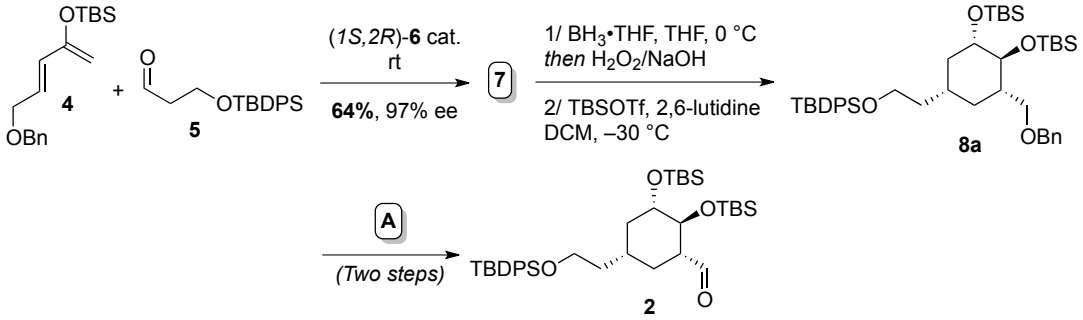
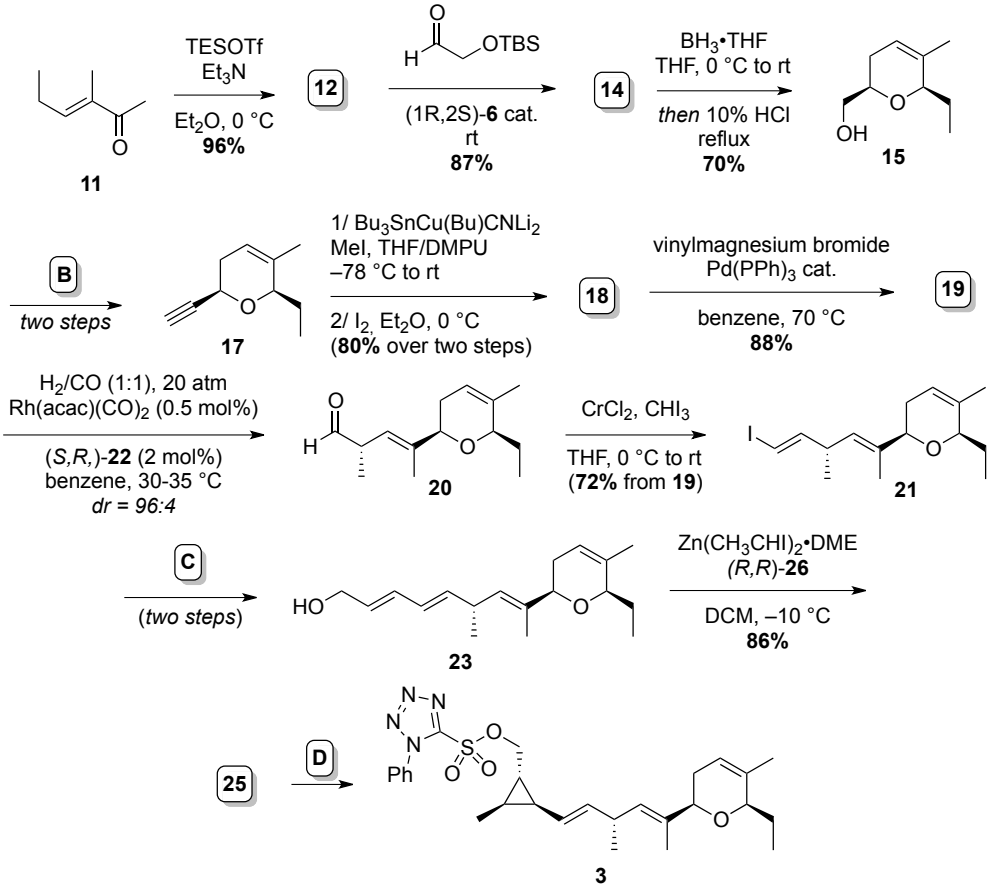
Submitted by Julien

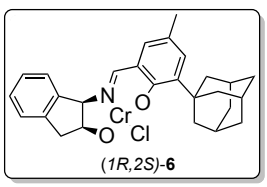
Total synthesis of (+)-Ambruticin

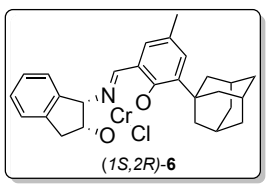
Synthesis of fragment **2**:

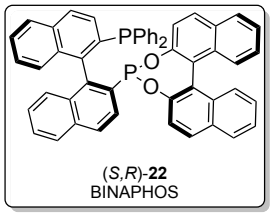


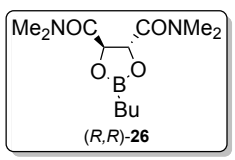
Synthesis of fragment **3**:



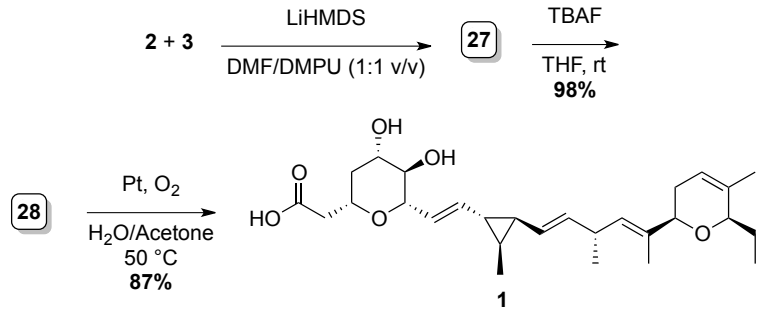








End of the synthesis:



1/ Give the reaction condition **A, B, C** and **D** and the structure **7, 12, 14, 18, 19, 25, 27** and **28**

2/ Give a transistion state for the formation of compound **7** or compound **14**. What the name of the reaction?

3/ What the name of the reaction with $Bu_3SnCu(Bu)CNLi_2$ (**18** from **17**, step 1) ? And explain the selectivity.

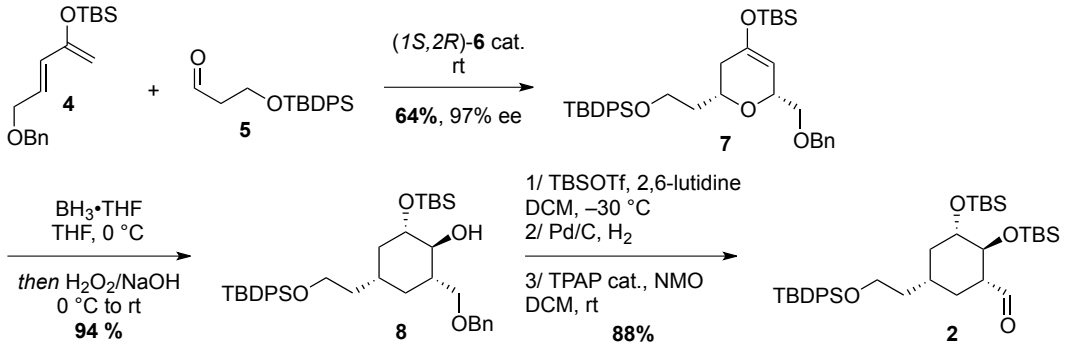
4/ Give a catalytic cycle and the name of the reaction for the formation of **19** (from **18**) and the aldehyde **20** (from **19**).

5/ Give the name and a mechanism for the coupling reaction between **2** and **6** and explain the selectivity. What happens if KHMDS or NaHMDS is used as base ?

