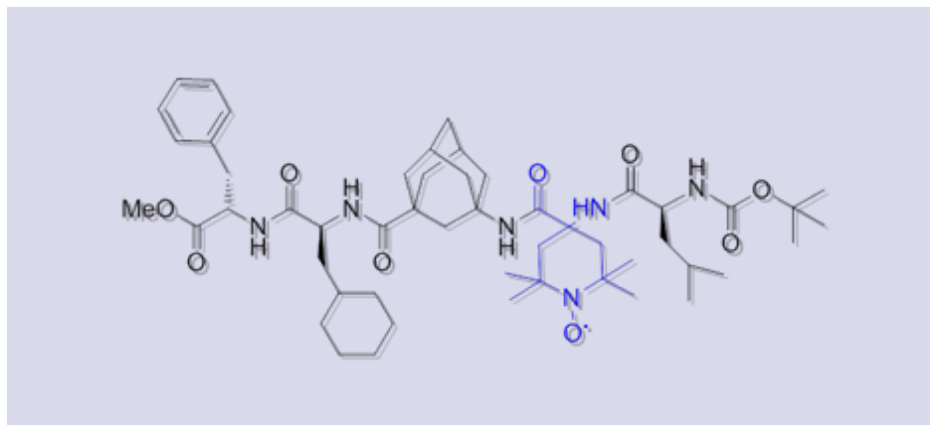


Stereoselective Oxidations of Alcohols using TEMPO-Peptidocatalysts

17.02.2011

Christine Hofmann

*Institute of Organic Chemistry
Justus-Liebig-University
35435 Giessen, Germany*





a) Oxidation of Alcohols using TEMPO as Catalyst

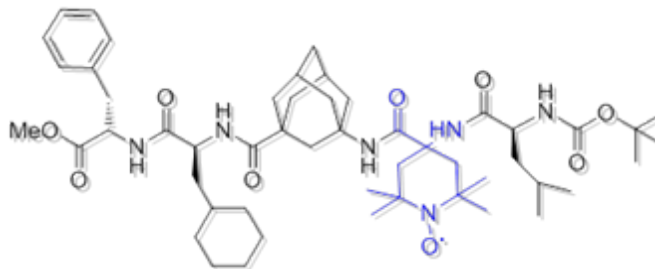
b) Selective Oxidation of Alcohols

↳ Desymmetrization / Oxidative Kinetic Resolution

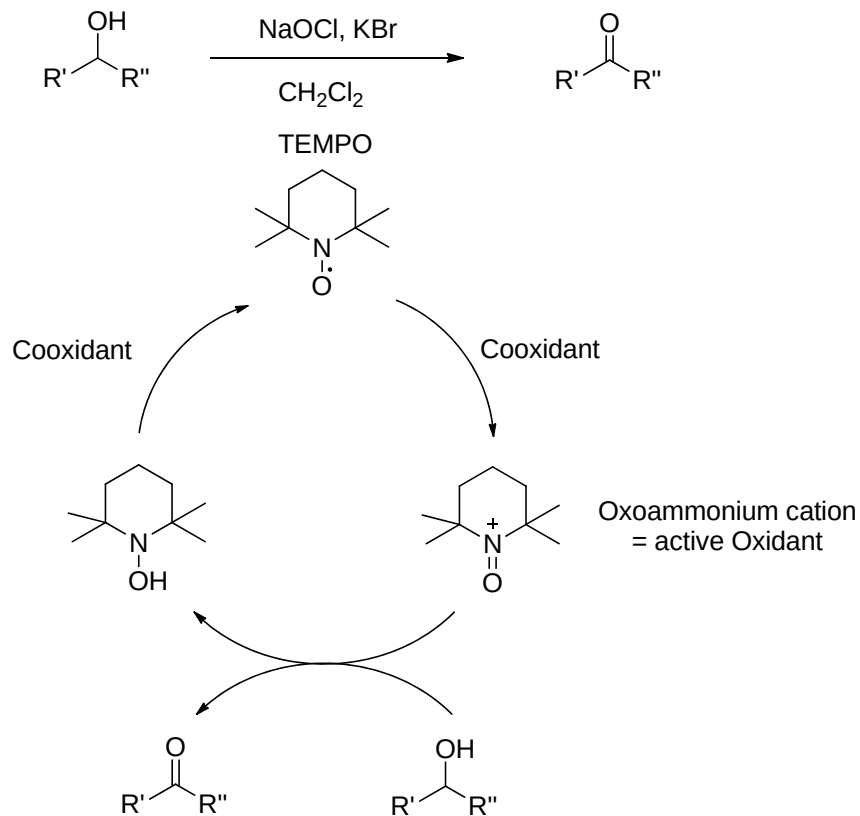
