ASÜMMEETRILINE ORGANOKATALÜÜS: KLASSIKALISED JA UUED VÕIMALUSED

Tõnis Kanger
Tallinna Tehnikaülikool

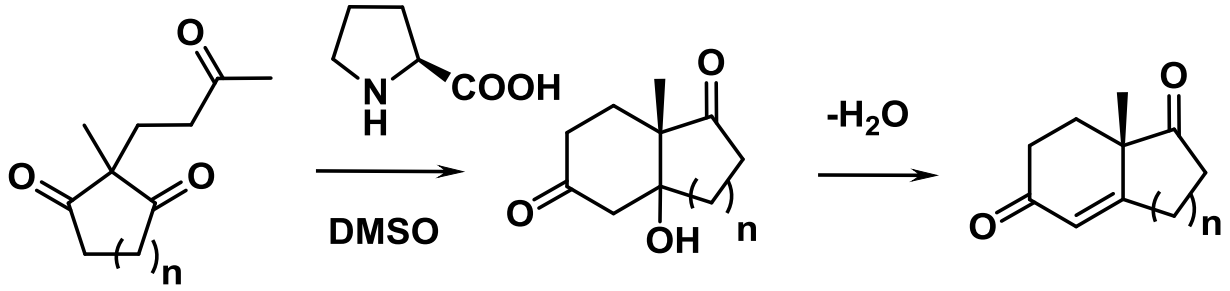
"Die Fermente and ihre Wirkungen" C. Oppenheimer, Leipzig, 1900

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

Ostwald, W. Z. *Phys. Chem.* ***1900,*** 34**,** 510

Sisemolekulaarne aldoolreaktsioon

Hajos-Parrish-Eder-Sauer-Wiecherti reaktsioon



1: n = 2, ee 76%
2: n = 1, ee 93%

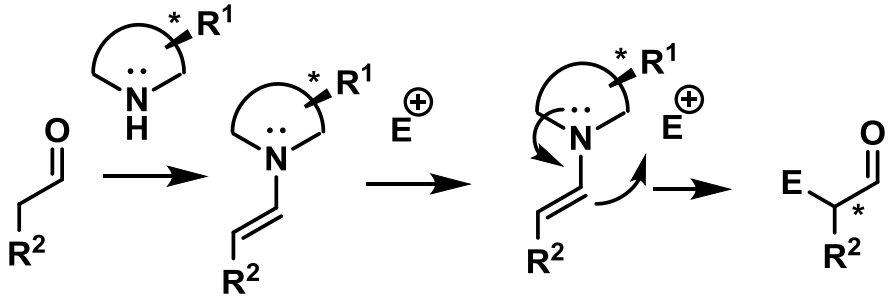
Hajos, Parrish, 1974

Eder, U.; Sauer, G.; Wiechert, R. *Angew. Chem., Int. Ed. Engl.* ***1971****, 496.*

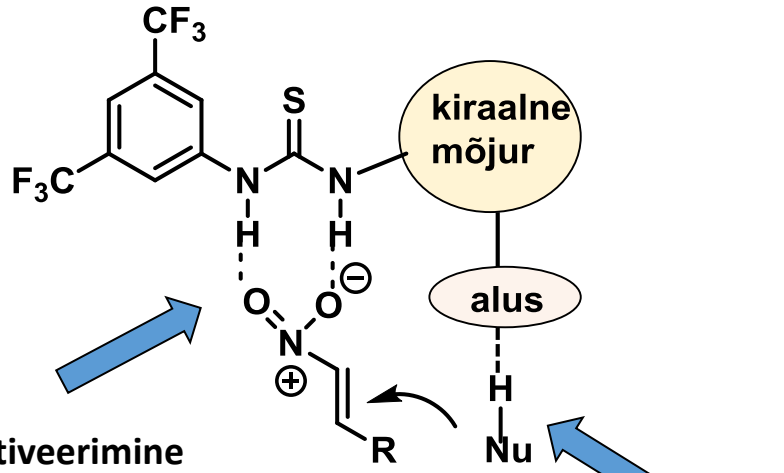
Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* ***1974****,1615.*

ORGANOKATALÜÜS

KOVALENTE ⟷ **MITTEKOVALENTNE**



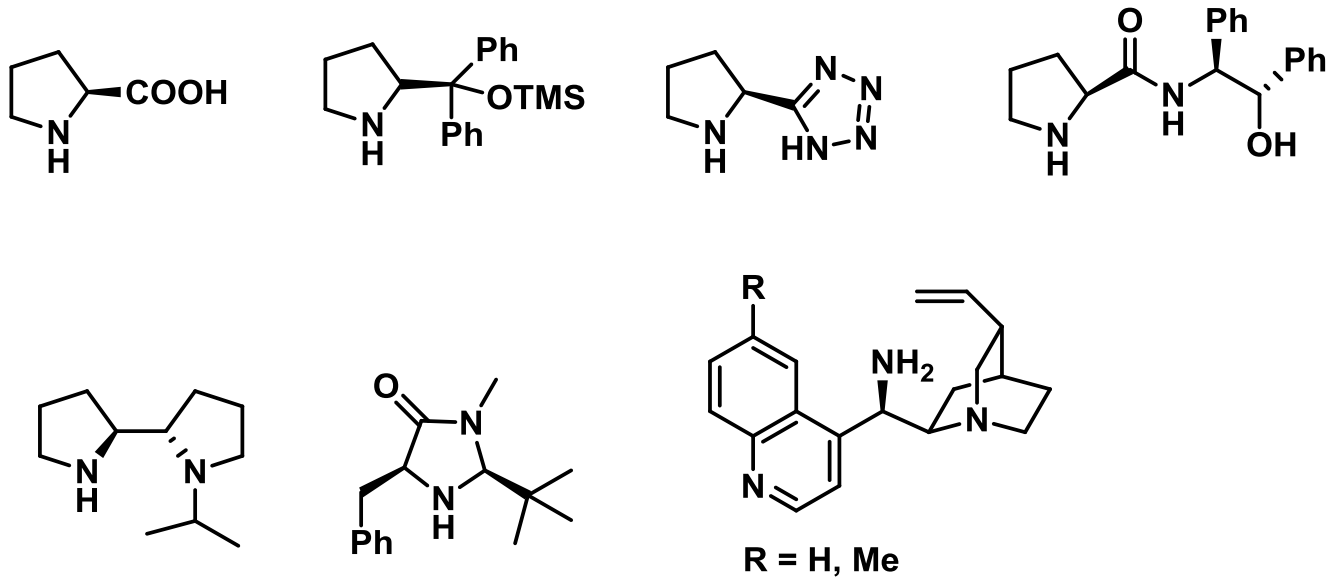
Nukleofiilii aktiveerimine



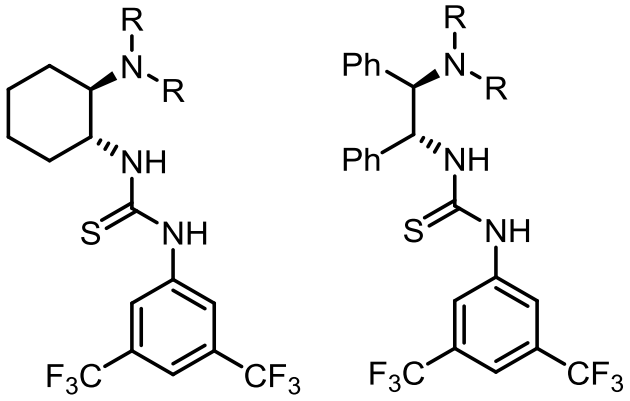
Elektrofiili aktiveerimine

Nukleofiili aktiveerimine

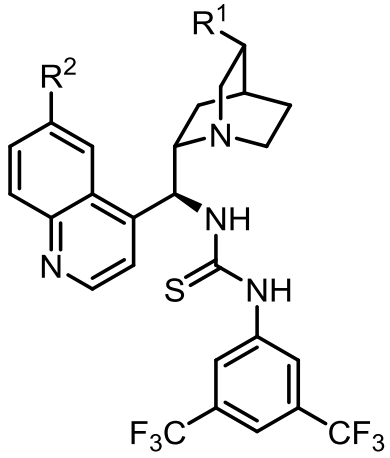
Enamkasutatavad aminokatalüsaatorid

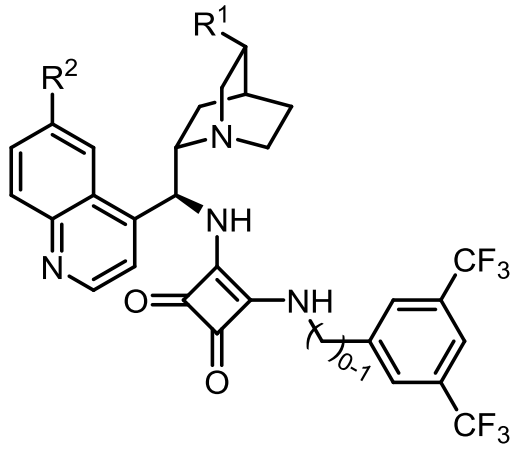


Enamkasutatavad H-sideme katalüsaatorid

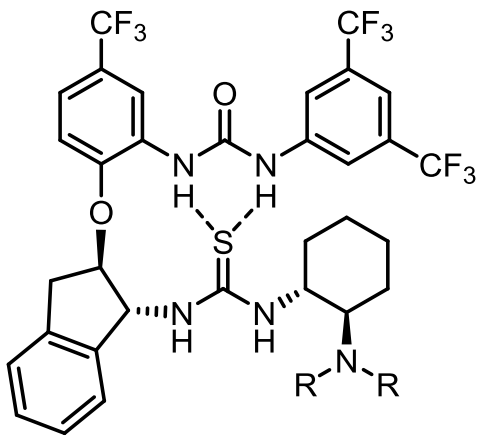


R = alküül või C_4-C_5 tsüklid

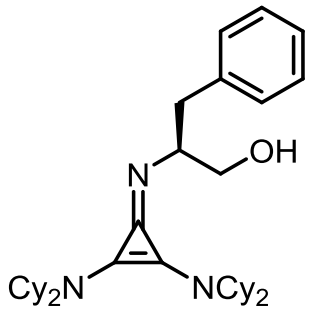


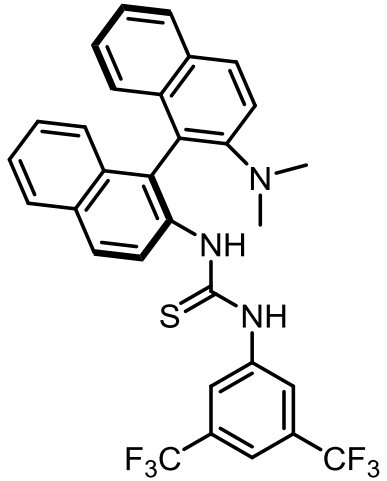


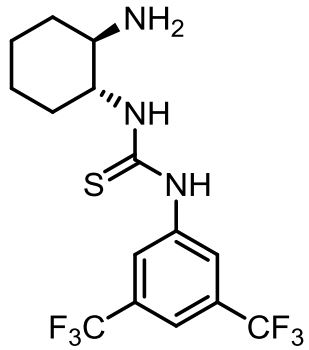
R^1 = etüül või vinüül
R^2 = H, OH või OMe



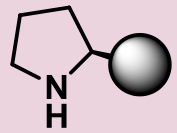
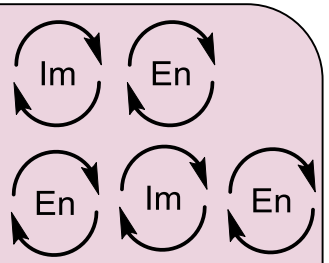
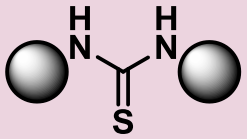
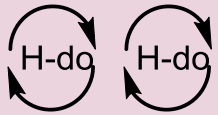
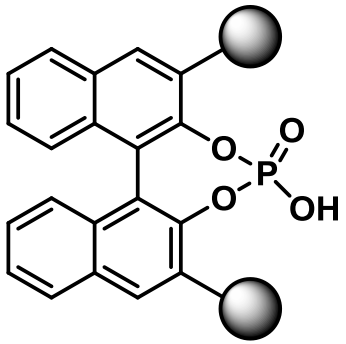
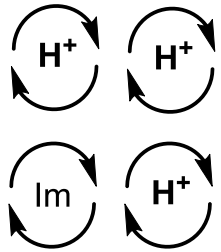
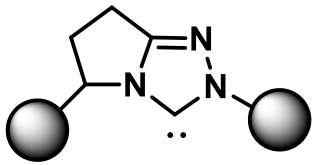
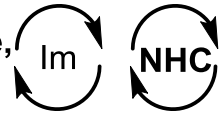
R = alküül või C_4-C_5 tsüklid





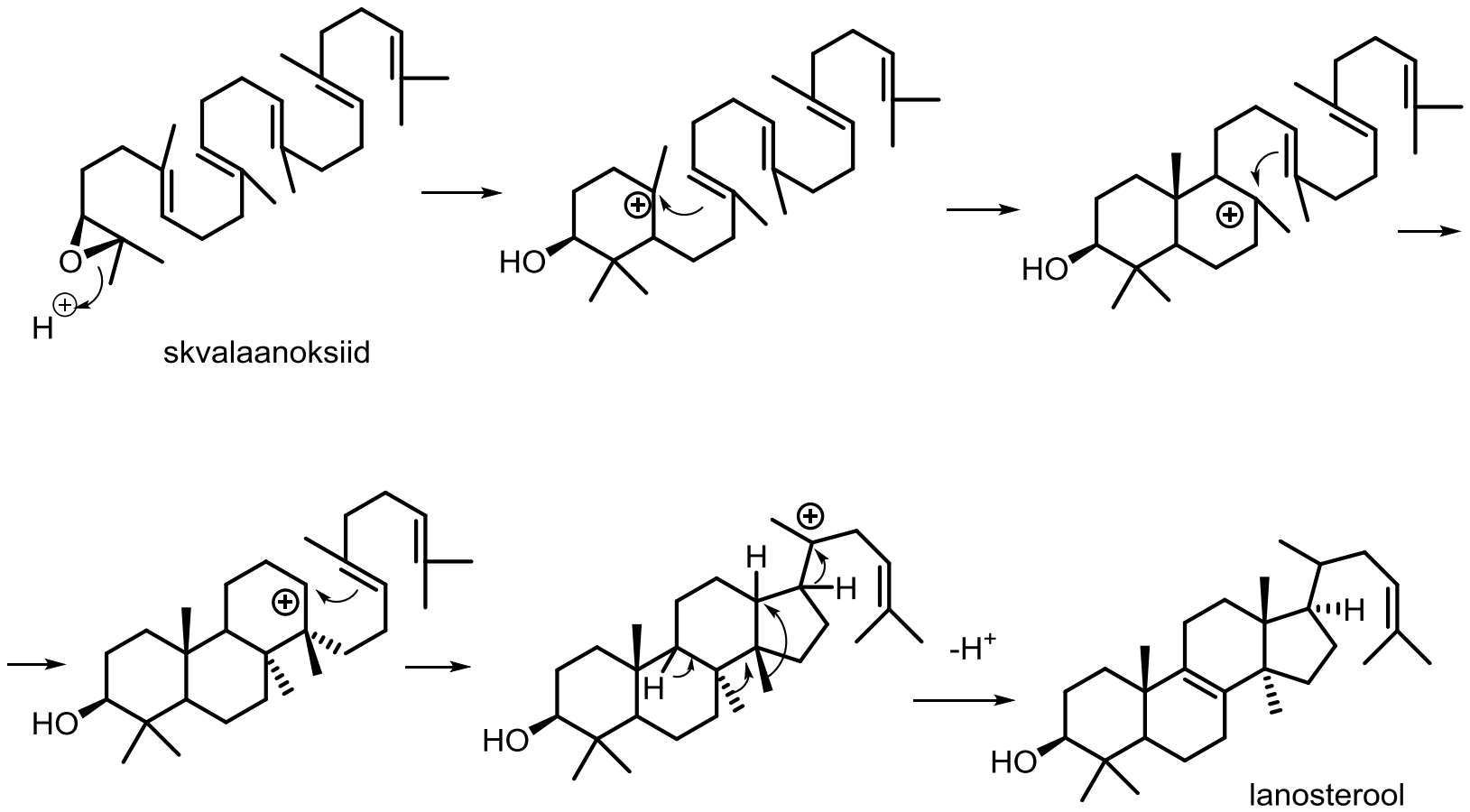


Organokatalüütilised reaktsioonid

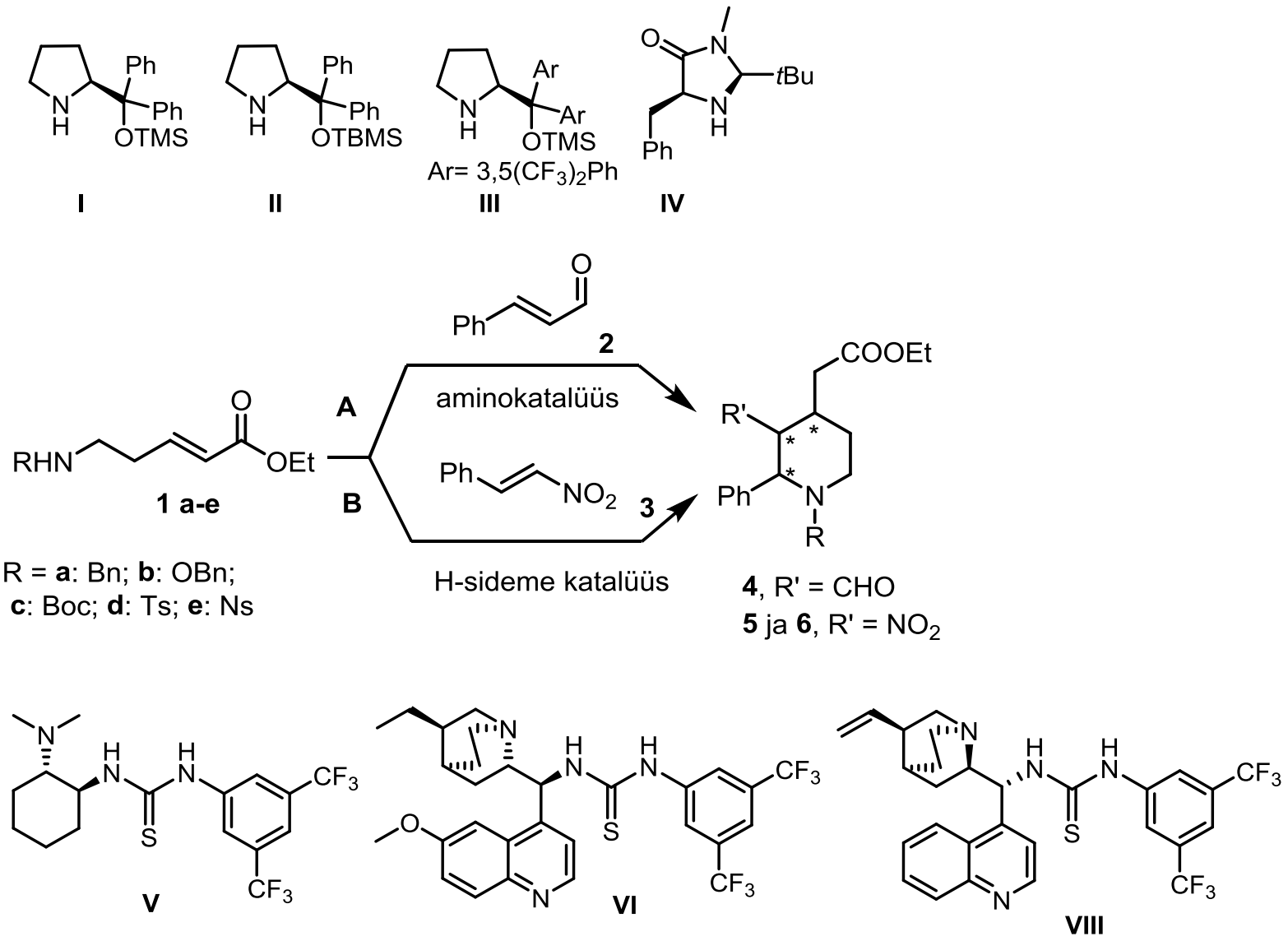
Katalüsaator	Aktiveerimine	Tüüpilised reaktsioonid	Kaskaadid
	Enamiini aktiveerimine, aldehüüdid ja ketoonid	Aldoolreaktsioon α-funktsionaliseerimine Michaeli reaktsioon Mannichi reaktsioon	
	H-side	Michaeli reaktsioon Henry reaktsioon Mannichi reaktsioon Streckeri reaktsioon	
	Protoneerimine (vastasiooni katalüüs)	Taandamine, Mannichi reaktsioon, Fridel-Craftsi reaktsioon, Michaeli reaktsioon	
	N-heterotsükliline karbeen	Nukleofiilne atsüleerimine, Stetteri reaktsioon	

