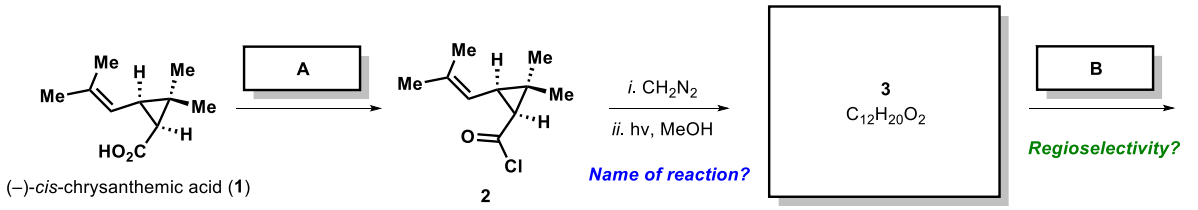
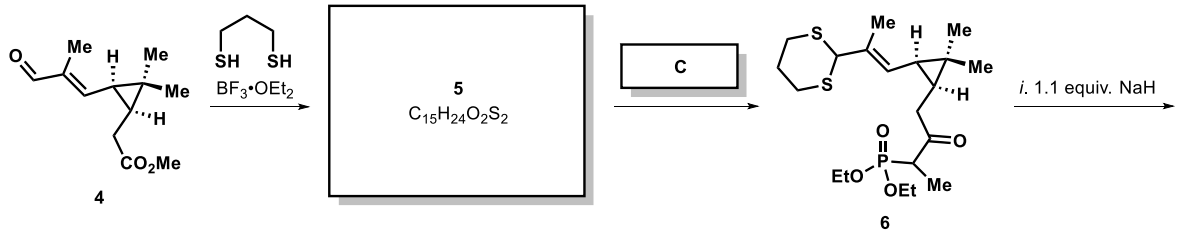
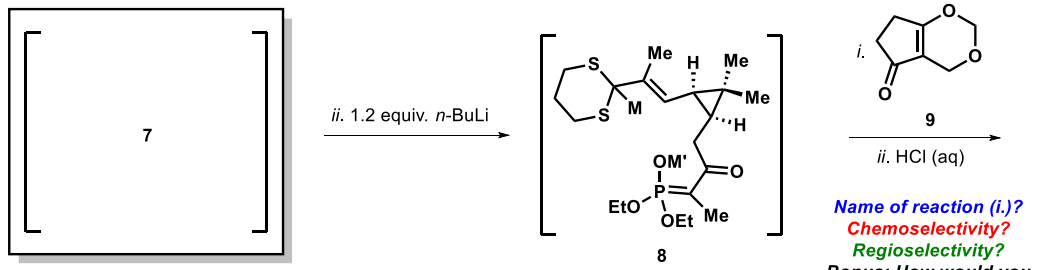
By Frederik Simonsen Bro

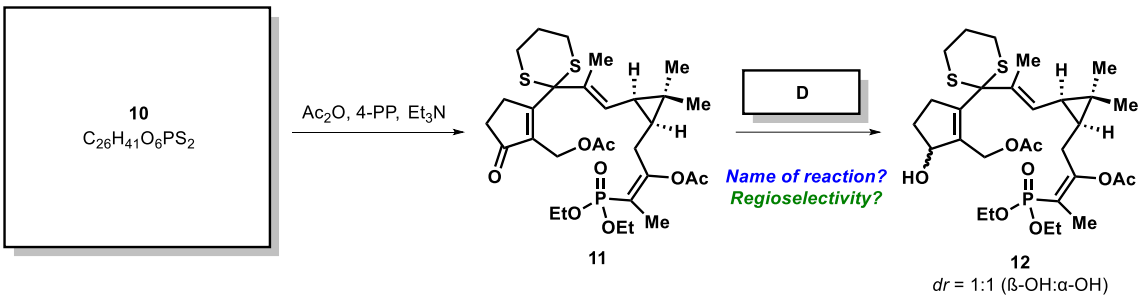
Strand-Clementson Problem Session – 2026.02.27

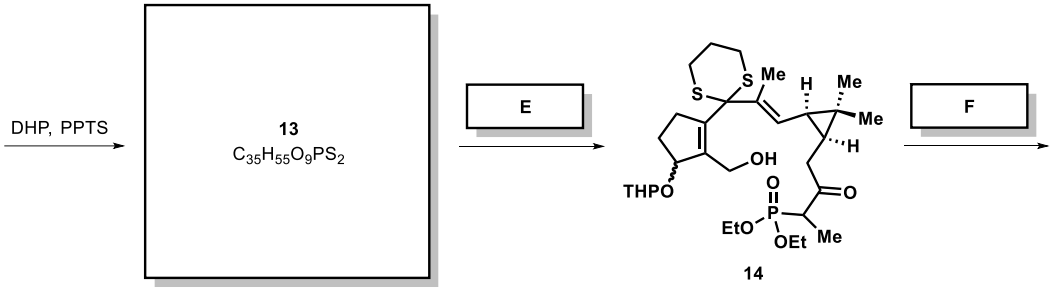
This problem set presents the synthesis of the lathyrane diterpene α-**23**. Propose suitable reagents/conditions and determine the structures missing in the boxes. Determine the **name of the reaction**, answer the **specific questions**, and explain **chemo**-, **regio**-, and **stereoselectivity** when explicitly asked for. 4-PP = 4-pyrrolidinepyridine, DHP = 3,4-dihydropyran, PPTS = pyridinium *p*-toluenesulfonate.



