

Old Meets New – Further Applications of Organocatalysts

PRS Group Seminar

20th February 2015

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Epoxidation

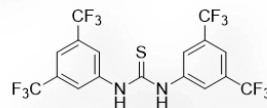
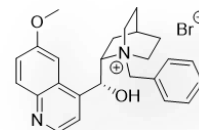
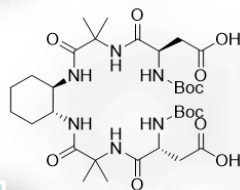
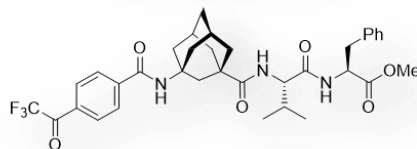
Lactam opening

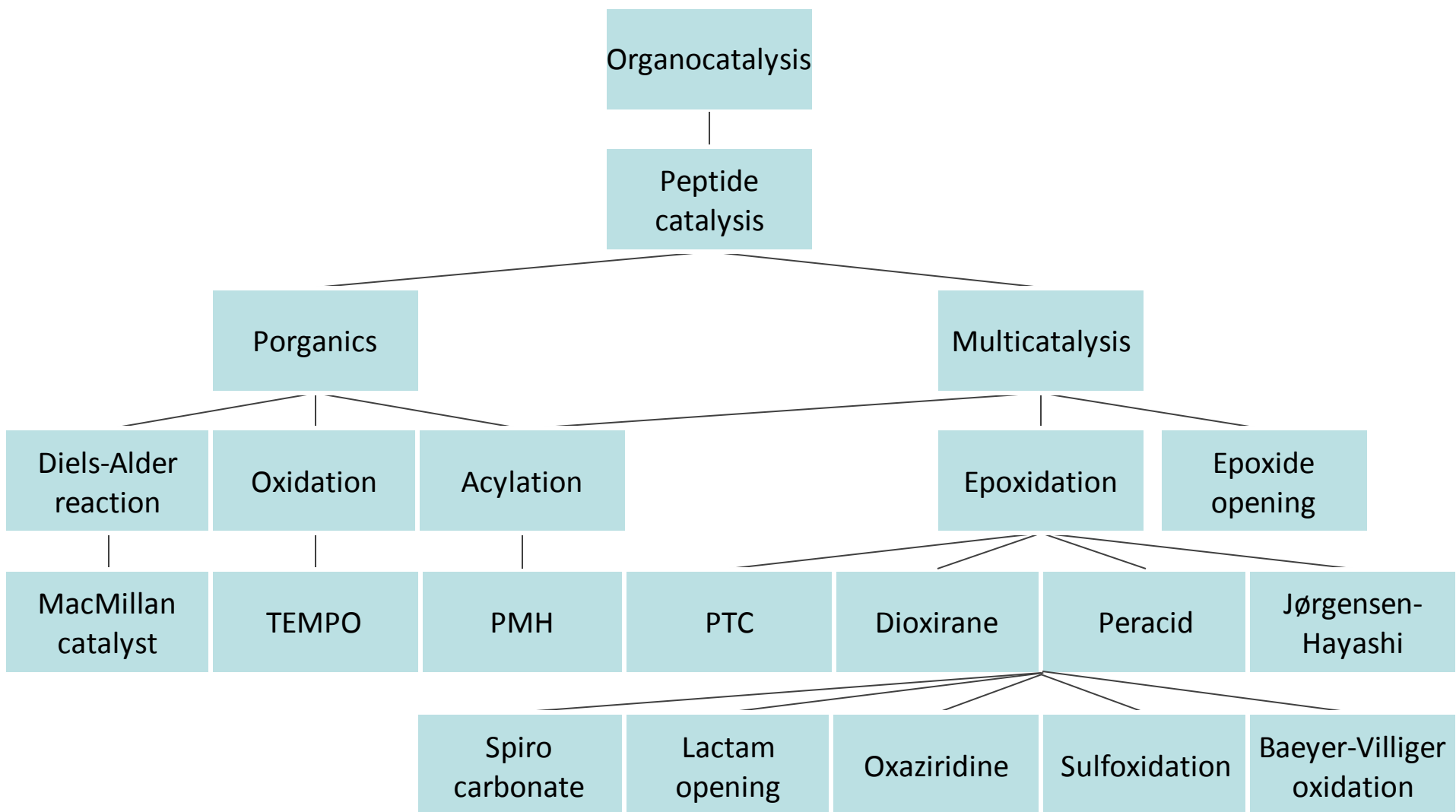
Sulfoxidation

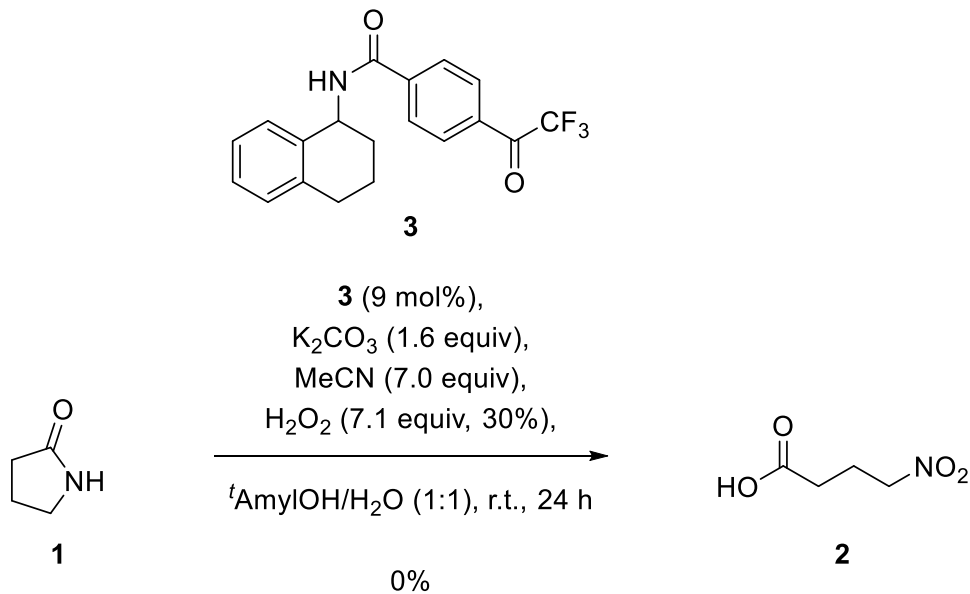
Spiro carbonate

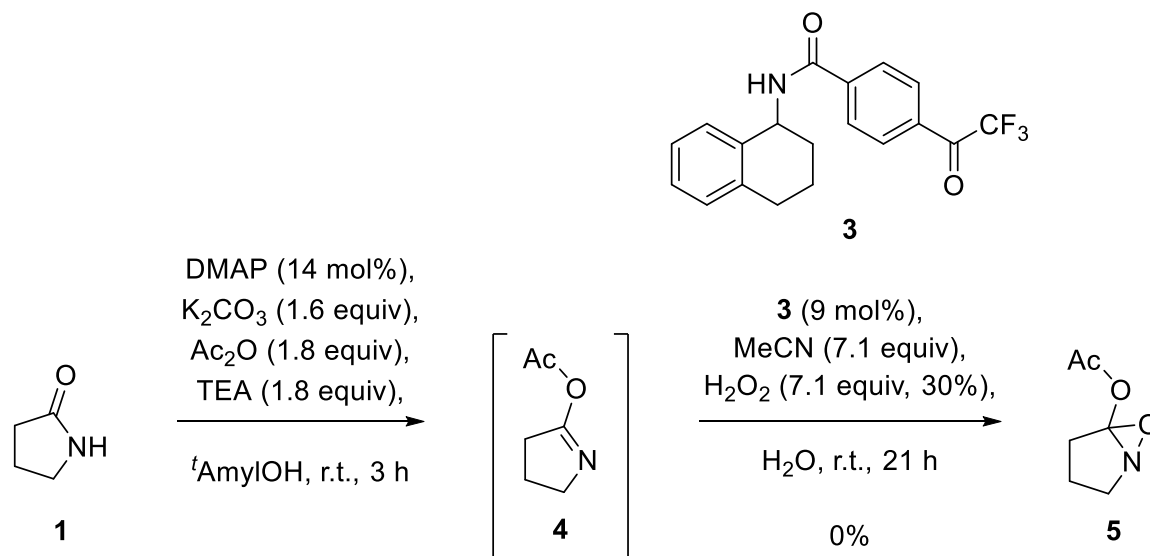