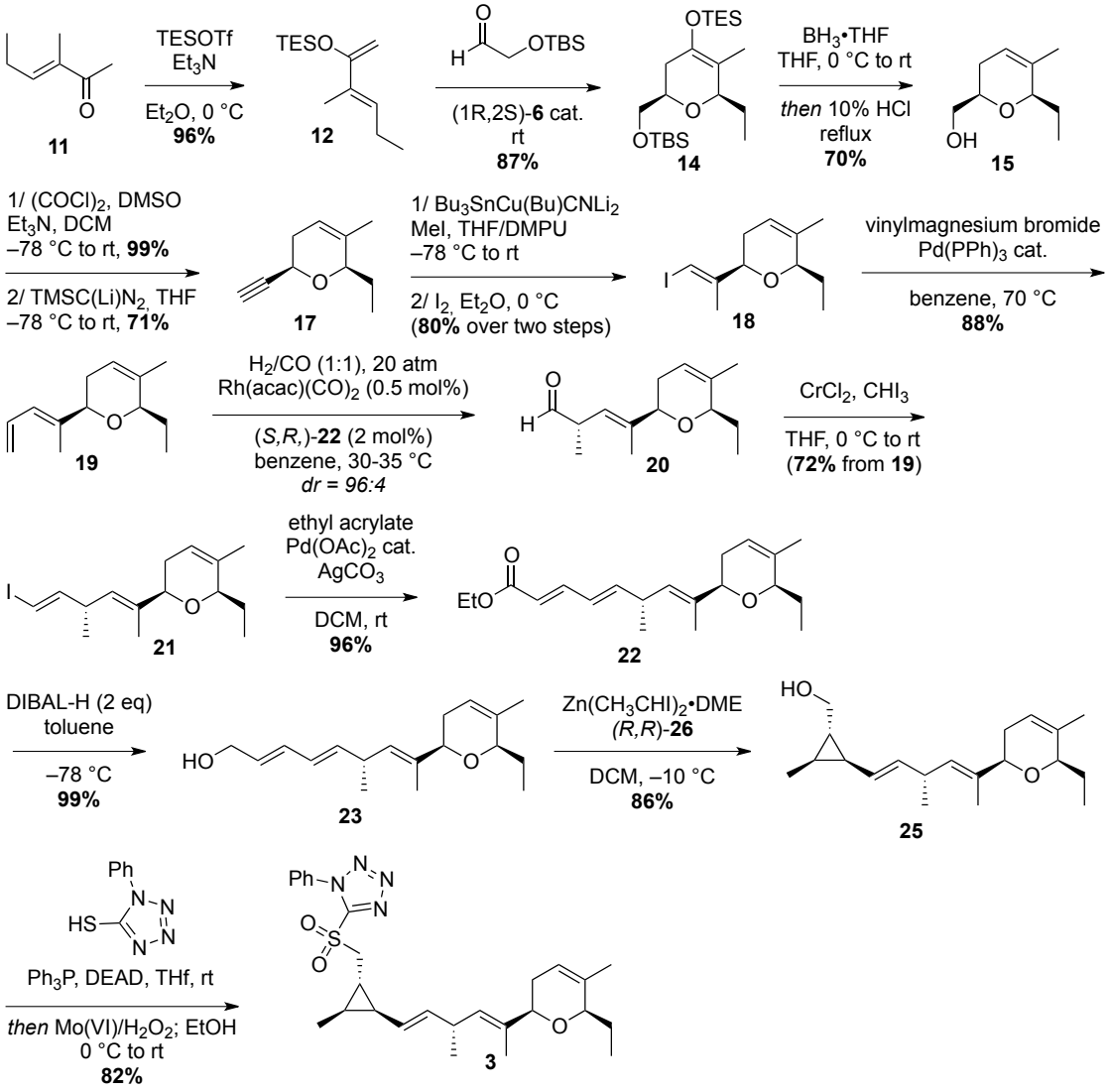
6/ Give a mechanism for the generation of the compound **21** (from **20**). What the name of this reaction.

Solution:

1/ Synthesis of fragment **2**:



Synthesis of fragment **3**:



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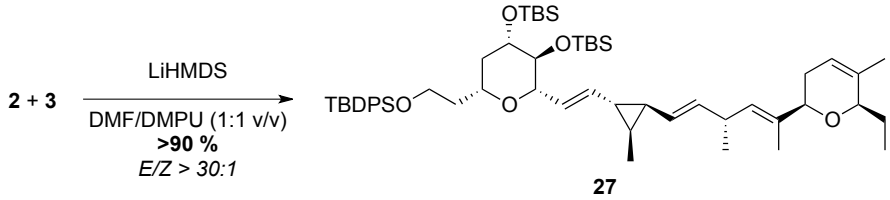
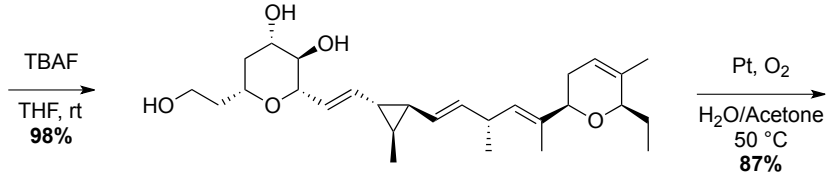
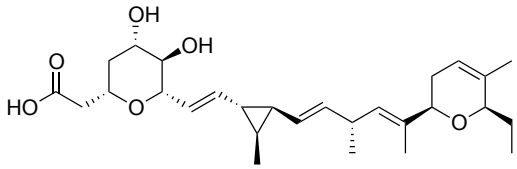


27

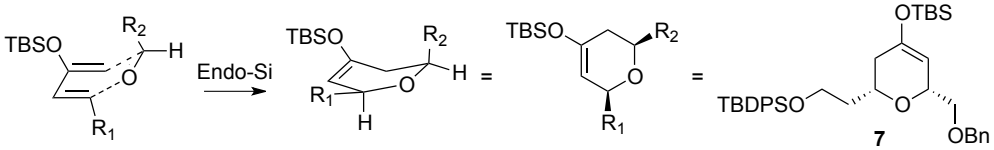


28



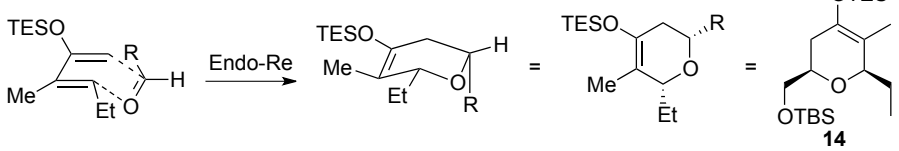
1

2/ Hetero-Diels-Alder.
Compound **7** : Endo-Si



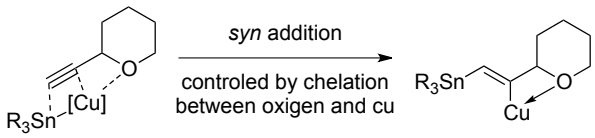
7

Compound **14 :** Endo-Re approach



14

3/ Carbocubration.



4/ **19** from **18** : Kumada cross-coupling

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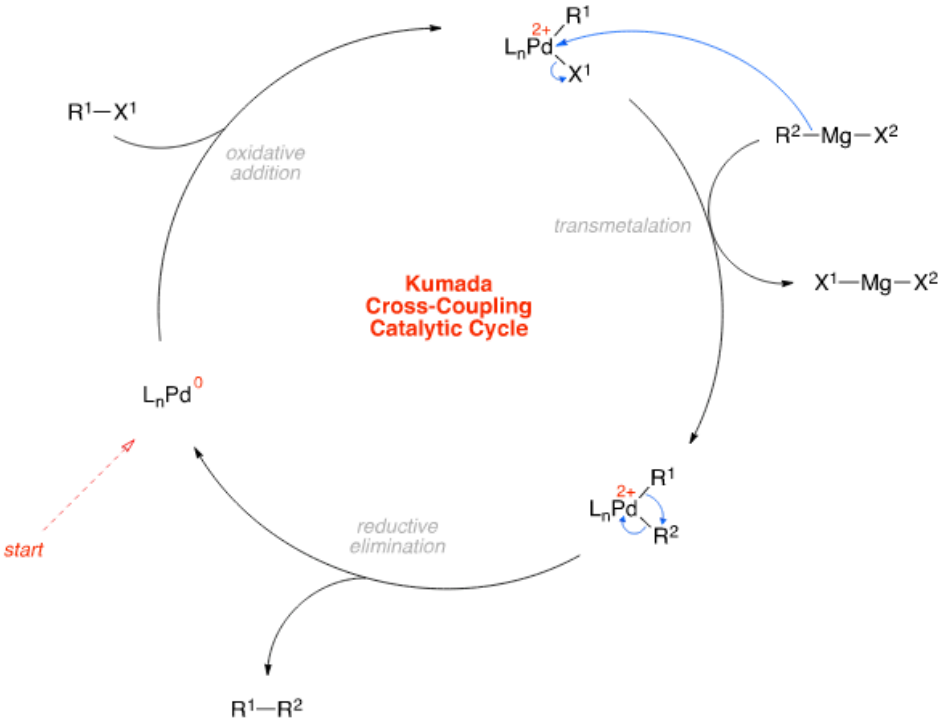
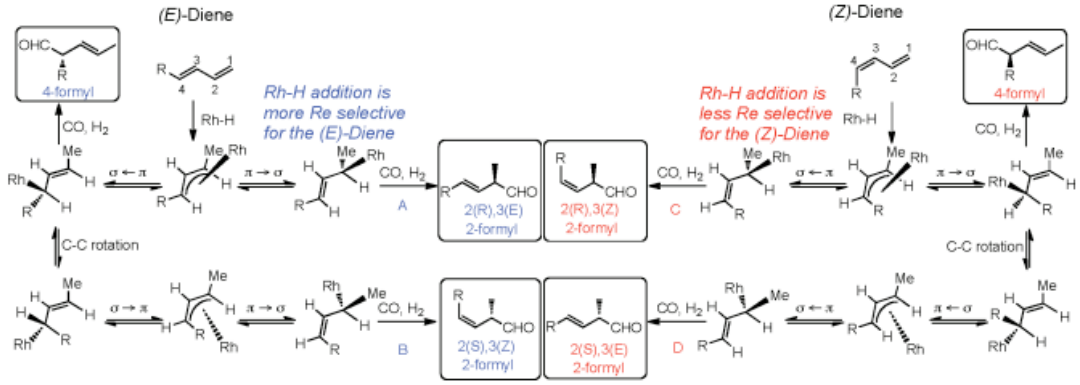
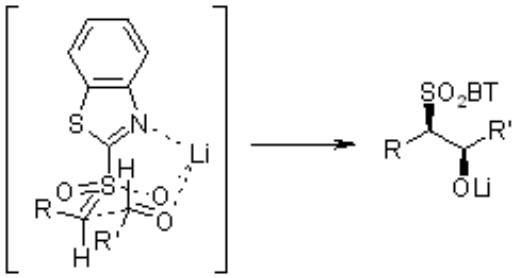
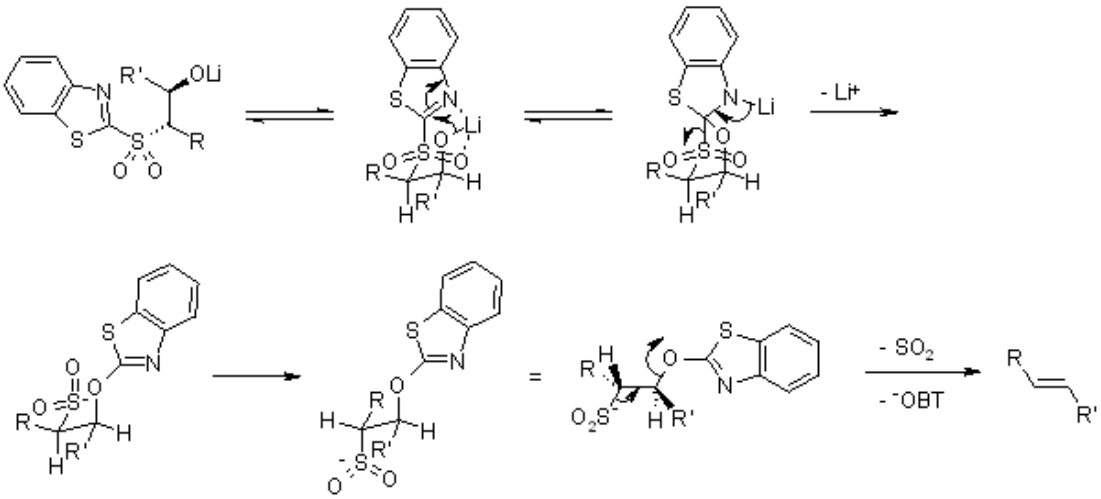


