

Cascade Reactions

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Minteer/Sigman lab

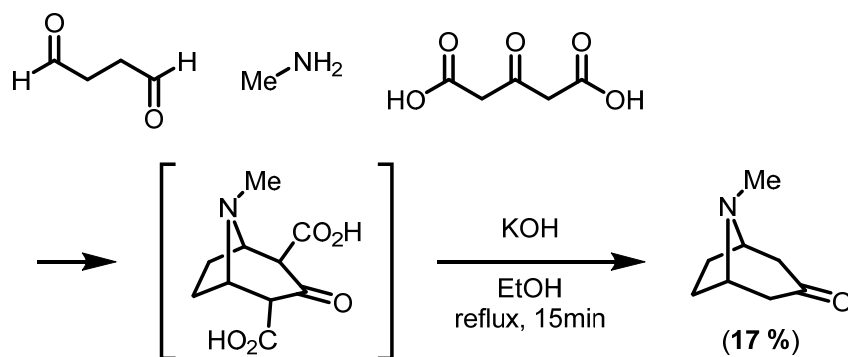
August 25th, 2021

Cascade reaction Types

- I. Cationic
- II. Anionic
- III. Radical
- IV. Pericyclic
- V. Photochemical
- VI. Carbenoid
- VII. TM Cat
- VIII. RedOx

