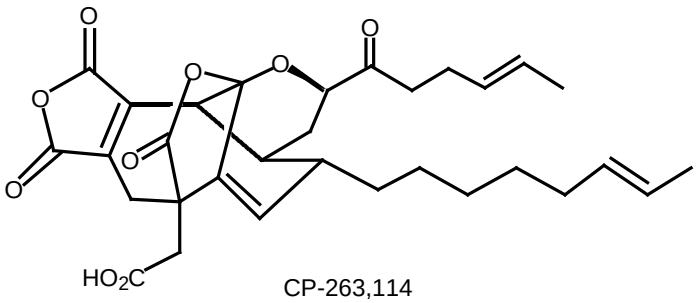
Organic Chemistry Day Lectures

Organic Cumulative Exam Saturday, June 3, 2000

9:00 AM- 12:00 noon, 201 Schlundt

NAME:_____

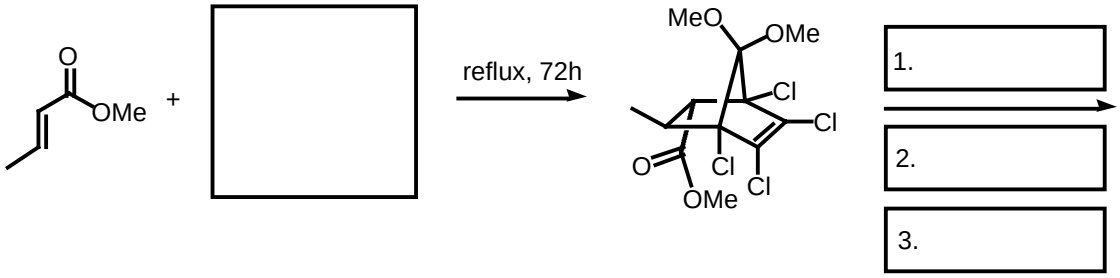
The questions found on this cumulative exam are derived from the lectures of Professors James L. Leighton and Lutz F. Tietze during our Organic Chemistry Day Symposium on Saturday, April 22, 2000. When answering the questions be as clear and concise as possible. Write your answers in a neat and organized manner, there are blank pages at the end of the exam if you need additional space.

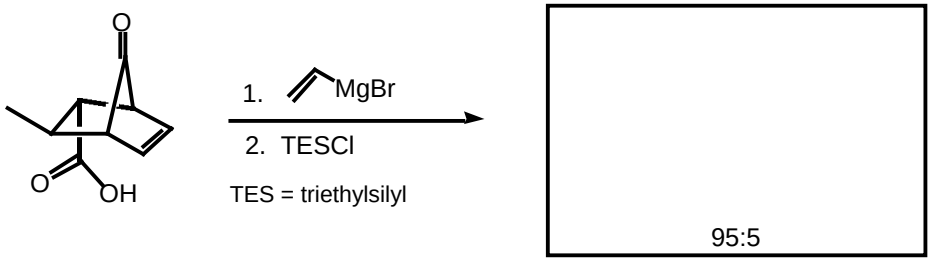


CP-263,114

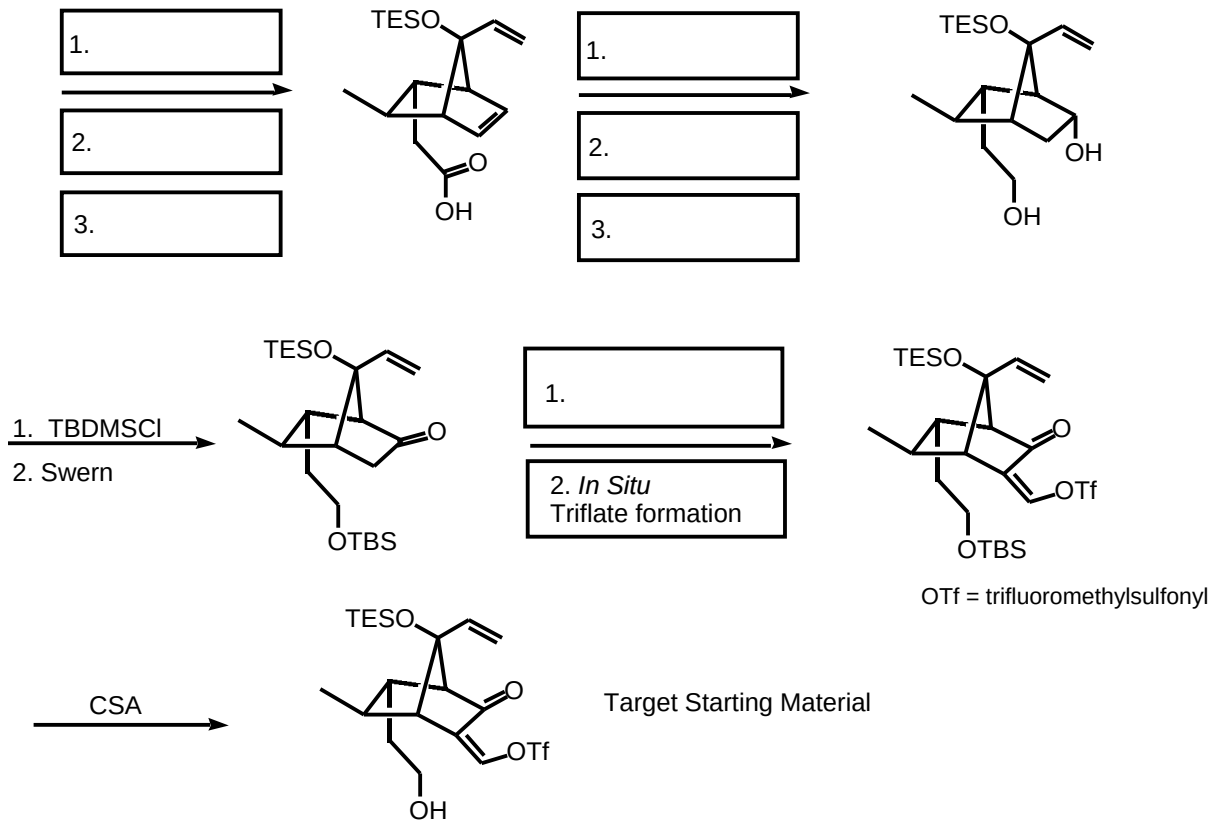
Recently the CP molecules, such as CP-263,114, have attracted a considerable amount of interest due to their structural complexity and their activity against protein farnesyl transferase. Professor Leighton presented a very interesting and exciting approach to the bicyclic core of the CP family. The following questions will address Professor Leighton's approach. *J. Am. Chem. Soc.* **1999**, *121*, 890-891

I. We will begin with a synthesis of the starting material in Professor Leighton's approach to the core of the CP molecules. In the synthetic scheme presented below provide the missing reagents or substrates. (25 Points)

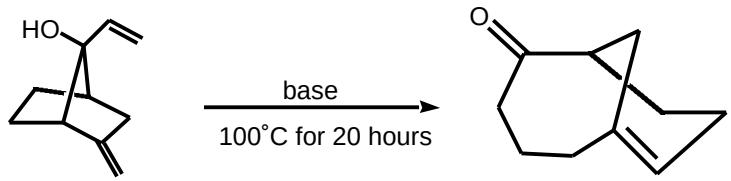




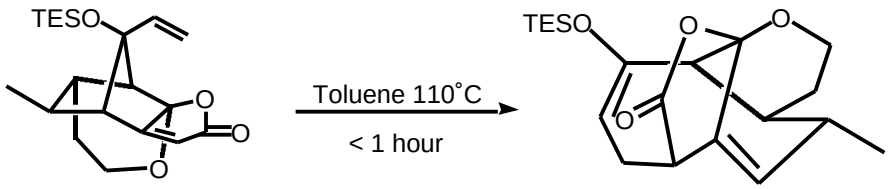
I Continued.


1.
2.
3.
TESO
O
OH
1.
2.
3.
TESO
OH
OH
1. TBDMSCl
2. Swern
TESO
O
OTBS
1.
2. In Situ
Triflate formation
TESO
O
OTf
OTBS
OTf = trifluoromethylsulfonyl
CSA
TESO
O
OTf
OH
Target Starting Material

II. Key to Professor Leighton's approach to the bicyclic core of CP-263,114 is a Cope rearrangement. Precedent for this key step is provided in the following example of an anionic oxy-Cope rearrangement in a similar molecule (Eq. 1). The rate acceleration due to the anion effect in an anionic oxy-Cope is reported to be on the order of $10^{10\text{-}17}$. Compare the two rearrangements given below and suggest an explanation for the rate acceleration observed in Professor Leighton's example (Eq. 2) which is a normal Cope rearrangement. (15 Points)

