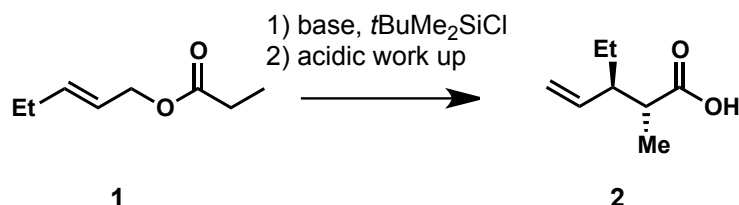


Reactivity in Organic Chemistry

Exam 19-04-2012

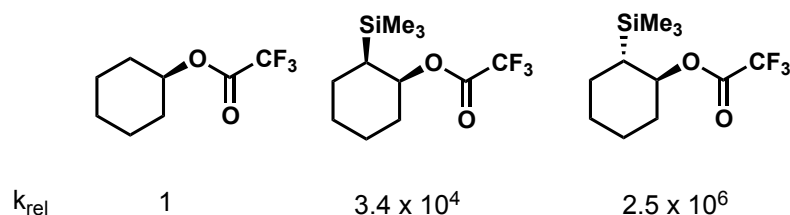
Problem 1

Which enolate has to be generated from ester **1** to provide acid **2**? Which base would you use for this transformation? Explain your answer.



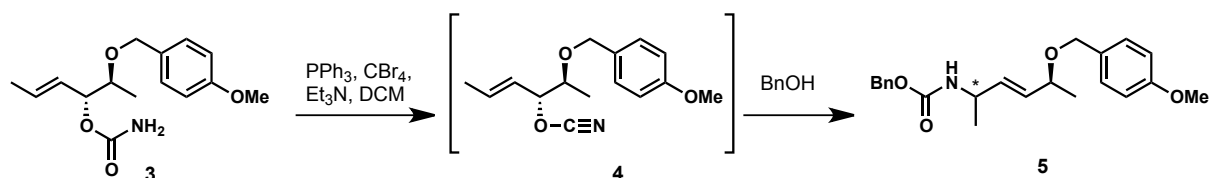
Problem 2

The solvolysis of the trifluoroacetates in trifluoroethanol depicted below proceeds with the relative rate constants given. Explain the trend observed for the rate constants.



Problem 3

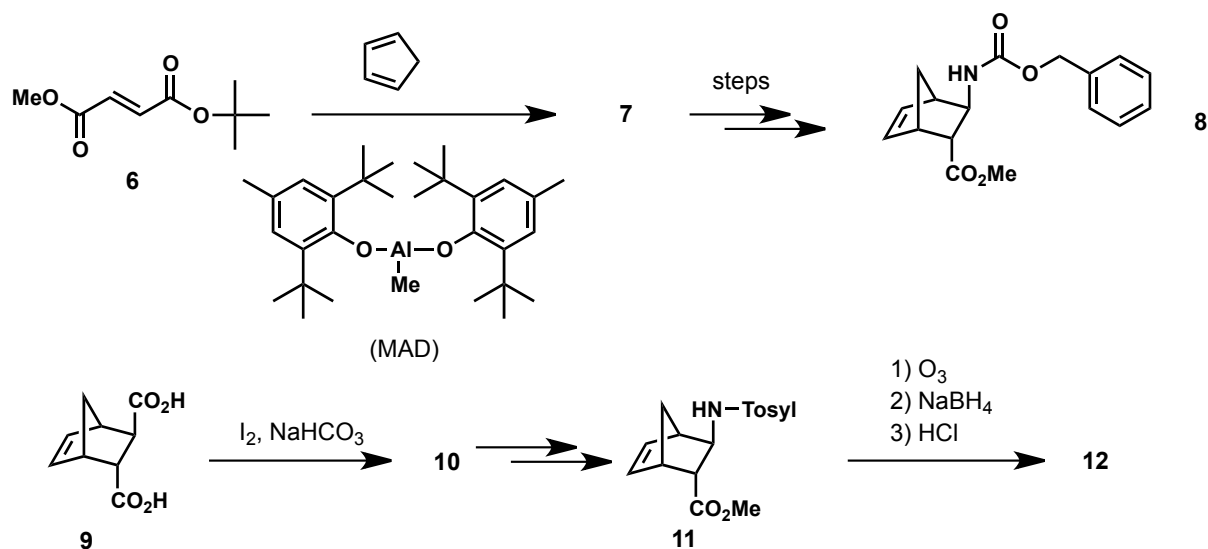
Compound **3**, is dehydrated under so called Appel conditions to provide allyl cyanate **4**. This compound reacts with benzyl alcohol to give compound **5**. Provide a mechanism for the transformation of **4** into **5**. Predict the stereochemistry of the newly formed stereocenter in **5**.