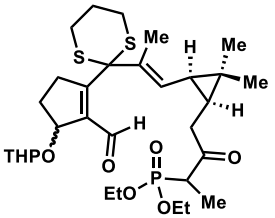








By Frederik Simonsen Bro



15

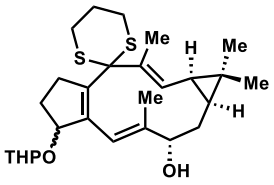
NaH

Name of reaction?
Stereoselectivity?

16
$C_{27}H_{38}O_3S_2$

$NaBH_4$, $CeCl_3$
MeOH

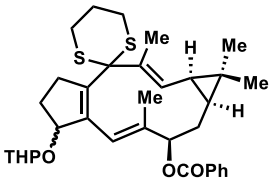
Name of reaction?
Regioselectivity?
Stereoselectivity?



17

G

Name of reaction?
Stereoselectivity?



18

1. 0.2 M HCl (aq)
2. CrO_3•2 pyr, DCM

Name of reaction (2.)?

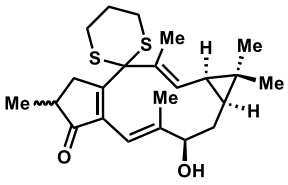
19
$C_{29}H_{34}O_3S_2$

i. LiHMDS
ii. MeI

Stereoselectivity?
(Hint: see X-ray and ChemDraw 3D structure of related compound 21)

20
dr = 4.3:1 (ß-Me:α-Me)
$C_{30}H_{36}O_3S_2$

NaOH, EtOH



22

"Pummerer-like" hydrolysis

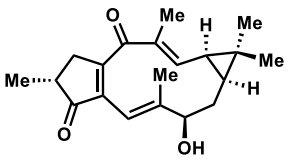
i. 1.0 equiv. *m*CPBA
ii. Ac_2O, Et_3N, THF (aq)

Chemoselectivity (i.)?

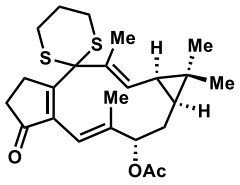
23
dr = 1.2:1 (ß-Me:α-Me)
$C_{20}H_{26}O_3$

iii. HPLC

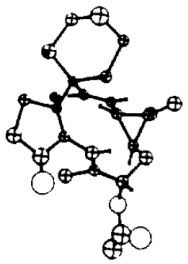
Why the change in dr compared to compound 20?



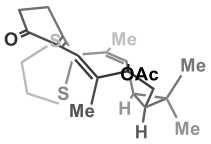
α-**23**
Lathyrane diterpene natural product



21



21 [X-ray]

