STRATEGIES IN SYNTHESIS

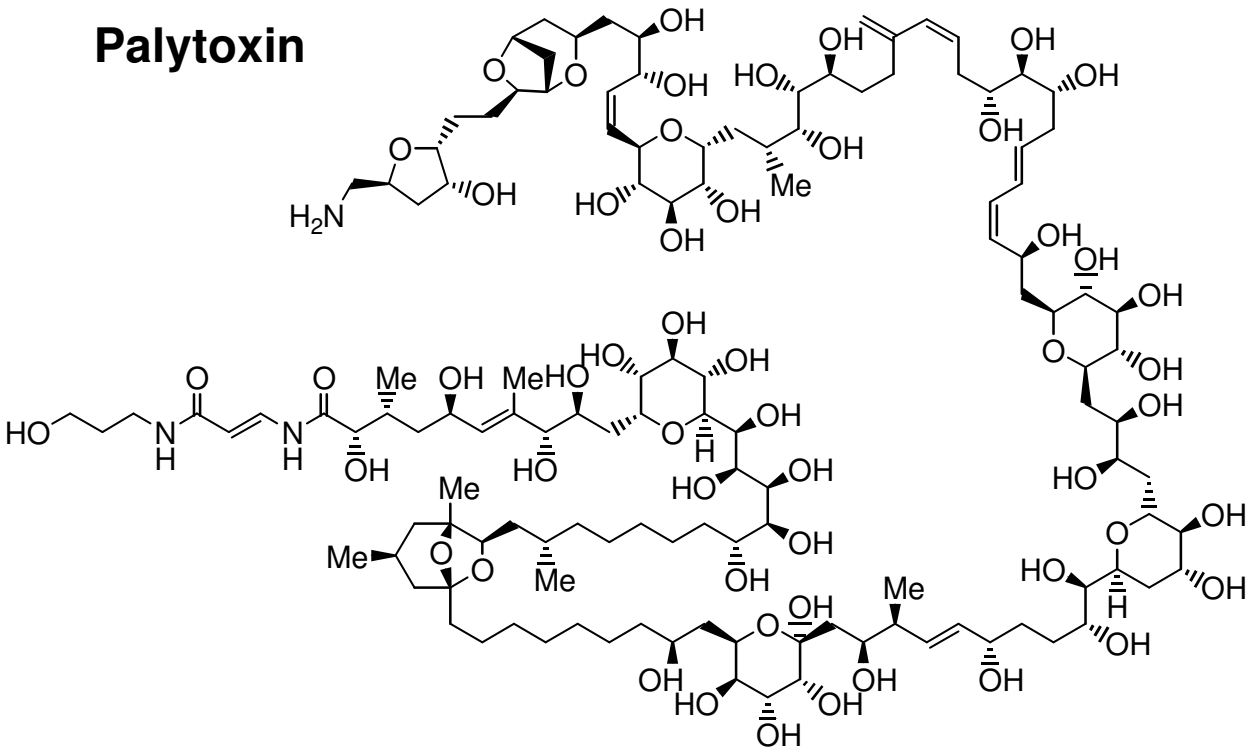
Professor T. J. Donohoe

MT 2004

6 Lectures: Tuesday at 10 am; Thursday at 9 am (weeks 6-8)

HANDOUT B

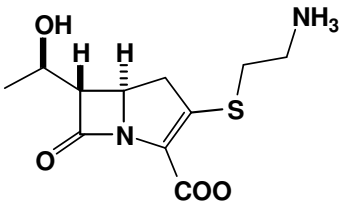
Palytoxin



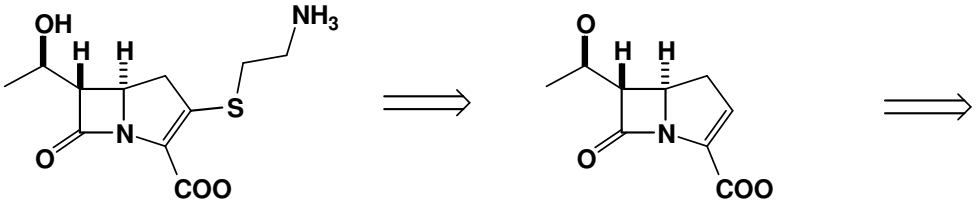
Total synthesis see :- Y. Kishi et al. J. Am. Chem. Soc., 1989, **111**, 7525, 7530; ibid. 1994, **116**, 11205

