Modification of Adamantane based Peptide Catalysts

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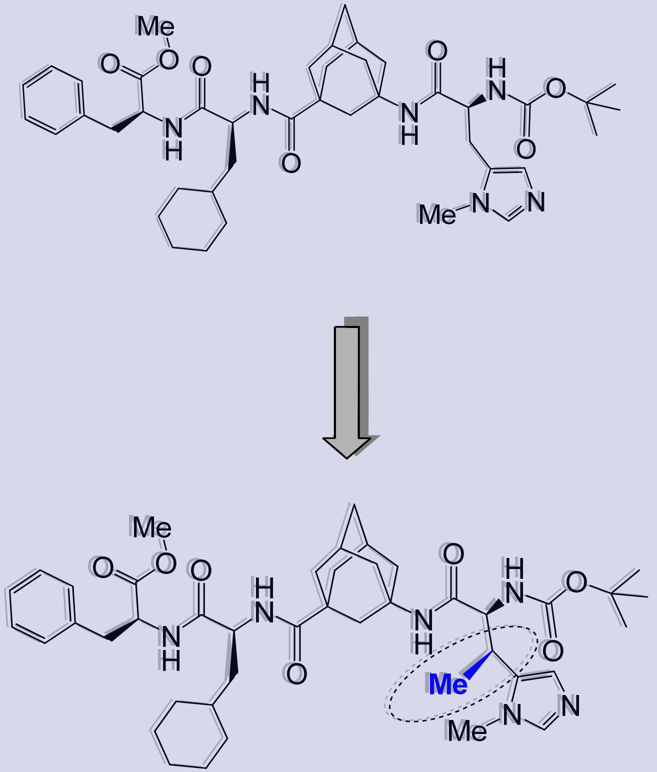

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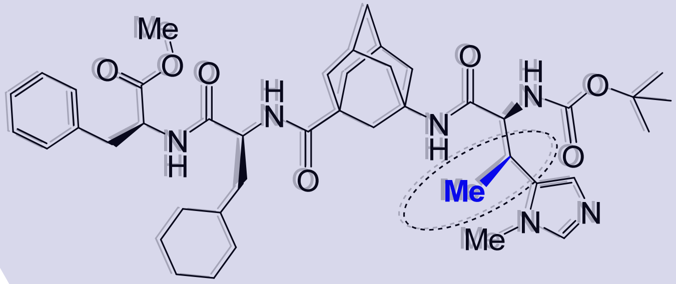
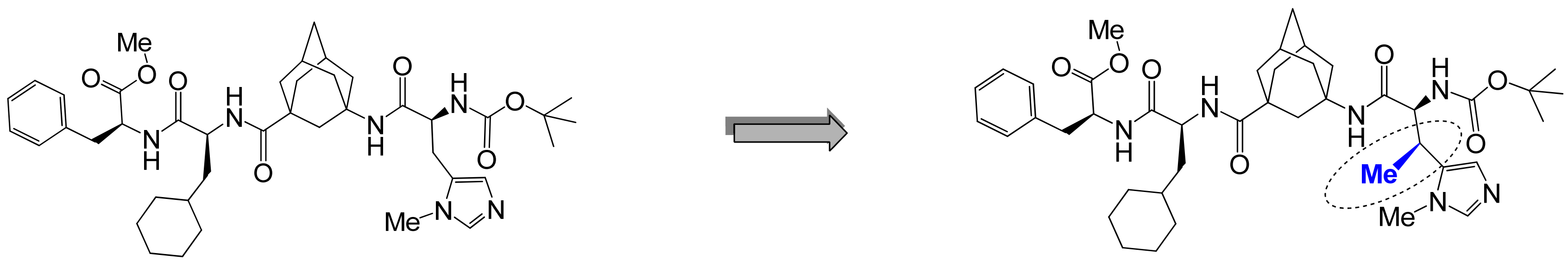


Goal

Amplification of the catalytical active moiety by one stereogenic centre



Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OMe [1]

