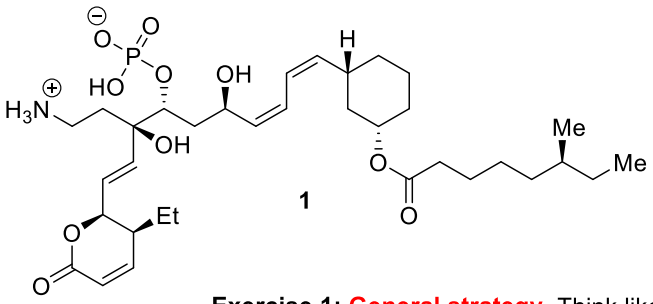
A Highly Convergent Total Synthesis of Leustroducsin B

Trost, B. M.; Biannic, B.; Brindle, C. S.; O'Keefe, B. M.; Hunter, T. J.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2015**, *137*, 11594



1

- Isolated from a culture broth of soil bacterium *Streptomyces Platensis* in 1993
- Antibacterial, antifungal, antitumor activity:
* Inhibition of protein serine/threonine phosphatase 2A (which regulates cell growth and inhibits metastasis)
* Produces increased *in vivo* resistance to *E. coli* infections.

Shortest prior total synthesis: 37 linear and 64 total steps!!

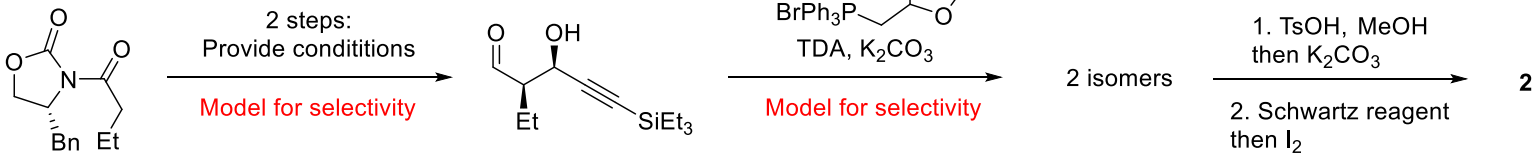
Exercise 1: General strategy. Think like Trost! Identify the two main disconnections, which leads to fragments **2**, **3**, **4**.
(Hint: reason broadly and not stepwise - there are 9 steps between 1 and **2**, **3**, **4**)

