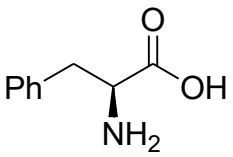
STRATEGIA DEL CHIRAL POOL

CHIRAL POOL

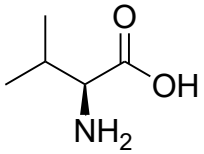
- Insieme di composti NATURALI ENANTIOMERICAMENTE PURI che viene incorporata nella molecola TARGET utilizzando la sua chiralità e le sue funzionalità

CHIRAL POOL

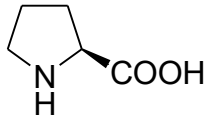
Amino acidi



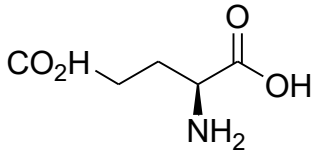
S-Phe



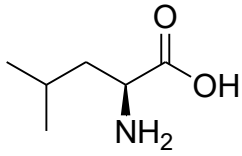
S-Val



S-Pro

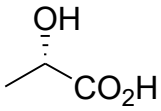


S-Glu

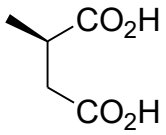


S-Leu

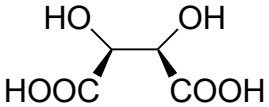
Idrossi acidi



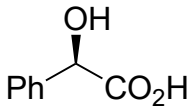
S-lattico



R-malico