C. Grondal, M. Jeanty, D. Enders. *Nature Chemistry*, **2010**, 2, 167.

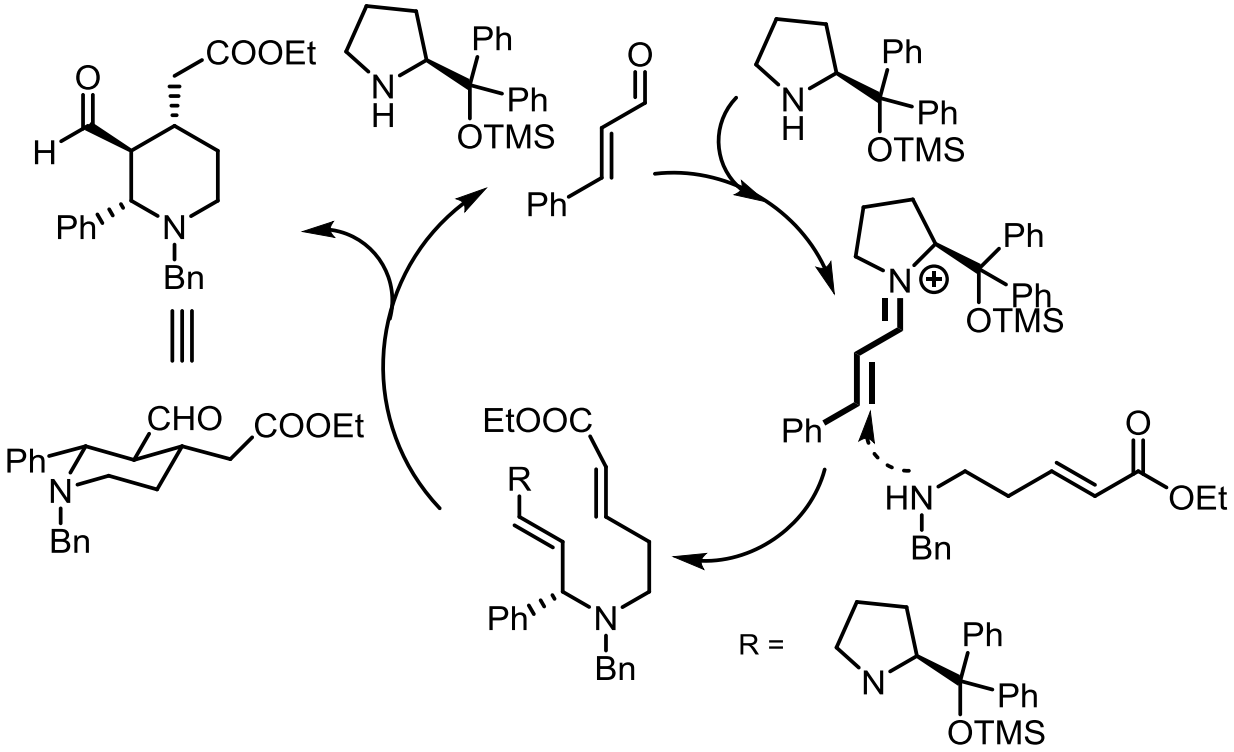
Lanosterooli biosünteesi kaskaad



2,3,4-triasendatud piperidiinide süntees

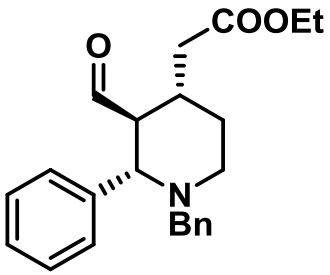


2,3,4-triasendatud piperidiinide süntees: aminokatalüüs

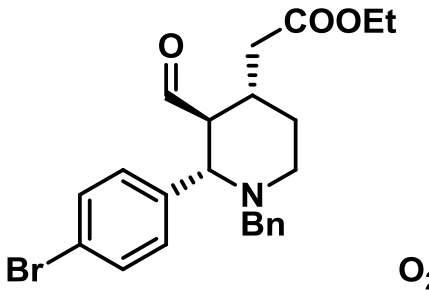


Aminokatalüütilise kaskaadreaktsiooni mehhanism

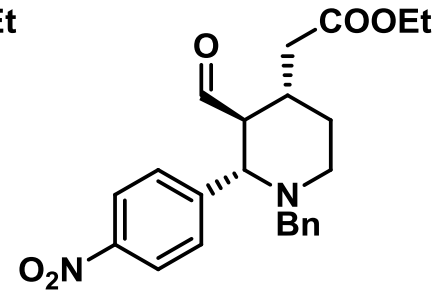
2,3,4-triasendatud piperidiinide süntees: aminokatalüüs