Baeyer-Villiger oxidation

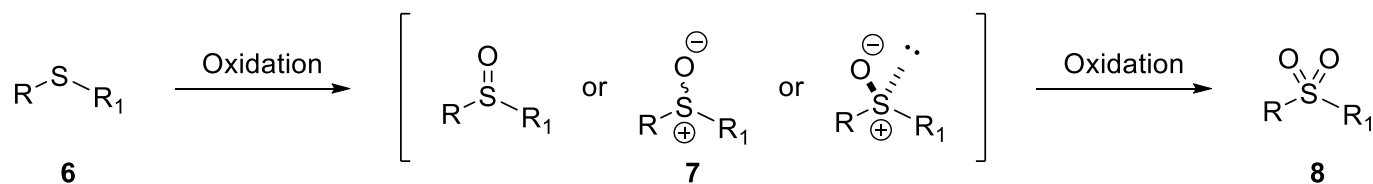
Oxaziridine



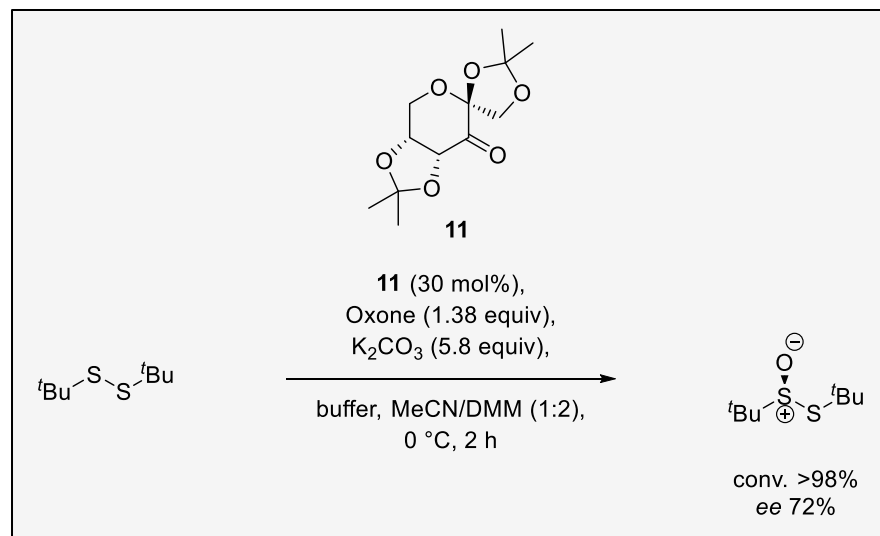
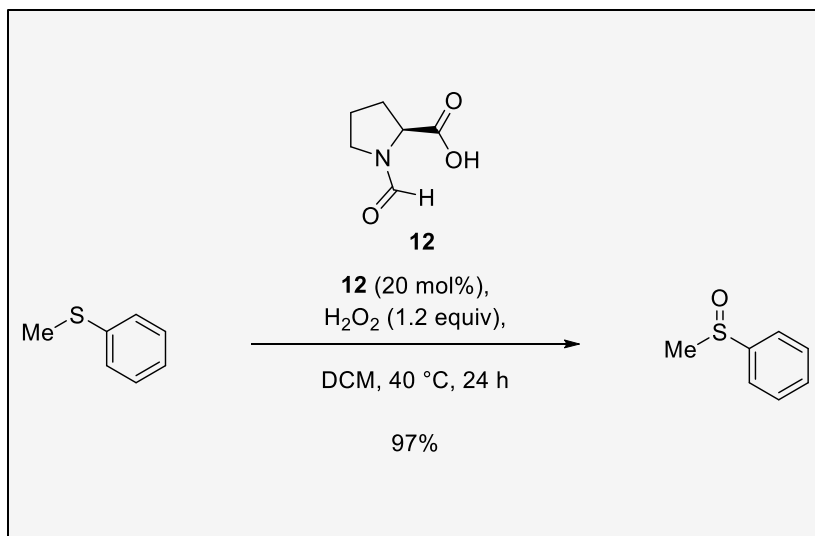
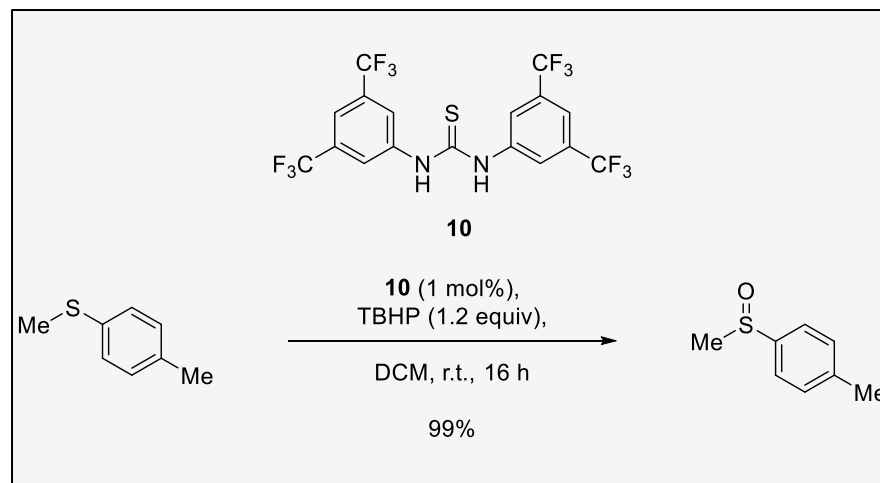
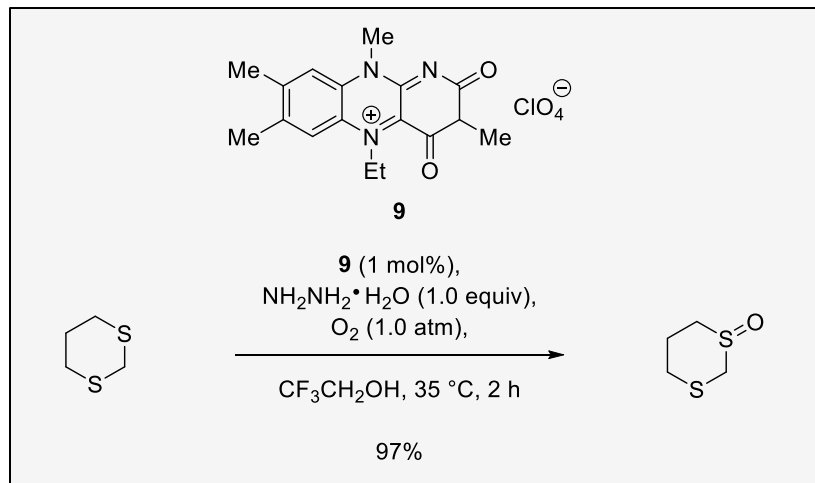