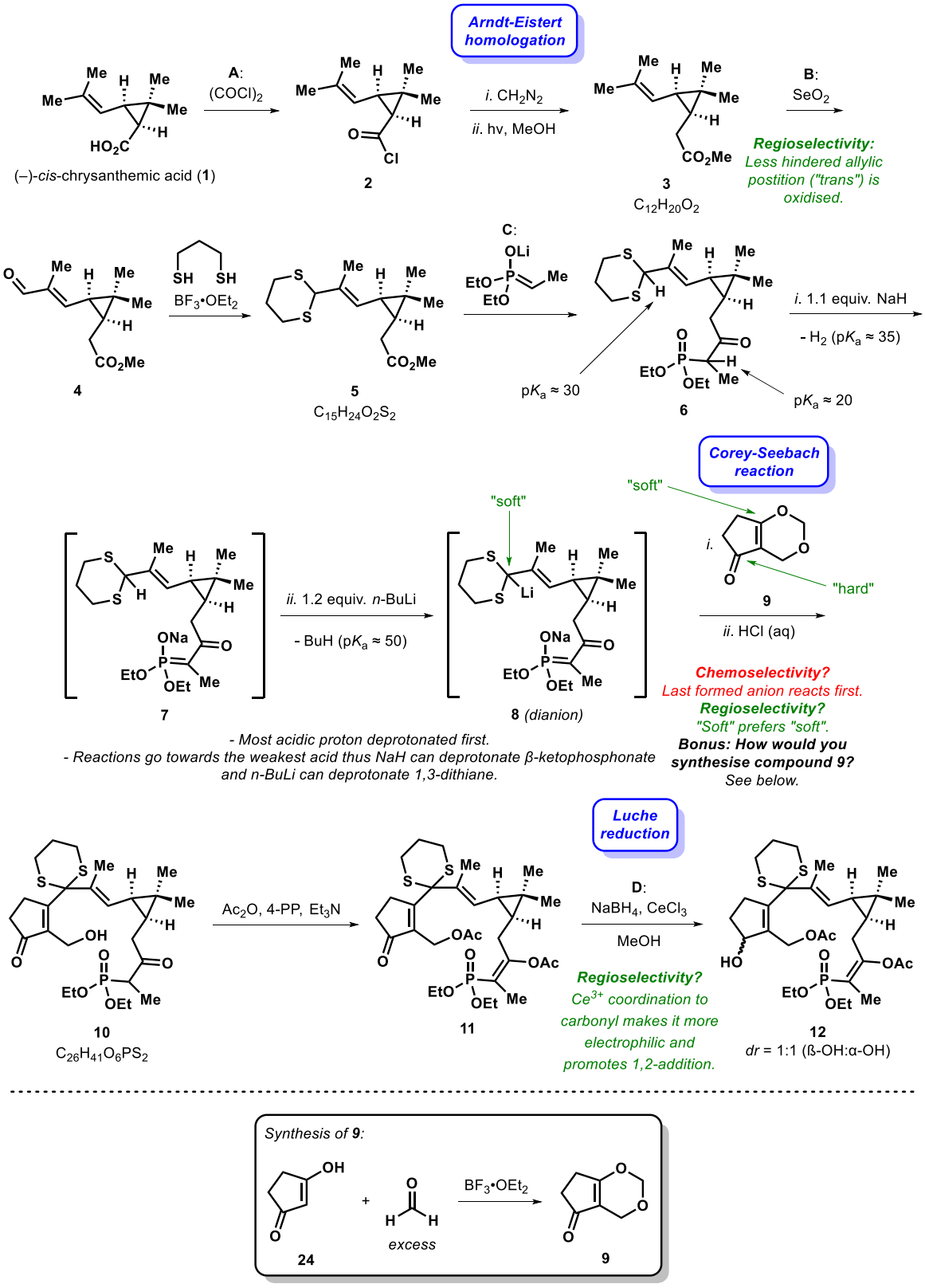


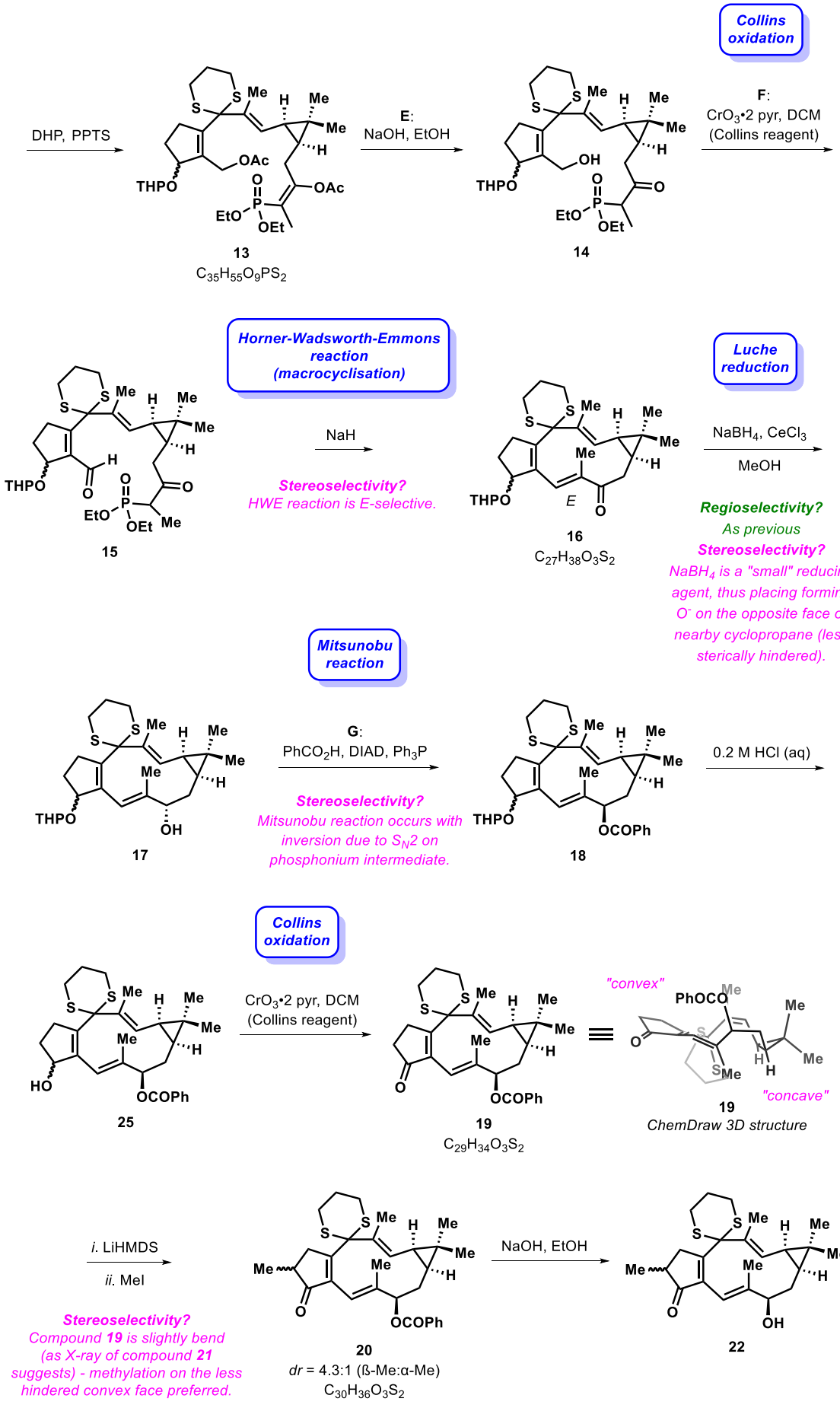
21 [ChemDraw 3D]

