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Communication

Enantioselective Total Synthesis of Cotylenin A

Masahiro Uwamori, Ryunosuke Osada, Ryoji Sugiyama, Kotaro Nagatani, and Masahisa Nakada*

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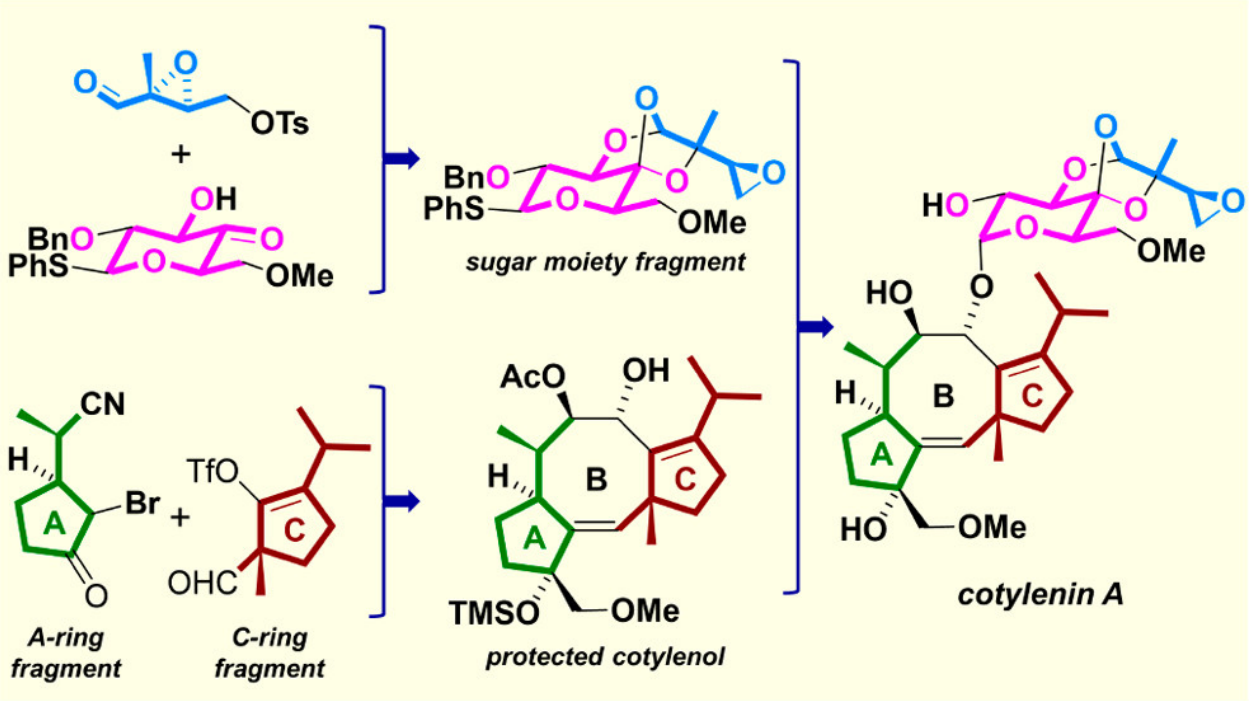
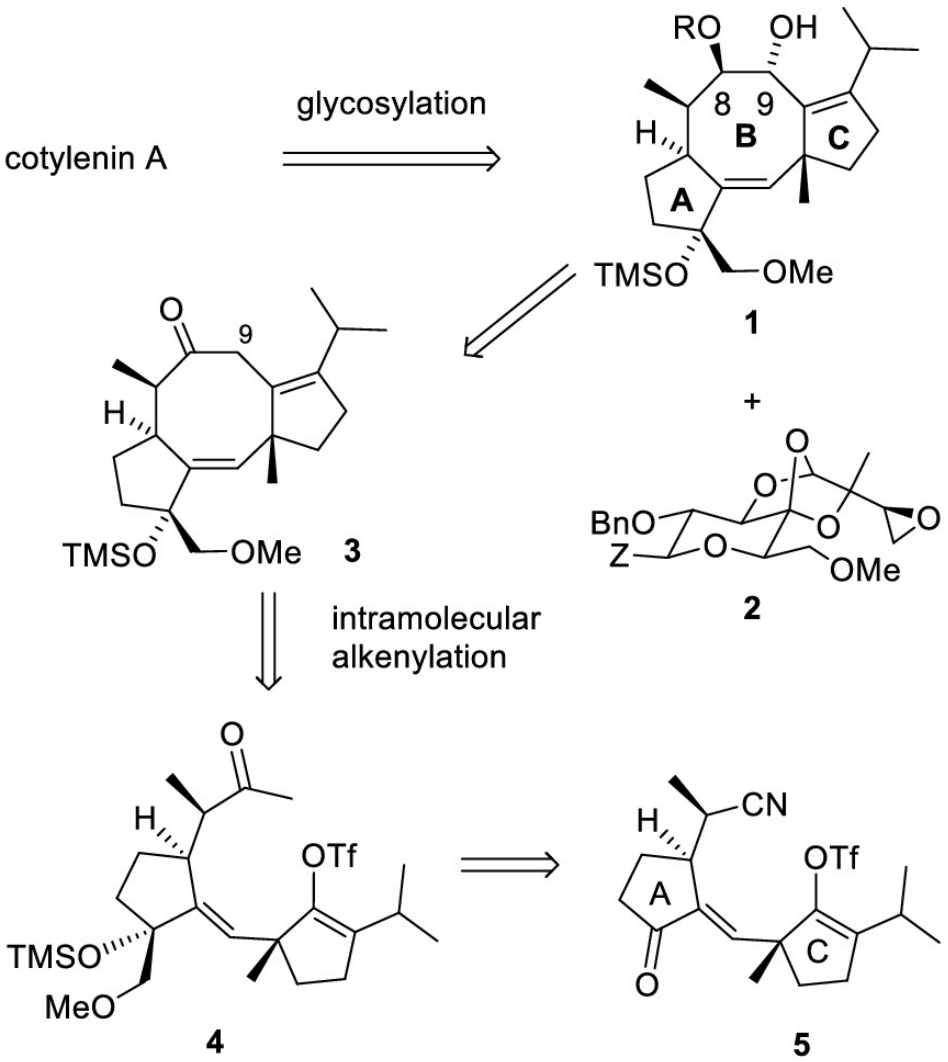
Jiangpeng Liu
Liu Research Group
4/14/2020

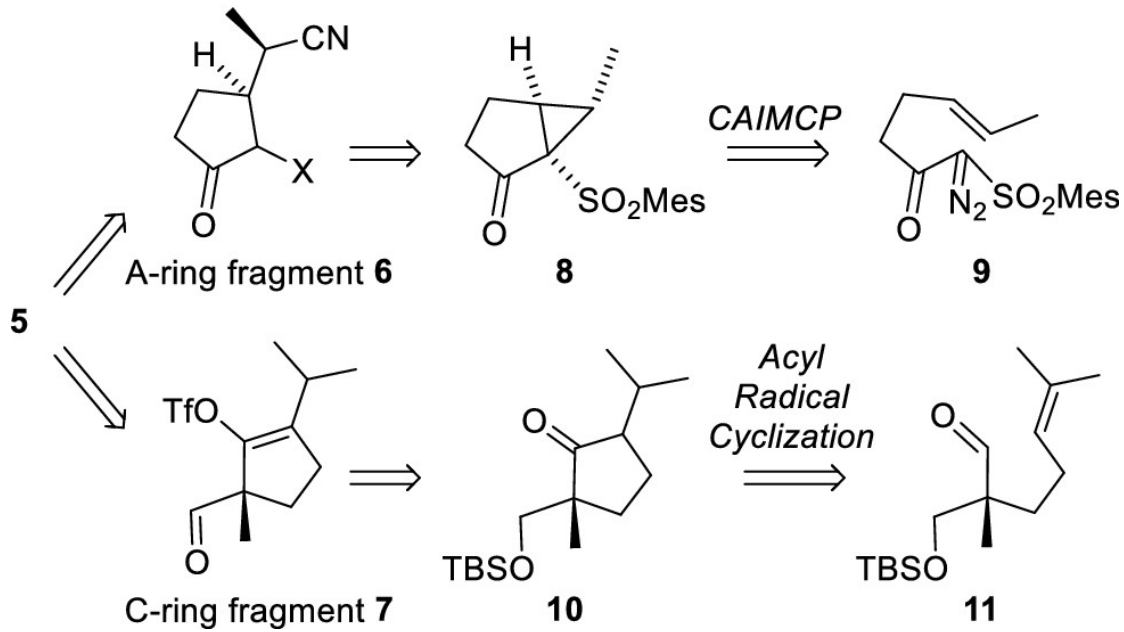


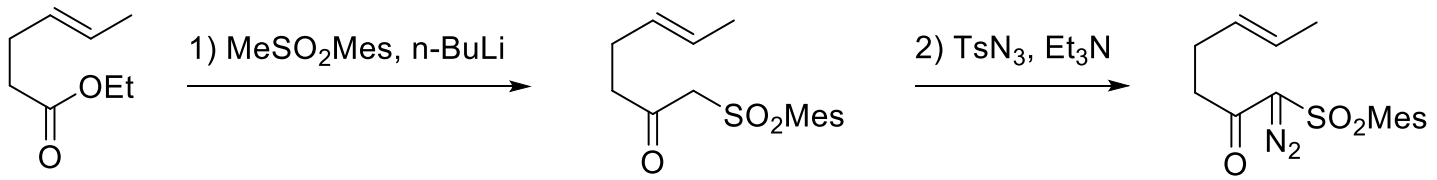
Introduction:

- Cotylenin A was isolated as a plant growth regulator.
- It has promising bioactivity as an anti-cancer agent.
- It features a fused 5-8-5 carbocyclic ring system includes a all carbon quaternary stereogenic center, a trans-1,2-diol, and a four-substituted alkene with an isopropyl group.
- Moreover, It bears a structurally unique glucose-fused trioxabicyclo[2.2.1]heptane with epoxyethly group.

Retro-synthetic route

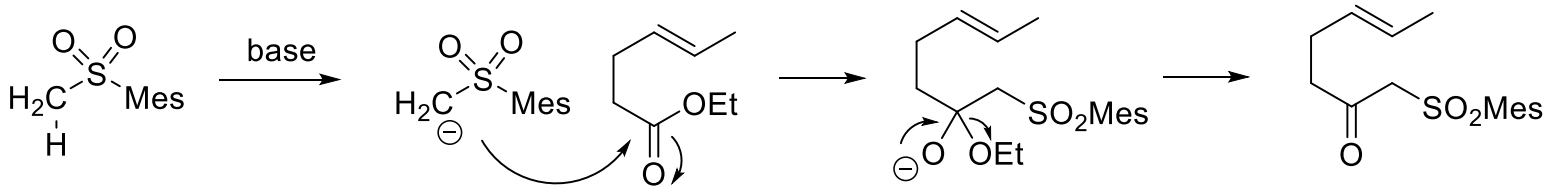




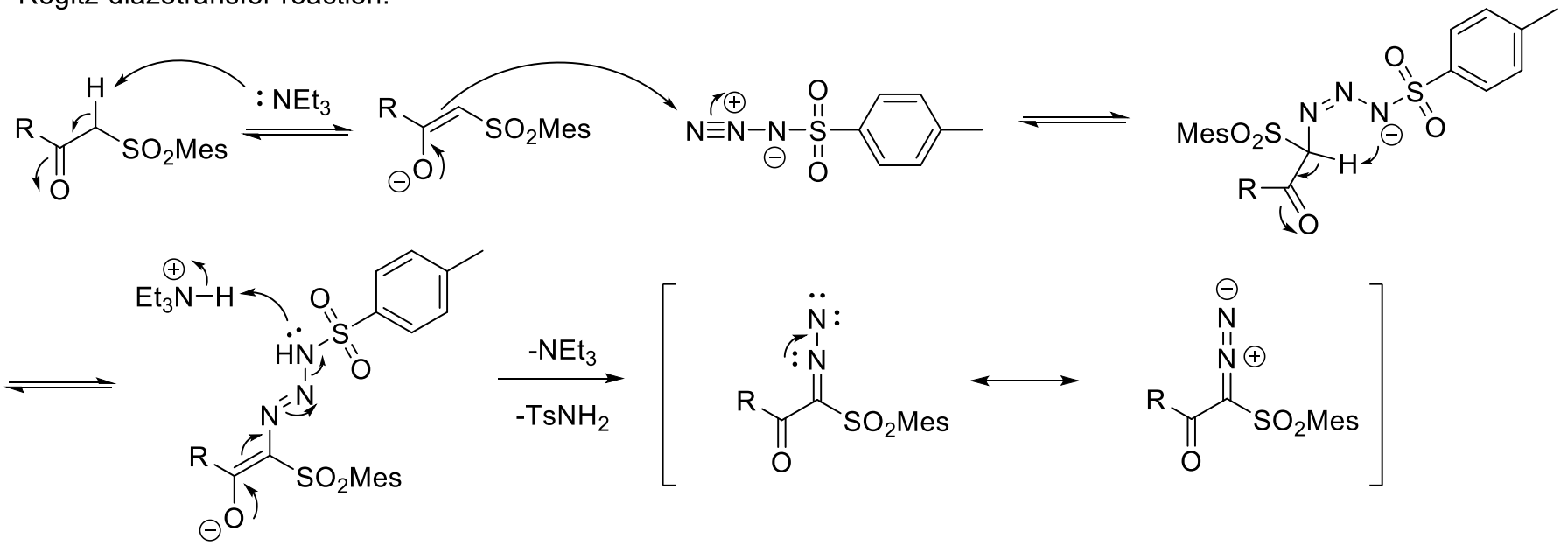


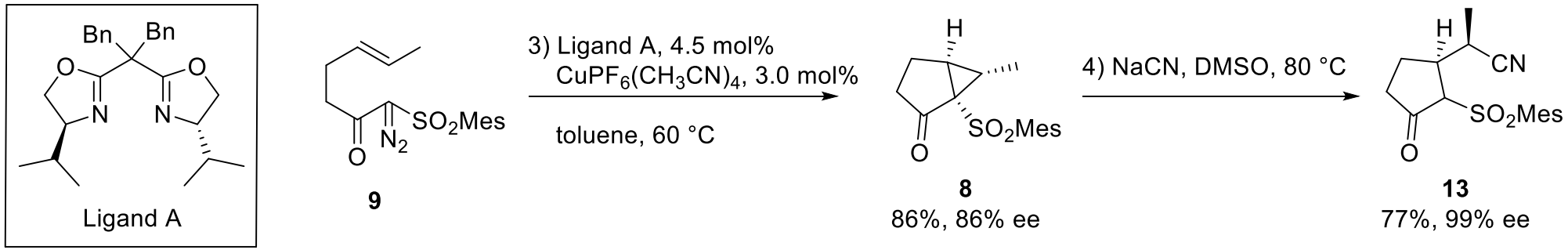
12 **12a** 97% **9** 98%

Formation of β-keto sulfone:

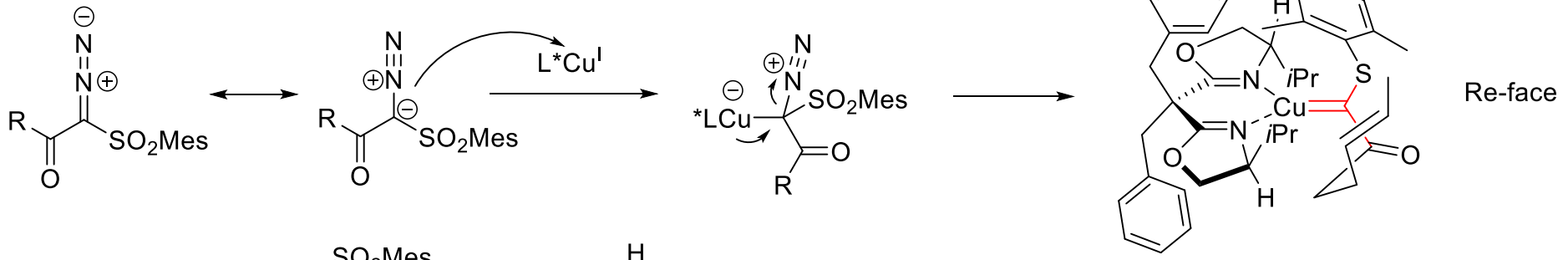


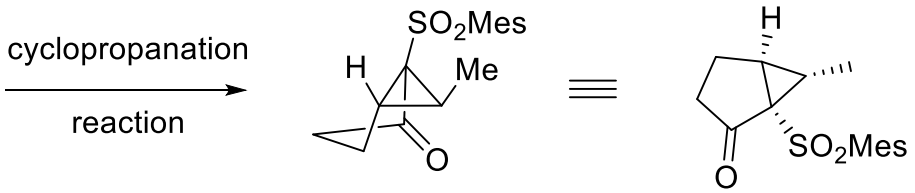
Regitz-diazotransfer reaction:



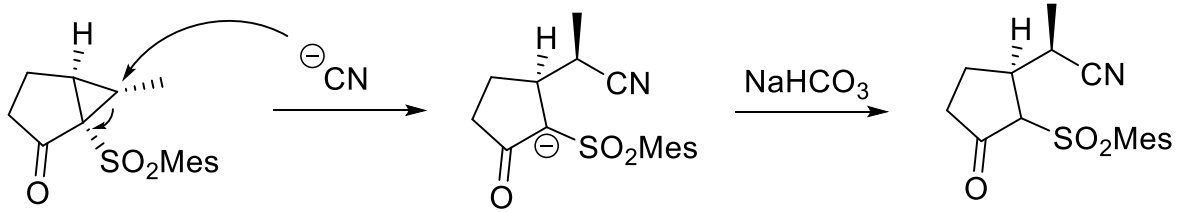


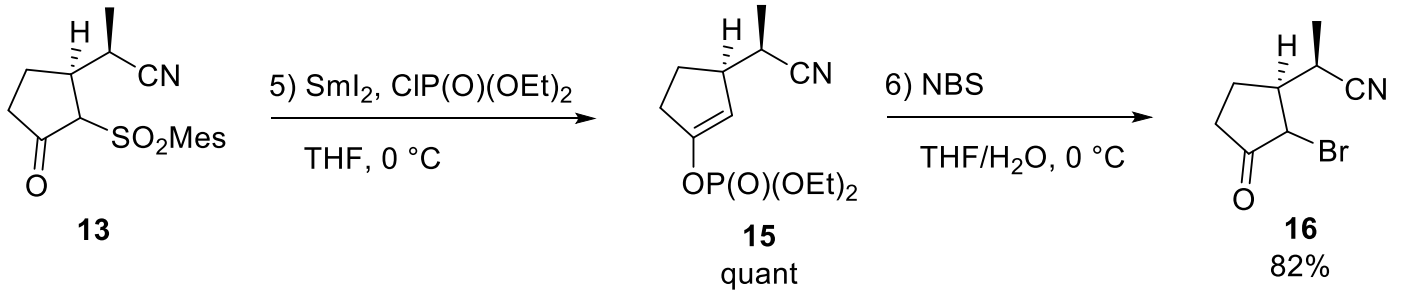
Catalytic asymmetric intramolecular cyclopropanation (CAIMCP)



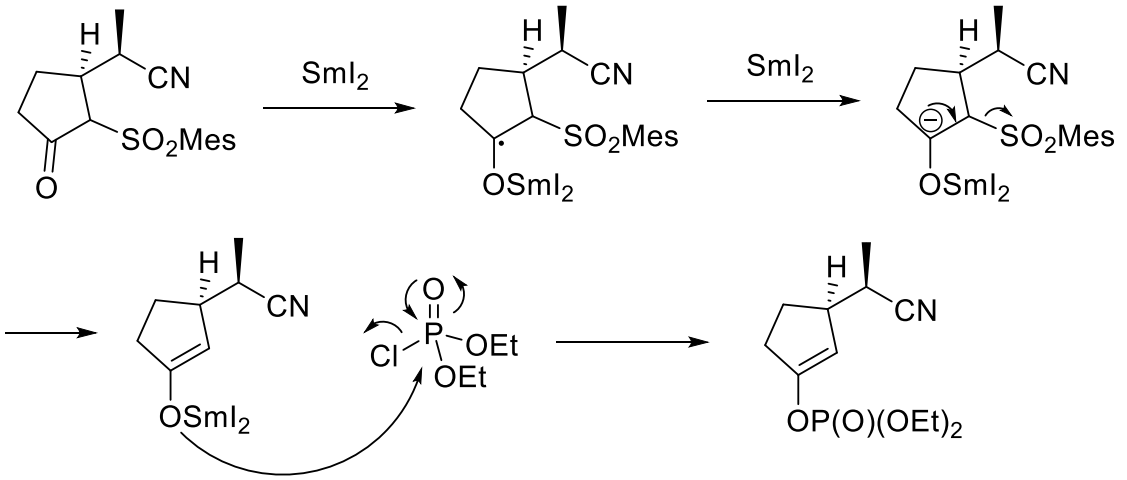


Electrophilic cyclopropane opening:

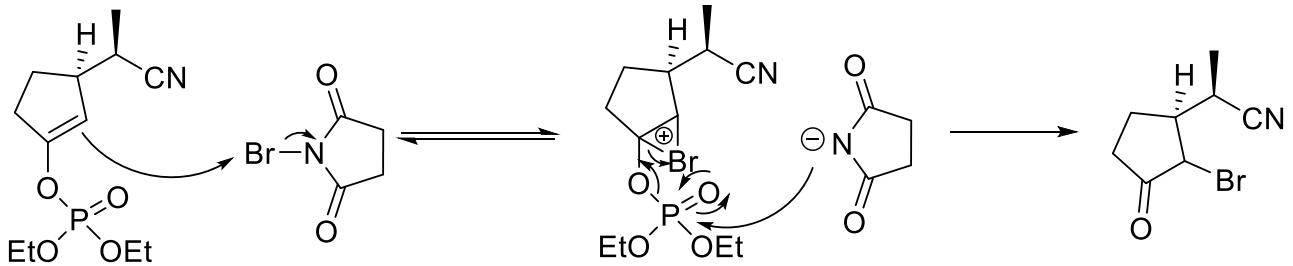


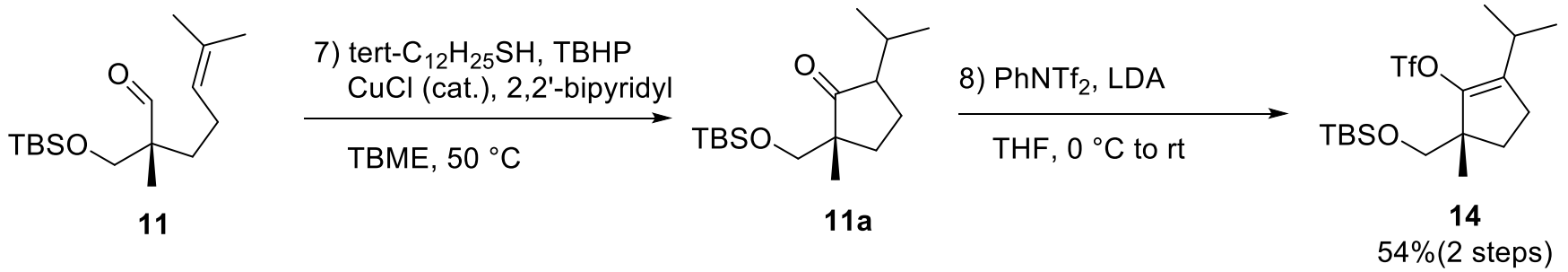


Reduction of β-keto sulfone with samarium iodide:

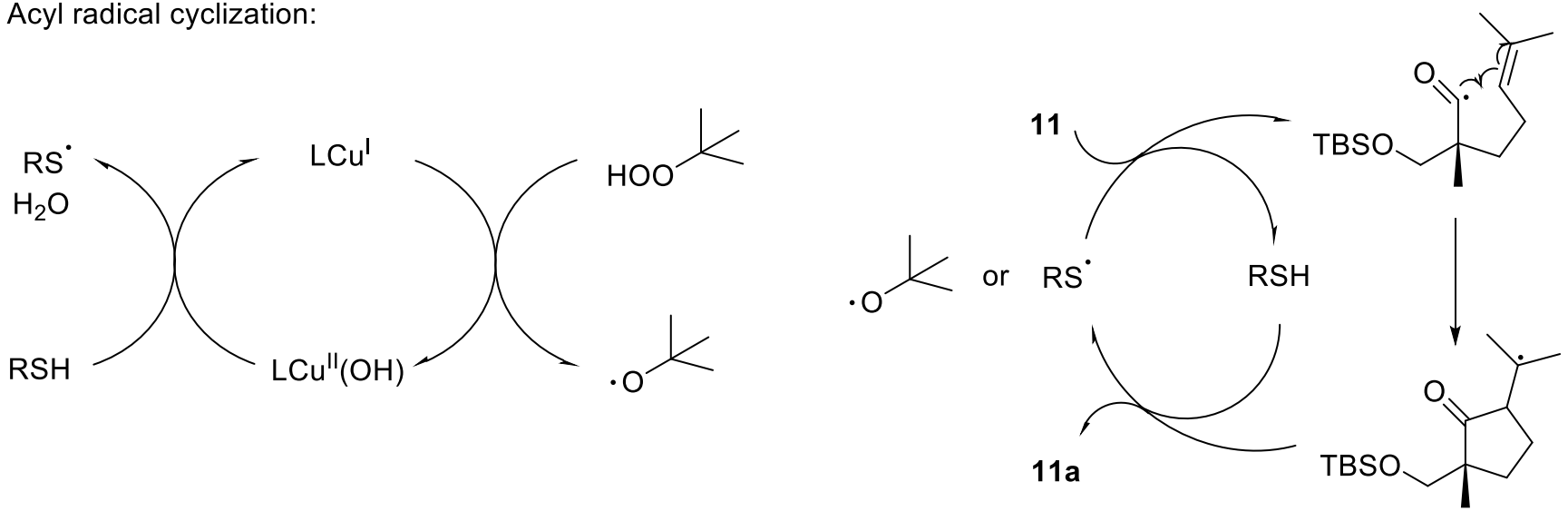


Formation of α-bromo ketone:

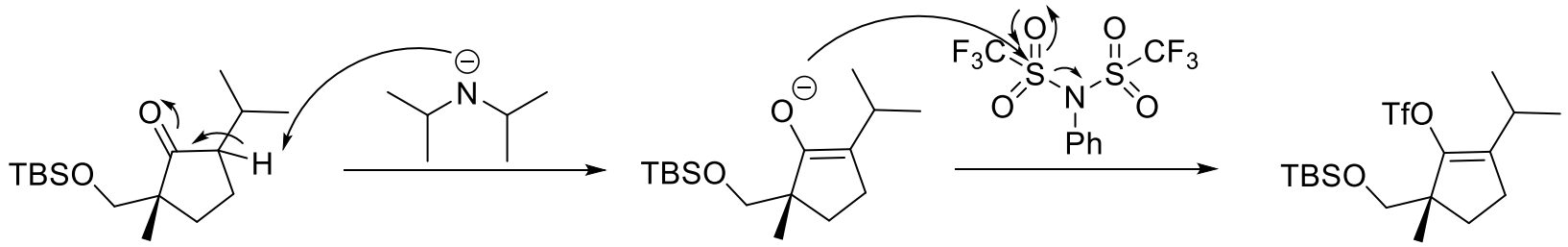


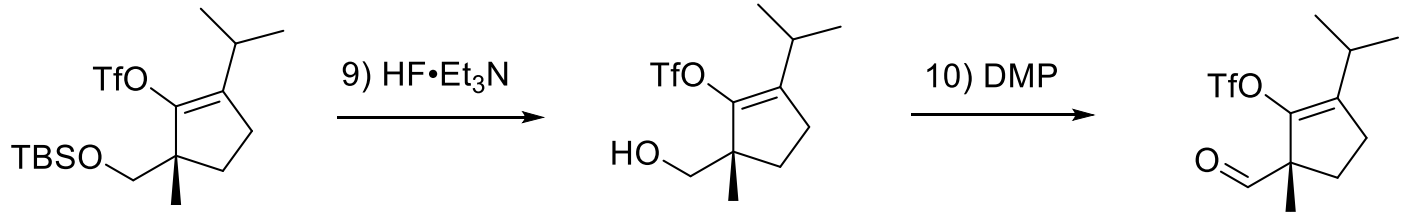


Acyl radical cyclization:



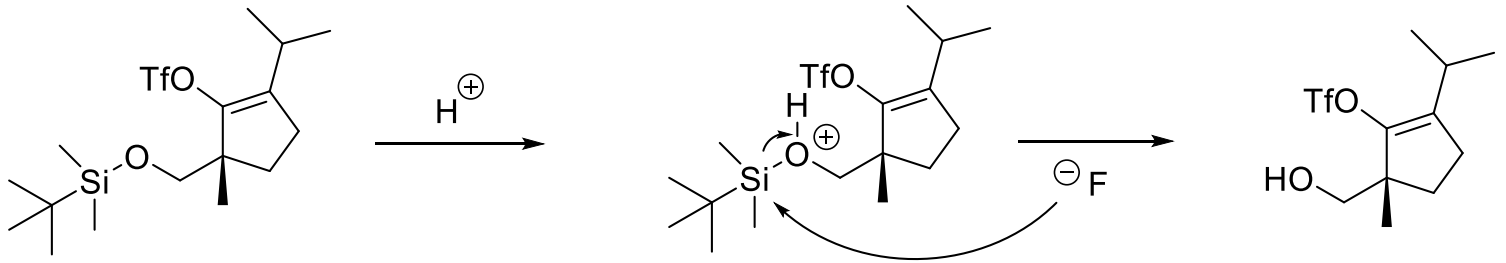
Formation of enol triflate:



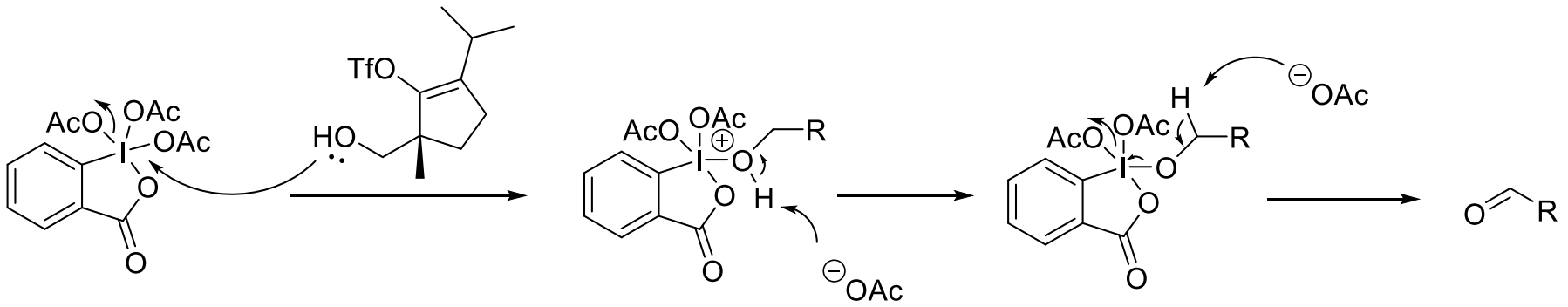


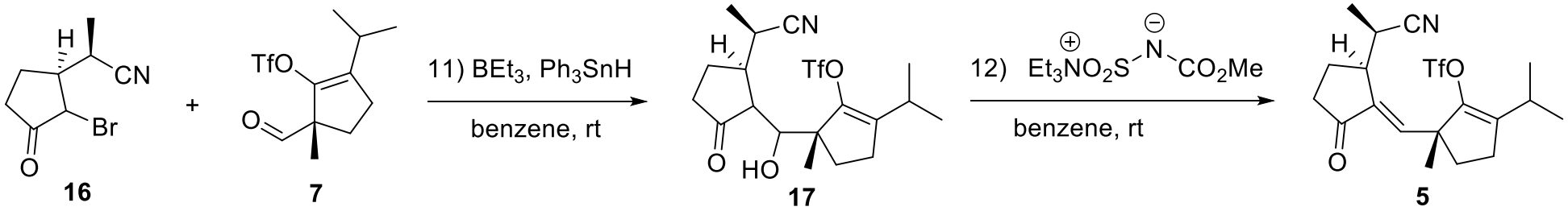
14 **14a** 88% **7** 89%

Deprotection of silyl group:

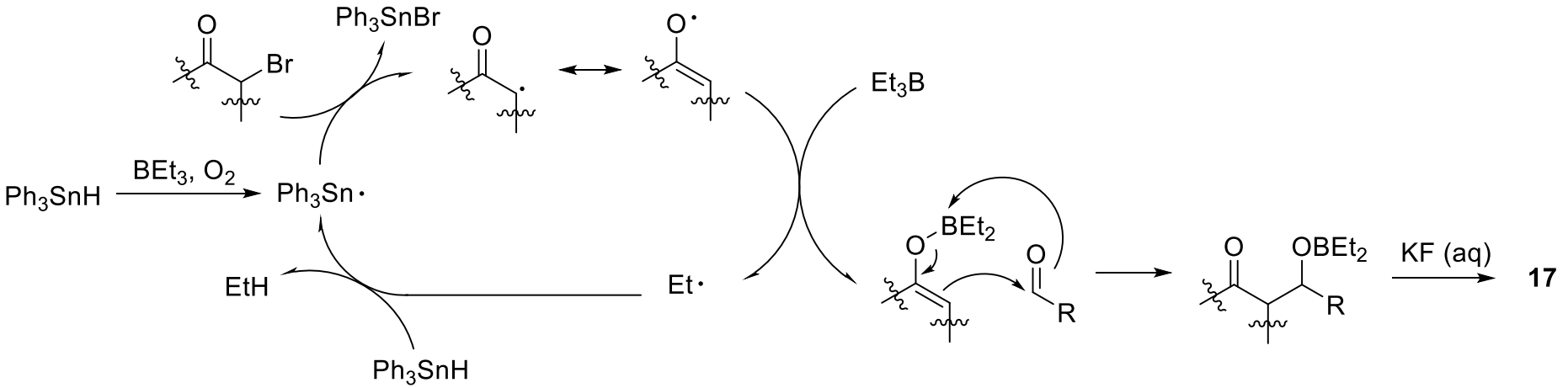


Dess-Martin oxidation:

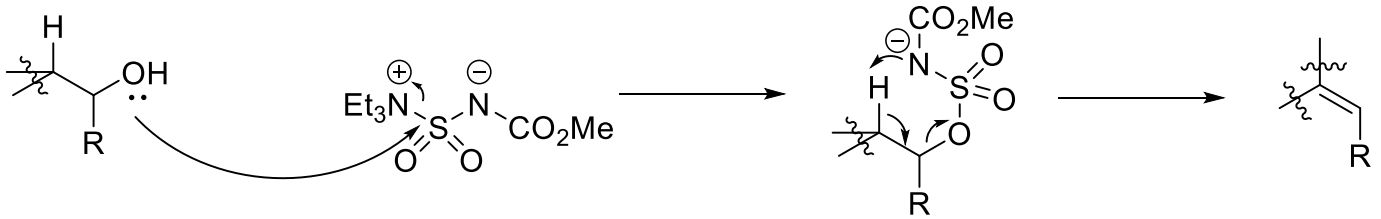


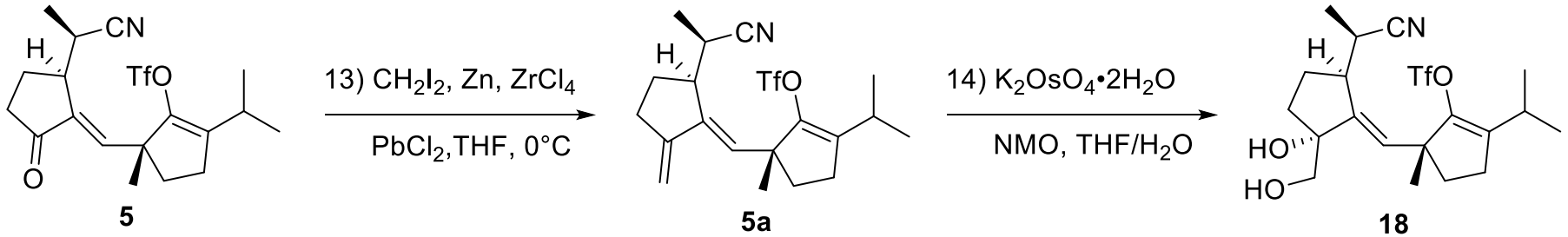


Utimoto coupling reaction:



Dehydration with the Burgess reagent:

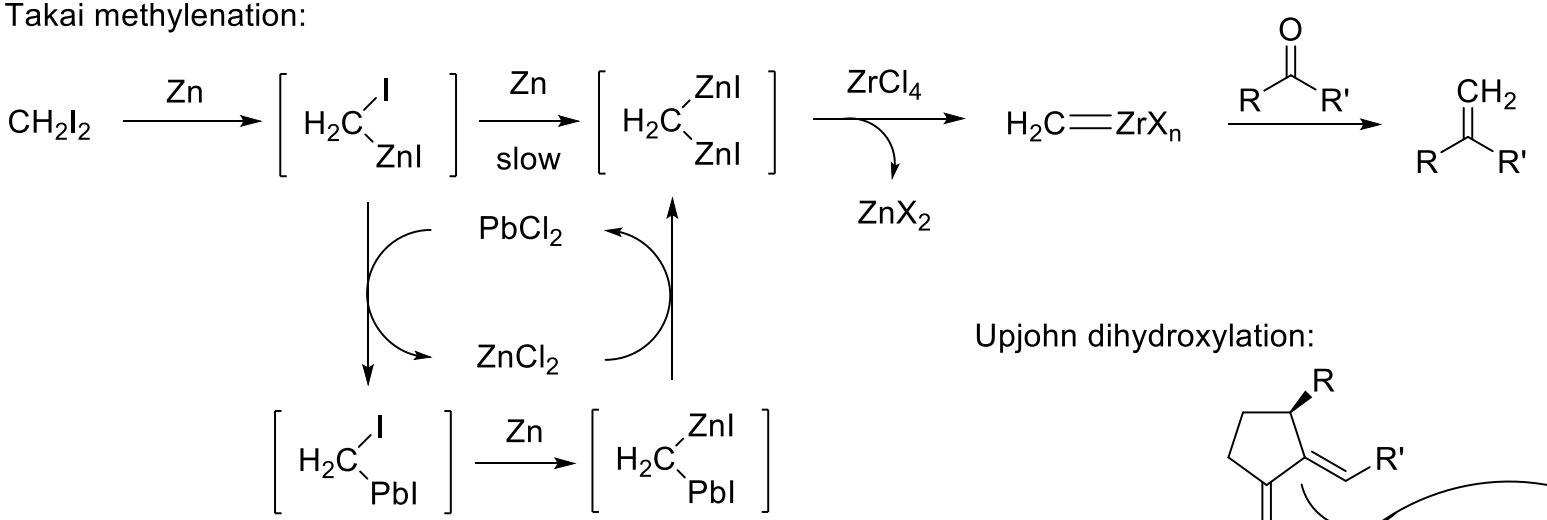




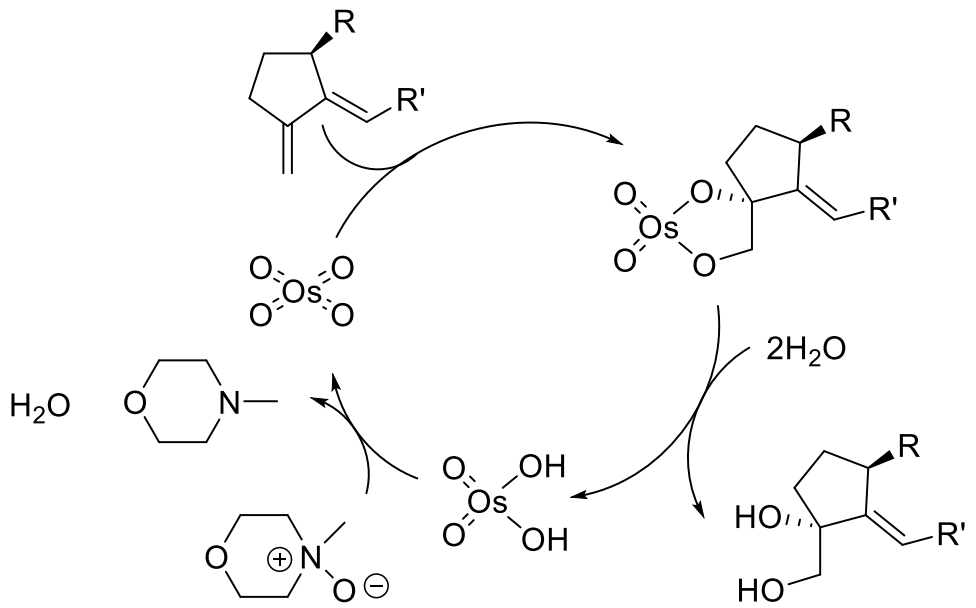
5 **5a** **18**

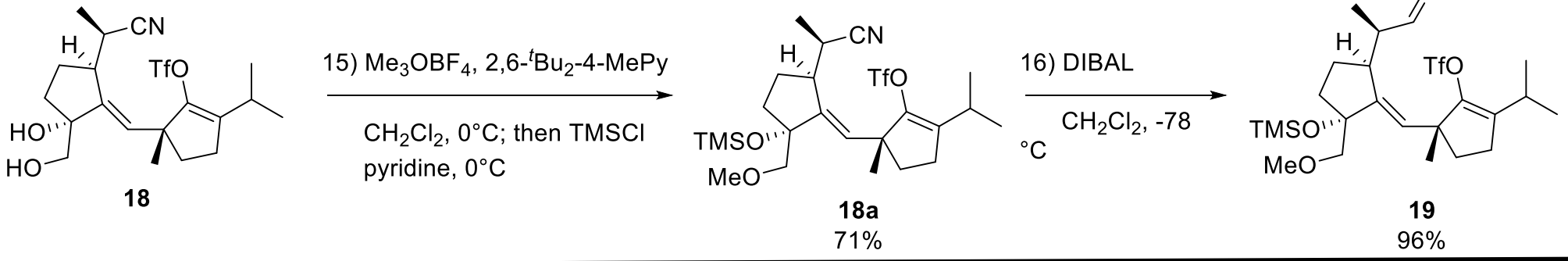
71% (2 steps), d.r. = 7:1

Takai methylenation:

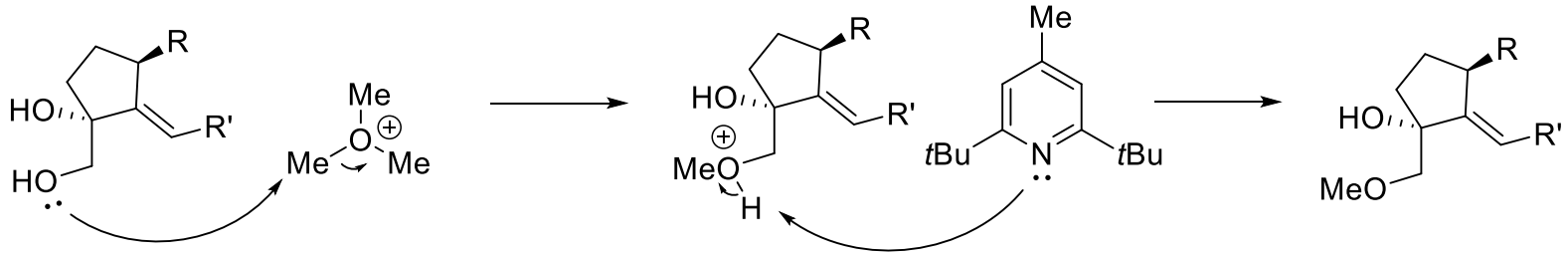


Upjohn dihydroxylation:

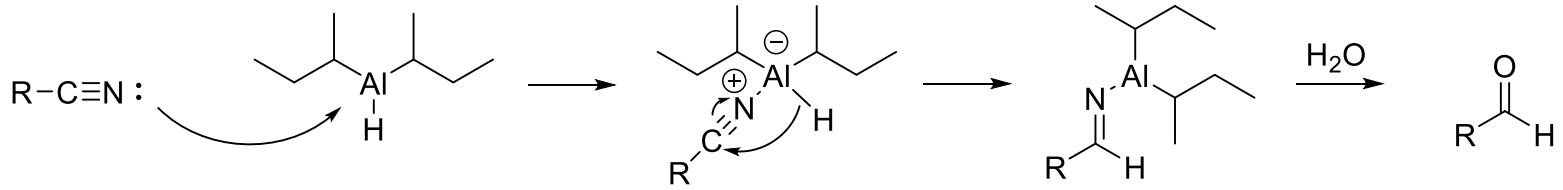


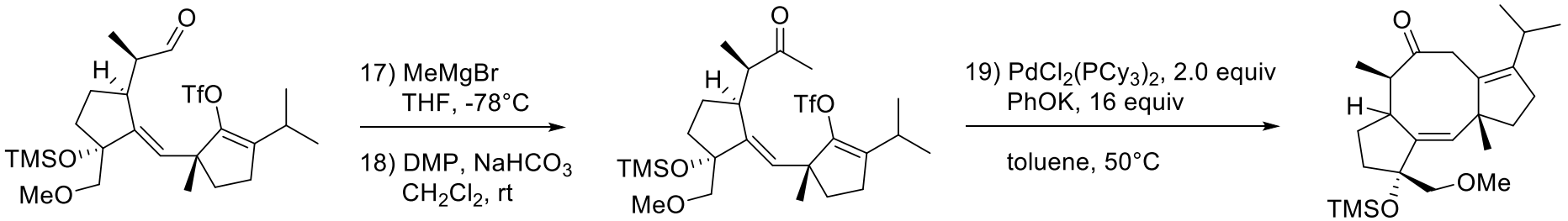


Methylation with Meerwein reagent:

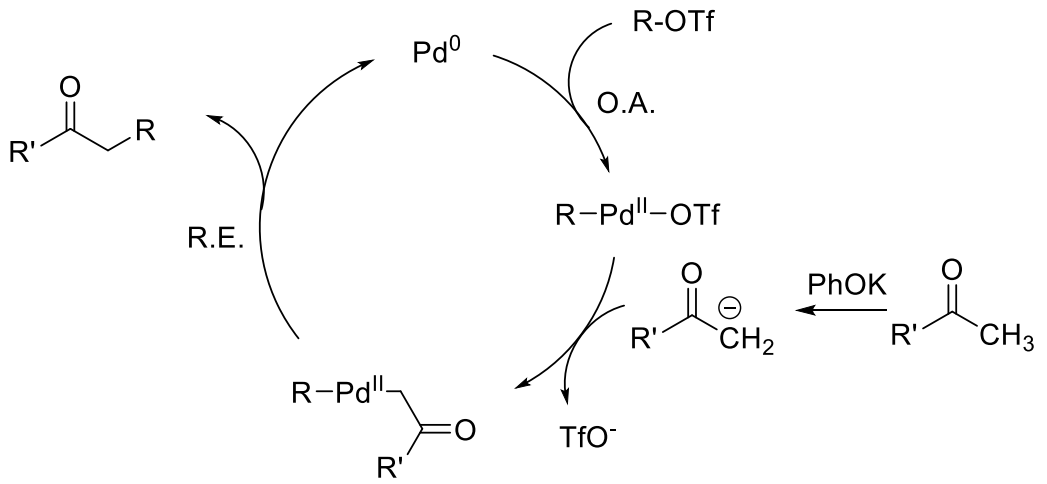


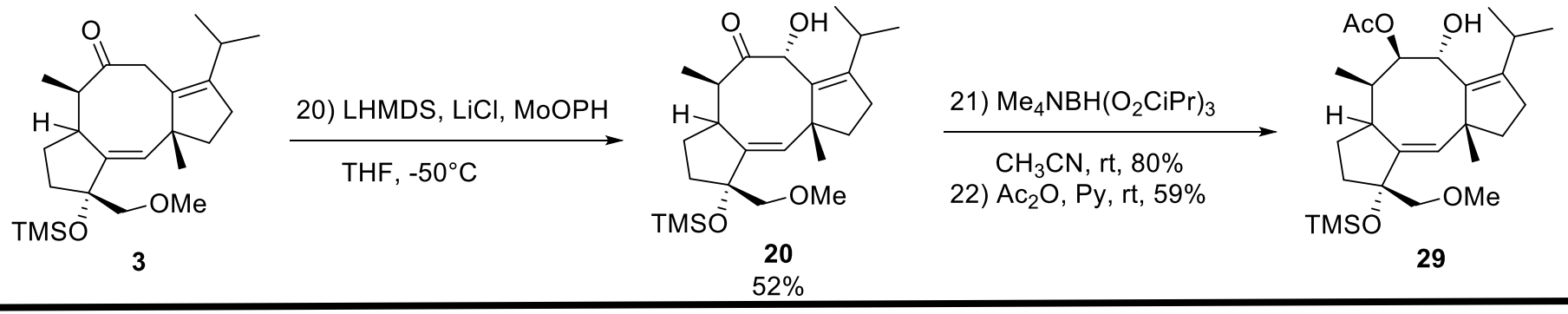
Reduction of nitrile:



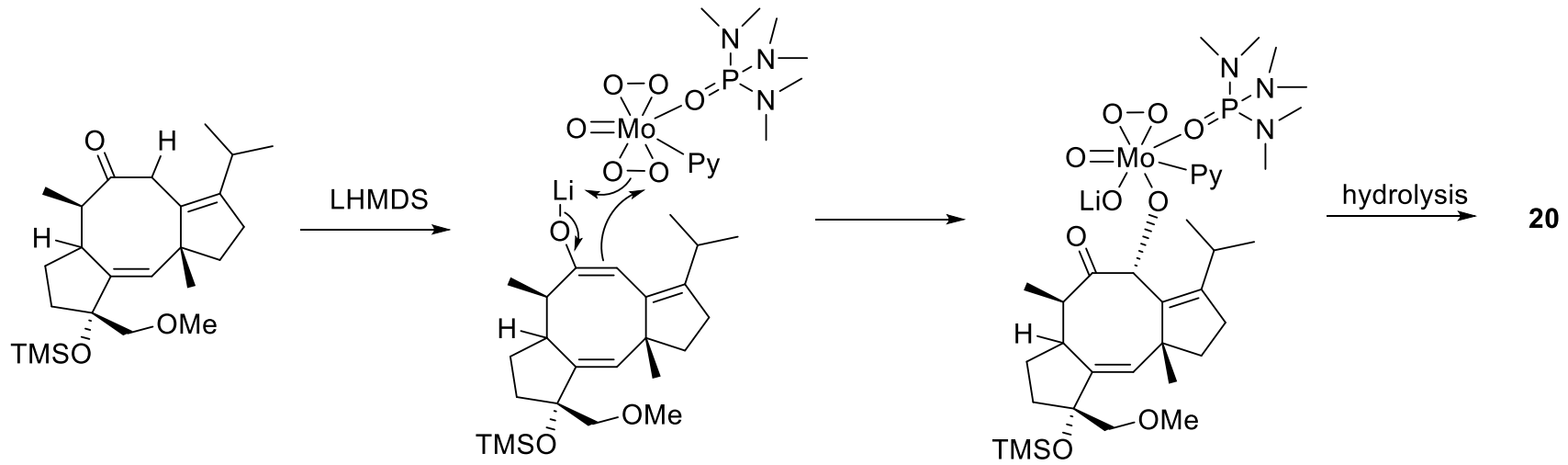


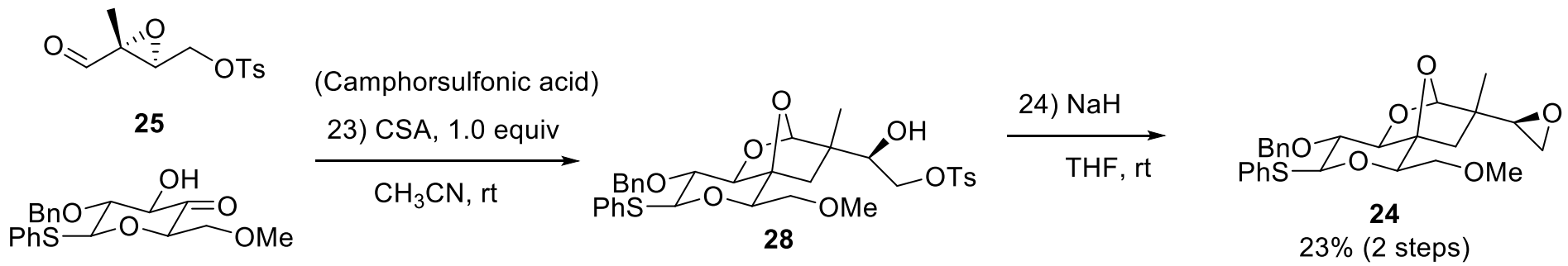
Palladium-catalyzed intramolecular alkenylation:



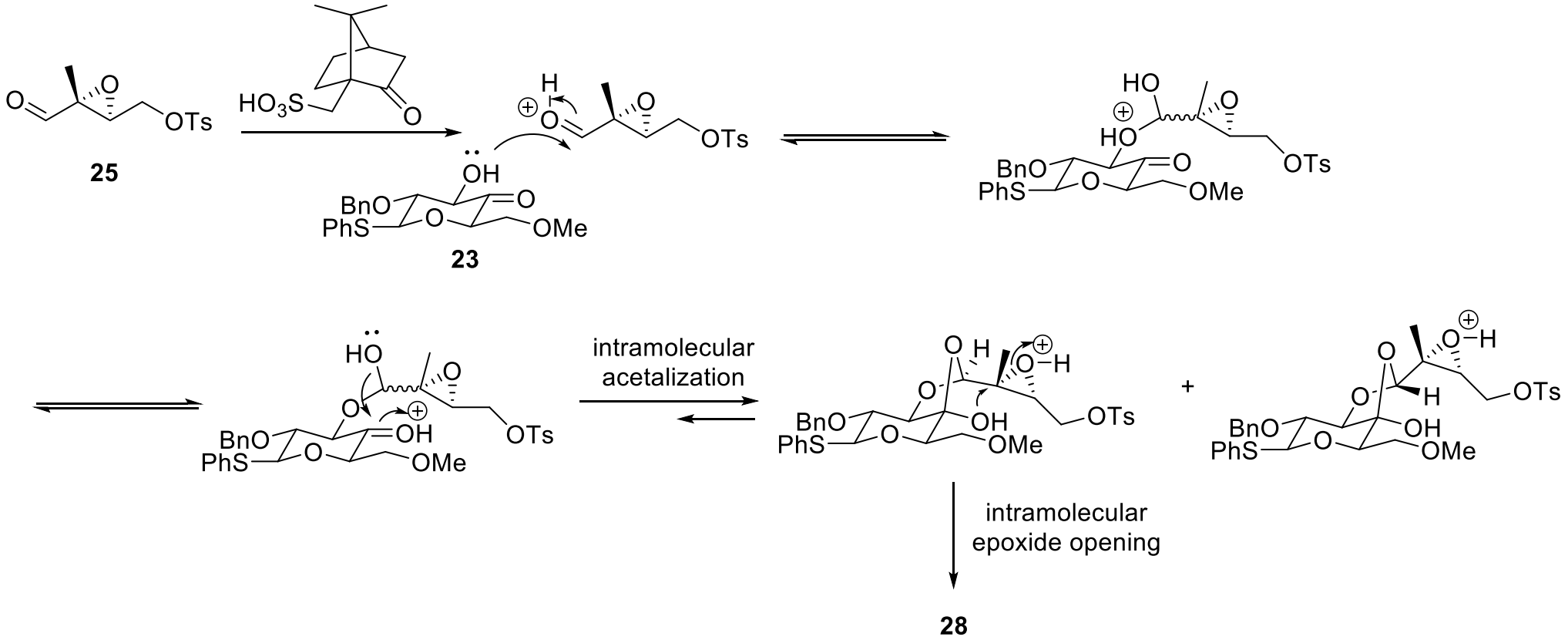


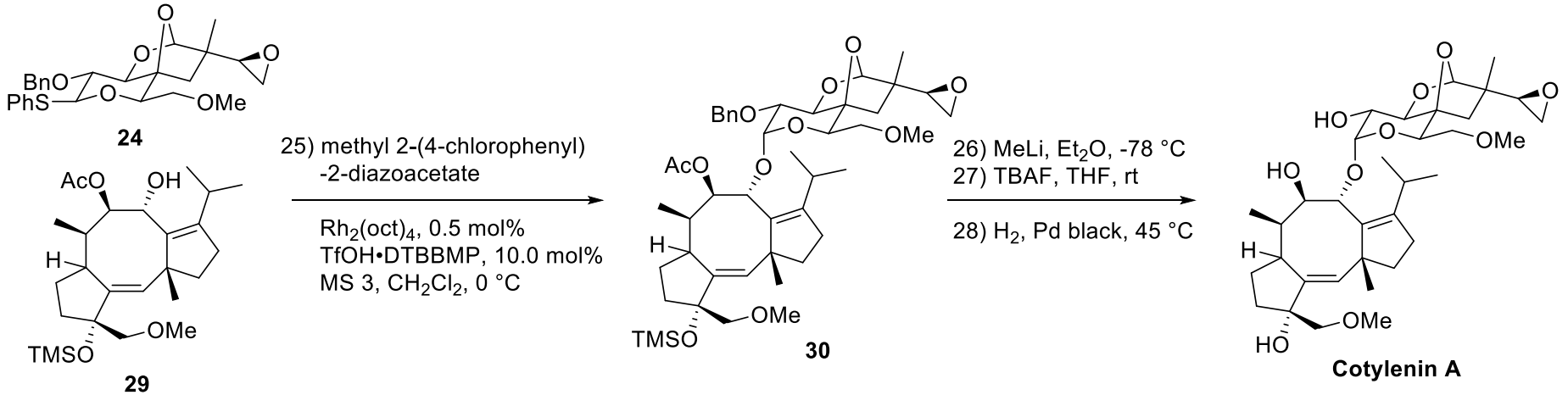
α-hydroxylation with MoOPH:



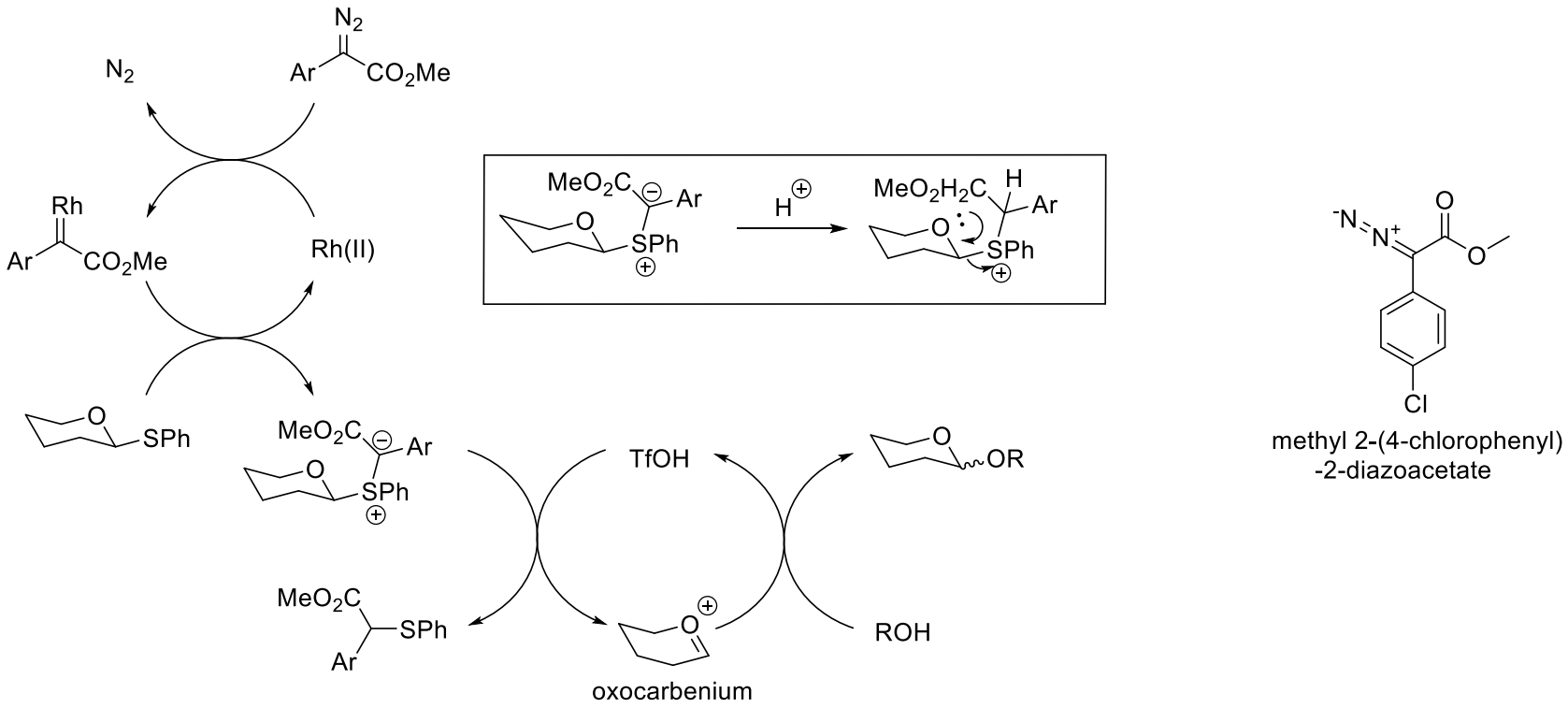


Acetalization and epoxide-opening cascade:





Rhodium-catalyzed sulfonium ylide formation and subsequent Bronsted-acid-catalyzed glycosylation:



methyl 2-(4-chlorophenyl)
-2-diazoacetate