↳ Chiral Nitroxides

↳ TEMPO-Derivats in Peptides

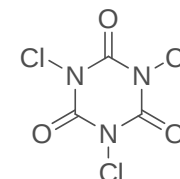
c) Oxidazing Agents, Catalysts & Substrates



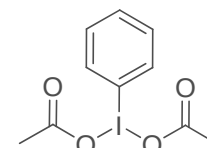
a) Oxidation of Alcohols using TEMPO as Catalyst



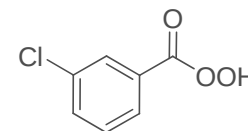
other Cooxidants



TCCA



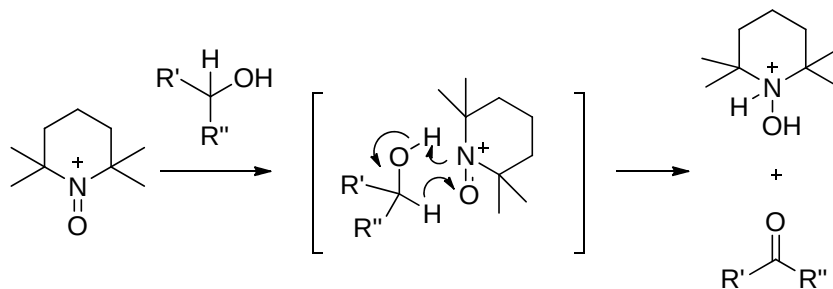
DAIB



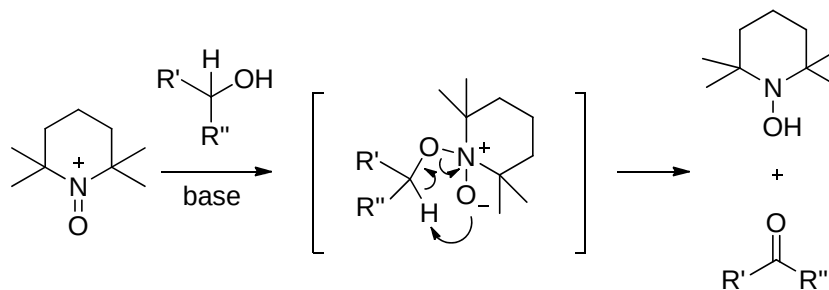
mCPBA



Oxidation of alcohols in acidic media ...

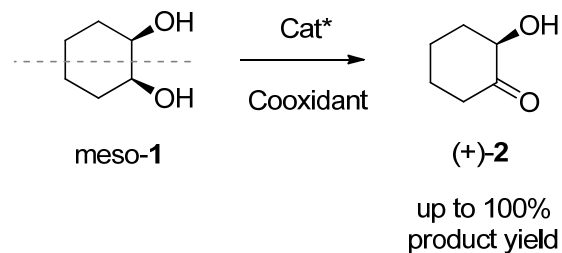


... and in basic media

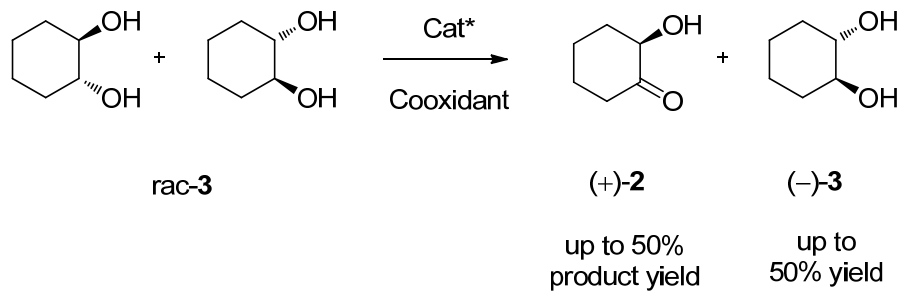




Desymmetrization of *meso* compounds



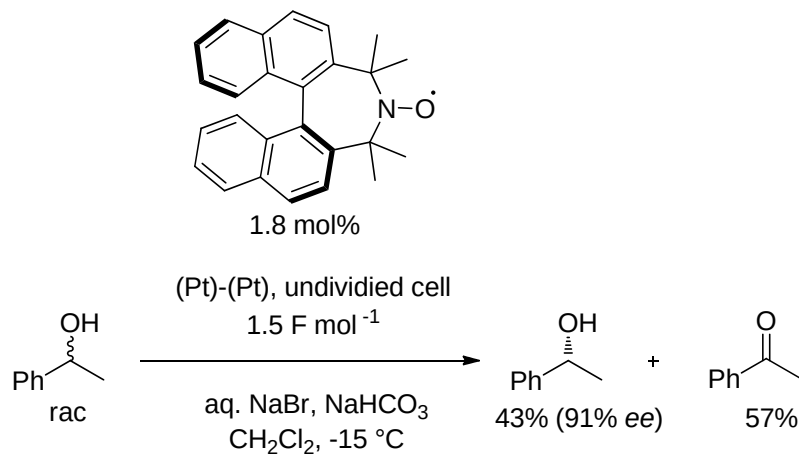
Oxidative kinetic resolution (OKR) of alcohols



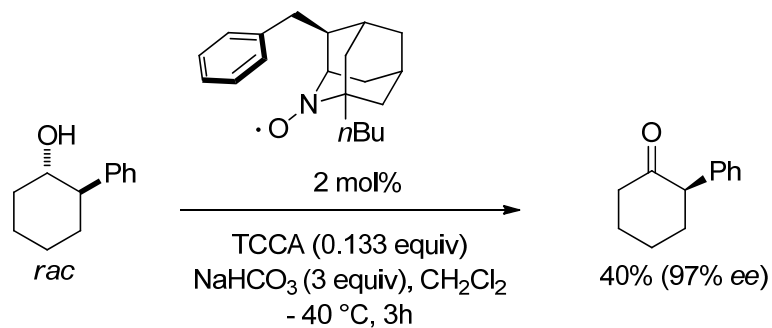
b) Selective Oxidation of Alcohols



Axially chiral C₂-symmetric nitroxide

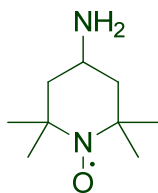


Chiral AZADO

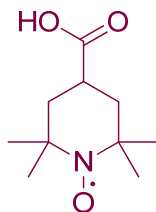




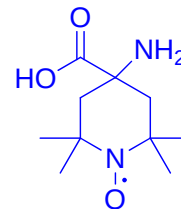
Catalytic Moieties: TEMPO-Derivatives in Peptides



TEMPO-NH₂



TEMPO-COOH



TOAC

(2,2,4,4-tetramethylpiperidine-
1-oxyl-4-amino-4-carboxylic acid)

