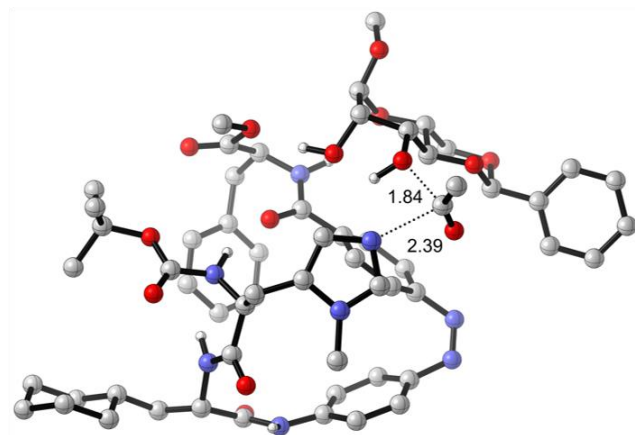
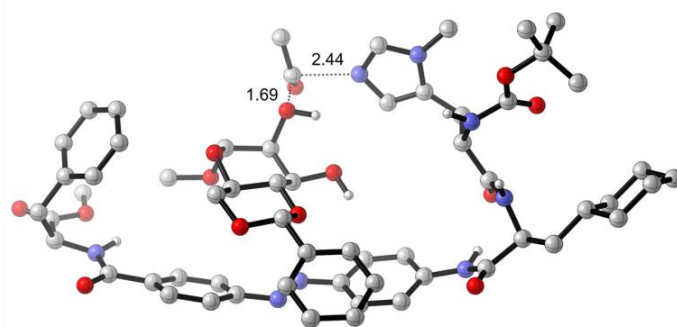


Photoswitchable Azo-Oligopeptides as Organocatalysts

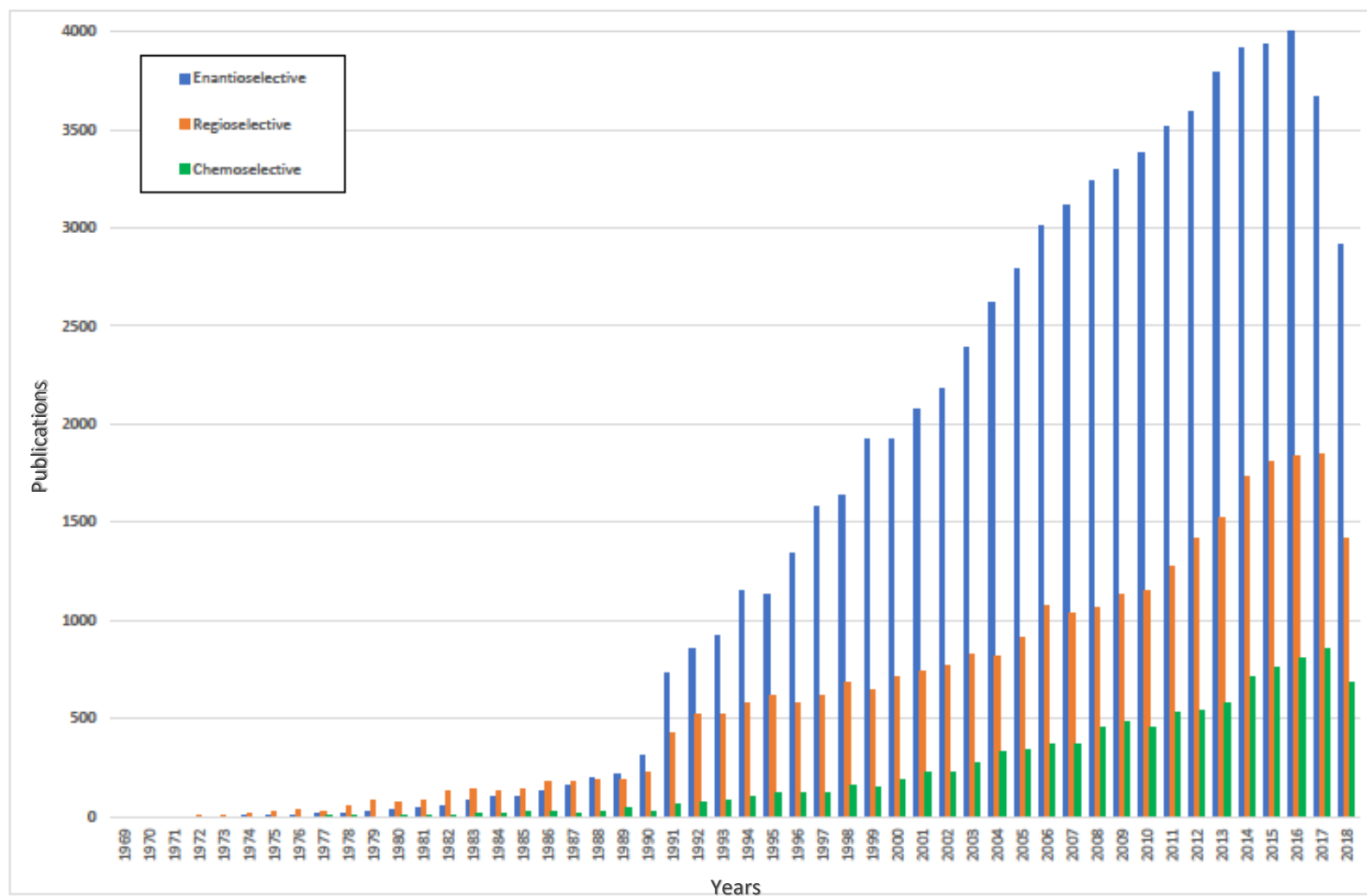
23.11.2018

Christopher Topp, Masterthesis

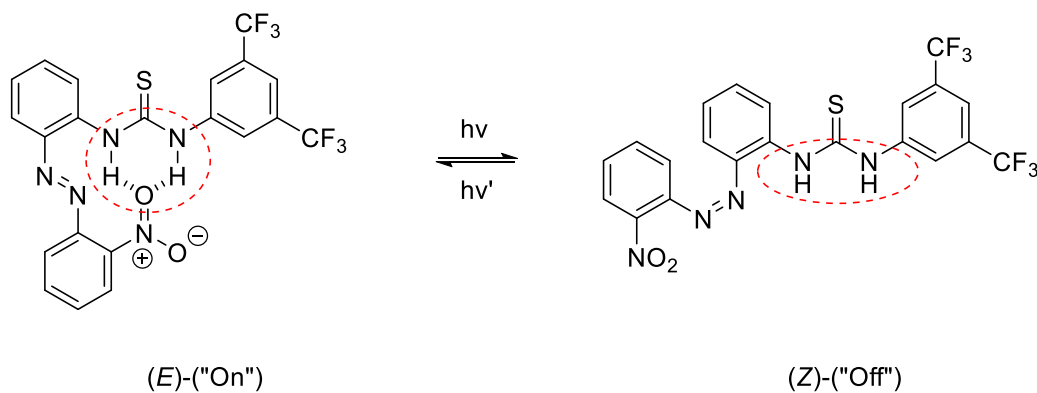
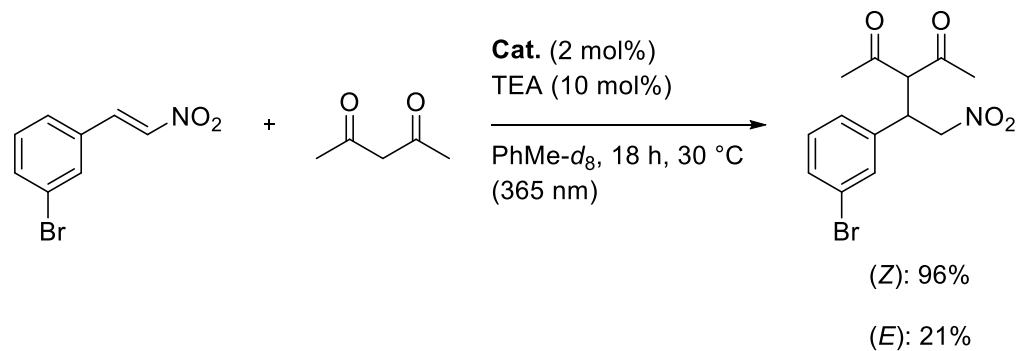
*Institute of Organic Chemistry
Justus-Liebig-University
35392 Giessen, Germany*

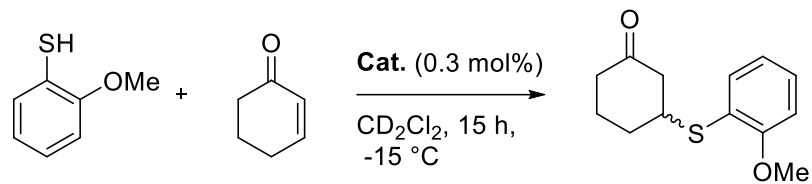


B3LYP-D3(BJ)/6-31G(d)



Number of Publications in the context of „organocatalytic“, since 1945, Web of Science® (25.10.2018, 13²¹).