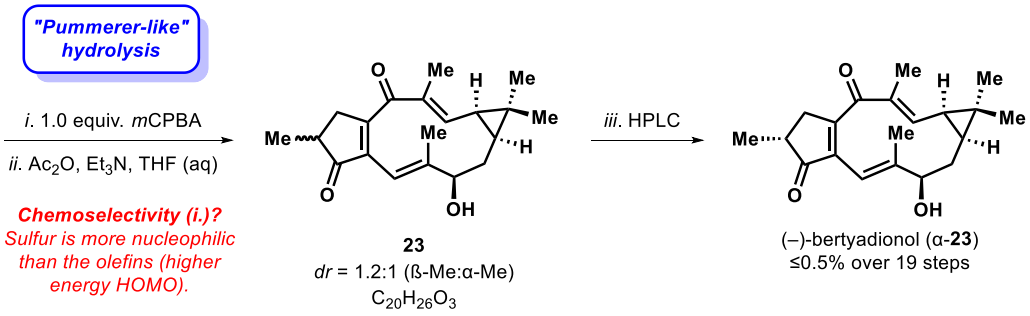
By Frederik Simonsen Bro

Strand-Clementson Problem Session – 2026.02.27 – Solution

This problem set presents the synthesis of the lathyrane diterpene (–)-bertyadionol (α-**23**) reported by Smith III (A. B. Smith III *et al.*, *J. Am. Chem. Soc.*, **1986**, *108*, 3110-3112, https://doi.org/10.1021/ja00271a054).




Collins oxidation
DHP, PPTS
E:
NaOH, EtOH
F:
CrO3•2 pyr, DCM
(Collins reagent)
13
C35H55O9PS2
14
Horner-Wadsworth-Emmons reaction (macrocyclisation)
NaH
Stereoselectivity?
HWE reaction is E-selective.
15
Luche reduction
NaBH4, CeCl3
MeOH
Regioselectivity?
As previous
Stereoselectivity?
NaBH4 is a "small" reducing agent, thus placing forming O- on the opposite face of nearby cyclopropane (less sterically hindered).
16
C27H38O3S2
Mitsunobu reaction
G:
PhCO2H, DIAD, Ph3P
Stereoselectivity?
Mitsunobu reaction occurs with inversion due to SN2 on phosphonium intermediate.
0.2 M HCl (aq)
17
18
Collins oxidation
CrO3•2 pyr, DCM
(Collins reagent)
25
19
C29H34O3S2
"convex"
"concave"
19
ChemDraw 3D structure
i. LiHMDS
ii. MeI
Stereoselectivity?
Compound 19 is slightly bend (as X-ray of compound 21 suggests) - methylation on the less hindered convex face preferred.
20
dr = 4.3:1 (ß-Me:α-Me)
C30H36O3S2
NaOH, EtOH
22



23
dr = 1.2:1 (ß-Me:α-Me)
$C_{20}H_{26}O_3$

(–)-bertyadionol (α-**23**)
≤0.5% over 19 steps

Why the change in dr compared to compound 20?

Initial methylation is under kinetic control and gives a kinetic mixture. Subsequent treatment with base (NaOH/NaOEt and Et_3N) is thermodynamic control and gives the thermodynamic mixture.