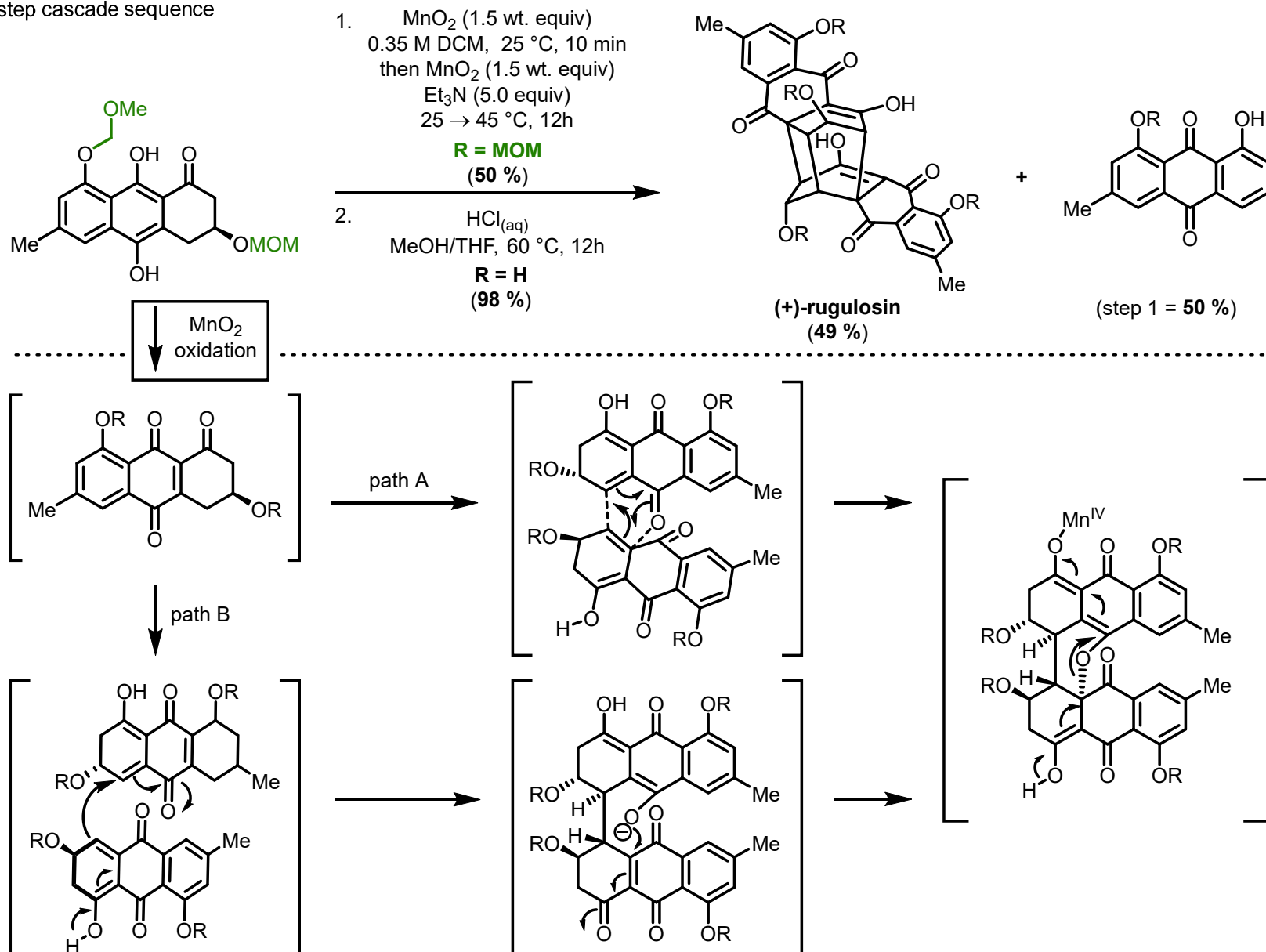
Tropinone

First biomimetic domino reaction, 1917 synthesis by Schopf and Robinson

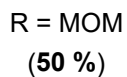