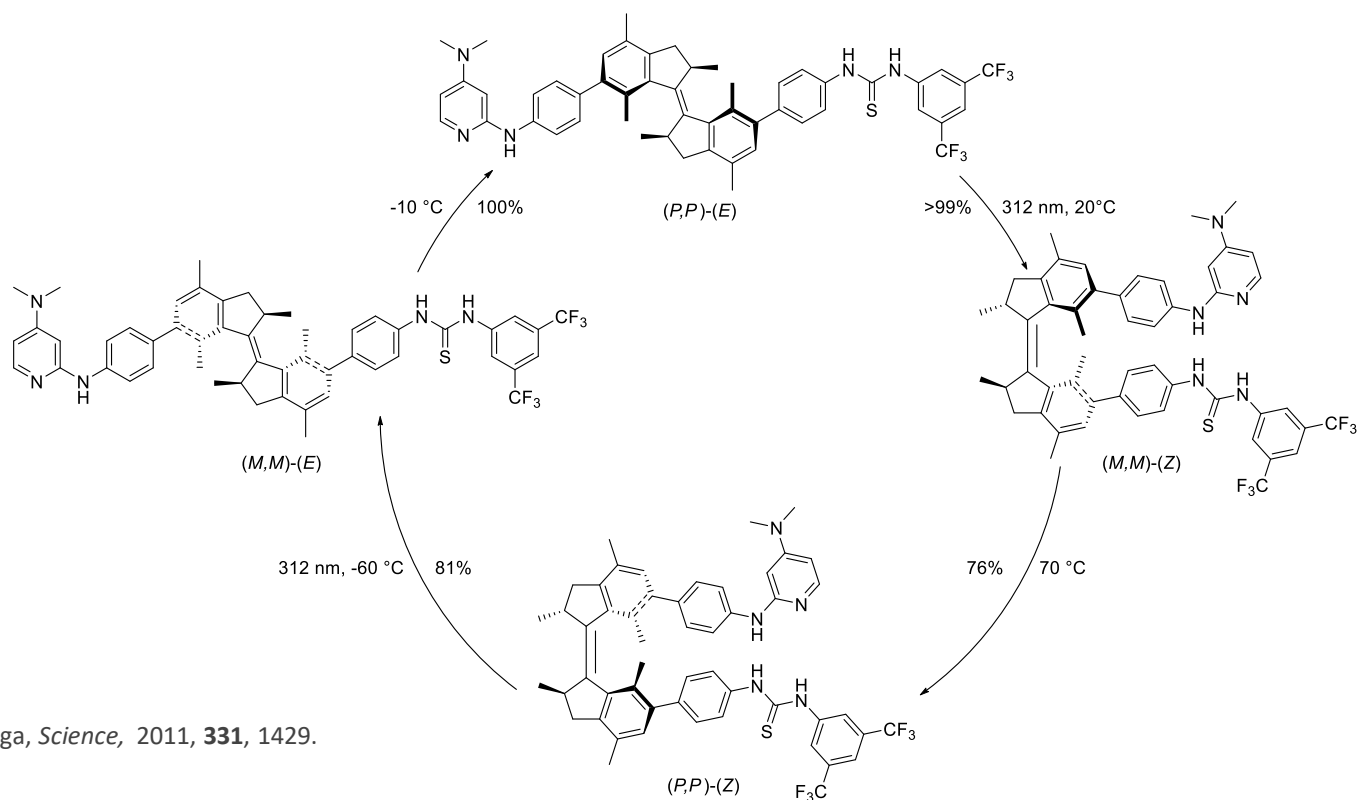
*Photoswitchable catalysis in the past*

*"Photoswitchable" catalysis in the past*

(*M,M*)-(Z): 75 **S** / 25 **R**

(*P,P*)-(Z): 23 **S** / 77 **R**

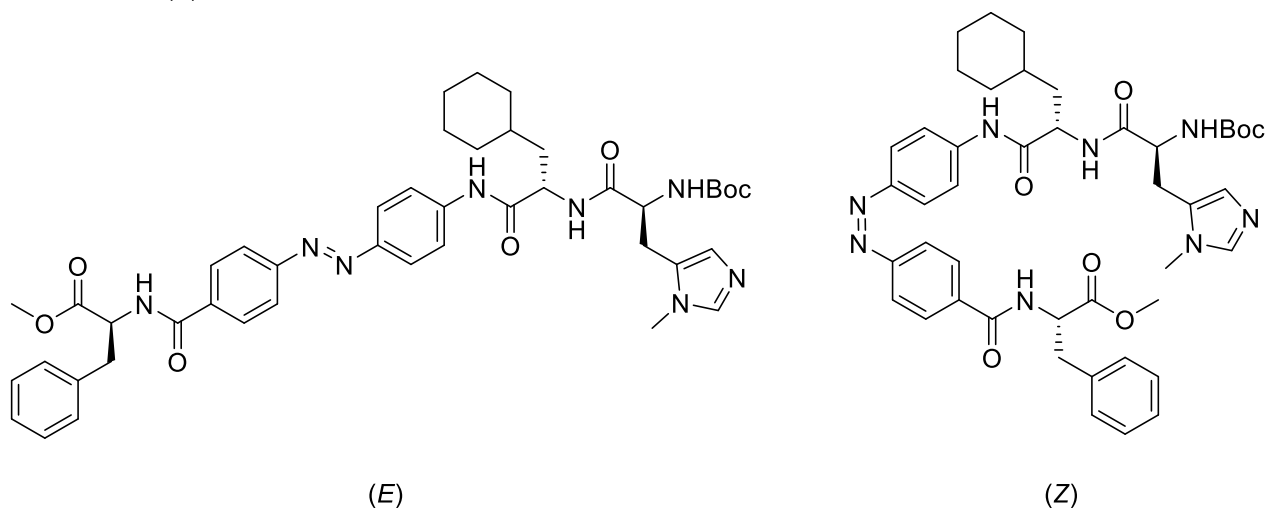
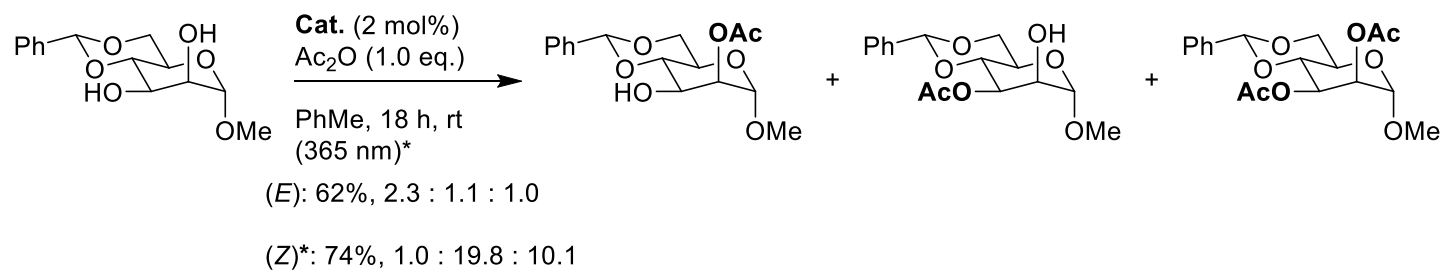
(*P,P*)-(E): 49 **S** / 51 **R**