TEMPO-NH₂ / TEMPO-COOH

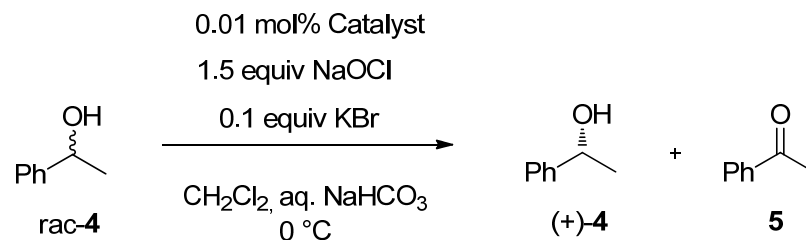
↳ inserting at the C- or N-terminus

TOAC

↳ inserting at the C-, N-terminus or in an internal position

↳ C^α-tetrasubstituted α-amino acid → a possible β-turn inducer

b) Selective Oxidation of Diols



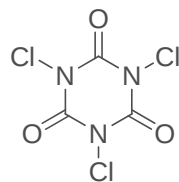
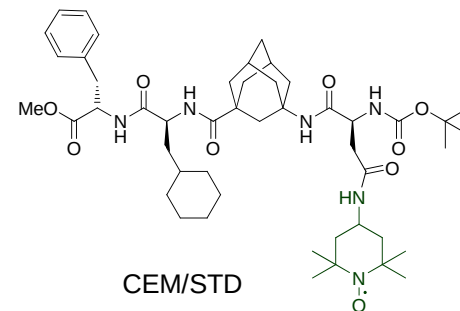
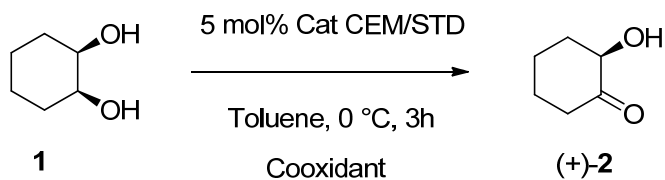
Catalyst	ee 4 /%	C /%	S*
Fmoc-TOAC-L-(α Me)Val-NHtMe	50	84	1.8
Fmoc-TOAC-L-(α Me)Val-NHtBu	67	83	2.3
Boc-TOAC-[L-(α Me)Val] ₃ -NHtBu	74	81	2.7

$$* S = \ln[(1-C)(1-ee)] / \ln[(1-C)(1+ee)]$$

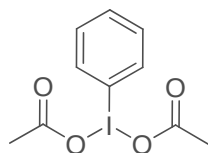
- Best peptide catalysts have large lipophilic blocking groups at either terminus
- TOAC residue is folded in a stable (intramolecular C=O $\cdots$ H-N hydrogen-bonded) β -turn conformation



Desymmetrization of *meso* Compounds



TCCA



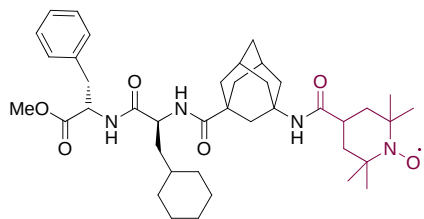
DAIB

Other Cooxidants

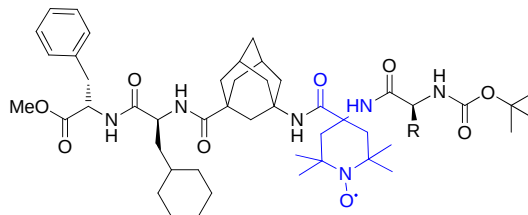
Cooxidant	C /%	ee 2 /%
mCPBA (1.8 equiv)*	66	15
TCCA (0.133 equiv)	88	5
DAIB (1.0 equiv)	59	12