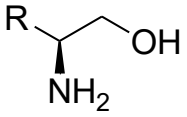


R,R-tartarico

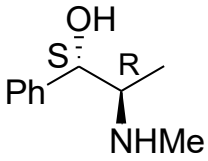


R-mandelico

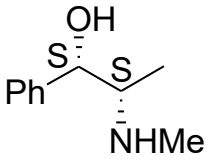
Amminoalcoli



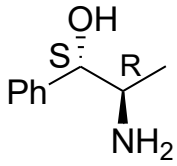
S-aminoalcoli



(+)-efedrina



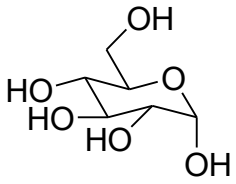
(+)-pseudoefedrina



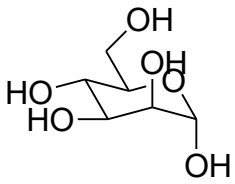
(+)-norefedrina

CHIRAL POOL

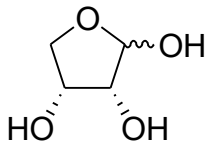
Carboidrati



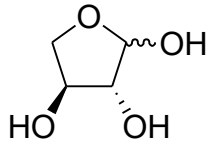
Glucosio



Mannosio

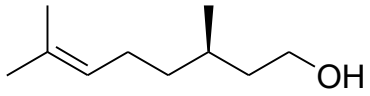


eritrosio

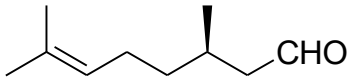


treosio

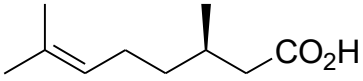
Terpeni



R-(+)-citronellolo