J. Wang, B. L. Feringa, *Science*, 2011, **331**, 1429.

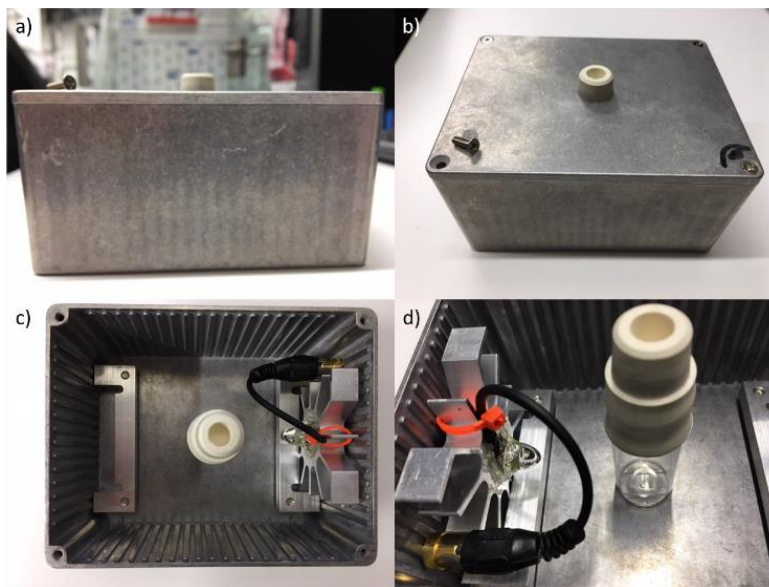


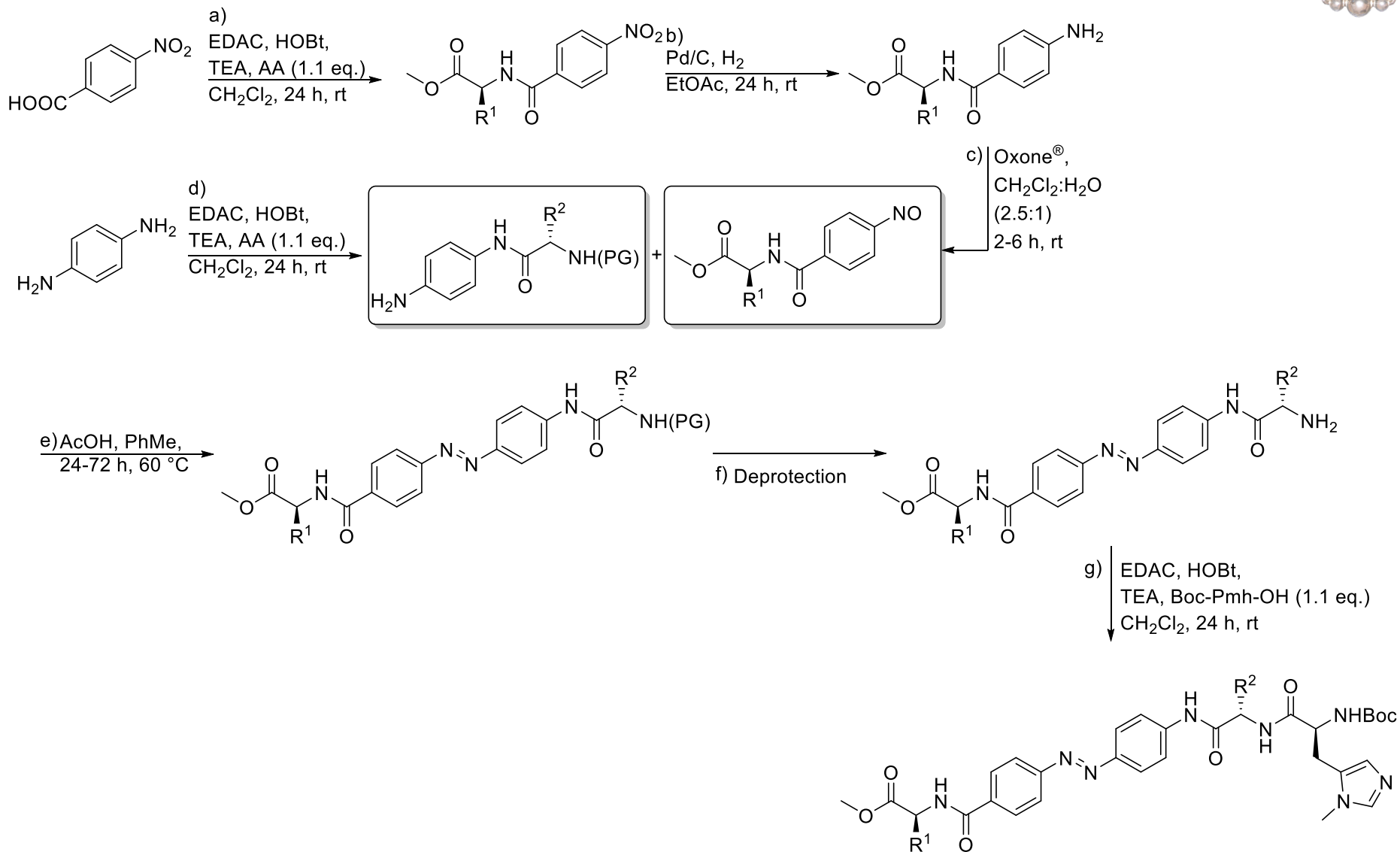
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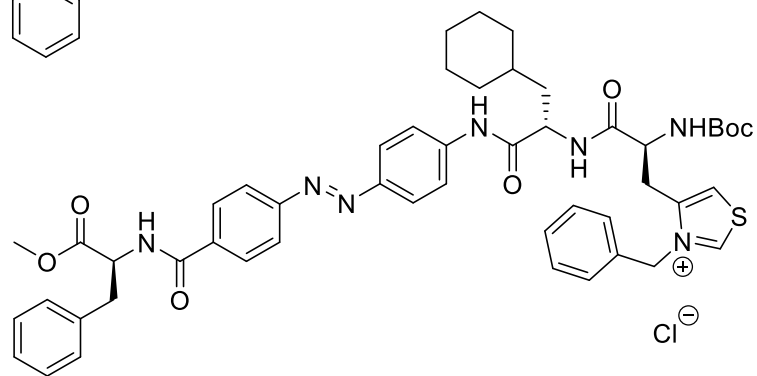
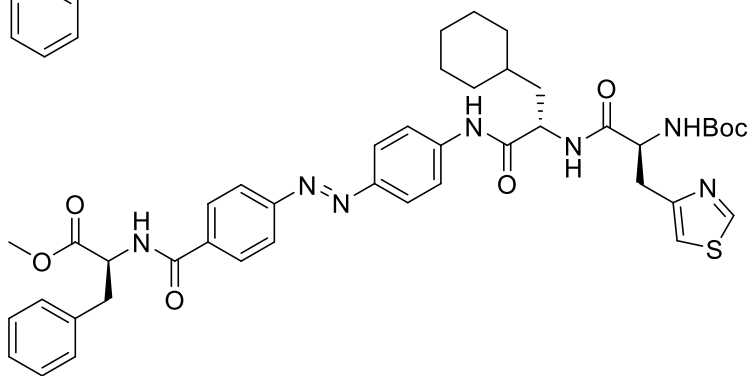
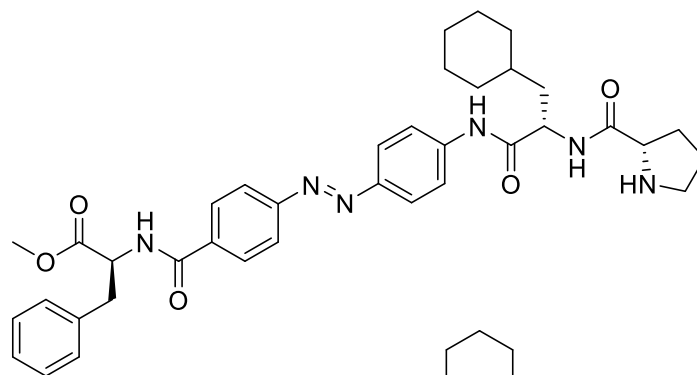
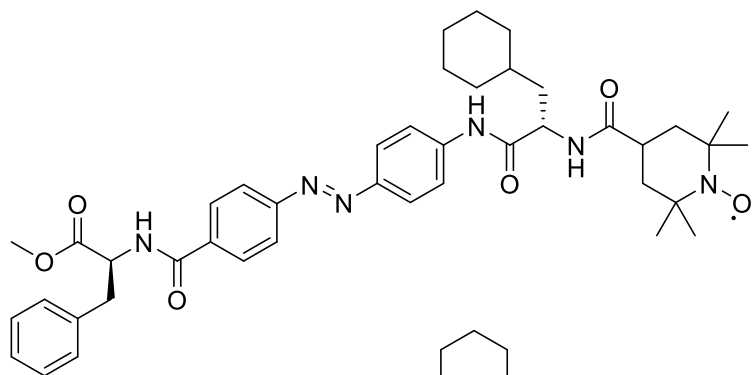
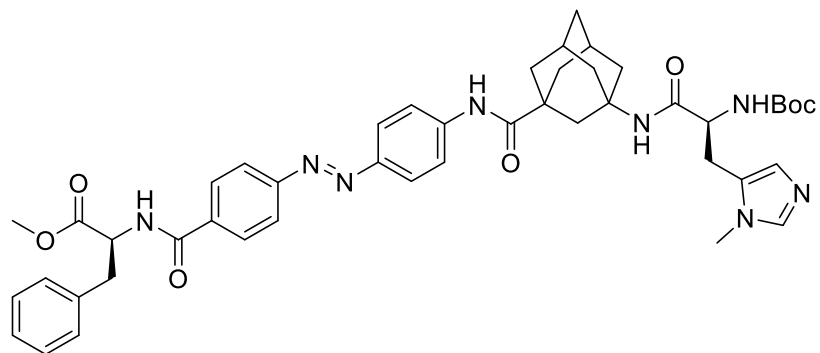
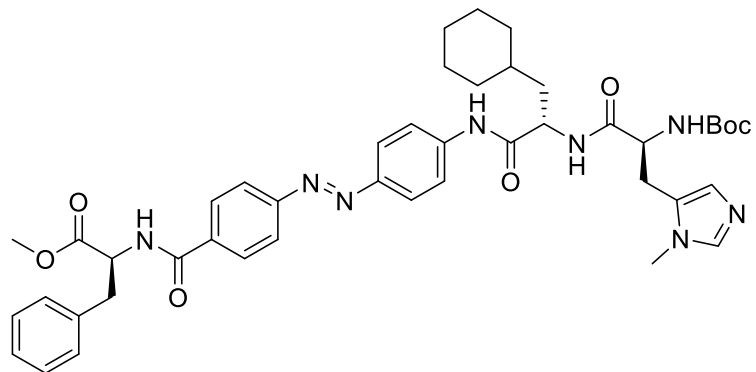


