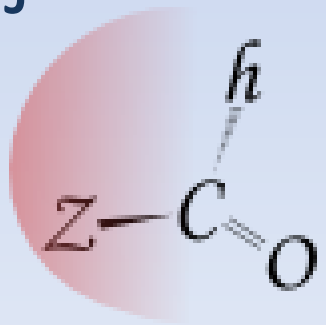
SYNTEZA ASYMETRYCZNA

Dr inż. Tomasz Rowicki

ZAKŁAD CHEMII ORGANICZNEJ



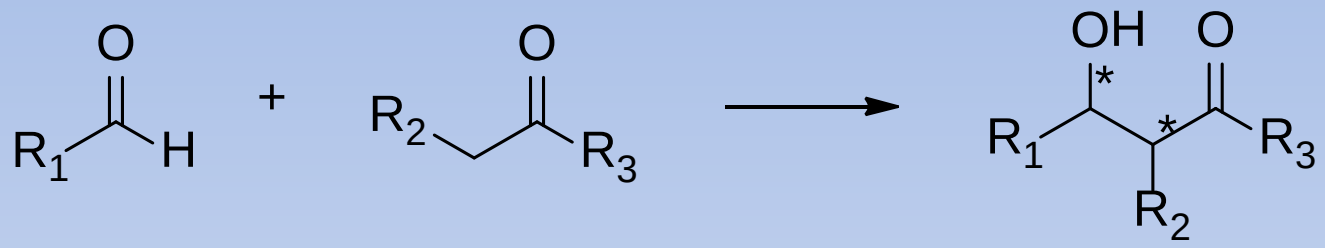
Konsultacje: pon. 14^{15}-16^{00}, pok. 135, G.Ch.

Zagadnienia na dziś

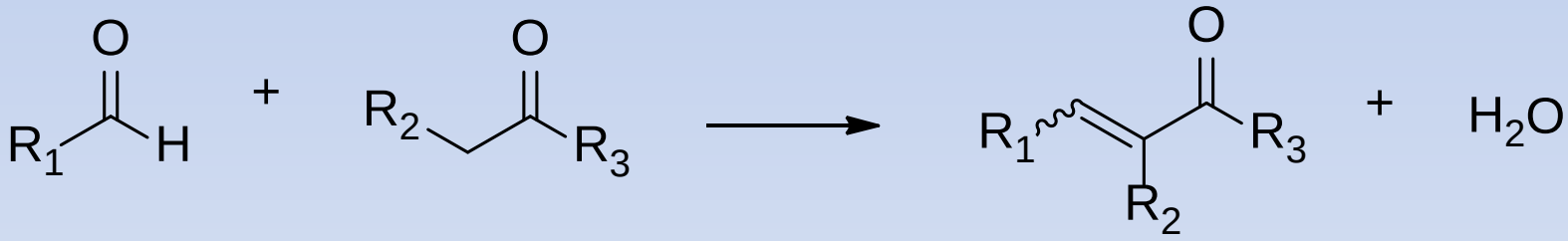
1. Reakcja aldolowa
2. Reakcja aldolowa Mukaiyamy
3. Reakcja aldolowa-Tishchenko
4. Reakcja Mannicha
5. Reakcja Michaela
6. Kaskady reakcji

Reakcja vs kondensacja aldolowa

Reakcja aldolowa

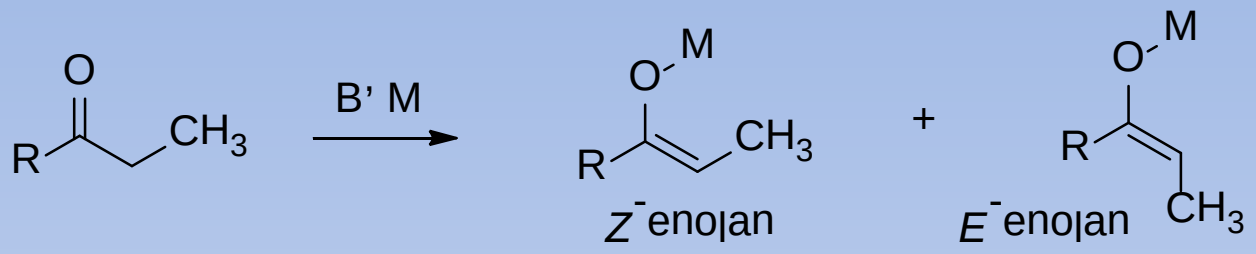


Kondensacja aldolowa

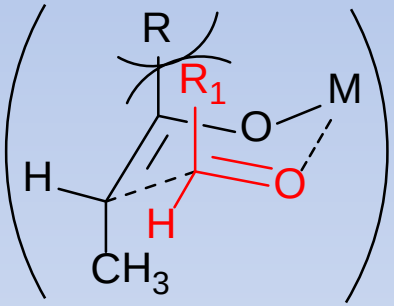


W przypadku jakiejkolwiek KONDENSACJI jednym z produktów jest cząsteczka prostego związku nieorganicznego lub organicznego (woda, alkohol).

