

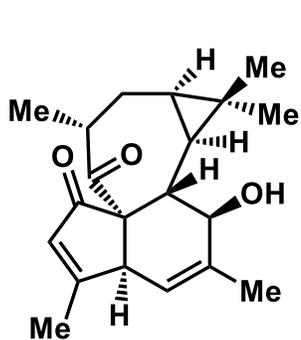
Total Synthesis of the *Euphorbia* Diterpenoid Pepluacetal

Meng Liu, Chuanhua Wu, Xingang Xie, Huilin Li,* and Xuegong She*

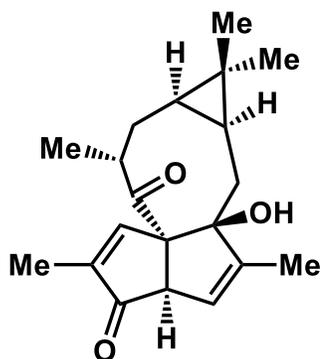


南欧大戟

A. Pepluanols with reported total synthesis.

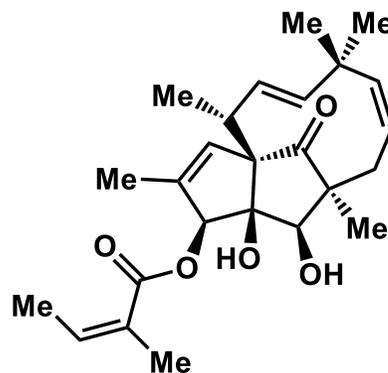


Pepluanol A (1)
Ding (2017), Racemic
Gaich (2021), Asymmetric

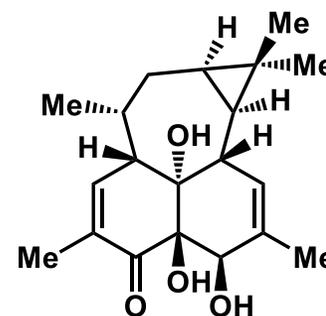


Pepluanol B (2)
She (2020),
Racemic & asymmetric

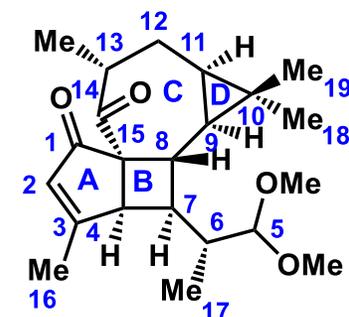
B. Pepluanols without synthesis to date.



Pepluanol C (4)

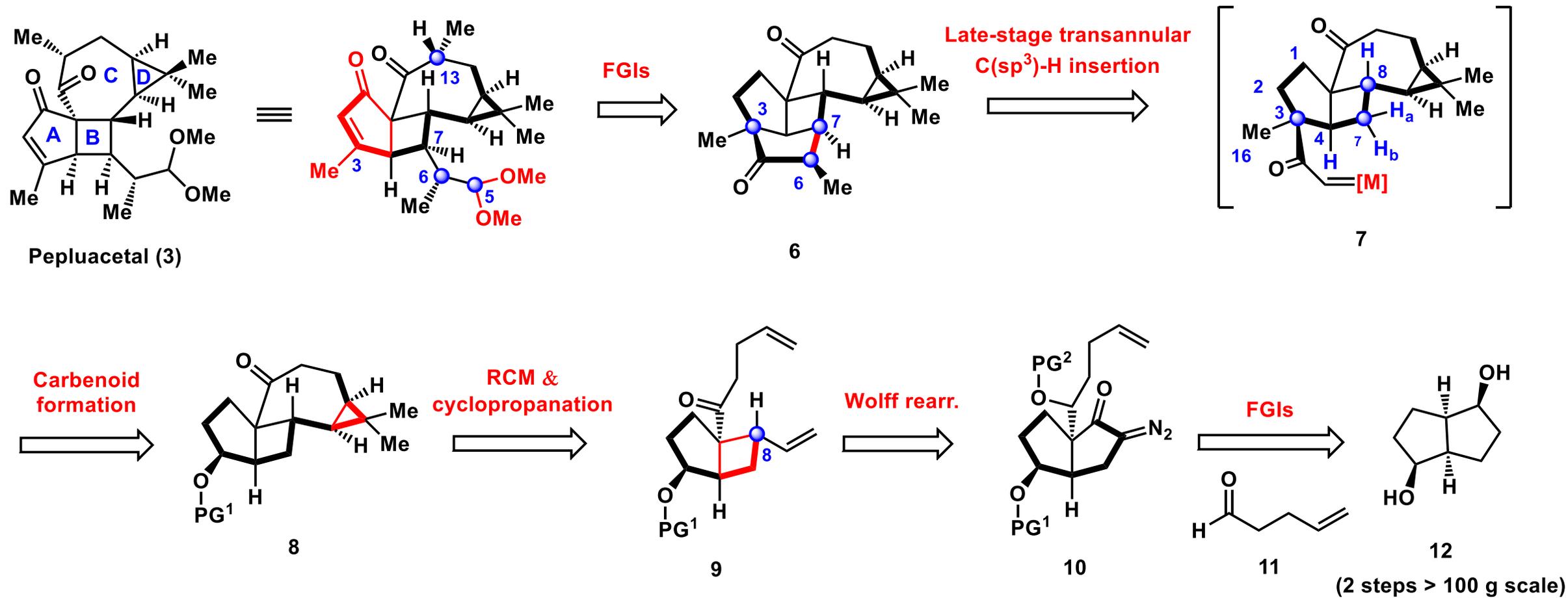


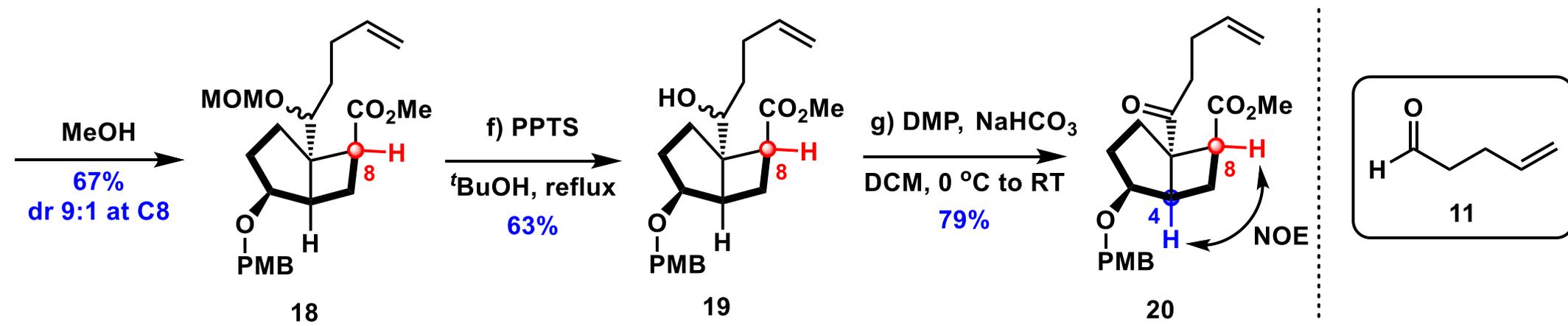
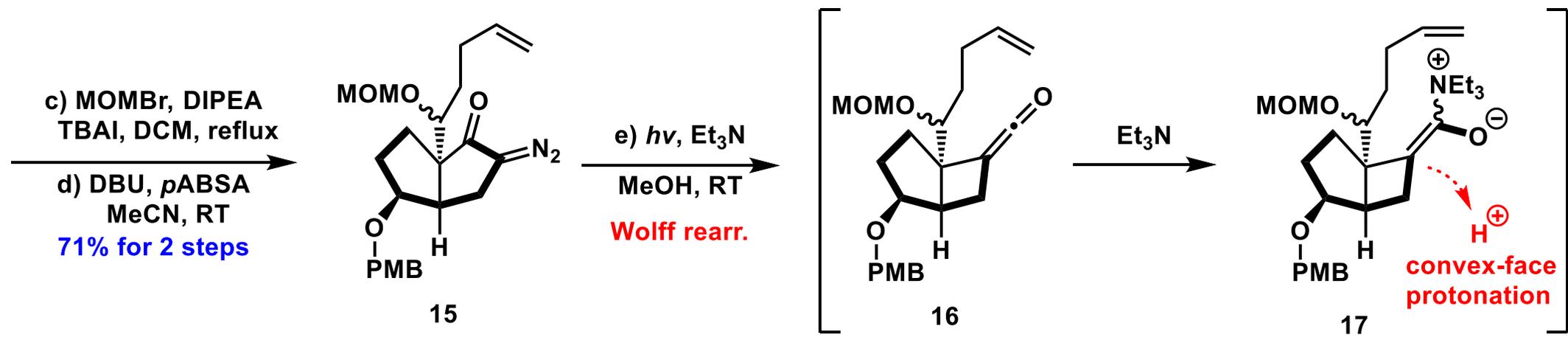
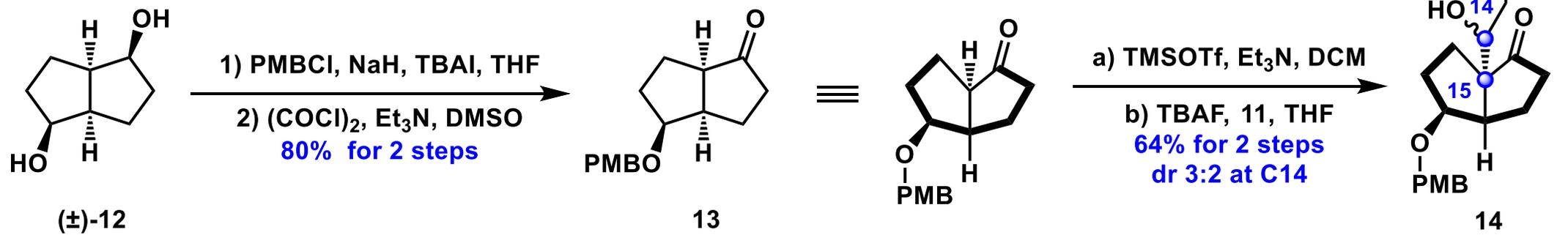
Pepluanol D (5)



Pepluacetal (3)
This work,
Racemic & asymmetric

Structural features:
△ [5-4-7-3] Carbocycle
△ Unique cyclobutane
△ 8 Stereocenters:
7 contiguous centers,
1 quaternary center

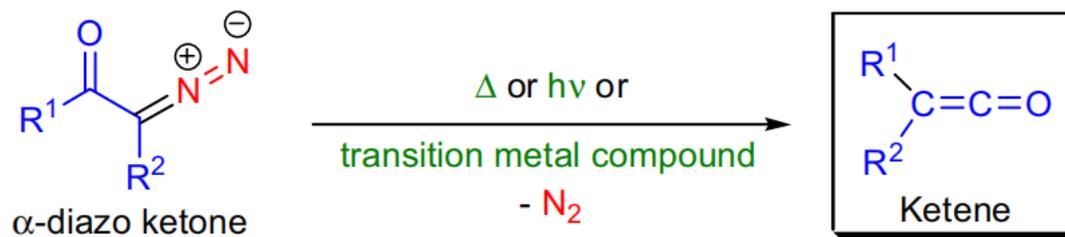




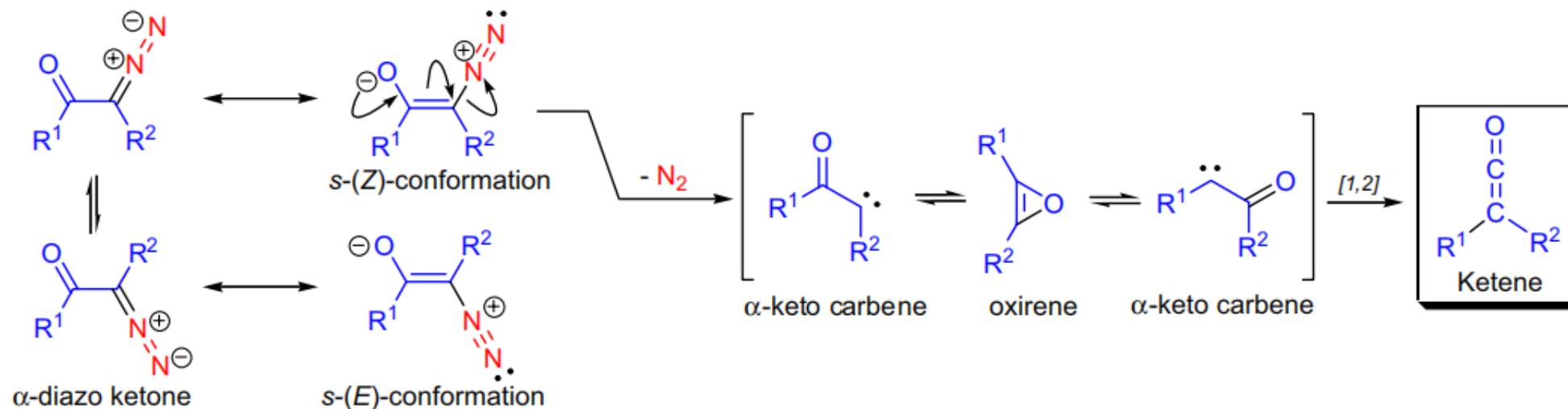
WOLFF REARRANGEMENT

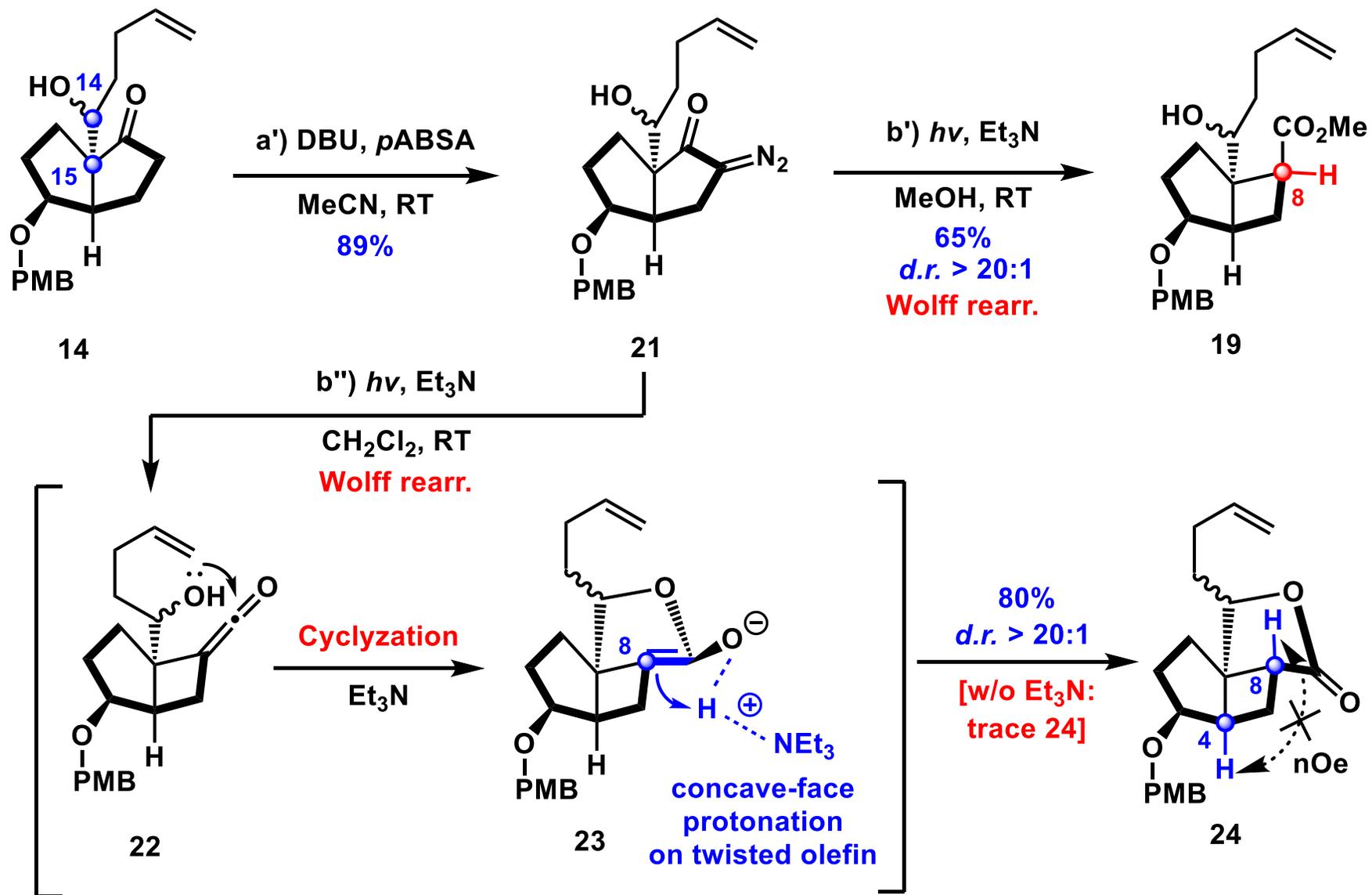
(References are on page 711)

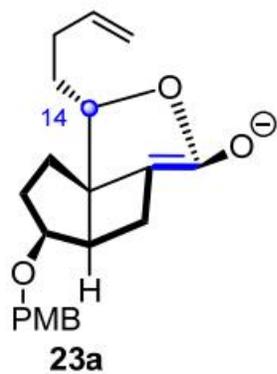
Wolff rearrangement:



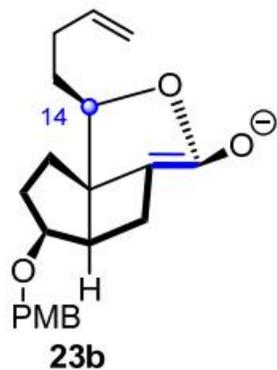
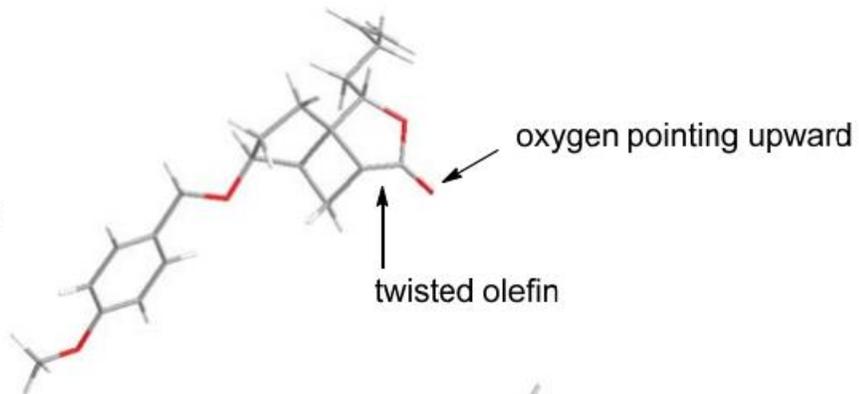
Mechanism: 65,9,13



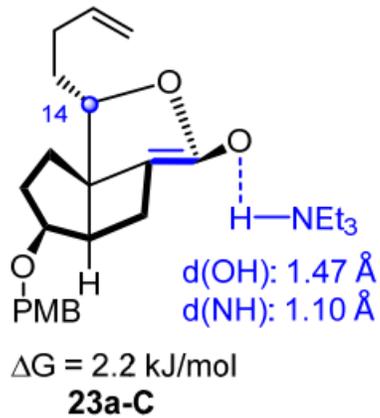
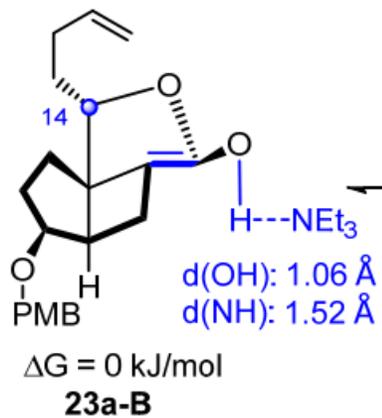
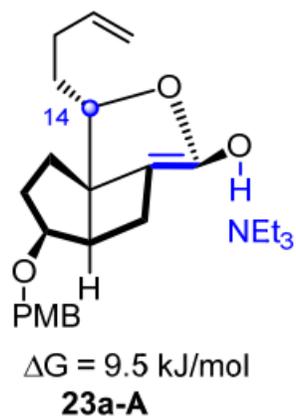
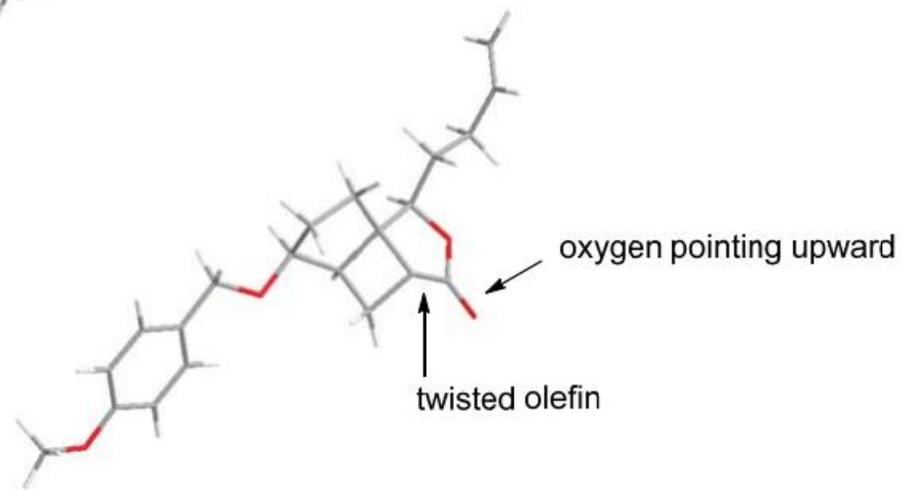


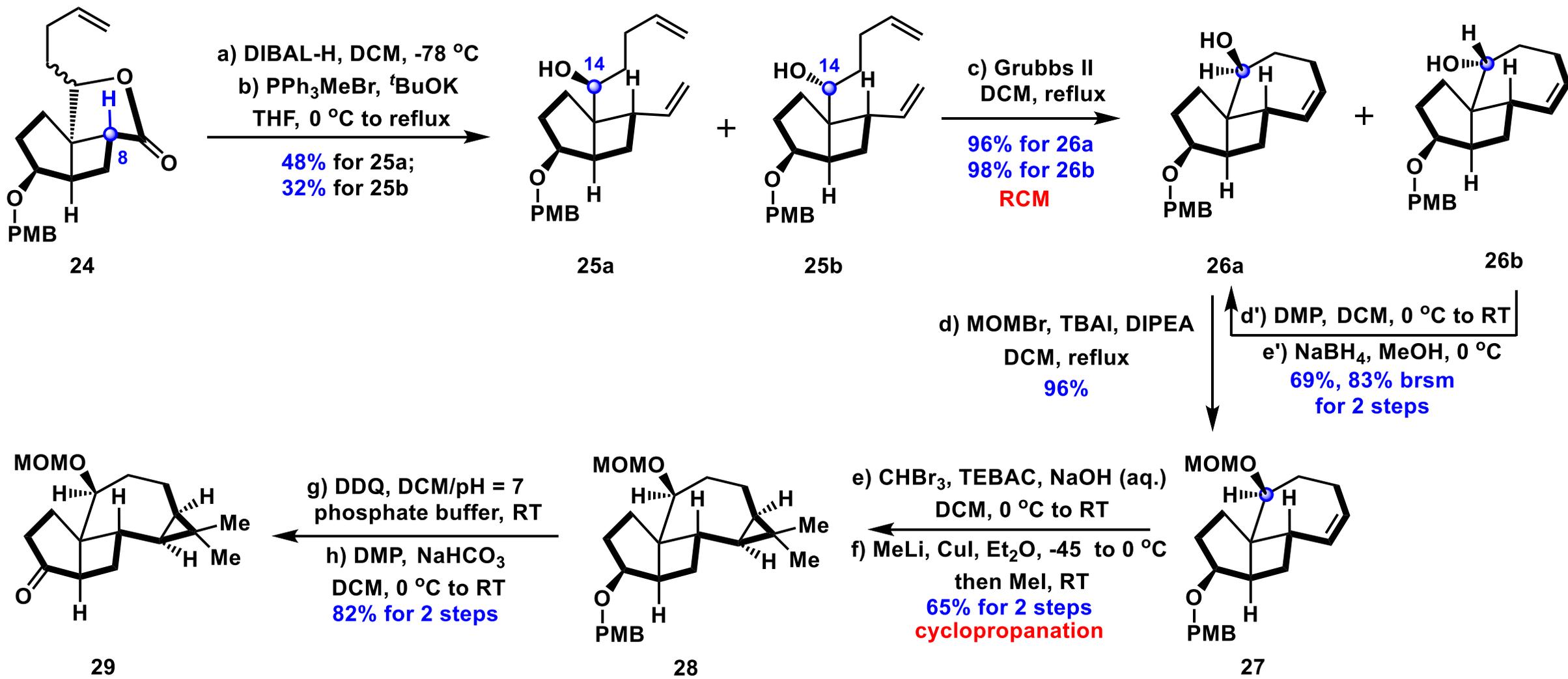


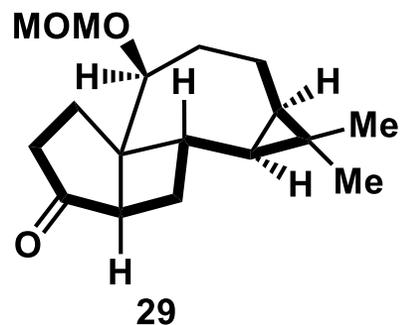
≡



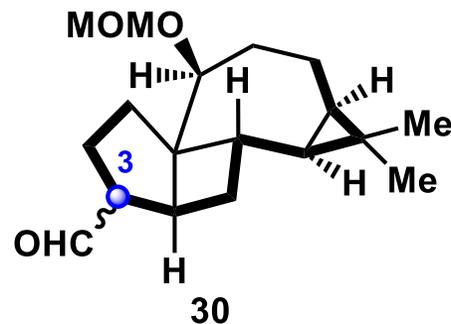
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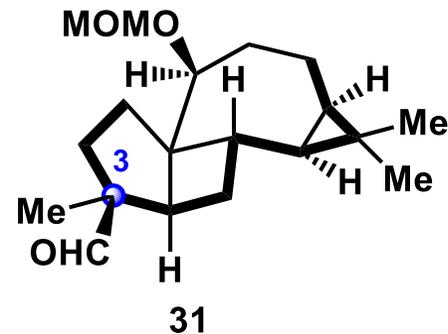




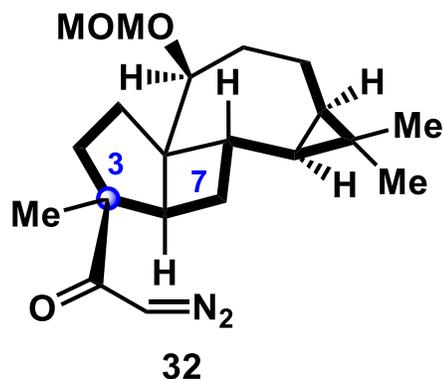
a) MOMPh₃Cl, ^tBuOK
THF, 0 °C to RT
b) Cl₃CCO₂H, DCM, RT
86% for 2 steps
d.r. = 1:1 at C3



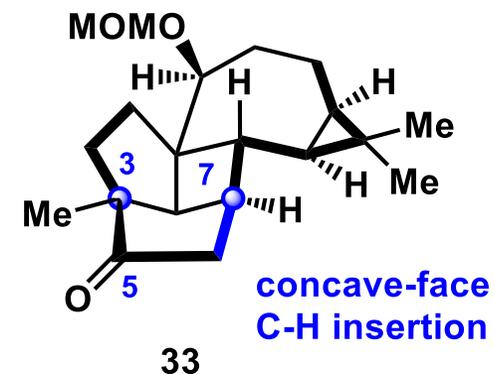
c) MeI, ^tBuOK
THF, -40 °C
78%, d.r. > 20:1 at C3
convex-face
methylation



d) NaClO₂, NaH₂PO₄
2-methyl-2-butene
THF/H₂O/^tBuOH, 0 °C
e) Ghosez's reagent, DCM
0 °C, then TMSCH₂N₂
MeCN, RT
73% for 2 steps

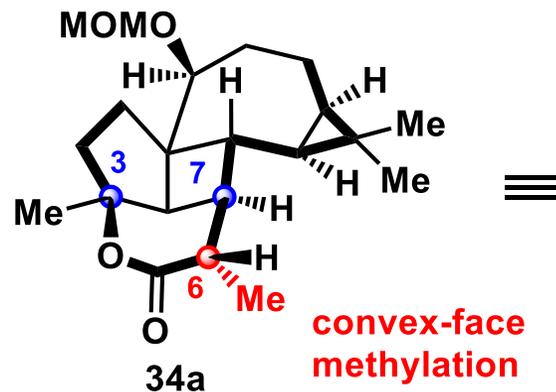


f) Rh₂(OAc)₄
DCM, RT
90%, d.r. > 20:1 at C7
Transannular C(sp³)-H insertion:
sole regio- & diastereoselectivities

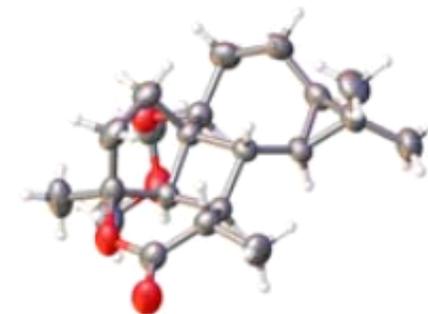


X-ray of 33
CCDC: 2253544

g) *m*CPBA, NaHCO₃
DCM, RT
h) LiHMDS, MeI
THF, -78 °C
68% for 2 steps
d.r. > 20:1 at C6