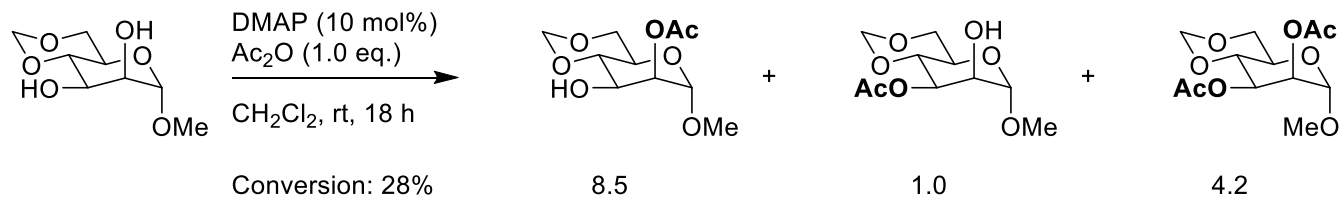
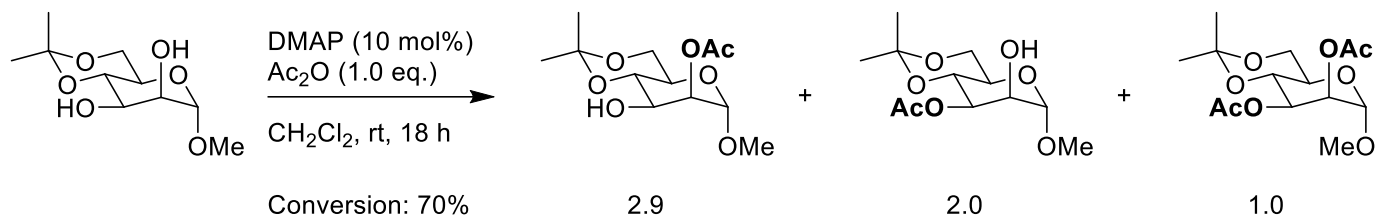
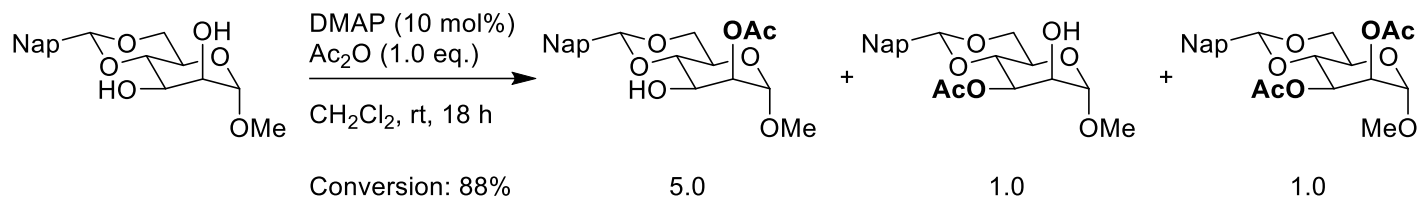


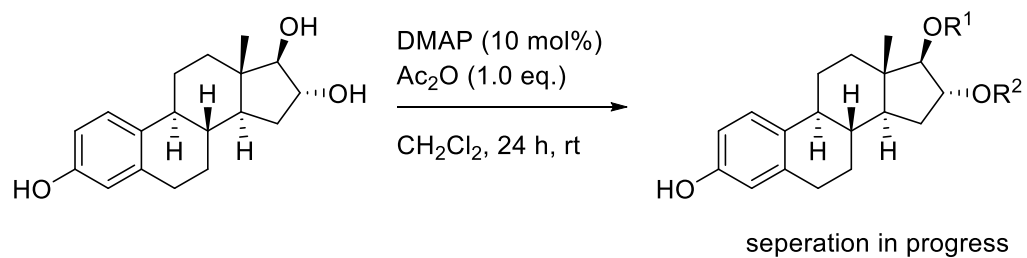
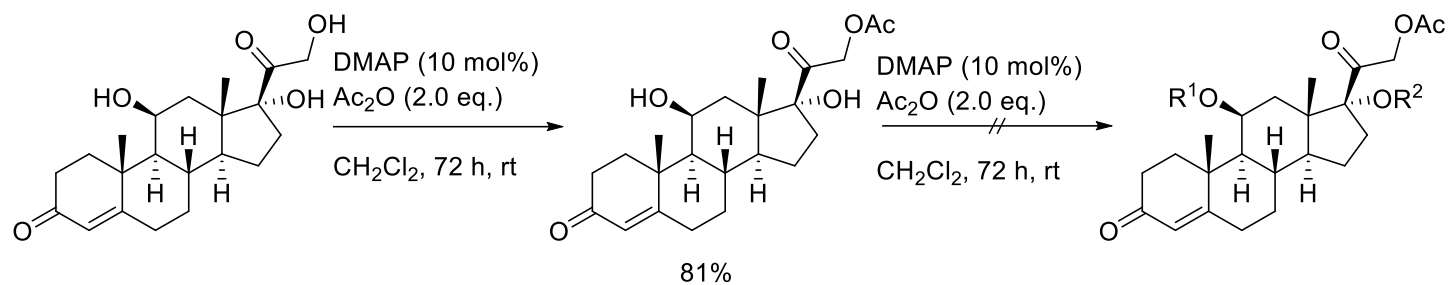
- *Synthesis of new catalysts*
 - *Permutation of amino acids in the peptide-backbone.*
 - *Variation of the catalytic motif.*
- *Synthesis of standard substrates for oxidations and acylations.*
- *Photoswitchable N-terminal proline peptide for selective Aldol reactions.*
- *'Design of Experiments' for a selective silylation of (4,6-O-benzylidene)methyl- α -D-mannopyranoside*

