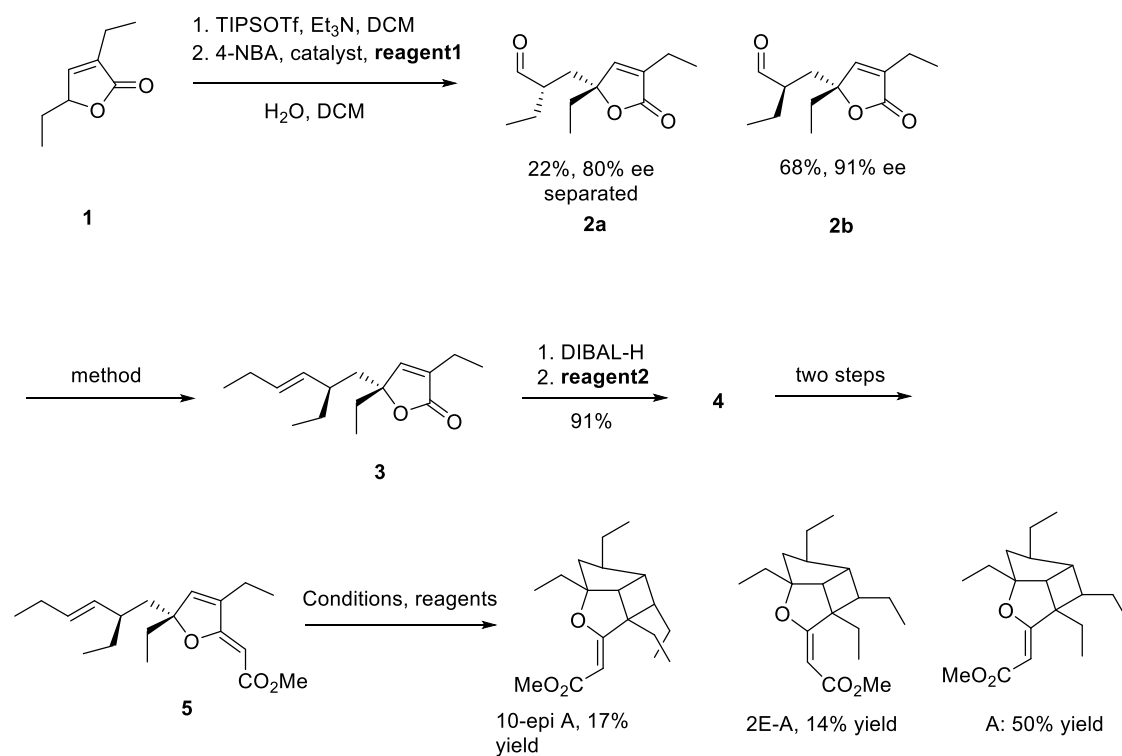


Exercise 7.2.18, submitted by Mănu



Q1: What kind of reaction is the transformation of 1 to 2? Give a plausible catalyst and the missing reagent1.

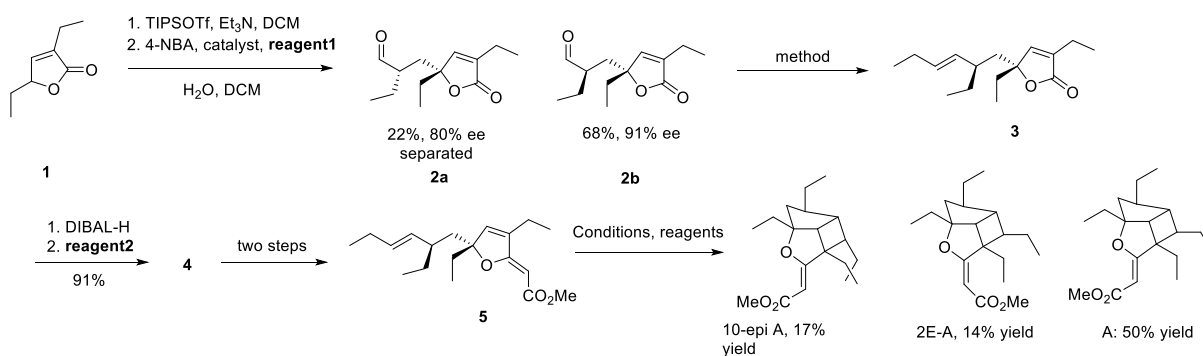
Q2: Give methods for the transformation of 2b to 3. Which would you choose/ which one should(n't) work?

Q3: Give reagent2 and a structure for the missing compound 4

Q4: What kind of reaction is the transformation of 5 to the target compound A (and its byproducts)

Q5: With Q4 solved, propose a different strategy to obtain the product A from 3, forming the cycles first.

## Exercise 7.2.18



Q1: What kind of reaction is the transformation of 1 to 2? Give a plausible catalyst and the missing reagent1.

Q2: Give methods for the transformation of 2b to 3. Which would you choose/ which one should(n't) work?