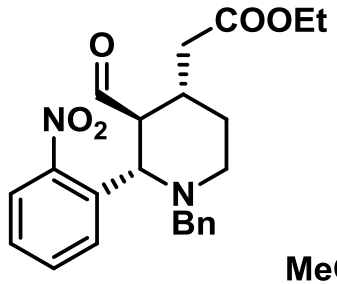
y: 77%
ee 86%



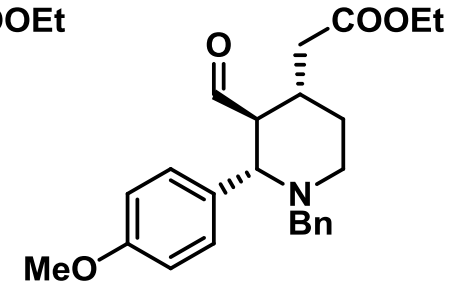
y: 75%
ee 86%



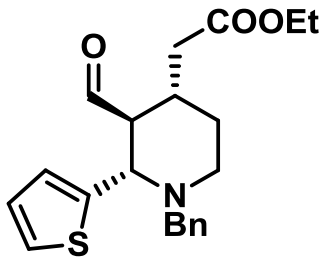
y: 89%
ee 92%



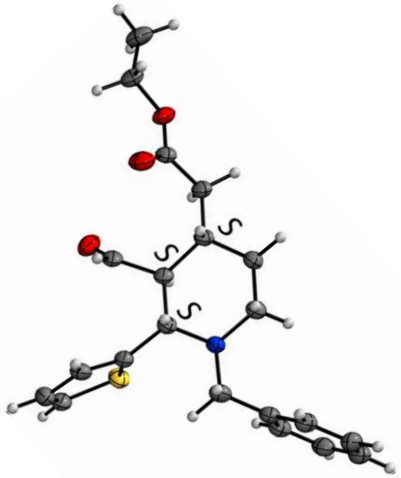
y: 55%
ee 68%



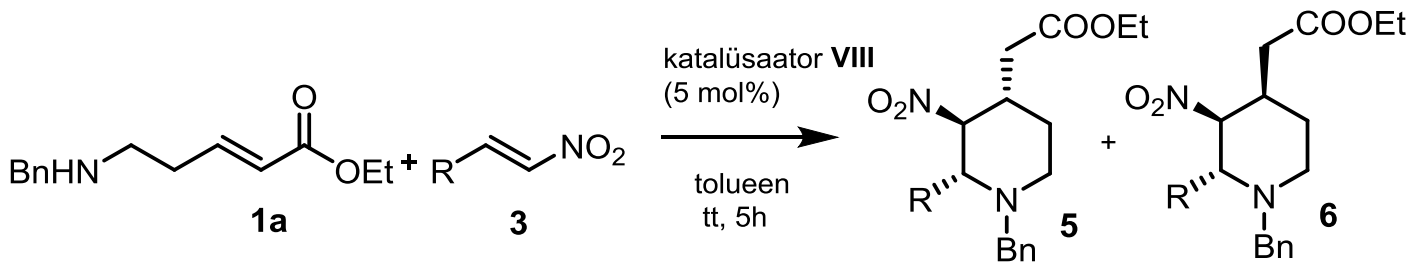
y: 34%
ee 85%

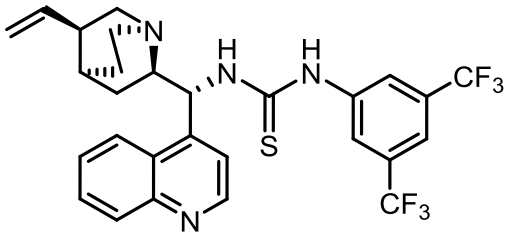


y: 63%
ee 88%



2,3,4-triasendatud piperidiinide süntees: H-sideme katalüüs

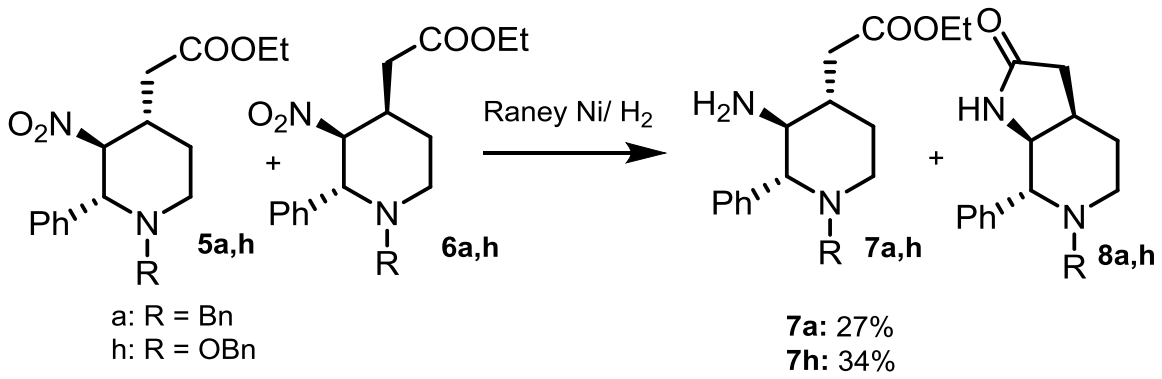




katalüsaator VIII

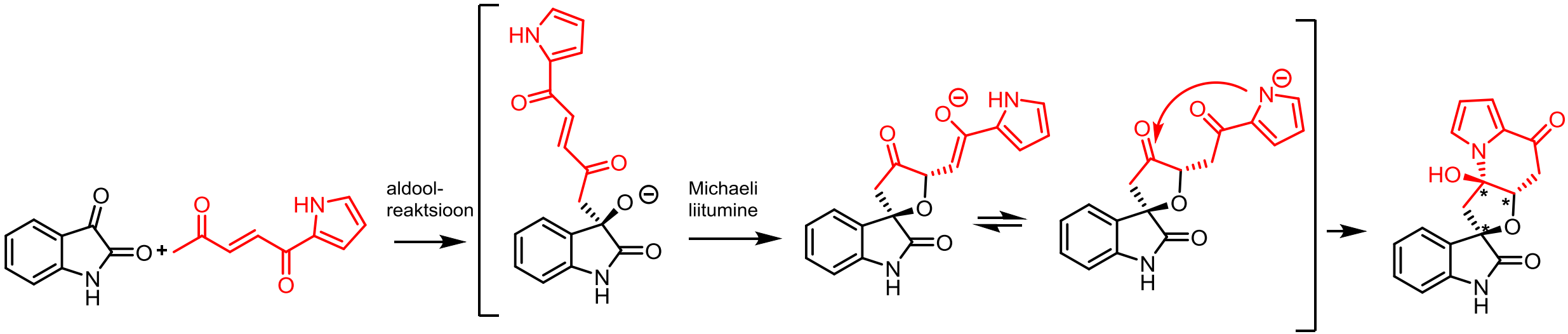
Nr	R	saagis (%)	dr	ee 5/6 (%)
1	a: Ph	95	1.4:1	97/97
2	b: p-MeOPh	89	1.2:1	97/98
3	c: p-F_3COPh	98	1.3:1	85/91
4	d: p-ClPh	79	1.3:1	89/94
5	e: m-MePh	73	1.3:1	n.d.
6	f: p-NO_2Ph	85	1:1	88/93
7	g: thiophen-2-üül	68	1.3:1	96/96

2,3,4-triasendatud piperidiinide süntees: H-sideme katalüüs

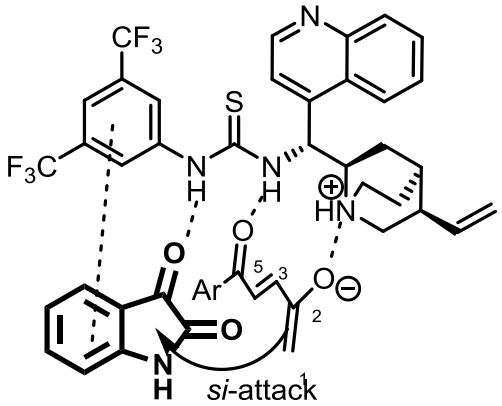


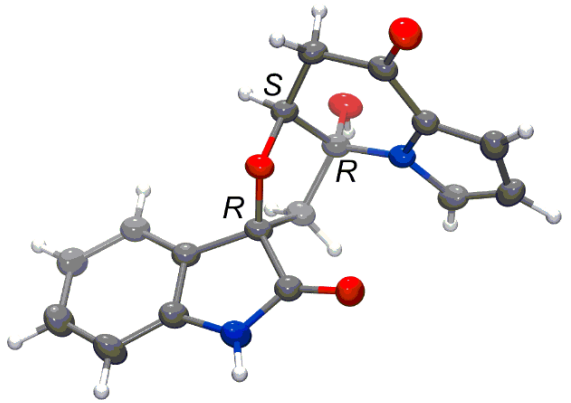
Kriis, K.; Melnik, T.; Lips, K.; Juhanson, I.; Kaabel, S.; Järving, I.; Kanger, T. Asymmetric Synthesis of 2,3,4-Trisubstituted Piperidines. *Synthesis*, **2017**, *49*, 604-614. (**SYNTHESIS Best Paper Award 2017)**