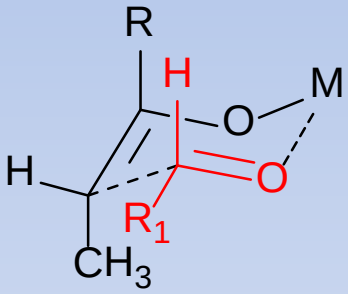
Geometria enolanów



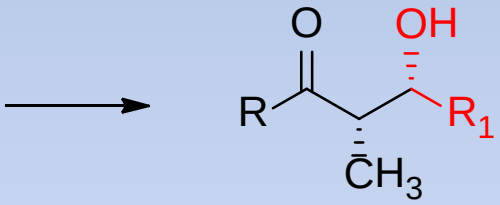
Z-enolany



niefaworyzowany

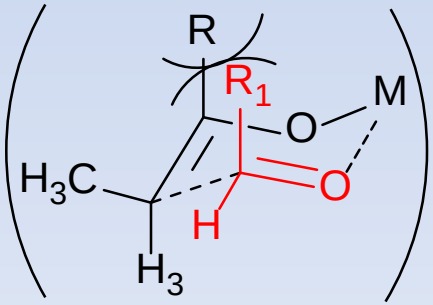


faworyzowany

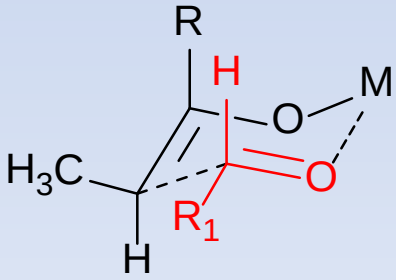


produkt 1,2-*syn*

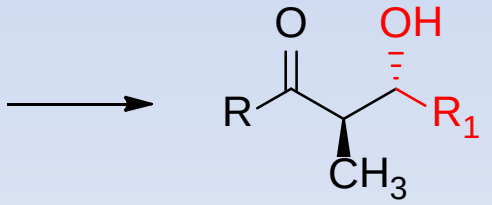
E-enolany



niefaworyzowany

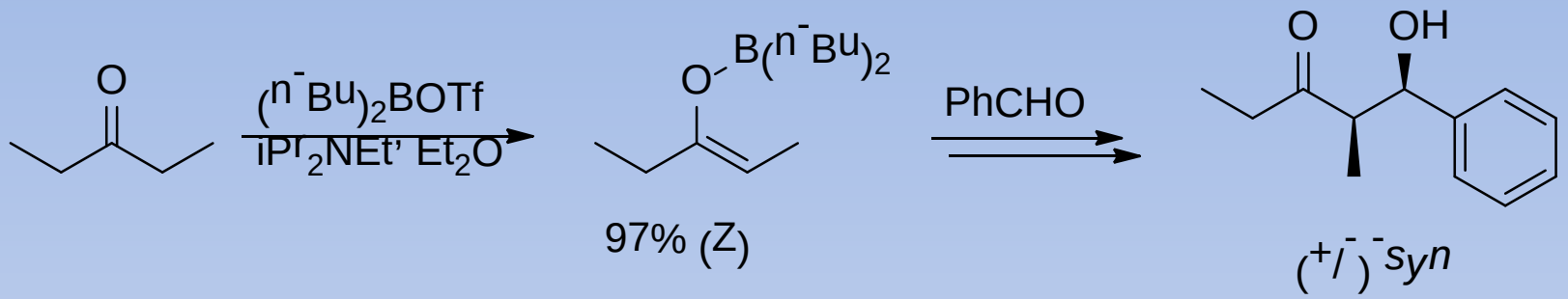


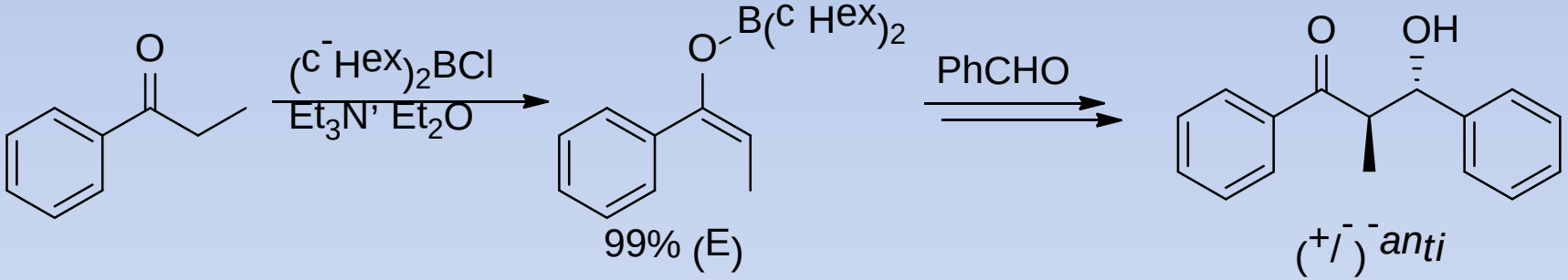
faworyzowany

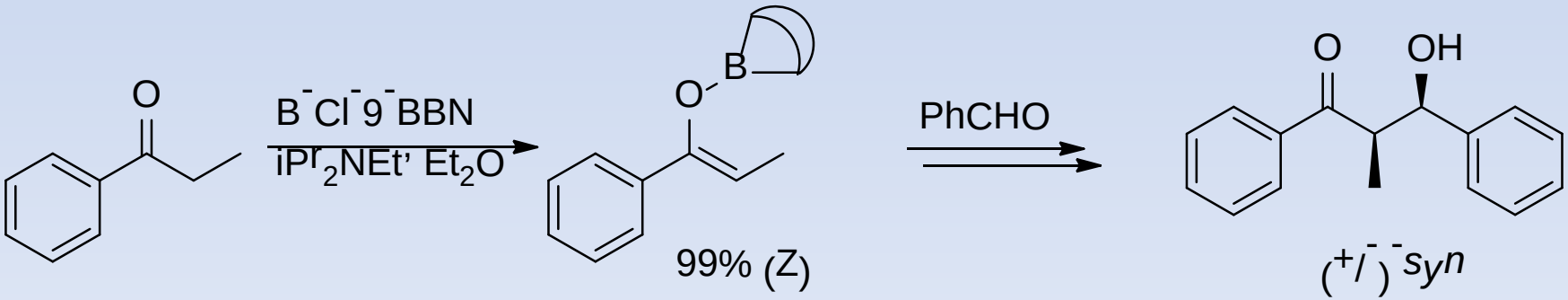


produkt 1,2-*anti*

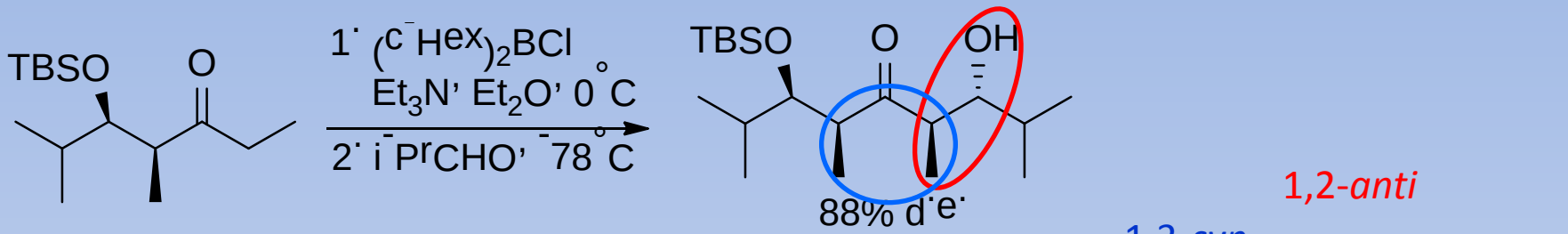
Geometria enolanów

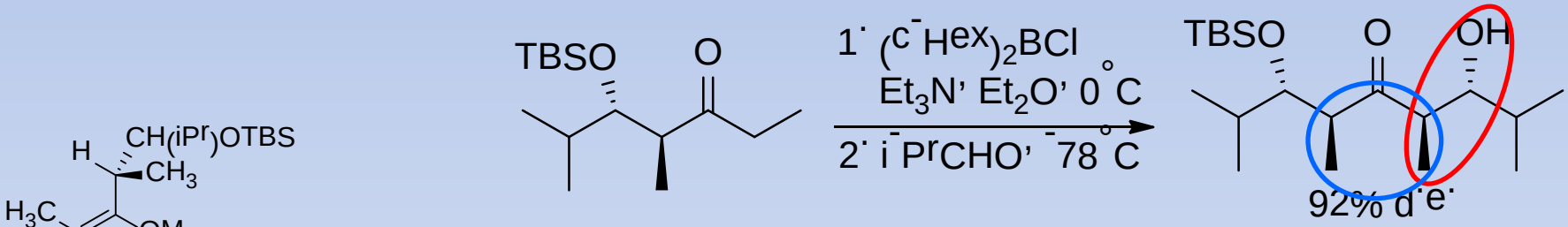




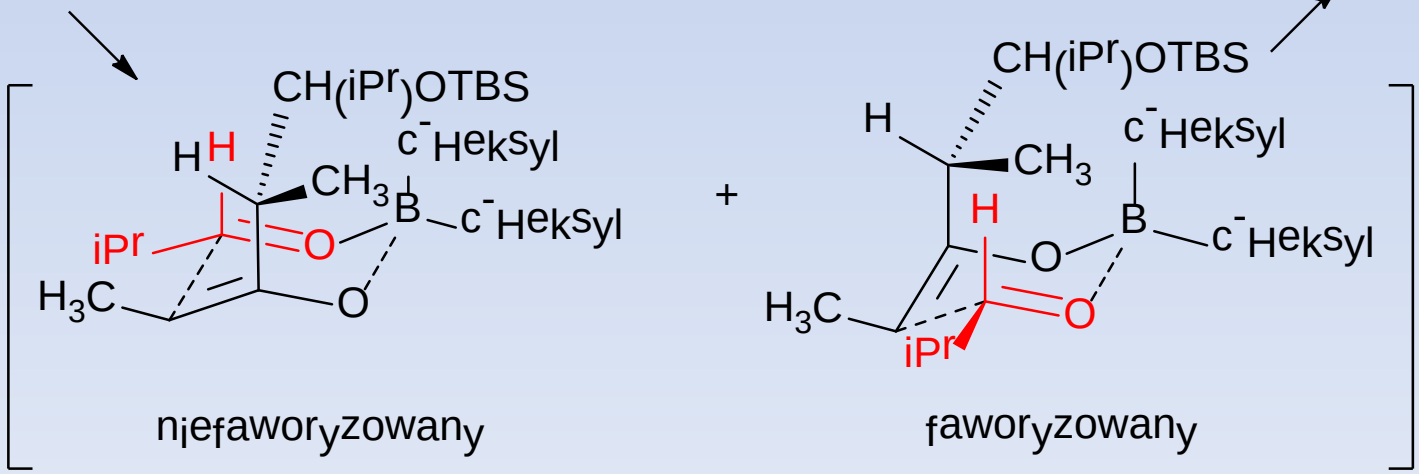


Reakcja aldolowa - centrum chiralności w enolanie





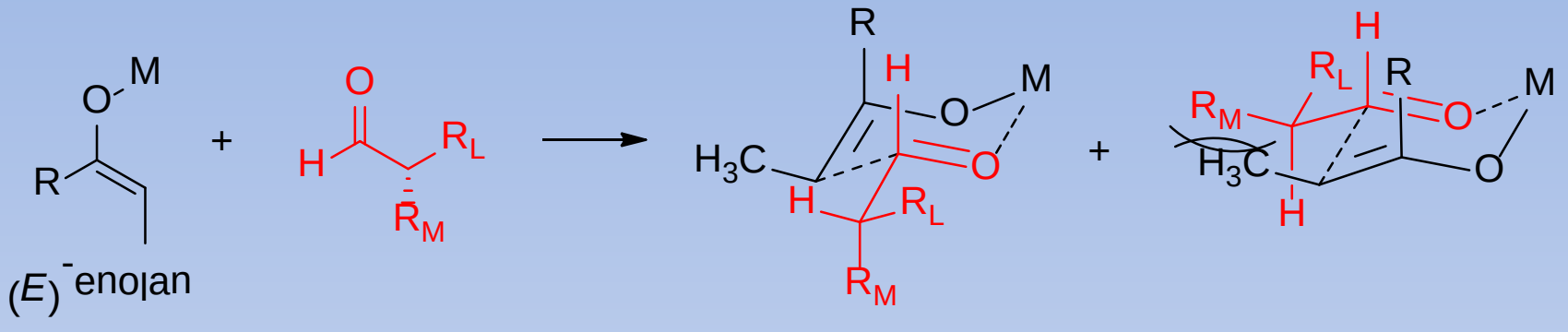
E-enolan



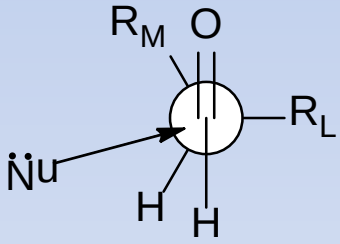
niefaworyzowany

faworyzowany

Reakcja aldolowa - centrum chiralności w akceptorze

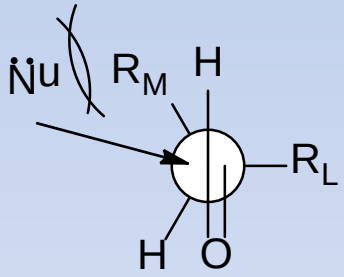


1. Zgodny z modelem Felkina-Ahna

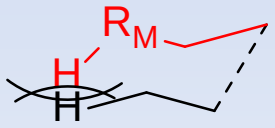


2. Brak zawad sterycznych

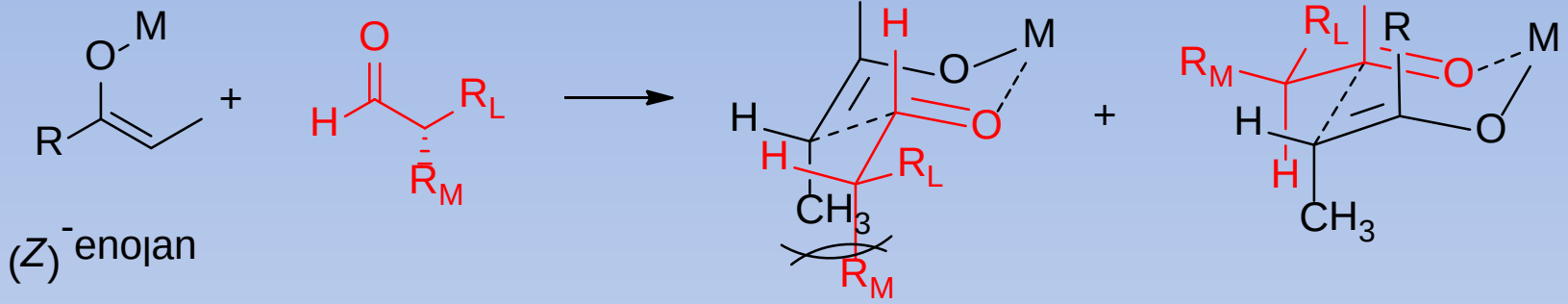
1. Niezgodny z modelem Felkina-Ahna



2. Konformacja syn-pentanu – zawada steryczna