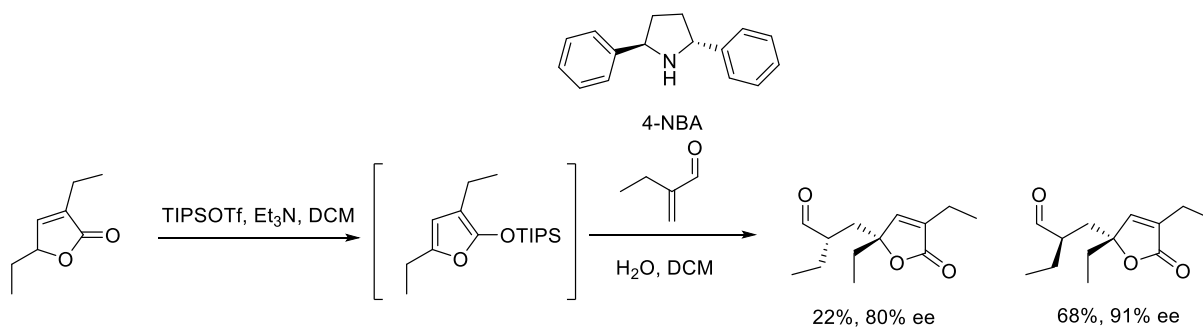
Q3: Give reagent2 and a structure for the missing compound 4

Q4: What kind of reaction is the transformation of 5 to the target compound A (and its byproducts)

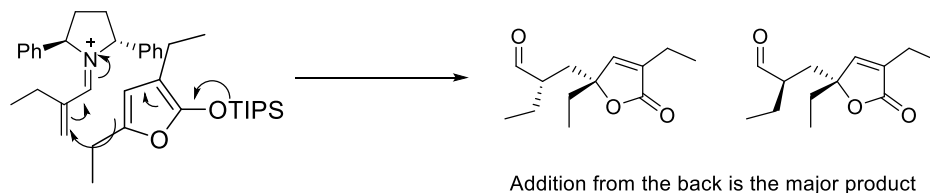
Q5: With Q4 solved, propose a different strategy to obtain the product A from 3, forming the cycles first.

Solutions:

A1: Mukaiyama-Michael Addition.



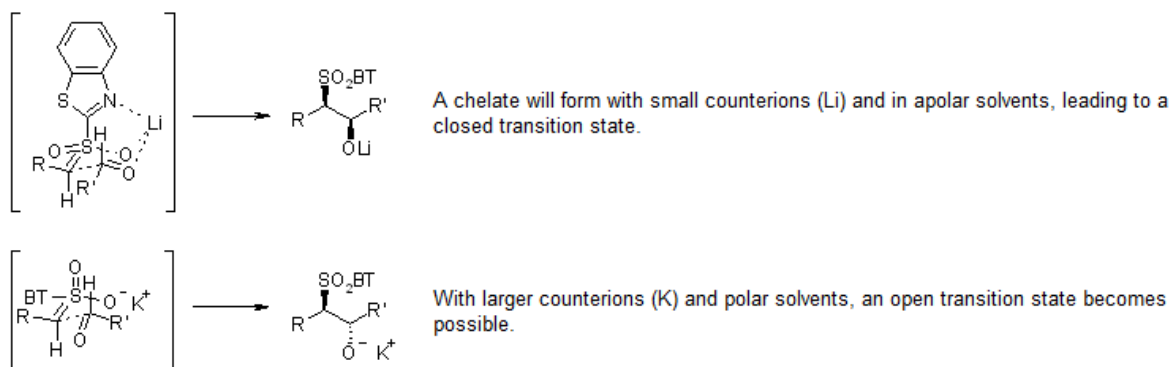
Enantioselectivity:



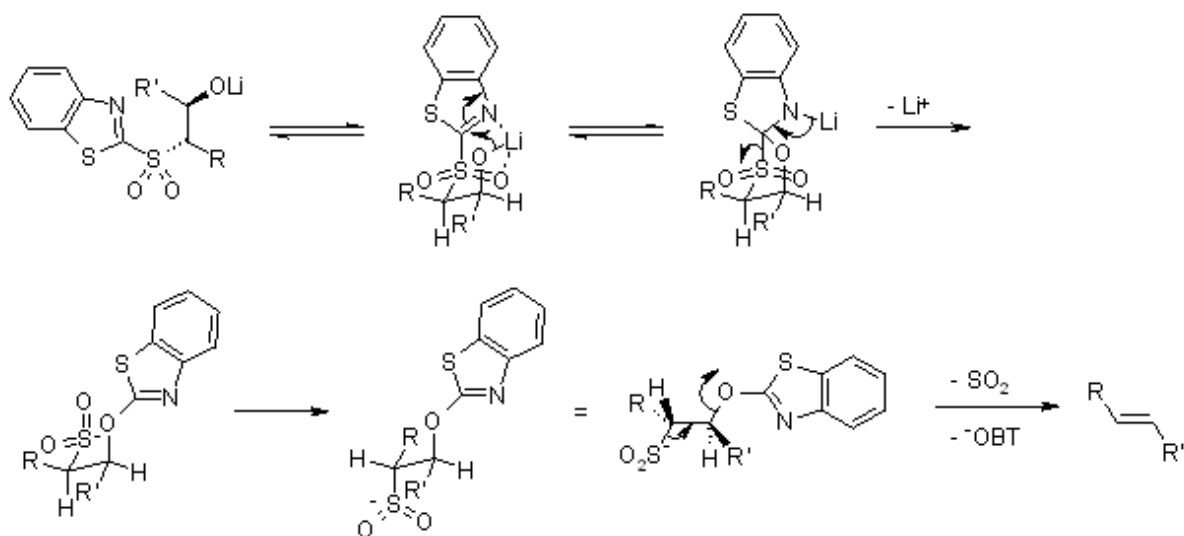
SM in in front, trap in the back, to minimize steric interaction of Ph and the SM

Protonation from behind (more accessible) would account for the diastereoselectivity.