Tetrahüdrofuranüülspirooksindoolide süntees: kolmikkaskaad



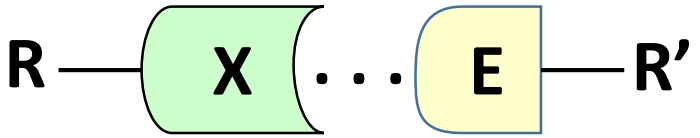
saagis 77%, ee 99%





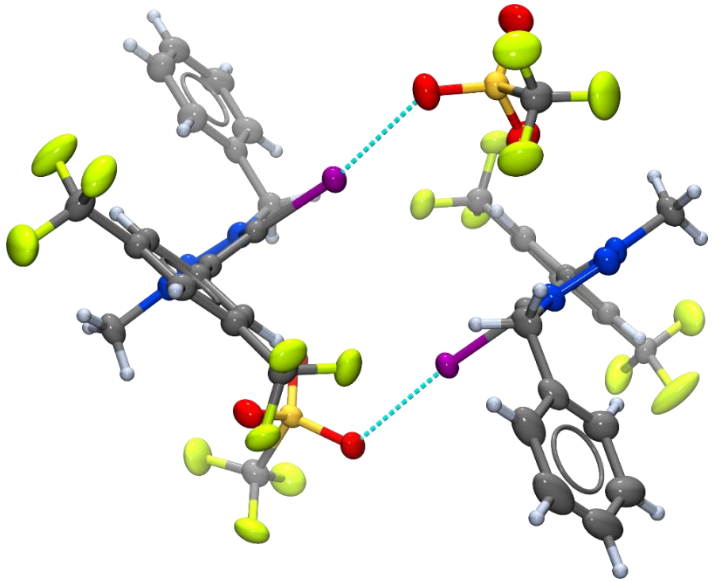
Halogeensideme (XB) katalüüs

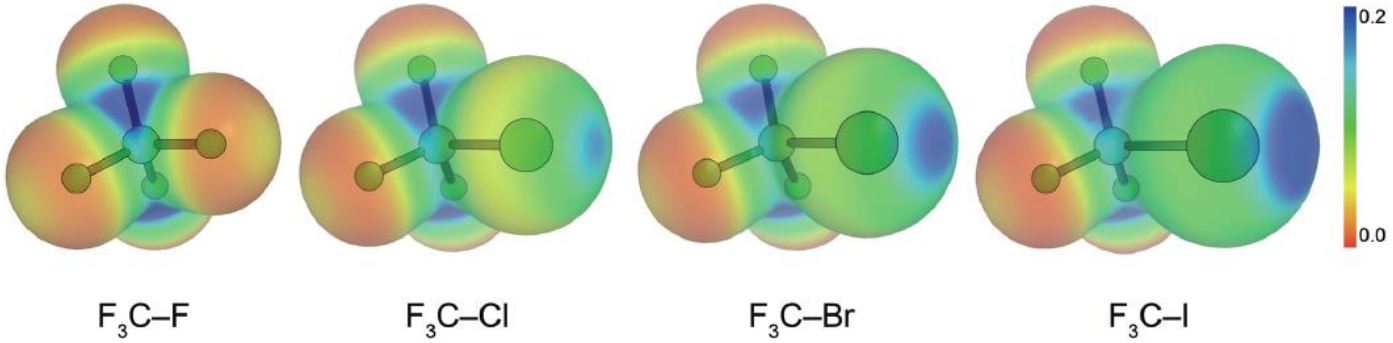
XB-doonor XB-aktseptor

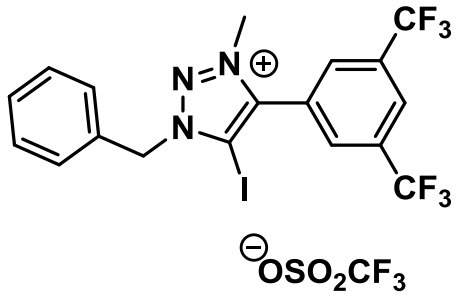


X = I, Br, Cl, F E = doonorne aatom

R = elektronaktseptoorne rühm

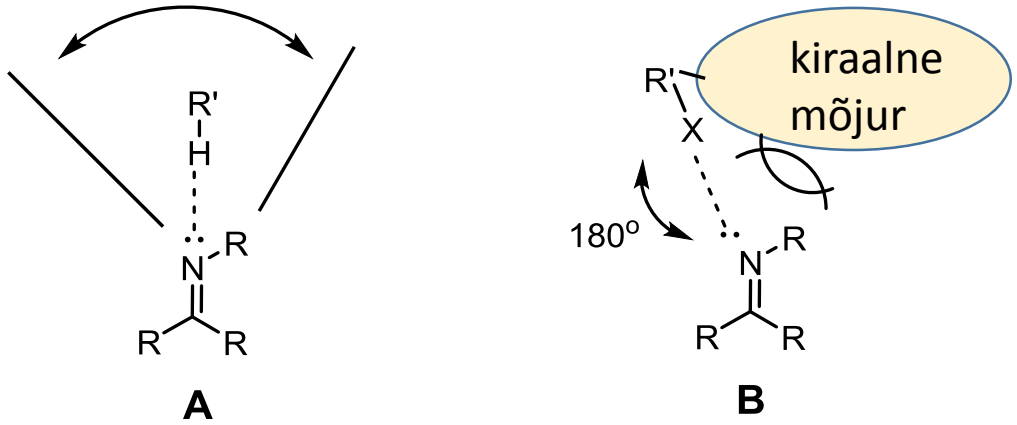




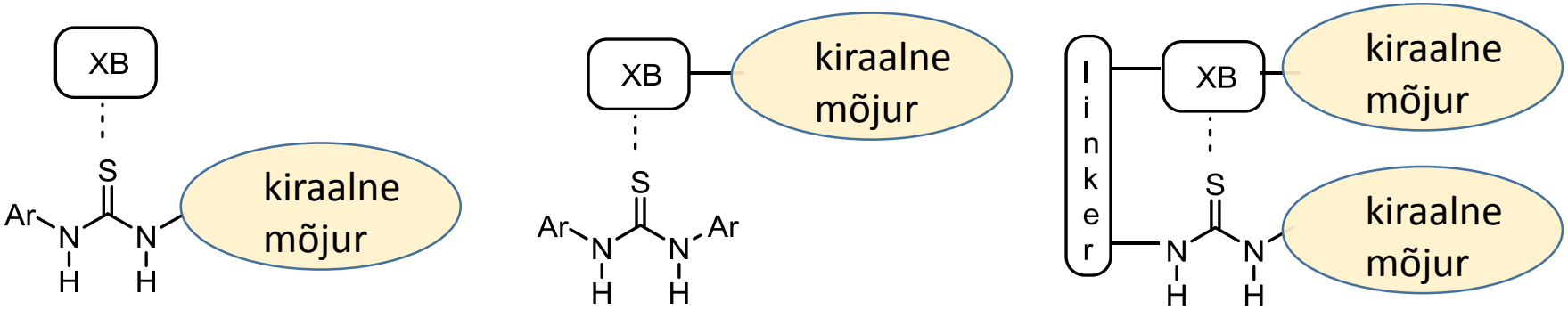


M. Breugst et al. *Synthesis* **2017**; 49, 3224

Halogeensideme (XB) katalüüs

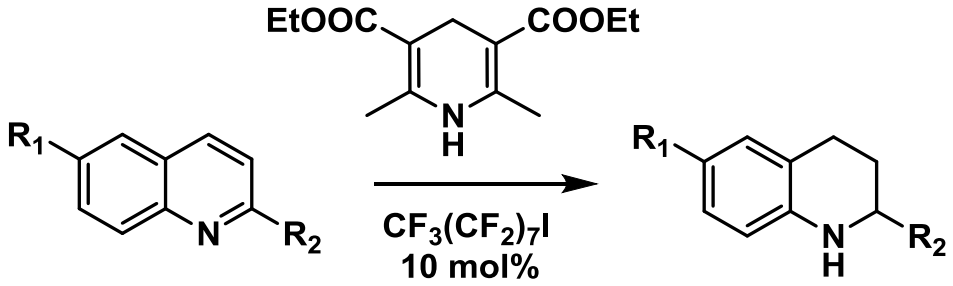


C

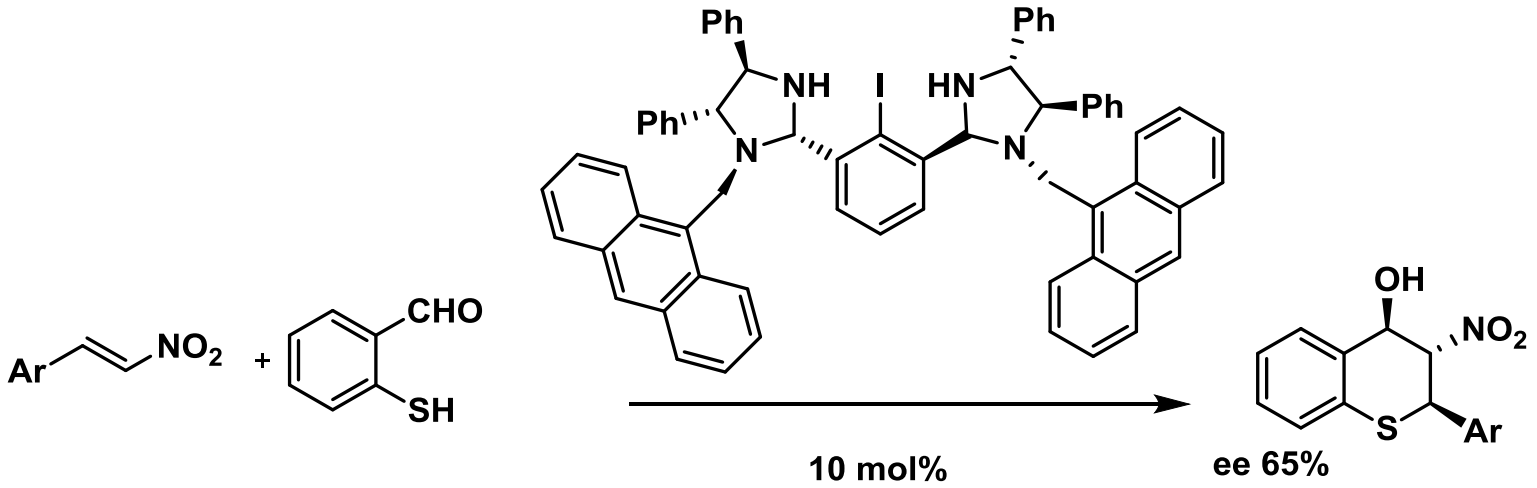


A. H-sideme katalüüs; B: XB-katalüüs; C. Kokatalüüs

XB-katalüüs

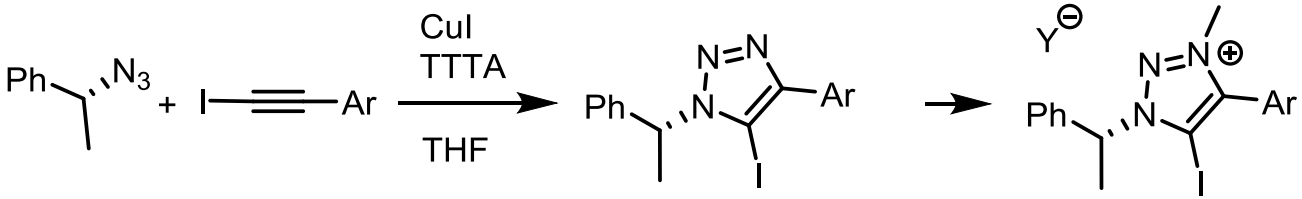


Bolm, C. *et al. Synlett* **2008**, *6*, 900



Arai, T. *et al. Synlett* **2017,** *28*, 122

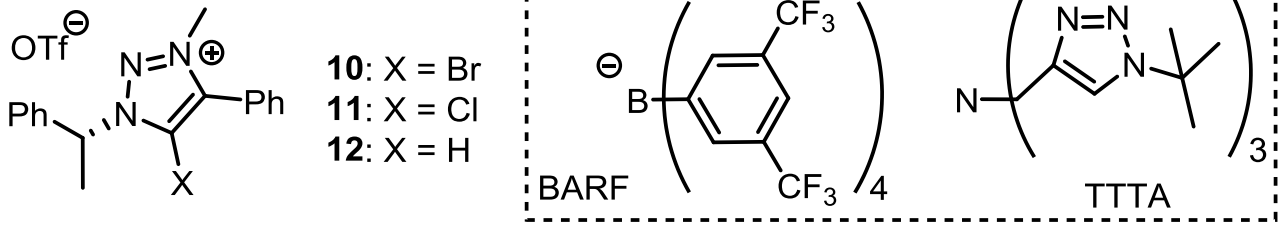
Halogeensideme doonorite süntees



4 **5**

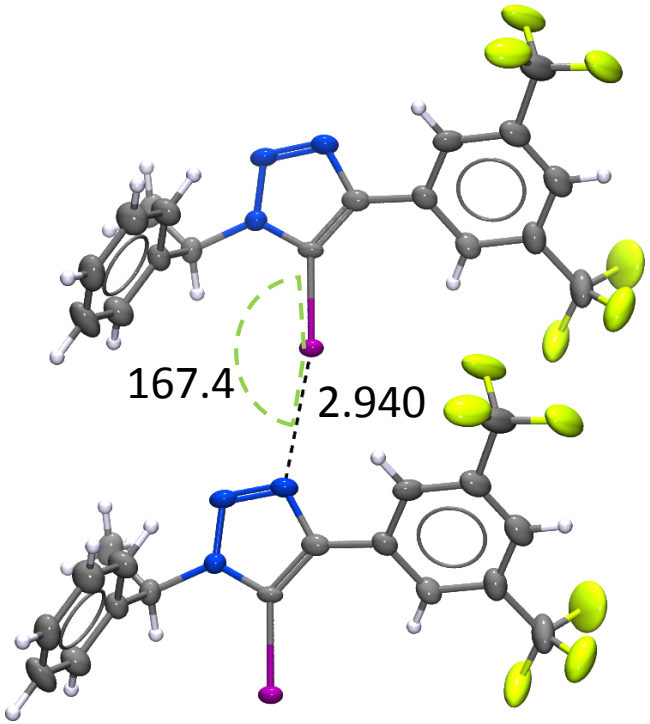
6(a-d)
a: Ar = Ph
b: Ar = C_6F_5
c: Ar = 4-NO_2-C_6H_4
d: Ar = 3,5-$(CF_3)_2$-C_6H_3