Anionic - initiated

7-step cascade sequence

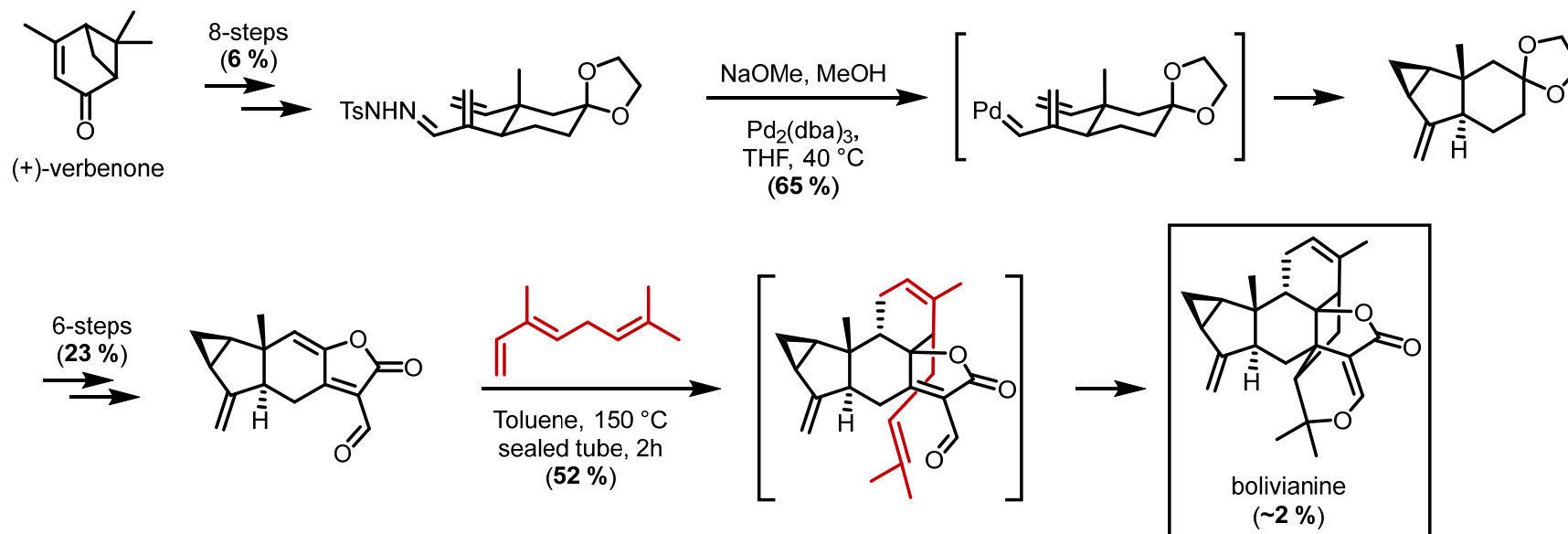


7-step cascade sequence

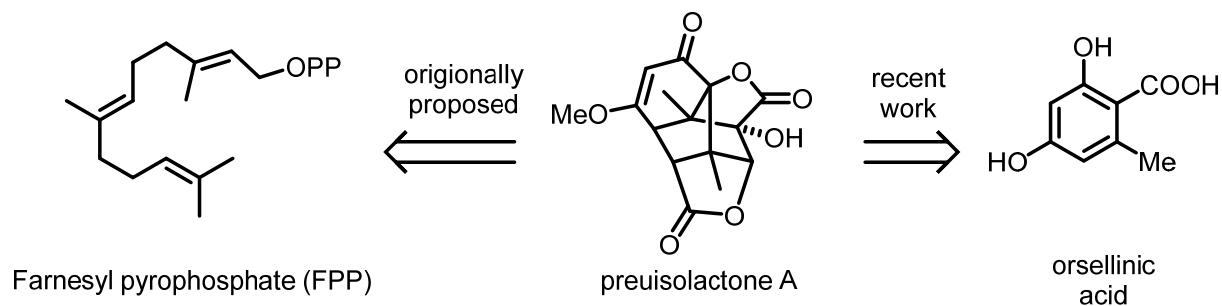