2

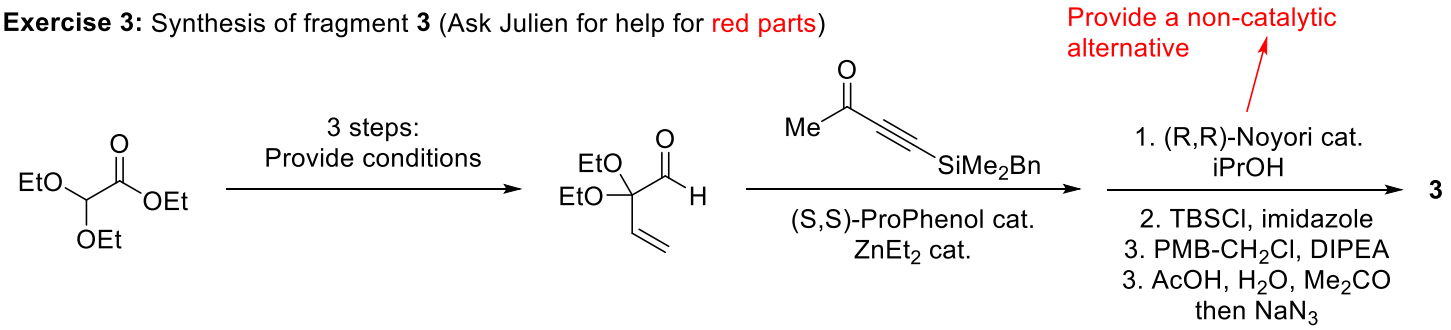
3

4

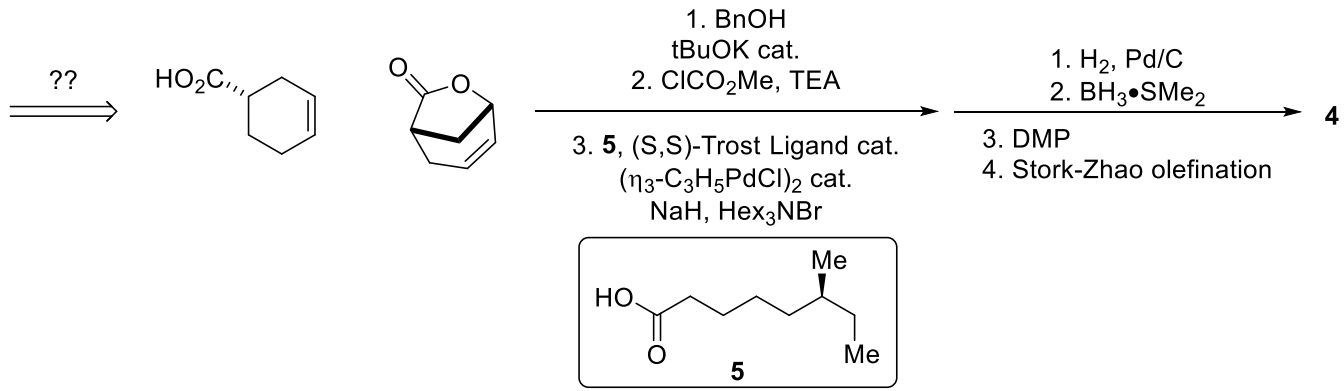
Exercise 2: Synthesis of fragment **2** (Ask Julien for help for red parts)



Exercise 3: Synthesis of fragment **3** (Ask Julien for help for red parts)