Problem 4

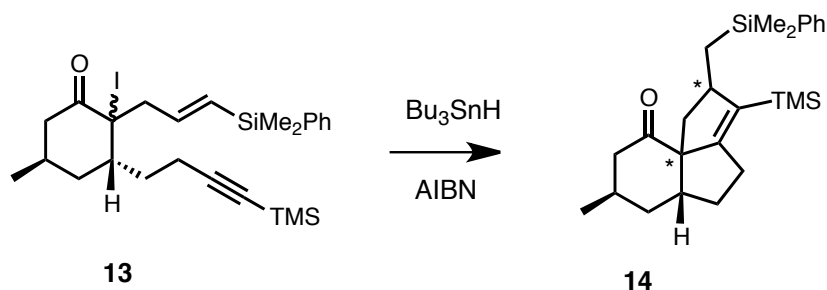
As part of a program directed at the synthesis of serotonin antagonists the chemical transformations depicted below were reported.

- Provide the mechanism of the Lewis acid catalyzed diastereoselective reaction of starting compound **6** with furan to give compound **7**. Provide the structure of **7**. (Hint: the bulky Lewis acid, MAD, selectively coordinates at one carboxylic acid ester functionality only)
- How would you transform **7** into compound **8**?
- Provide the structure of compound **10** and the mechanism of its formation from **9**.
- Provide the structure of bicycle **12** (the Tosyl group does not count as a cycle!)



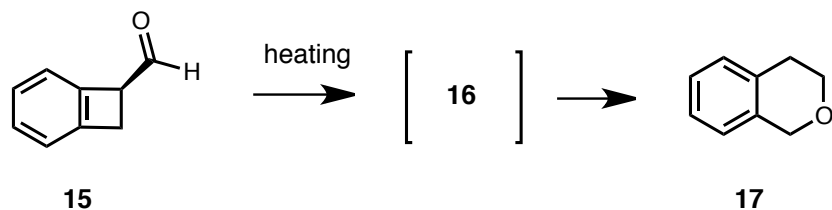
Problem 5

Provide a detailed mechanism of the transformation of alkenyne **13** into tricyclic structure **14**. Predict the stereochemistry of the newly formed stereo-centers in **14**.



Problem 6

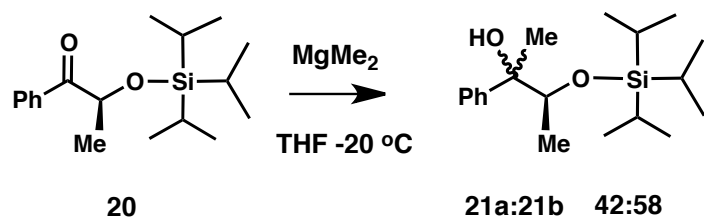
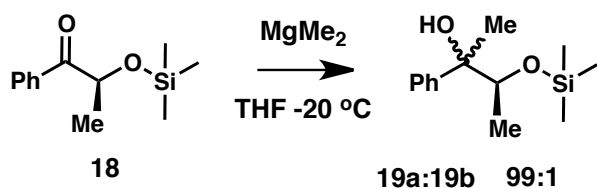
Benzocyclobutene **15** was converted into bicyclic compound **17** by heating. Intermediate **16** was not isolated. Give the structure and the stereochemistry of **16** and explain how it is formed. Give the mechanism for the transformation of **16** into **17**.



Problem 7

Chiral silyloxyketone **18** was treated with dimethylmagnesium to obtain tertiary alcohol **19** virtually as a single diastereoisomer. When silyloxyketone **20** was subjected to the same reaction condition the stereoselectivity severely degraded. Two diastereomeric products were obtained in a ratio 42:58.

- Predict the stereochemistry of **19a** (the major diastereomer) and justify your answer.
- Give an explanation for the loss of stereoselectivity in case of transformation of **20** into **21**.