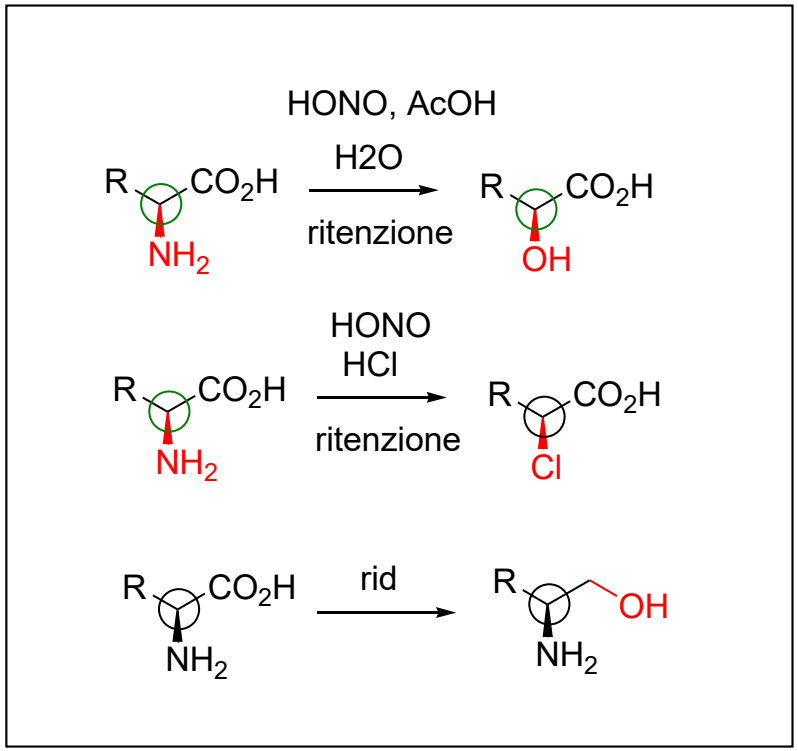
R-(+)-citronellale



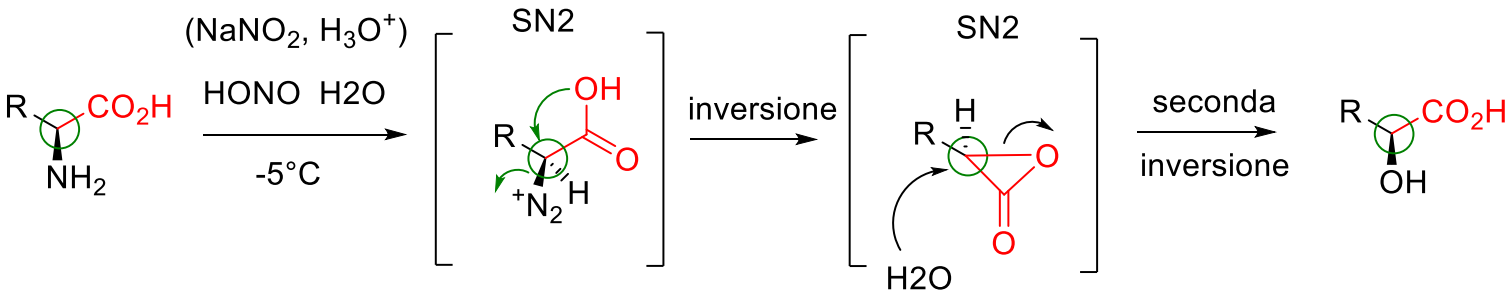
acido R-(+)-citronellalico

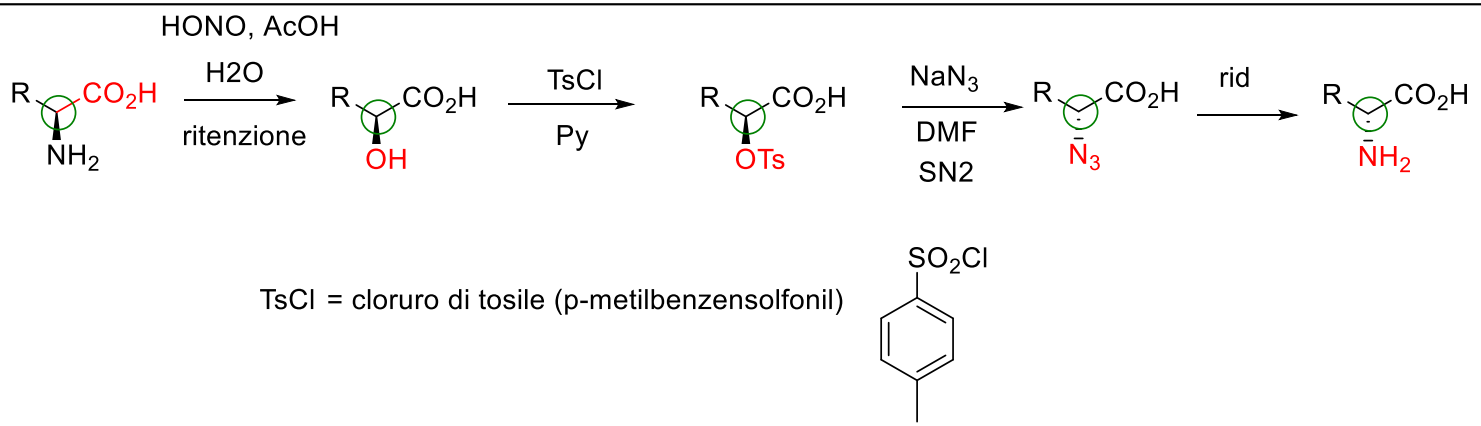
CHIRAL POOL

Trasformazioni di amino acidi



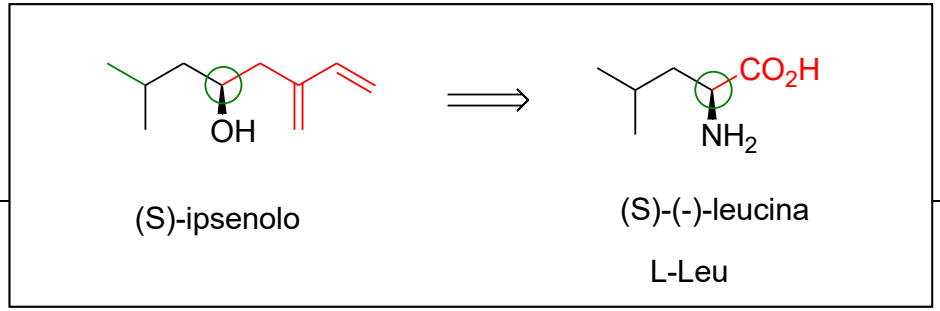
CHIRAL POOL



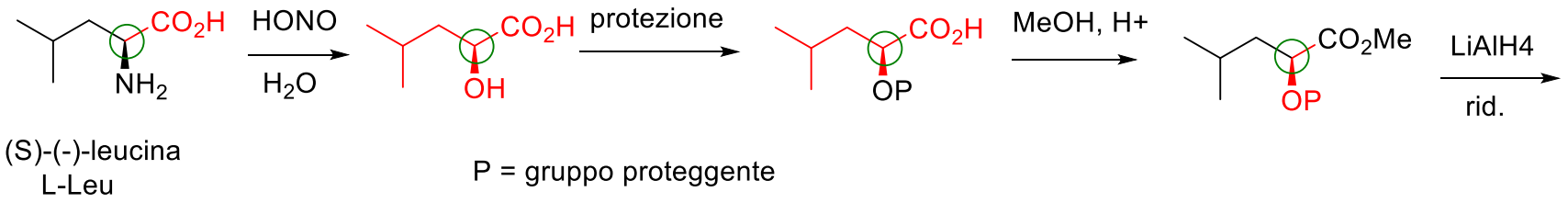


TsCl = cloruro di tosile (p-metilbenzensolfonil)

CHIRAL POOL

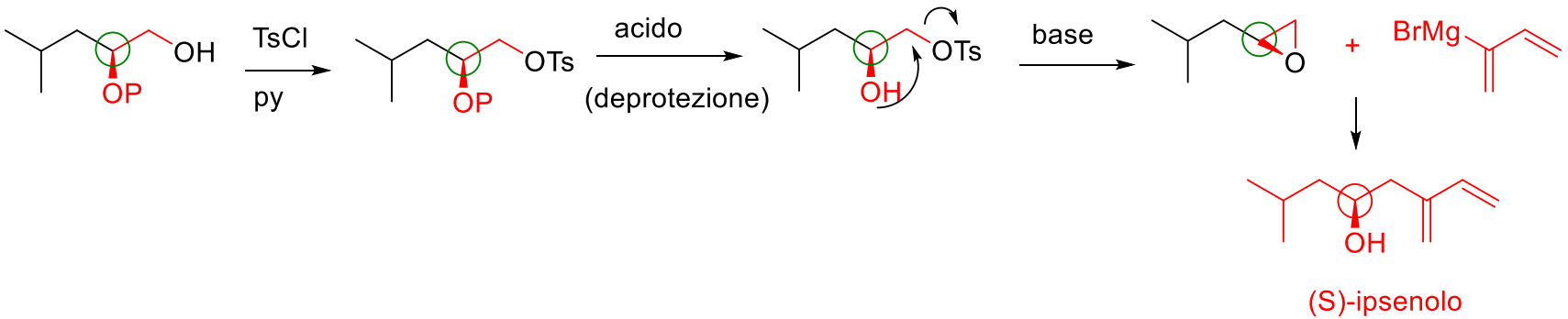


Feromone del coleottero della corteccia



(S)-(-)-leucina
L-Leu

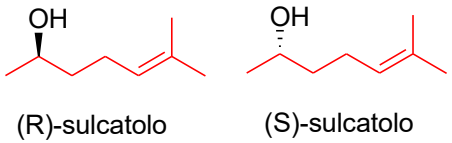
P = gruppo proteggente



(S)-ipsenolo

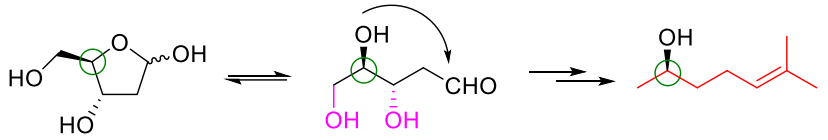
Un centro stereogenico: ritenzione di configurazione

CHIRAL POOL



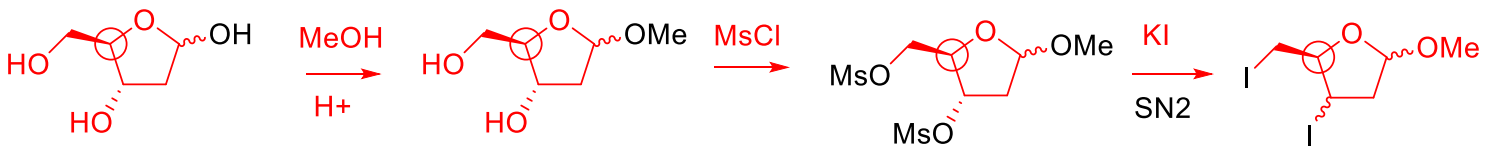
(R)-sulcatolo (S)-sulcatolo

R/S = 65/35



D-deossiribosio emiacetale

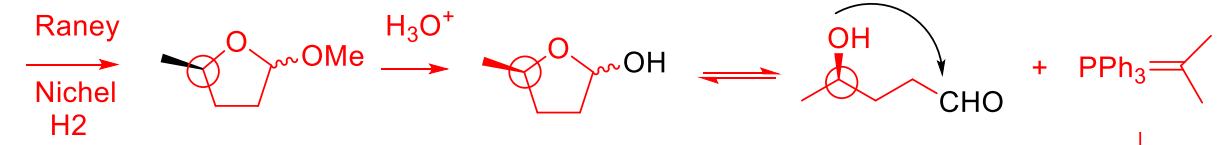
(R)-sulcatolo



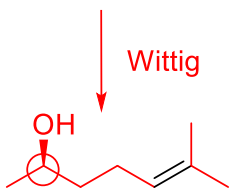
D-deossiribosio (emiacetale)

D-1-OMe-deossiribosio acetale

MsCl = cloruro di mesile (metansolfonile) CH_3SO_2Cl



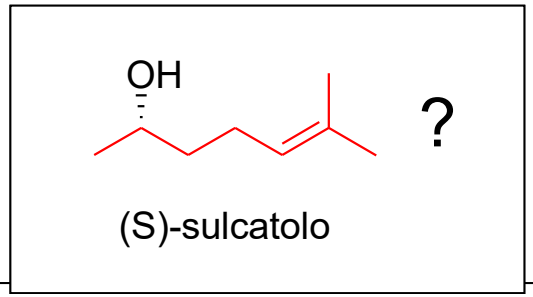
(idrogenolisi C-I)

