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Communication

Two-Stage Syntheses of Clionastatins A and B

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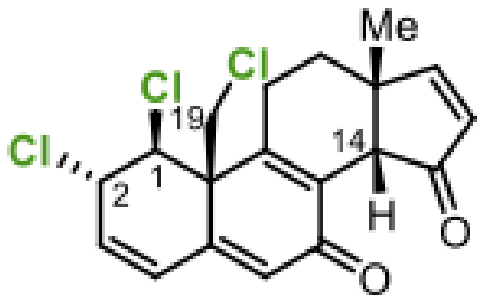
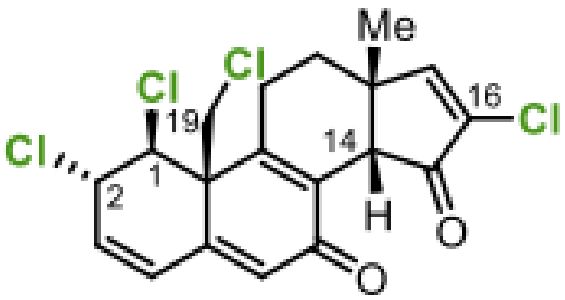
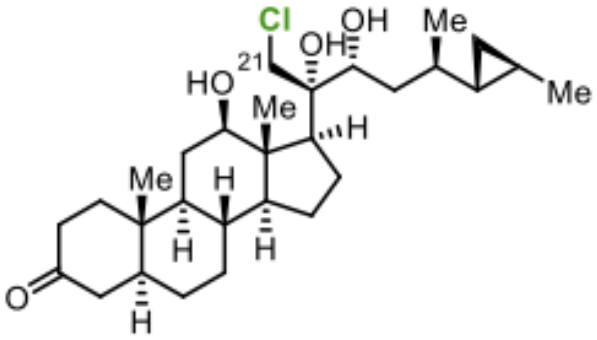


clionastatin A (**7**)

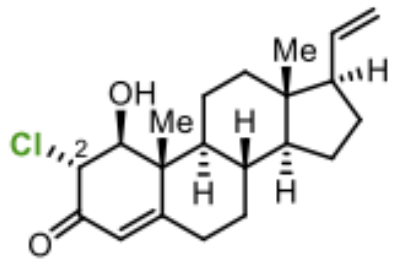


clionastatin B (**8**)

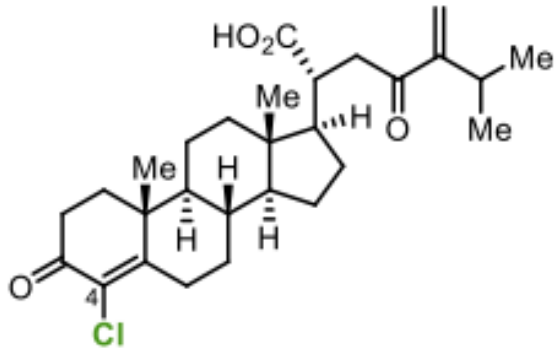
A. Selected examples of marine chlorinated steroids



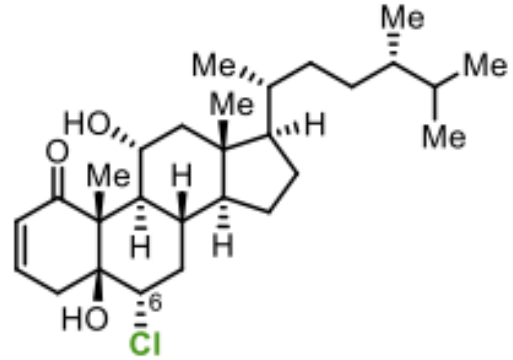
aragusterol C (**1**)