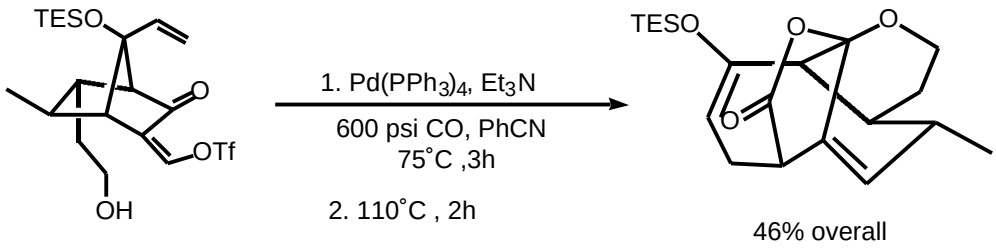


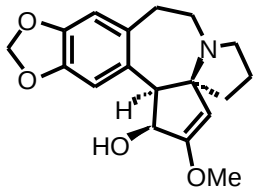
(1)



(2)

III. Professor Leighton demonstrated, in a one pot reaction, the material synthesized in question I could be converted to the cyclic core of CP-263,114. Provide a detailed step by step mechanism for the following transformation. Remember there are two separate events in this transformation and an intermediate is involved. You can isolate the intermediate but it is not necessary. (20 Points)

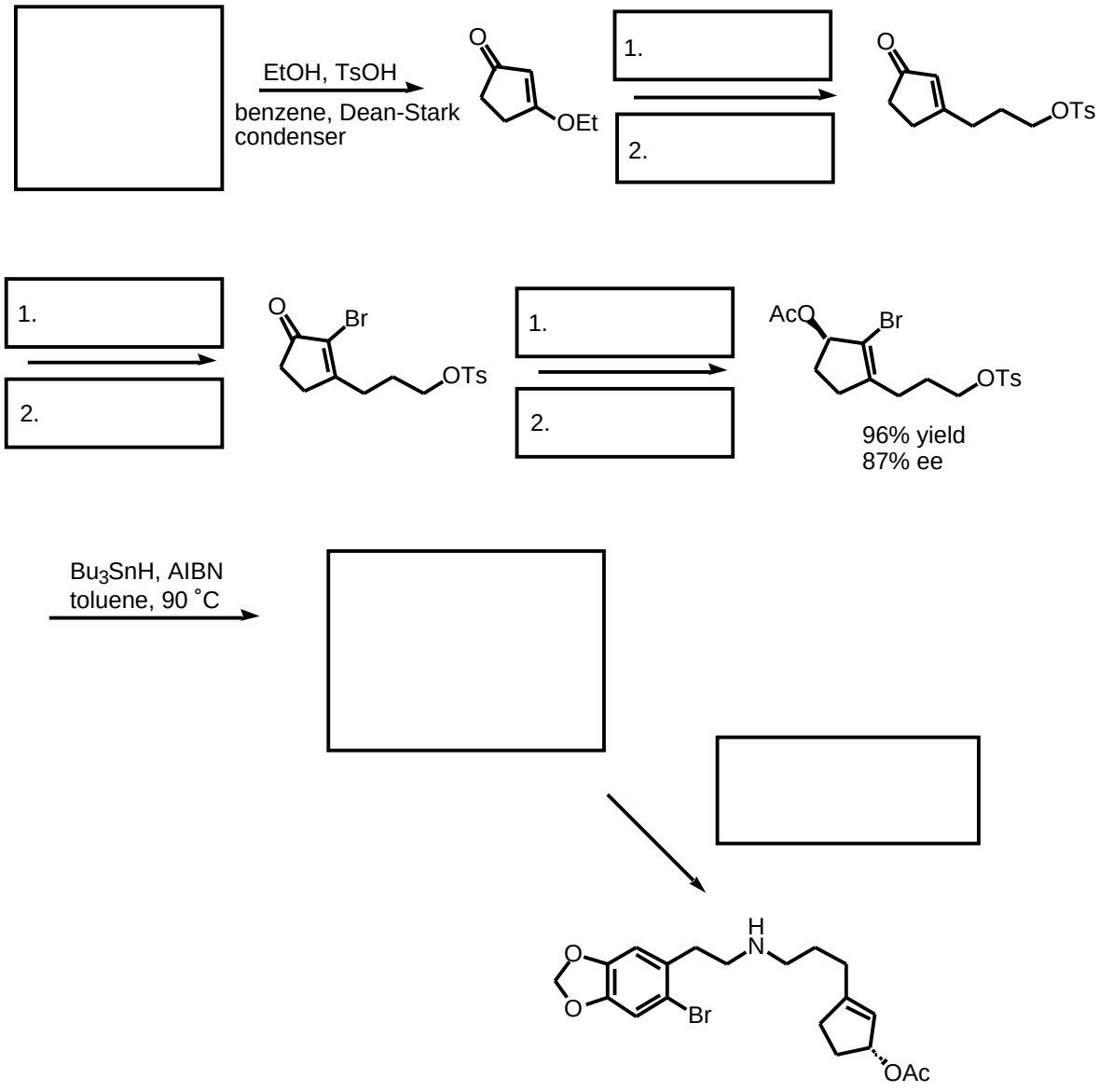




(-)-Cephalotaxine

Professor Tietze presented us with two lectures highlighting the use of domino palladium reactions in the synthesis of natural products. The domino concept was recently applied to the synthesis of (-)-Cephalotaxine the parent to a number of compounds with antileukemic activity *J. Am. Chem. Soc.* **1999**, *121*, 10264-10269.

IV. In the synthetic scheme presented below provide the missing reagents or substrates. (30 Points)



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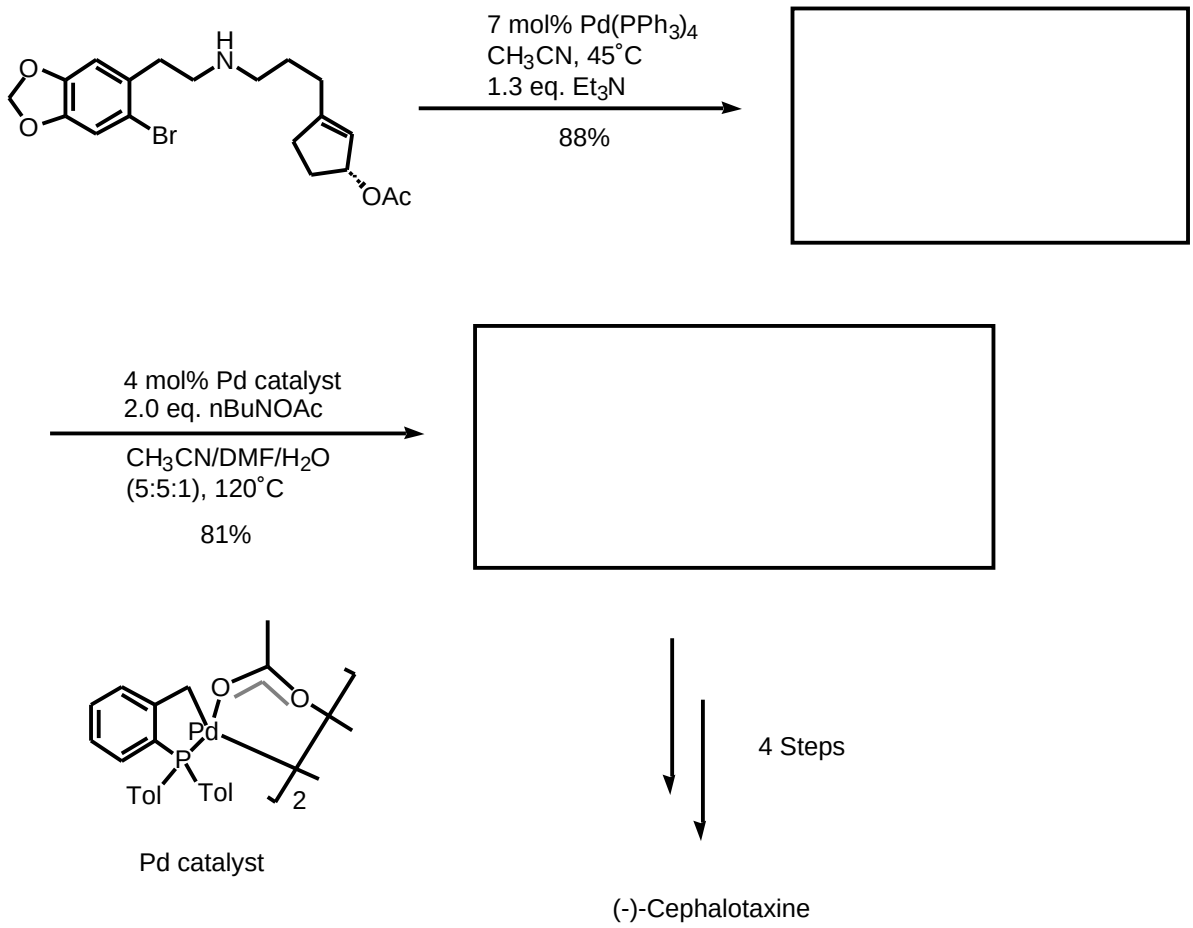

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