Reakcja aldolowa - centrum chiralności w akceptorze

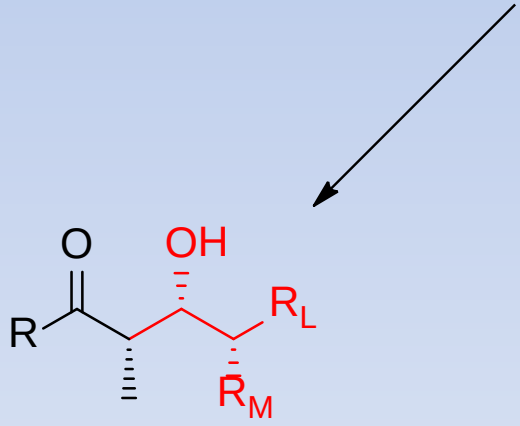


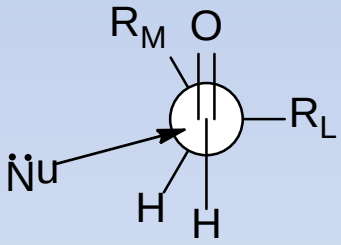
NIEFAWORYZOWANY

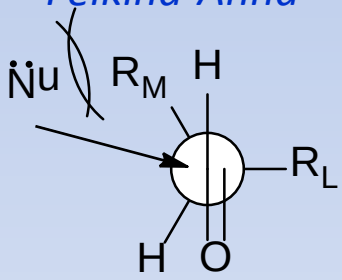
1. Zgodny z modelem Felkina-Ahna

FAWORYZOWANY

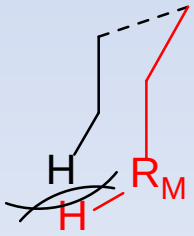
1. Niezgodny z modelem Felkina-Ahna





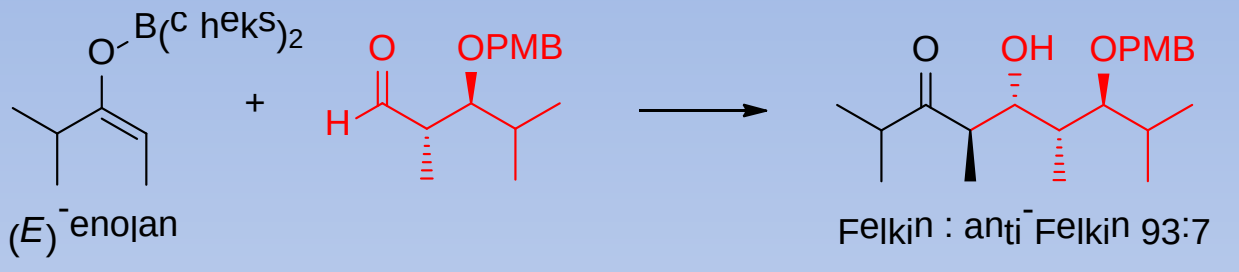


2. Konformacja syn-pentanu – zawada steryczna



2. Brak innych zawad sterycznych

Reakcja aldolowa - centrum chiralności w akceptorze

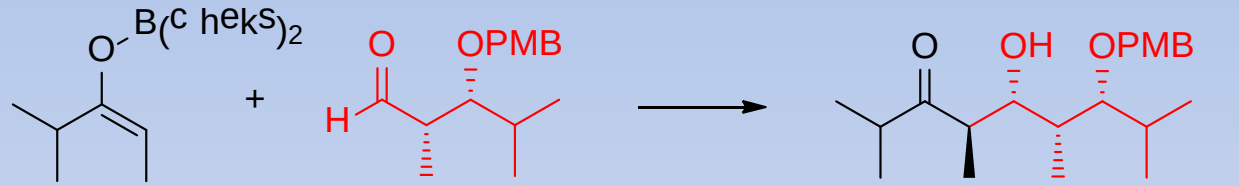


(*E*)-enolan

Felkin : anti-Felkin 93:7

(*E*)-enolany

Wysoka selektywność zgodna z modelem Felkina-Ahna

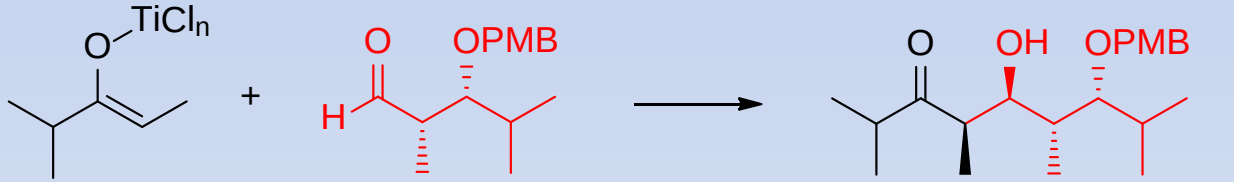


(*E*)-enolan

Felkin : anti-Felkin 74:26

(*Z*)-enolany

Umiarkowana selektywność przeciwna do modelu Felkina-Ahna



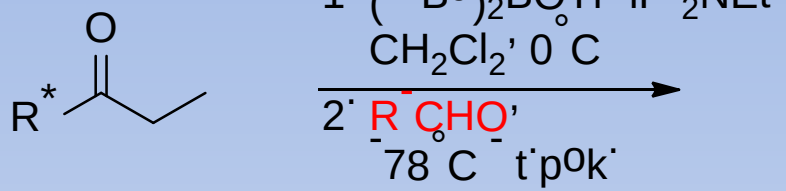
(*Z*)-enolan

Felkin : anti-Felkin 23:77

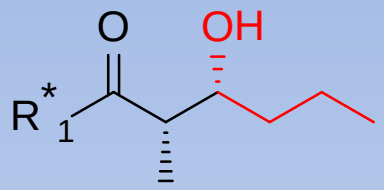
(*Z*)-enolan

Felkin : anti-Felkin 44:56

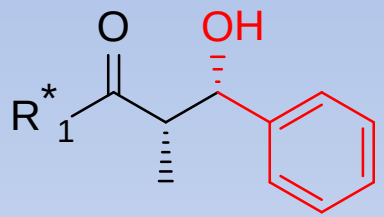
Chiralne pomocniki w r. aldolowej



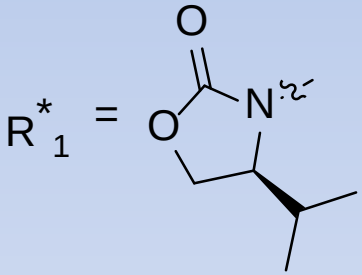
d.r.



