PRIMAARSED AMIINID KUI HETEROGEENSED KATALÜSAATORID: VÄLJAKUTSED, LAHENDUSED JA RAKENDUSED

Tõnis Kanger

TALLINNA TEHNIKAÜLIKOOL

Asümmeetrilise katalüüsi arendamine:

- oligopeptiidsete halogeensideme doonoritega katalüsaatorite konformatsioonanalüüs ja reaktsiooniteede modelleerimine;
- rinnapiima oligosahhariidide süntees;
- immobiliseeritud katalüsaatorite süntees ja rakendamine asümmeetrilises [2,3]-Wittigi ümberasetusreaktsioonis.

Asümmeetrilise katalüüsi arendamine:

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“Katalüüs on aeglaselt kulgeva reaktsiooni kiirendamine välise aine poolt.“

W. Ostwald, *Zeitschrift für Physikalische Chemie*, **1894**, *15*, 705.

…dass man später Fermente oder **organische Katalysatoren** auffinden Wird, welche auch höhere Temperaturen vertragen.

W. Ostwald, *Zeitschrift für Physikalische Chemie* , ***1900,*** 34**,** 510

TAL TECH

Enantioselektiivne organokatalüüs

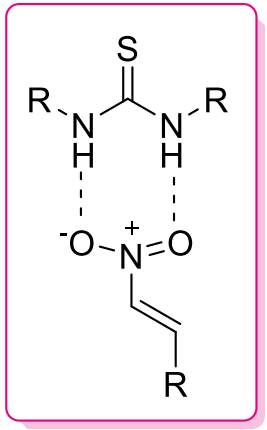
Gomollón-Bel, F. *Chem. Int.* **2019**, *41*, 12–17

TAL TECH

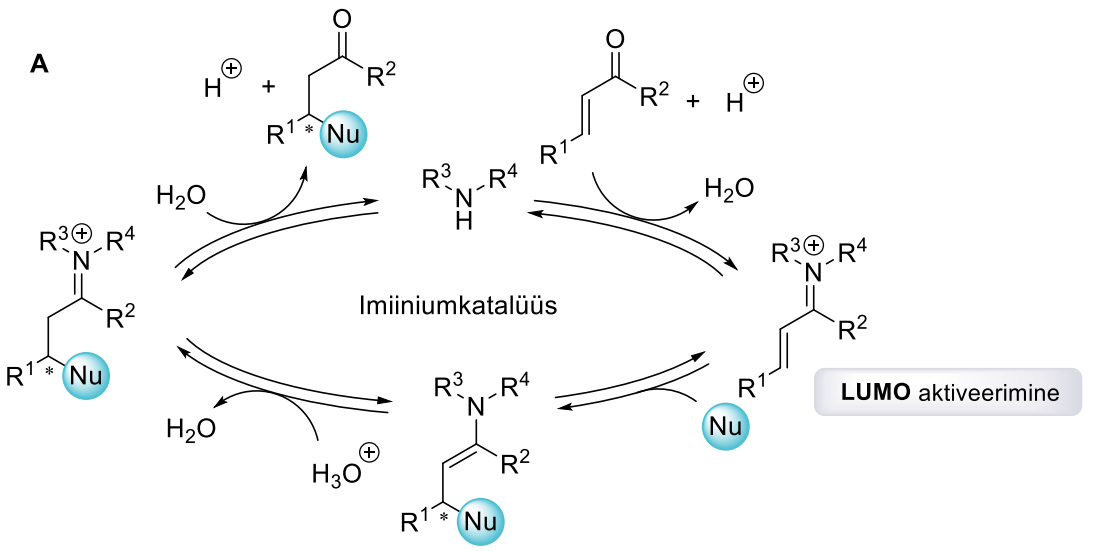
Organokatalüüs

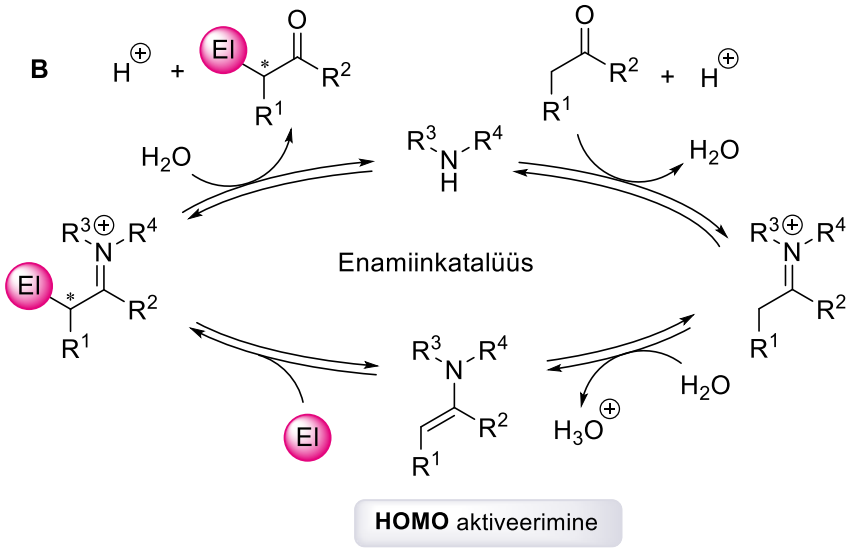
Nobeli keemiapreemia 2021
Benjamin List ja David W.C. MacMillan

Vesiniksideme katalüüs

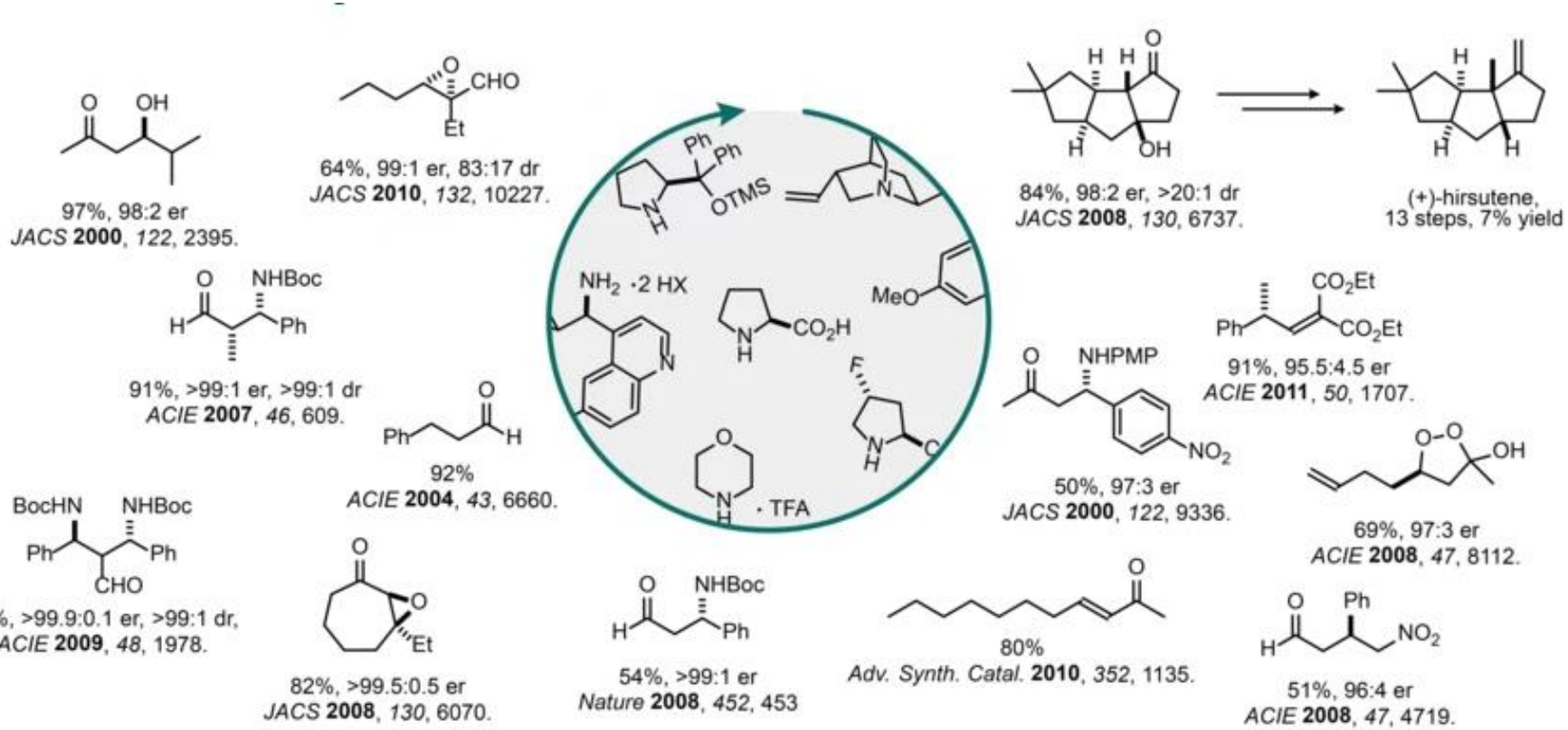


Aminokatalüüs



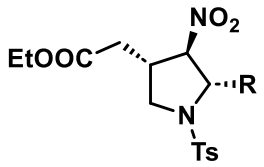


TAL TECH

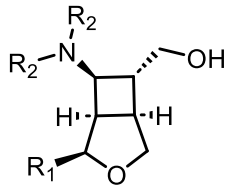


MAX-PLANCK-INSTITUT
FÜR KOHLENFORSCHUNG

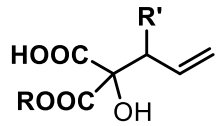
TAL TECH



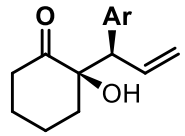
Tetrahedron: Asymmetry 2012



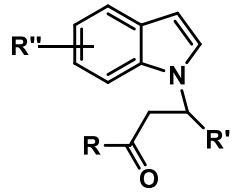
J. Org. Chem. 2012



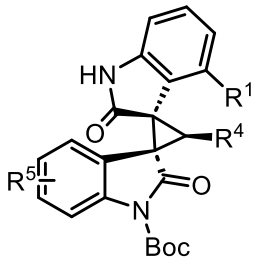
ACS Omega 2021



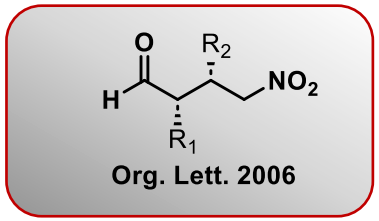
Eur. JOC 2021



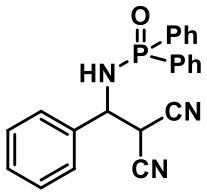
Org. Lett. 2021



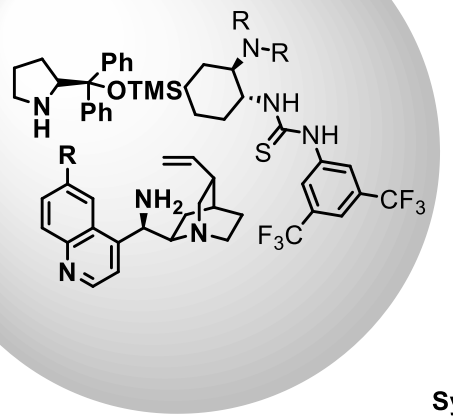
Adv. Synth. Cat. 2013

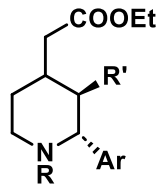


Org. Lett. 2006

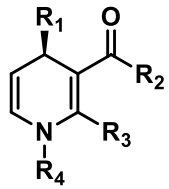


J. Org. Chem. 2022

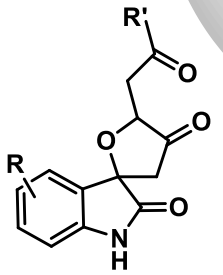




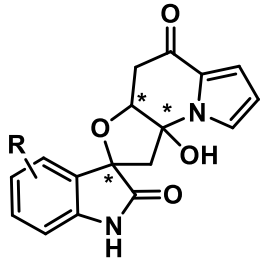
Synthesis 2017



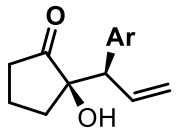
J. Org. Chem. 2011



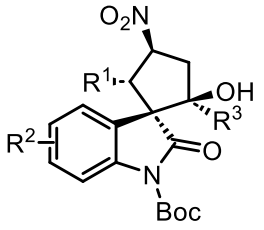
Synthesis 2018



Synthesis 2018



Org. Lett. 2019

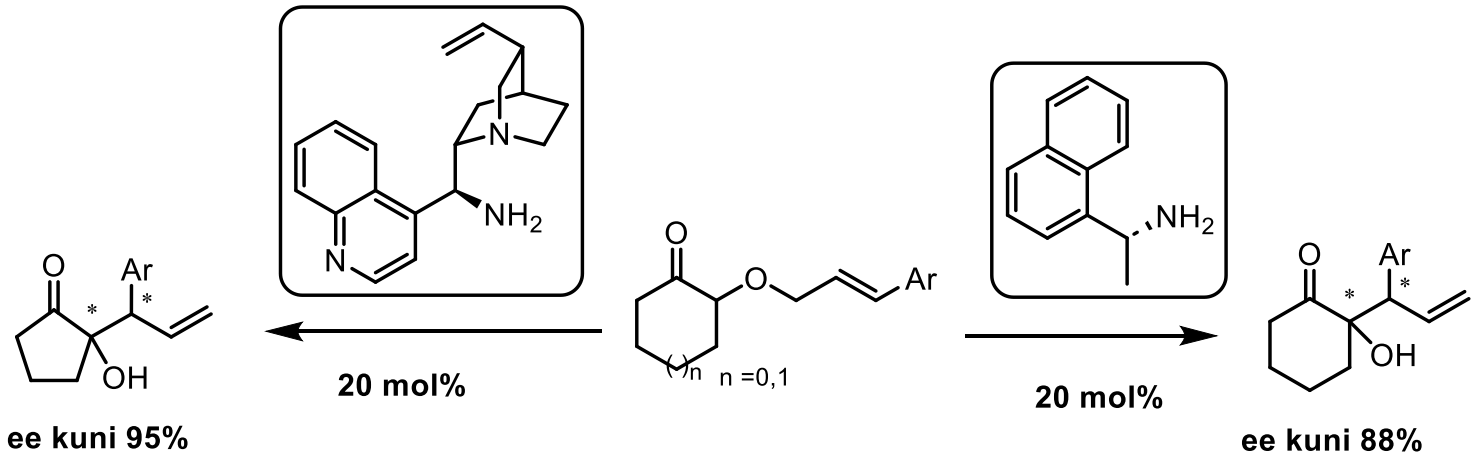


J. Org. Chem. 2013

TAL TECH

Kanger et. al.

[2,3]-Wittigi ümberasetus – homogeenne katalüüs

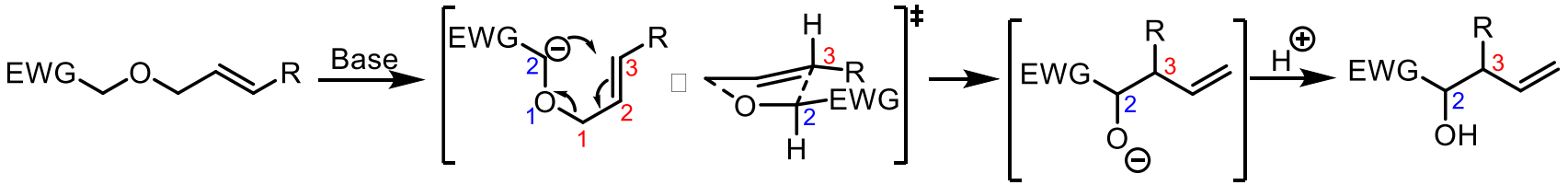


Kimm, M. et. al. *Org. Lett.* **2019**, *21*, 4976-4980.

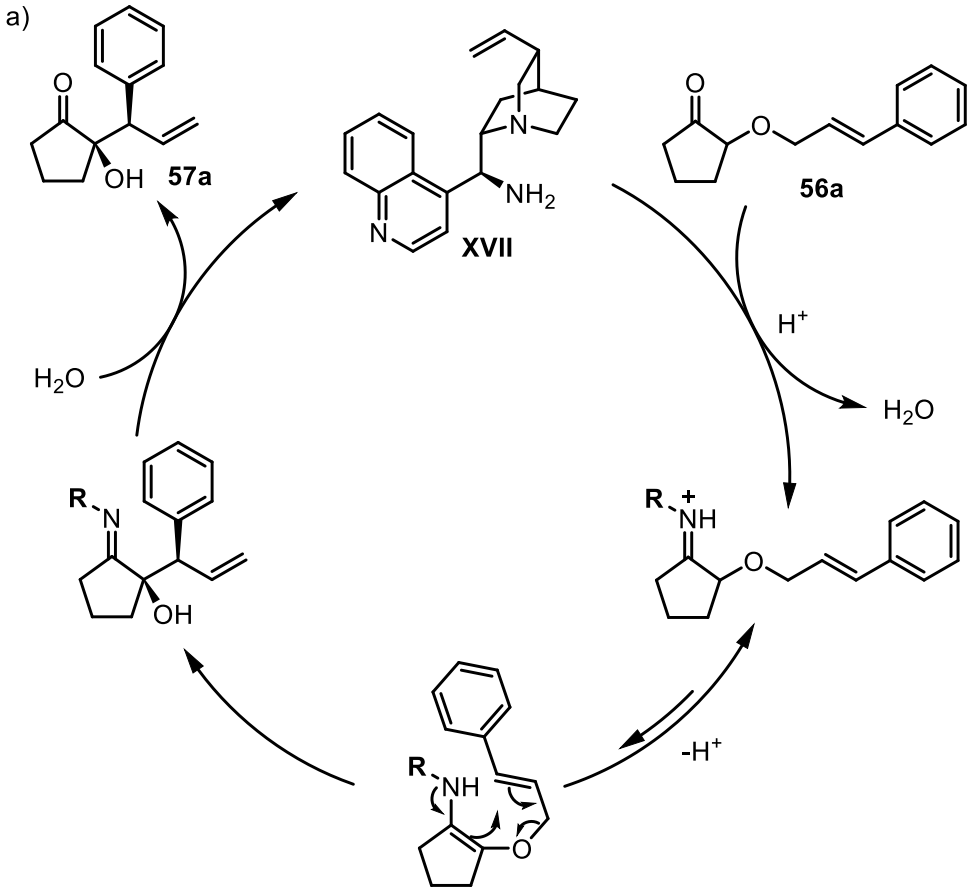
Kimm, M. et. Al. *Eur. J. Org. Chem.* **2021**, 3113-3120.

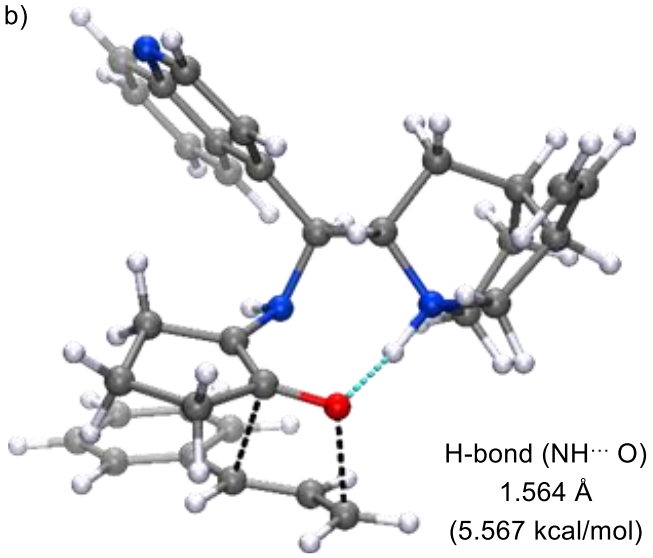
TAL TECH

[2,3]-Wittigi ümberasetus



EWG - elektronaktseptoorne rühm



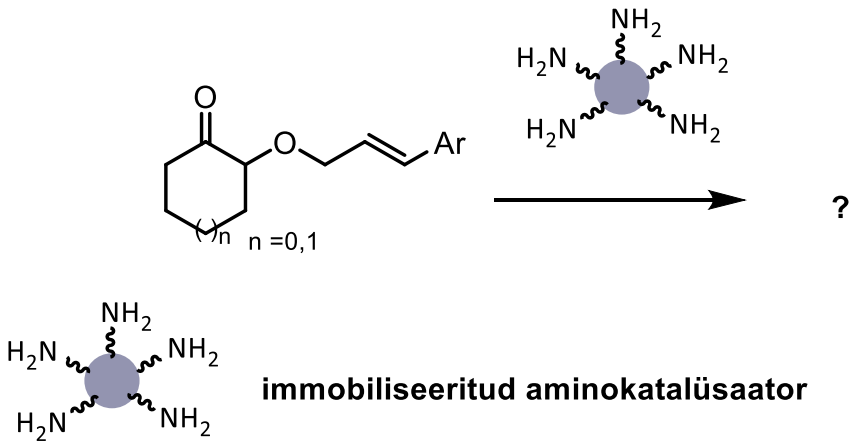


TAL TECH

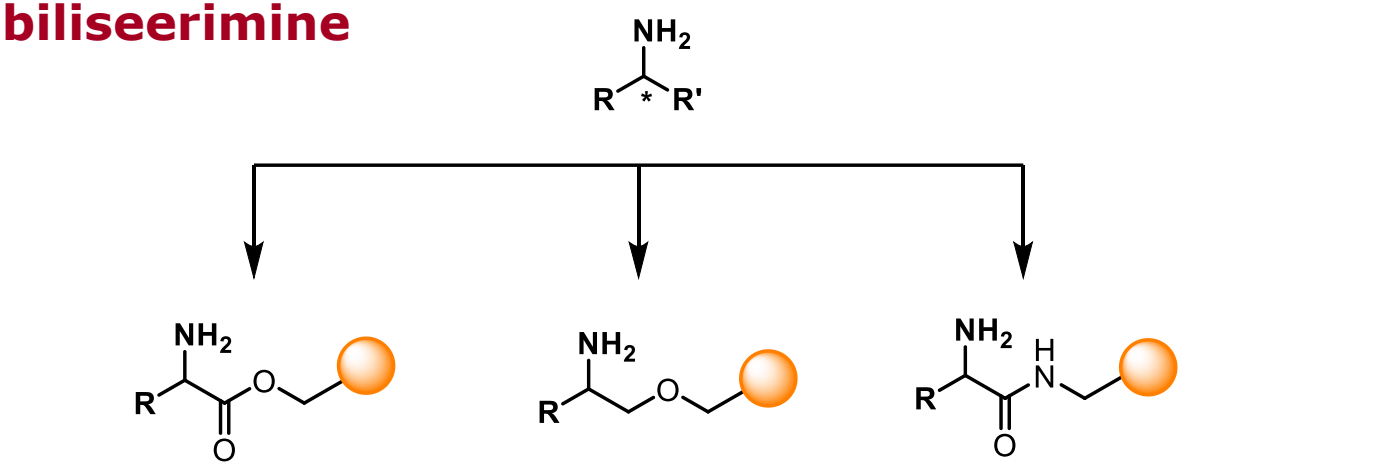
[2,3]-Wittigi ümberasetus

- 100% aatomefektiivne
- katalüütiline
- 20 mol% katalüsaatorit

Heterogeenne katalüüs

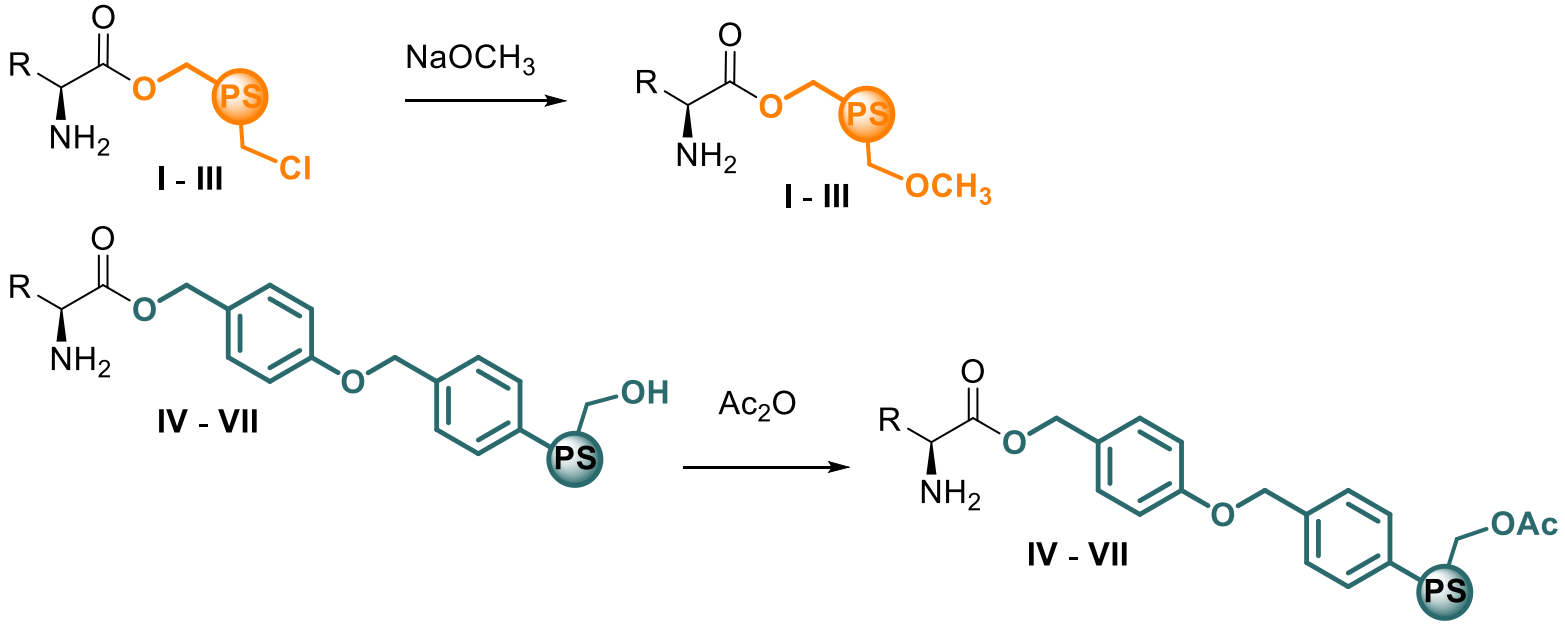


Katalüsaatorite immobiliseerimine

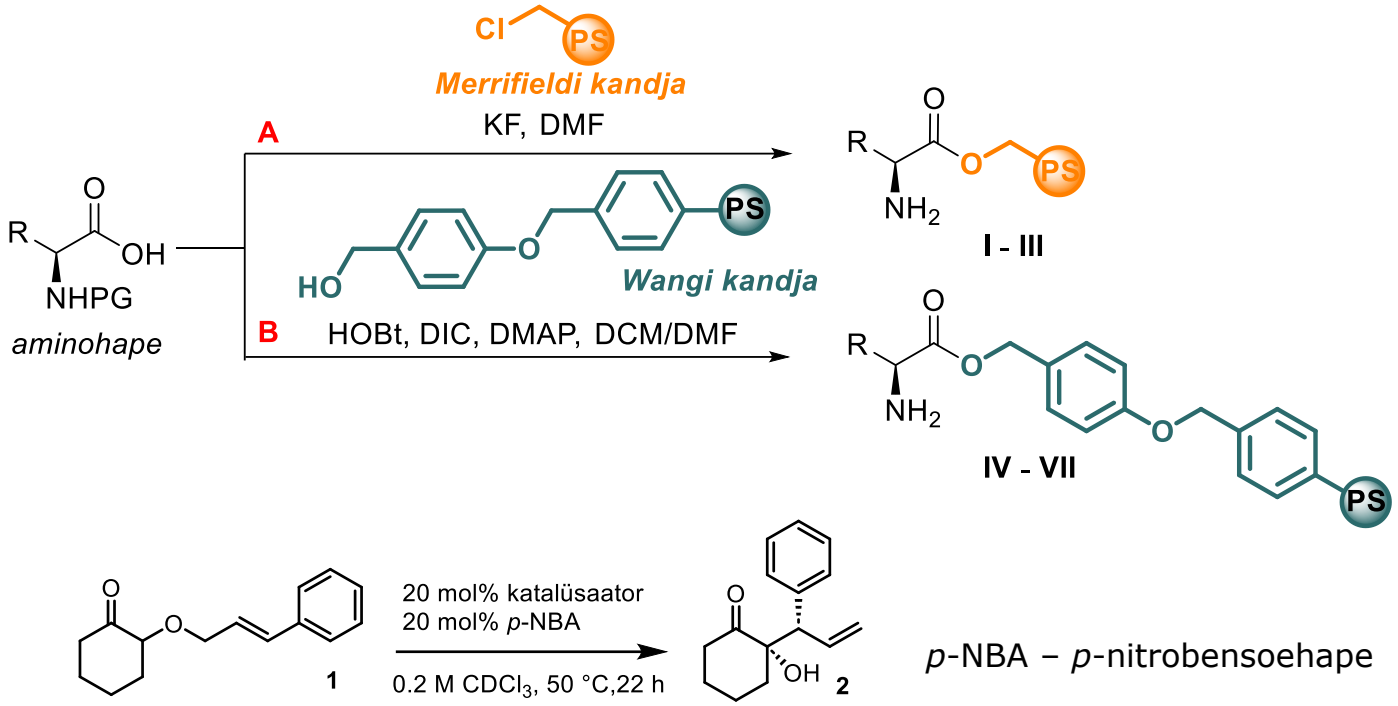


seotud estersidemega seotud eetersidemega seotud amiidsidemega

Kandja lõpprühmade blokeerimine



Estersidemega kandjale seotud katalüsaatorite süntees

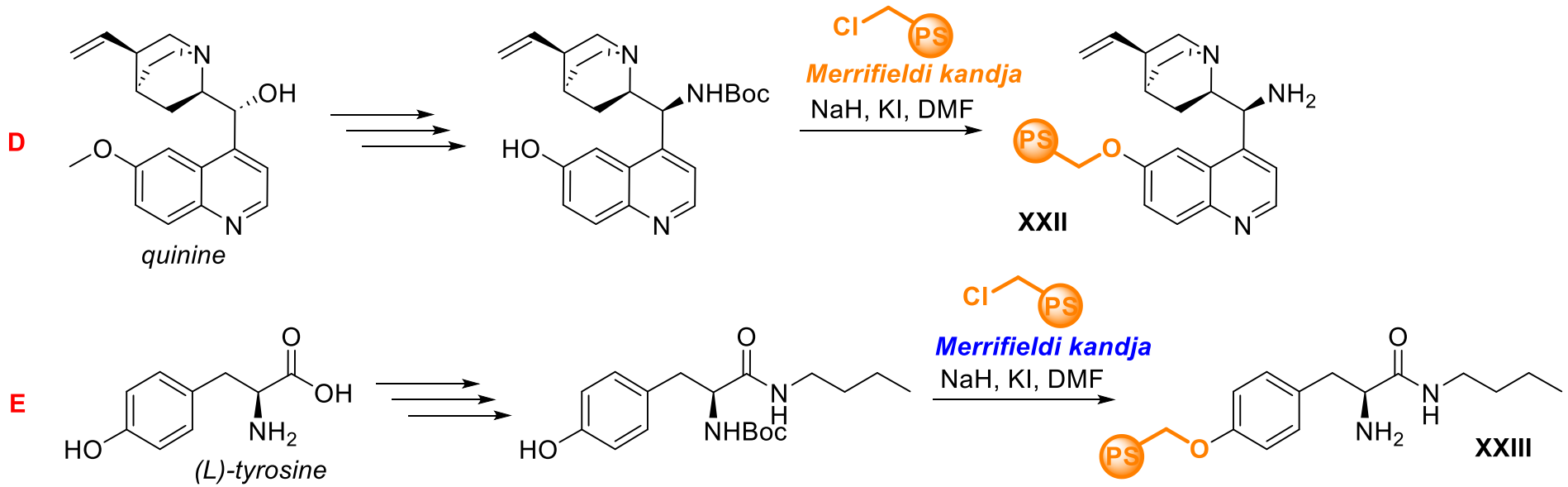


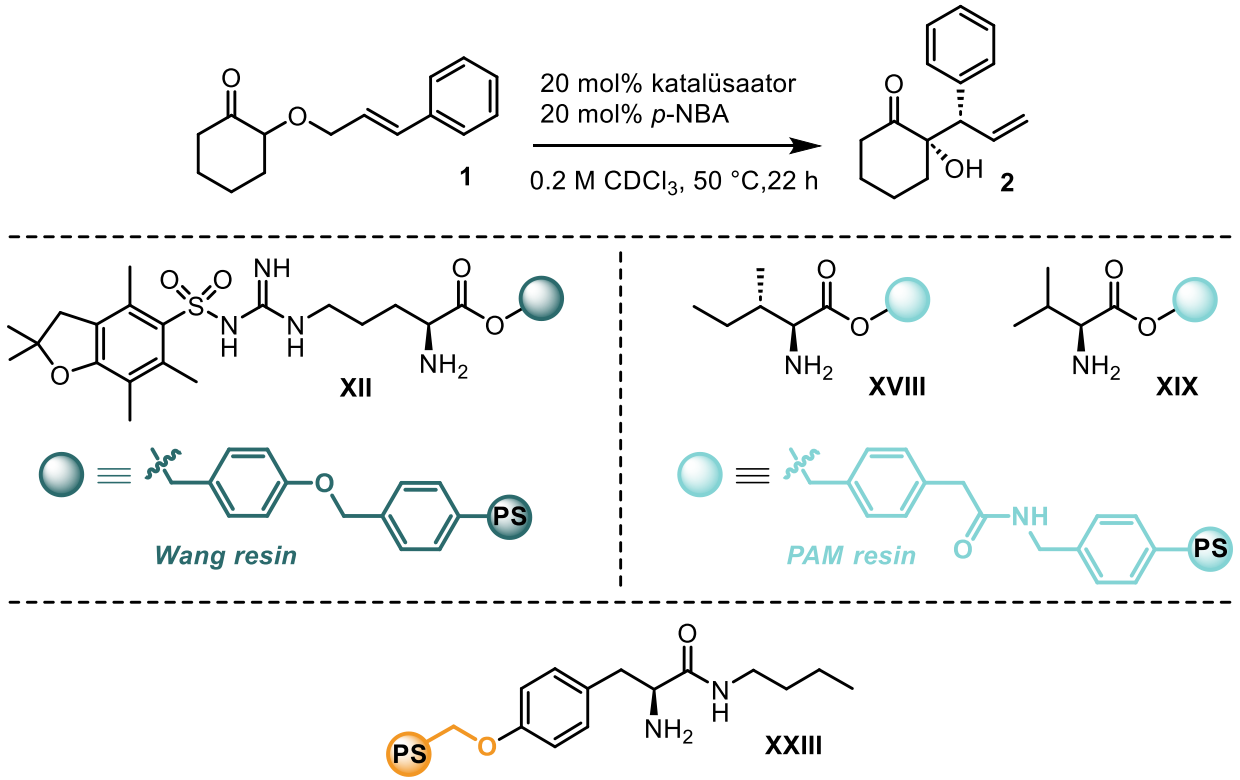
p-NBA – *p*-nitrobensoehape

Katalüsaator	R	Konversioon %	dr	ee, % major	ee, % minor
I	Me	80	6:1	6	14
II	iBu	63	3.1:1	rac	20
IV	Bn	20	4.3:1	14	4
VI	sec-Bu	jäljed	nd		nd
VII	Me	32	5.7:1	rac	14

TAL TECH

Eetersidemega kandjale seotud katalüsaatorite süntees

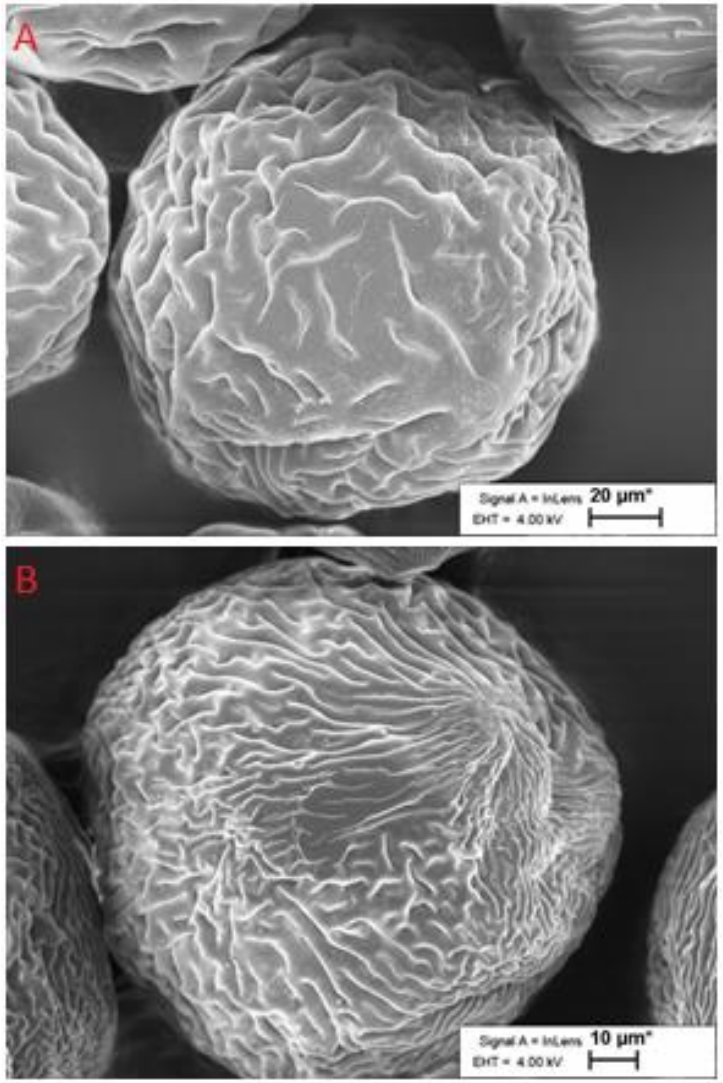




I tsükkel				II tsükkel		
Katalüsaator	Konv.	ee_{maj}	ee_{min}	Konv.	ee_{maj}	ee_{min}
XII	96	21	35	48	5	7
XVIII	78	39	38	15	23	19
XIX	62	46	46	5	nd	nd
XXIII	44	88	88	12	44	50

TAL TECH

Katalüsaatori morfoloogia muutus

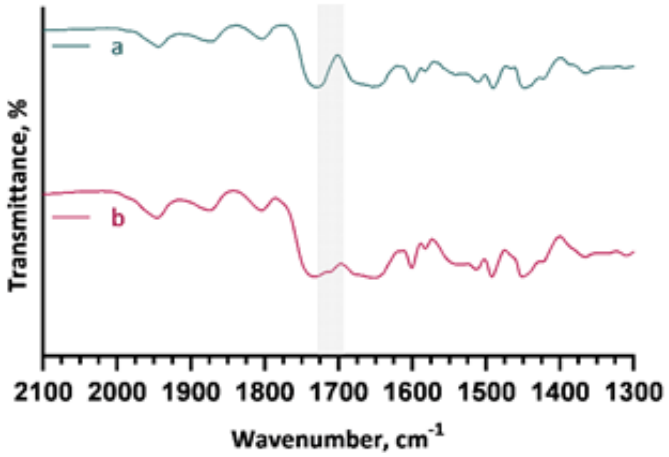


A. Kasutamata katalüsaatori **XXIII** SEM pilt

B. Kasutatud katalüsaatori **XXIII** SEM pilt

TAL TECH

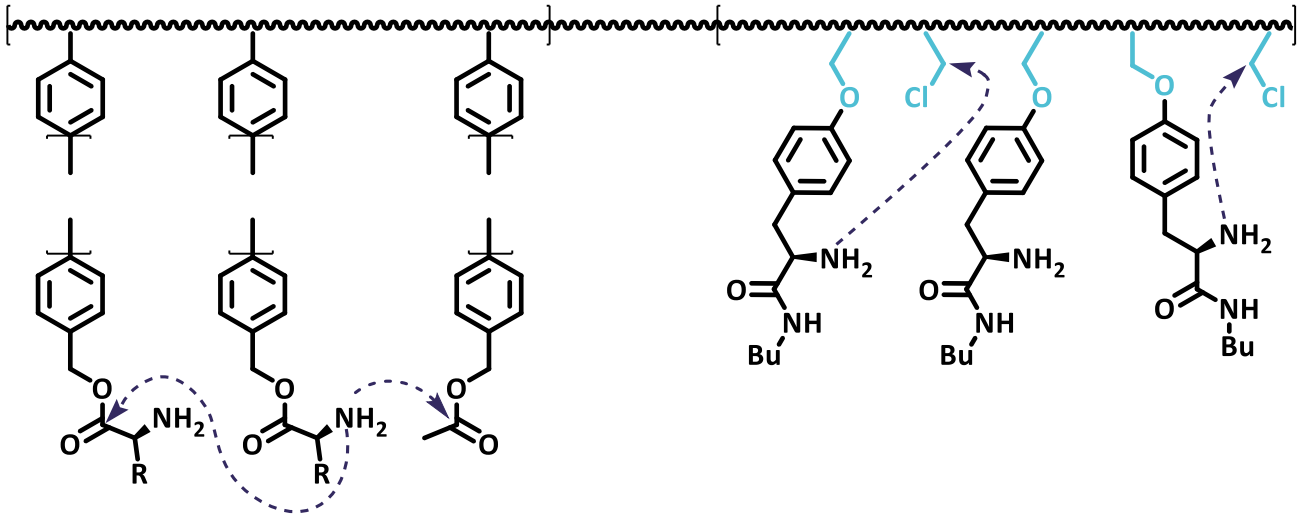
A



Kasutamata katalüsaatori IP spekter.

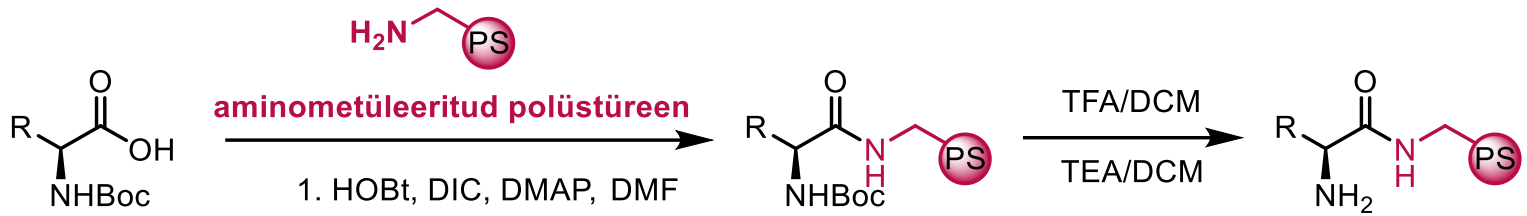
Kasutatud katalüsaatori IP spekter

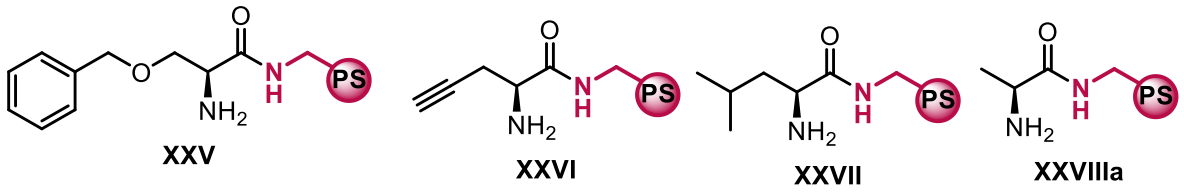
B

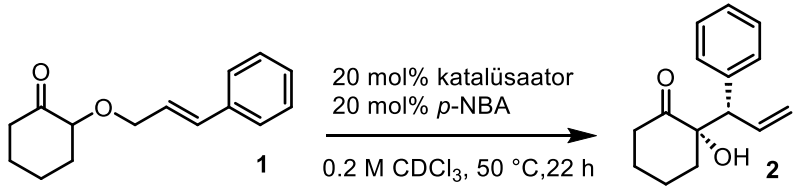


Võimalik katalüsaatori deaktiveerimine

Amiidsidemega kandjale seotud katalüsaatorite süntees

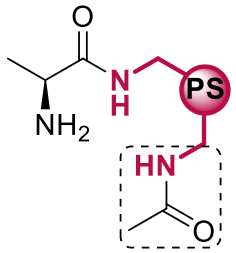






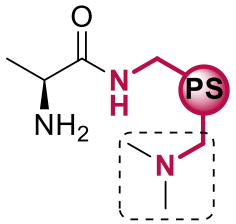
Katalüsaator	Konv.%	dr	ee	
			maj	min
XXV	100	6:1	78	78
XXVI	82	5.1:1	92	84
XXVII	95	3.7:1	88	76
XXVIIIa	100	8.9:1	82	72

TAL TECH



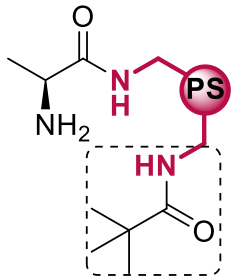
lõpprühm blokitud atsüleerimisega

XXVIIIa



lõpprühm blokitud alküülimisega

XXVIIIb

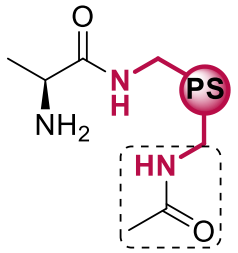


lõpprühm blokitud pivaloüülkloriidiga

XXVIIIc

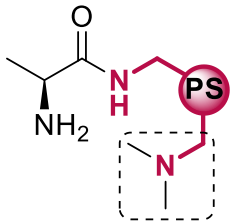
Katalüsaator	I tsükkel				II tsükkel			
	Konv. %	dr	ee		Konv. %	dr	ee	
			maj	min			maj	min
XXVIIIa	100	8.9:1	82	72	42	8.3:1	48	30
XXVII	95	3.7:1	88	76	31	3.7:1	56	38
XXVIIIa	100	7:1	82	58	45	5.7:1	42	16
XXVIIIb	100	8.6:1	87	73	73	8:1	70	50
XXVIIIc	100	8.6:1	86	71	100	8.4:1	82	65

TAL TECH



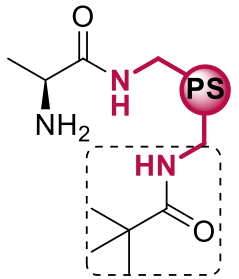
lõpprühm blokitud atsüleerimisega

XXVIIIa



lõpprühm blokitud alküülimisega

XXVIIIb

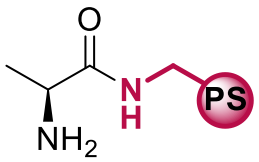


lõpprühm blokitud pivaloüülkloriidiga

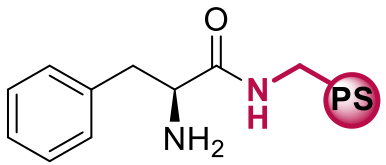
XXVIIIc

Katalüsaator	I tsükkel				II tsükkel			
	Konv. %	dr	ee		Konv. %	dr	ee	
			maj	min			maj	min
XXVIIIa	100	8.9:1	82	72	42	8.3:1	48	30
XXVII	95	3.7:1	88	76	31	3.7:1	56	38
XXVIIIa	100	7:1	82	58	45	5.7:1	42	16
XXVIIIb	100	8.6:1	87	73	73	8:1	70	50
XXVIIIc	100	8.6:1	86	71	100	8.4:1	82	65

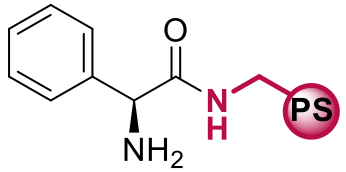
TAL TECH



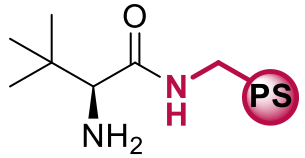
XXVIIIc



XXIX



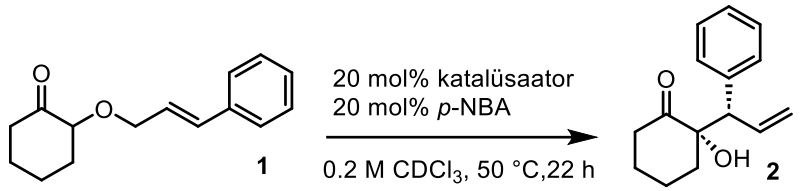
XXX

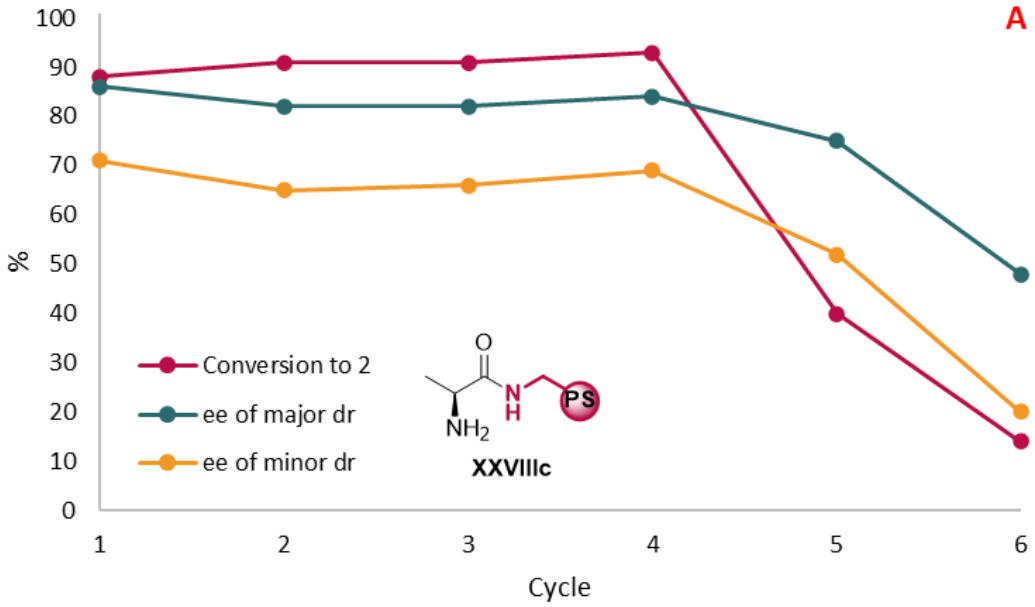


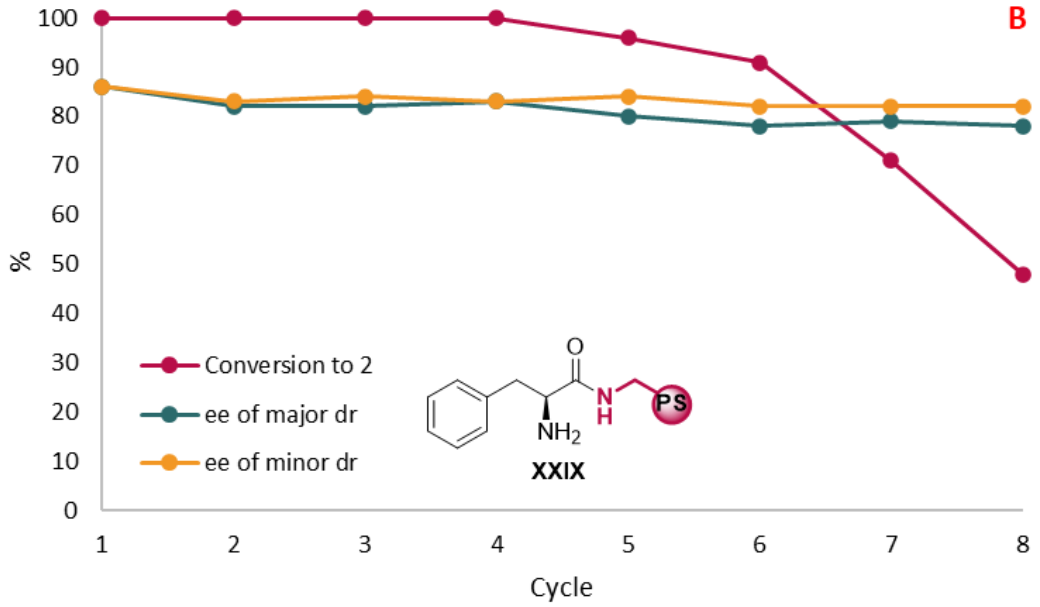
XXXI

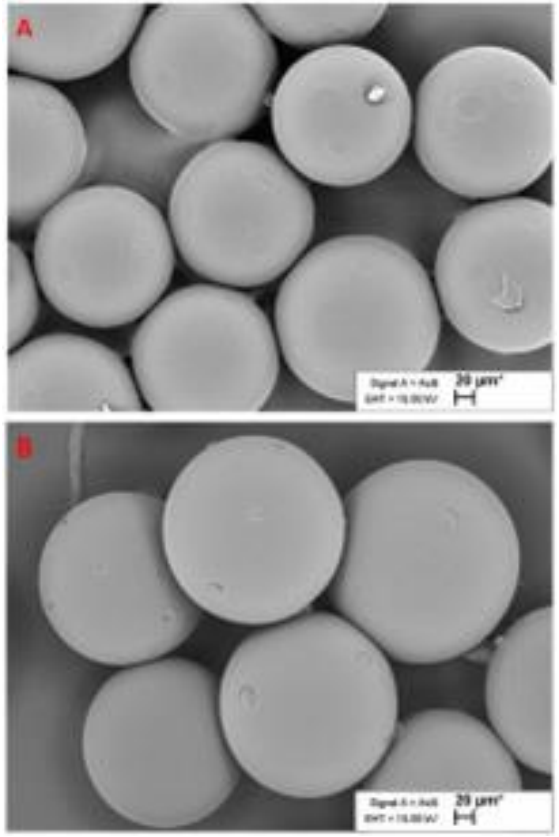
Katalüsaator	Konv.%	dr	ee	
			maj	min
XXVIIIc	100	8.6:1	86	71
XXIX	100	3.2:1	86	86
XXX	83	5:1	24	22
XXXI	65	1.8:1	37	32

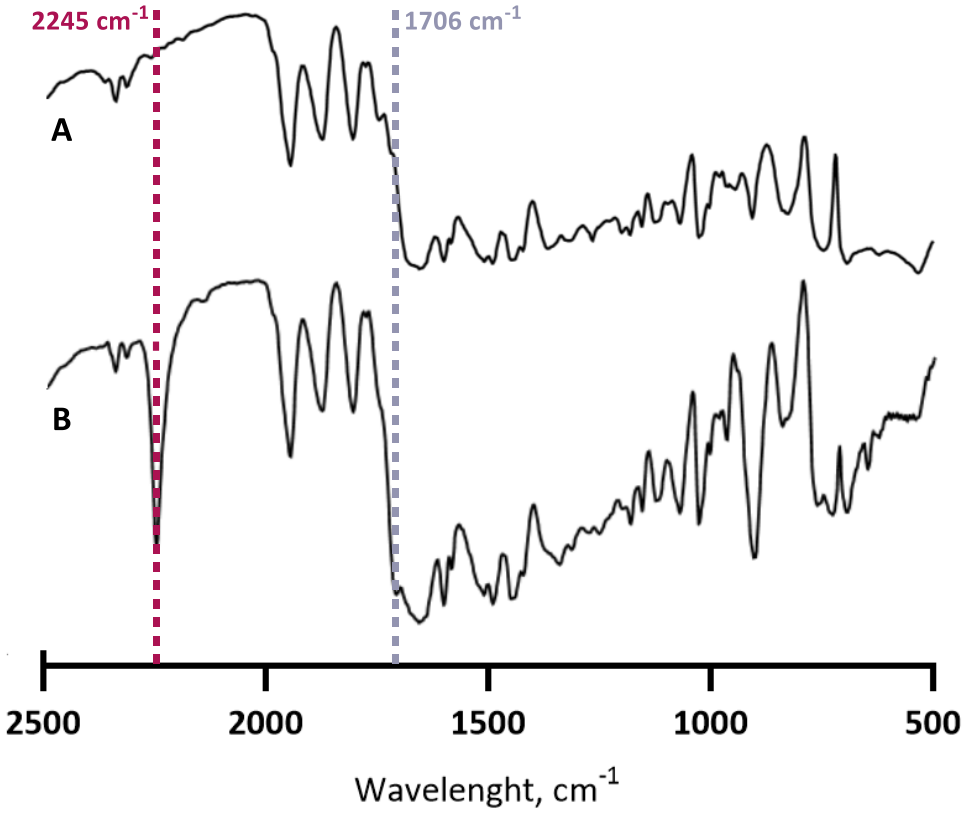
TAL TECH


20 mol% katalüsaator
20 mol% p-NBA
0.2 M CDCl3, 50 °C,22 h
1
2
OH


A
100
90
80
70
60
50
40
30
20
10
0
%
1
2
3
4
5
6
Cycle
Conversion to 2
ee of major dr
ee of minor dr
PS
XXVIIIc


B
100
90
80
70
60
50
40
30
20
10
0
%
1
2
3
4
5
6
7
8
Cycle
Conversion to 2
ee of major dr
ee of minor dr
PS
XXIX





A. Kasutamata katalüsaatori **XXIX** SEM pilt ja IP spekter

B. 6x taaskasutatud katalüsaatori **XXIX** SEM pilt ja IP spekter

TAL TECH

A. Murre, V. Mikli, K. Erkman, T. Kanger. *iScience*, **2023,** *26***,** 107822.

Kokkuvõtteks

- Heterogeenne katalüüs on konkurentsivõimeline alternatiiv homogeensele katalüüsile [2,3]-Wittigi ümberasetusreaktsioonis
- Sobivamaks kandjaks on aminometüleeritud polüstüreen
- Kriitilise tähtsusega on kandja vabade lõpprühmade blokeerimine
- Blokeerimine steeriliselt mahuka pivaloüülkloriidiga tagab immobiliseeritud katalüsaatori korduvkasutamise
- Aminohapped on sobivad lähteained immobiliseeritud katalüsaatorite sünteesiks

TAL TECH

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Dr Kristin Erkman
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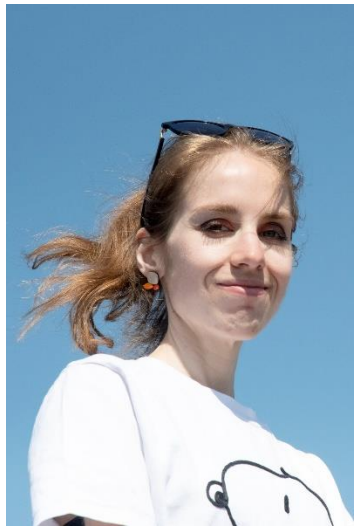
Dr Andrus Metsala



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Harry Martõnov
Annette Miller
Kerli Tali