7(a-d): Y = OTf
8(a;c): Y = BF_4
9a: Y = BARF

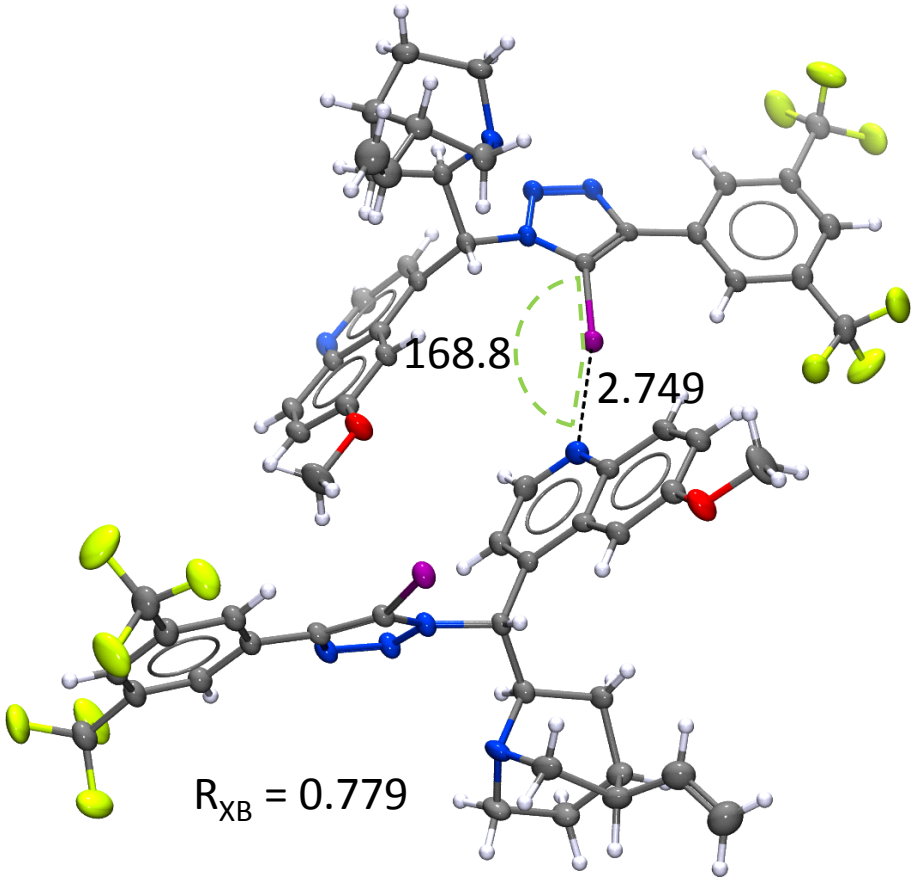


10: X = Br
11: X = Cl
12: X = H

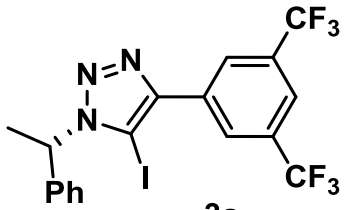
Halogeenside tahkes faasis



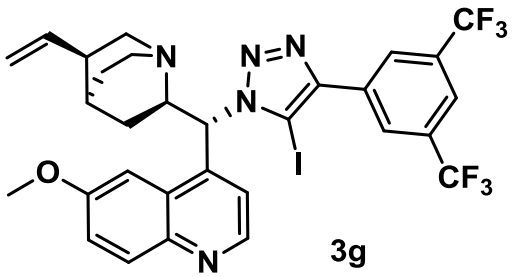
R_{XB} = 0.833



R_{XB} = 0.779

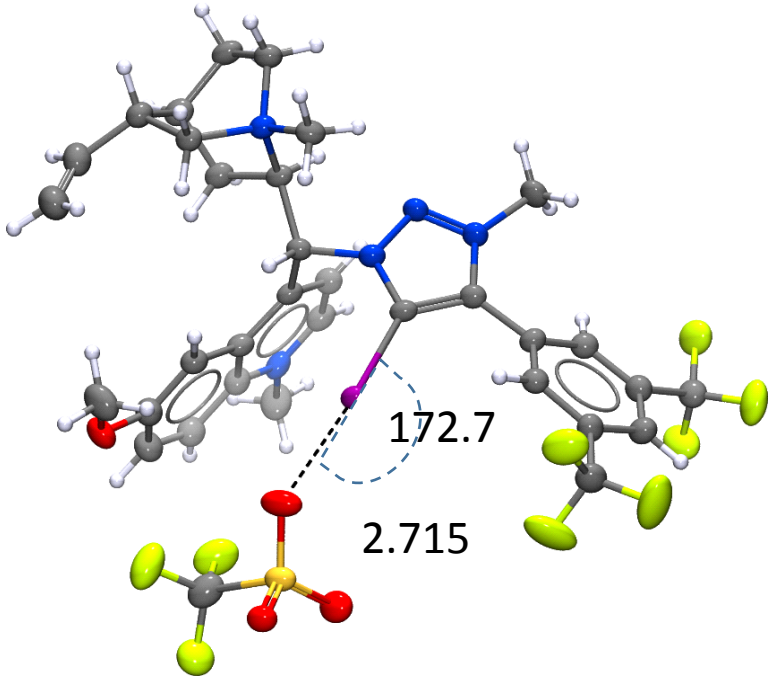


3a

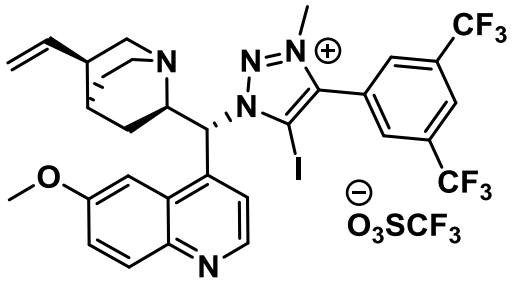


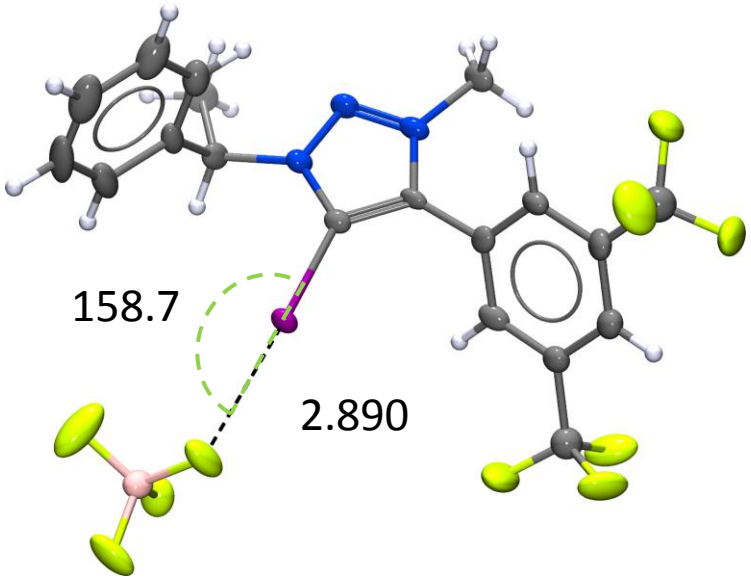
3g

Halogeenside tahkes faasis



R_{XB} = 0.776





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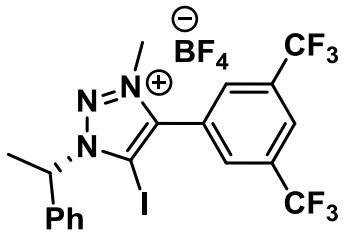
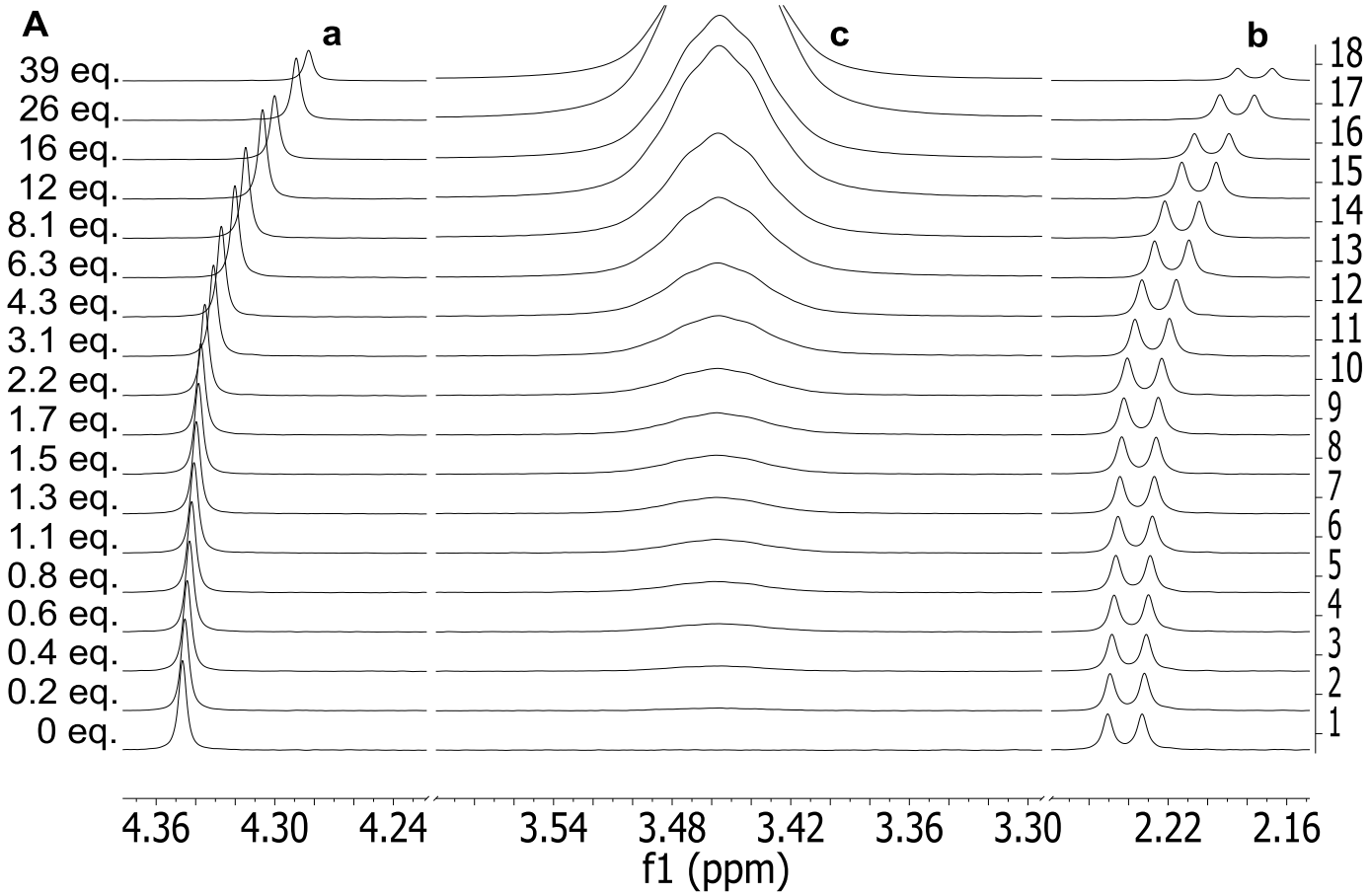
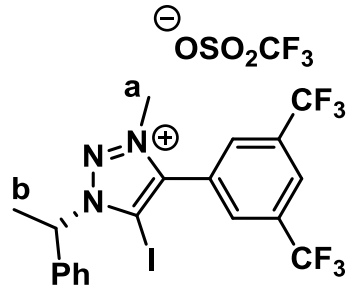
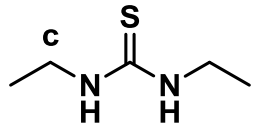