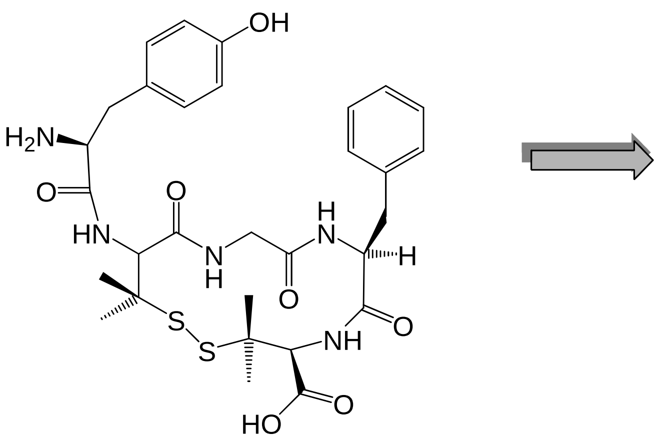
Boc-L-(π-Me)-(β-Me)-His-^{A}Gly-L-Cha-L-Phe-OMe

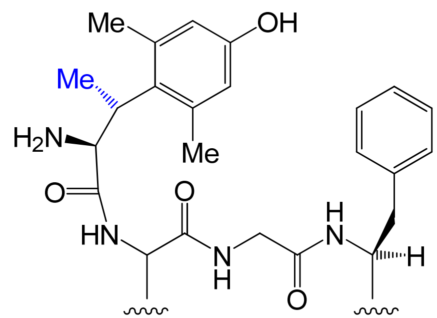
[1] C. E. Müller, L. Wanka, K. Jewell, P. R. Schreiner, *Angew. Chem.* **2008**, *120*, 6275-6278

β-substituted Amino Acids

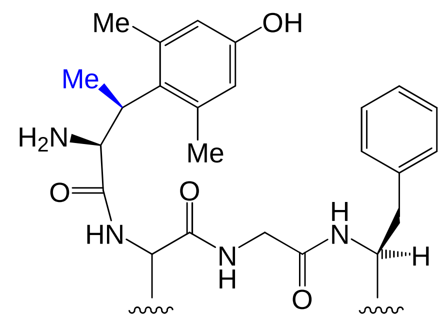
Binding affinity of bioactive peptides to their receptors and subsequent biological transduction depend on:

- the backbone conformation of the peptides
- the side-chain orientation of key parmacophore groups





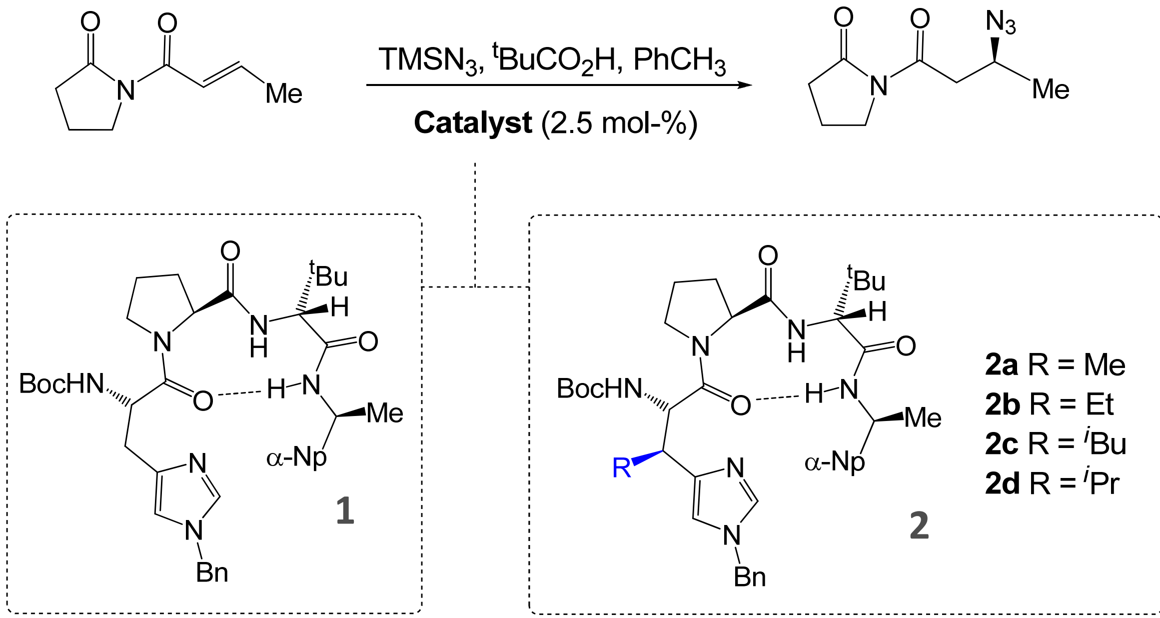
improved binding
and selectivity [2]



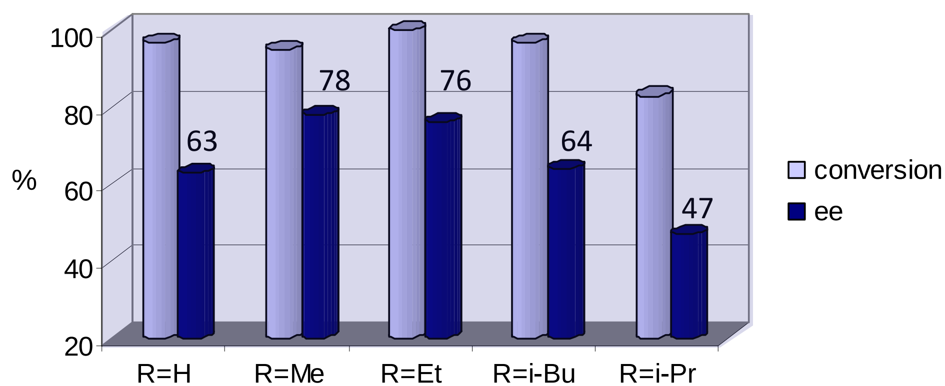
impaired selectivity [2]

[2] V. J. Hruby, *Acc. Chem. Res.* **2001**, *34*, 389-397

Asymmetric Azidation with Miller's Peptides [3]

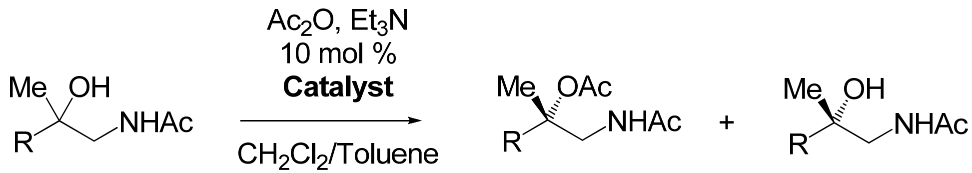


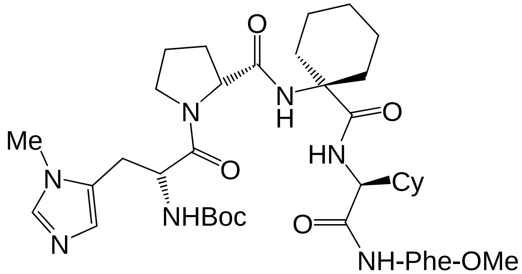
Catalysts Screen for β-azidation
with Catalyst 1 and 2



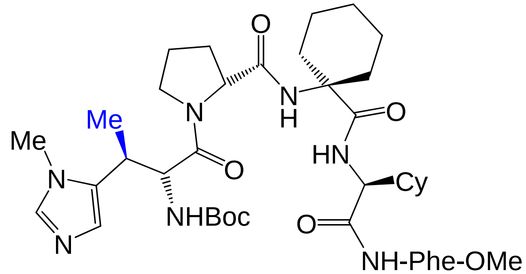
[3] D. J. Guerin, S. J. Miller, *J. Am. Chem. Soc.* **2001**, *124*, 2134-2136

Kinetic Resolutions of tertiary Alcohols with Catalysts **3** versus **4** [4]

