After the Dakin-West Reaction – Challenges and Opportunities

Group Seminar

05.02.2016

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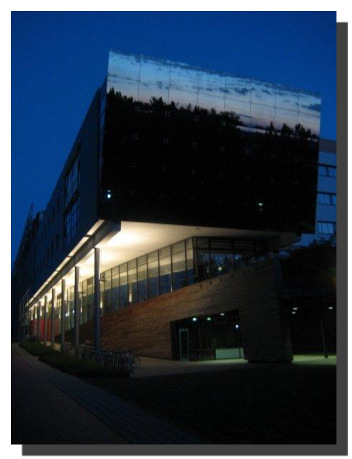
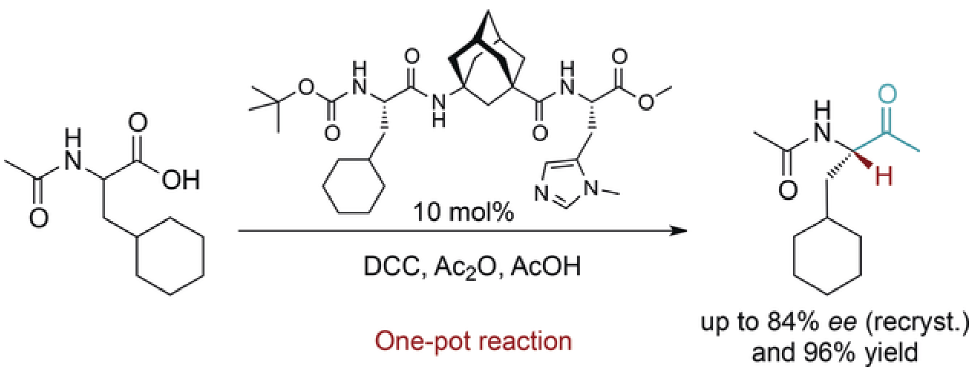
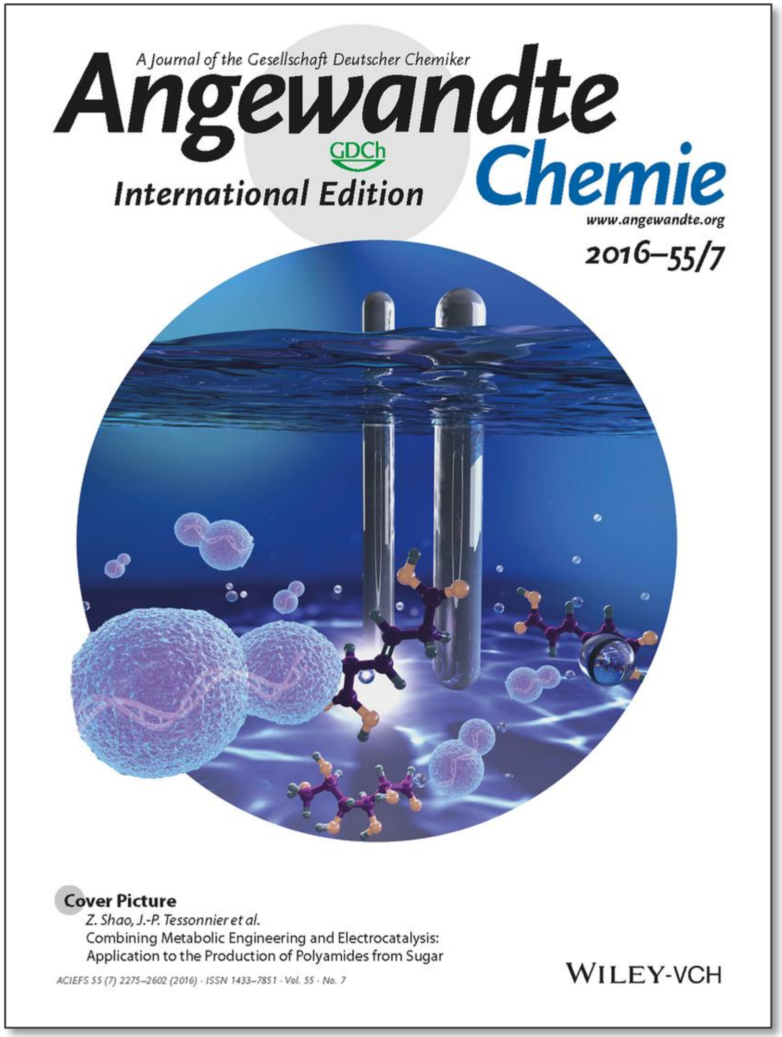
Justus-Liebig University
35392 Giessen, Germany



The Enantioselective Dakin-West Reaction





R. C. Wende, A. Seitz, D. Niedek, S. M. M. Schuler, C. Hofmann, J. Becker, P. R. Schreiner, *Angew. Chem. Int. Ed.* **2016**, DOI: 10.1002/anie.201509863.

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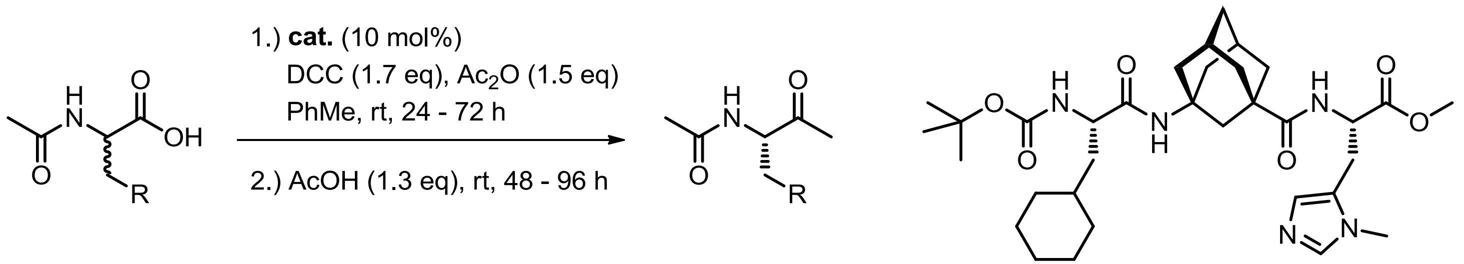
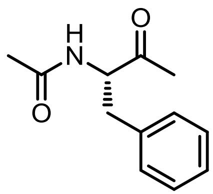
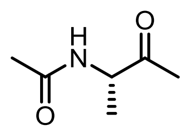
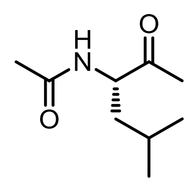




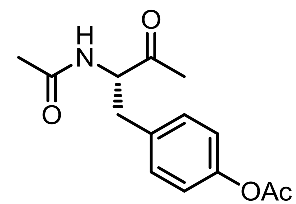
36% *ee*, 69% yield
(84% *ee* after cryst.)