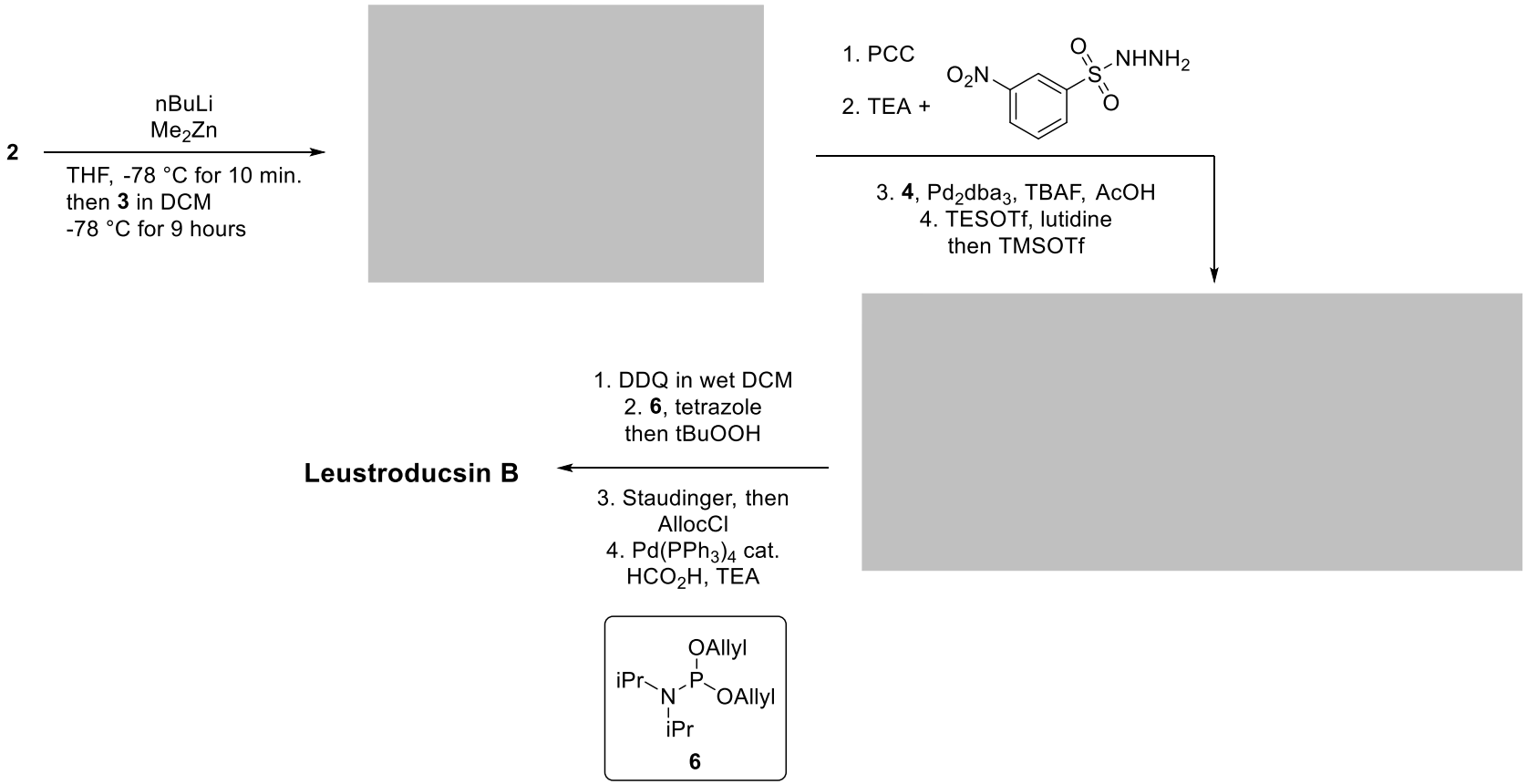


Exercise 4: Synthesis of fragment **4**



Exercises 5, 6, 7 (based on the remaining time)

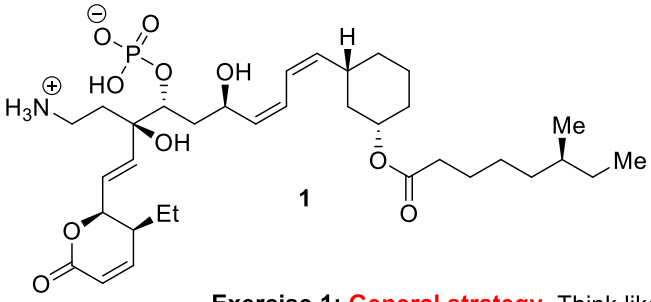
Propose a synthetic route for **5**



SOLUTION

A Highly Convergent Total Synthesis of Leustroducsin B

Trost, B. M.; Biannic, B.; Brindle, C. S.; O'Keefe, B. M.; Hunter, T. J.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2015**, *137*, 11594

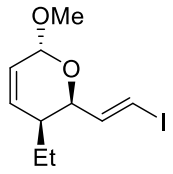


1

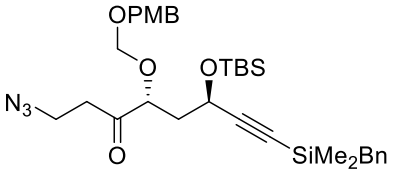
- Isolated from a culture broth of soil bacterium *Streptomyces Platensis* in 1993
- Antibacterial, antifungal, antitumor activity:
* Inhibition of protein serine/threonine phosphatase 2A (which regulates cell growth and inhibits metastasis)
* Produces increased *in vivo* resistance to *E. coli* infections.

Shortest prior total synthesis: 37 linear and 64 total steps!!

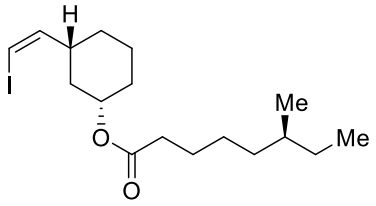
Exercise 1: General strategy. Think like Trost! Identify the two main disconnections, which leads to fragments **2**, **3**, **4**.
(Hint: reason broadly and not stepwise - there are 9 steps between 1 and **2**, **3**, **4**)



2

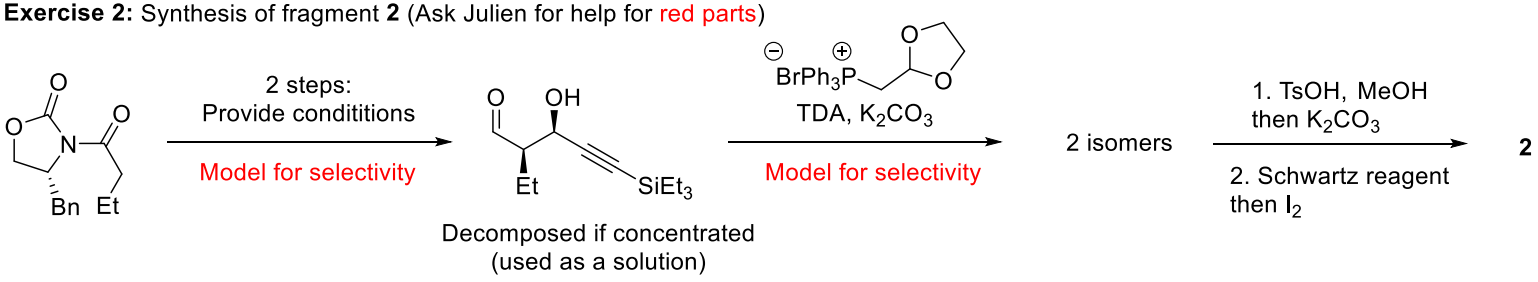


3

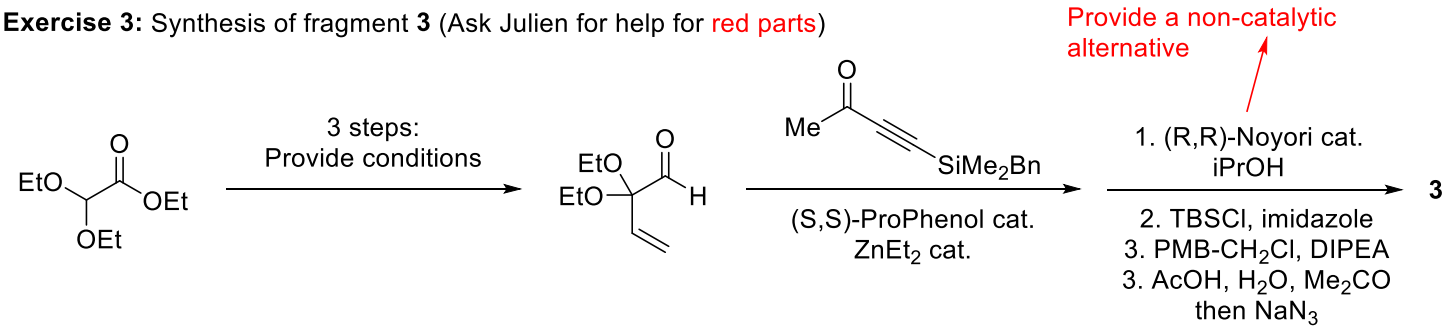


4

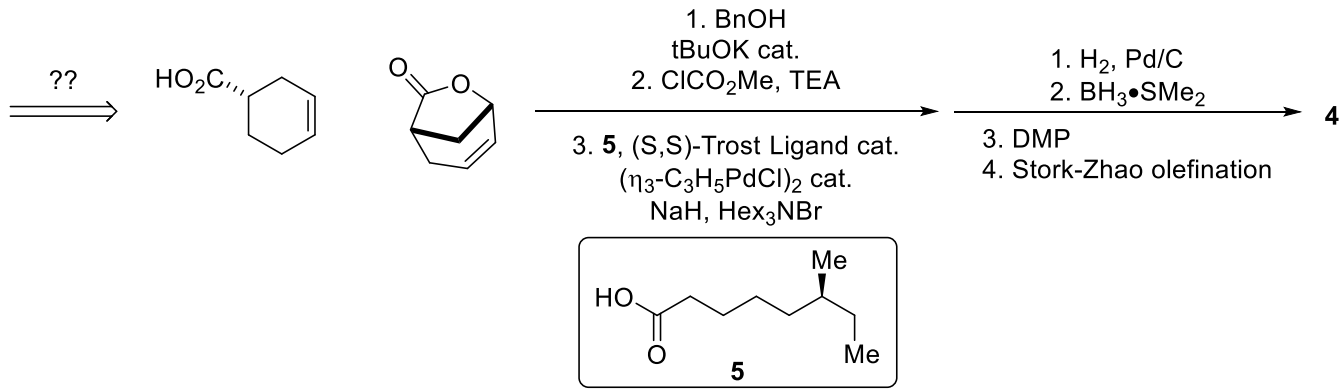
Exercise 2: Synthesis of fragment **2** (Ask Julien for help for red parts)