* 5 mol% Bu₄NBr as cocatalyst

c) Synthesized Catalysts

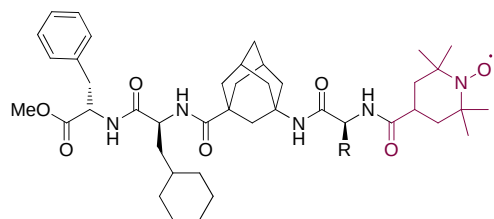


Cat. 1



R = Me, Cat. 5

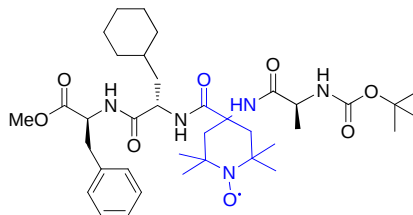
R = *i*Pr, Cat. 2



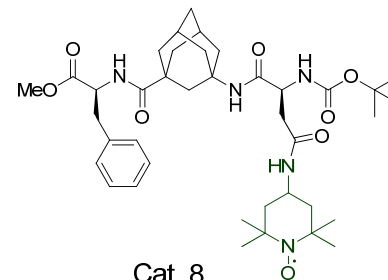
R = Dimethyl, Cat. 3

R = Cy, Cat. 4

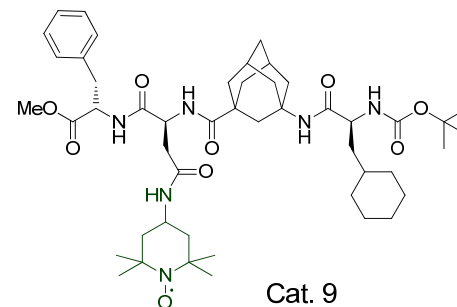
R = Phe, Cat. 7



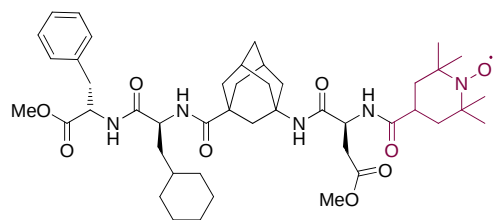
Cat. 6



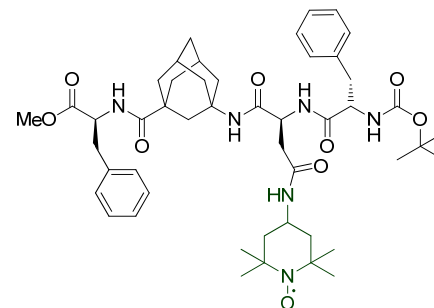
Cat. 8



Cat. 9

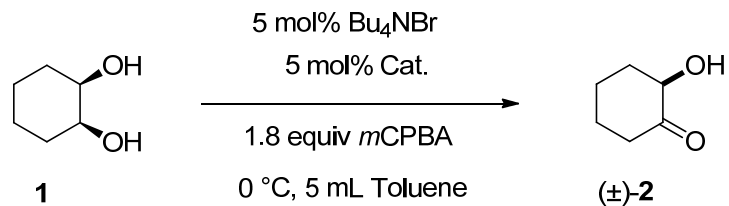


Cat. MR

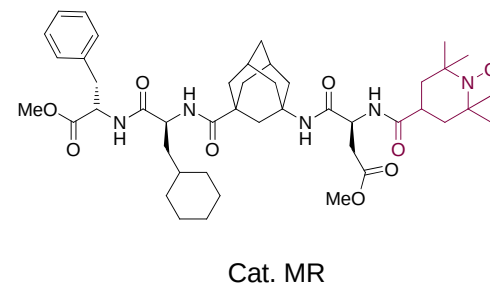
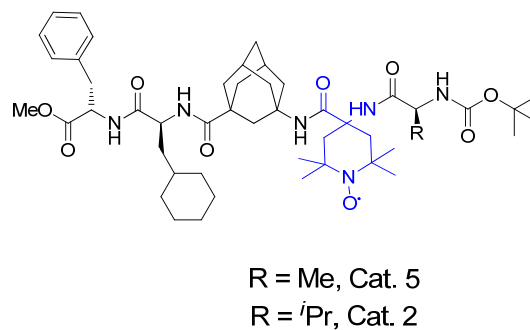
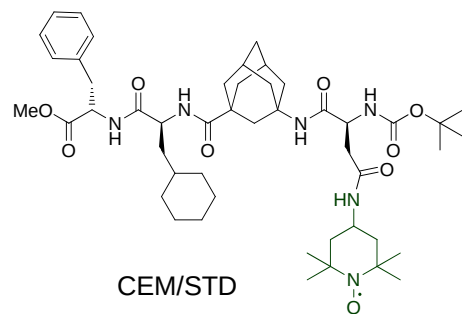


Cat. 10

c) Desymmetrization of *cis*-1,2-Cyclohexandiol

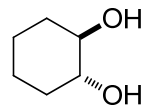
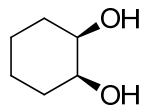


Catalyst	1h		3h	
	C /%	ee 2 /%	C /%	ee 2 /%
CEM/STD	56	15	69	15
Cat. 2,5,6	-	-	-	-
Cat. MR	51	7	80	11

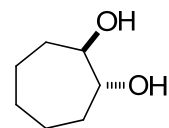
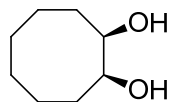
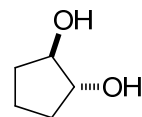
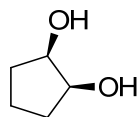




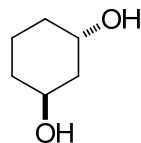
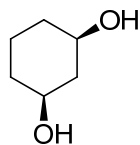
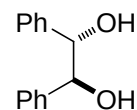
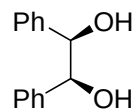
meso compounds



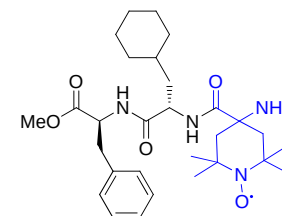
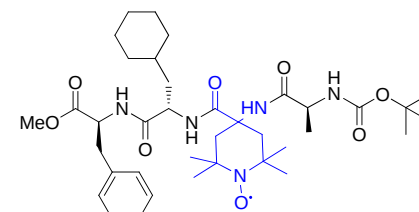
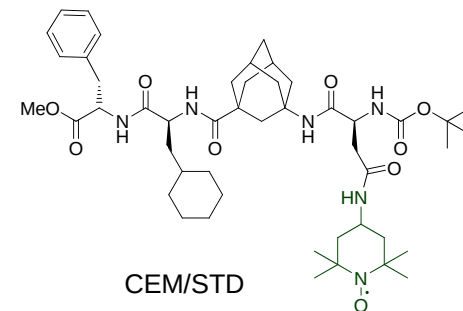
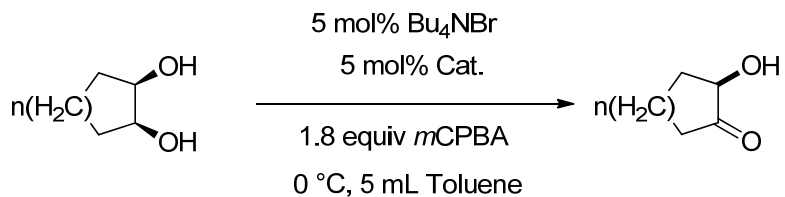
racemic compounds

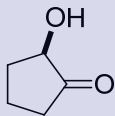
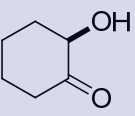
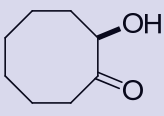


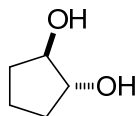
Diols



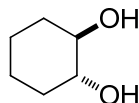
c) cis-1,2-Diols



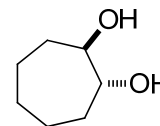
Catalyst	 C (ee) /%	 C (ee) /%	 C (ee) /%
CEM/STD	64 (3)	69 (15)	100 (21)
Cat. 6	53 (2)	-	79 (31)
Cat. 6.1	No Data	No Data	80 (51)