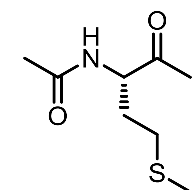
11% *ee*, 82% yield



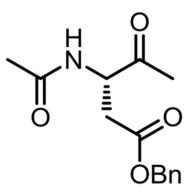
54% *ee*, 63% yield



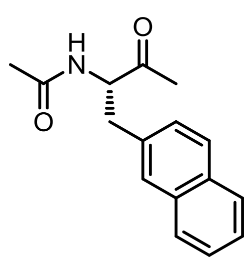
31% *ee*, 77% yield
(54% *ee* after cryst.)



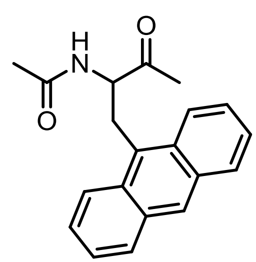
25% *ee*, 81% yield



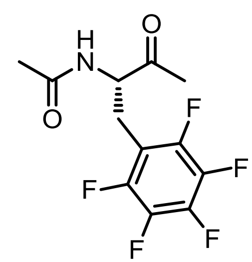
17% *ee*, 62% yield



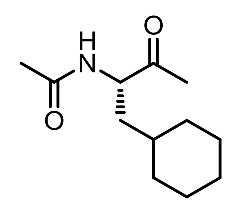
31% *ee*, 78% yield



0% *ee*, 52% yield



18% *ee*, 96% yield



58% *ee*, 67% yield

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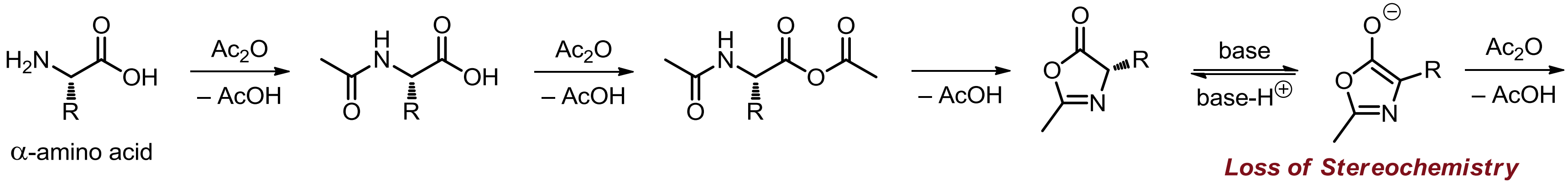
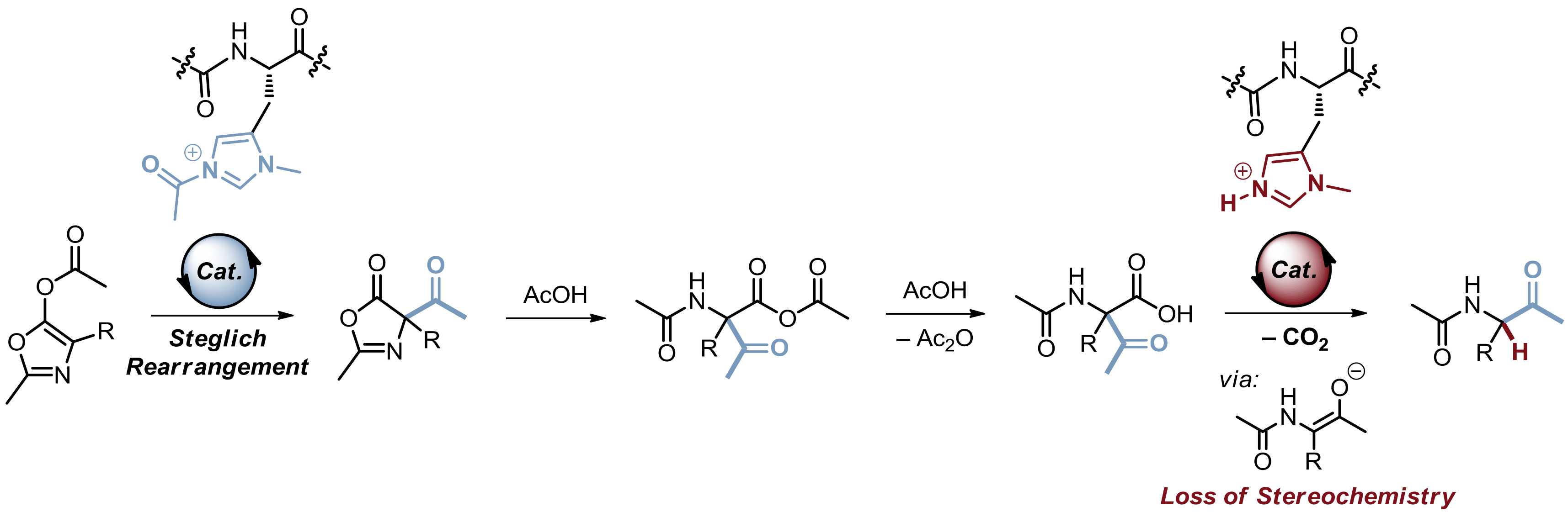
The Enantioselective Dakin-West Reaction





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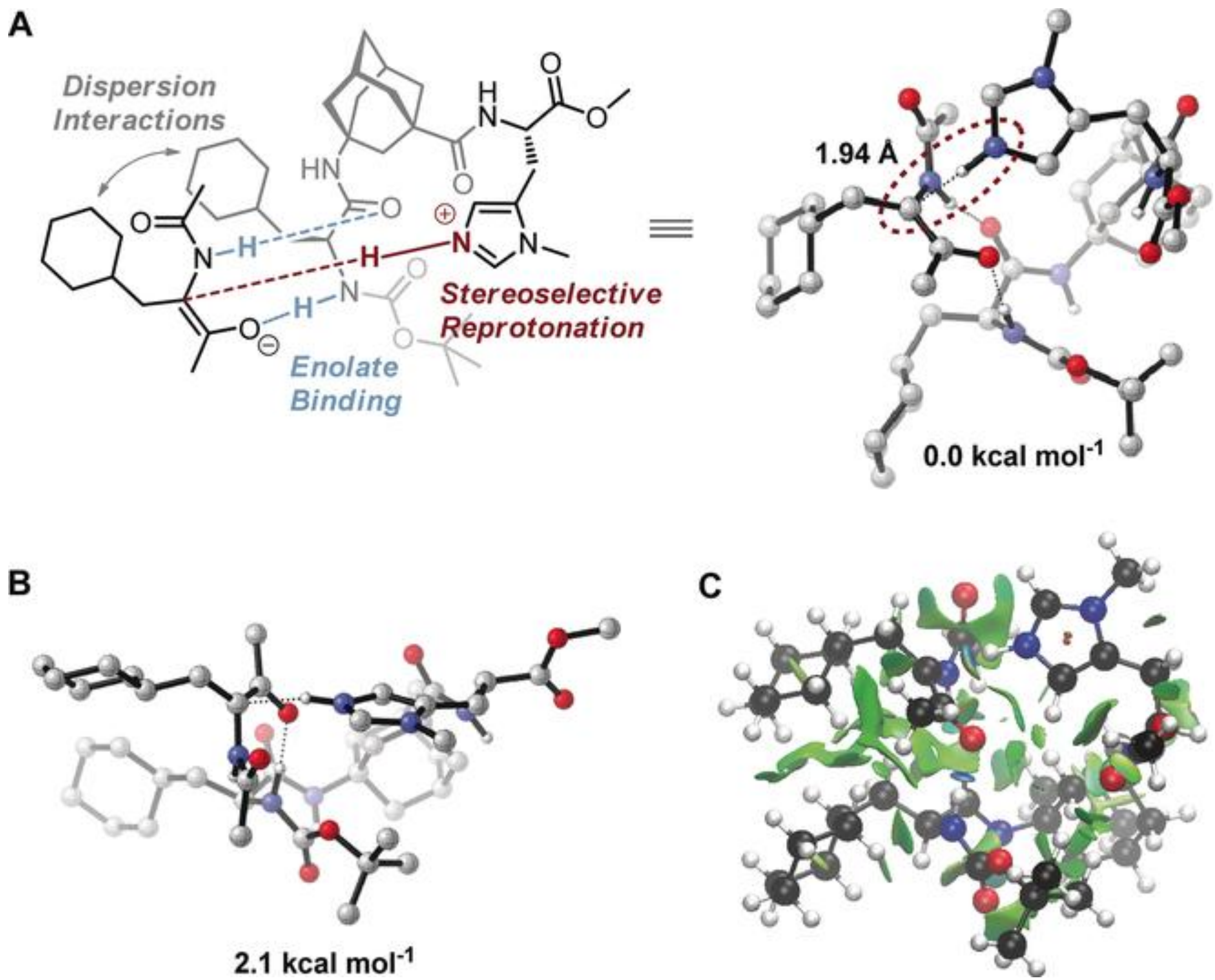

MMFF conformer distribution, lowest lying conformers were reoptimized at B3LYP-D3(BJ)/6-31+G(*d*,*p*), PCM solvent model in toluene.

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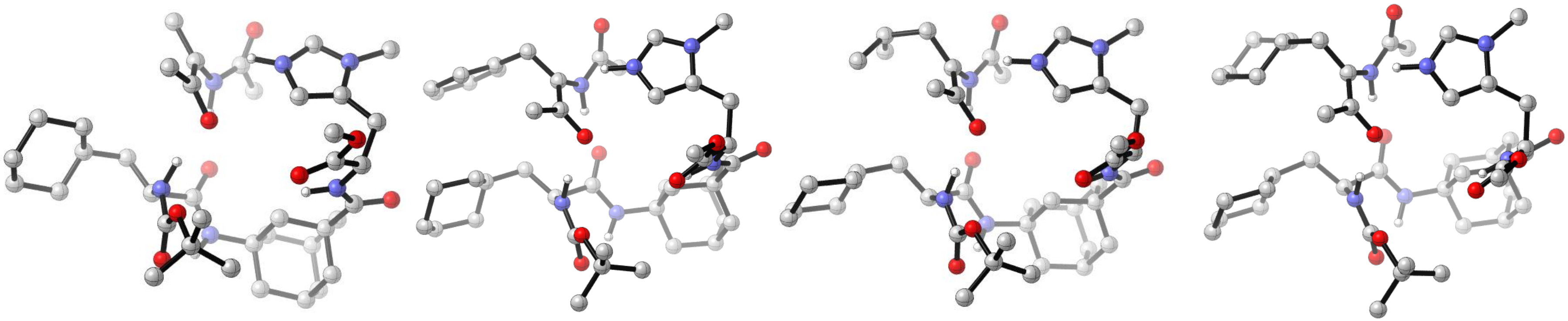
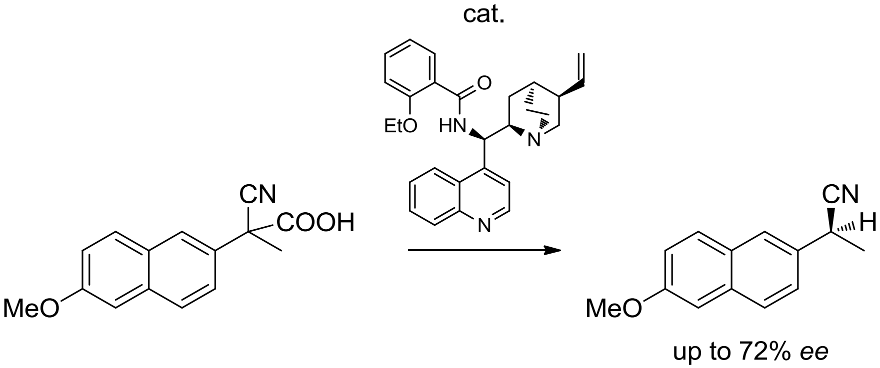
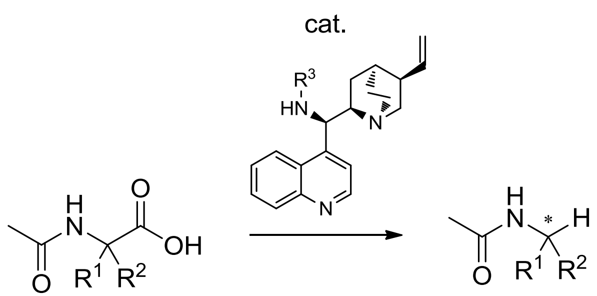


