Reactivity in Organic Chemistry

Exam 16-01-2014 14:00

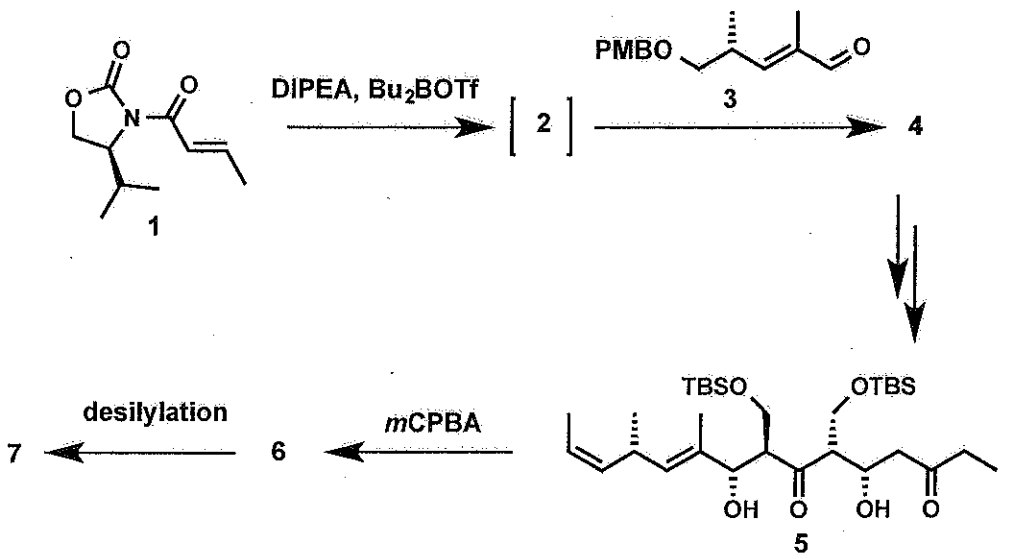
Problem 1

Below parts of the synthesis of myriaporone, a compound with suspected anti cancer activity, are depicted.

A) In the first step, **1** is treated with DIPEA and Bu_2BOTf to give **2**, which is immediately reacted with aldehyde **3**. Provide the structure of intermediate **2**. Provide the structure of **4**, including stereochemistry and the mechanism of its formation.

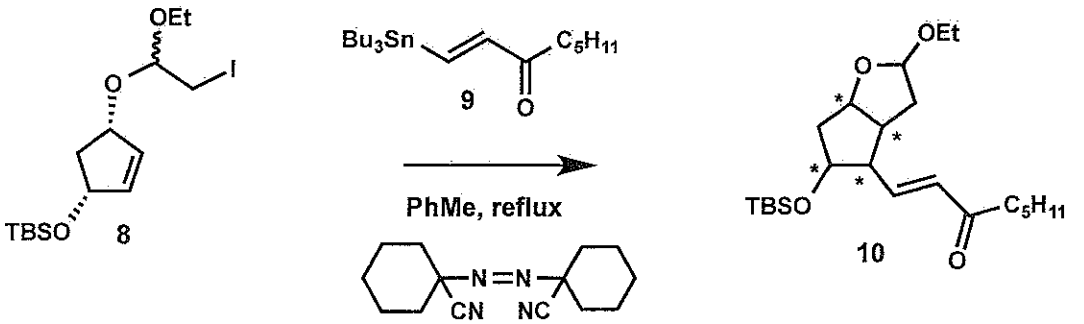
B) After a couple of steps diketone **5** is obtained. This compound is treated with *m*CPBA to give **6**. Give the structure of this compound, including stereochemistry and the mechanism of its formation.

C) Finally, the silyl groups in **6** are removed under mild conditions. The resulting long chain product is in equilibrium with a cyclic compound. Give the structure of this cyclic compound **7**, including stereochemistry.



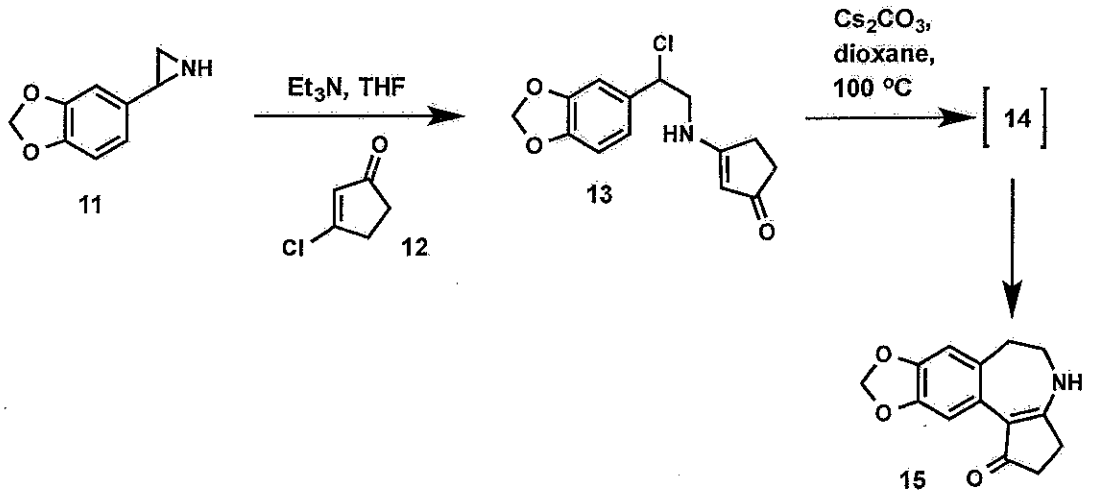
Problem 2

Compound **8** was combined with organotin reagent **9** under the conditions specified below to give bicyclic product **10**. Provide the mechanism for the formation of **10.** Specify the stereochemistry of the indicated chiral centres in **10** and justify your answer. Explain why the configuration of the douple bond in **10** is as shown.