Organometallic and Pericyclic

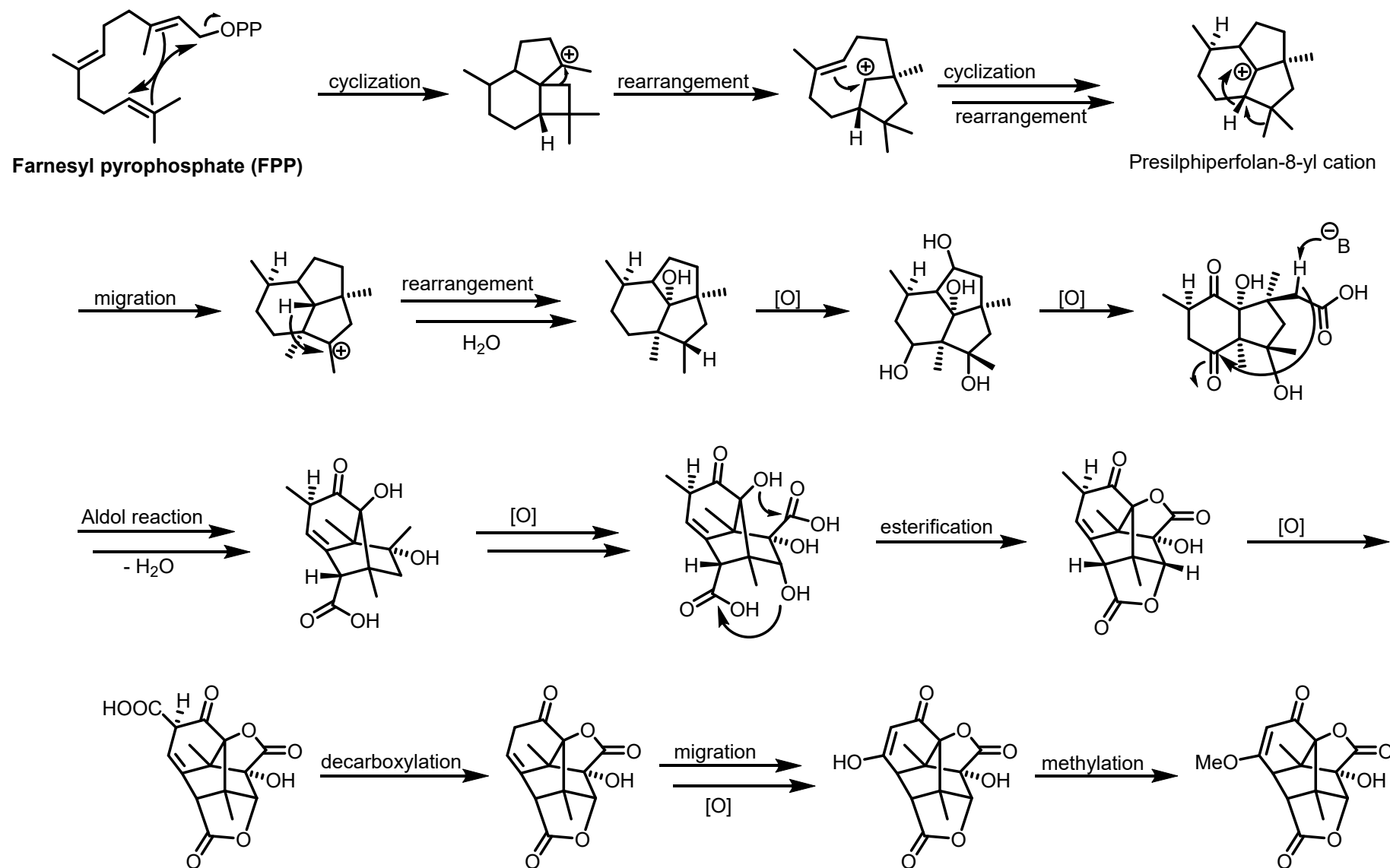
3 cycles, 4 C–C bonds and 5 stereogenic centers; no other isomers detected.