	Ala	Phe	Leu	Cha
$\Delta\Delta G_{298}$	0.0		-0,74	-1,43
$\Delta\Delta H_{298}$	0.0		-1,03	-2,32

MMFF conformer distribution, lowest lying conformers were reoptimized at B3LYP-D3(BJ)/6-31+G(*d*,*p*), PCM solvent model in toluene.

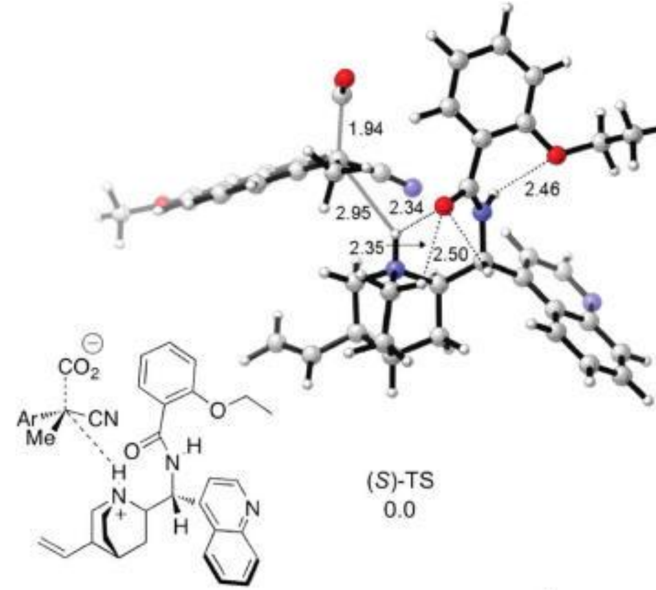
Enantioselective Decarboxylative Protonation

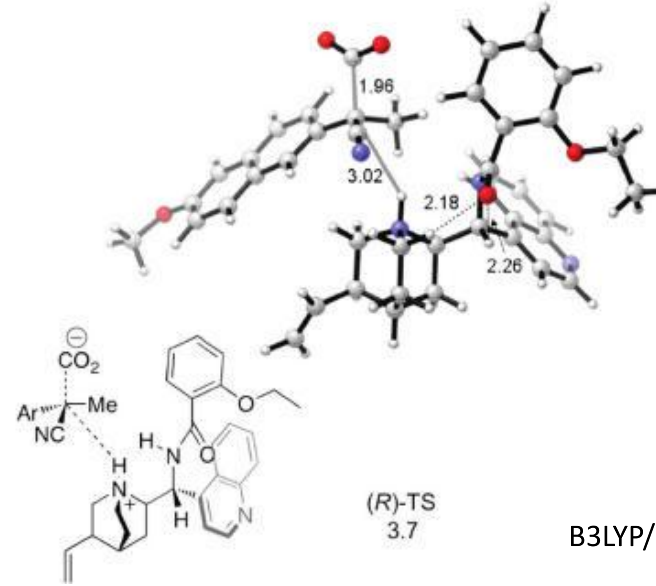




R^1 = COOEt, COOH, CN
R^2 = Me i-Pr, Bn

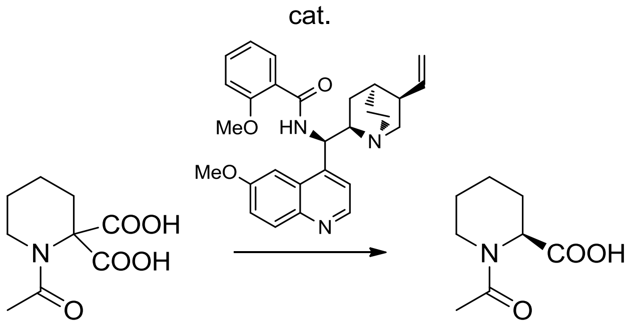
up to 70% *ee*



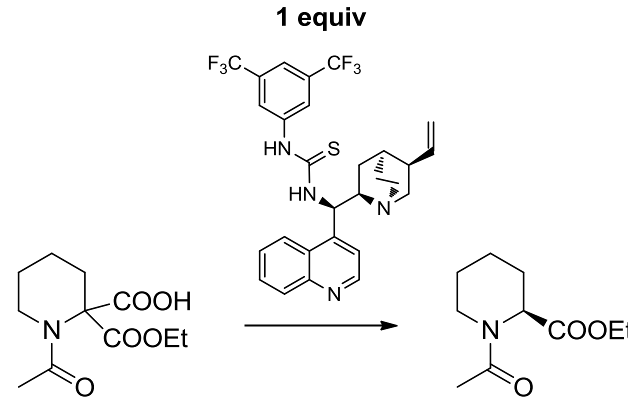


B3LYP/6-31G(d)