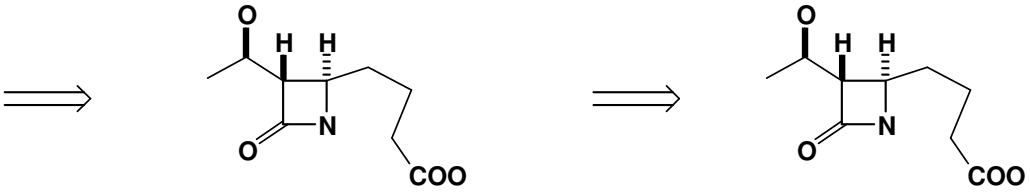
71 stereochemical elements (64 stereogenic centres, 7 geometrical)
Therefore there are 2^{71} possible stereoisomers ie:
2.3×10^{21} = 23000000000000000000 isomers !!!

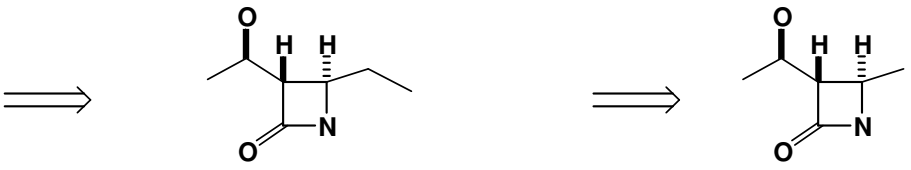
Thienamycin (Merck-1980)

