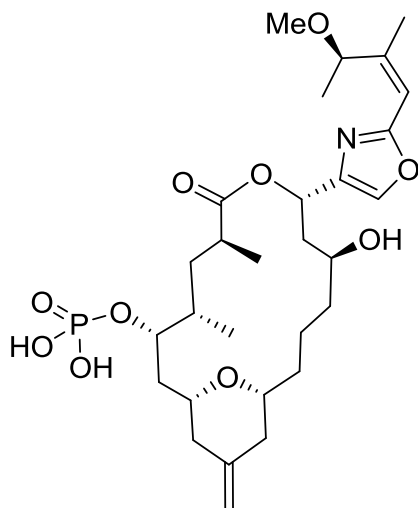


Concise Total Synthesis of Enigmazole A

Andreas Ahlers, Teresa de Haro, Barbara Gabor, and Alois Fuerstner

DOI: 10.1002/anie.201510026



Enigmazole A

Enigmazole A was isolated from a sponge of the genus *Cinachyrella enigmata*.

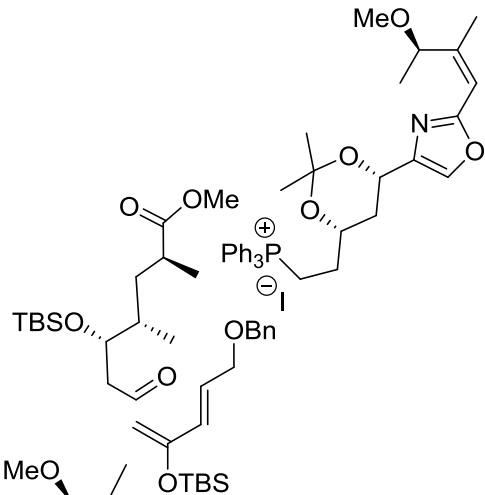
The first phosphorylated macrolides of marine origin but were reported to elicit an exceptionally rare phenotypic response in that they interfere with c-Kit signaling.

Eight stereogenic center exist.

Retro synthesis:

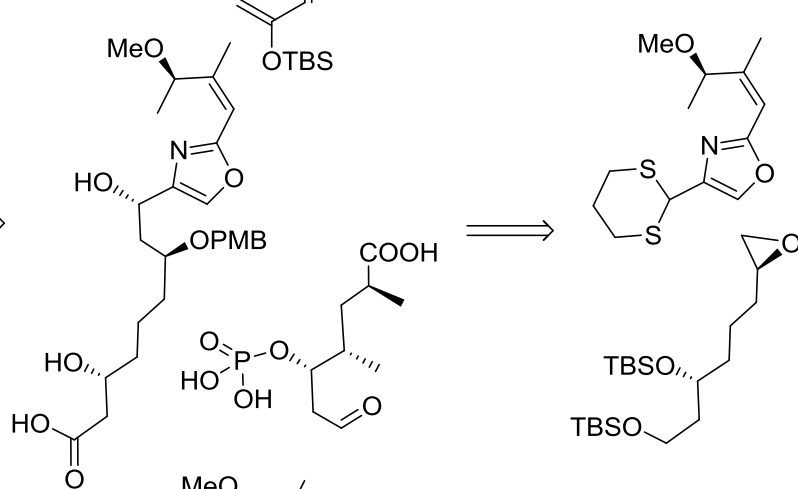
Keck
esterification
Hetero-D-A
Wittig reaction

By Molinski, JACS, **2010**, 10286 22 steps 0.41% yield



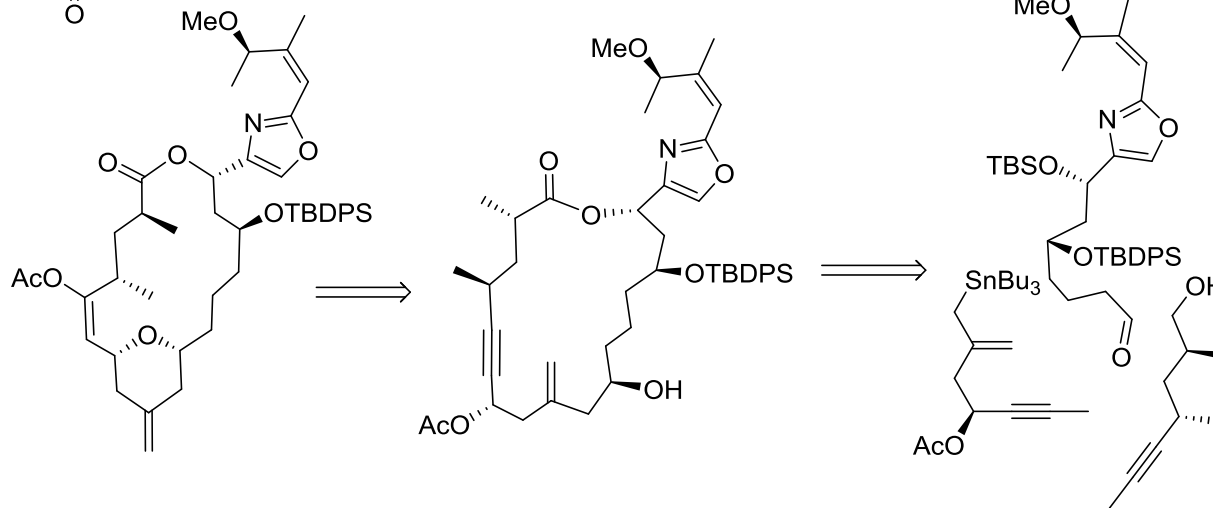
Yamaguchi
esterification
Petasis-Ferrier
rearrangement

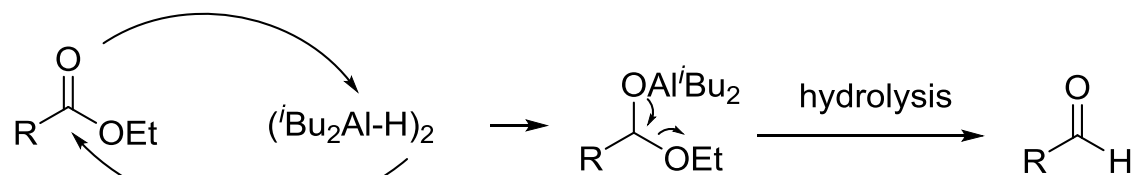
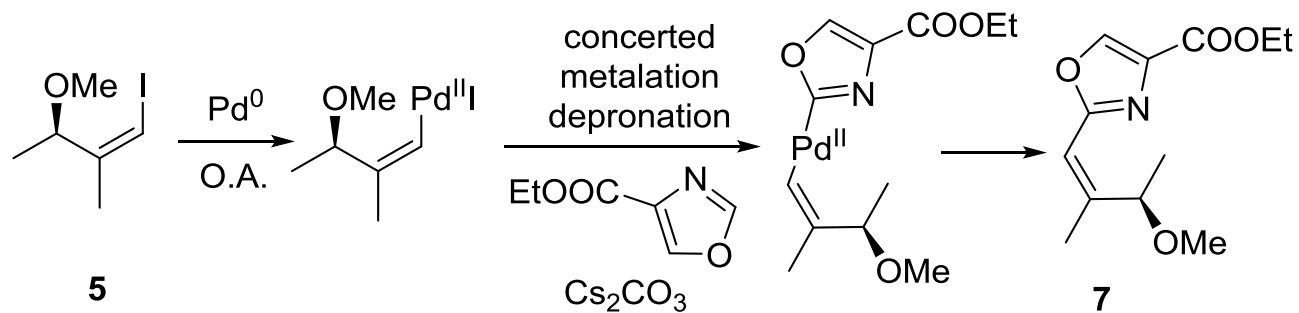
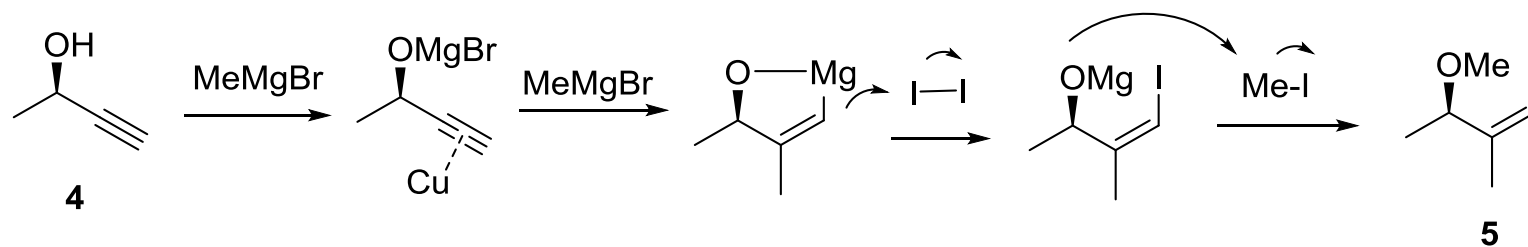
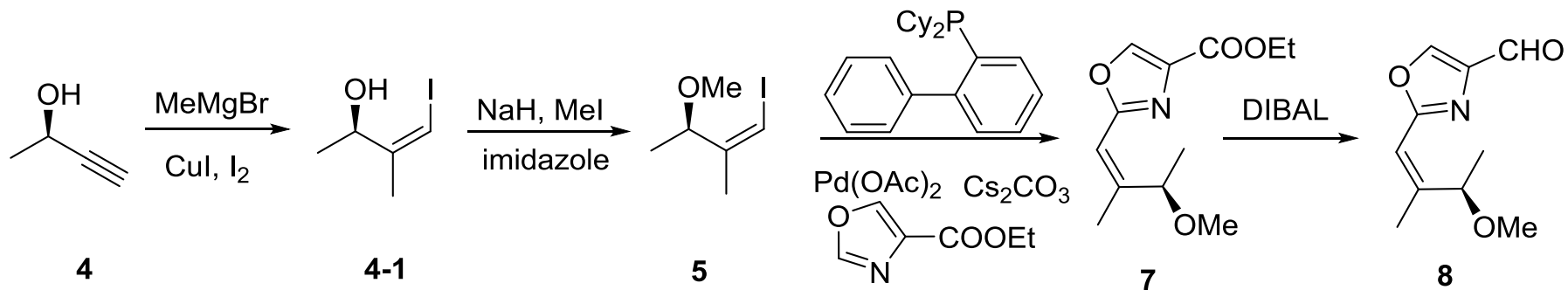
By Smith III, JACS, **2015**, 15426 22 steps, 4.4% yield



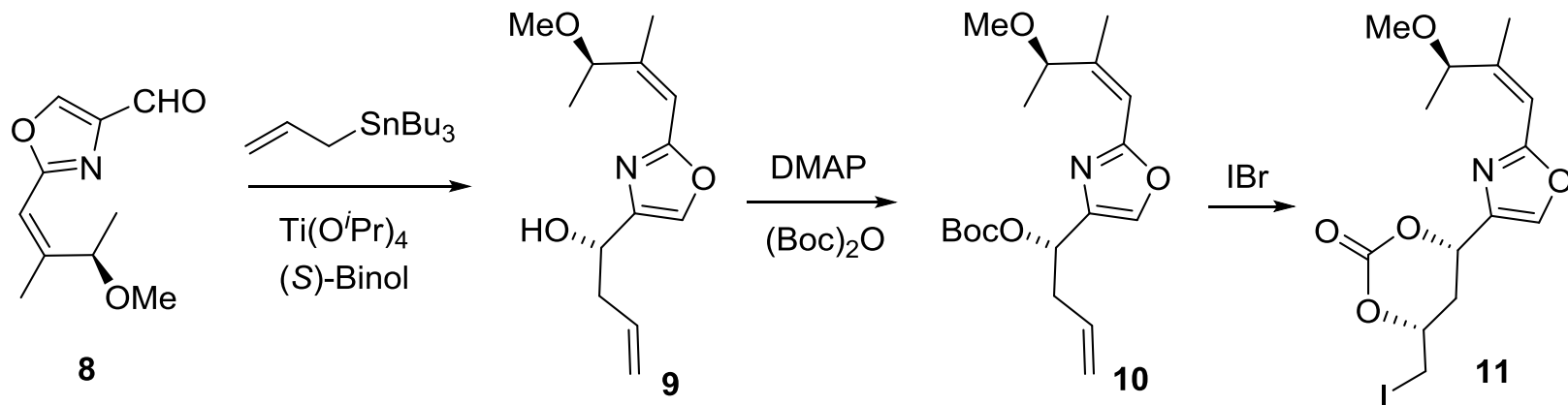
Yamaguchi
esterification
RCAM
pi-acid catalysis

23 steps 3.3% yield

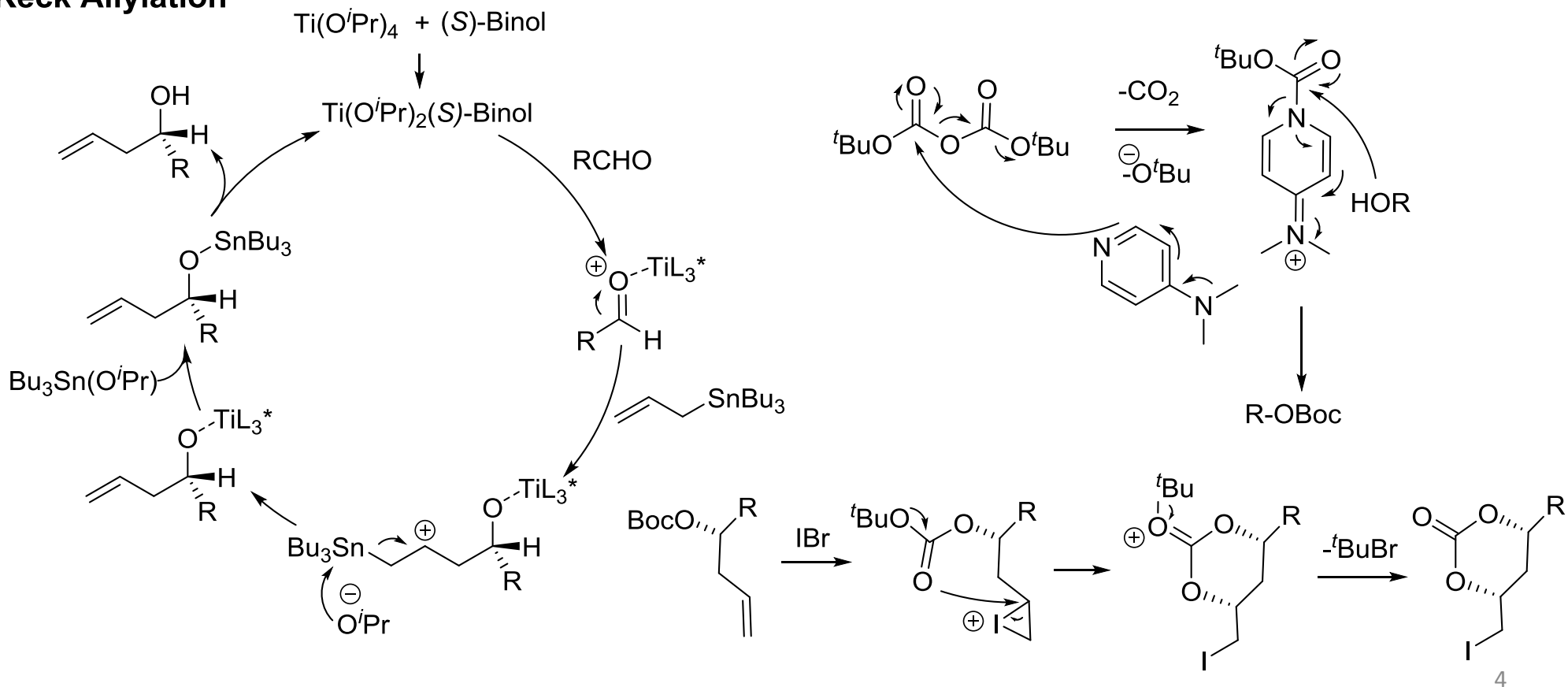


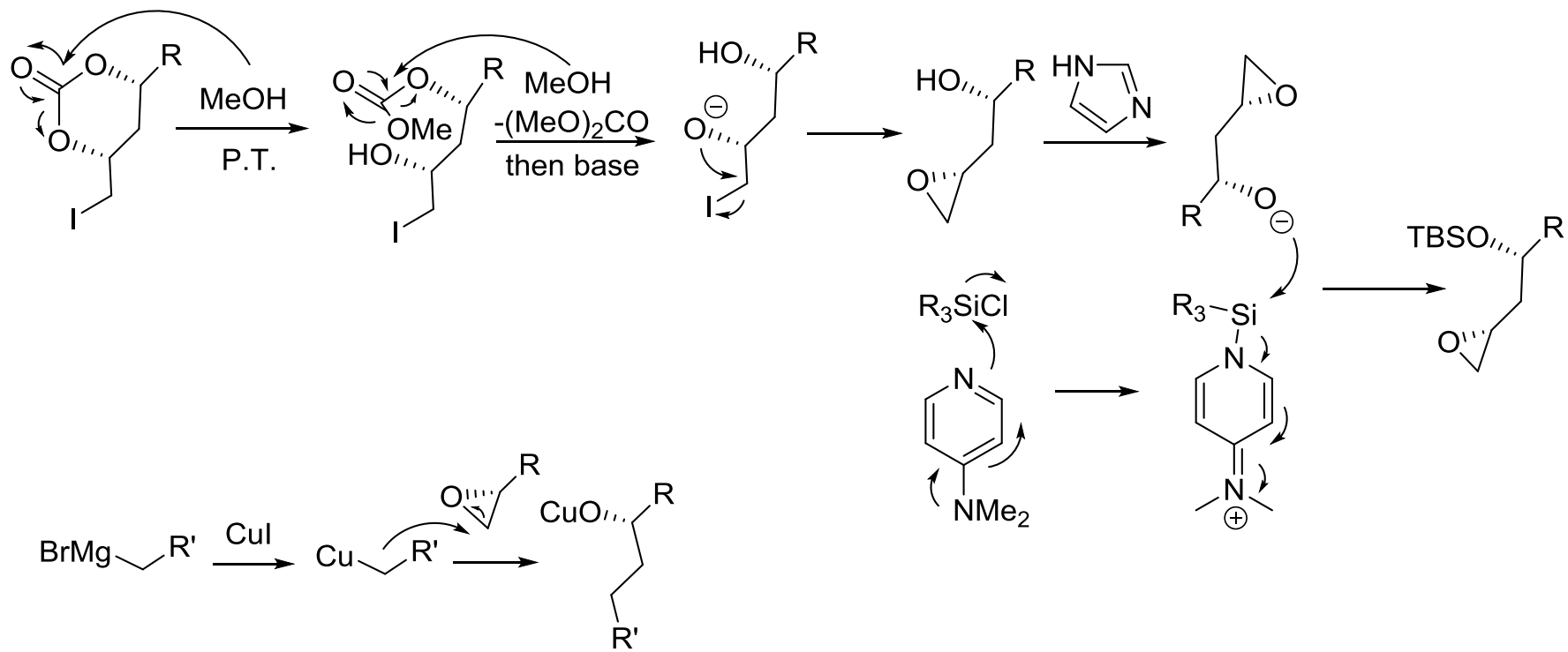
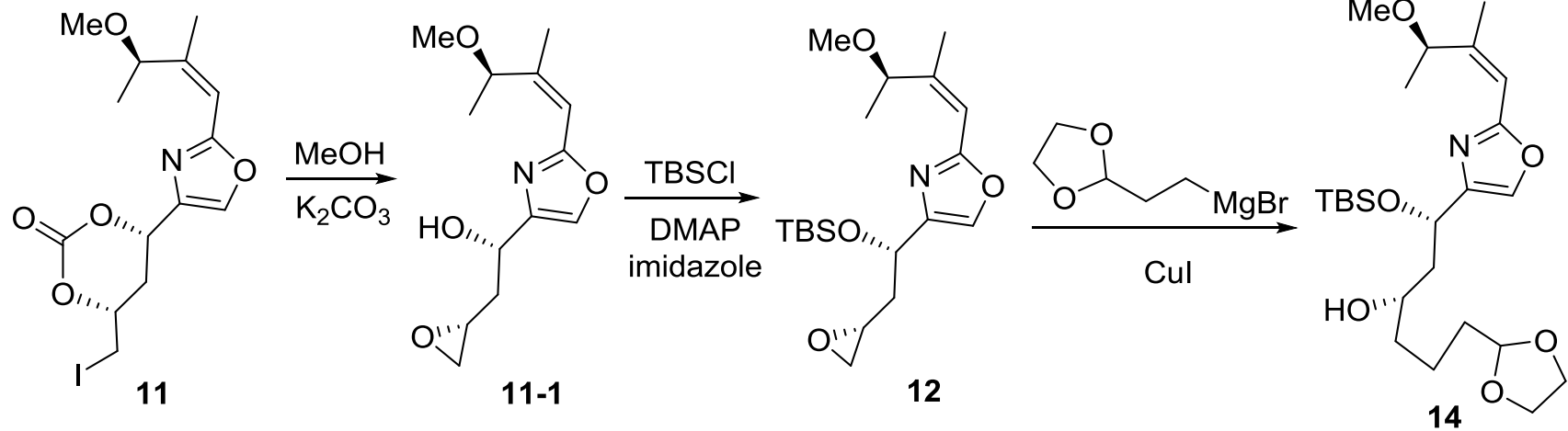


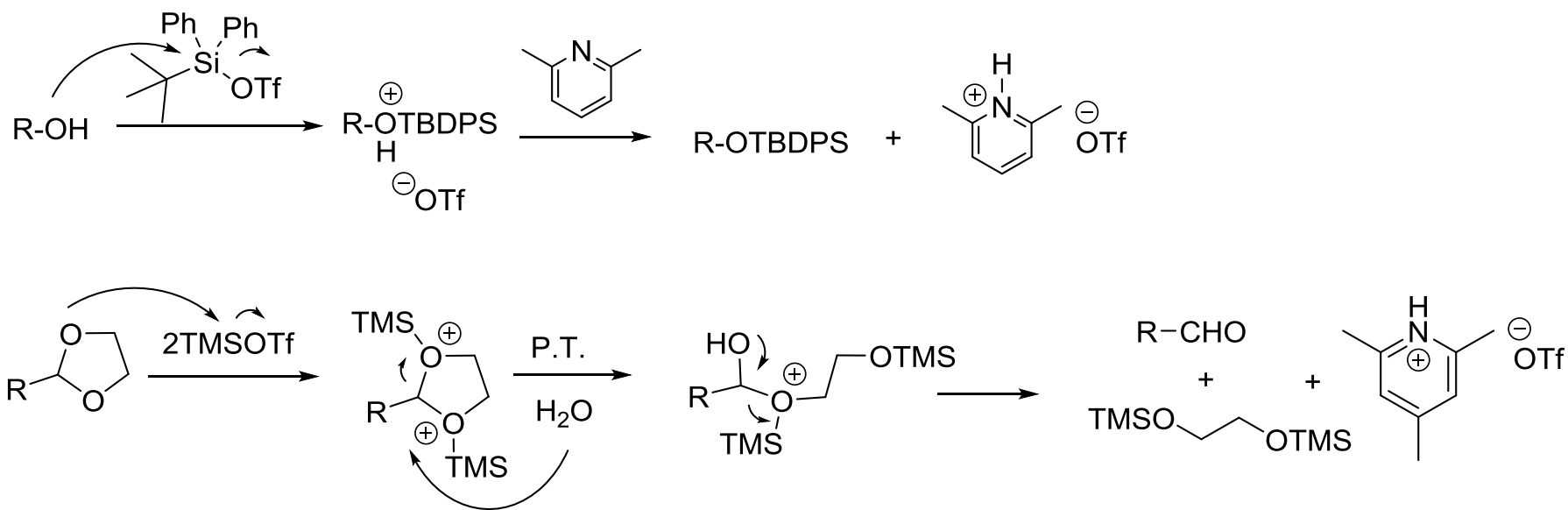
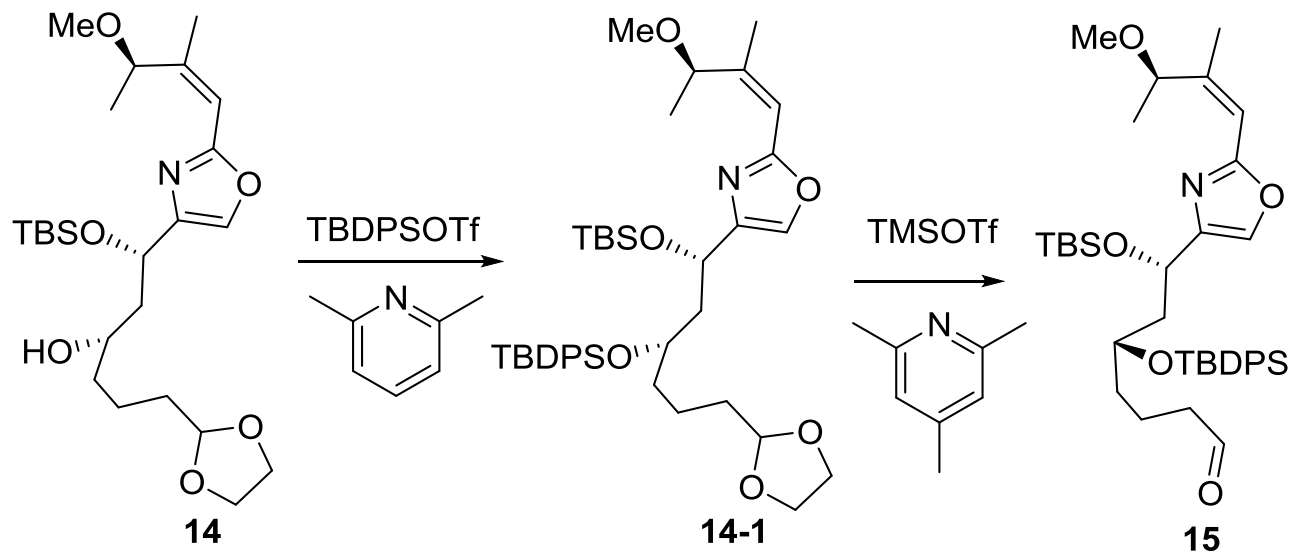
low temperature can prevent over-reduction

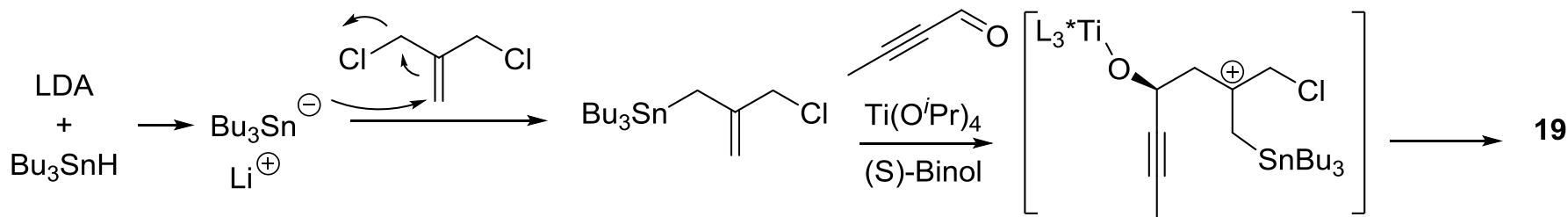
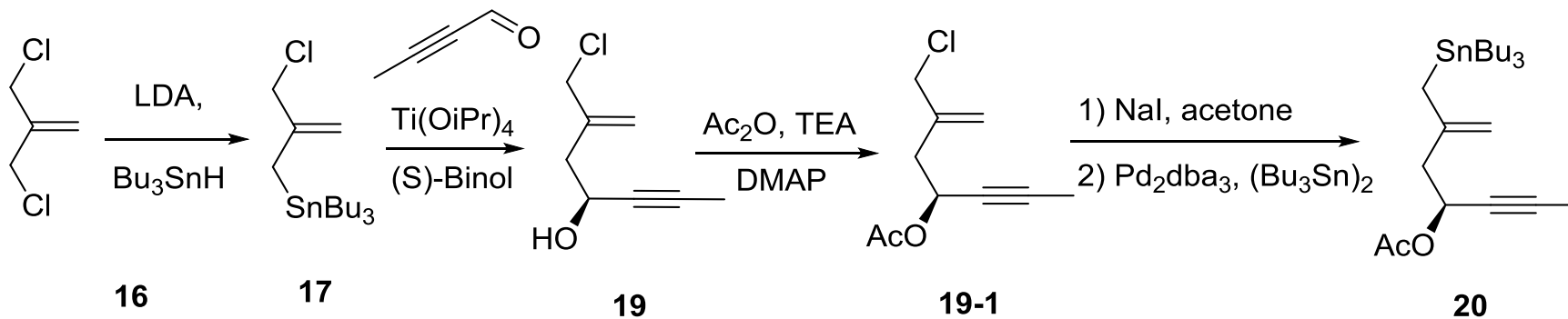


Keck Allylation

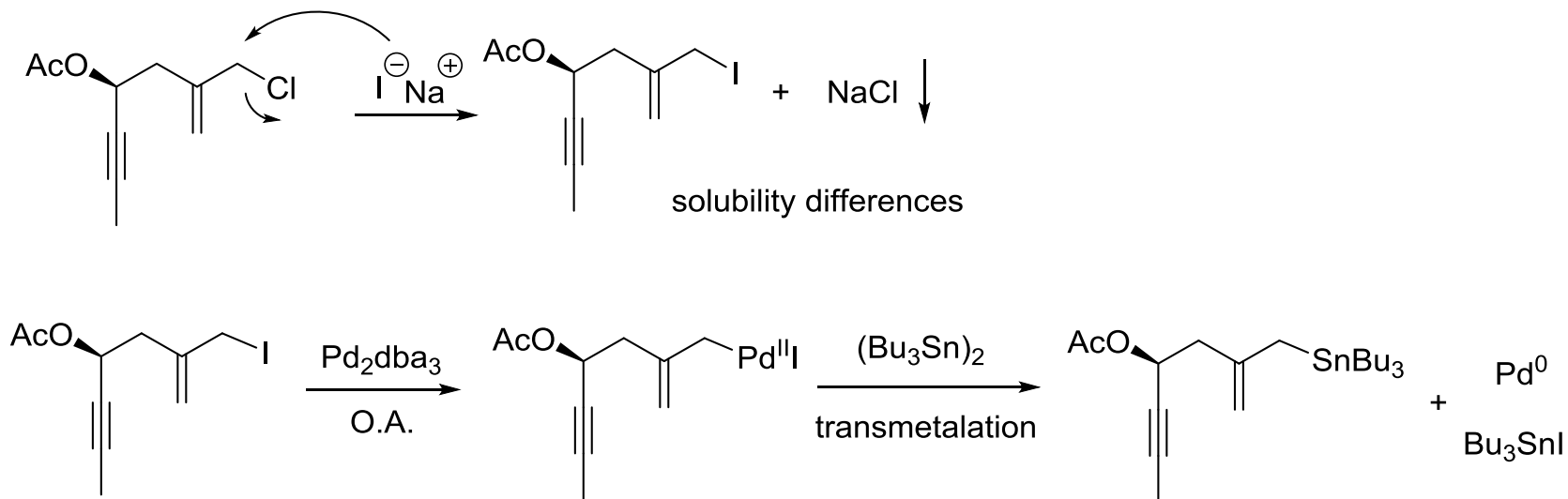


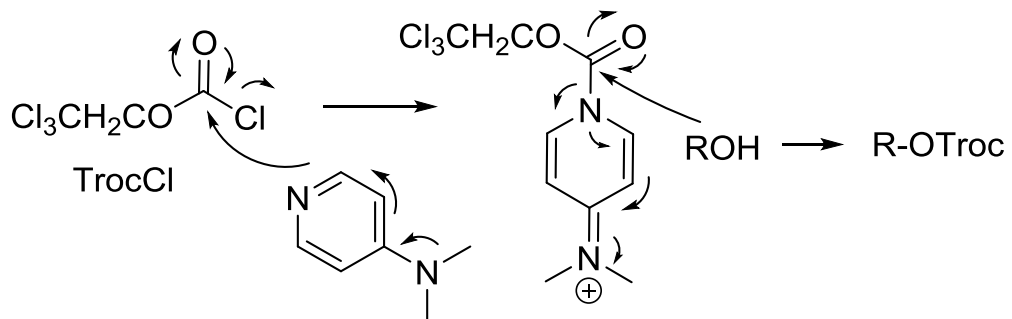
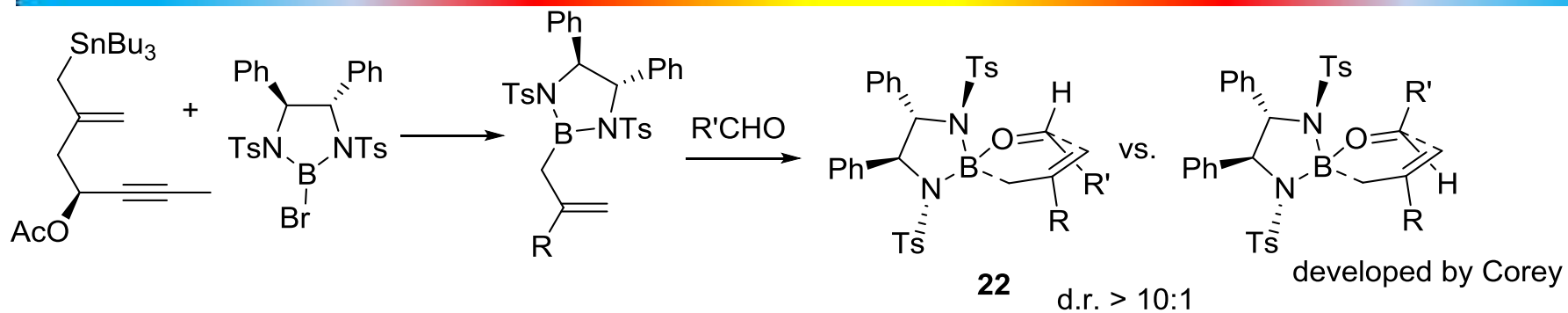
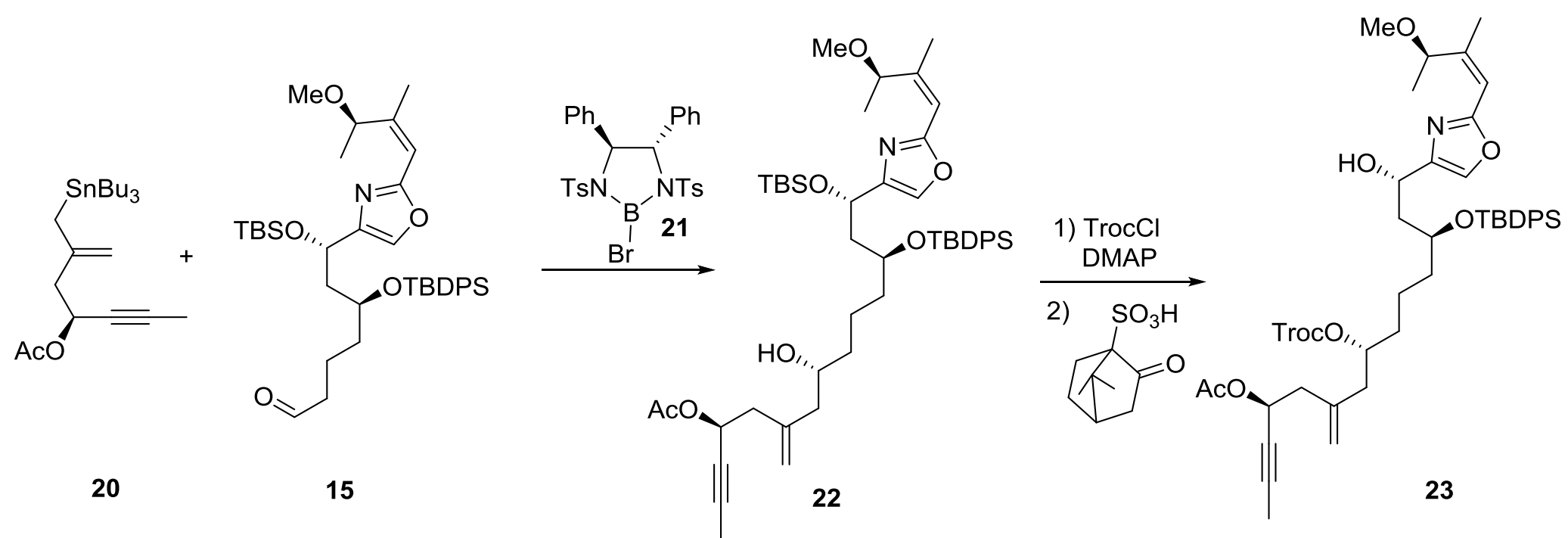


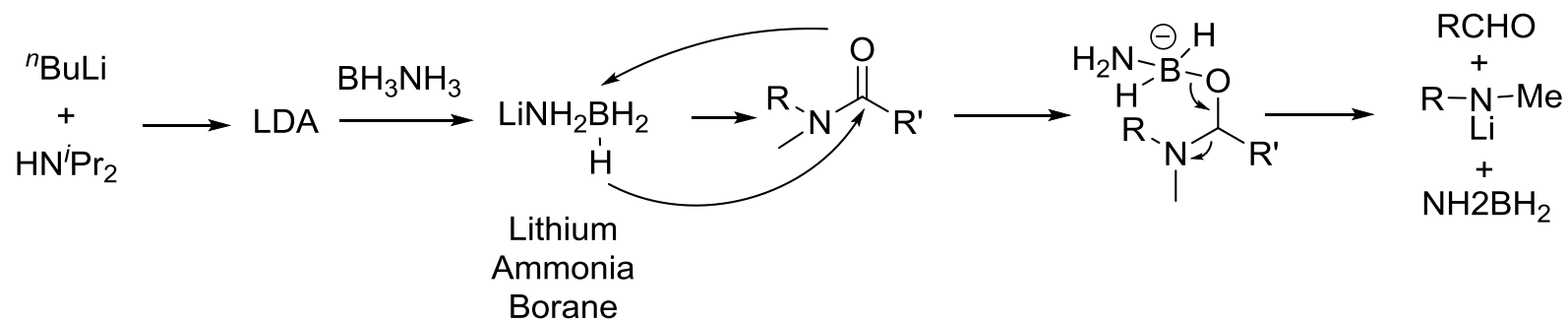
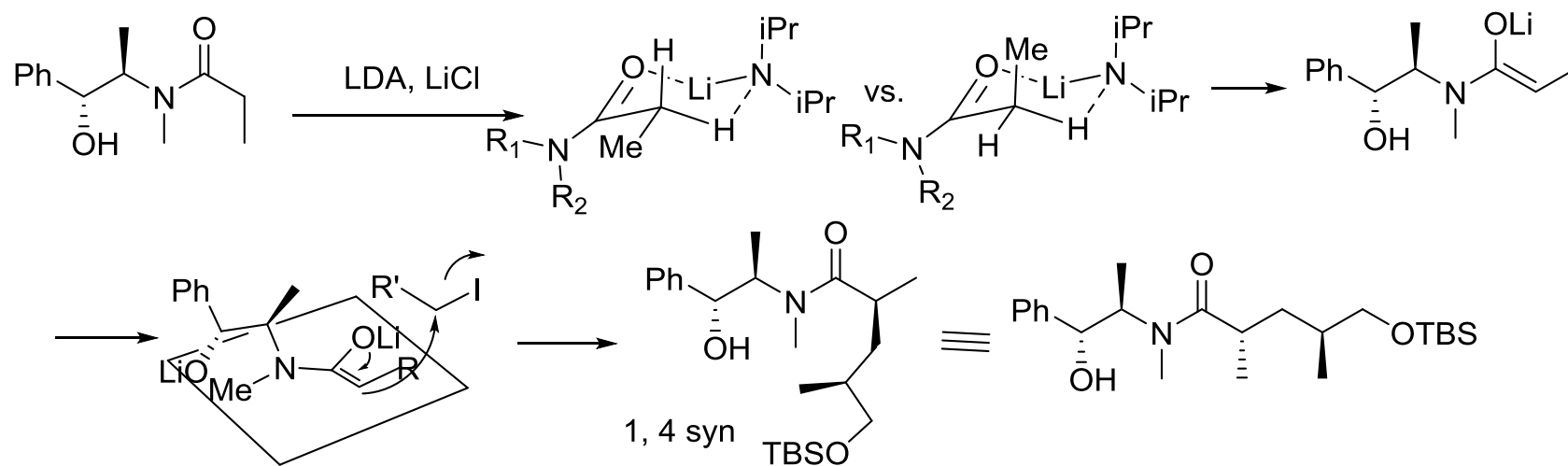
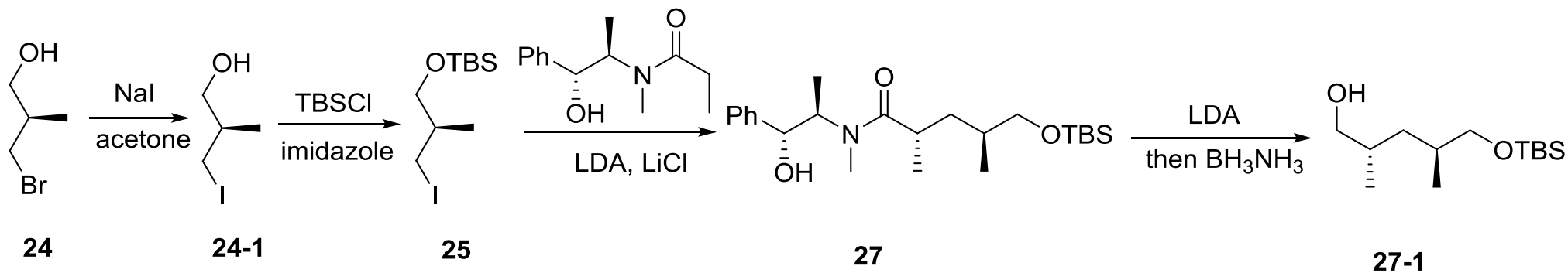


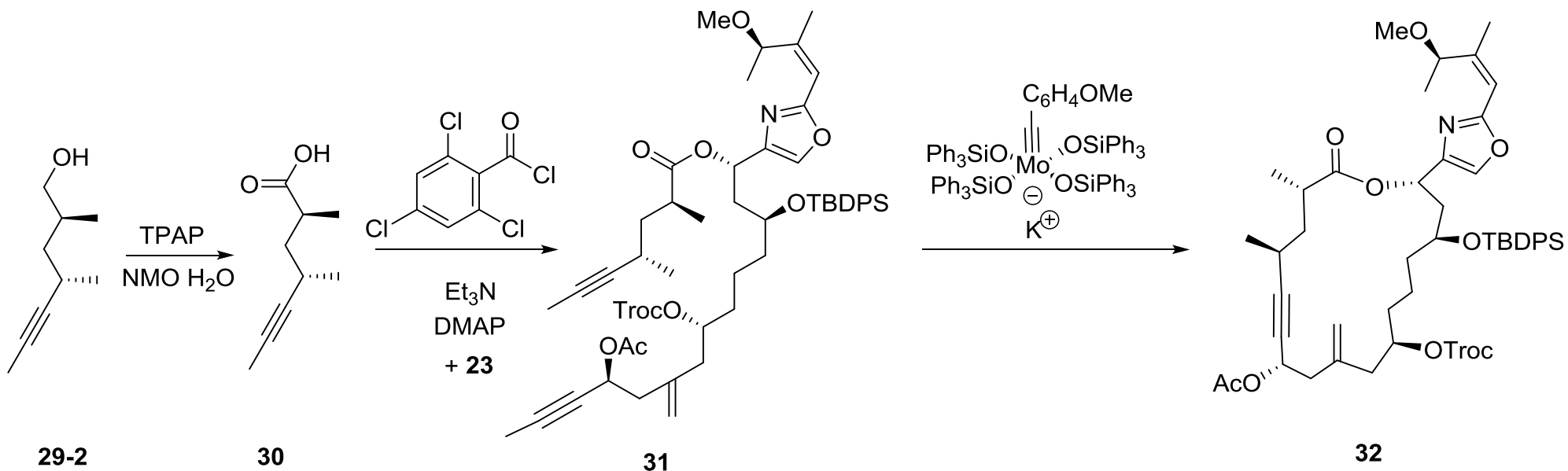


Finkelstein Reaction

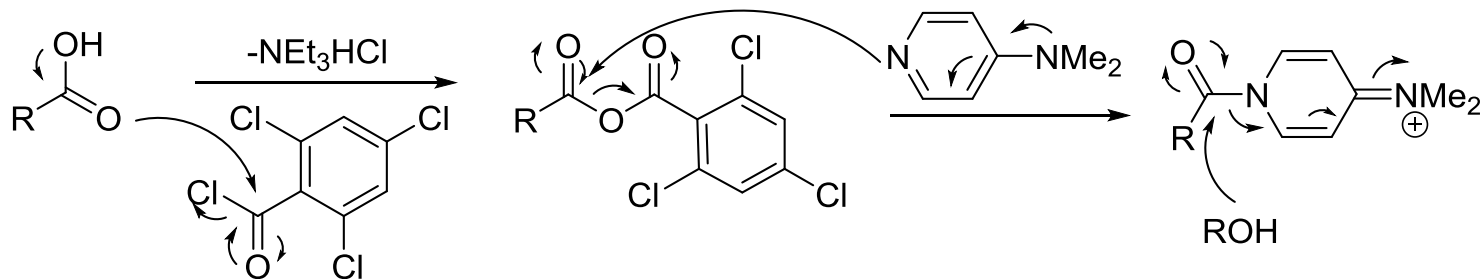




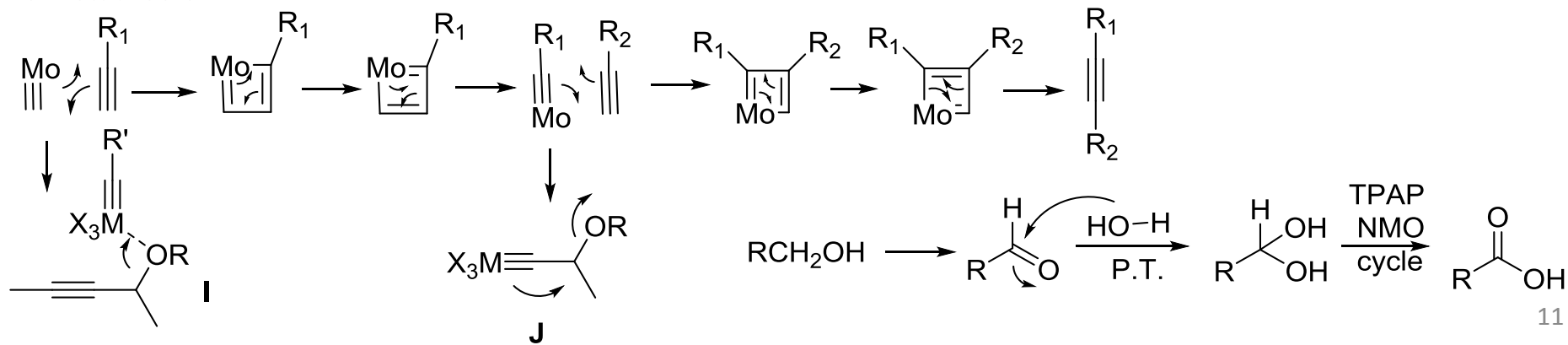


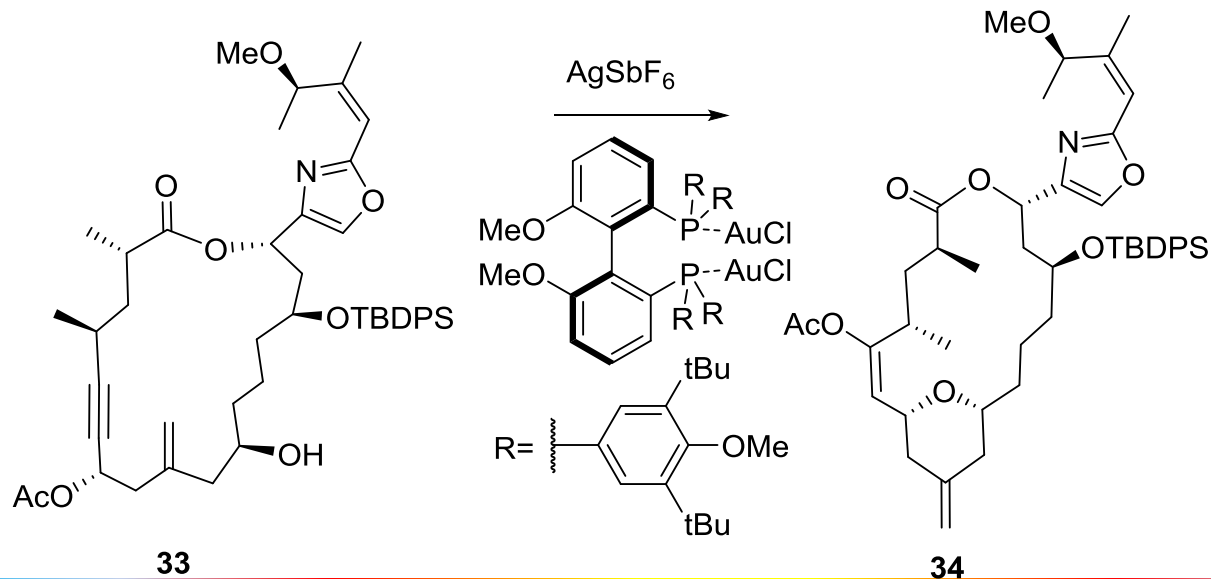


Yamaguchi esterification

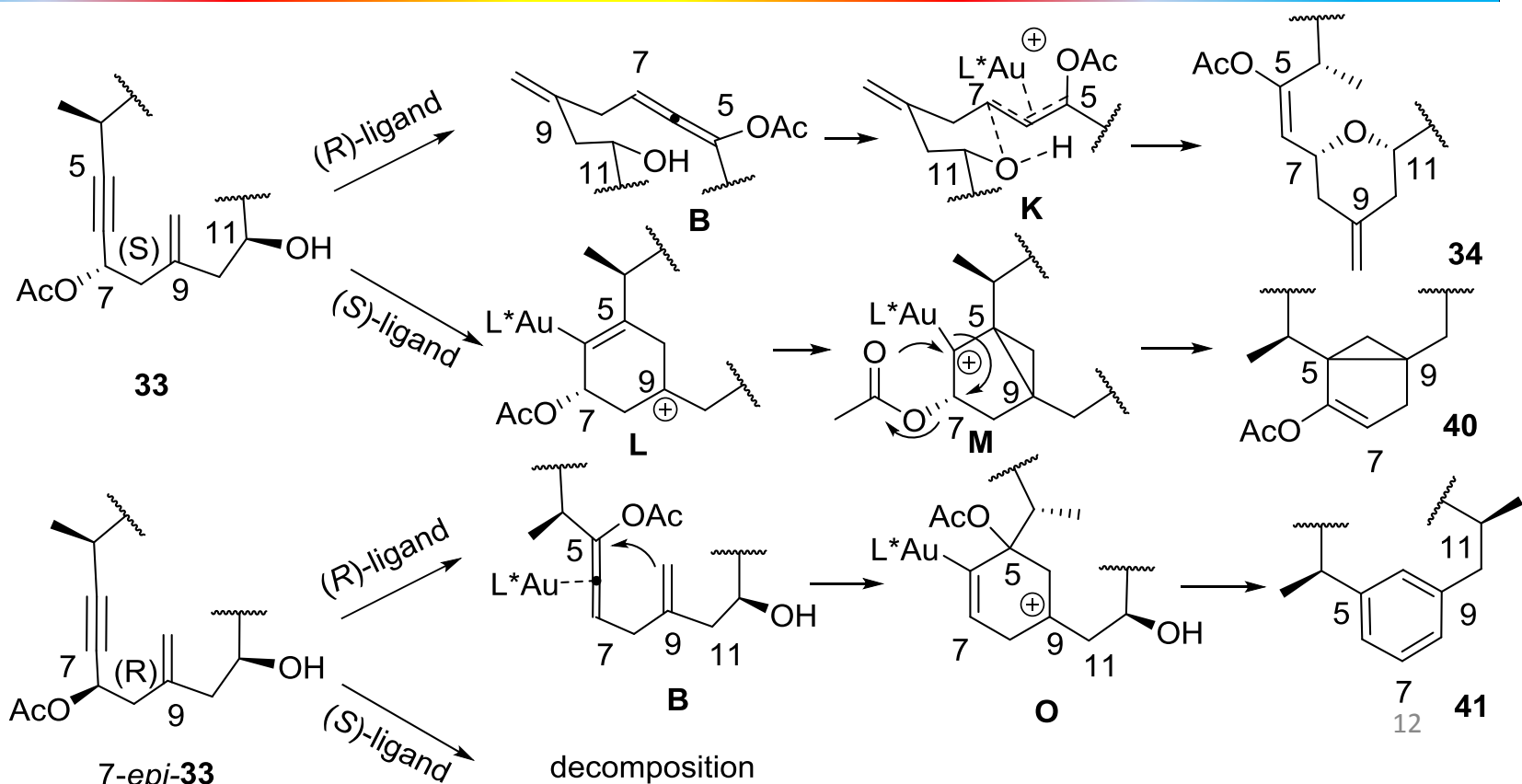
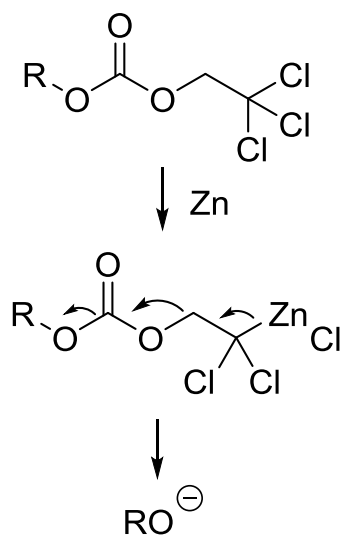


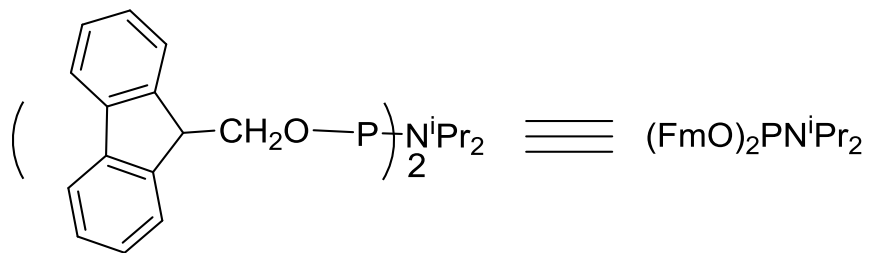
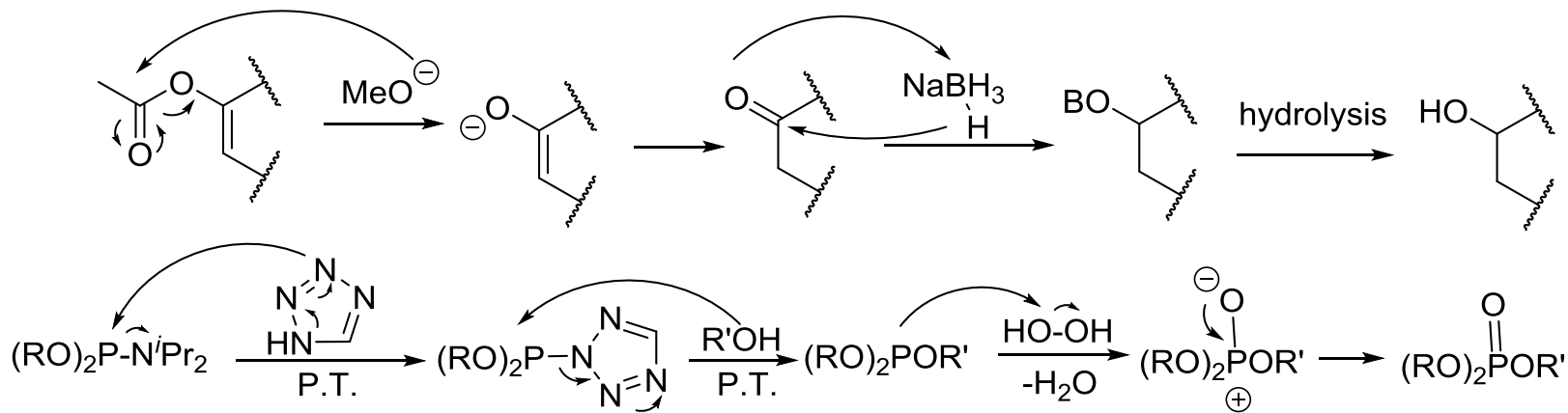
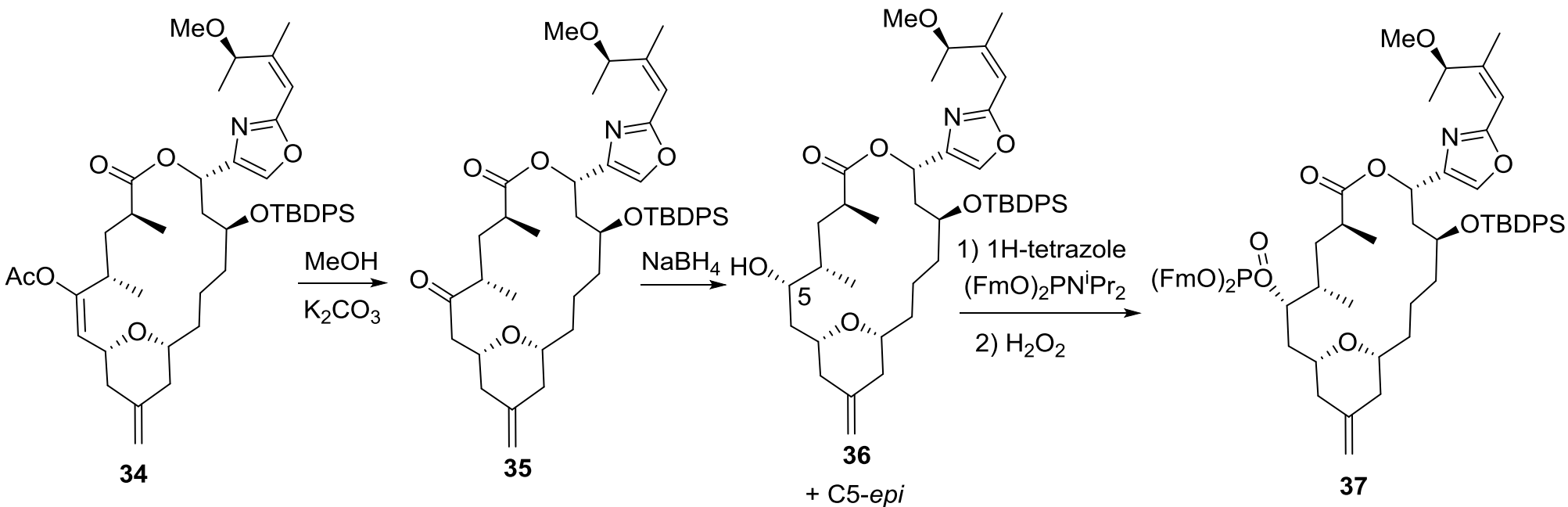
Alkyne Metathesis

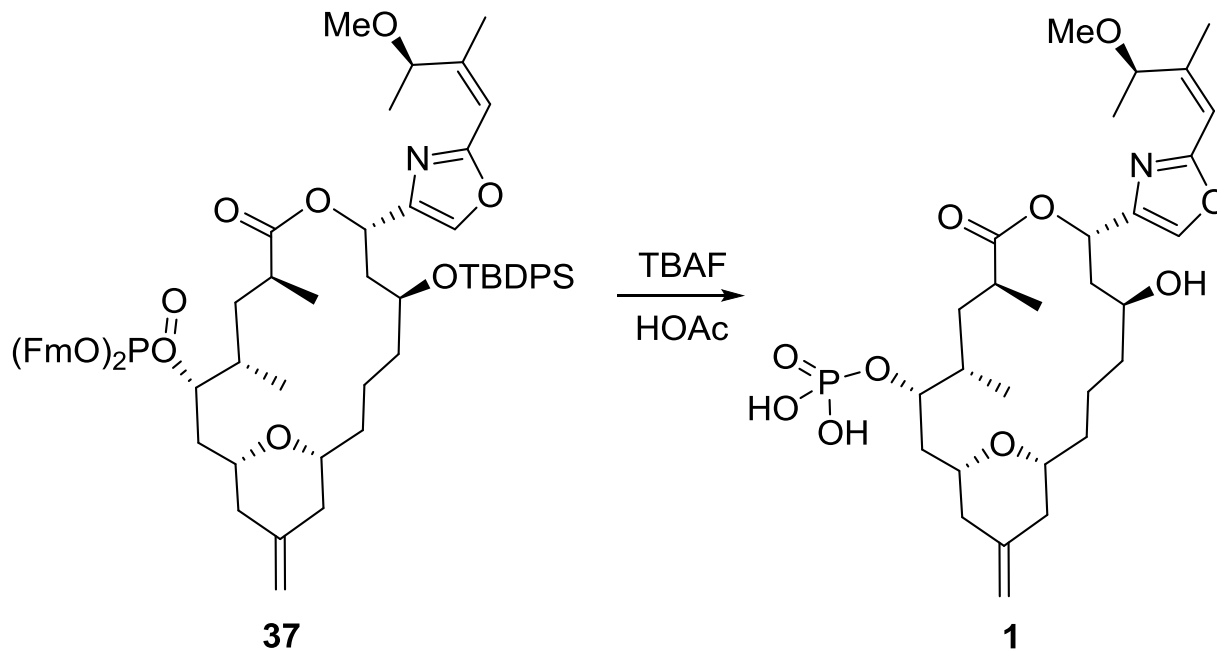




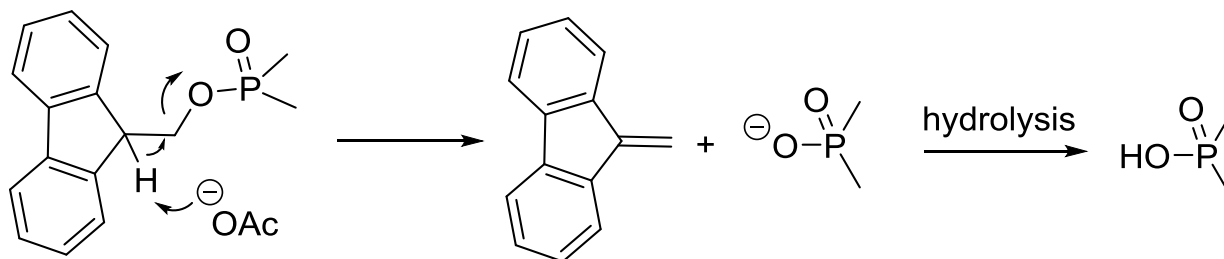
Troc Deprotection







Fmoc deprotection



Conclusion: 23 steps for the longest linear route, 3.3% overall yield.