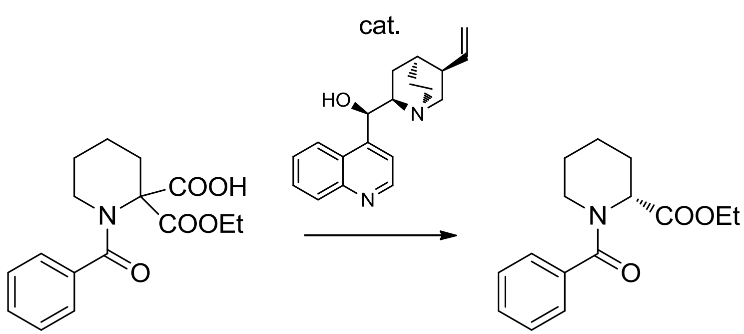
H. Brunner, P. Schmidt, *Eur. J. Org. Chem.* **2000**, 2119-2133; H. Brunner, Markus A. Baur, *Eur. J. Org. Chem.* **2003**, 2854-2862; M. Drees, L. Kleiber, M. Weimer, T. Strassner, *Eur. J. Org. Chem.* **2002**, 2405-2410; P. H.-Y. Cheong, C. Y. Legault, J. M. Um, N. Çelebi-Ölçüm, K. N. Houk, *Chem. Rev.* **2011**, *111*, 5042-5137.