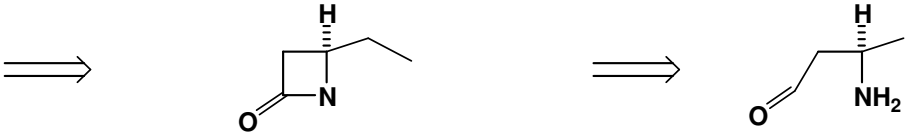


Retrosynthesis

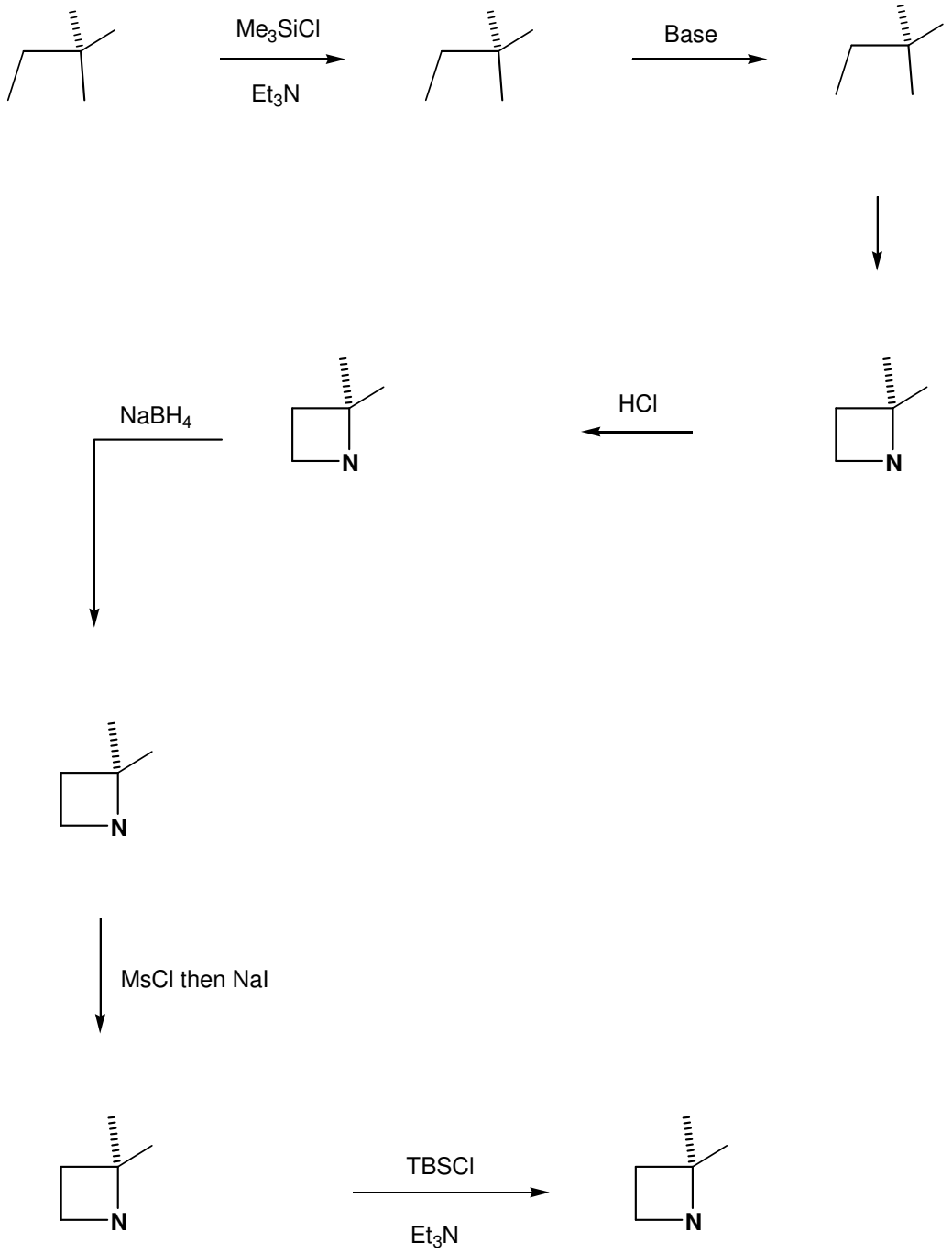