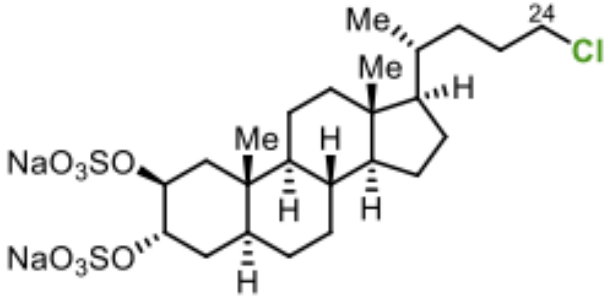
(1β,2α)-2-chloro-1-hydroxypregna-4,20-dien-3-one (**2**)



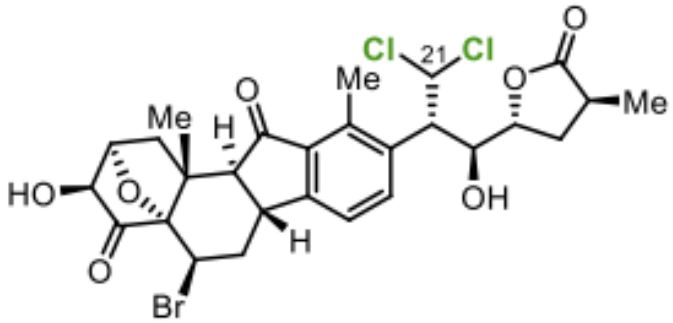
kiheisterone C (**3**)



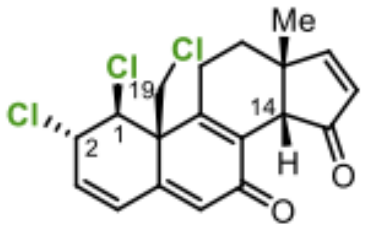
yonarasterol H (**4**)



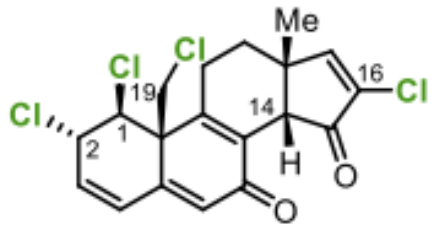
chalinulasterol (**5**)



nakiterpiosinone (**6**)

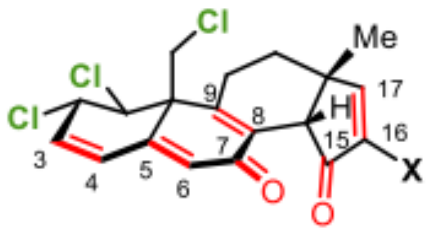


clionastatin A (**7**)



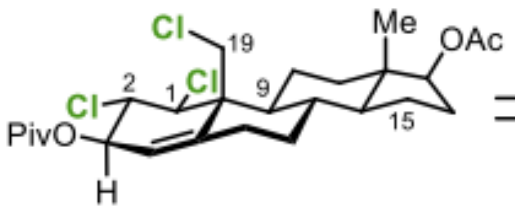
clionastatin B (**8**)

B. General synthetic strategy toward clionastatins from testosterone



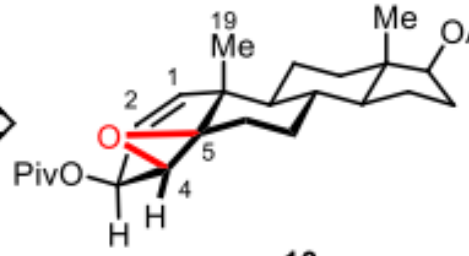
X = H: clionastatin A (**7**)
X = Cl: clionastatin B (**8**)