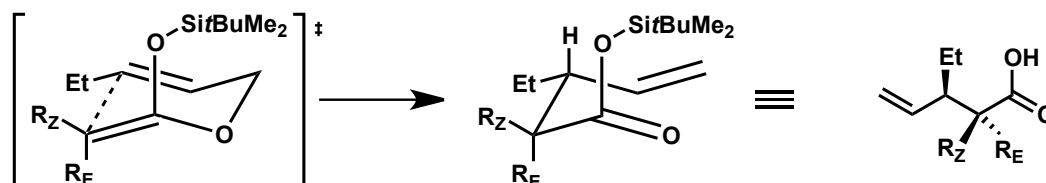


Reactivity in Organic Chemistry

Exam 19-04-2012

Problem 1

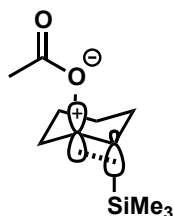
The following transition state leads to the products:



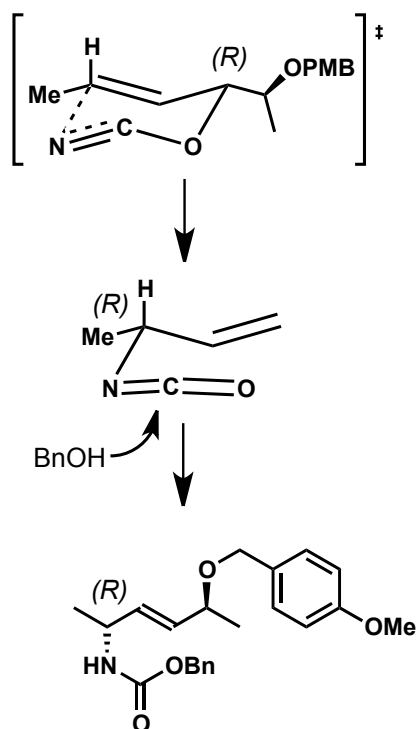
Generation of the *E*-enolate gives the *trans* product, where the *Z*-enolate generates the *syn* product. LDA can be used as a base.

Problem 2 (JACS 1985, 107, 1496-1500)

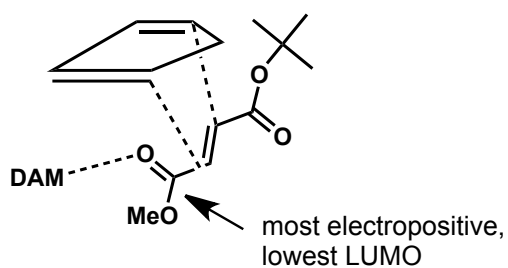
The order of relative rate constants can be explained by the fact that the solvolysis of the compounds occurs through an $\text{S}_{\text{N}}1$ mechanism. And formation of a carbocationic product will be the rate determining step. β -silicon groups can stabilize a β -positive charge through efficient hyperconjugation. Therefore the two cyclohexanes bearing silyl groups will react faster. The product with the silyl group *trans* with respect to the leaving group will react fastest because it can directly stabilize the developing positive charge (in an empty p -orbital) because it is perfectly perpendicularly aligned with the leaving group:



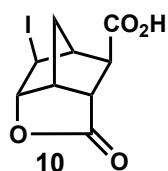
Problem 3 (Org Lett 2006, 8, 5737-5740)