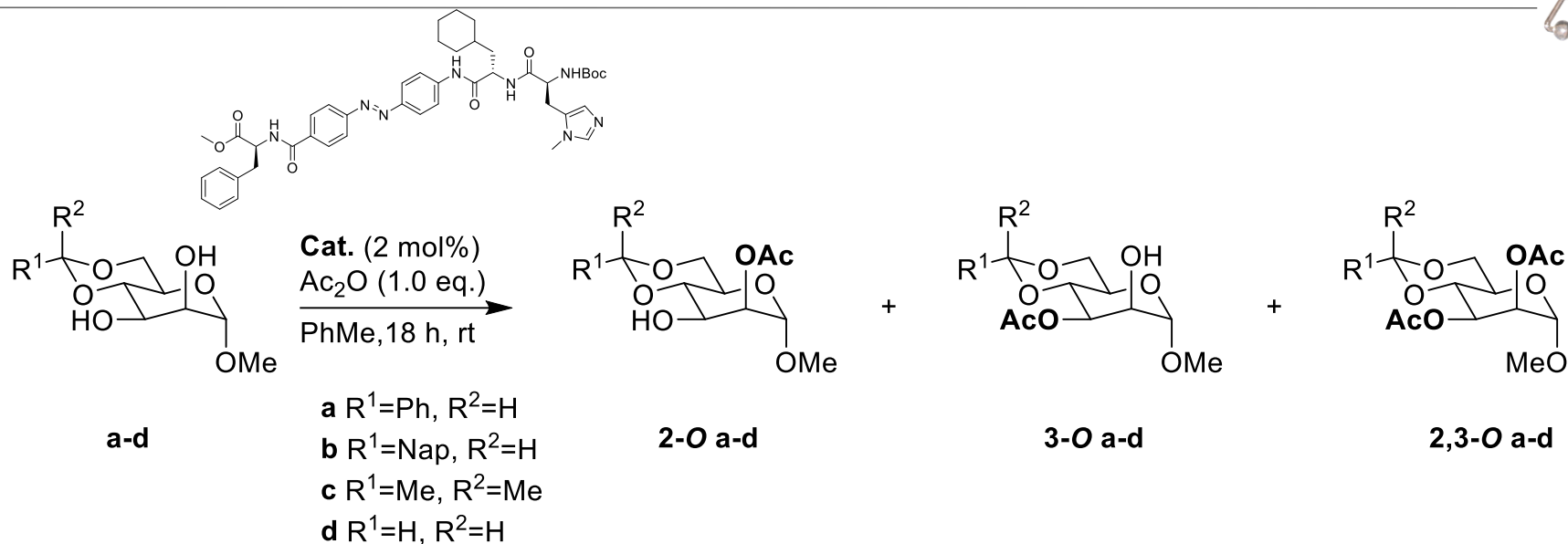








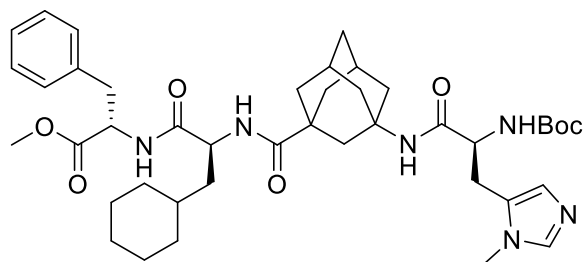
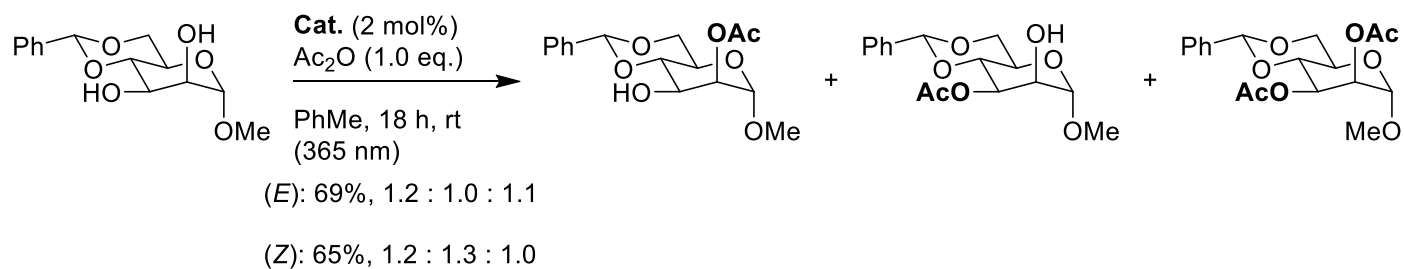
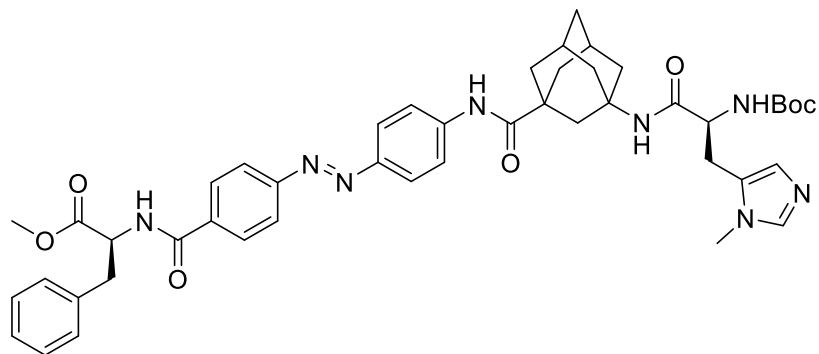


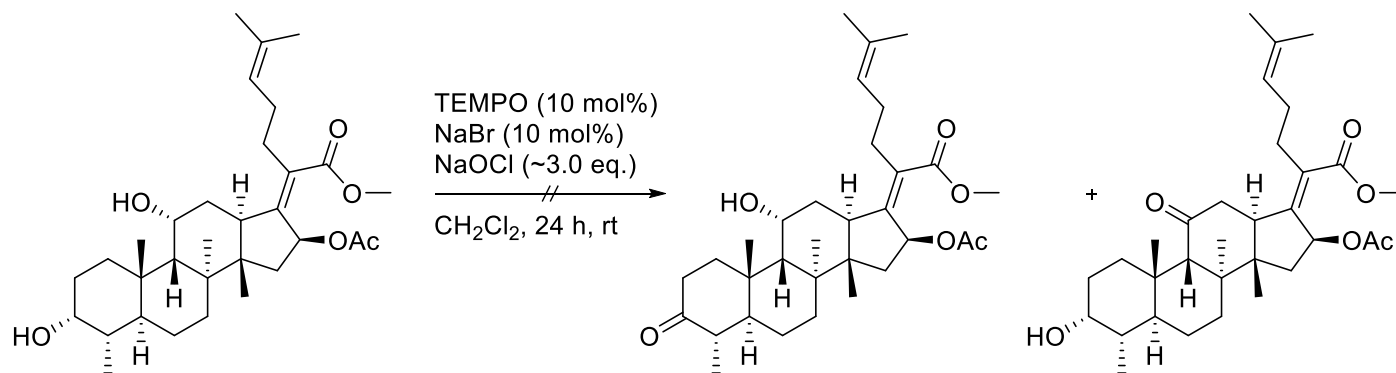
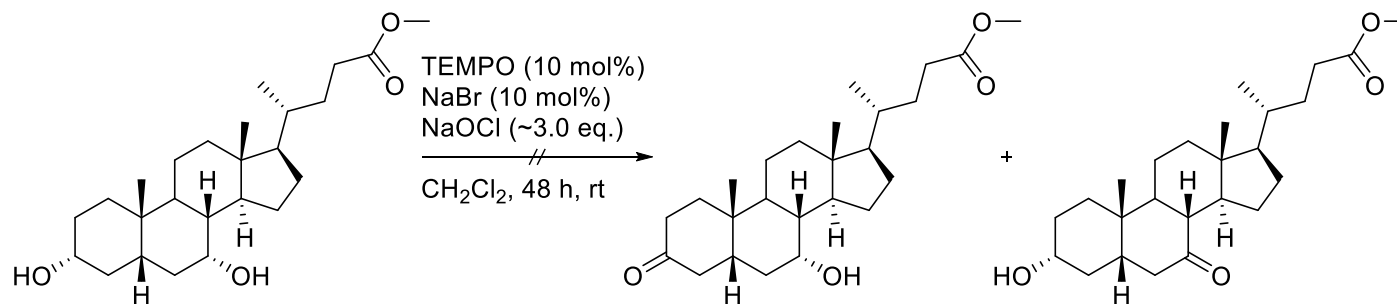
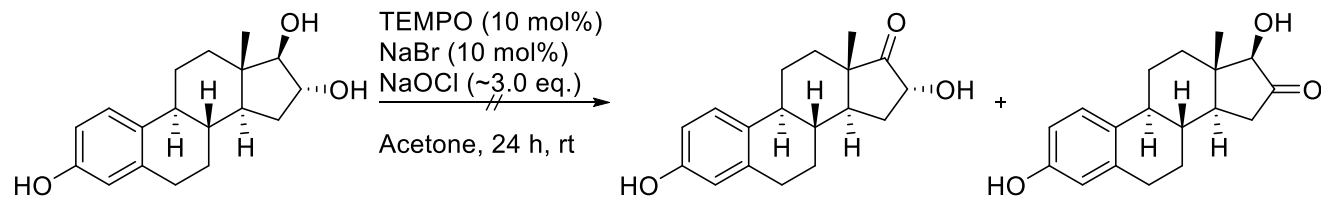


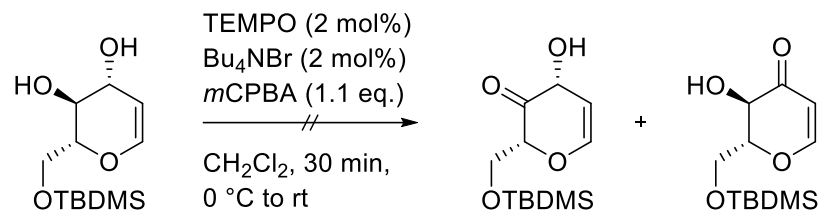
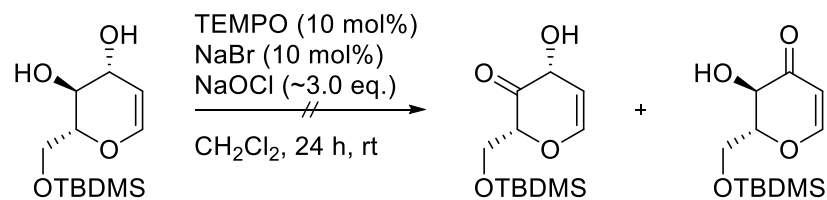
Substrate	2-O a-d ^[a]	3-O a-d ^[a]	2,3-O a-d ^[a]	Yield / % ^[a]
a	2.3	1.1	1.0	62
a (365 nm)^[b]	1.0	19.8	10.1	74
b	2.0	1.0	2.2	42 ^[d]
b (365 nm)^[b]	1.0	10.7	9.5	25 ^[d]
c	3.9	3.6	1.0	75
c (365 nm)^[b]	1.8	4.0	1.0	91
d	4.1	1.7	1.0	44 ^[c]
d (365 nm)^[b]	1.0	10.4	6.1	54 ^[c]

[a] Yield and ratio determined *via* ¹H-NMR. [b] Reaction at 0° C. [c] Yield not determined exactly due to some decomposition of the methyldene protecting group.