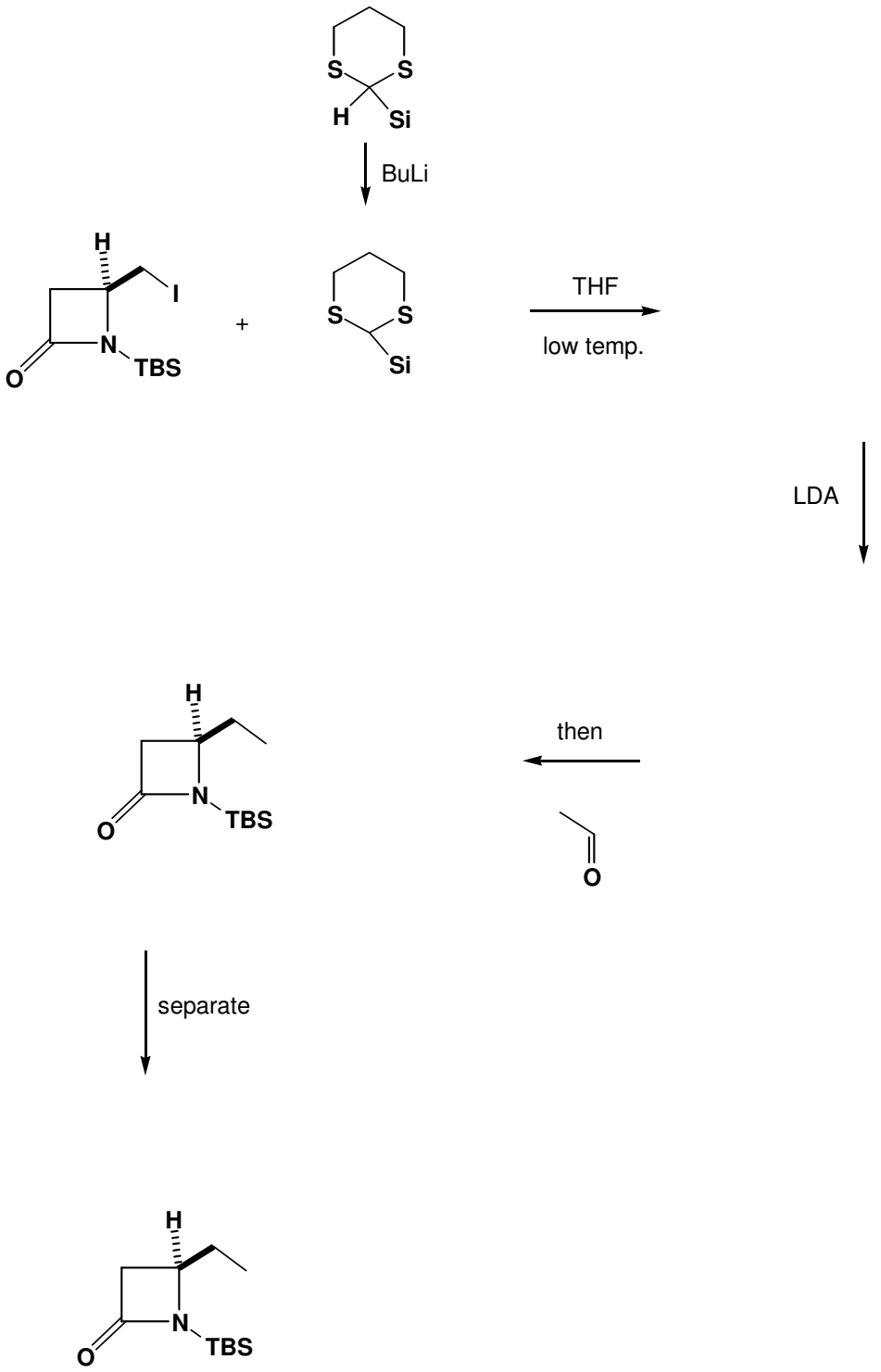


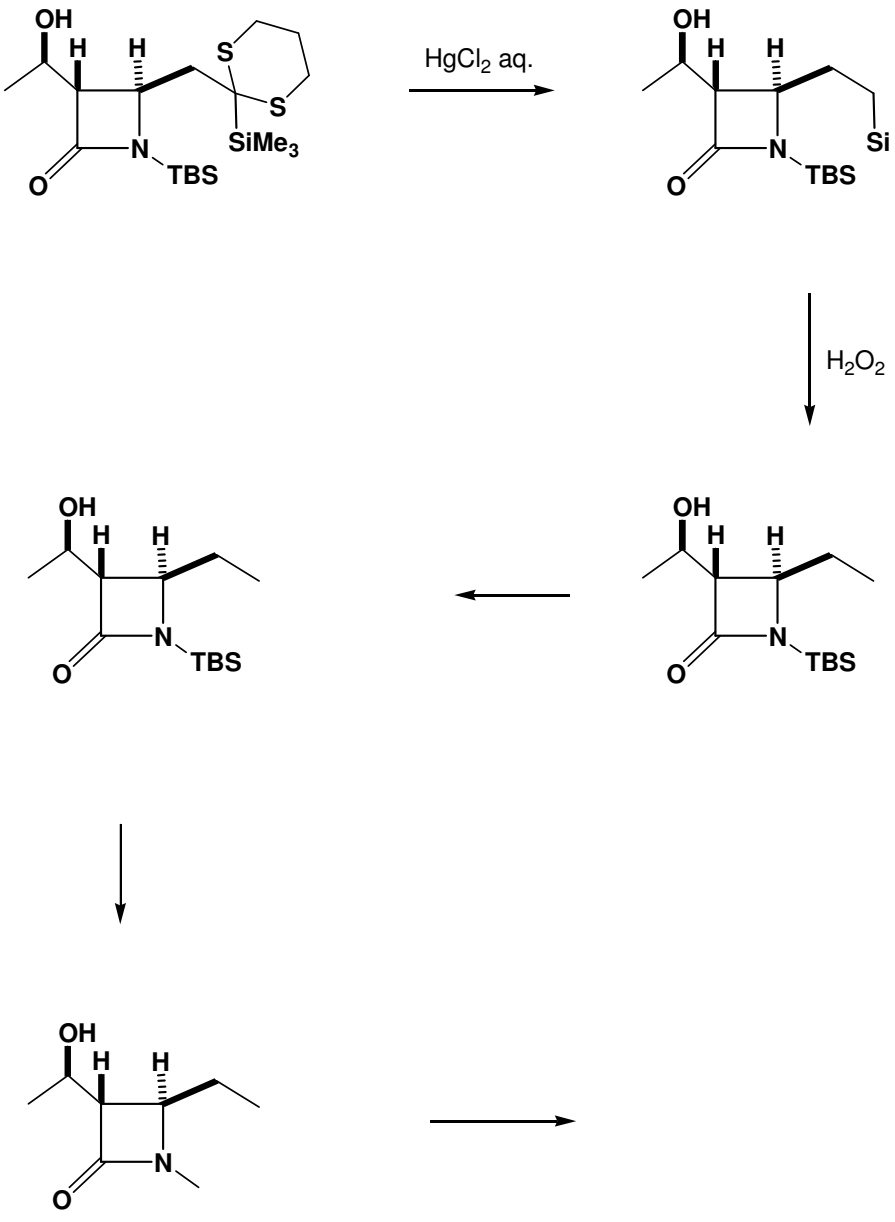