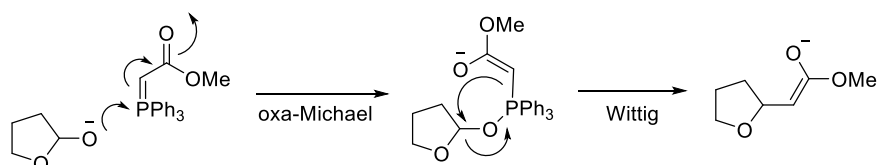
A2: Wittig reaction – Julia-Kocienski. Here Julia Kocienski, because Wittig would give Z-alkene most likely (unstabilized ylide). Julia Kocienski gives E, because KHMDS is used, LiHMDS leads to Z as well.



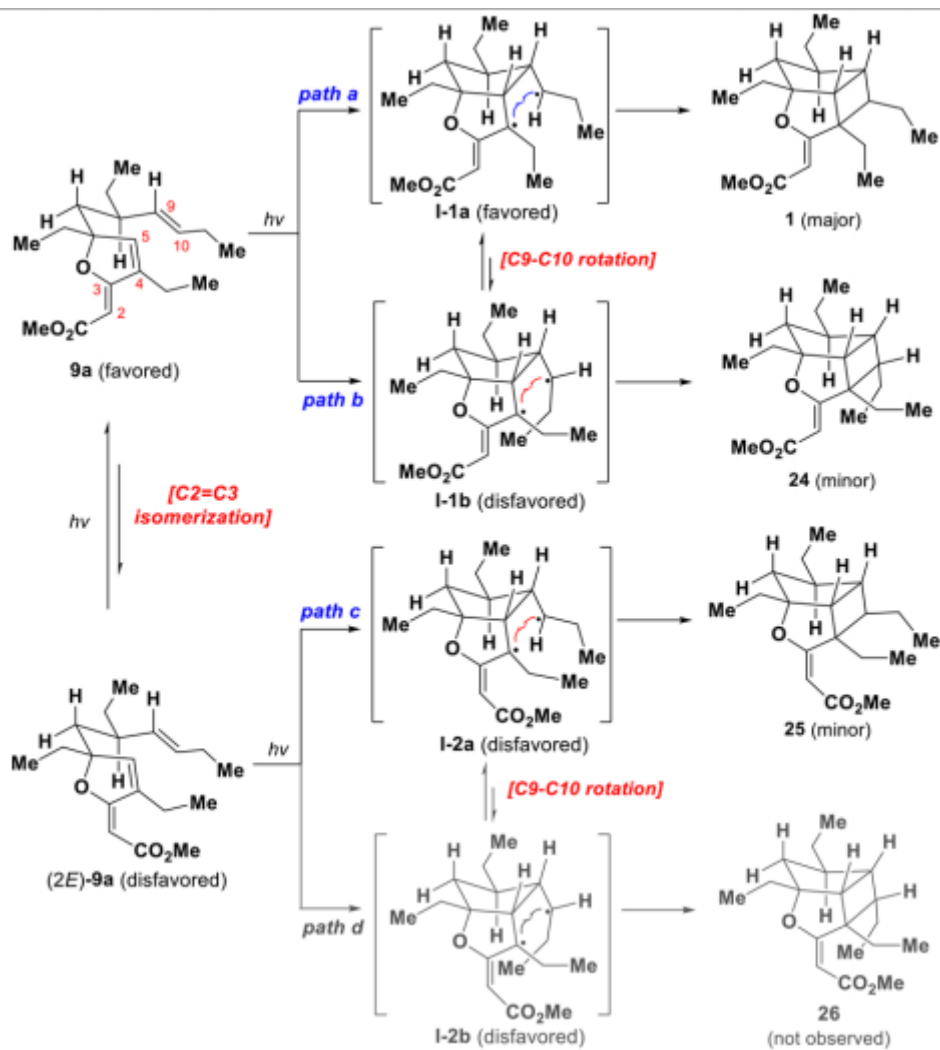
The anti then gives the E-alkene:



A3: Reduction with DIBAL-H, then tandem Wittig/oxa-Michael addition:



A4: [2+2] Photocycloaddition



A5: It is now obvious that you could also make the [2+2] Photocycloaddition first and replace the ketone second. Since such a transformation was already published (JACS, 2016, 138, 2437-2442) this would have resulted in a formal total synthesis.

Scheme of the overall synthesis:

