

# A General Entry to Antifeedant Sesterterpenoids: Total Synthesis of (+)-Norleucosceptroid A, (–)-Norleucosceptroid B, and (–)-Leucosceptroid K

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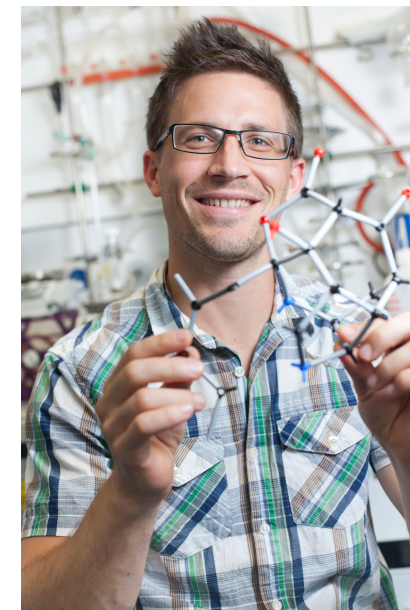
Ludwig-Maximilians-University Munich, Germany

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# Introduction

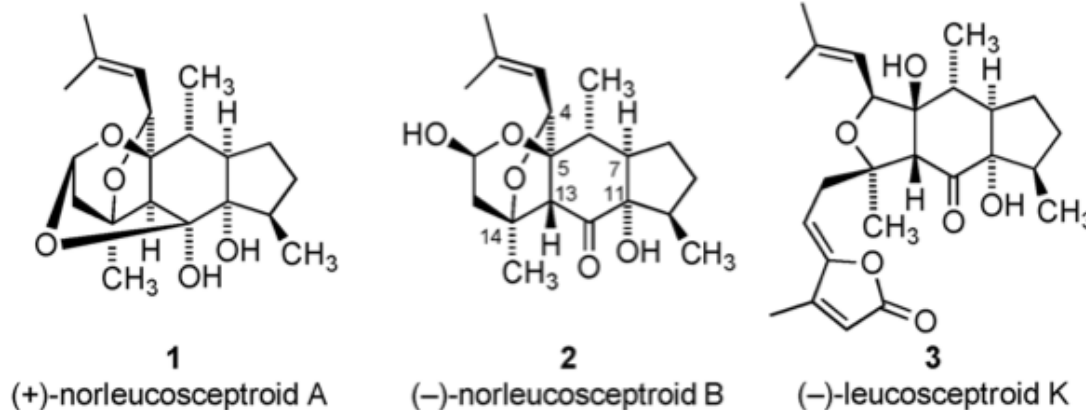
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- > Thomas Magauer, born in 1983 in Linz, Austria
  - PhD in Vienna under the supervision of Johann Mulzer (2007)  
*Enantioselective syntheses of the complex polyketide kendomycin and the sesquiterpenoid echinopines A and B*
  - Post-Doc in Harvard University with Andrew G. Myers (2009)  
*worked on chiral silicon protecting groups, synthesis of natural and diverse unnatural antiproliferative trioxacarcins*
  - Liebig-junior research group leader at the LMU Munich (2012)



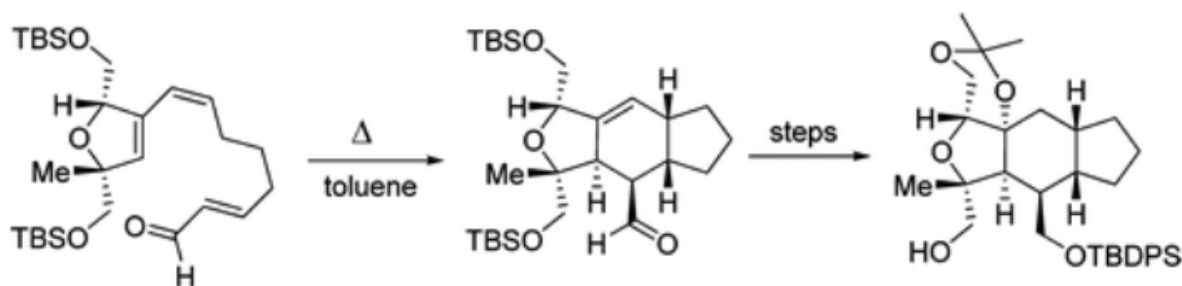
# Antifeedant Sesterterpenoids

- > Isolated from *Leucosceptrum canum* Smith (“Bird’s Coca Cola tree”) and *Colquhounia coccinea* var. *mollisa* found in China and Nepal
- > Both plants are remarkably resistant to herbivores and pathogens
- > showed potent **antifeedant activity** against the cotton bollworm and the beet armyworm
- > concept of employing **nontoxic antifeedant compounds** to protect plants
- > Extracted many different novel **sesterterpenoids** as norleucosceptroids A–C, Leucosceptroids A–O, ... etc. (23 members)
- > 5,6,5 skeleton

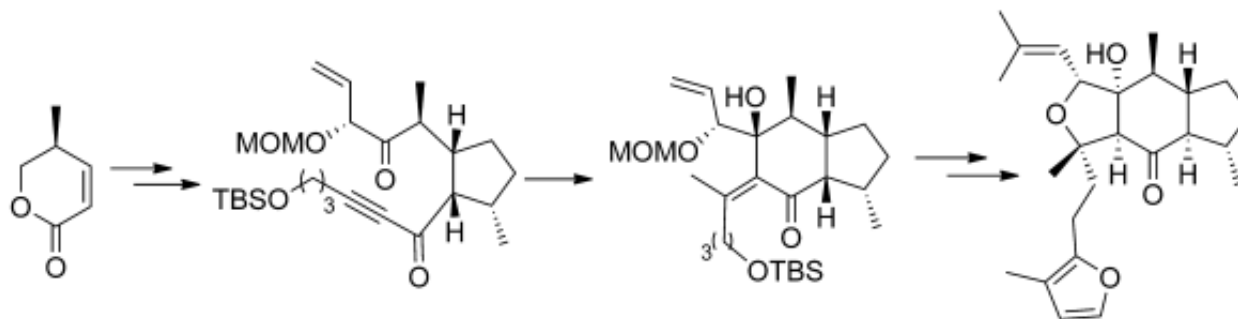


# Previous Synthesis

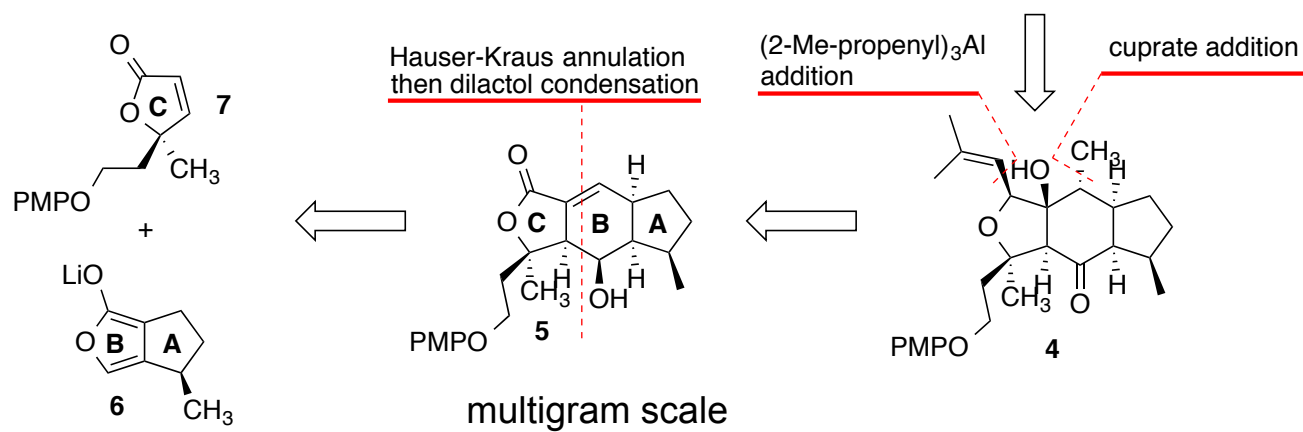
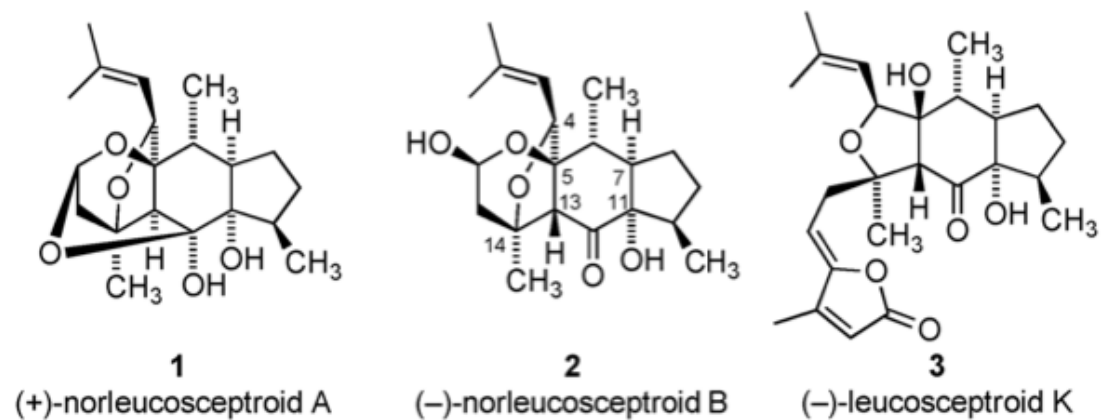
- > Horne and coworkers, **2011**: approach to core of leucosceptroids (IMDA)



- > Liu and coworkers, **2013**: First (asymmetric) total synthesis of leucosceptroid B (Micheal/Aldol/oxy-Micheal sequence)

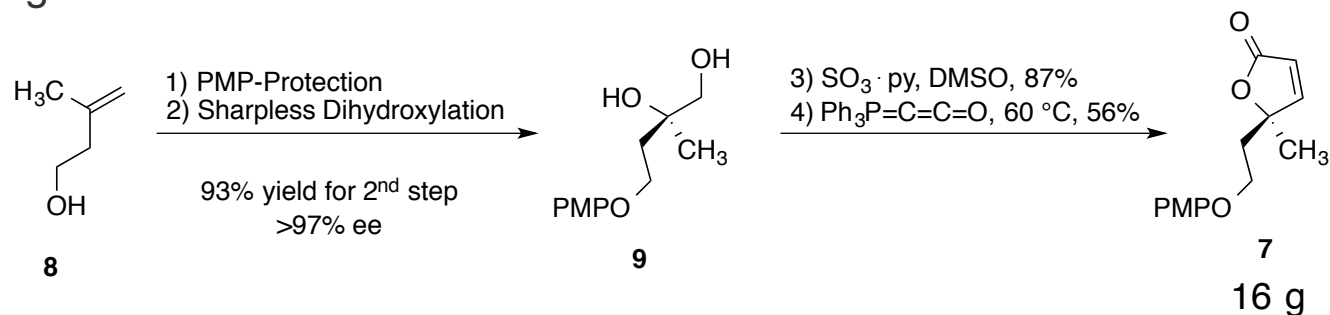


# Retrosynthetic Analysis

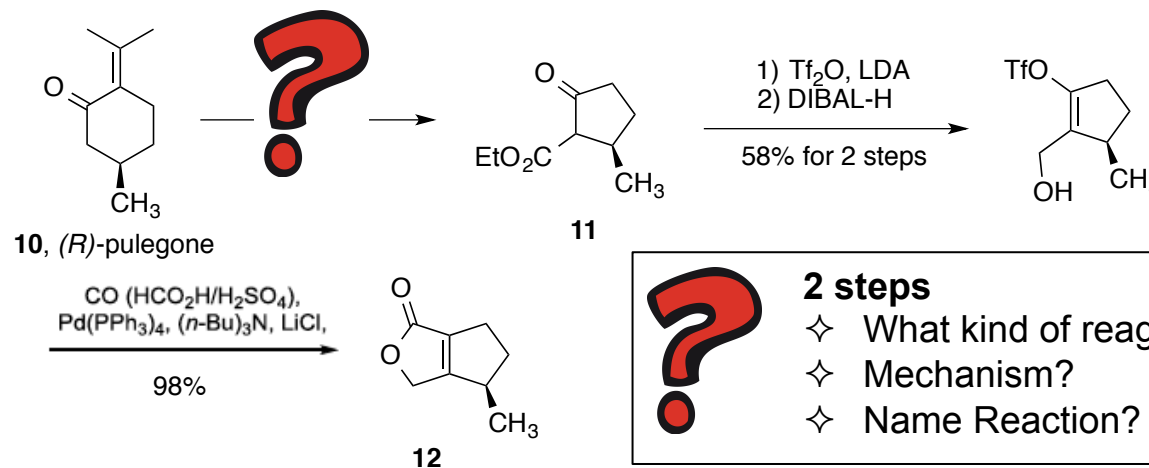


# Synthesis of C-ring butenolide 7 and AB segment 12 (→ 6)

## > C fragment 7

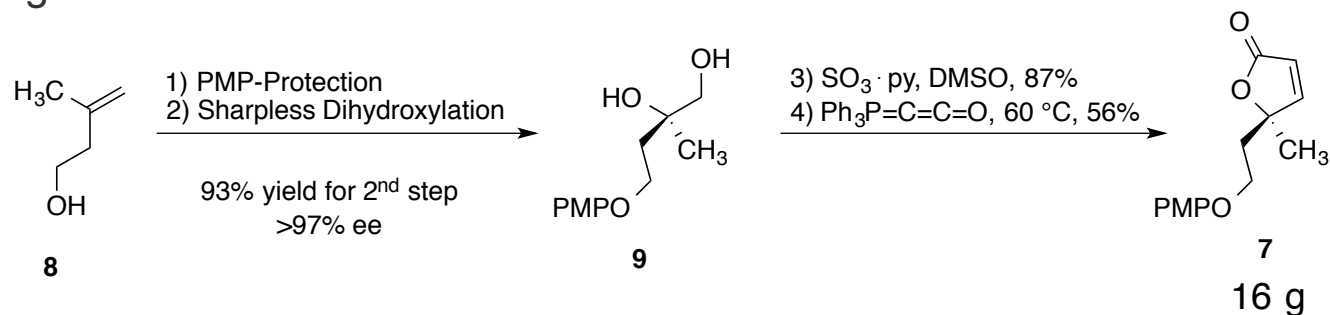


## > AB fragment 12 (→ 6)

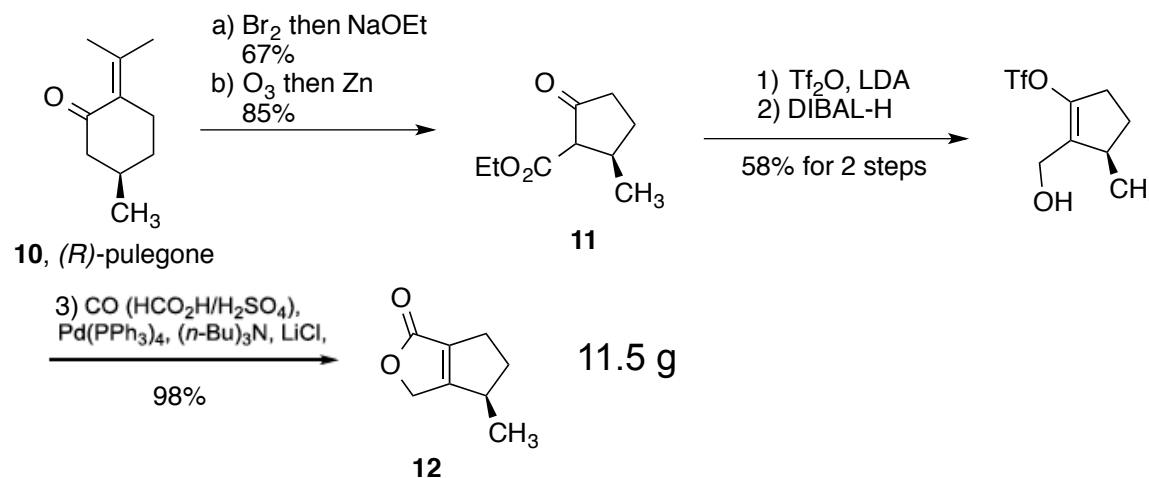


# Synthesis of C-ring butenolide 7 and AB segment 12 (→ 6)

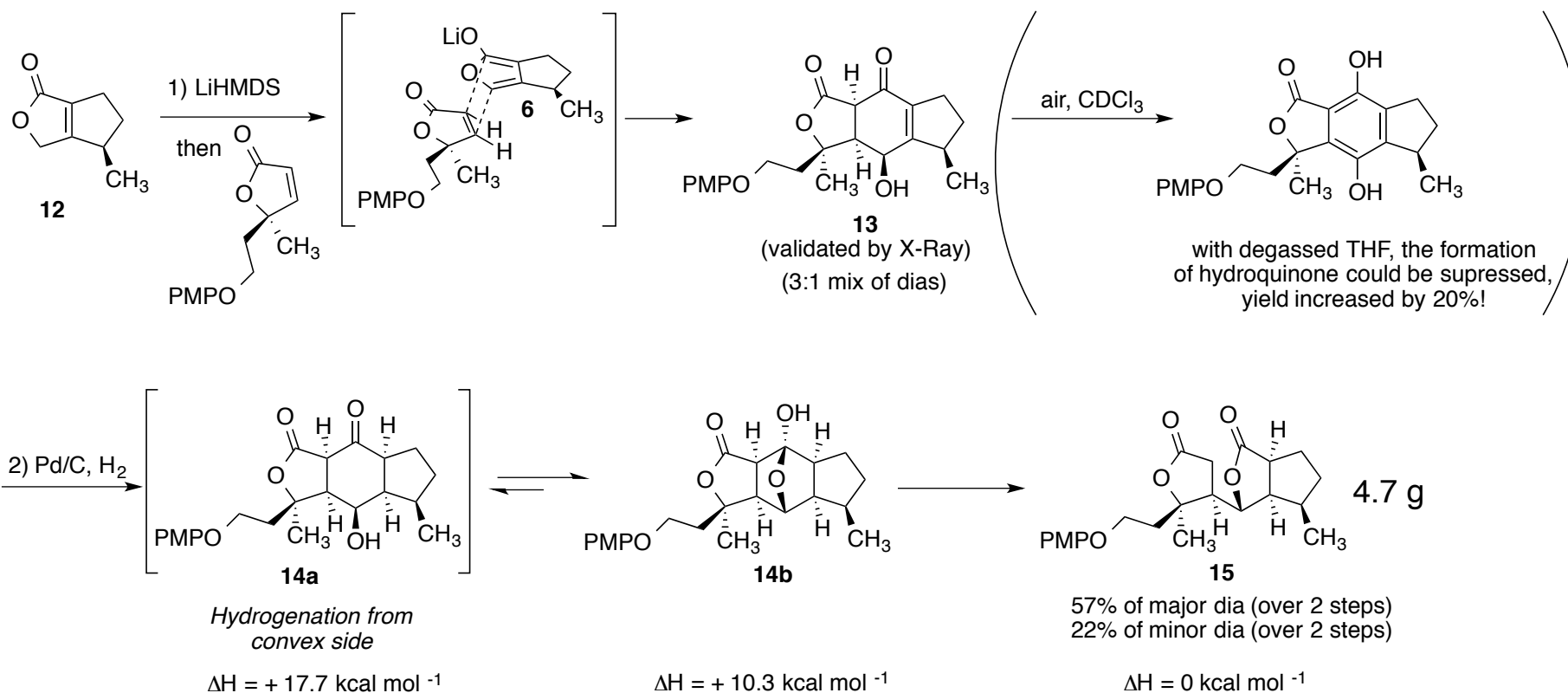
## > C fragment 7



## > AB fragment 12 (→ 6)



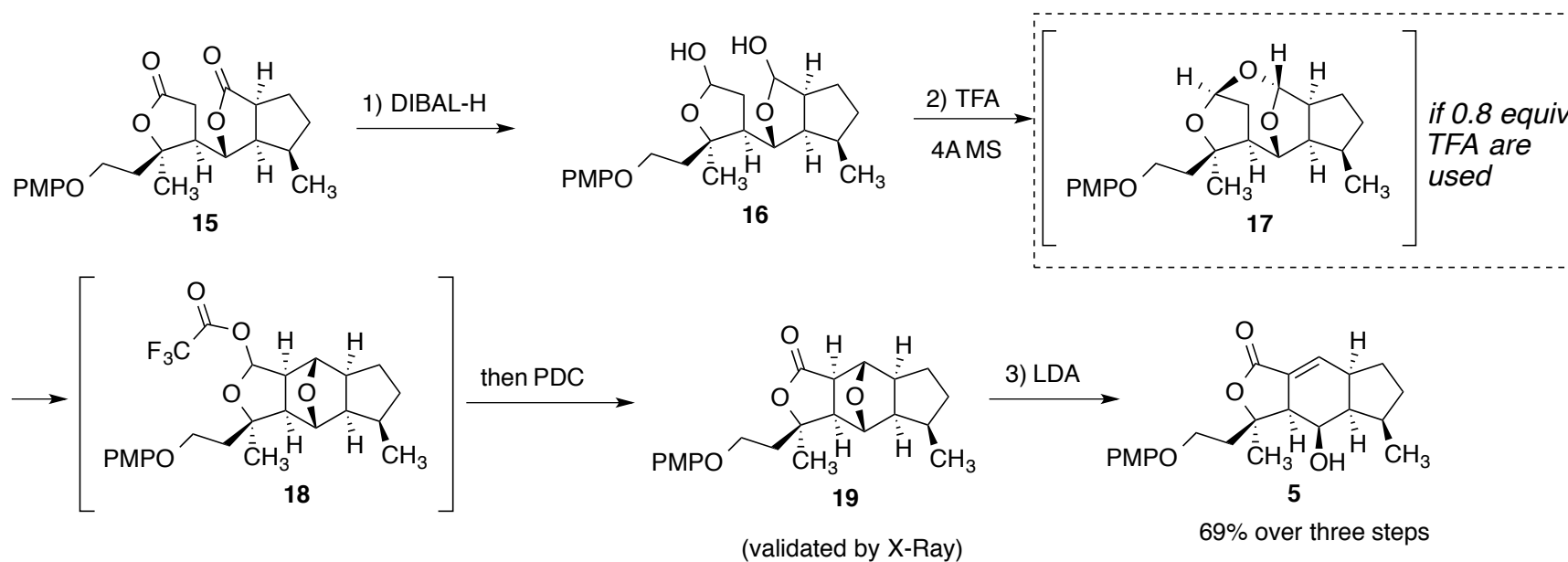
# Fragment coupling to ABC tricycle I



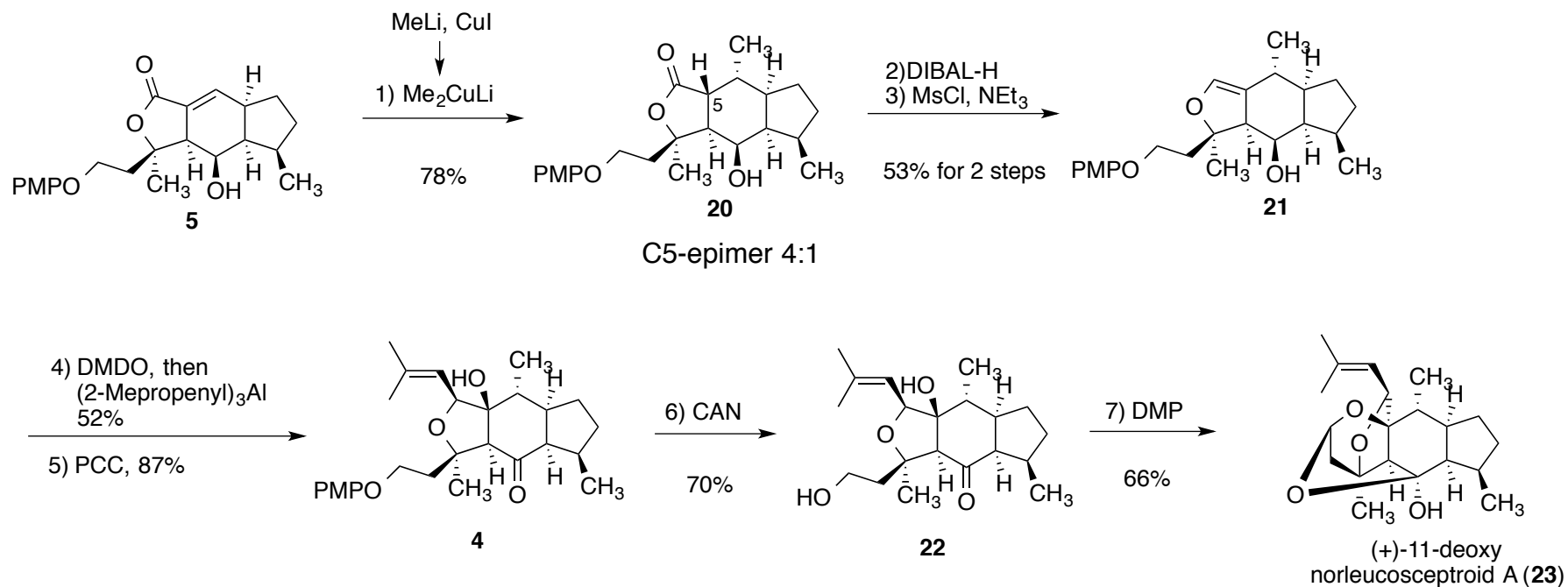
DFT calculations B3LYP/6-31G(d)



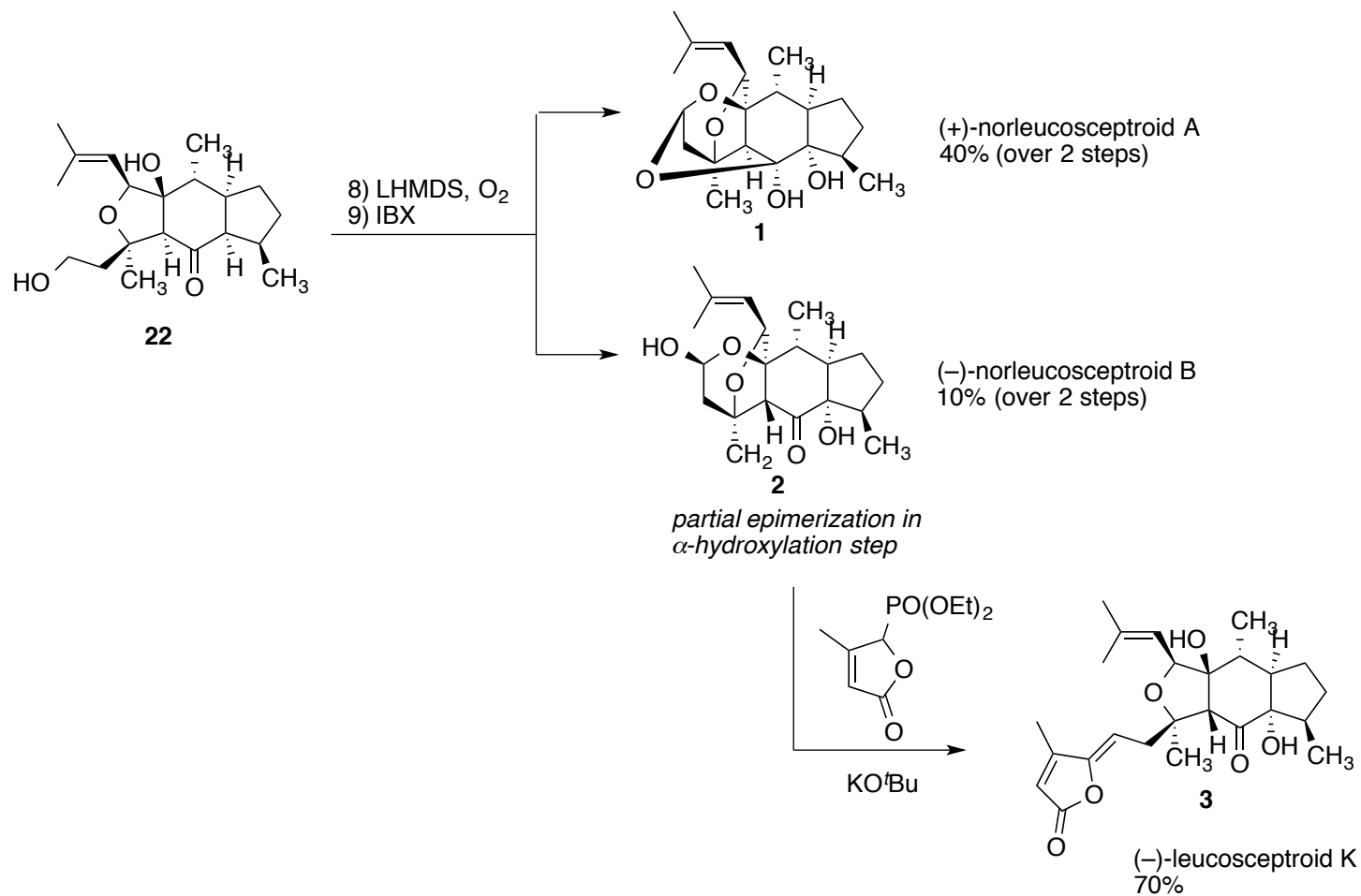
# Fragment coupling to ABC tricycle II



# Functionalization of ABC core and completing total syntheses I

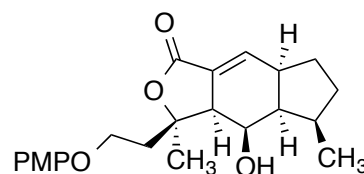


# Functionalization of ABC core and completing total syntheses II



## Conclusion

- > Concept of employing antifeedant compounds from plants to protect plants from insects → natural and nontoxic pesticide (alternative to synthetic)
- > Hauser-Kraus annulation (alternative to [4+2]-cycloaddition with substituted furans)
- > intramolecular aldol-type condensation as key step to produce 5,6,5-skeleton in multigram scale (3.0 g)



- > 16 steps (longest linear sequence) for norleucosceptroid A and B