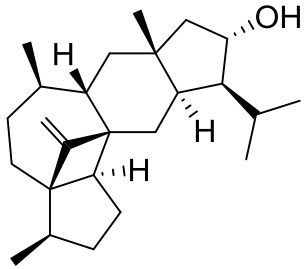


Total Synthesis of Astellatol

Angew. Chem. Int. Ed. **2018**, *57*, 3386 –3390

Jing Xu
Associate Professor

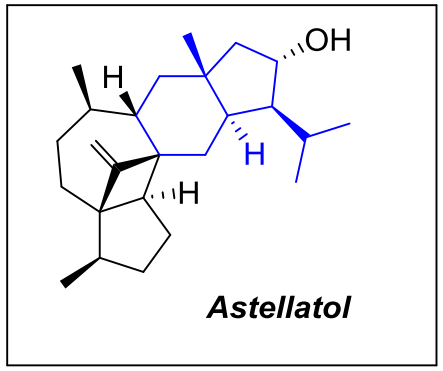
- BS Nanchang University (2000)
- MS Tongji University (2004)
- PhD Leipzig University, Professor Athanassios Giannis (2009)

Nan Zhao, Shuqiang Yin, Shengling Xie, Hao Yan, Pan Ren, Gui Chen, Fang Chen, and Jing Xu.

Department of Chemistry
South University of Science and Technology of China

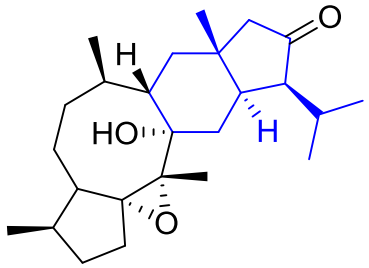
Journal Club. Camilo Meléndez
Renaud Group
DCB, UniBe
29.03.2018

Sesterterpenoids

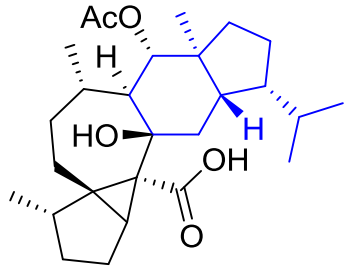


Astellatol

Isolated from
Aspergillus stellatus

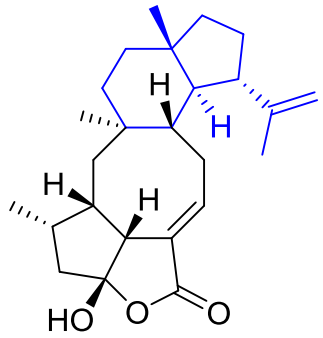


Nitidasin
-Trauner, 2014

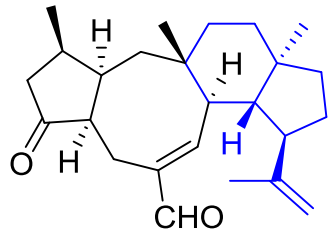


Aspterpenacids

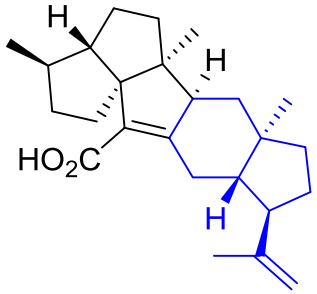
"Isopropyl *trans*-hydrindane sesterterpenoids"



Variecolactone

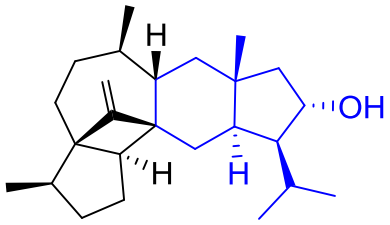


Variecolin

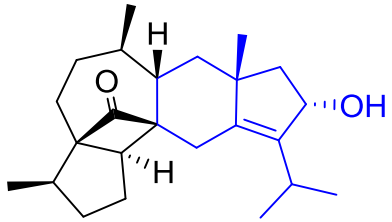


Retigenaric acid A
-Corey, 1985
-Wender, 1990

Retrosynthetic Analysis

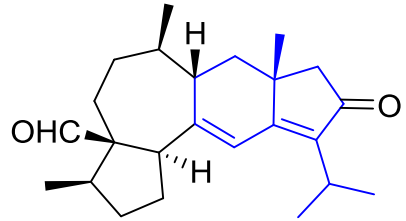


OH-Directed hydrogenation

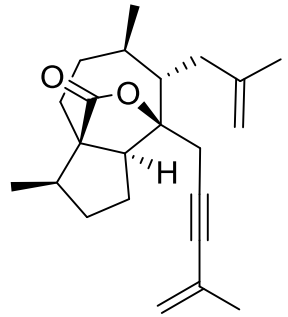


Advanced precursor A

SmI_2-mediated Reductive 1,6-addition

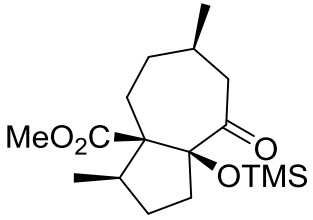


Pauson-Khand reaction

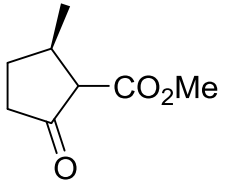


Key Precursor B

Hg-catalyzed Grignard reaction

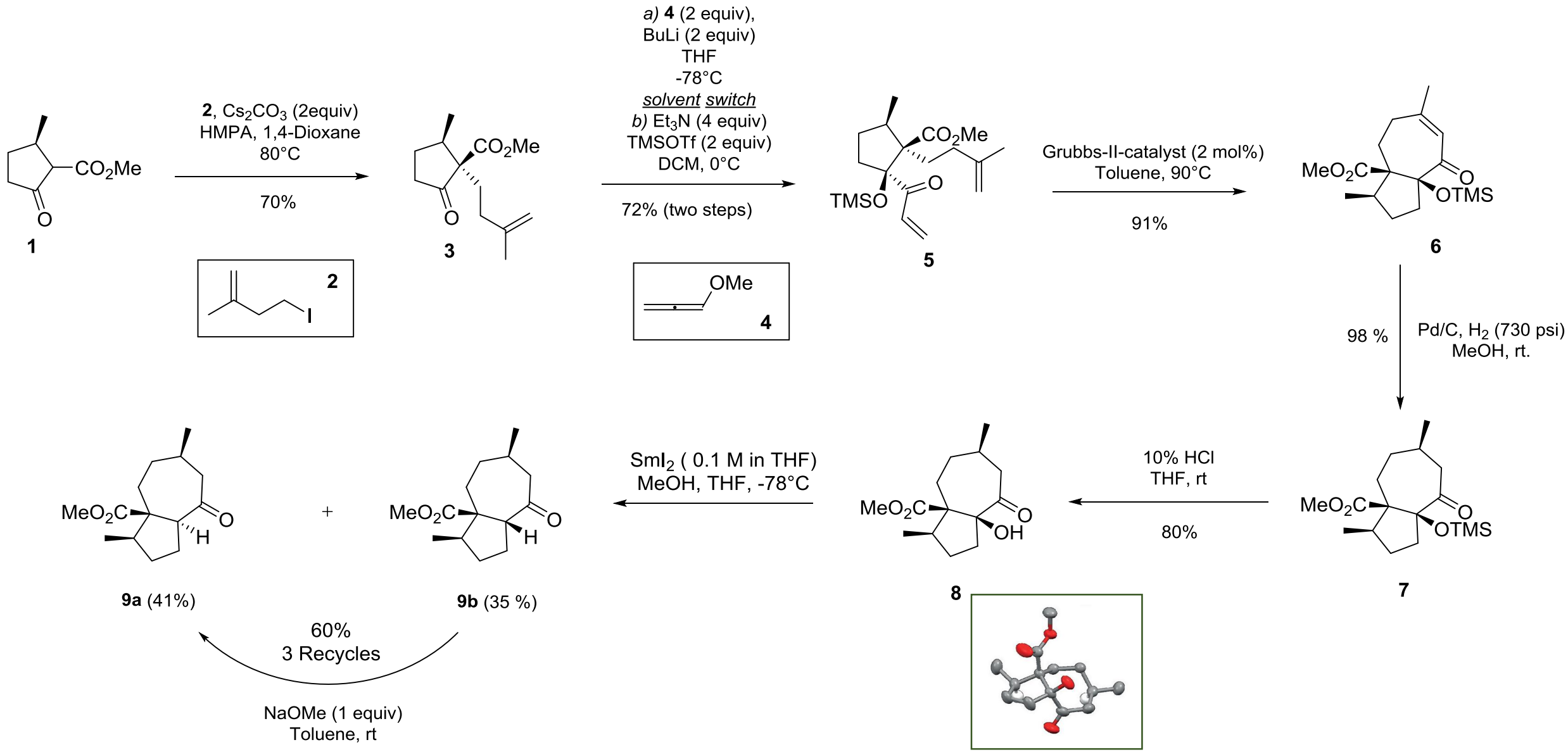


RCM

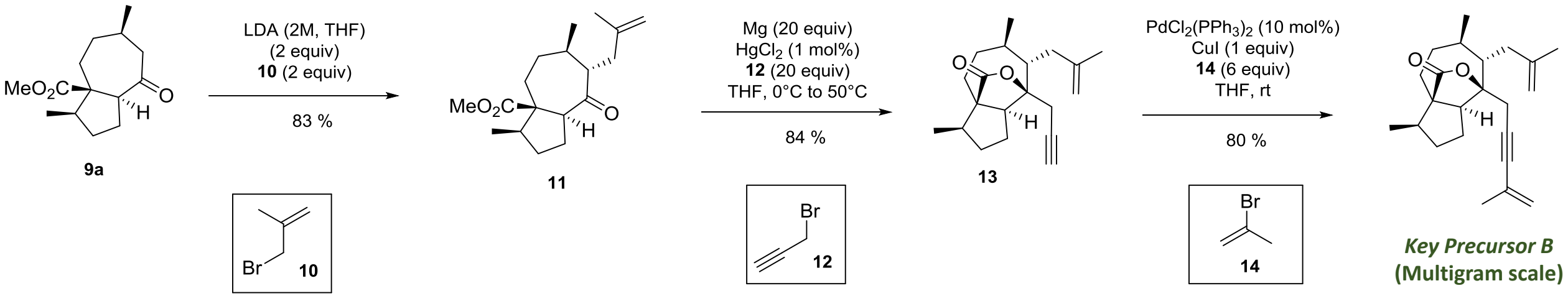


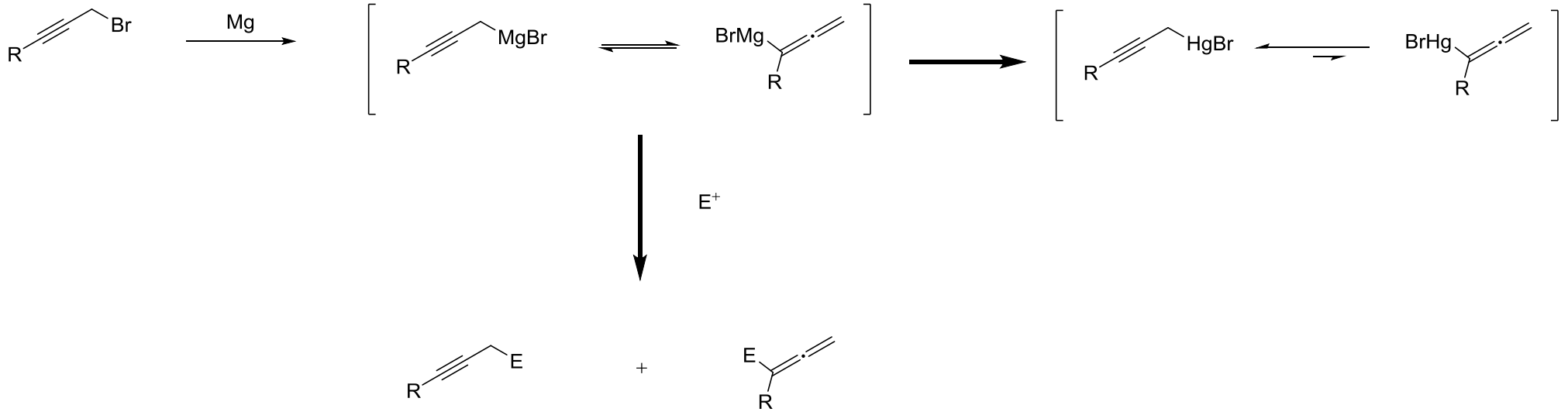
Prepared in two steps From *(R)-(+)*-pulegone

Synthesis of key precursor B

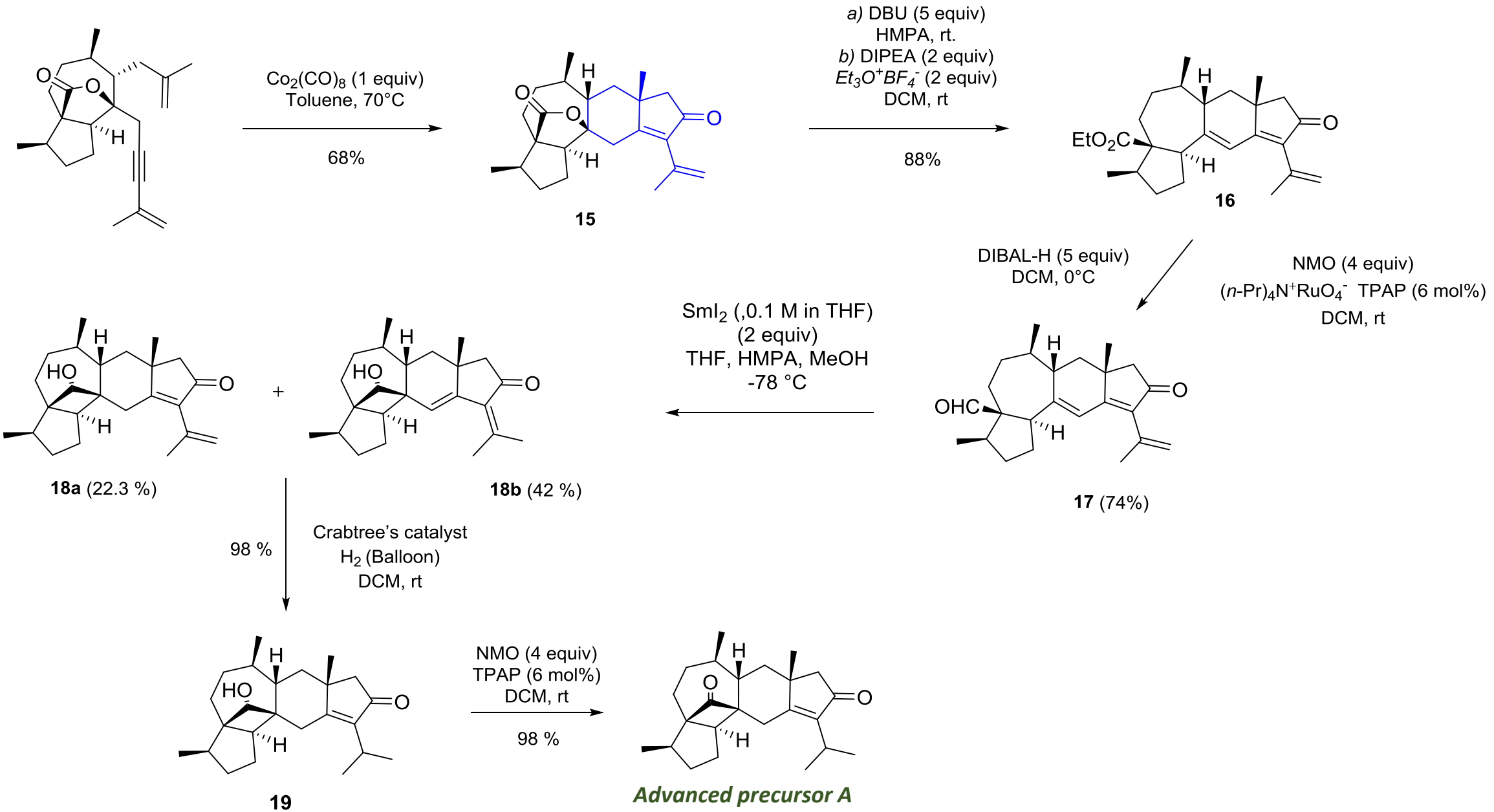


Synthesis of key precursor B

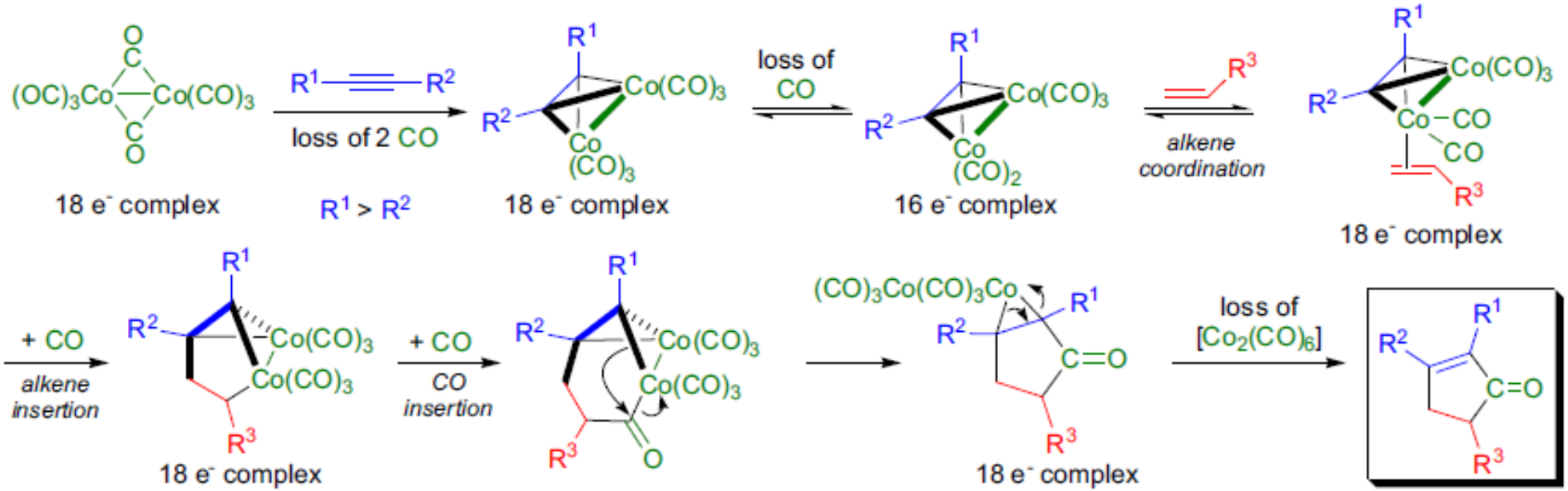




Construction of the hydrindane core and advanced precursor A

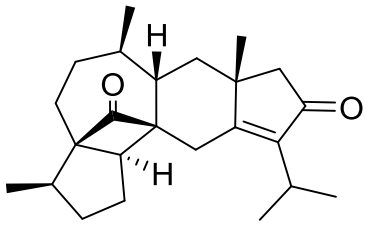


Pauson-Khand reaction



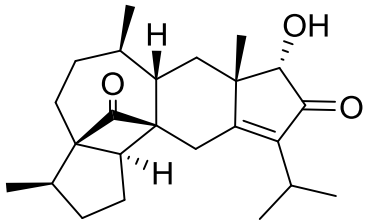
Strategic Applications of Named Reactions in Organic Synthesis: Background and Detailed Mechanisms (Kürti, László; Czakó, Barbara).

End of the Game



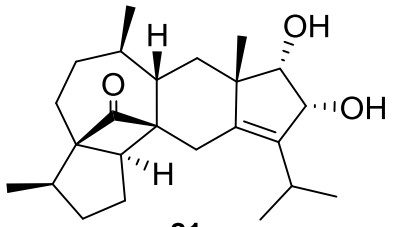
NaHMDS (3.8 equiv)
THF, -78°C
then Davis oxaziridine

99%



20

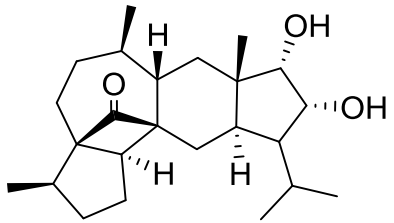
$CeCl_3 \cdot 7H_2O$ (1 equiv)
$NaBH_4$ (2 equiv)
MeOH, 0 °C.



21

79%

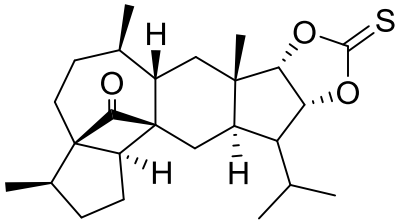
Crabtree's catalyst
$C_{31}H_{50}F_6IrNP_2$, H_2 (500 psi)
DCM, rt



22

$(Im)_2C{=}S$ (10 equiv)
Toluene, reflux

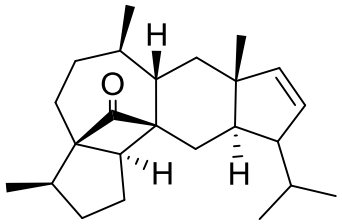
80%



22a

$P(OCH_3)_3$ (60mL/mmol)
Reflux

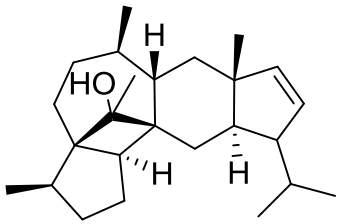
93%



23

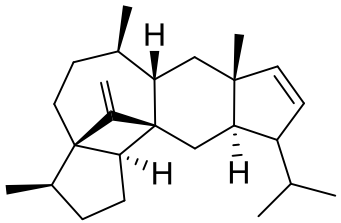
88%

MeLi (5 equiv)
THF, 0 °C to 50 °C



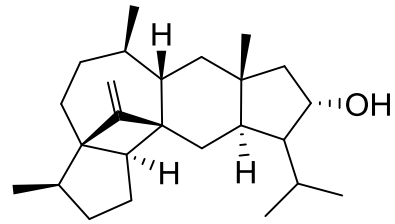
24

pyridine (5 equiv)
$SOCl_2$ (3 equiv)
DCM 0°C



25

$BH_3 \cdot Me_2S$ (1.5 equiv)
THF, 0°C
Then, MeOH, NaOH, H_2O_2



Astellatol (56%)
+ 15% of regioisomer

Conclusion

- First and enantiospecific total synthesis of the ***Astellatol*** in 25 steps (0.63% overall yield)
  Scalable key transformations (multigram scale)

- Development of a synthetic strategy for the preparation of the *trans*-hydrindane core

- Unprecedent SmI_2-mediated reductive radical 1,6-addition to furnish a cyclobutane moiety

Thank you for the attention