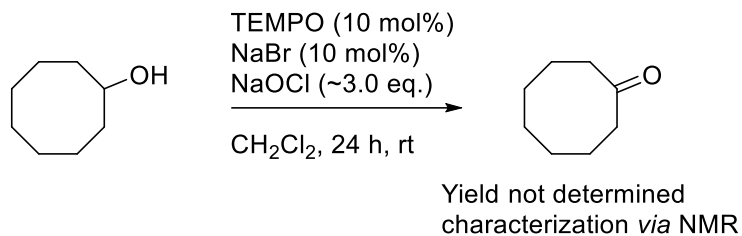
[d] Low conversion due to solubility issues.

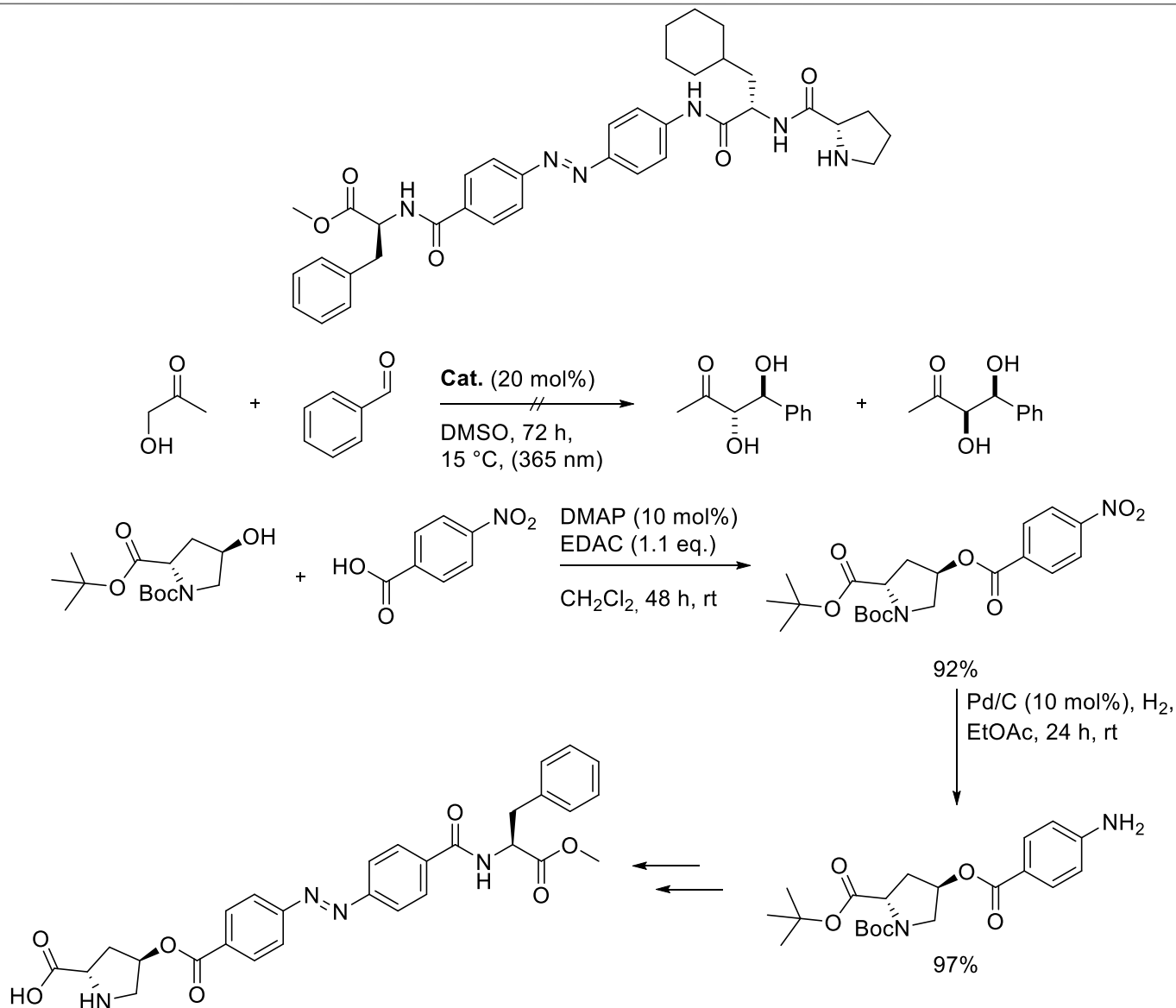






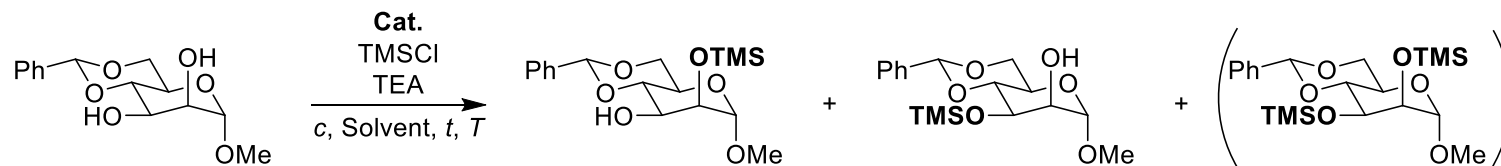
Validation of the protocol







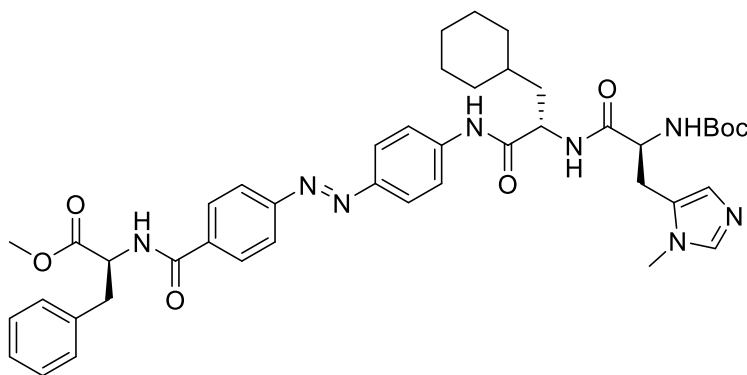
General reaction

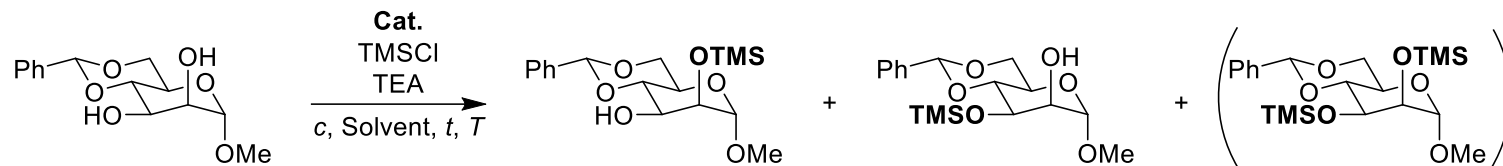


'Factors Table'

$c / \text{mol L}^{-1}$	TMSCl / eq.	TEA / eq.	$n_{\text{Cat}} / \text{mol}\%$	$T / ^\circ\text{C}$	t / h	Solvent
0,01	0,9	1	1	10	1	PhMe
0,1	2	5	10	30	72	DMF
						CHCl_3
						Dioxane

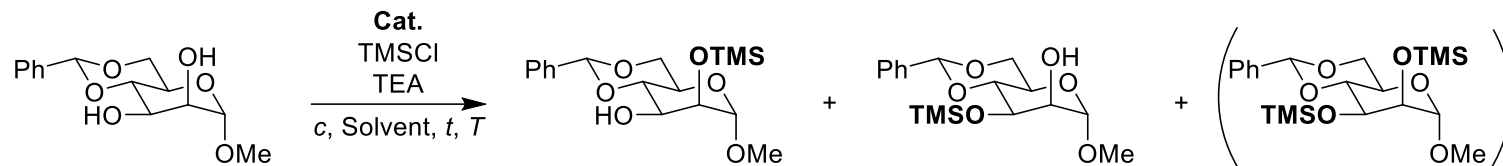
Catalyst (Cat.)