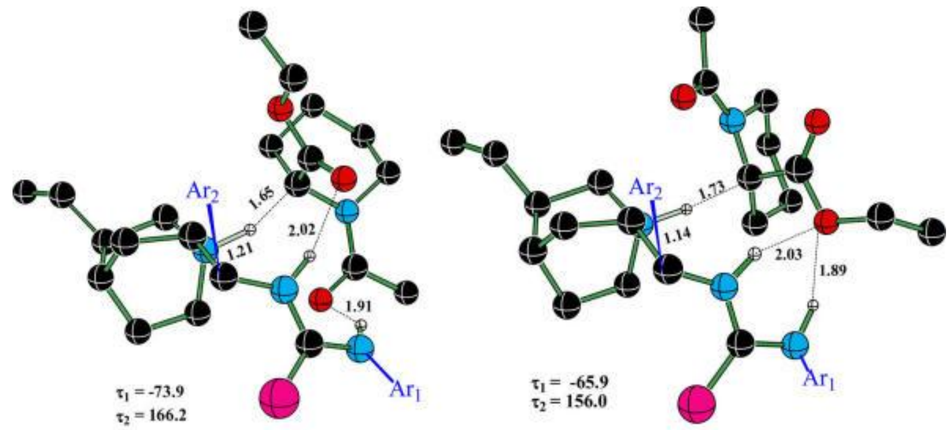
up to 52% *ee*



up to 93% *ee*



up to 71% *ee*

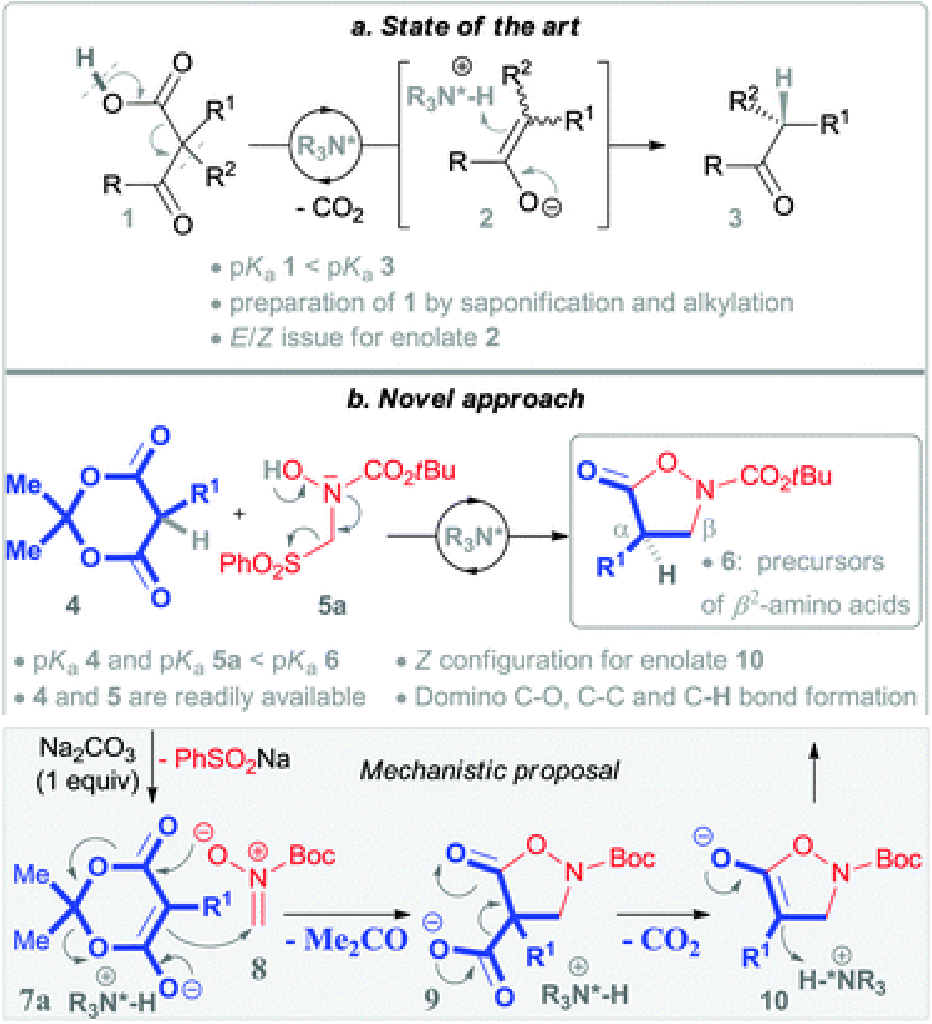


TS4 ΔG_{rel}= 0.0 kcal/mol

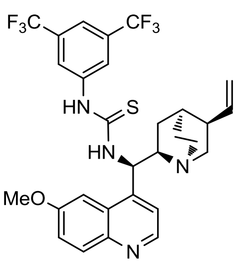
TS4$_{enan}$ ΔG_{rel}= 2.61 kcal/mol

M06-2X/6-311+G**//ONIOM2

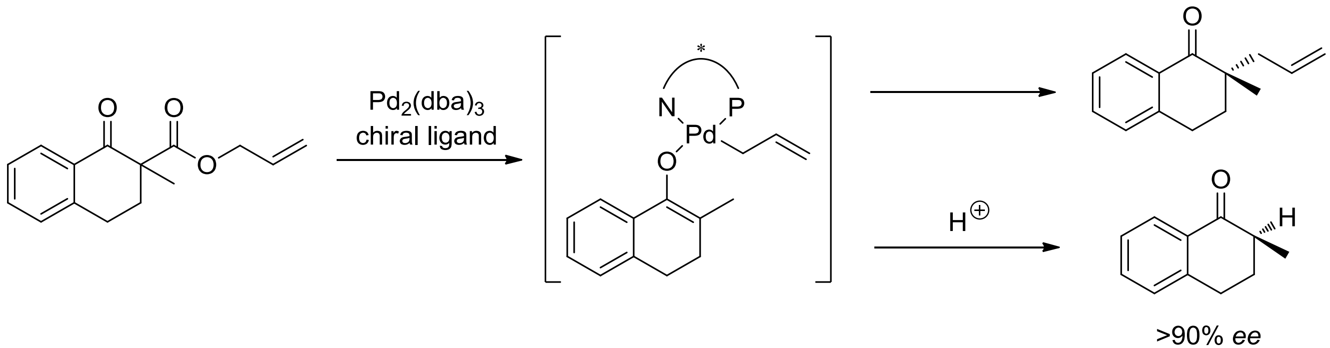
L. M. A. Rogers, J. Rouden, L. Lecomte, M.-C. Lasne, *Tetrahedron Lett.* **2003**, *44*, 3047-3050; T. Seitz, J. Baudoux, H. Bekolo, D. Cahard, J.-C. Plaquevent, M.-C. Lasne, J. Rouden, *Tetrahedron* **2006**, *62*, 6155-6165; M. Amere, M.-C. Lasne, J. Rouden, *Org. Lett.