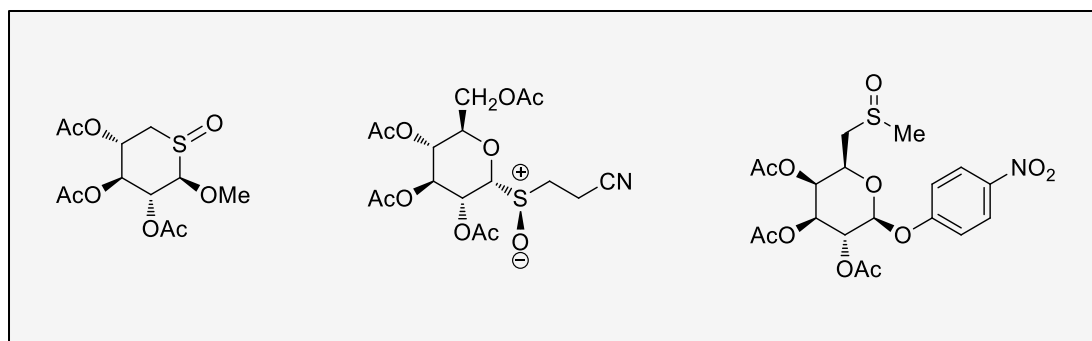
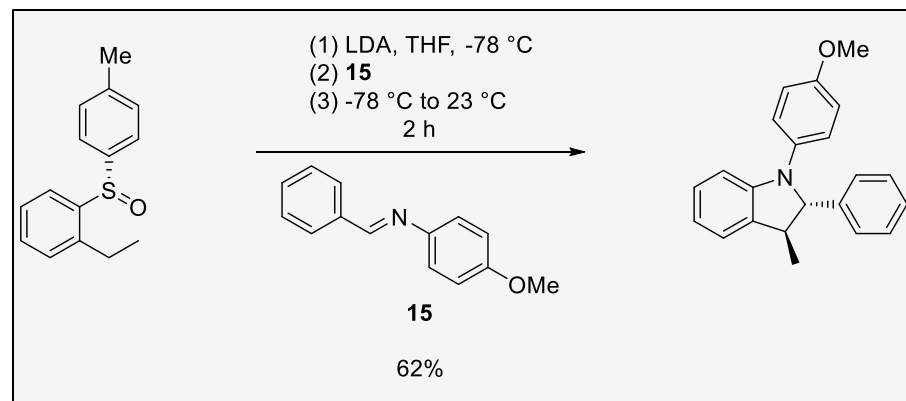
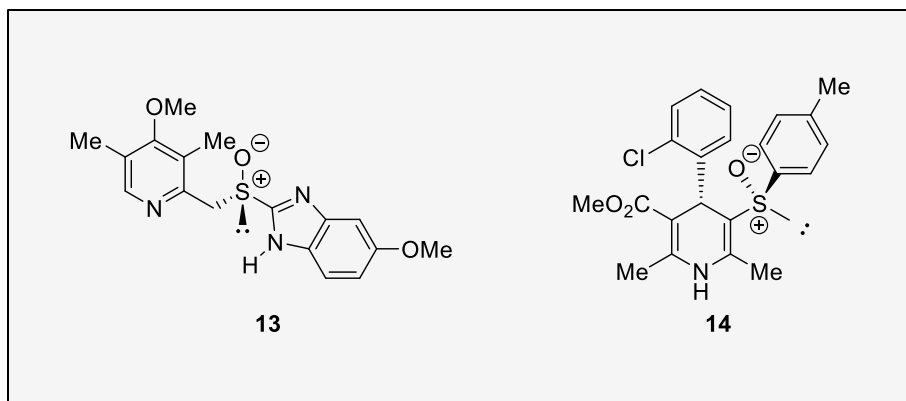
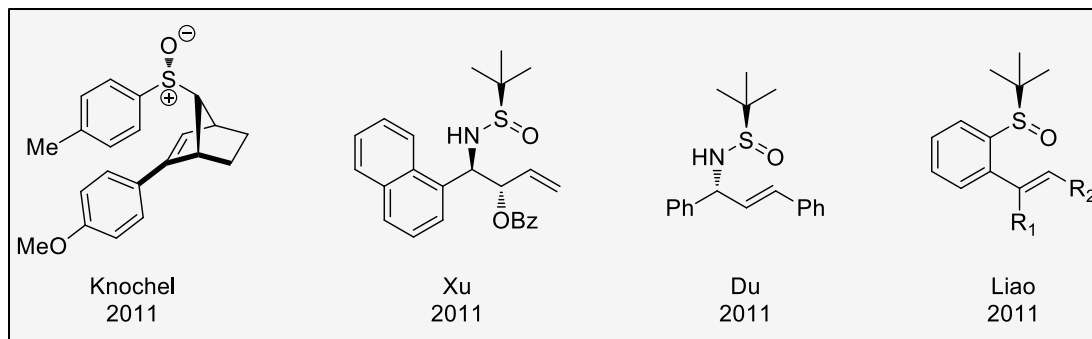




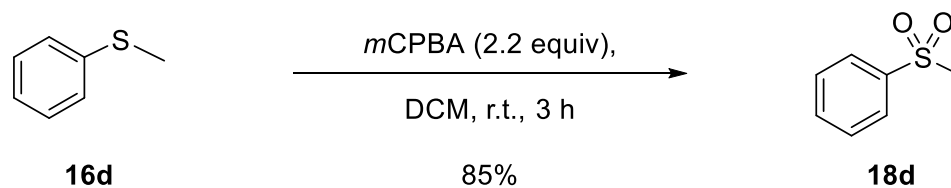
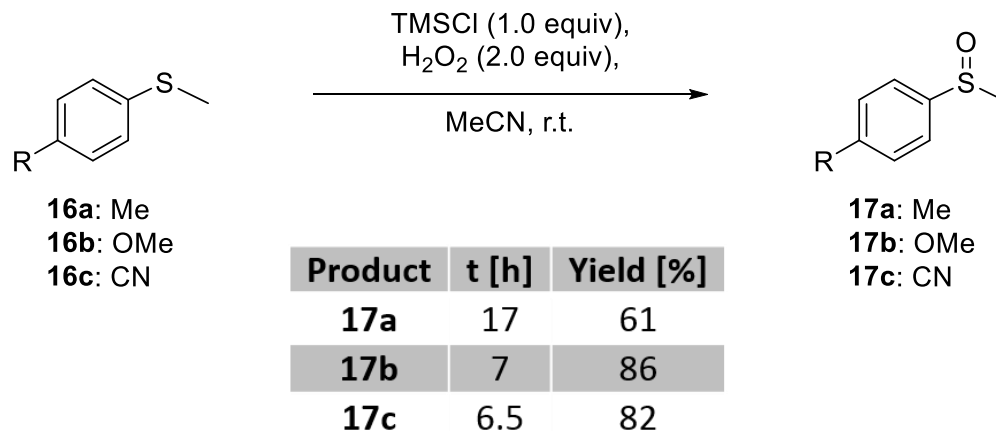


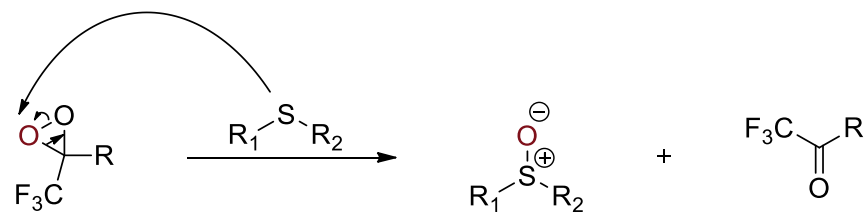
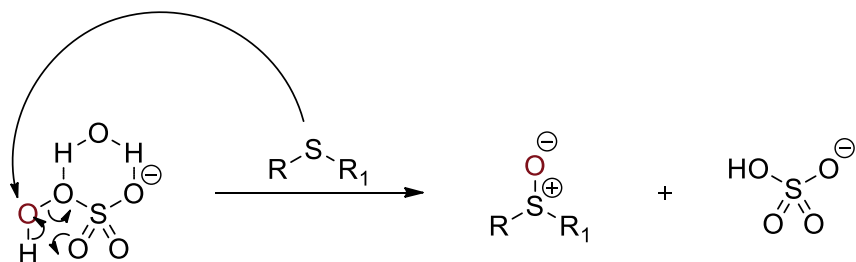
R, R₁ = aliphatic, aromatic