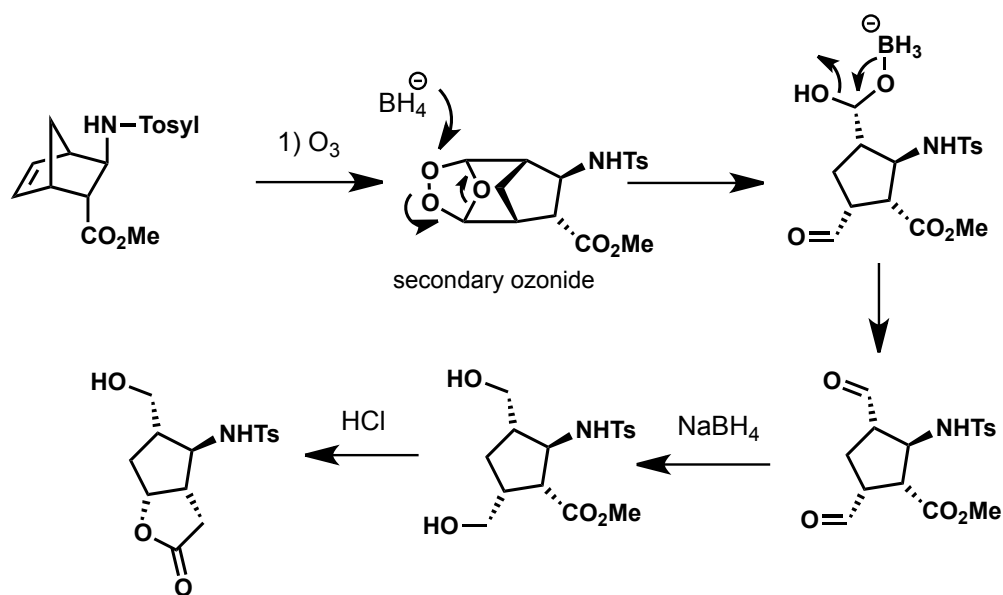
Problem 4 (JACS1992, 114, 1089-1090; Tetrahedron 1999, 55, 11787-11802)



- A)
 B) TFA in DCM to remove the *t*Butyl ester, then DPPA (diphenylphosphoryl azide) to form the acyl azide, heating in the presence of benzylalcohol leads, *via* a Curtius rearrangement, to product **8**
 C) A iodolactonisation provides the following compound:

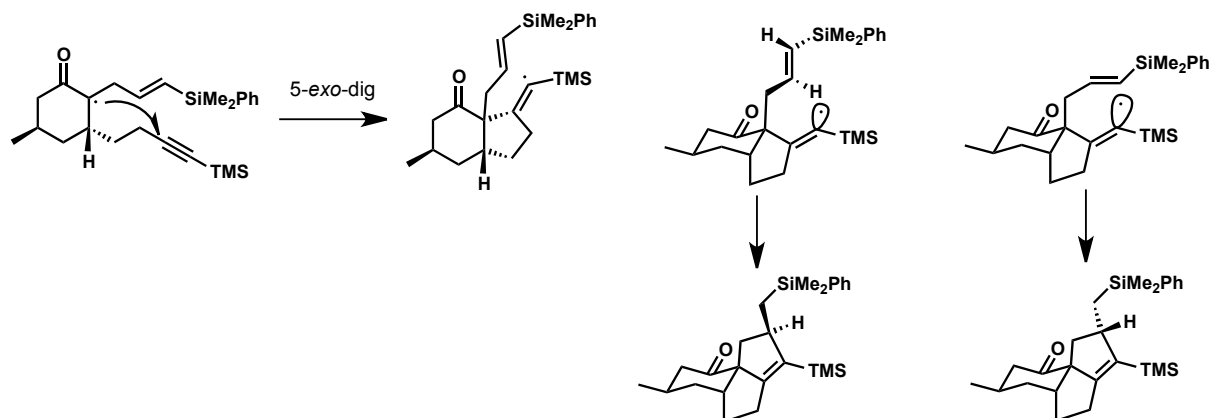


- D)



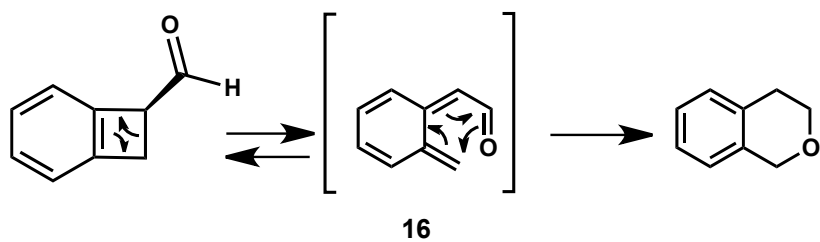
Problem 5

Provide a detailed mechanism of the transformation of alkenyne **13** into tricyclic structure **14**. Predict the stereochemistry of the newly formed stereo-centers in **14**.



Problem 6

Benzocyclobutene **15** was converted into bicyclic compound **17** by heating. Intermediate **16** was not isolated. Give the structure and the stereochemistry of **16** and explain how it is formed. Give the mechanism for the transformation of **16** into **17**.



Problem 7