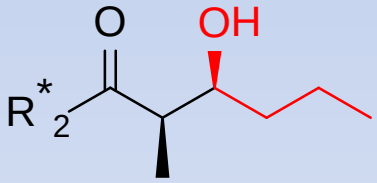
141:1



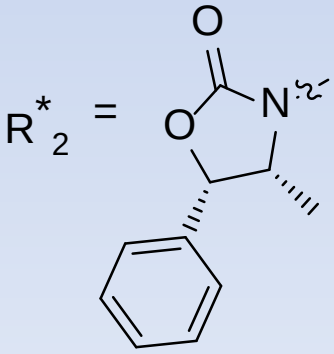
>500:1

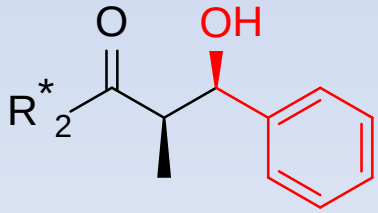


d.r.



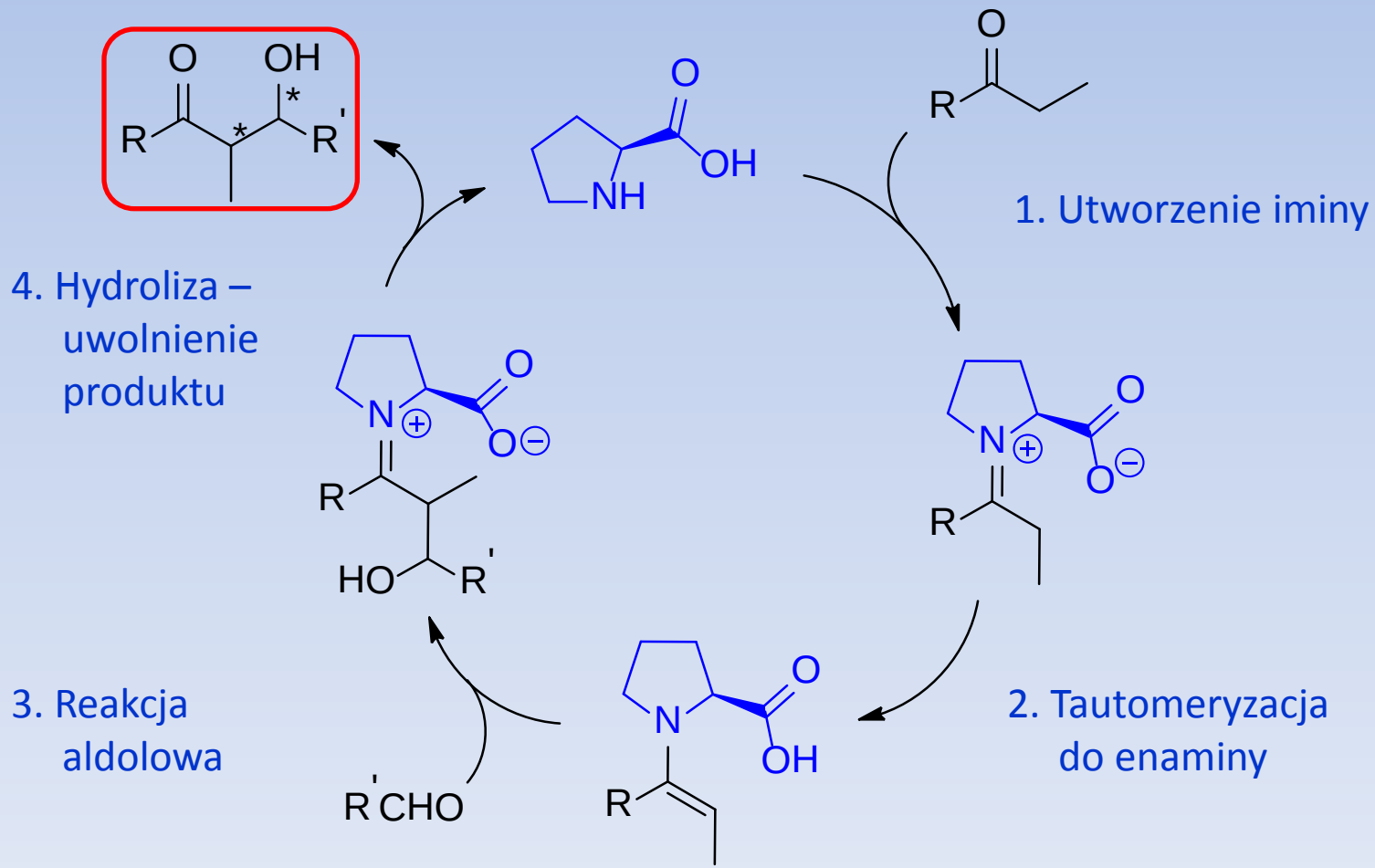
>500:1



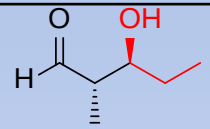
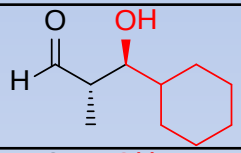
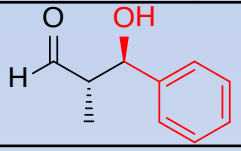
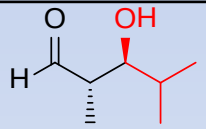
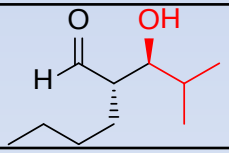
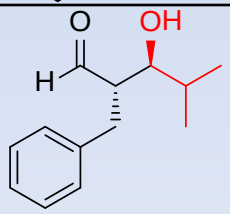