* **2007**, *9*, 2621-2624; A. Sengupta, R. B. Sunoj, *J. Org. Chem.* **2012**, *77*, 10525-10536.

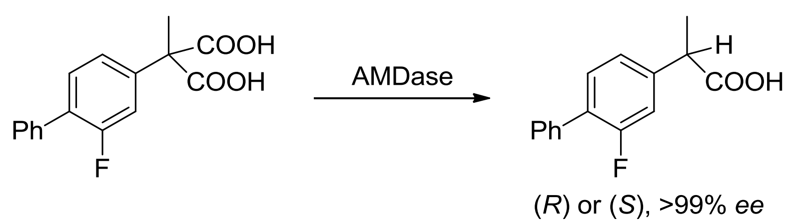


up to 88% *ee* with cat.



Enantioselective Decarboxylative Protonation





J. T. Mohr, T. Nishimata, D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2006**, *128*, 11348-11349; S. K. Gaßmeyer, J. Wetzig, C. Mügge, M. Assmann, J. Enoki, L. Hilterhaus, R. Zuhse, K. Miyamoto, A. Liese, R. Kourist, *ChemCatChem* **2016**, DOI: 10.1002/cctc.201501205.

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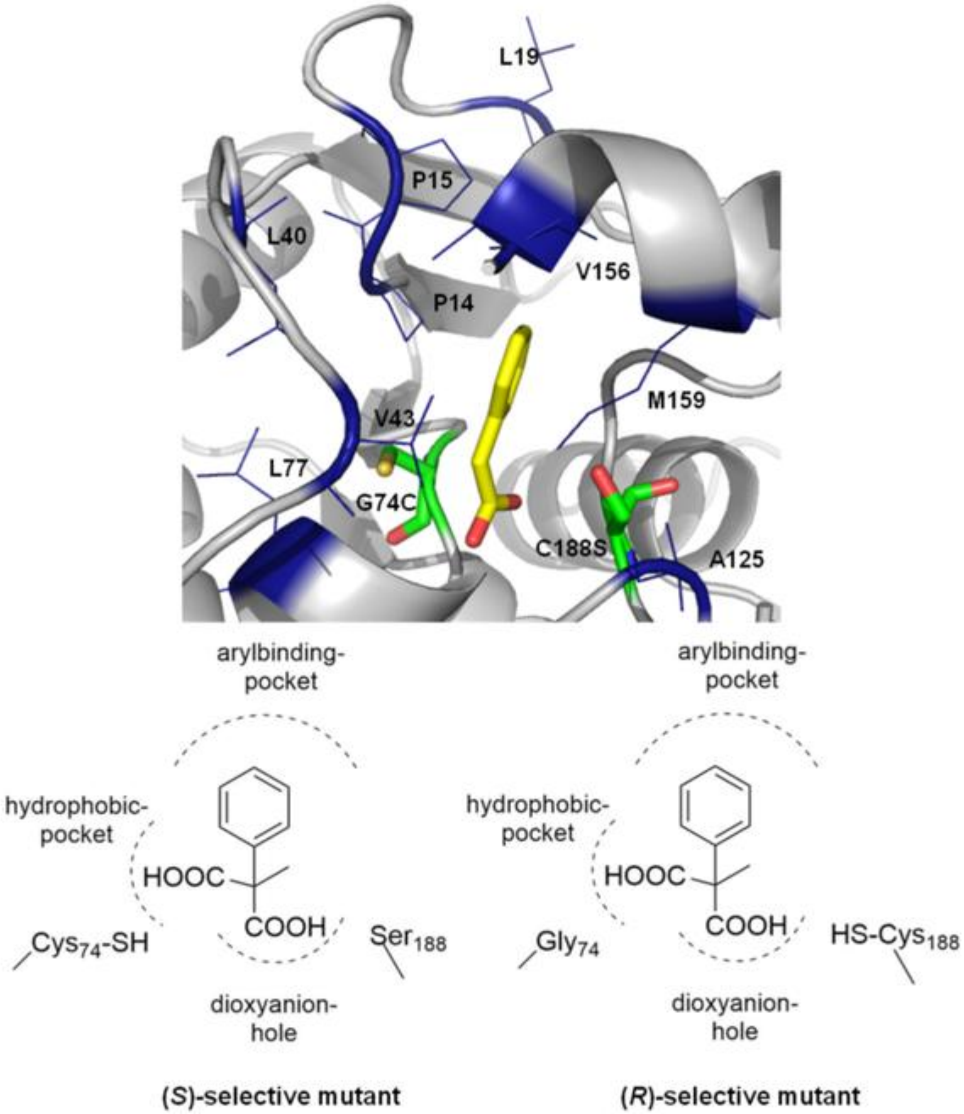