[O]
4×C=C
2×C=O



9

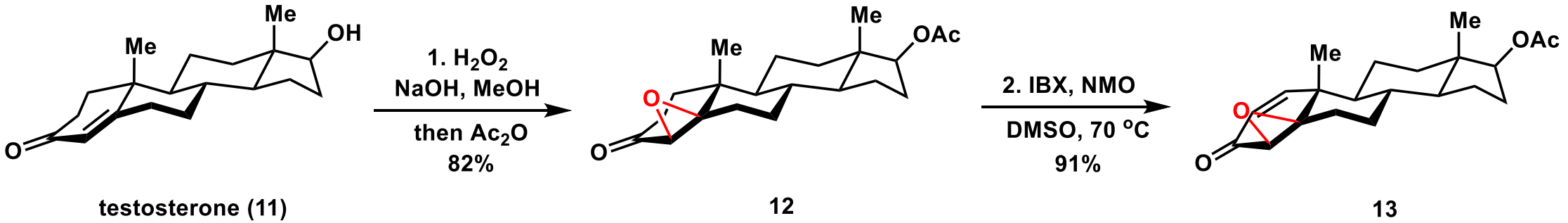
[Cl]
3×C–Cl

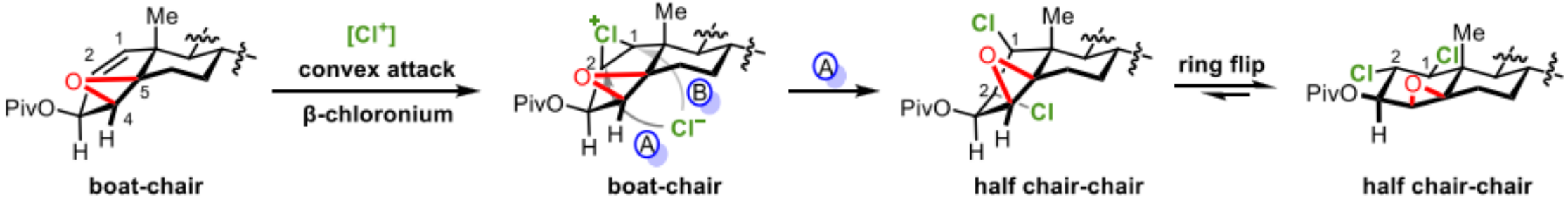


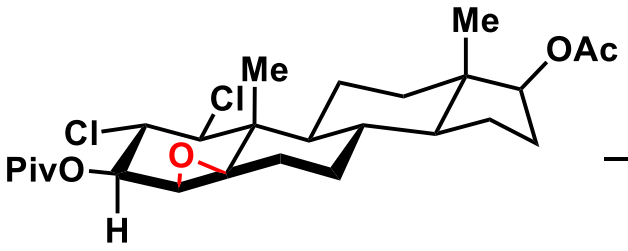
10

Conformational design

testosterone (**11**)


Me
OH
O
1. H_2O_2
NaOH, MeOH
then Ac_2O
82%
OAc
2. IBX, NMO
DMSO, 70 °C
91%
testosterone (11)
12
13
3. NaBH4
then PivCl
75%
PivO
H
10
4. Et_4NCl, oxone
DCM
84%
[20 g scale]
Cl
14


[Cl+]
convex attack
β-chloronium
boat-chair
Cl⁻
A
B
half chair-chair
ring flip

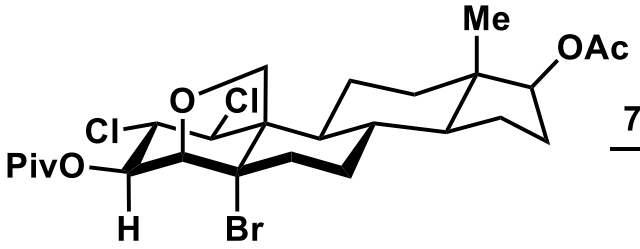


14

5. 40 % HBr, 79%

6. $Pd(OAc)_4$, I_2, *hv*

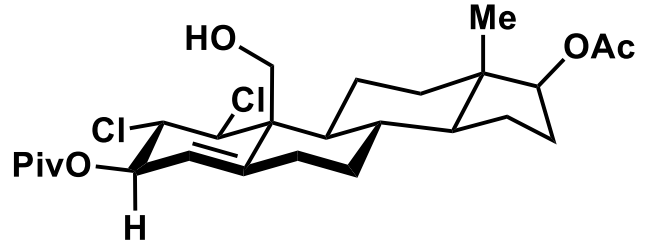
80%



15

7. Zn, AcOH

88%



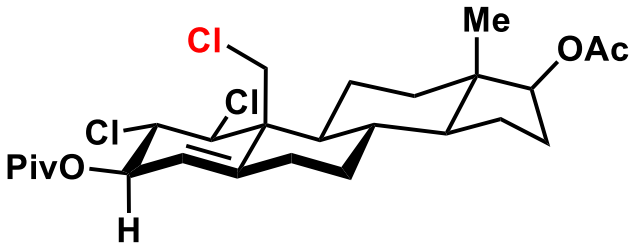
16

8. TBAI, PPh_3

$ClCH_2CH_2Cl$

120 °C, 84%

[10 g scale]



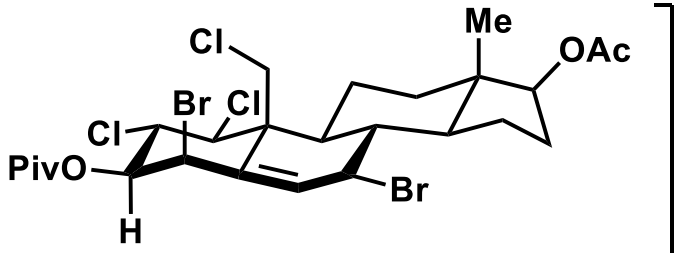
9

9. NBS

Ph_2CO

MeCN

violet LED



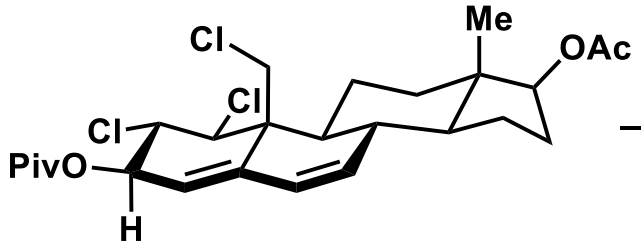
17

then

Zn, AcOH

60%

[2.5 g scale]