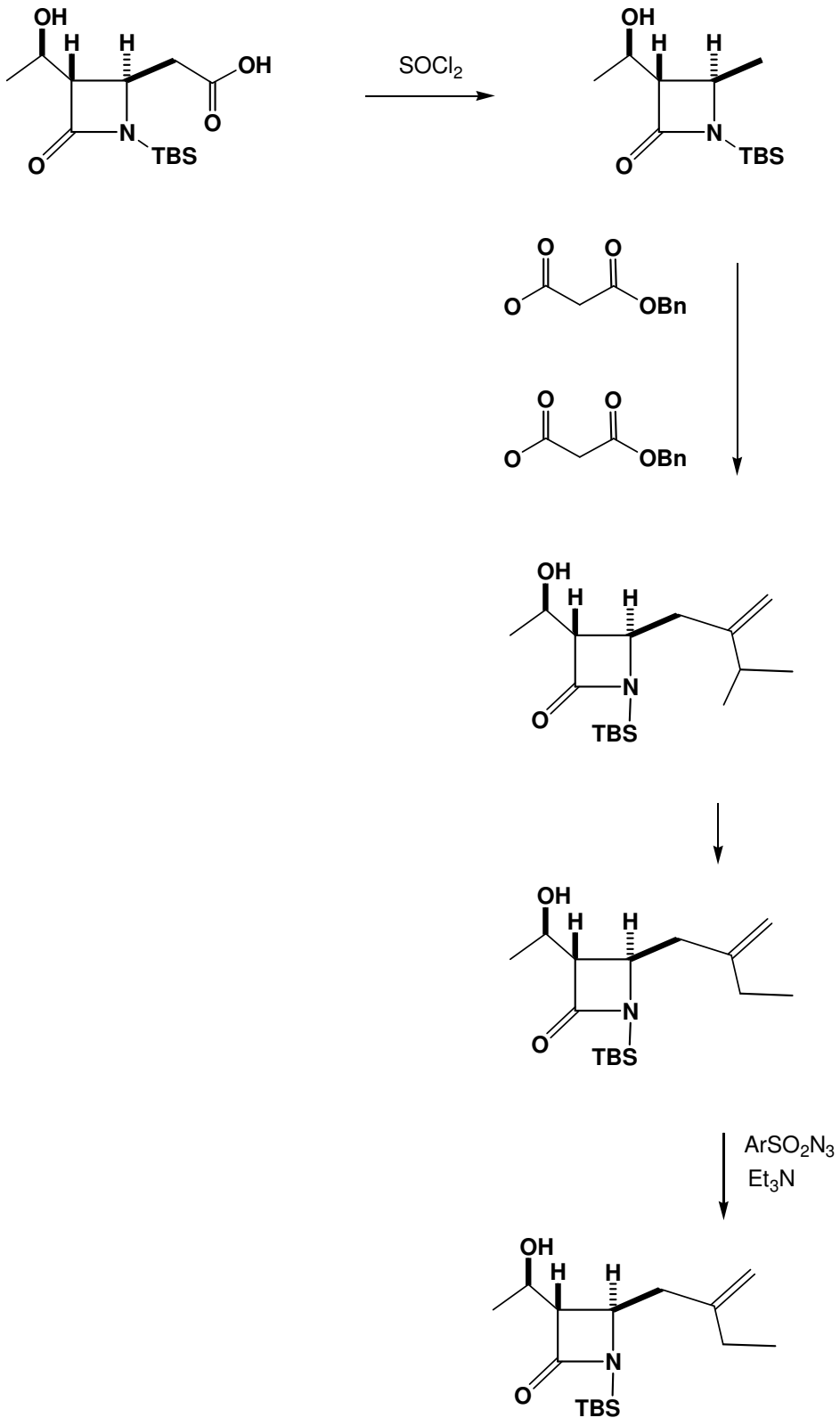
Now the synthesis is detail.