>500:1

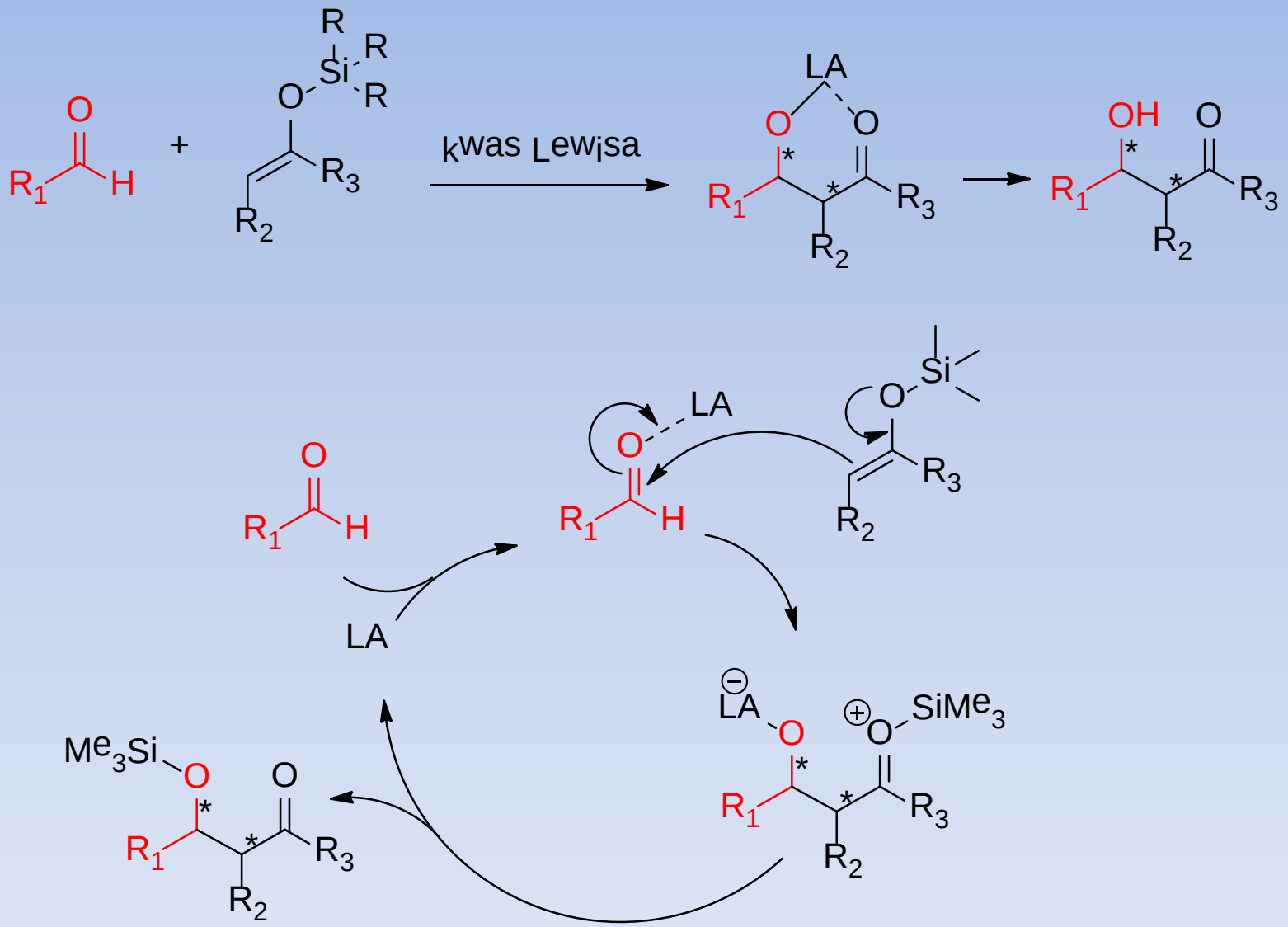
Bezpośrednia reakcja aldolowa



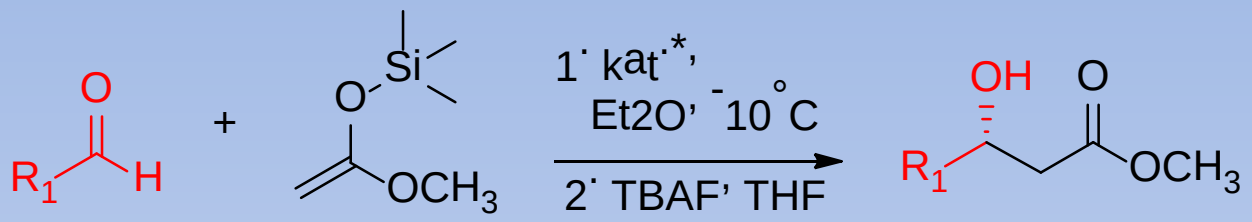
Bezpośrednia reakcja aldolowa

R1	R2	Produkt	anti : syn	e.e. [%]
Me	Et		4 : 1	99
Me	c-C_6H_{11}		14 : 1	99
Me	Ph		3 : 1	99
Me	^{i}Pr		24 : 1	>99
n-Bu	^{i}Pr		24 : 1	98
Bn	^{i}Pr		19 : 1	91

Reakcja aldolowa Mukaiyamy

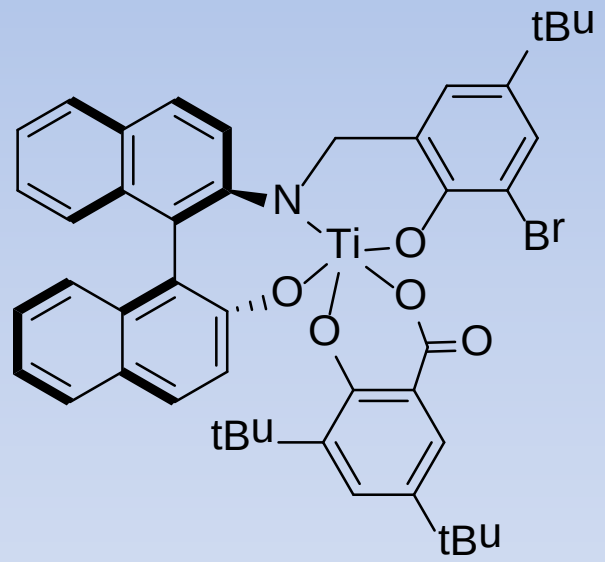


Reakcja aldolowa Mukaiyamy

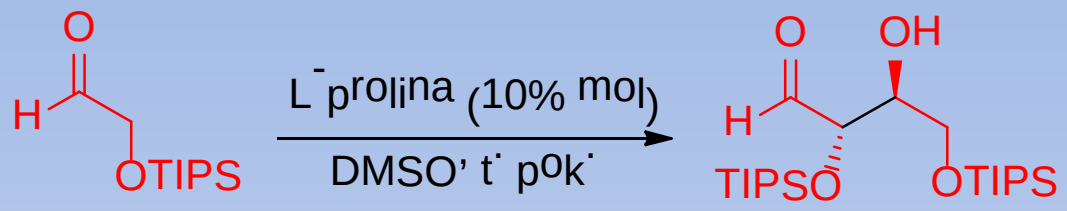


R	e.e. [%]
(*E*)-CH_3CH=CH	97
n-Pr	95
(*E*)-PhCH=CH	97
$PhCH_2CH_2$	94
C_6H_{11}	95
Ph	96

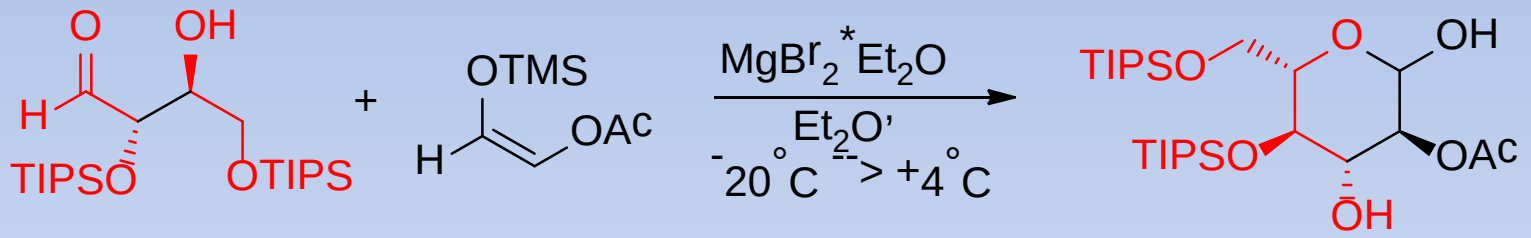
kat˙* =



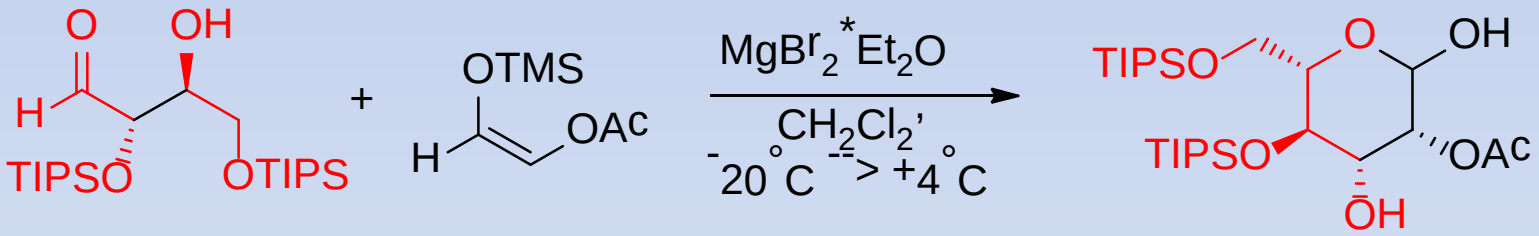
Reakcja aldolowa Mukaiyamy



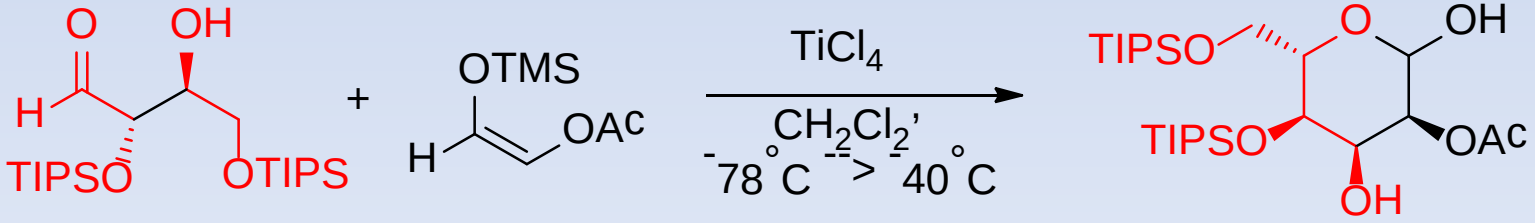
wyd. 92%,
d.r. 4:1,
e.e. 95%



glukoza
wyd. 79%,
d.r. 10:1,
e.e. 95%

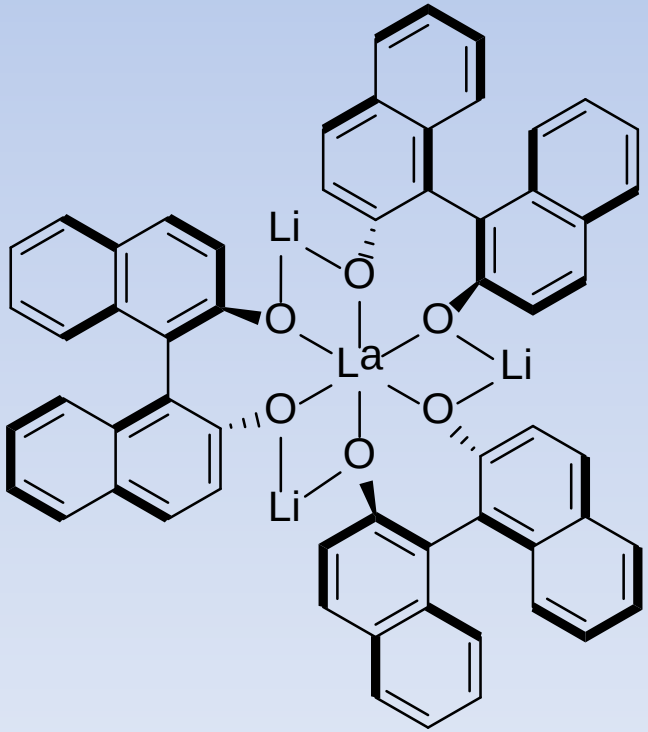


mannoza
wyd. 87%,
d.r. >19:1,
e.e. 95%



alloza
wyd. 97%,
d.r. >19:1,
e.e. 95%

Asymetryczna r. aldolowa-Tishchenko

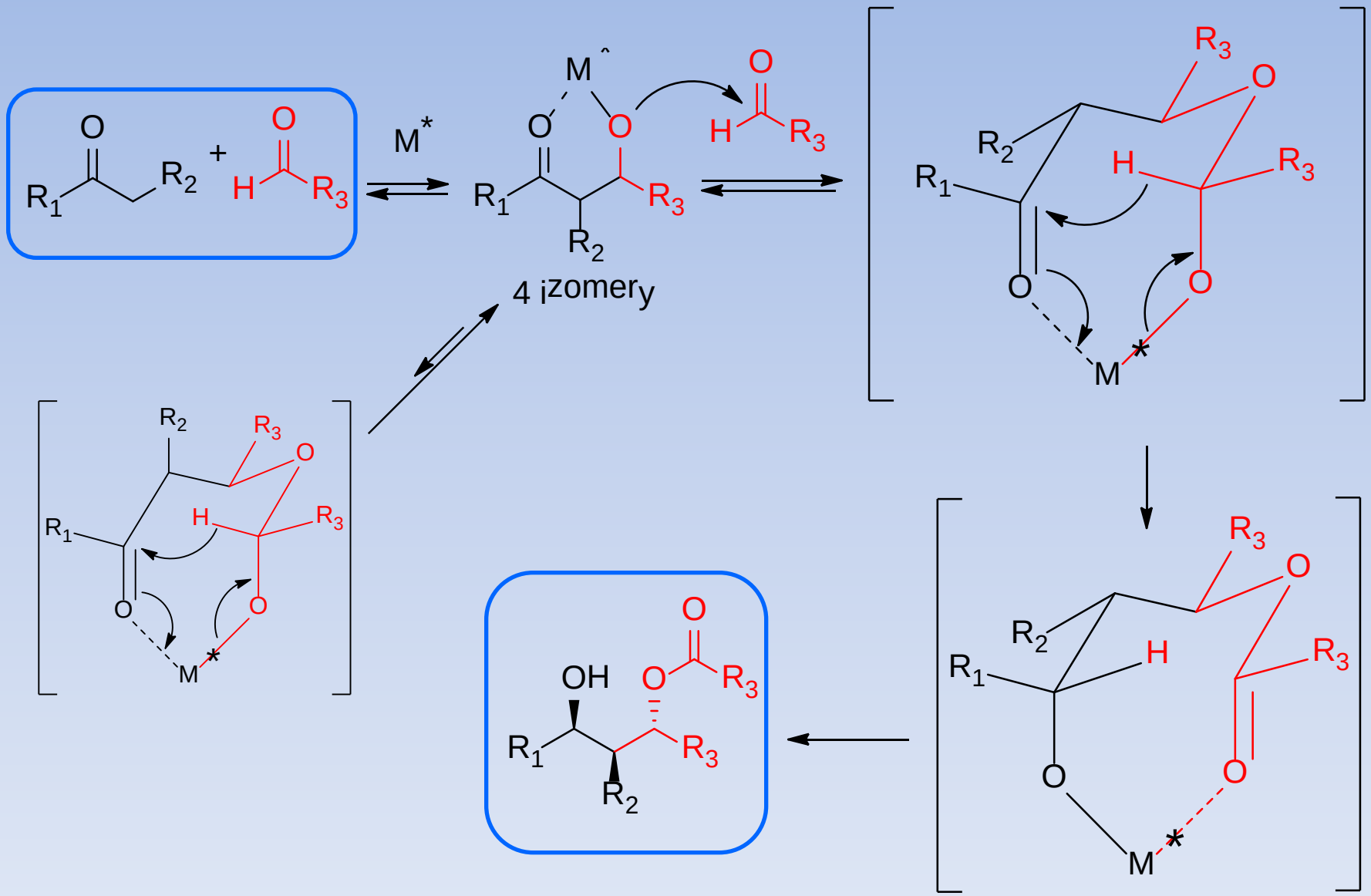


$La(OTf)_3$ + (*R*)-BINOL + $BuLi$

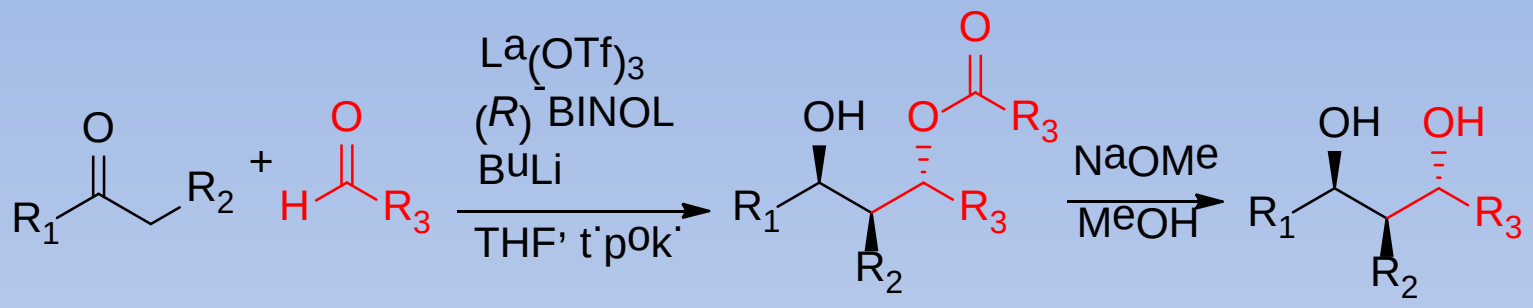
1 : 3 : 5’6

THF, t·pok·

Asymetryczna r. aldolowa-Tishchenko

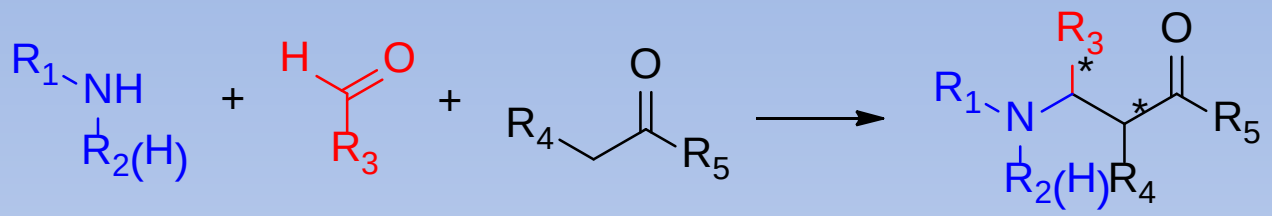


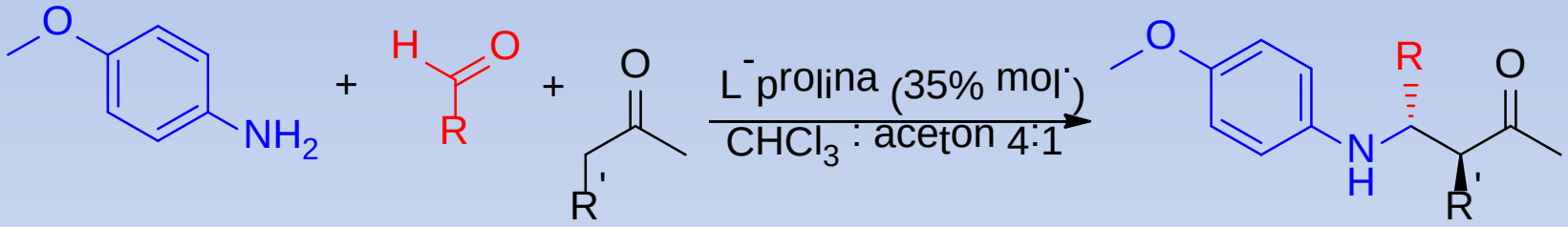
Asymetryczna r. aldolowa-Tishchenko

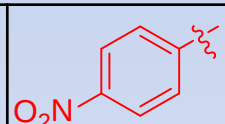
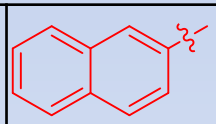
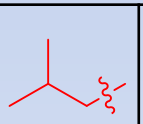
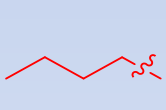
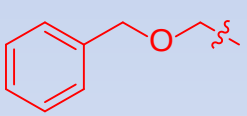
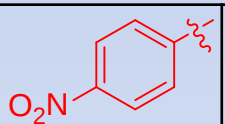
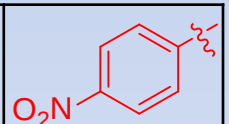