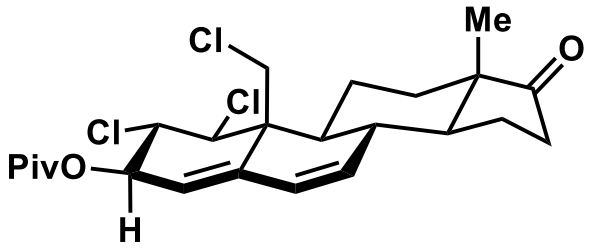
18

10. AcCl

MeOH

then DMP

87%



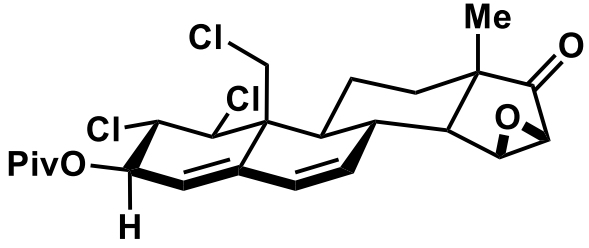
19

11. TMSOTf, Et_3N

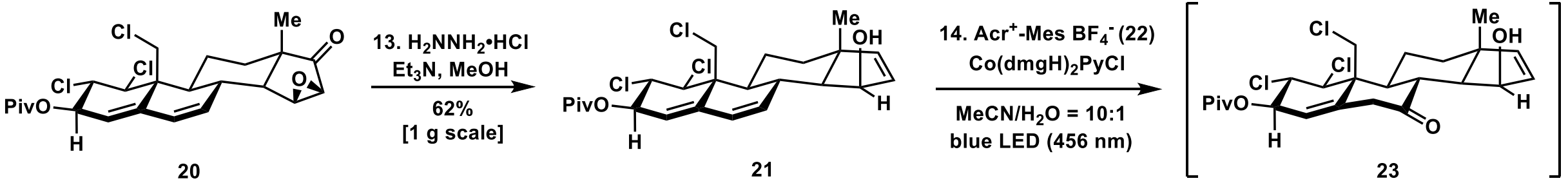
then $Pd(OAc)_2$, 83%

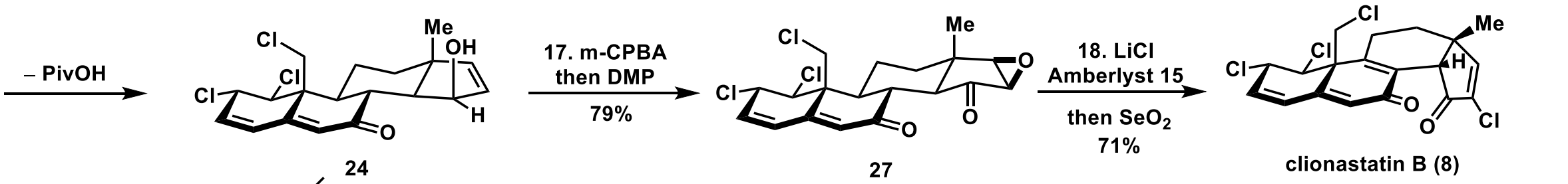
12. TBHP, DBU

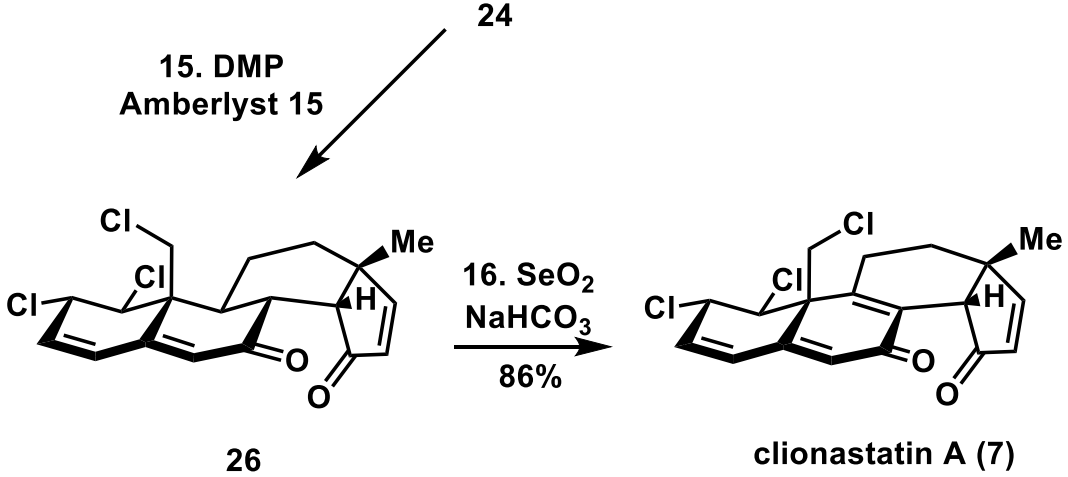
88%

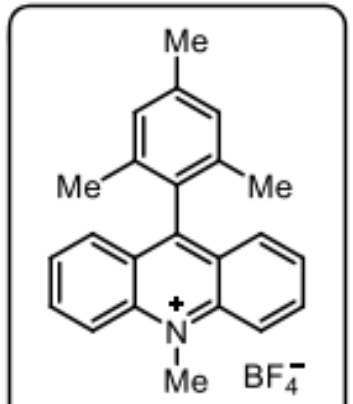


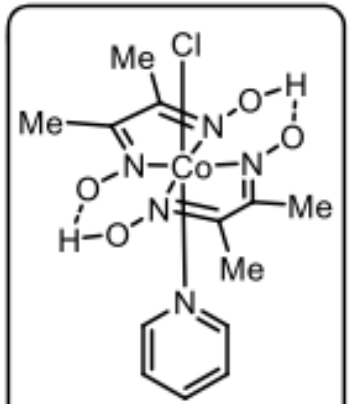
20


20
13. H_2NNH_2•HCl
Et_3N, MeOH
62%
[1 g scale]
21
14. Acr^+-Mes BF_4^- (22)
$Co(dmgH)_2PyCl$
MeCN/H_2O = 10:1
blue LED (456 nm)
23


– PivOH
24
17. m-CPBA
then DMP
79%
27
18. LiCl
Amberlyst 15
then SeO_2
71%
clionastatin B (8)


15. DMP
Amberlyst 15
26
16. SeO_2
$NaHCO_3$
86%
clionastatin A (7)


22: Acr^+-Mes BF_4^-


$Co(dmgH)_2PyCl$

SAEGUSA OXIDATION

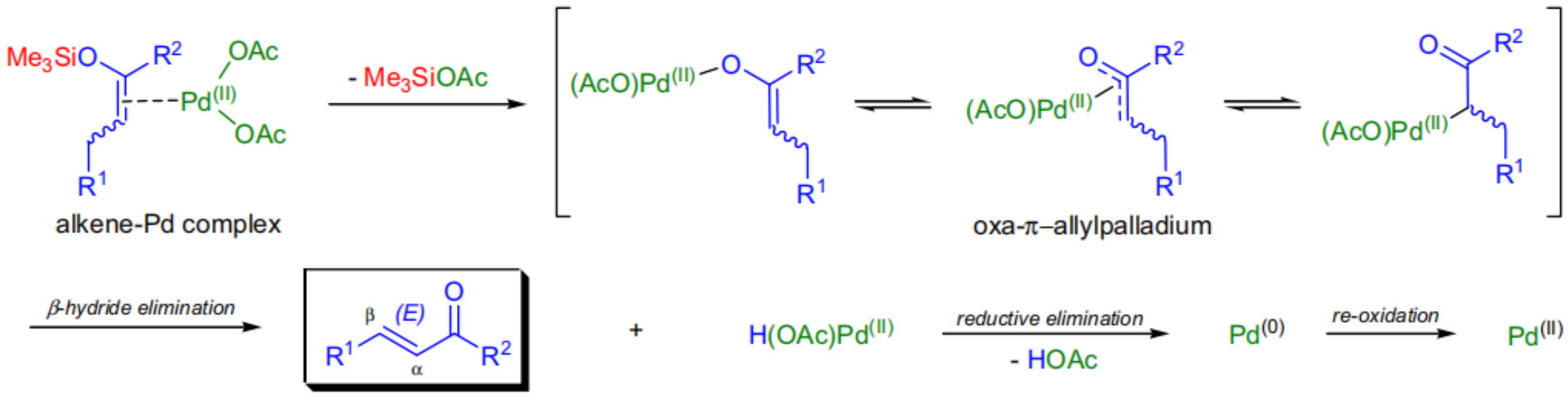
(References are on page 667)

Importance:

[*Seminal Publications*[1,2]; *Reviews*[3-7]; *Modifications & Improvements*[8-11]]

Mechanism: [15,7]

When substoichiometric/stoichiometric amounts of $Pd(OAc)_2$ is used:



WHARTON OLEFIN SYNTHESIS (WHARTON TRANSPOSITION)

(References are on page 706)

Importance:

[*Seminal Publications*[1-4]*; Reviews*[5]*; Modifications & Improvements*[6-8]]

Mechanism:[4,6,8]

The mechanism of the *Wharton transposition* is very similar to that of the *Wolff-Kishner reaction*. The epoxyhydrazone is first deprotonated, which triggers the facile and irreversible epoxide ring-opening. The C-N bond of the resulting vinyl diazene[11,12] is broken upon another deprotonation, releasing N_2 and a vinyl anion, which in turn affords the desired allylic alcohol. Alternatively, the formation of a vinyl radical has been proposed.[6]