Halogeenside lahuses

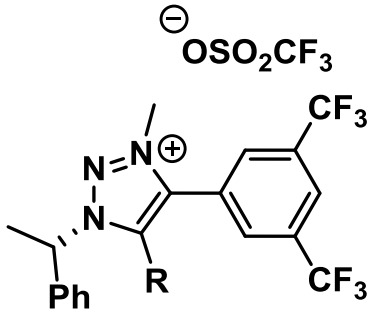




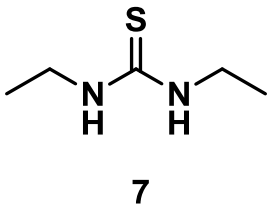


Halogeenside lahuses

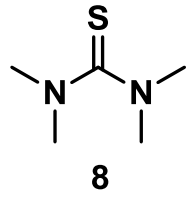
XB doonor	XB aktseptor	$K_A[M^{-1}]$
4a	**7**	42
4b	**7**	11
4c	**7**	29
4a	**8**	12
4b	**8**	0.1
4c	**8**	0.05
4k	**7**	-



4a: R = I
4b: R = Br
4c: R = Cl
4k: R = H

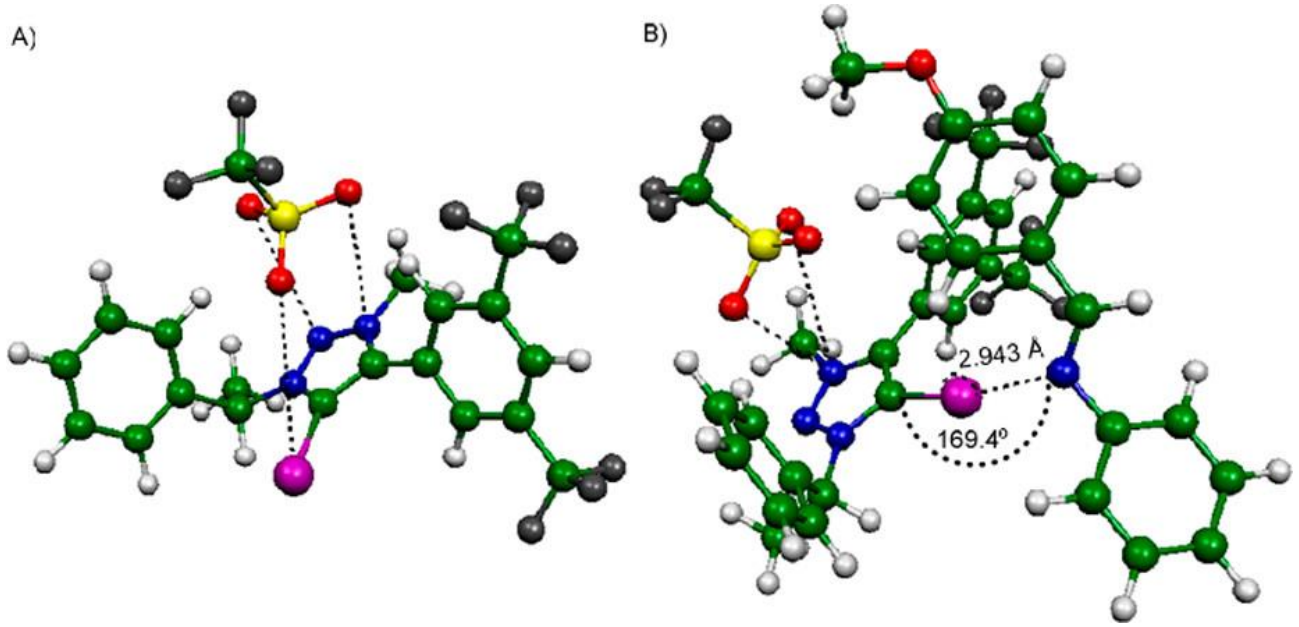


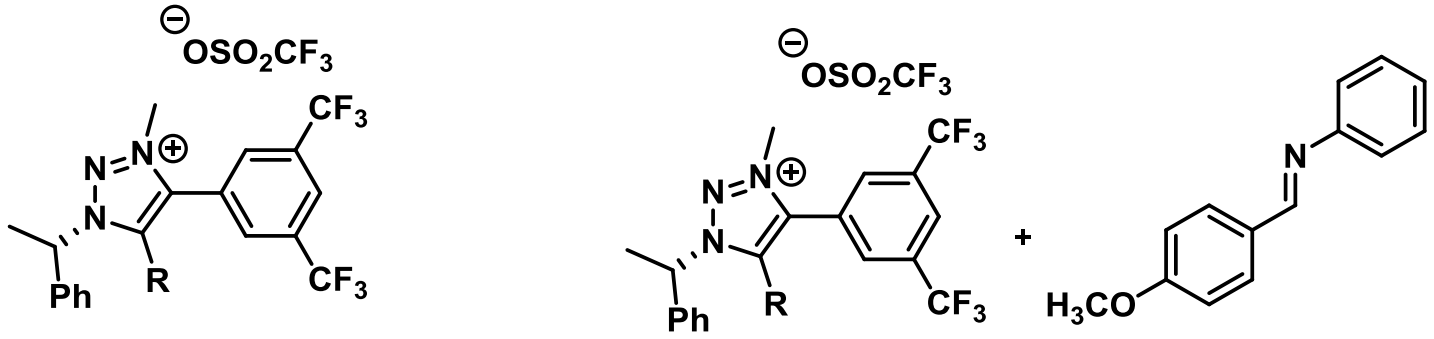
7



8

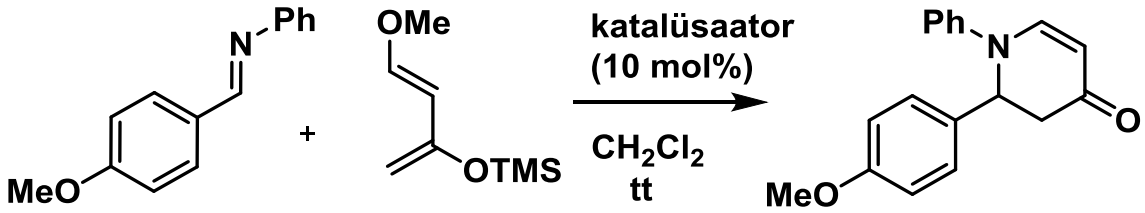
Konformatsioonanalüüs



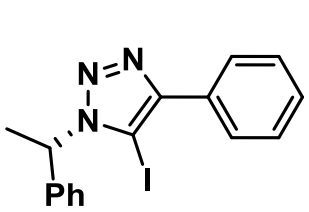


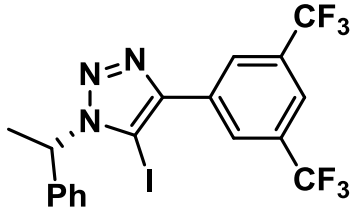
DFT arvutustega leitud kõige stabiilsemad konformatsioonid

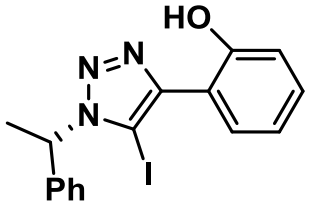
XB-katalüüs



Elektroneutraalsed katalüsaatorid

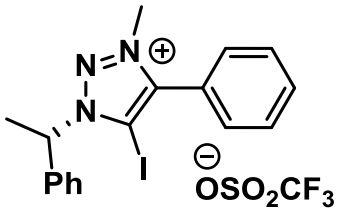


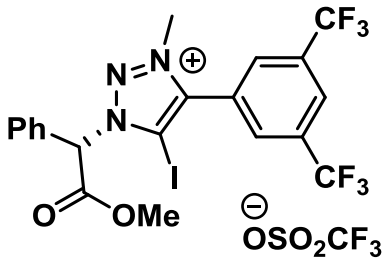


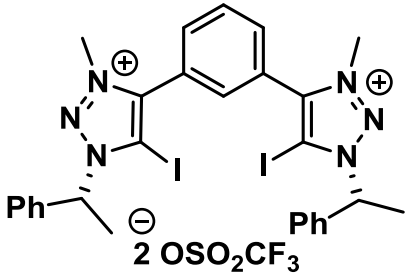


Reaktsiooni ei toimunud

Triasooliumsoolad

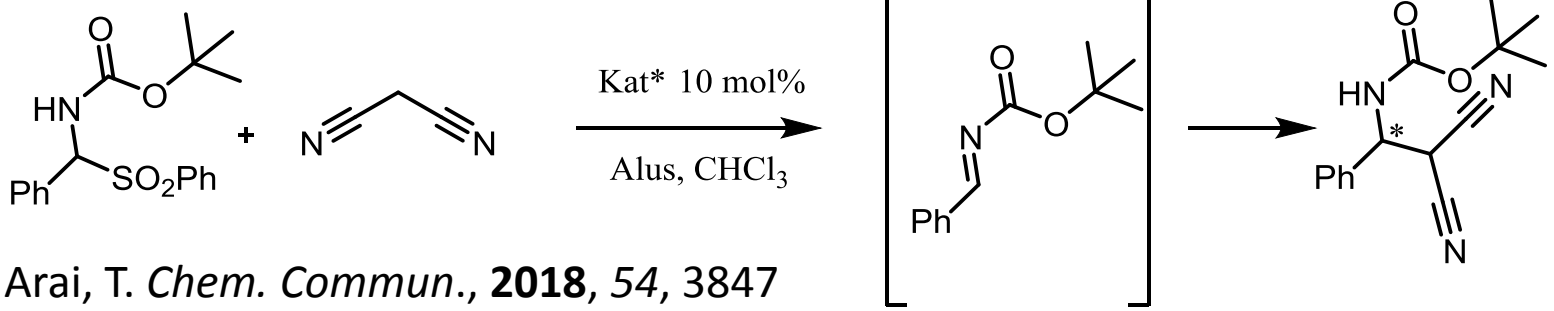






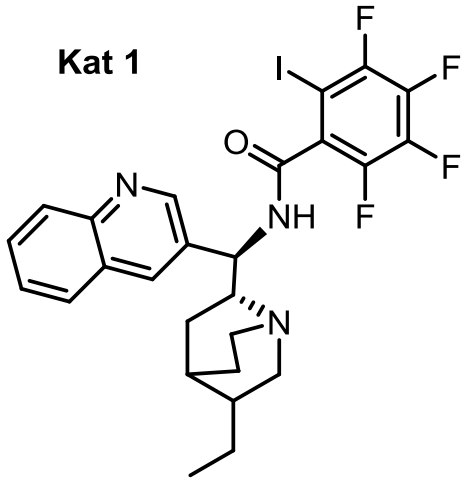
100% konversioon 1-2 tunniga. Produkt ratseemiline