Solvent	<i>c</i> / mol L ⁻¹	TMSCl / eq.	TEA / eq.	Cat. / mol%	<i>T</i> / °C	<i>t</i> / h	Ratio ^[a]
PhMe	0.01	0.9	5	10	-10	1	6.6
PhMe	0.01	2	1	1	30	1	1.7
PhMe	0.1	0.9	1	10	-10	72	9.4
PhMe	0.1	2	5	1	30	72	6.8
DMF	0.1	0.9	5	1	-10	1	0.2
DMF	0.1	2	1	10	30	1	0
DMF	0.01	2	1	1	-10	72	0
DMF	0.01	0.9	5	10	30	72	3.5
CHCl ₃	0.1	0.9	1	1	-10	1	1.7
CHCl ₃	0.1	2	5	10	30	1	1.5
CHCl ₃	0.01	2	5	1	-10	72	7.1
CHCl ₃	0.01	0.9	1	10	30	72	4.7
Dioxane	0.01	2	1	10	-10	1	/
Dioxane	0.01	0.9	5	1	30	1	0
Dioxane	0.1	2	5	10	-10	72	/
Dioxane	0.1	0.9	1	1	30	72	1.6

[a] Yield and ratio determined *via* ¹H-NMR.



Solvent	c / mol L ⁻¹	TMSCl / eq.	TEA / eq.	Cat. / mol%	T / °C	t / h	Ratio ^[a]
PhMe	0.01	2	1	1	30	1	1.7
PhMe	0.1	0.9	1	10	-10	72	9.4
PhMe	0.1	2	5	1	30	72	6.8
DMF	0.1	2	1	10	30	1	0
DMF	0.01	0.9	5	10	30	72	3.5
CHCl ₃	0.1	2	5	10	30	1	1.5
CHCl₃	0.01	2	5	1	-10	72	7.1
CHCl ₃	0.01	0.9	1	10	30	72	4.7
Dioxane	0.01	0.9	5	1	30	1	0
Dioxane	0.1	0.9	1	1	30	72	1.6

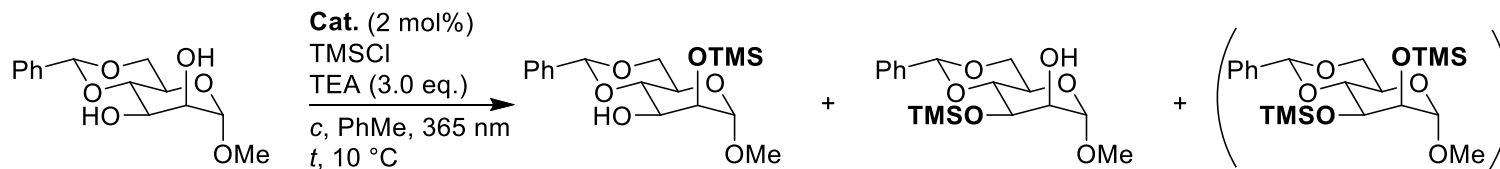
[a] Yield and ratio determined *via* ¹H-NMR.



'Effect Summary'

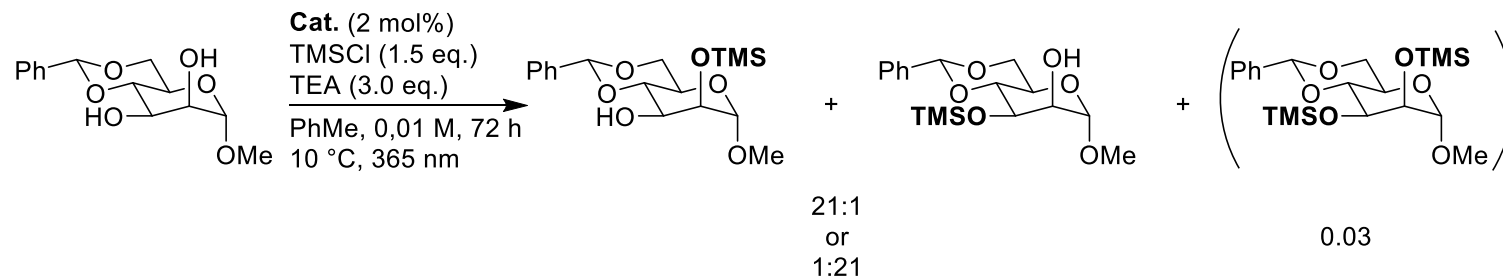
Source	LogWorth	PValue
Solvent	1.891	0.01285
Time(1,72)	1.884	0.01307
TMSCl(0,9,2)	0.807	0.15590
Catalyst(0.01,0.1)	0.701	0.19927
Base(1,5)	0.681	0.20824
Temperature(-10,30)	0.332	0.46548
Concentration(0.01,0.1)	0.051	0.88865

General reaction



'Factors Table'

c / mol L ⁻¹	TMSCl / eq.	t / h
0.01	0.9	24
0.1	1.5	72

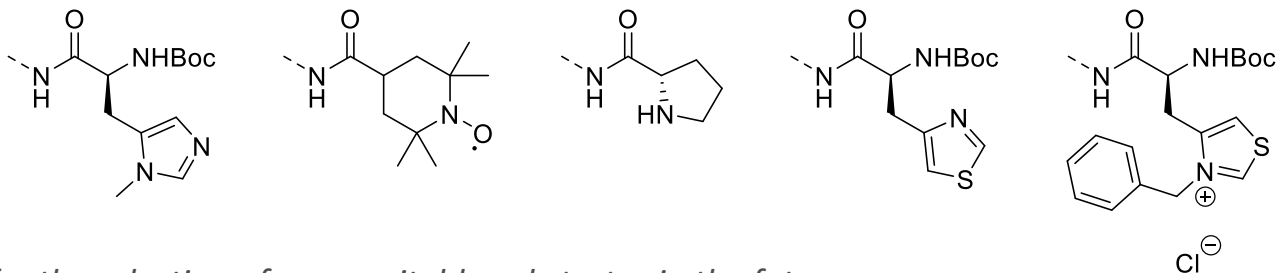


Solvent	Cat. / mol%	T / °C	t / h	Ratio ^[b]	Conversion / %
PhMe	2	10	72	21:1:(0)	37
PhMe	2 ^[a]	10	72	3:1:(0)	74
PhMe	0	10	72	2:1:(0)	20

[a]: Cat. = DMAP, [b]: Ratio and Conversion determined *via* ¹H-NMR spectroscopy.



- *Synthesis and characterization of six completely new photoswitchable azo-peptide organocatalysts, with various catalytic motifs.*

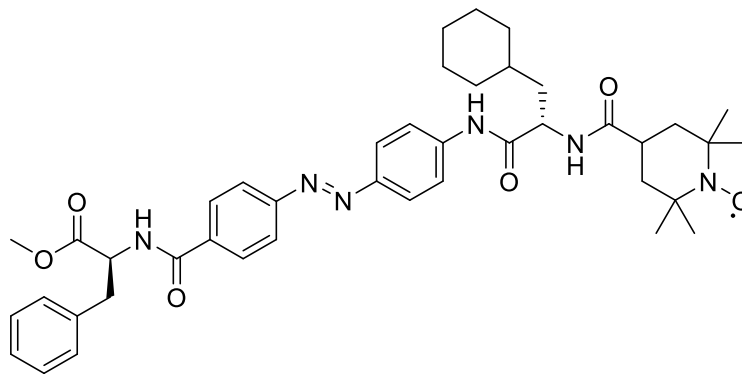


- *First hints for the selection of more suitable substrates in the future.*
- *Promising results for selective silylation of carbohydrates and further applications of JMP® 14.*

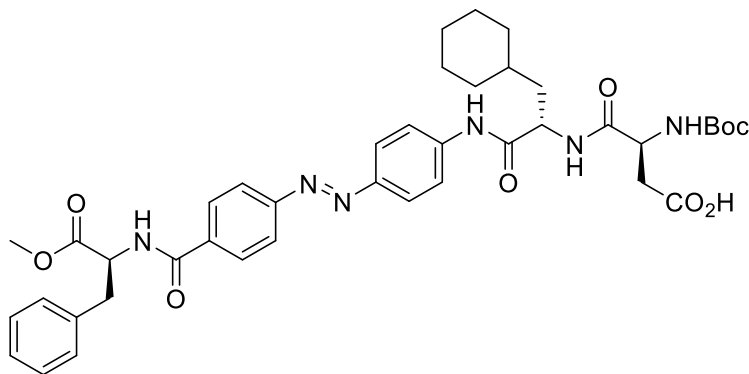




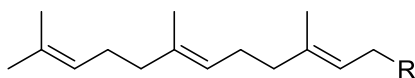
Cyclovoltammetry



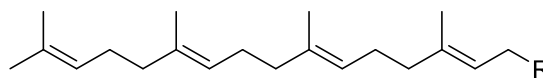
Change of the catalytic motif to aspartic acid, for selective epoxidation reactions.