R1	R2	R3	Wyd. [%]	e.e. [%]
C_6H_4-4-CF_3	Pr	C_6H_4-4-Br	88	87
C_6H_4-4-CF_3	Et	C_6H_4-4-Br	90	88
C_6H_4-4-CF_3	Me	C_6H_4-4-Br	96	95
C_6H_4-4-CF_3	Me	C_6H_4-4-Cl	95	93
C_6H_4-4-CF_3	Me	C_6H_4-4-F	85	92
C_6H_4-4-Br	Me	C_6H_4-4-Cl	70	85
C_6H_4-3-Cl	Me	C_6H_4-4-Cl	60	84
C_6H_4-4-CF_3	Me	Ph	95	91
C_6H_4-4-CF_3	Me	2-naftyl	67	88
C_6H_4-4-CF_3	Me	3-furyl	77	93

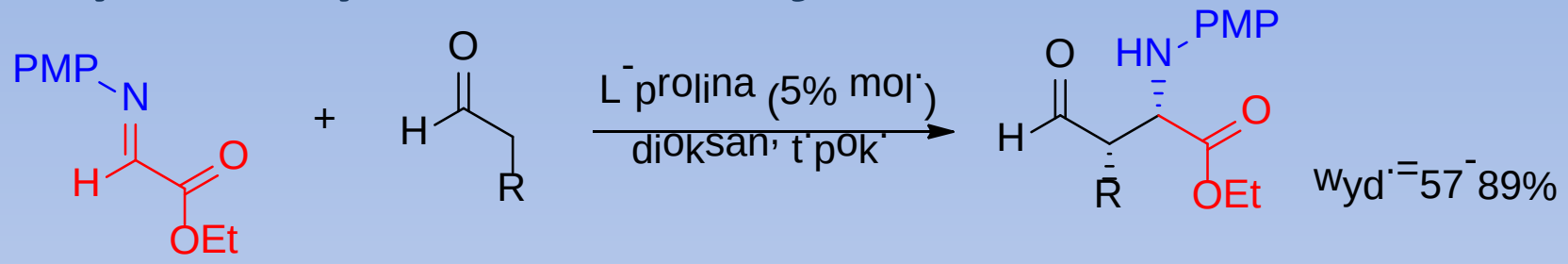
Asymetryczna reakcja Mannicha

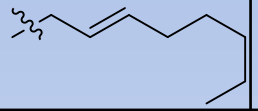
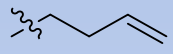


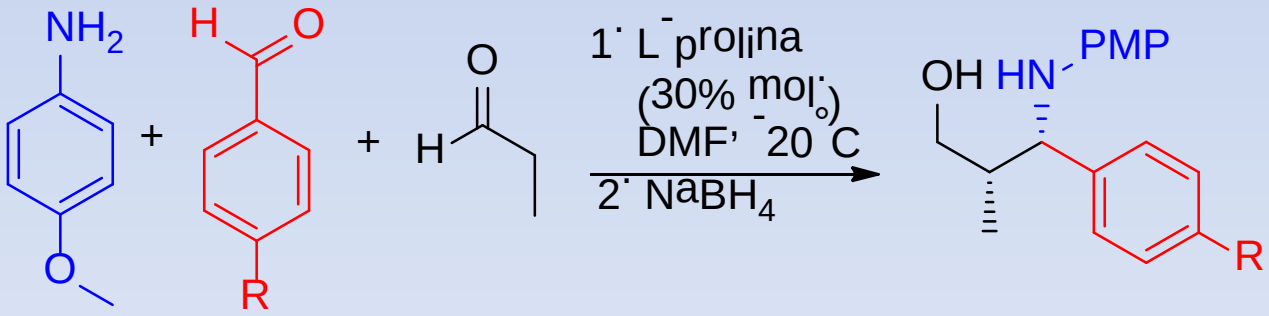


R								
R’	H	H	H	H	H	H	CH_3	OCH_3
e.e. [%]	94	96	93	73	70	75	99 d.r.>20:1	98 d.r.>20:1

Asymetryczna reakcja Mannicha

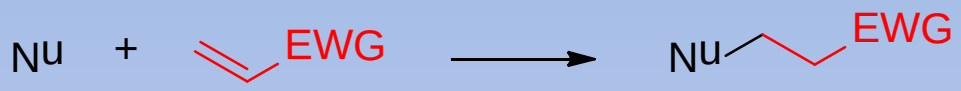


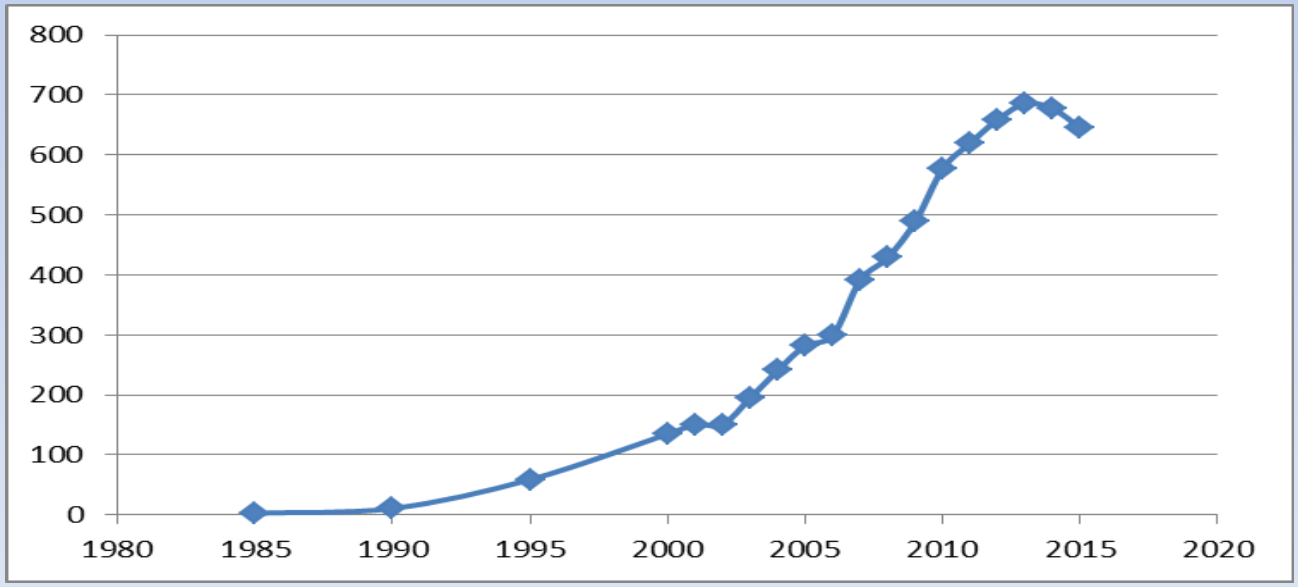
R	Me	Et	iPr	n-Bu	n-pentyl		
d.r.	3 : 1	7 : 1	19 : 1	>19 : 1	>19 : 1	>19 : 1	>19 : 1
e.e. [%]	99	99	93	99	>99	99	>99



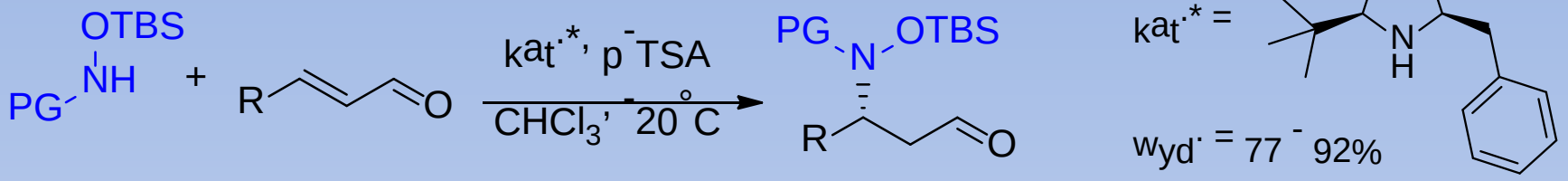
R	d.r.	e.e. [%]
H	4 : 1	94
Cl	12 : 1	84
Br	16 : 1	89
CN	65 : 1	99
NO_2	65 : 1	98