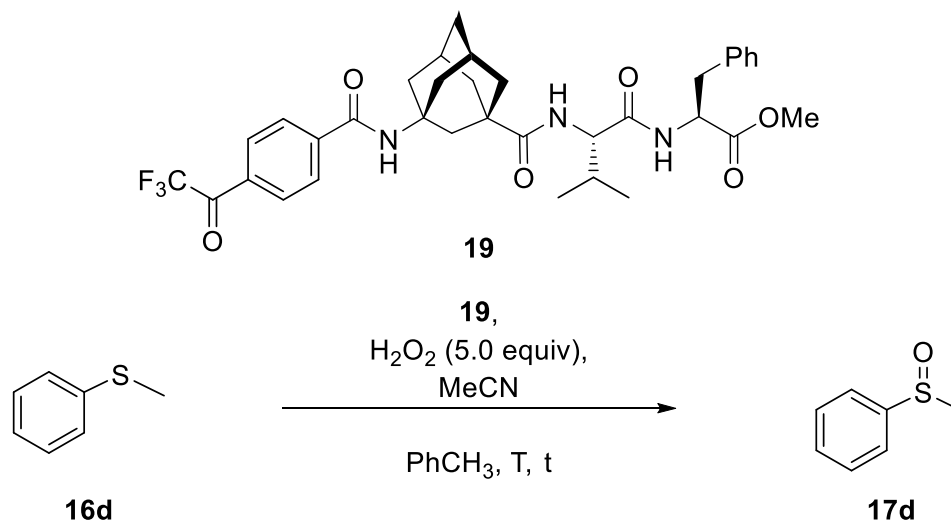




(a) M. C. Aversa, A. Barattucci, P. Bonaccorsi, *Tetrahedron* **2008**, 64, 7659-7683; (b) R. L. Whistler, T. V. Es, R. M. Rowell, *J. Org. Chem.* **1965**, 30, 2719-2721; (c) V. Aucagne, M. C. Aversa, A. Barattucci, P. Bonaccorsi, P. Giannetto, P. Rollin, A. Tatibouët, *J. Org. Chem.* **2002**, 67, 6925-6930; (d) U. Grabowska, D. A. MacManus, K. Biggadike, M. I. Bird, S. Davies, T. Gallagher, L. D. Hall, E. N. Vulfson, *Carbohydrate Research* **1997**, 305, 351-361.



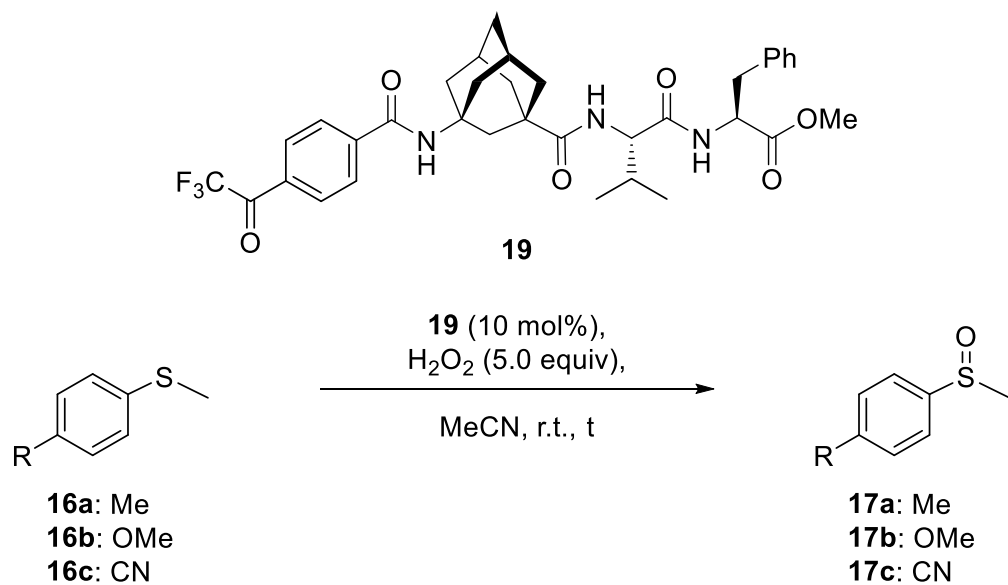




19 [mol%]	MeCN [mL]	Toluene [mL]	T [°C]	t [h]	Conv. to 17d^(a) [%]	Conv. to 18d^(a) [%]
7.5	1.60	-	r.t.	24	89	Traces
10	1.60	-	r.t.	24	93	1
10	3.20	-	r.t.	49	98	Traces
10	0.800	-	r.t.	24	95	5
10	1.60	-	0	46	32	1
10	0.800	0.800	r.t.	24	96	2
10	0.100 ^(b)	1.50	r.t.	48	85	15

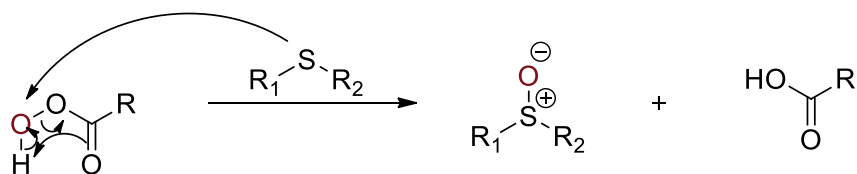
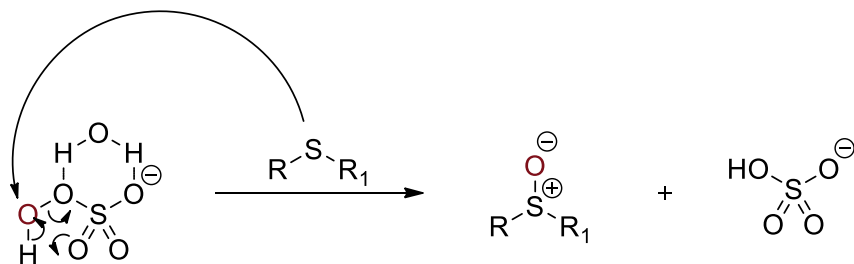
^(a): Conversion was determined using chiral GC without an internal standard;