Problem 3

A part of the synthesis of the anti-leukemia alkaloid (-)deoxyharringtonide is depicted below.



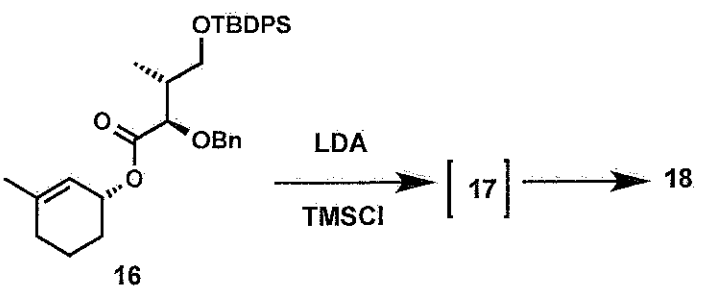
A) In the first step aziridine **11** is treated with cyclopentenone **12** under basic conditions. Provide the mechanism of formation of **13**.

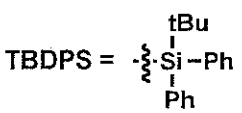
B) Next, **13** is heated in the presence of a weak base to provide **15**. Give the mechanism of this transformation, which proceeds *via* an aziridine intermediate **14**.

Problem 4

A) Upon treatment of **16** with LDA and TMSCl, silyl enol ether **17** is formed, which upon warming to room temperature reacts further to provide **18** (after aqueous work-up). Give the structure of **17** and **18** including stereochemistry and a mechanistic rationale for the formation of **18** from **17**. (Hint: In order to determine the configuration of enol ether **17** you have to consider that the OBn is able to chelate).

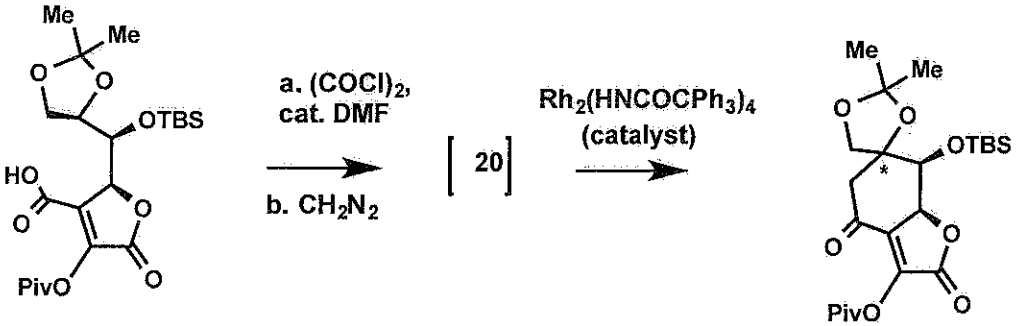
B) To prove the stereochemistry of product **18** it was treated with I_2 and $NaHCO_3$ to give a bicyclic product. Give the structure of this product including stereochemistry and the mechanism of its formation.





Problem 5

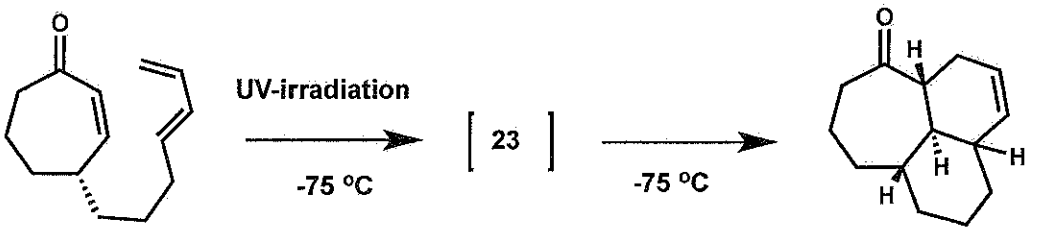
At the early stages of the synthesis of well known natural poison Tetrodotoxin compound **21** was prepared from precursor **19** via an intermediate (**20**). Give the structure of intermediate **20** and the mechanism of its transformation into **21.** Predict the stereochemistry of the indicated carbon in **21** (asterisk). Justify your prediction.



19 21

Problem 6

Alkenes are known to undergo cis-trans isomerisation under irradiation with UV-light. Compound **22** was irradiated with UV-light and subsequently underwent intramolecular thermal Diels-Alder reaction to give **24** at unusually low temperature. Provide the structure and the stereochemistry of the reactive intermediate **23** (stereoisomer of **22**). Justify your answer by evaluating the transition state for the conversion of **23** into **24**. What is the driving force of this extremely facile cycloaddition?



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