Asymetryczna reakcja Michaela

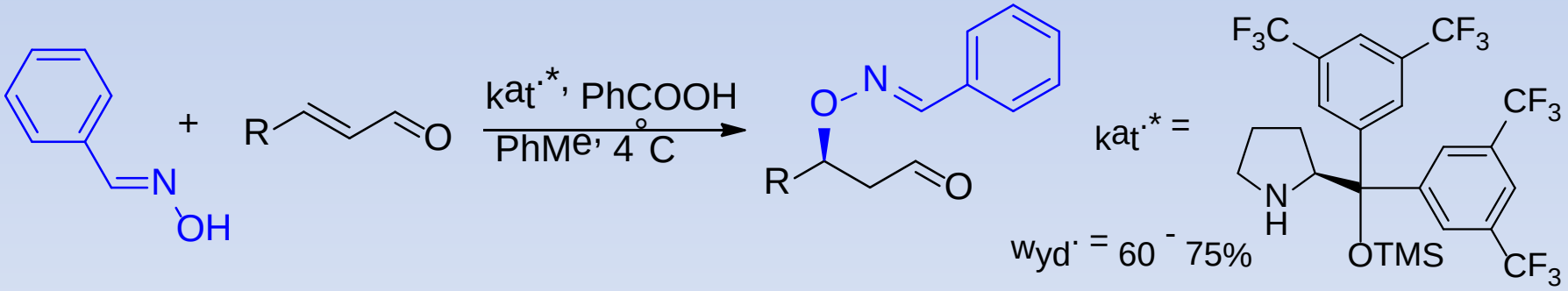




Asymetryczna reakcja Michaela

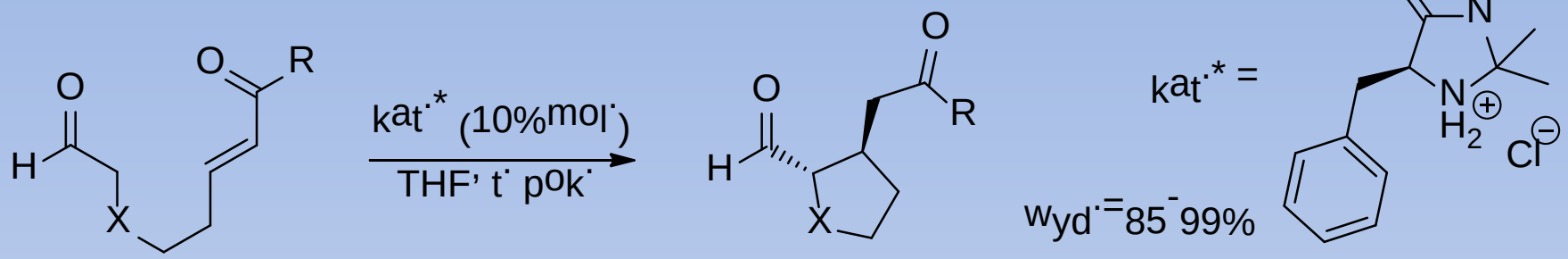


R	Me	n-Pr	n-Pr	n-Pr	$CH_2=CH(CH_2)_3$	$PhCH_2CH_2$	$BnOCH_2$	CO_2Me
PG	Cbz	Cbz	Boc	Fmoc	Cbz	Cbz	Cbz	Boc
e.e. [%]	92	95	92	89	96	90	96	97

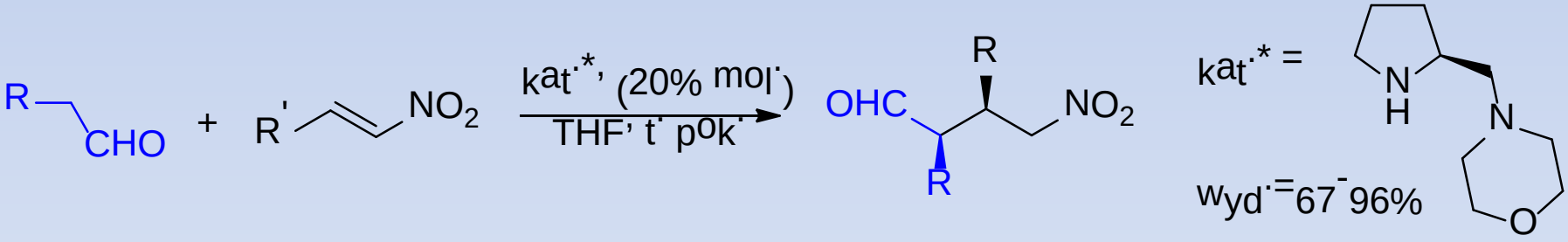


R	Me	Et	n-Pr	i-Pr	n-Bu	n-heptyl	heks-3-enyl	CO_2Me
e.e. [%]	92	95	92	89	96	90	96	97

Asymetryczna reakcja Michaela

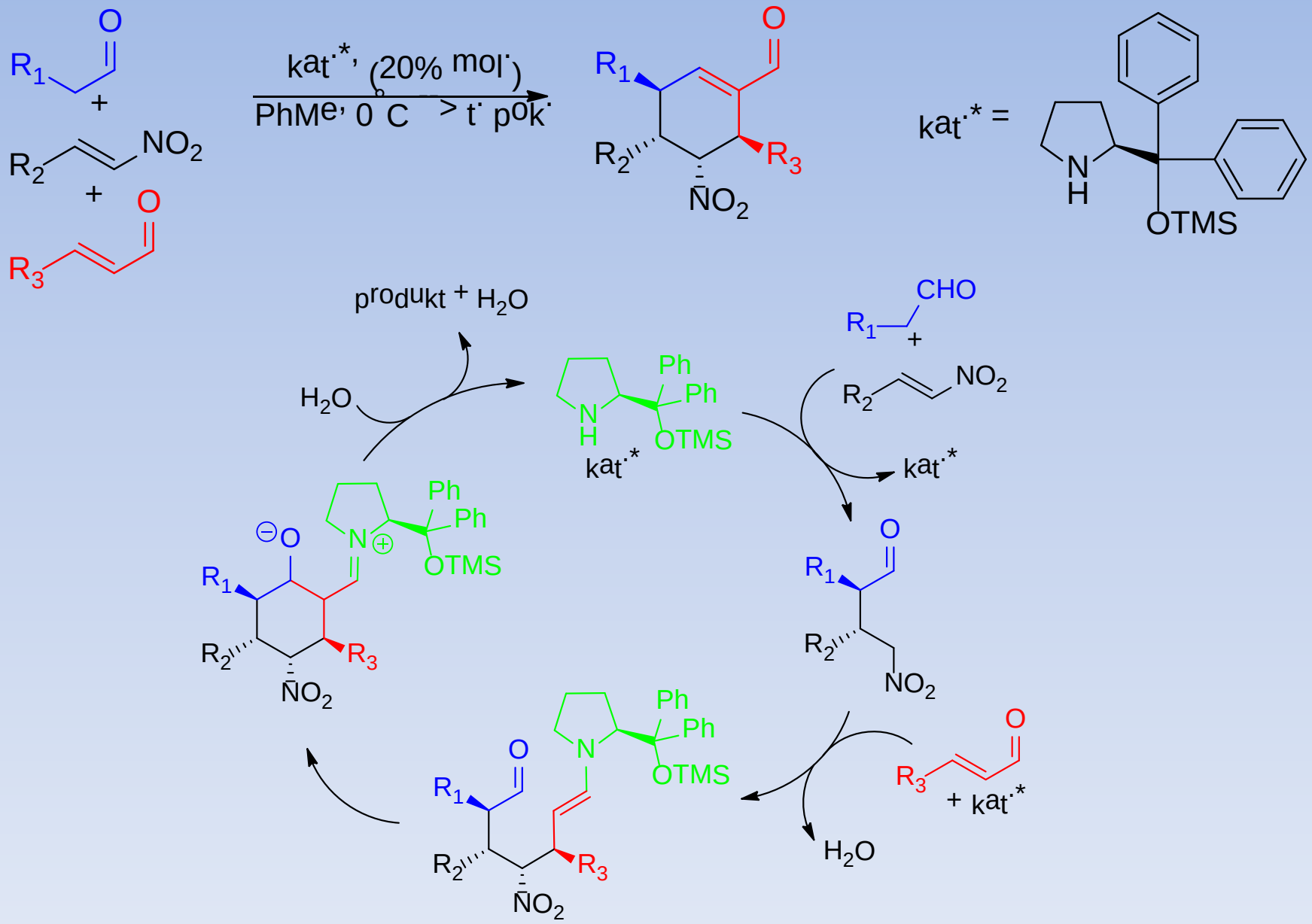


R	H	Me	Et	Ph	2-naftyl	Me
X	CH_2	CH_2	CH_2	CH_2	CH_2	p-Me-$C_6H_4SO_2N$
e.e. [%]	80	93	94	97	97	93



R	Me	Et	i-Pr	n-Bu	i-Pr	i-Pr	i-Pr	i-Pr
R’	Ph	Ph	Ph	Ph	1-naftyl	2-naftyl	o-CF_3-C_6H_4	2-tienyl
e.e. [%]	56	65	72	69	75	69	78	71

Asymetryczne reakcje kaskadowe



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SYNTEZA ASYMETRYCZNA

Dziękuję za uwagę

Konsultacje: pon. 14^{15}-16^{00}, pok. 135, G.Ch.