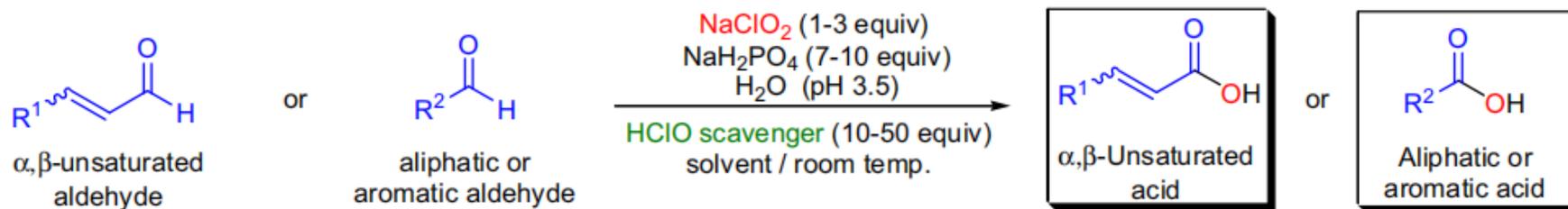
convex-face
methylation



X-ray of 34a
CCDC: 2268395

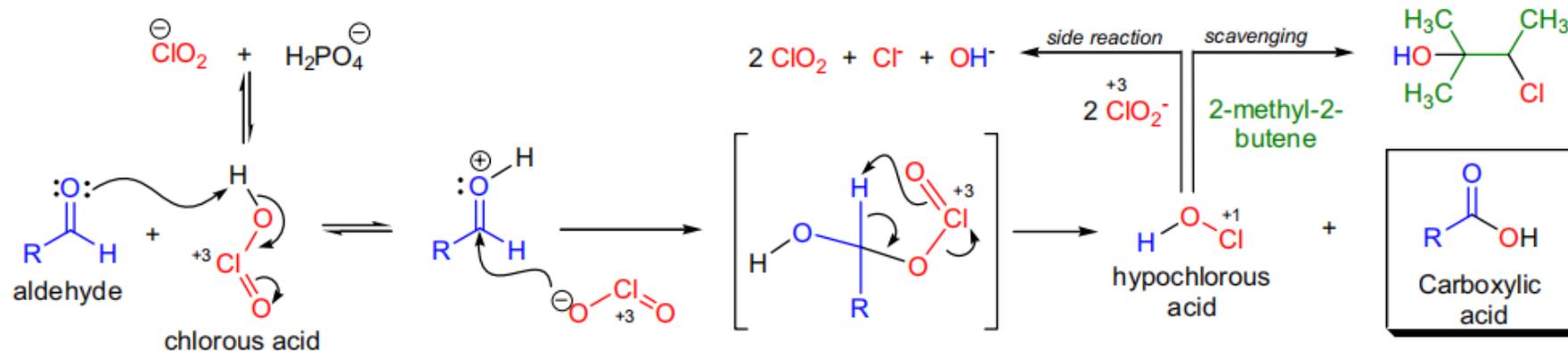
PINNICK OXIDATION

(References are on page 655)



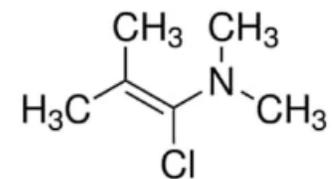
R^1 = H, alkyl, aryl, alkenyl, allyl; R^2 = alkyl, aryl, allyl, homoallyl; scavenger = 2-methyl-2-butene, H_2O_2 , $\text{H}_2\text{NSO}_3\text{H}$, $m\text{-C}_6\text{H}_4(\text{OH})_2$, DMSO; solvent = $t\text{-BuOH}$, $t\text{-BuOH/THF}$