Possible substrates



Farnesyl

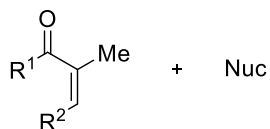
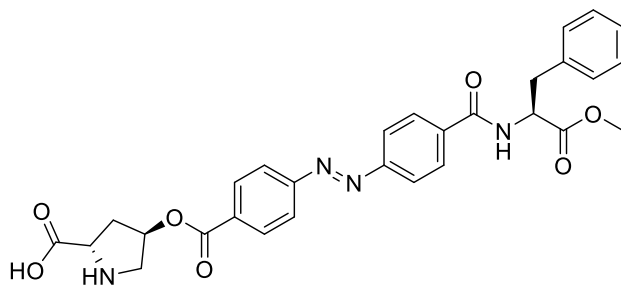


Geranyl

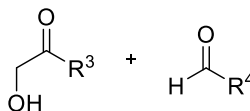
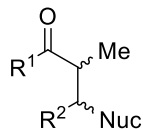


Finishing the synthesis of new Prolin containing photoswitchable azo-peptides for selective intermolecular Aldol reactions.

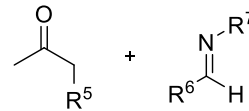
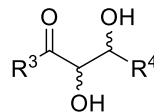
- Potentially viable for other enamin-catalyzed reactions, e.g. Michael addition or Mannich reaction.*



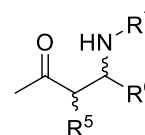
Michael addition



Aldol reaction

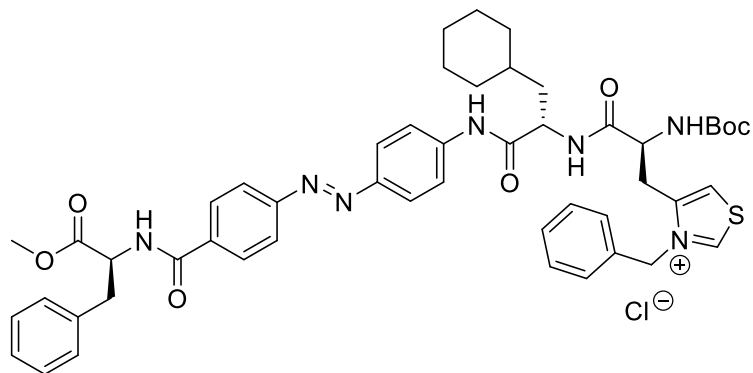


Mannich reaction





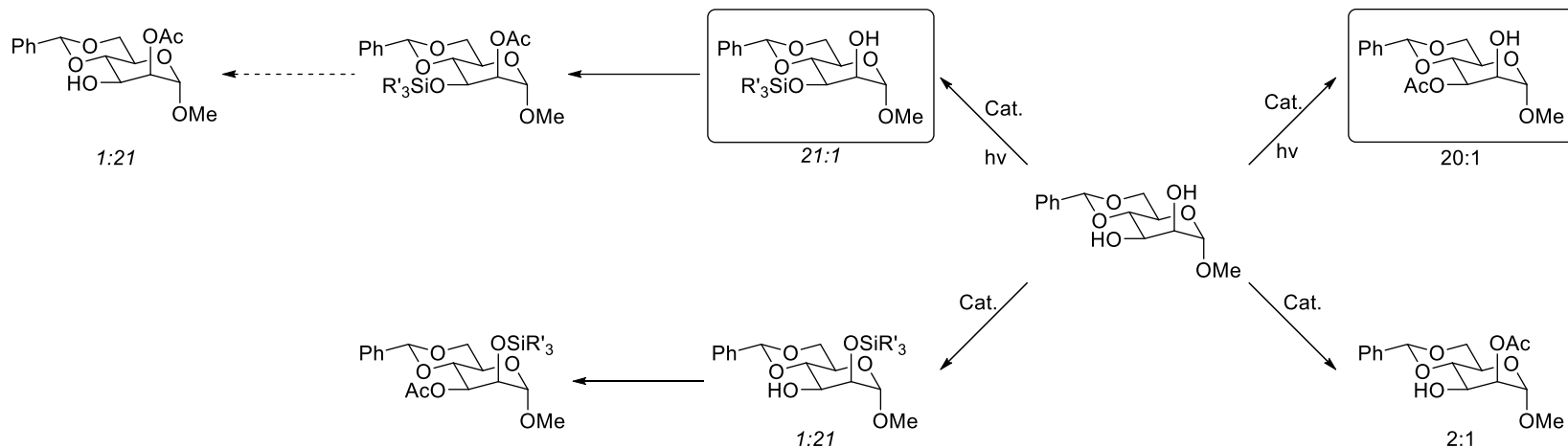
- *Optimizing the synthesis, especially the alkylation, of thiazolyl containing azo-peptides for possible applications as photoswitchable NHC-catalyst e.g., in Stetter reactions.*



- *Further optimization for the silylation of (4,6-O-benzylidene)methyl- α -D-mannopyranoside.*
 - *Variation of the electrophile*
 - *Variation of the base*
- *Application in an one pot orthogonal protection of carbohydrates, polyphenols or polyols in general.*

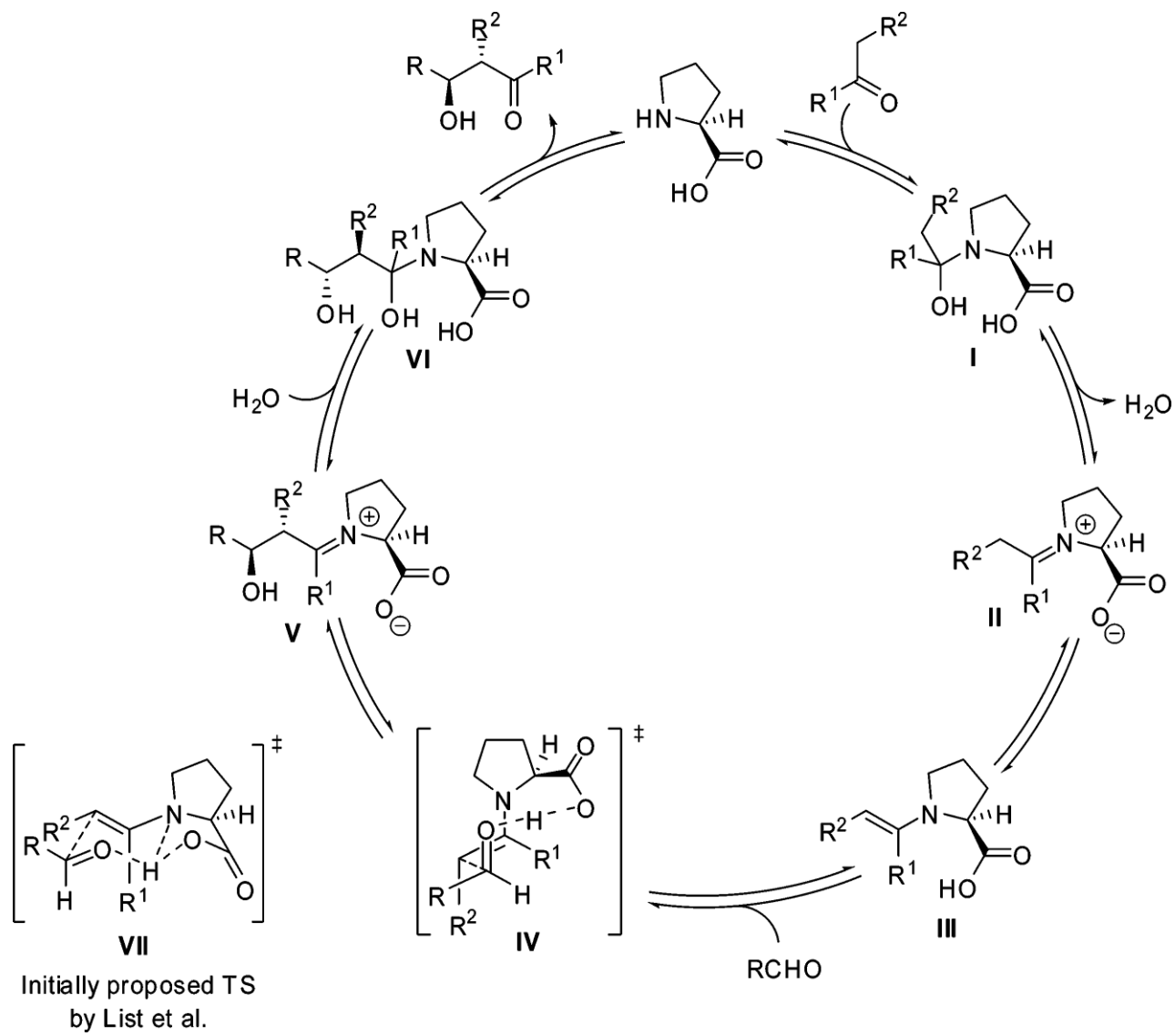


Strategy for an one pot orthogonal protection of carbohydrates.





- *Prof. Dr. Peter R. Schreiner*
- *Dominik Niedek*
- *B204 & B205*
- *OC-Analytik*
- *PRS Group*





Diastereoselective Mannich reaction

*Y. Li, X. Ren et al., J. Org. Chem., 2016, **81**, 9858–9866*



Educt

with DMAP

without Cat.

Mixture of isolated monosilylated products

with (Z) Cat.