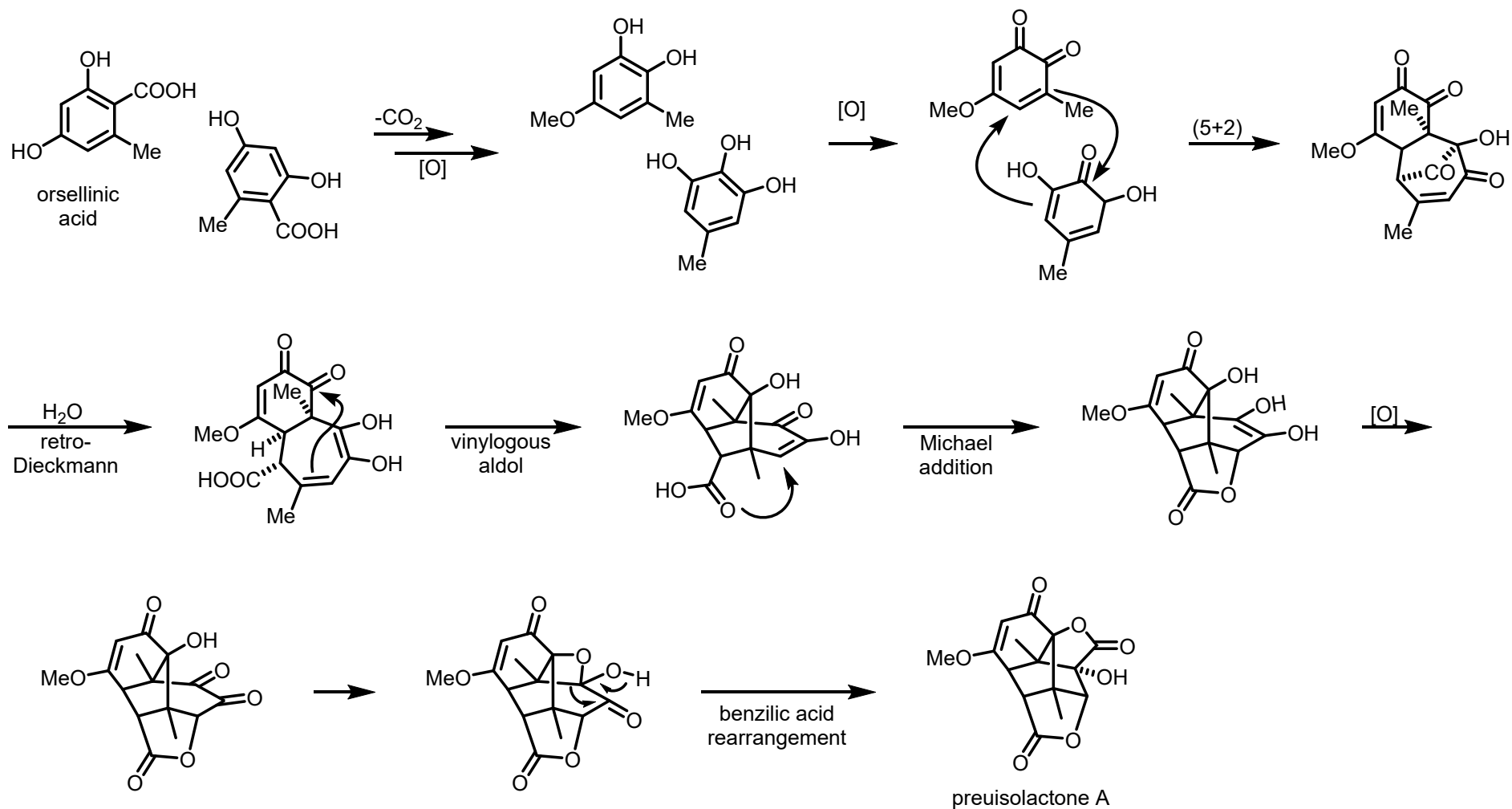
preisolactone A



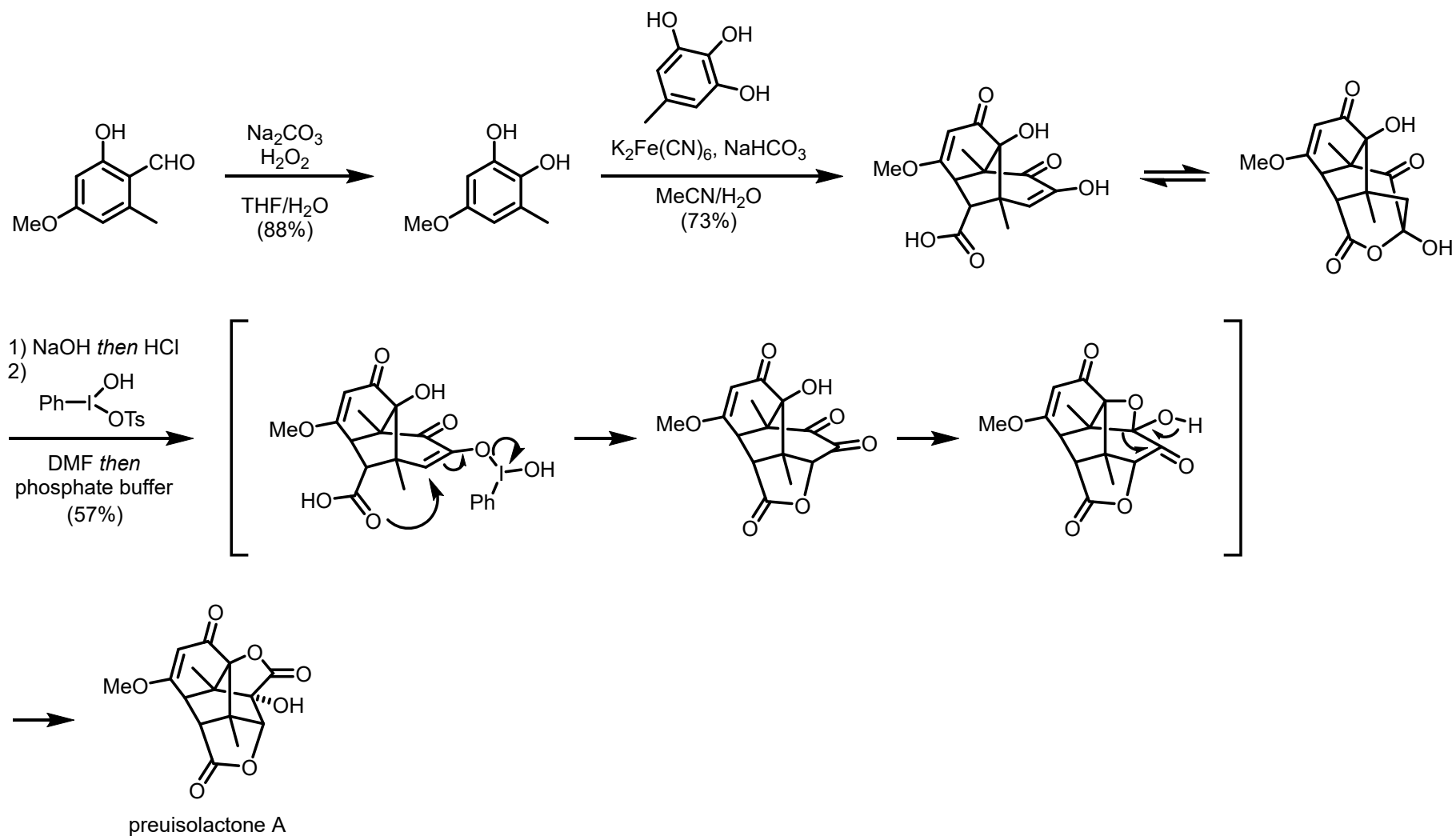
Cationic Proposed Biosynthetic Pathway