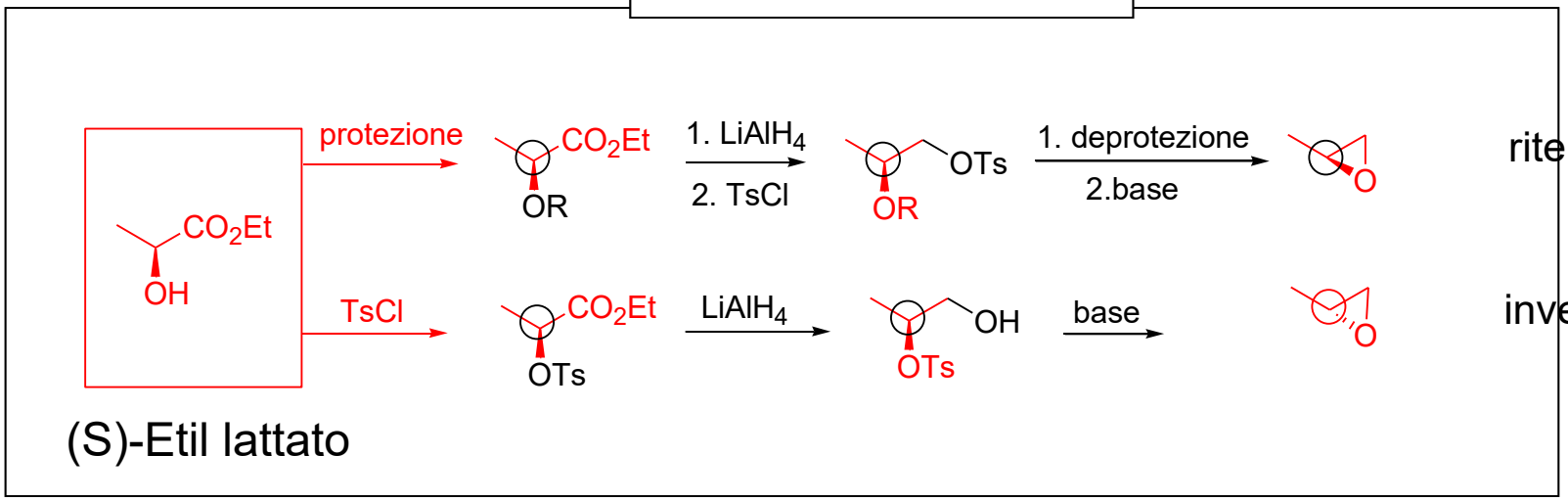


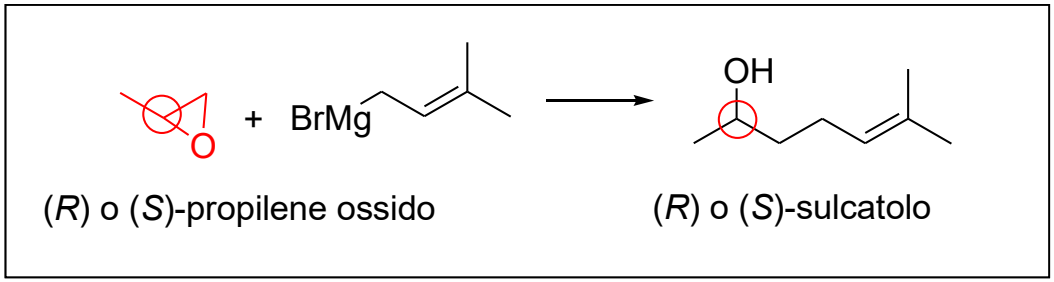
(R)-sulcatolo

Un centro stereogenico: ritenzione di configurazione
Due centri stereogenici eliminati

CHIRAL POOL


OH
?
(S)-sulcatolo


protezione
CO2Et
OH
TsCl
CO2Et
OR
CO2Et
OTs
1. LiAlH4
2. TsCl
OTs
OR
1. deprotezione
2.base
O
ritenzione
LiAlH4
OH
OTs
base
O
inversione
(S)-Etil lattato


O
+
BrMg
OH
(R) o (S)-propilene ossido
(R) o (S)-sulcatolo

CHIRAL POOL

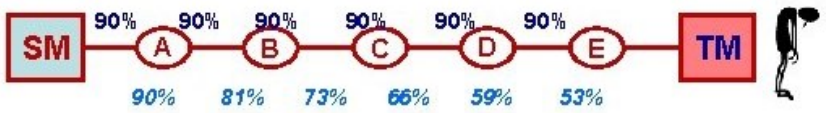
Svantaggi:

1. Sintesi per lo più lineari. Se ci sono molti passaggi può diventare più conveniente la risoluzione di un racemo

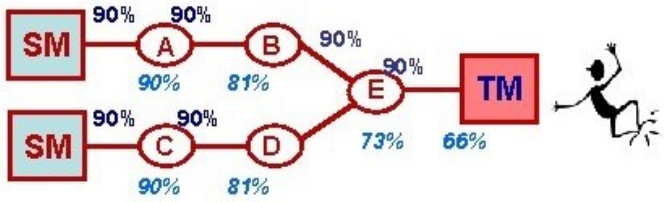
2. Disponibilità di un solo enantiomero.

Sintesi lineare (ramo lineare di una sintesi convergente):

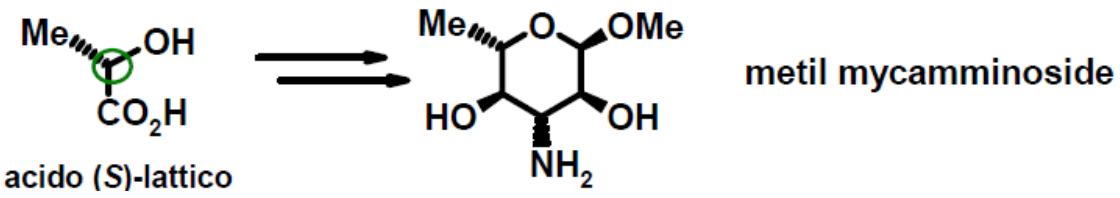
$$Y\,(\%) = (\Pi y_i/100)\times 100$$



reagenti = Starting Materials (SM);
molecola da sintetizzare = Target Material (TM)



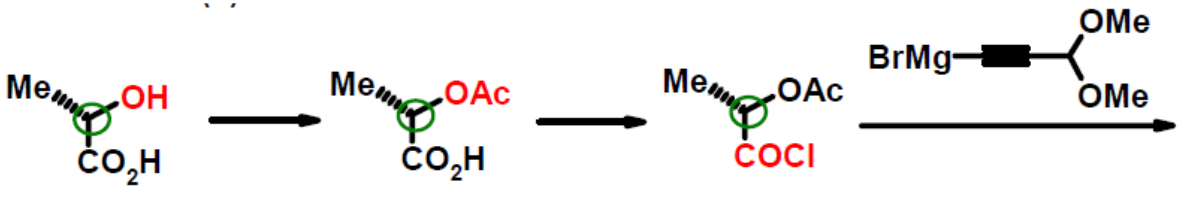
CHIRAL POOL



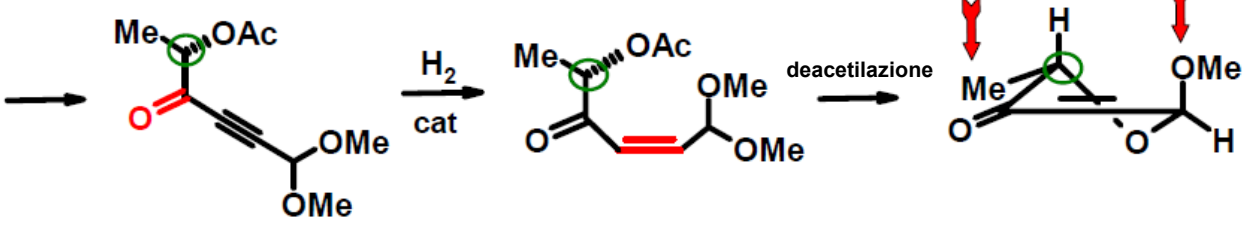
acido (*S*)-lattico

metil mycamminoside

Da uno a cinque centri stereogenici attraverso reazioni diastereoselettive: poiché il primo centro stereogenico ha una configurazione assoluta definita, qualsiasi reazione diastereoselettiva che controlli la stereochimica relativa di un nuovo stereocentro ne definisce anche la configurazione assoluta.

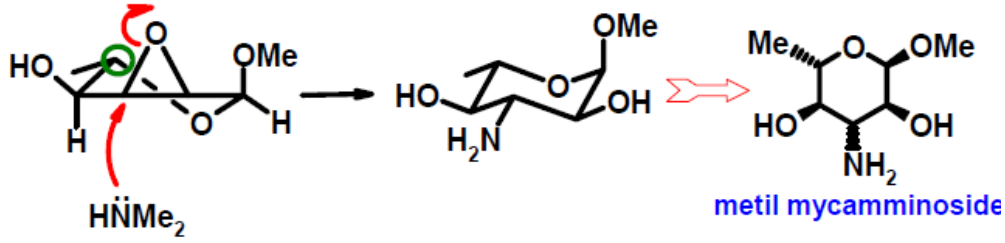


acido (*S*)-lattico



Il secondo centro stereogenico è introdotto selettivamente nello step di ciclizzazione in cui il Me si dispone pseudoequatoriale e il MeO pseudoassiale per effetto anomerico.

1. $NaBH_4$
2. epossidazione



metil mycamminoside

Il terzo centro stereogenico è controllato dalla riduzione del chetone che dà l'alcol equatoriale.

Il centro che si genera nella riduzione del chetone controlla l'epossidazione (di un alcol allilico) e quindi la stereochimica del quarto e del quinto stereocentro; L'apertura nucleofila dell'epossido avviene con inversione.