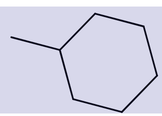
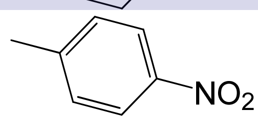




3



4

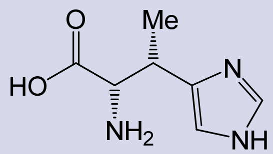
	s* (% Conv.)	s* (% Conv.)
R = Me	**14** (29)	**>50** (51)
R = 	**9** (33)	**>50** (53)
R = 	**10** (39)	**24** (60)
R = 	**3** (32)	**18** (65)

$$* \, \mathbf{s} = \frac{\ln\,[(1-C)(1-ee)]}{\ln\,[(1-C)(1+ee)]}$$

[4] M. C. Angione, S. J. Miller, *Tetrahedron* **2006**, *62*, 5254-5261

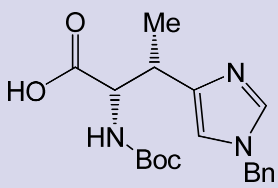
Synthesis of β-methylhistidine

First synthesis of an β-substituted histidine done by Hruby (6 steps) [5]

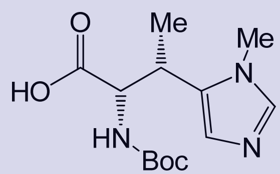


(β-Me)-His

First synthesis of (π-Me)-(β-Me)-histidine (10 steps) [6]



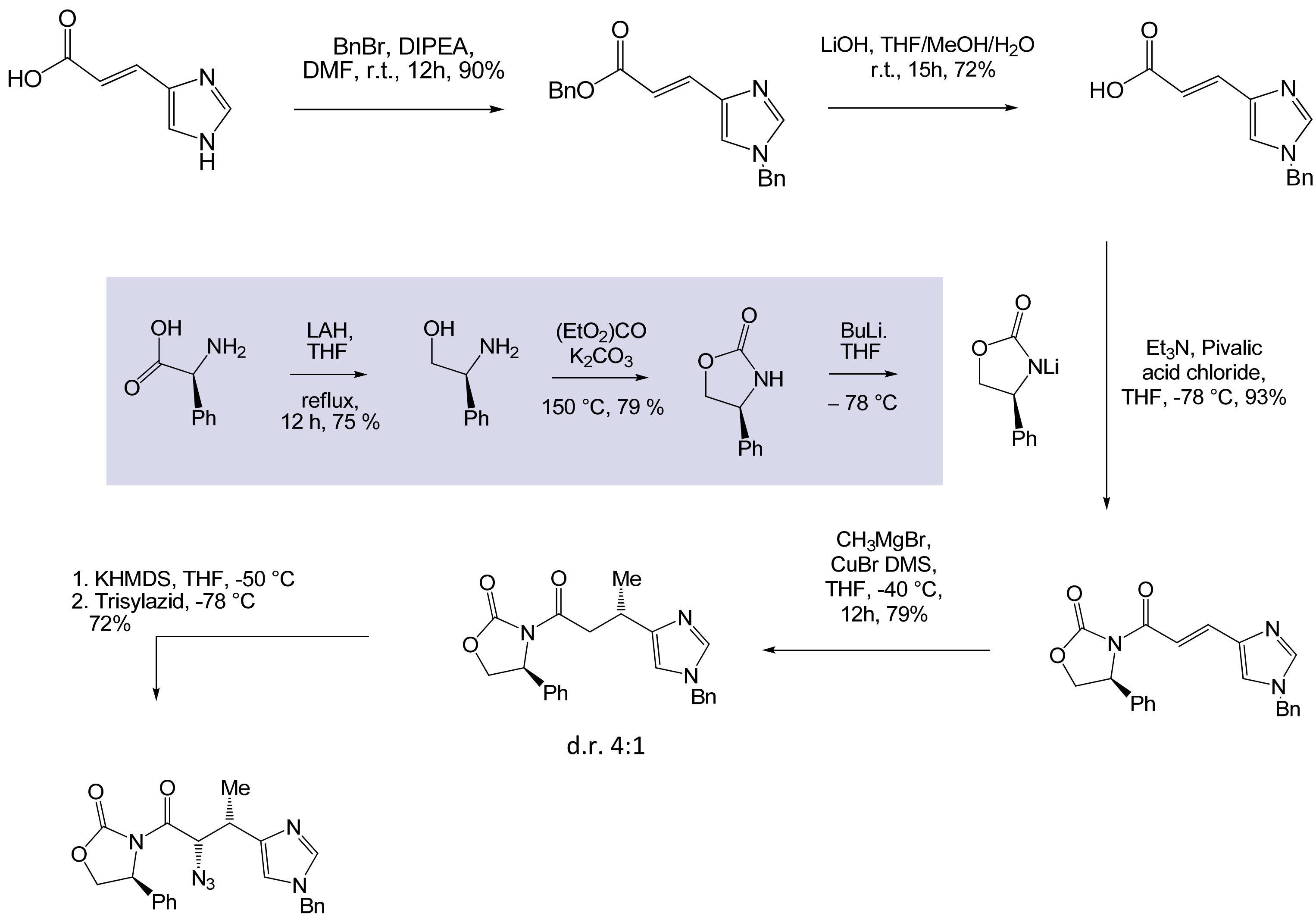
(τ-Bn)-(β-Me)-His



(π-Me)-(β-Me)-His

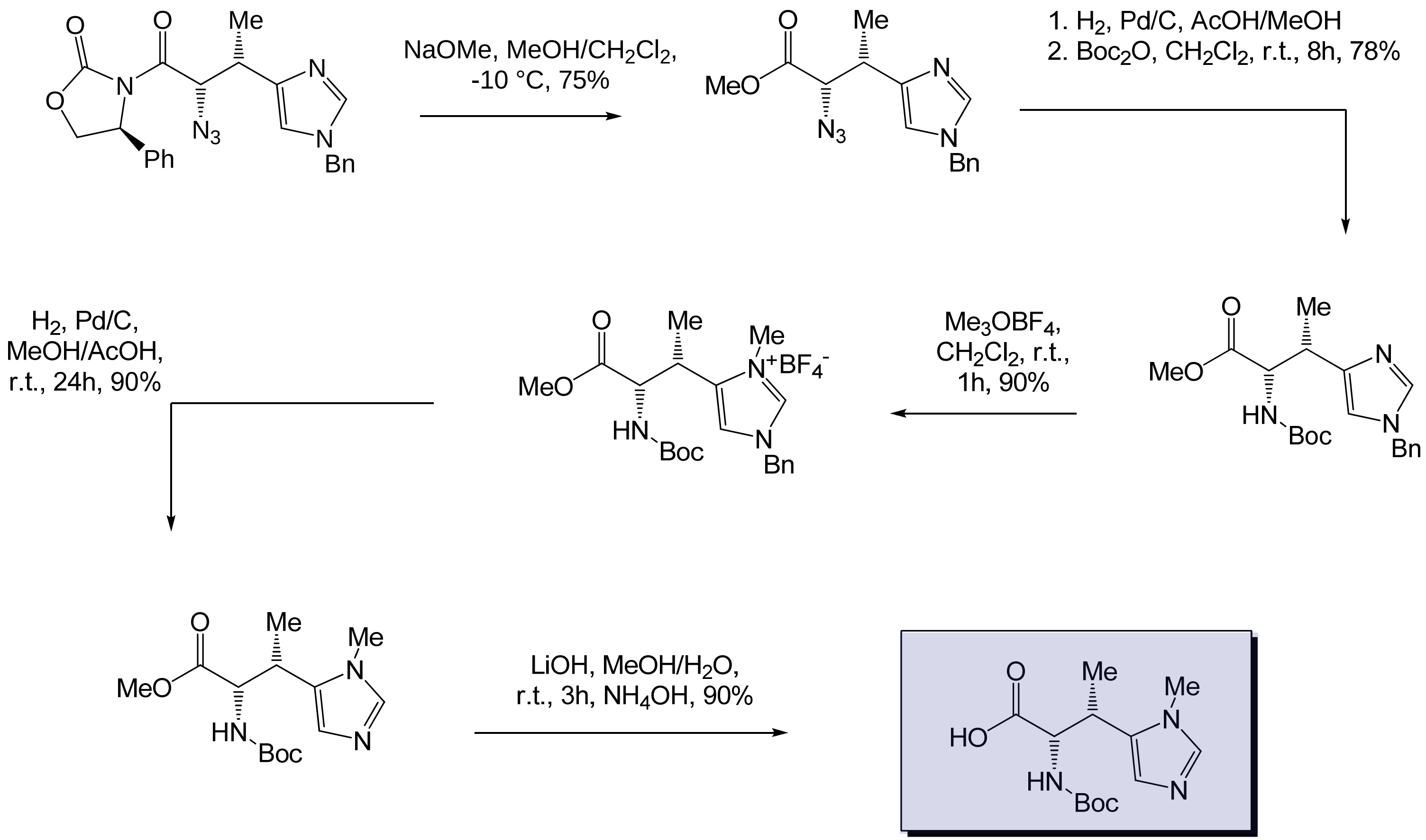
[5] S. Wang, X. Tang, V. J. Hruby, *Tetrahedron Lett.* **2000**, *41*, 1307-1310
[6] M. C. Angione, S. J. Miller, *Tetrahedron* **2006**, *62*, 5254-5261

Synthesis of β-methylhistidine [6]



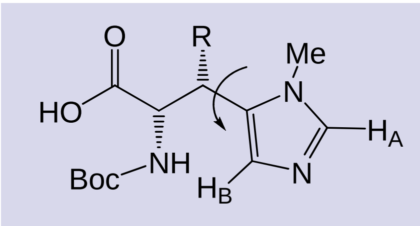
[6] M. C. Angione, S. J. Miller, *Tetrahedron* **2006**, *62*, 5254-5261

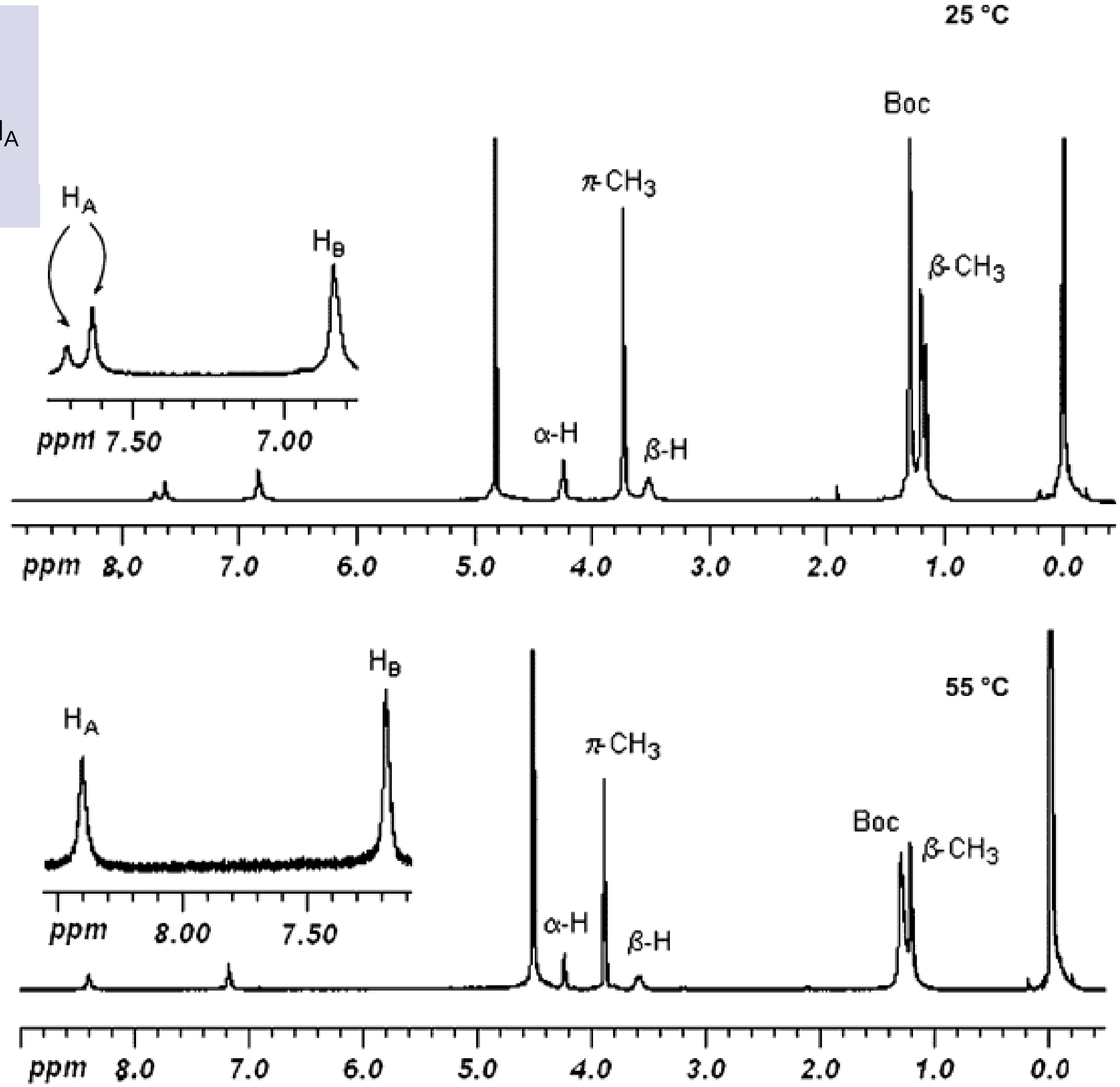
Synthesis of β-methylhistidine [6]



[6] M. C. Angione, S. J. Miller, *Tetrahedron* **2006**, *62*, 5254-5261

Synthesis of β-methylhistidine [6]

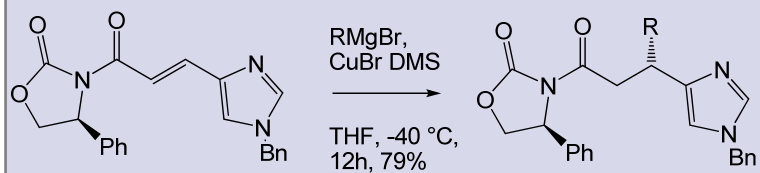




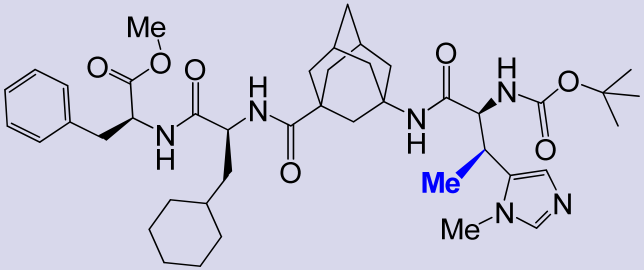
[6] M. C. Angione, S. J. Miller, *Tetrahedron* **2006**, *62*, 5254-5261

Approach

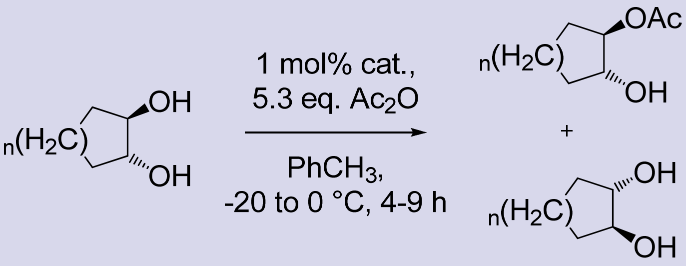
β-Alkyllhistidine



Peptide synthesis



Catalysis



Acknowledgments

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- *Prof. Dr. Peter R. Schreiner*
- *Daniela Zell*