Mechanism: ^{10,6}





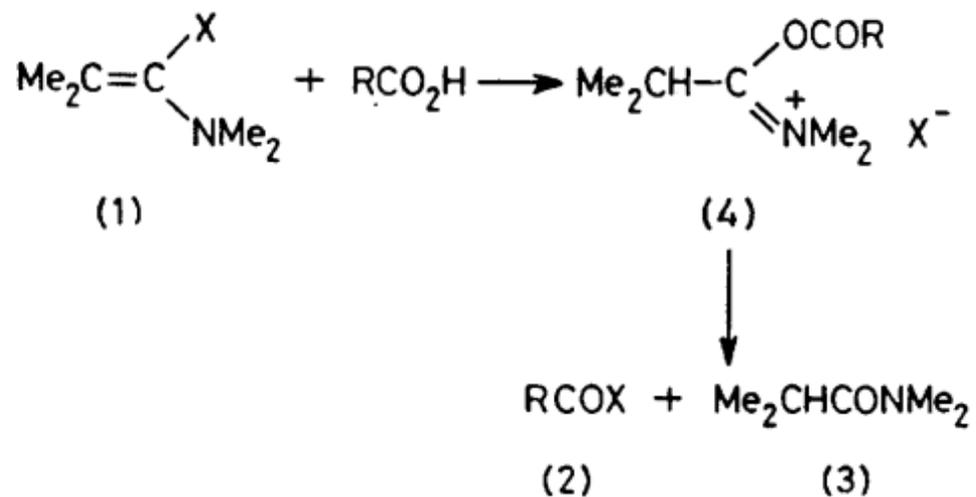
Ghosez试剂



1-氯-N, N, 2-三甲基-1-丙烯胺或四甲基-α-氯烯胺

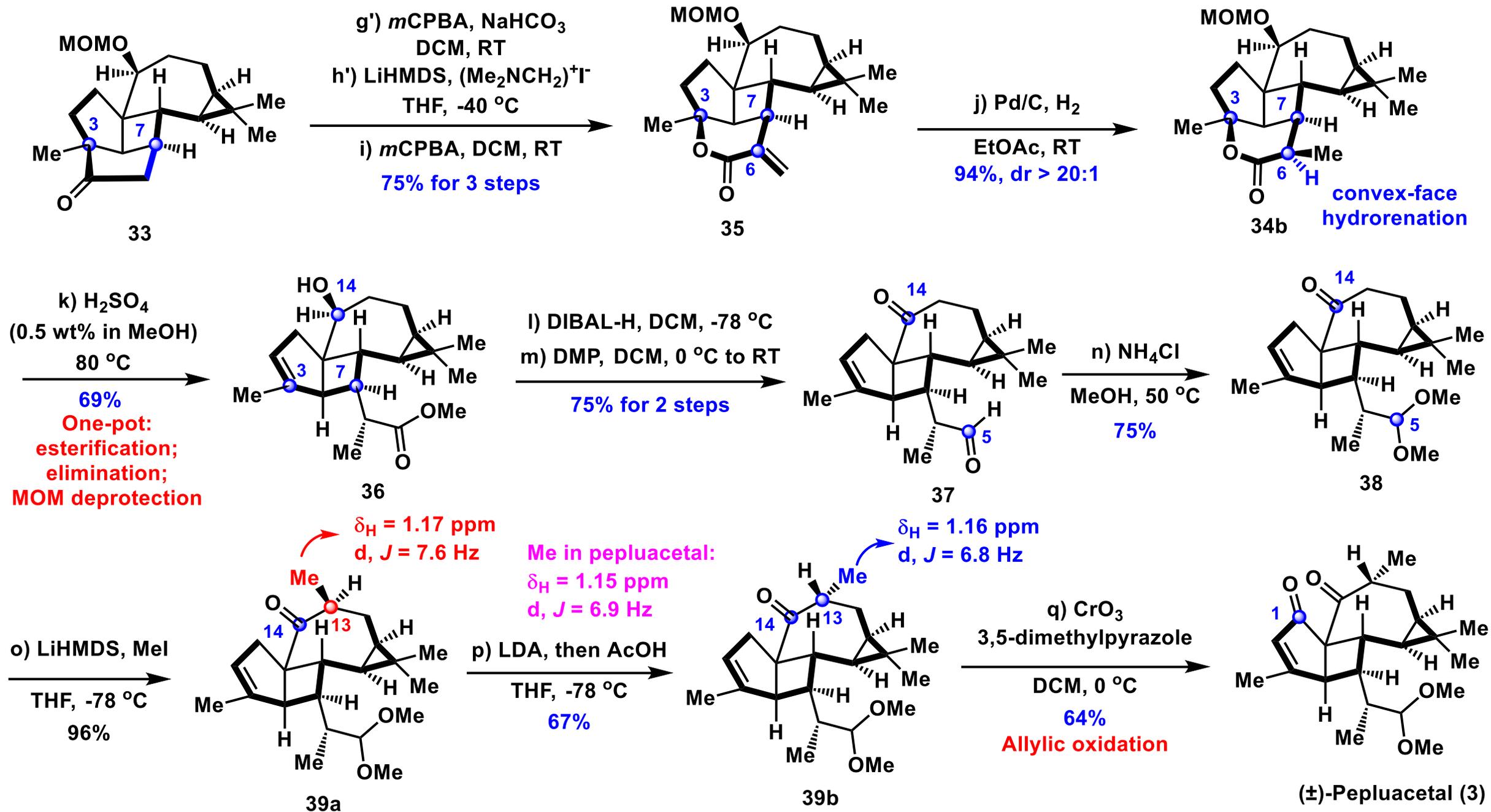
CAS: 26189-59-3

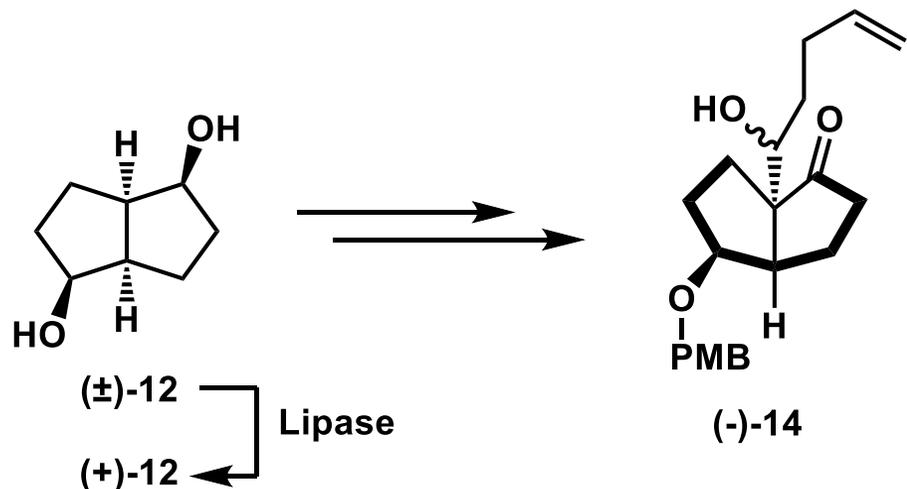
分子量:133.62



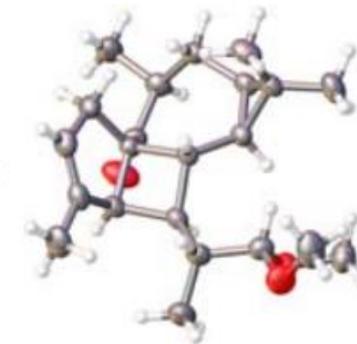
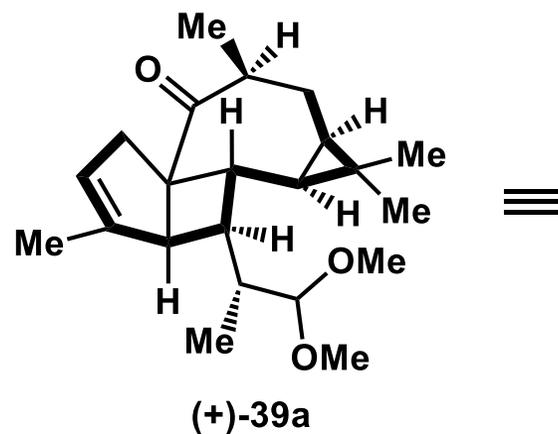
- a**; X = Cl
- b**; X = F
- c**; X = I
- d**; X = Br

J. Chem. Soc. Chem. Commun., **1979**, 1180.





14.4 g



20 mg made in one batch