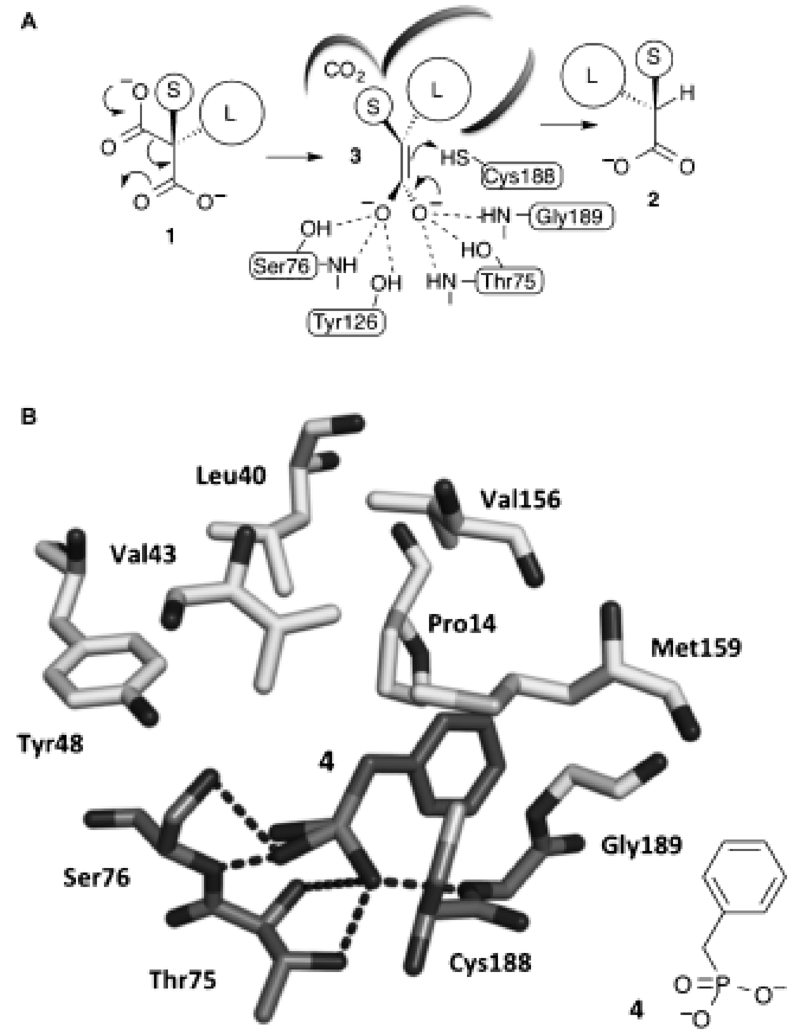

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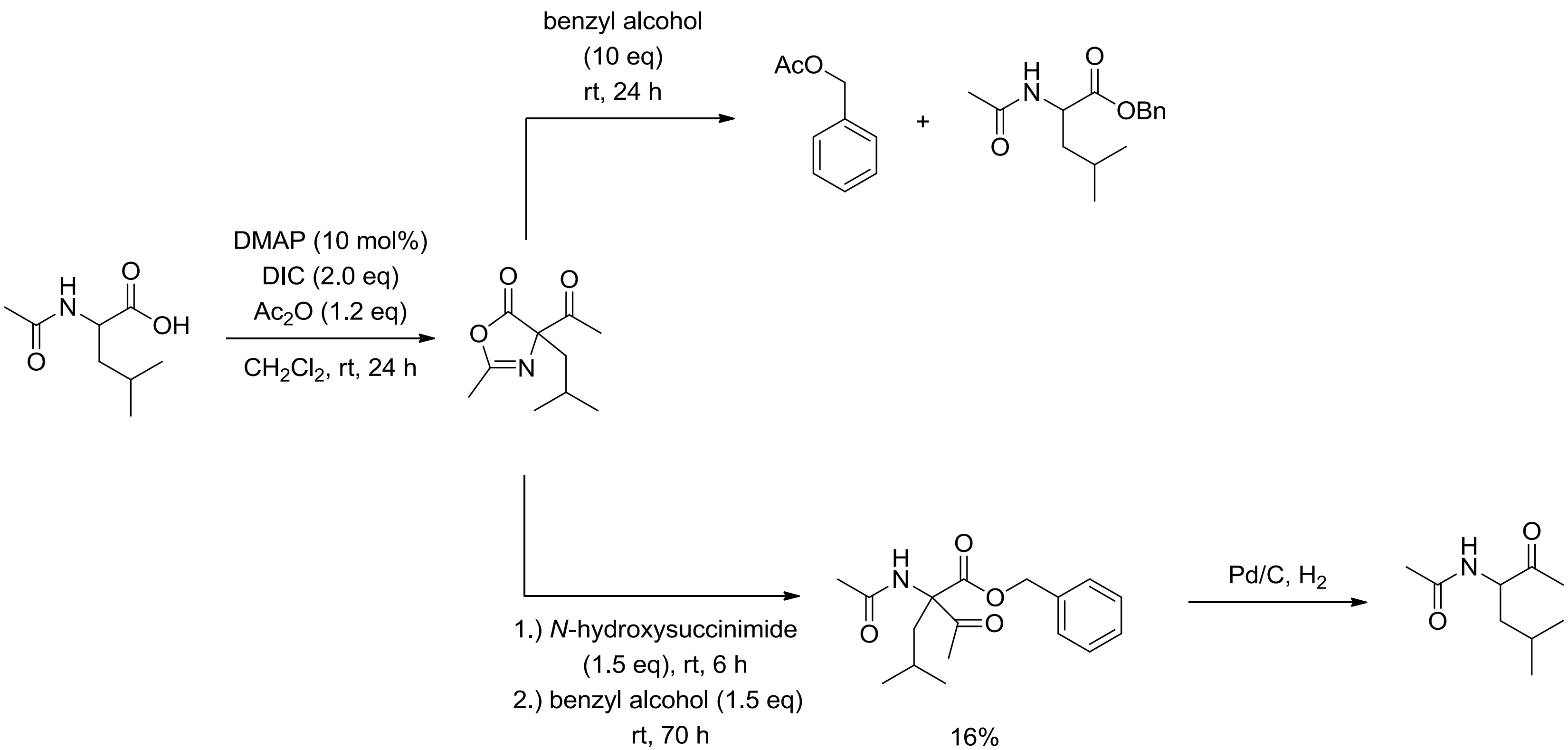
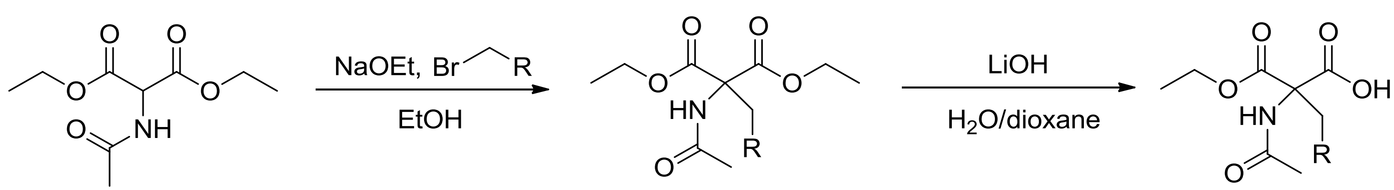
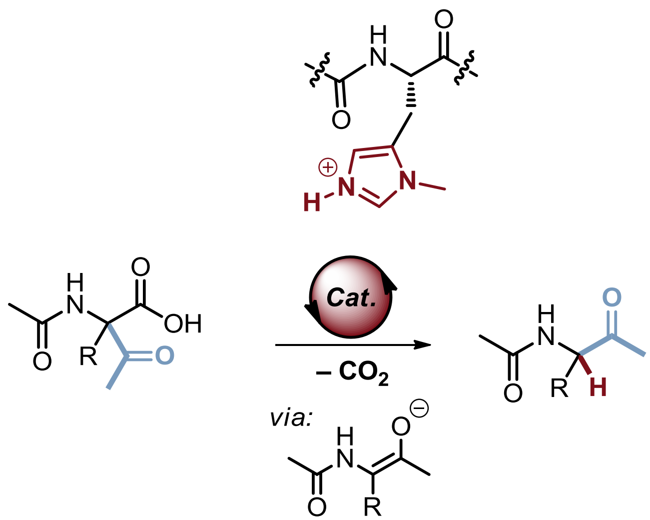
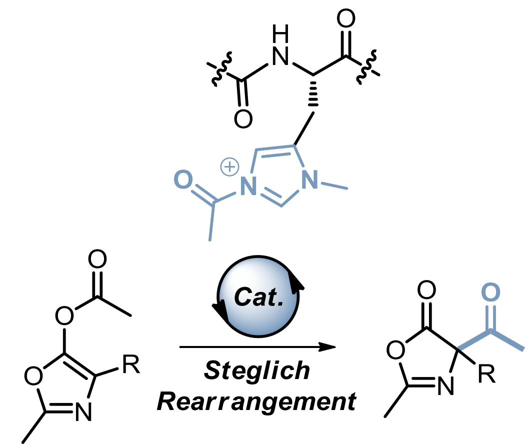
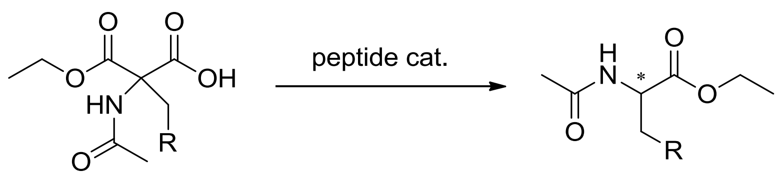
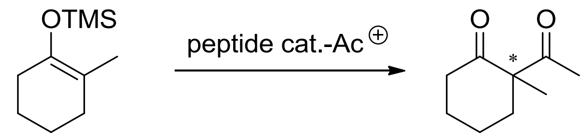


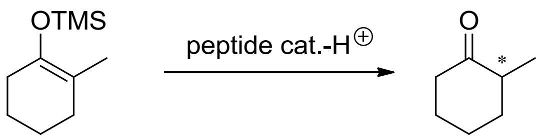



Cat.
– CO2
via:


Cat.
Steglich
Rearrangement


peptide cat.


OTMS
peptide cat.-Ac⊕


OTMS
peptide cat.-H⊕

Prof. Peter R. Schreiner

Dr. Dennis Gerbig

Dominik Niedek

Alexander Seitz

PRS group