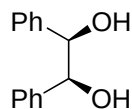
C = 9 - 35%, *ee* (ox.diol) < 5%



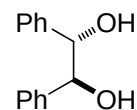
no conversion



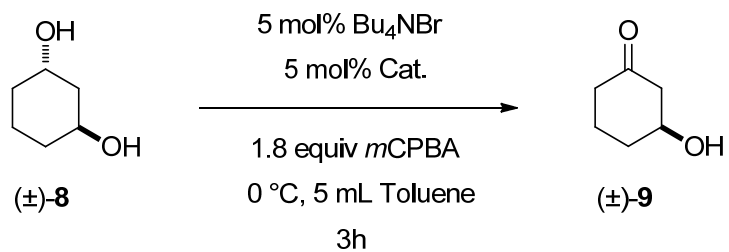
C = 41 - 87%, *ee* (ox.diol) < 9%



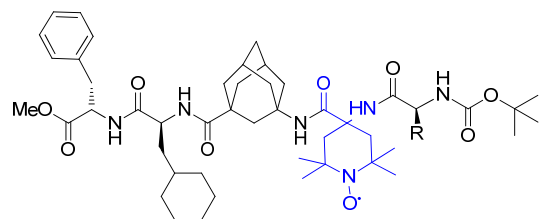
C = 74 - 87%, *ee* (ox.diol) < 4%



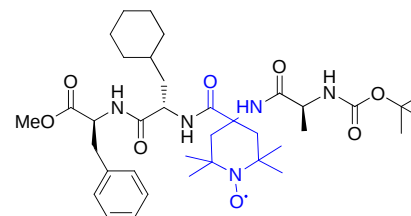
C = 49 - 68%, *ee* (ox.diol) < 5%



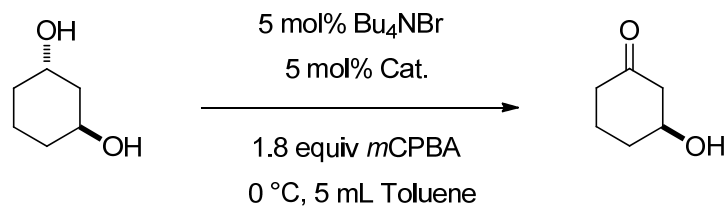
Catalyst	C /%	ee 8 /%	ee 9 /%
Cat. 5	29	8	33
Cat. 2	29	10	29
Cat. 6	32	1	4



R = Me, Cat. 5
R = *i*Pr, Cat. 2

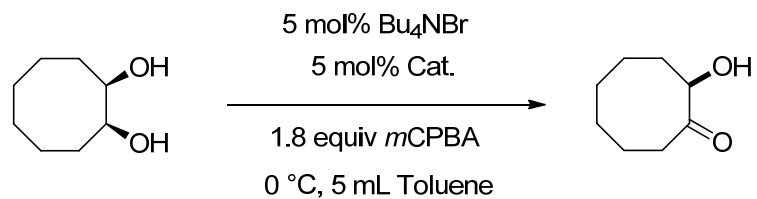
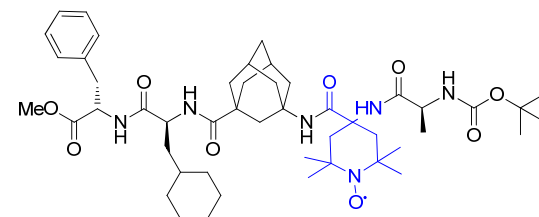


Cat. 6



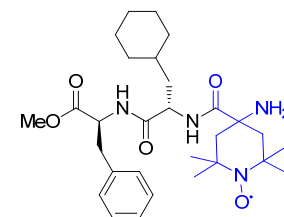
$C = 29\%$

$ee \text{ (ox.diol)} = 33\%$

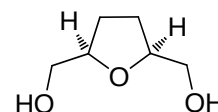
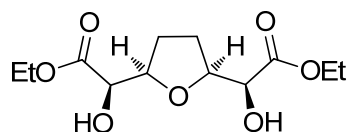
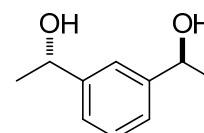
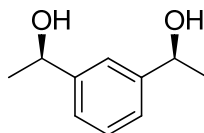


$C = 80\%$

$ee \text{ (ox.diol)} = 51\%$



Other Substrates



Thank you for your attention!