XB-katalüüs



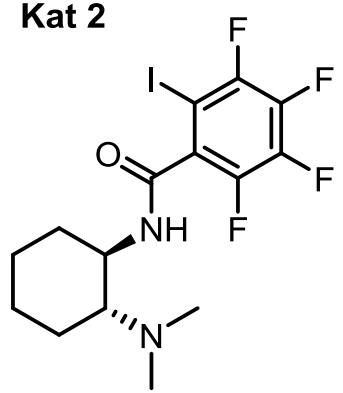
Arai, T. *Chem. Commun.*, **2018**, *54*, 3847

Kat 1



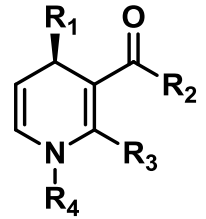
Katse	Kat.	Alus, Temp.	Saagis %	ee %
1	Kat 1	Na_2CO_3, rt	86	86
2	Kat 2	Na_2CO_3, rt	88	76

Kat 2

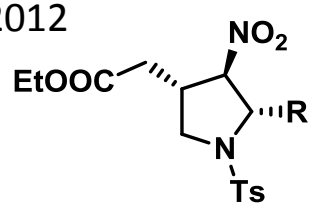


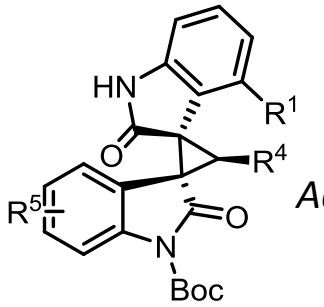
Kaksikkaskaadid

J. Org. Chem. 2011



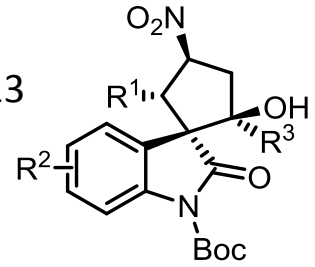
Tetrahedron: Asymmetry 2012

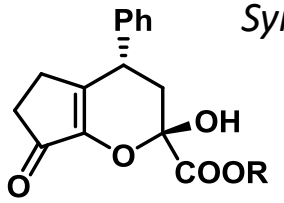




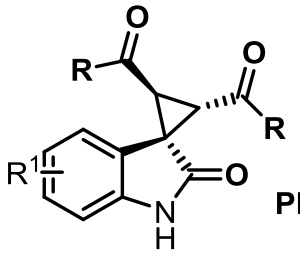
Adv. Synth. Cat. 2013

J. Org. Chem. 2013

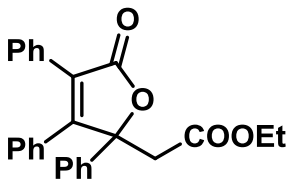




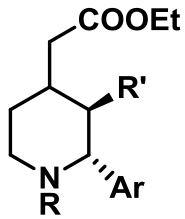
Synthesis 2015



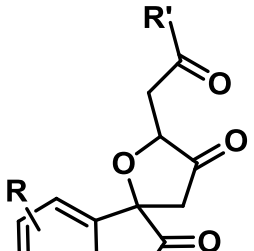
Eur. J. Org. Chem. 2014



Chem. Heterocycl. Comp. 2018

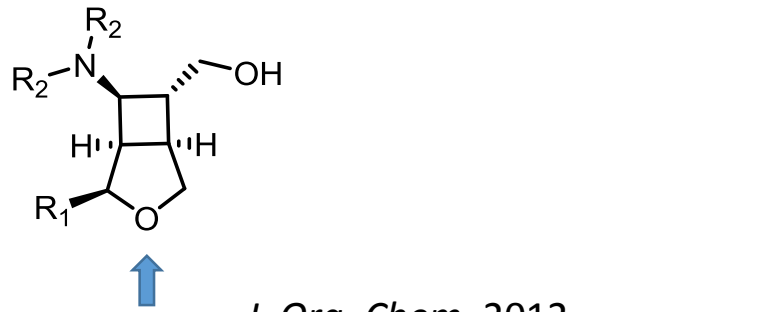


Synthesis 2017

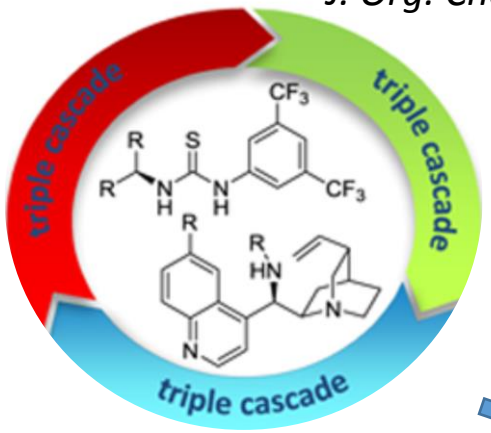


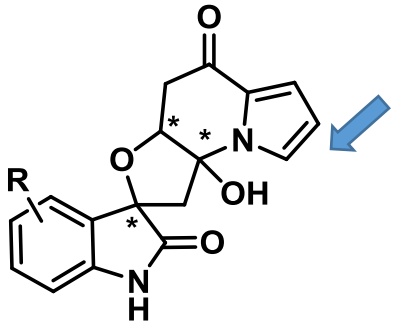
Synthesis 2018

Kolmikkaskaadid

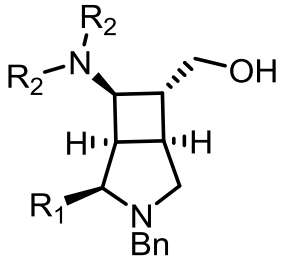


J. Org. Chem. 2012



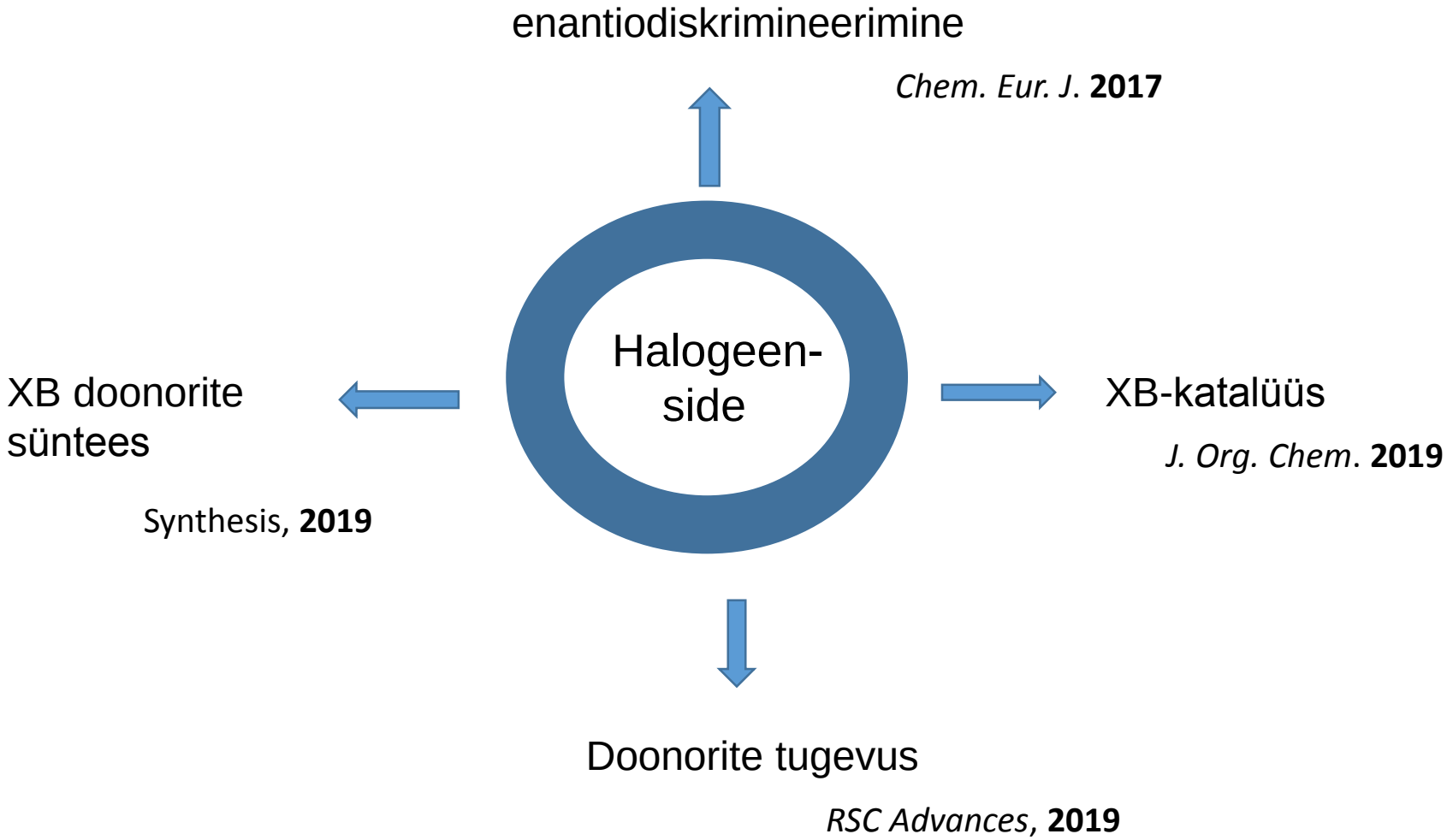


Synthesis 2018



Org. Lett. 2010

Halogeensideme uurimine



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