An alternative biosynthetic proposal



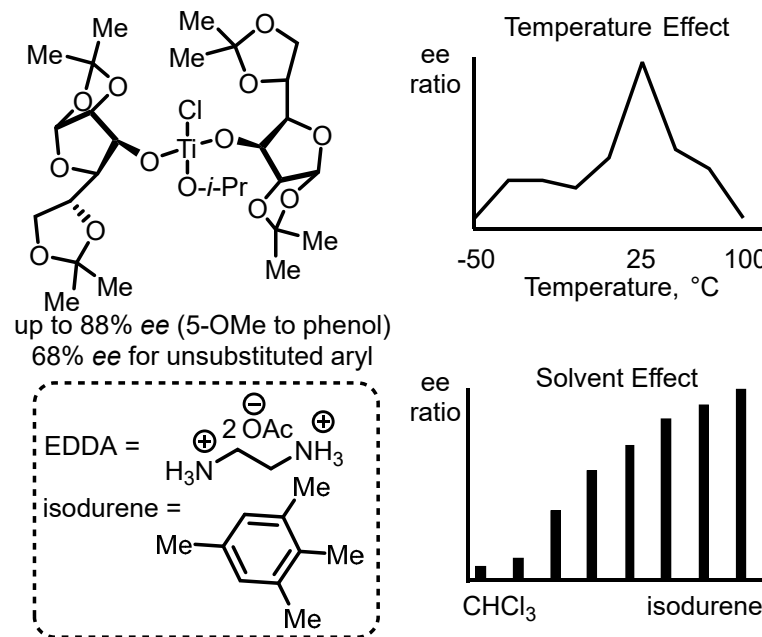
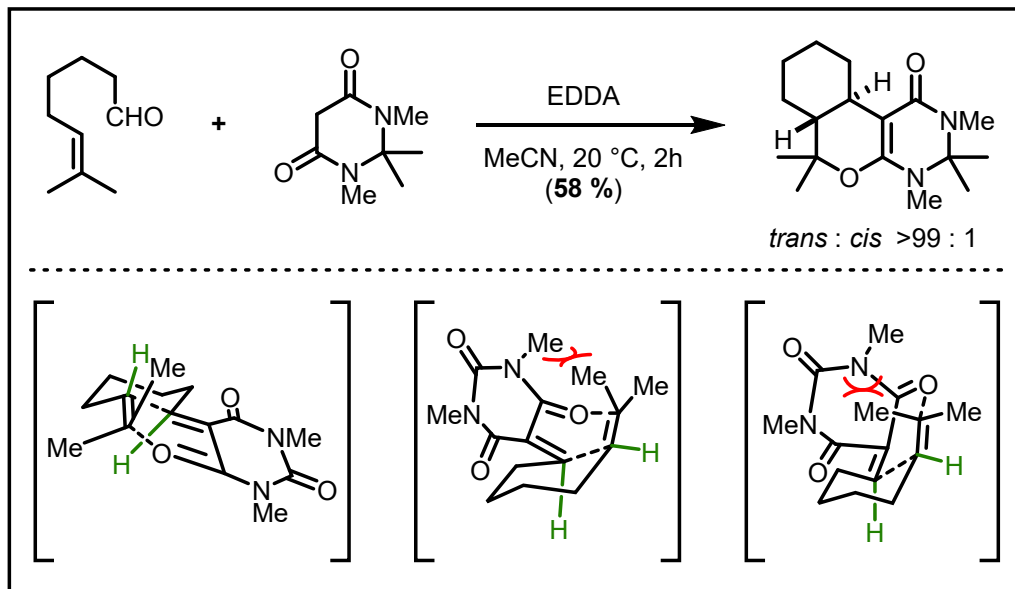
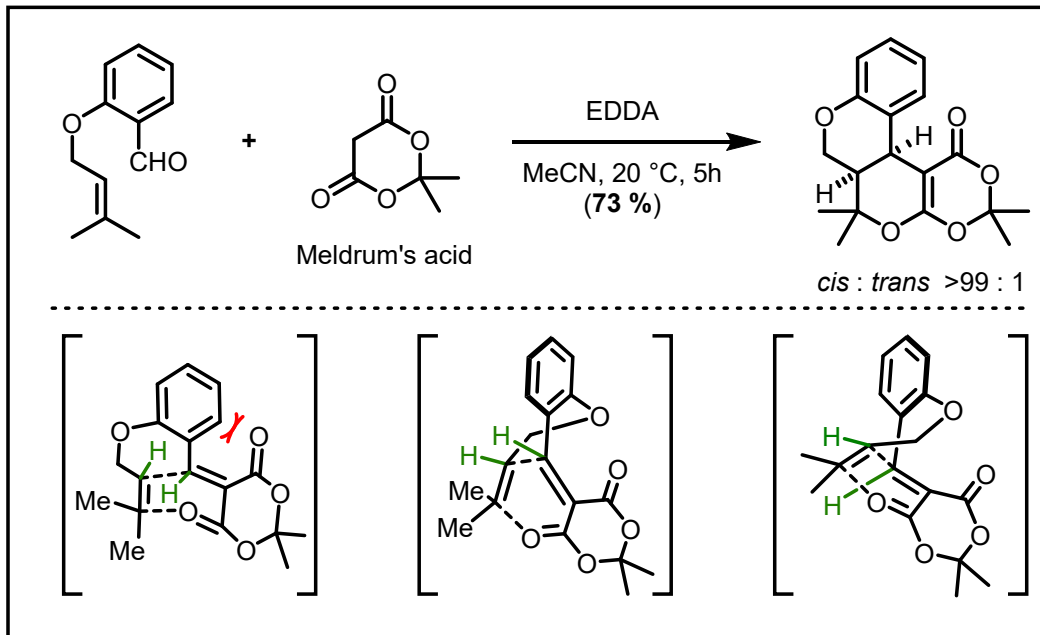
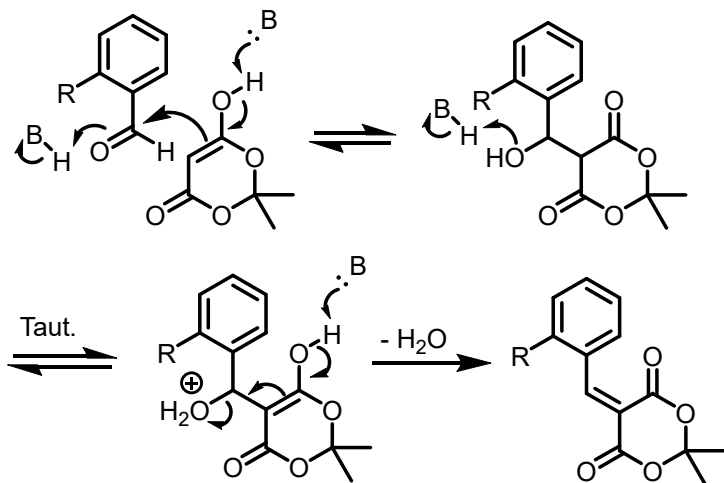
Validation through synthesis

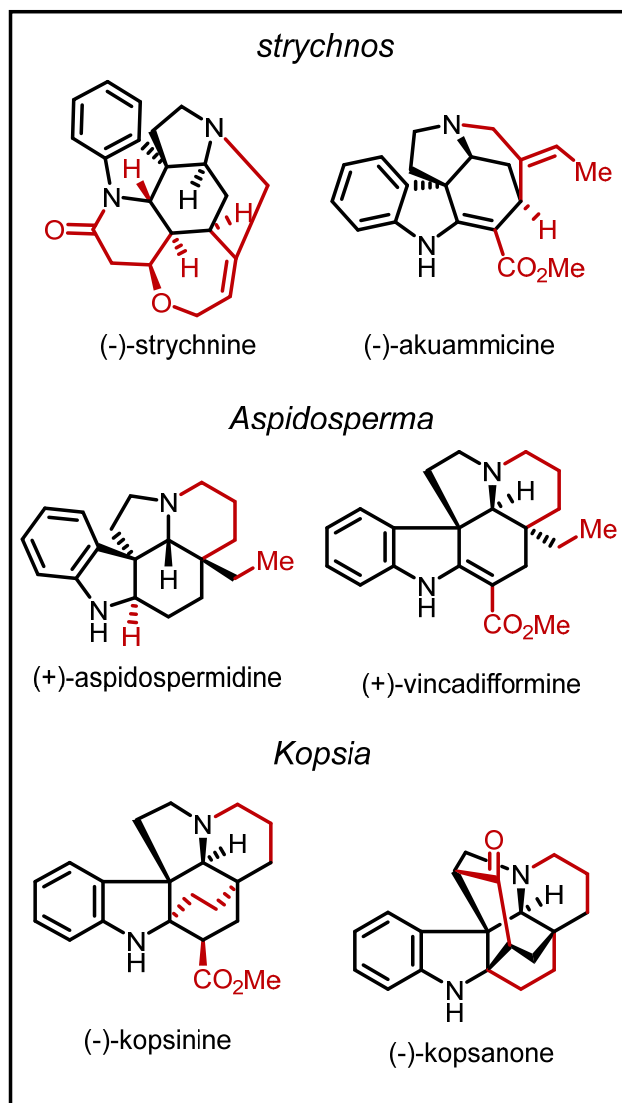
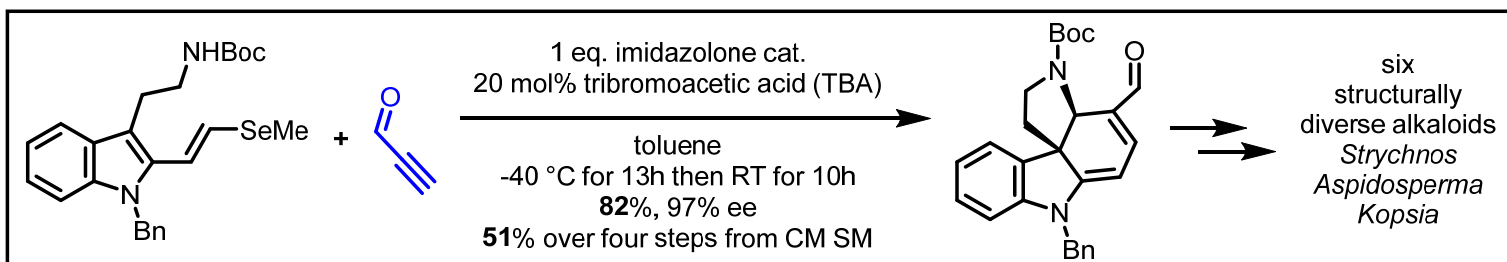


Anionic-Pericyclic sequence

Knoevenagel condensation, ene reaction

Knoevenagel condensation = "aldol" with a 1,3-diketone





	No. steps here	overall yield (%)	PSAC steps	PSCA steps
(-)-strychnine	12	6.4	25	16
(+)-aspidospermidine	9	24	13	11
(-)-kopsinine	9	14	NA	19
(-)-akuammicine	10	10	NA	NA
(+)-vincadifformine	11	8.9	NA	10
(-)-kopsanone	11	10	NA	NA

PSAC = previous shortest asymmetric catalytic synthesis
PSCA = previous shortest chiral auxiliary or chiral pool synth