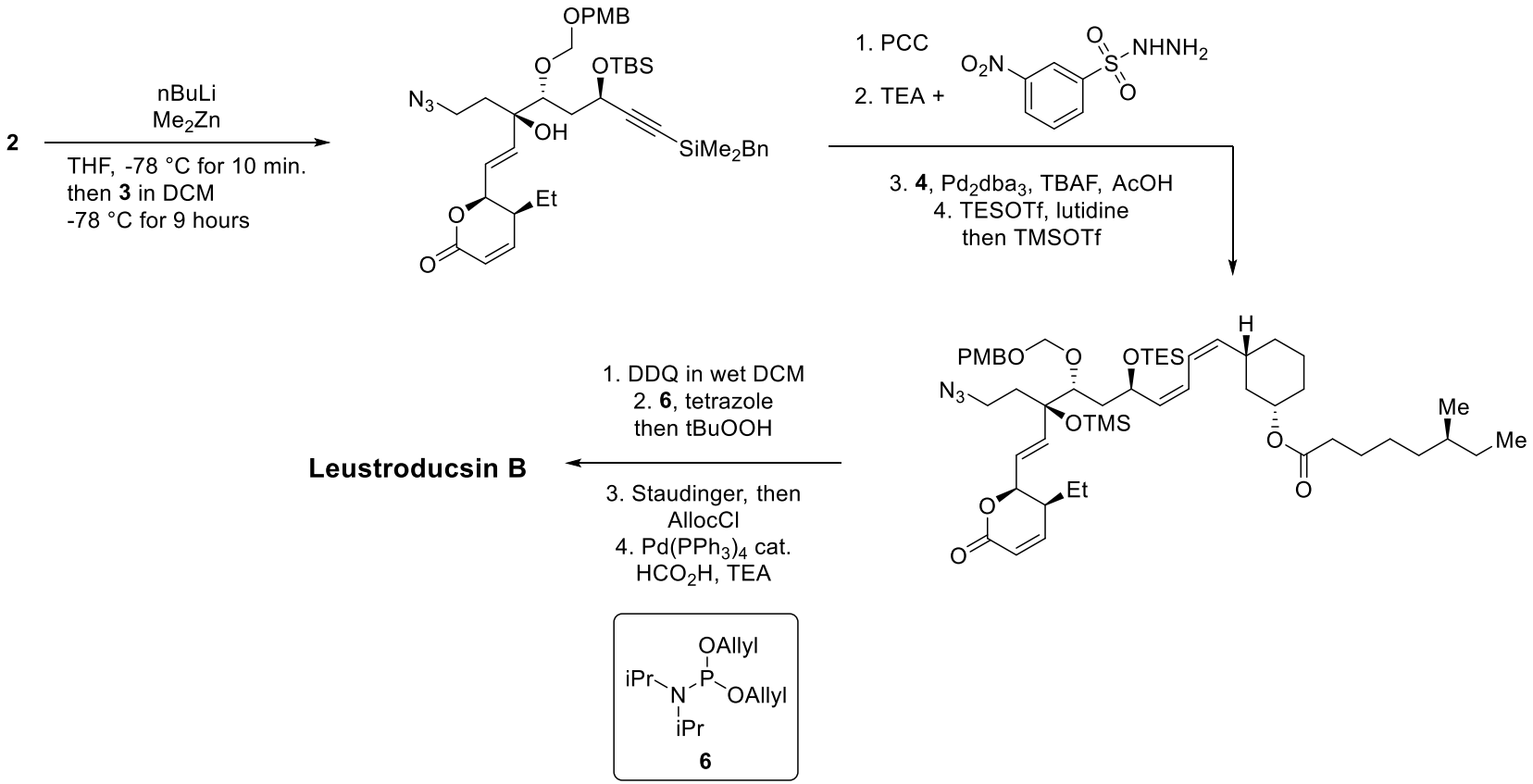


Exercise 3: Synthesis of fragment **3** (Ask Julien for help for red parts)



Exercise 4: Synthesis of fragment **4**



Exercises 5, 6, 7 (based on the remaining time)

Propose a synthetic route for **5**