20 from **19** : Takaya-Nozaki catalytic asymmetric hydroformylation (regioselective hydrofromylation of 1,3-diene

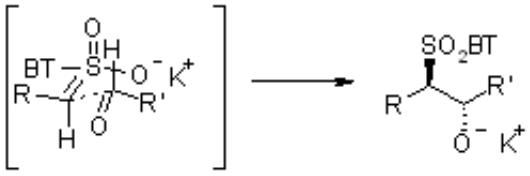


5/ Julia-kocienski olifination

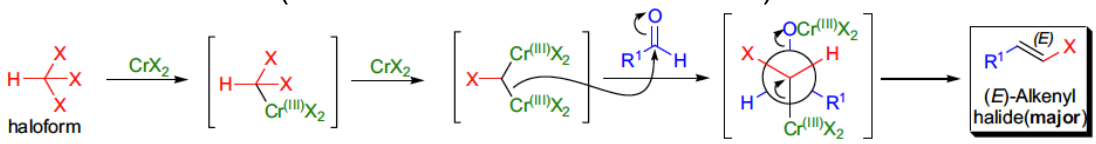




With KHMDS or NaHMDS : Z selectivity



6/ Takai olefination (TAKAI-UTIMOTO OLEFINATION)



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Julia-Kocienski olefination :
Paul R. Blakemorea, William. J. Colea, Philip J. KocieÆski*a, and Andrew Morley *Synlett* **1998**, 26-28.
Philip J. Kocienski*, Alan Bell, Paul R. Blakemore *Synlett* **2000**, 365-366.

Takai olefination:
Okazoe, T.; Takai, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 951–953.
Strategic Applications of Named Reactions in Organic Synthesis (Paperback) by Laszlo Kurti, Barbara Czako ISBN 0-12-429785-4

Keywords: hetero-Diels-Alder reaction, stannylcupration, Takaya-Nozaki hydroformylation, Takai olifenation, Heck cross-coupling, one-pot mitsunobu/oxidation process, Julia-Kocienski olifenation.