The CO_2R synthon uses UMPOLUNG methodology




OH
H
H
S
S
SiMe3
N
TBS
O
HgCl2 aq.
Si
H2O2


OH
H
H
OH
O
N
TBS
O
SOCl2
OH
H
H
N
TBS
O
O
O
OBn
O
O
O
OBn
OH
H
H
N
TBS
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OH
H
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N
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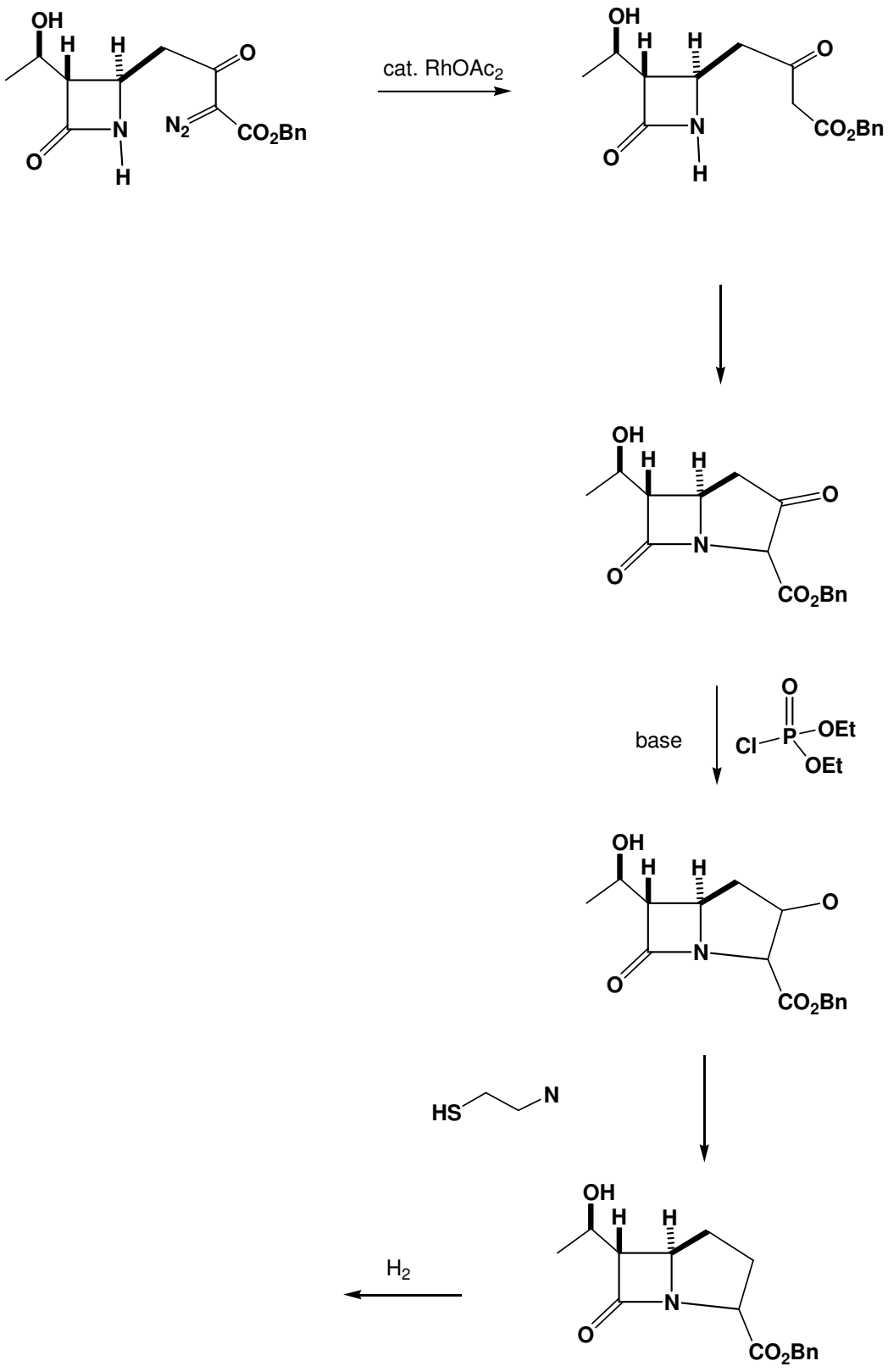
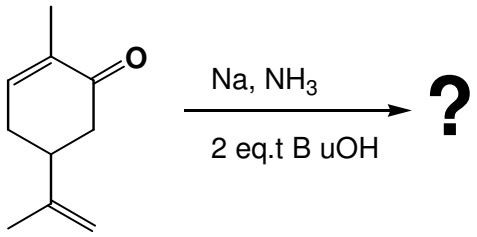
O
ArSO2N3
Et3N
OH
H
H
N
TBS
O

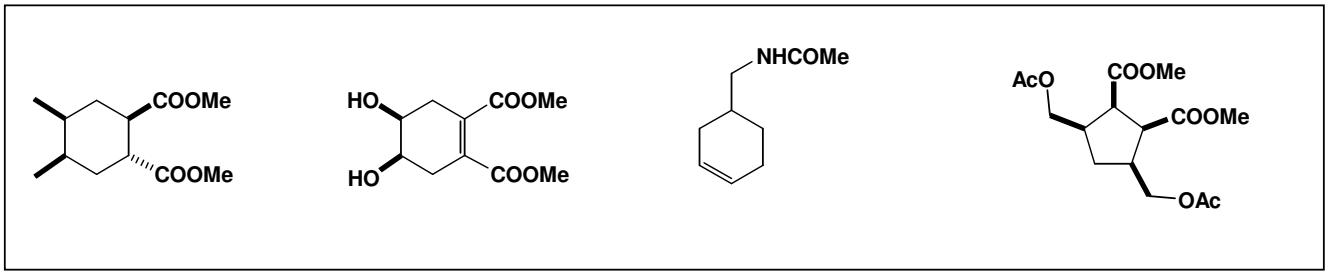

OH
H
H
O
N2
CO2Bn
O
N
H
cat. RhOAc2
OH
H
H
O
CO2Bn
O
N
H
OH
H
H
O
O
N
CO2Bn
base
O
Cl
P
OEt
OEt
OH
H
H
O
O
N
CO2Bn
HS
N
OH
H
H
H2
O
N
CO2Bn

ANSWERS TO PROBLEMS

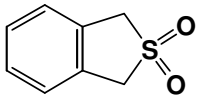
Q. What would happen if we added 2 eq. of tBuOH?



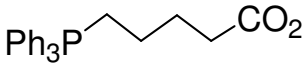
Some problems: How would you synthesise the following? (Hint: think about Diels Alder)



Synthesis?



How do you make the ylid?



Some problems to think about:

Disconnect the following and then devise forward syntheses: