h)	> 99	53	23
	64.9 (3 h)	> 99	54	24
	70 (4 h)	> 99	43	17
	39 ^[c]	> 99 ^[c]	78 ^[c]	> 50 ^[c]
	54	> 99	85	> 50



Katalysator	C / % ^[b]	(+)-25 ee / % ^[a]	(-)-26 ee / % ^[a]	S ^[b]
	53	64	57	7.0
	54	67	59	7.5



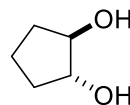
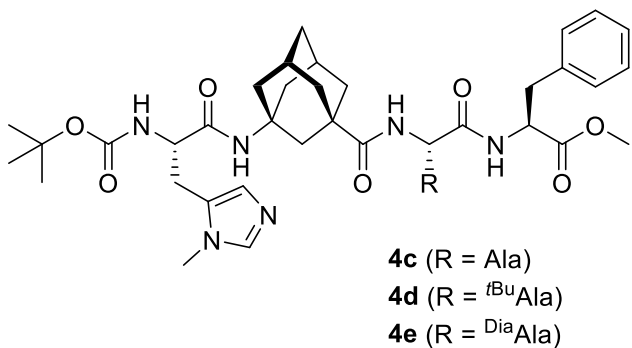
- Reproduced synthesis of L-adamantylalanine
- First synthesis of **4b**



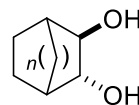
- Catalyst **4b** showed improved *S*-values and *ee*'s over **4a**
- Enlarging the DED lead to a slightly higher selectivity



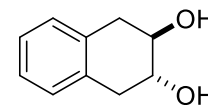
- Synthesize/Screen peptide series with DED increments **4c-e**
- Screen *trans*-1,2-diols that performed poor before e.g. **27**
- Kinetic resolutions of bicyclic *trans*-1,2-diols
 - Bridged bicyclic systems **28**
 - Fused bicyclic systems **29**



27



28



29



- Prof. Peter R. Schreiner
- Alexander Seitz & Dr. Raffael C. Wende
- PRS Group
- OC Analytical Department