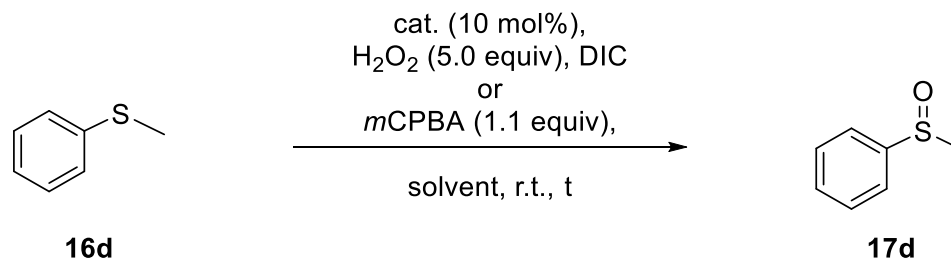
^(b): Corresponds 5.0 equiv of MeCN.



Sulfide	t	Conv. to 17 ^(a)	Conv. to 18 ^(a)
	[h]	[%]	[%]
16a	24	>99	Traces
16b	24	quant.	Traces
16c	48	80	Traces

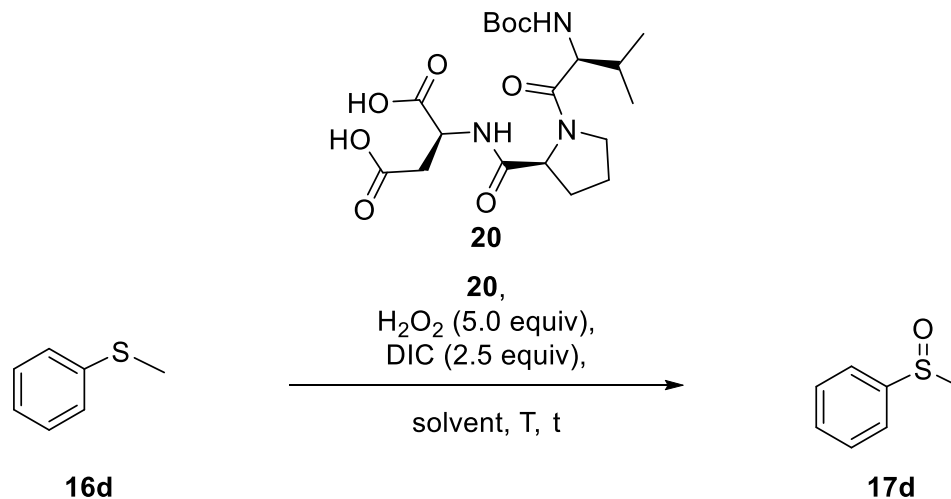
^(a): Conversion was determined using chiral GC without an internal standard.





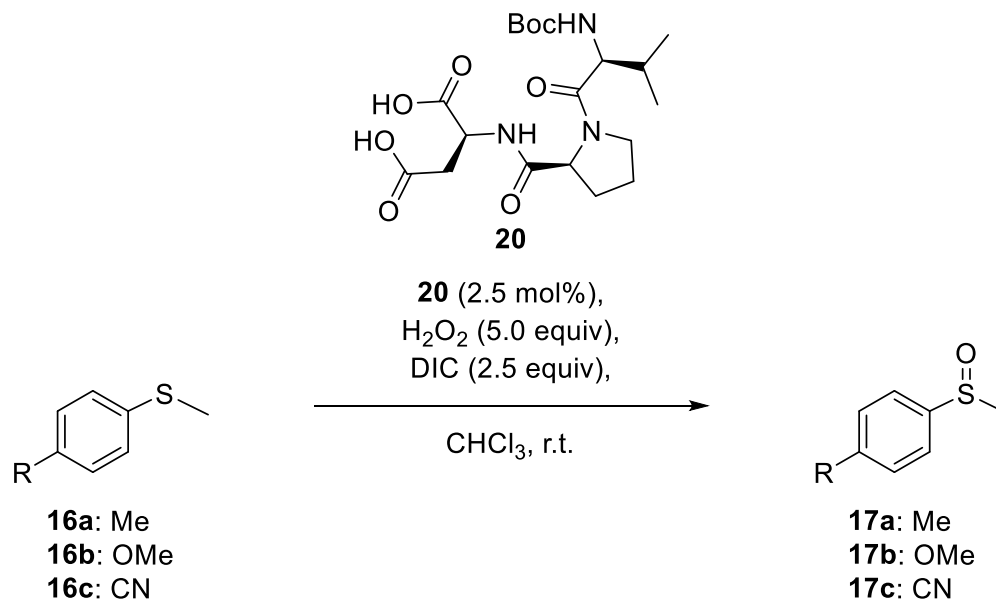
Cat.	Oxidizer	DIC	Solvent ^(a)	t [h]	Conv. to 17d ^(b)	Conv. to 18d ^(b)
		[equiv]			[%]	[%]
-	<i>m</i> CPBA	-	CH ₂ Cl ₂	1	94	6
benzoic acid	H ₂ O ₂	1.1	CH ₂ Cl ₂	48	30	0
<i>m</i> CBA	H ₂ O ₂	1.1	CH ₂ Cl ₂	48	25	0
phthalic acid	H ₂ O ₂	1.1	CH ₂ Cl ₂	48	90	0
phthalic acid	H ₂ O ₂	1.1	CHCl ₃	24	98	2
phthalic acid	H ₂ O ₂	2.5	CHCl ₃	4	98	Traces
phthalic acid	H ₂ O ₂	5.0	CHCl ₃	3	95	3
-	H ₂ O ₂	1.1	CH ₂ Cl ₂	48	6	0

^(a): Reaction performed in 1.60 mL solvent; ^(b): Conversion was determined using chiral GC without an internal standard.



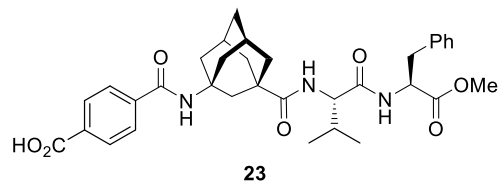
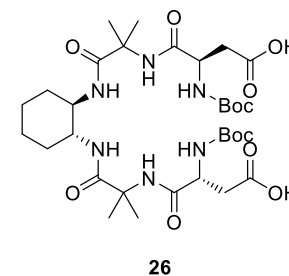
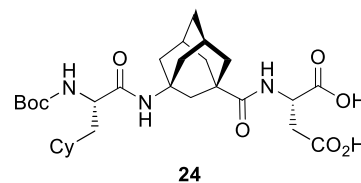
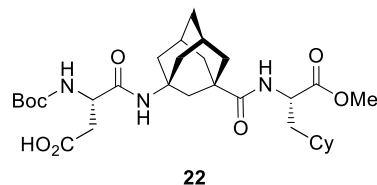
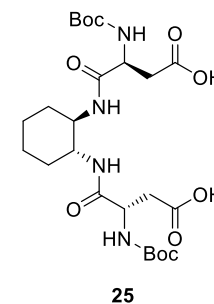
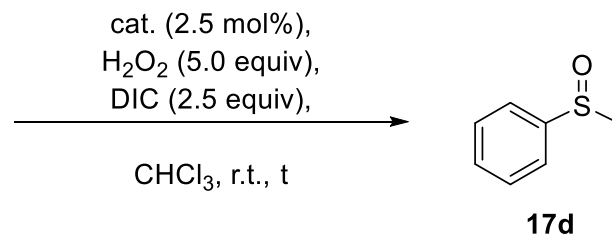
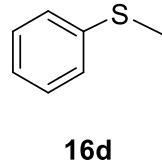
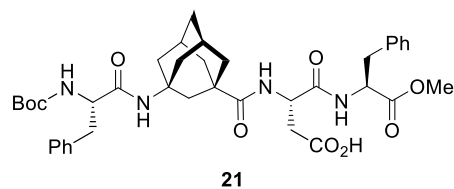
20 [mol%]	Solvent [mL]	t [h]	T [°C]	Conv. to 17d ^(a) [%]	Conv. to 18d ^(a) [%]
10	CHCl ₃ (1.6)	3	r.t.	96	4
10	CHCl ₃ (1.6)	4	0	96	2
10	PhCH ₃ (1.6)	7	r.t.	76	15
10	PhCH ₃ (1.6)	25	0	68	13
5	CHCl ₃ (1.6)	1	r.t.	97	2
2.5	CHCl ₃ (1.6)	2	r.t.	97	1
1	CHCl ₃ (1.6)	5	r.t.	89	0
-	CHCl ₃ (1.6)	5	r.t.	2	0
2.5	CHCl ₃ (0.8)	2	r.t.	95	Traces
2.5	CHCl ₃ (3.2)	8	r.t.	97	2

^(a): Conversion was determined using chiral GC without an internal standard.



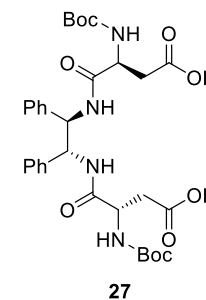
Sulfide	t	Conv. to 17 ^(a)	Conv. to 18 ^(a)
	[h]	[%]	[%]
16a	1	quant.	Traces
16b	2	quant.	Traces
16c	24	67	Traces

^(a): Conversion was determined using chiral GC without an internal standard.



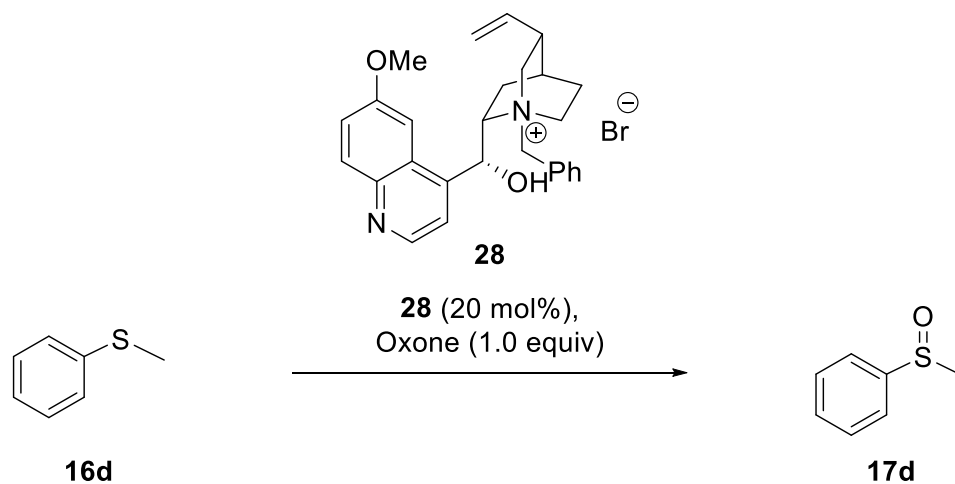
Cat.	t [h]	Conv. to 17d ^(a) [%]	Conv. to 18d ^(a) [%]
21	24	31	0
22	24	16	Traces
23	24	20	0
24	7	94	Traces
25	24	91	2
26	7	89	Traces
27	24	97	3

^(a): Conversion was determined using chiral GC without an internal standard.

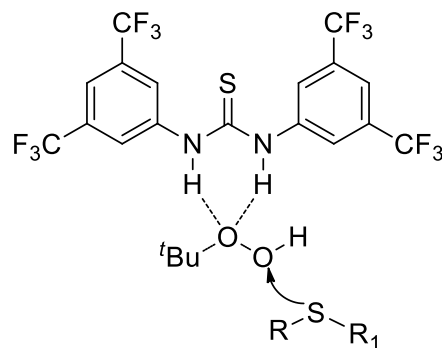


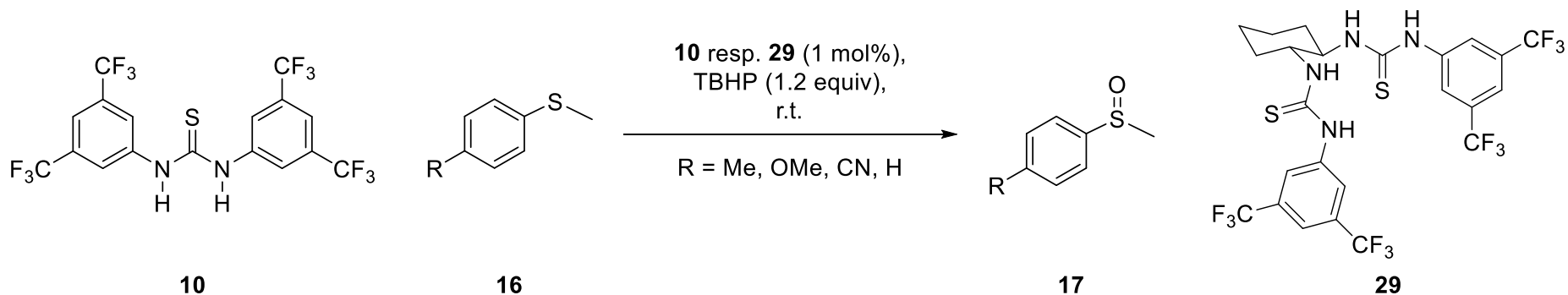


- ## Sulfoxidation



- Reaction parameters: solvent and addition of water
- Product is not formed enantiomerically enriched
- Uncatalyzed reaction





R	Cat.	Solvent	t [h]	Conv. to 17 ^(a) [%]	Conv. to 18 ^(a) [%]
Me	10	DCM	53	93	7 ^(b)
Me	29	DCM	54	91	9 ^(b)
OMe	29	DCM	52	97	3 ^(b)
CN	29	DCM	51	91	6 ^(b)
H	29	DCM	51	99	1 ^(b)
Me	29	PhCH ₃	48	79	2 ^(b)
Me	29	CHCl ₃	26	73	27 ^(b)
Me	-	DCM	50	38	Traces ^(b)

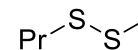
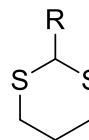
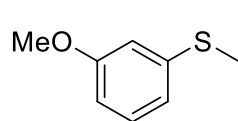
^(a): Conversion was determined using chiral GC without an internal standard;

^(b): Identification of the sulfones **18** via GC-MS.

- Oxidative lactam opening did not work
- Synthesis of oxaziridines did not work
- Three feasible optimized protocols for monooxidation of sulfides

	Dioxirane-based sulfoxidation	Peracid-based sulfoxidation	Thiourea-based sulfoxidation
Catalyst loading	10 mol%	2.5 mol%	1 mol%
Solvent	MeCN (1.6 mL)	CHCl ₃ (1.6 mL)	DCM (0.400 mL)
Oxidizer	H ₂ O ₂ (5.0 equiv)	H ₂ O ₂ (5.0 equiv)	TBHP (1.2 equiv)
Temperature	r.t.	r.t.	r.t.
Additive	-	DIC (2.5 equiv)	-

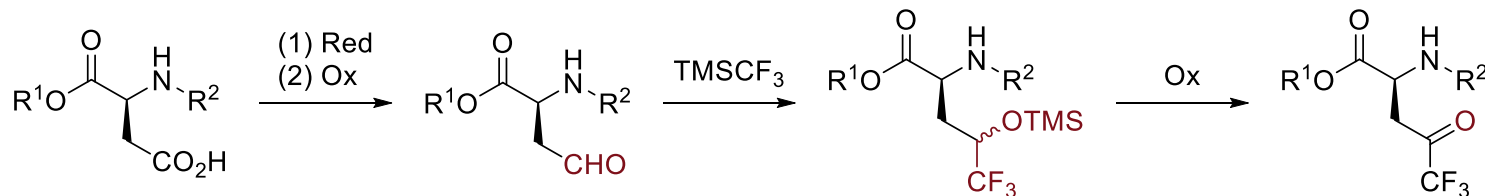
- Further substrates



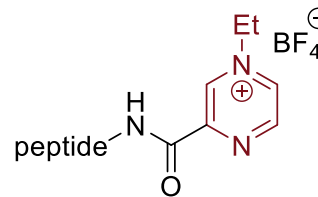
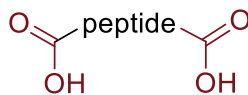
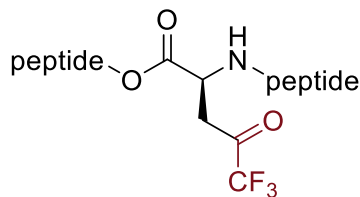
R = Et, ^tBu, allyl

R = H, Me, Ph

- Modification of the catalytic moiety

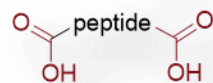
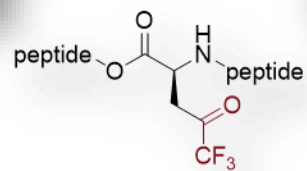


- Further catalysts



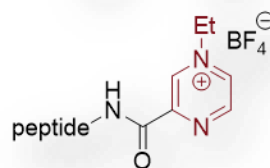
Sulfoxidation

Epoxidation



Spiro
carbonate

Baeyer-Villiger
oxidation



???

My thanks go to

... Prof. Peter Schreiner

... Sascha Combe, Katharina Lippert, and Dominik Niedek

... Prof. Daniel Seidel
