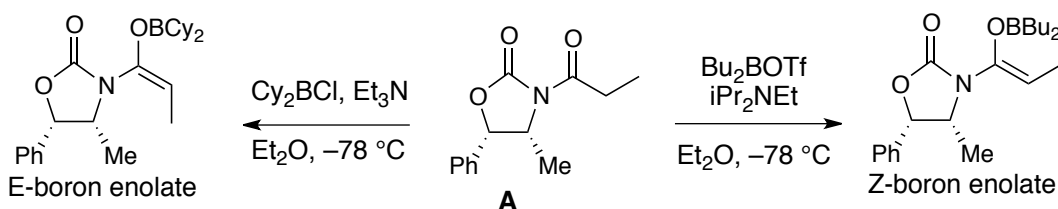


CEM 852 Exam-2

March 20, 2021

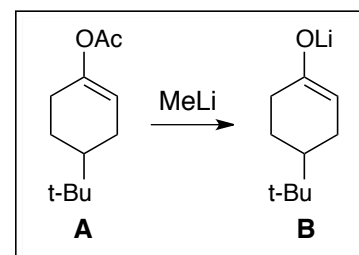
This exam consists of 5 pages. Please make certain that your exam has all of the necessary pages. Total points possible for this exam are 100. In answering your questions, please write legibly and draw all structures clearly. Write all your answers in the exam booklets. Good luck.

- I. Illustrate the following: (a) a Kumada coupling, (b) a Zimmerman-Traxler transition structure, (c) a Type III crotylation, and (d) a carbonyl reduction by a Grignard reagent. (12 pts)
- II. What advantage do the Shi or Jacobsen epoxidations have over the Sharpless epoxidation? (I'm not asking you to illustrate any of these epoxidations.) (3 pts) **allylic alcohol not required**
- III. Provide conditions to convert Evans' oxazolidinone **A** into its *E*- and *Z*-boron enolates. Be sure to draw the *E*- and *Z*-boron enolates. (6 pts)

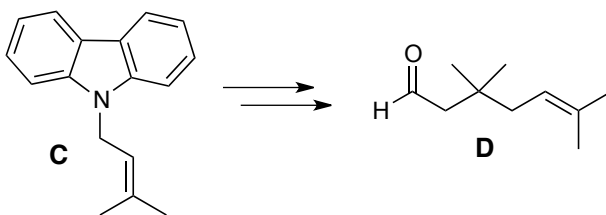


- IV. The enolate of 4-*t*-butylcyclohexanone (**B**) can be generated by the reaction of enol ester **A** with MeLi .

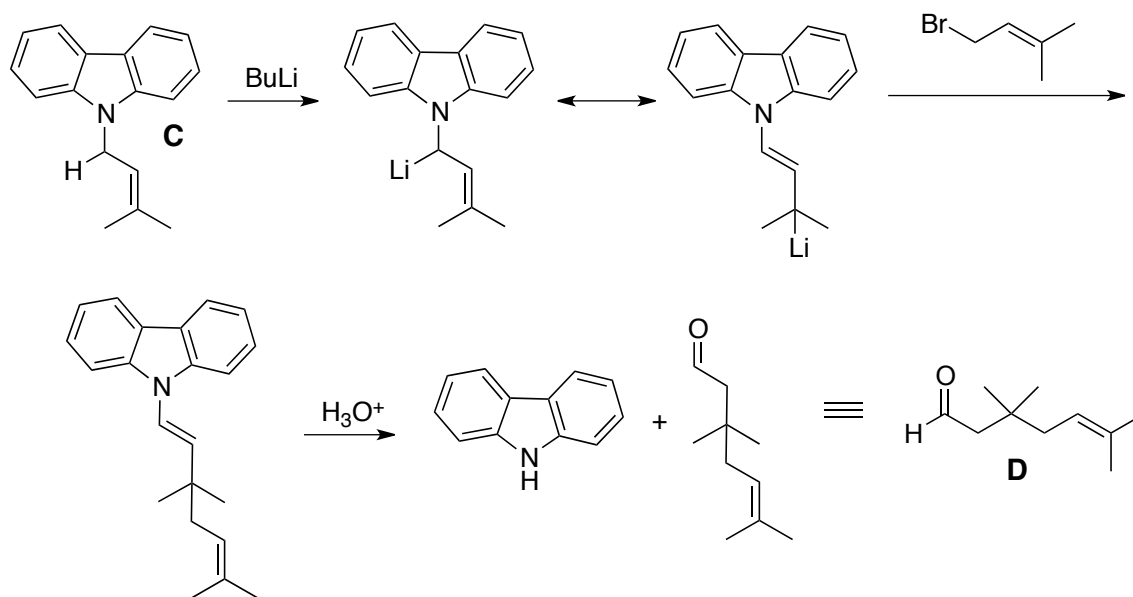
- (a) Provide a detailed arrow pushing mechanism for the reaction of **A** to **B** (2 pts)
- (b) Provide conditions that would best achieve C-alkylation of **B** (2 pts) **MeI**
- (c) Provide conditions that would best achieve O-alkylation of **B** (2 pts) **MeOTf, HMPA**



- V. Compound **C** can be viewed as a homo-enolate equivalent. Provide conditions/steps and a detailed arrow pushing mechanism that would transform **C** into **D**. (8 pts)

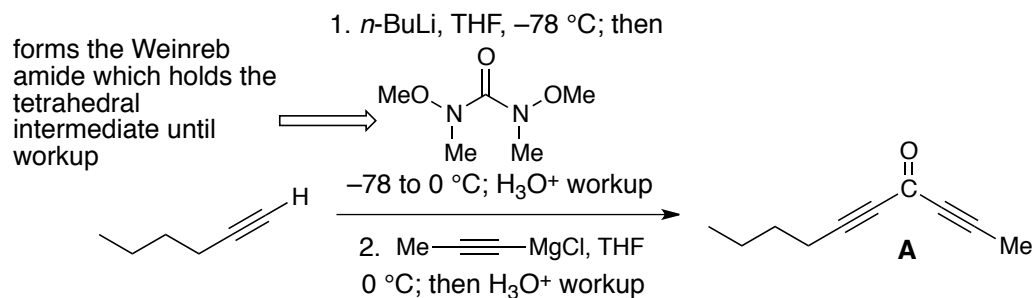


V. Compound **C** can be viewed as a homo-enolate equivalent. Provide conditions/steps *and* a detailed arrow pushing mechanism that would transform **C** into **D**. (8 pts)

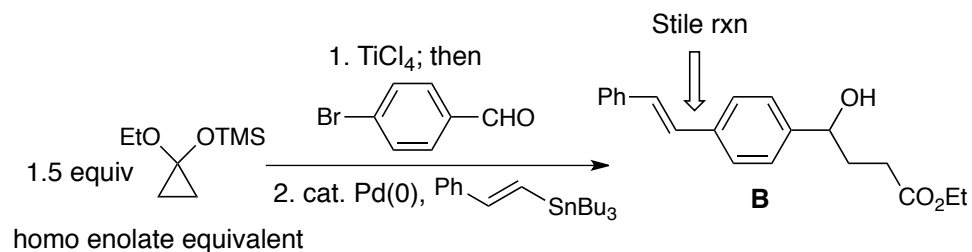


VI. Provide the product or products of the reactions outlined below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, be sure to indicate the major and minor species. (15 pts)

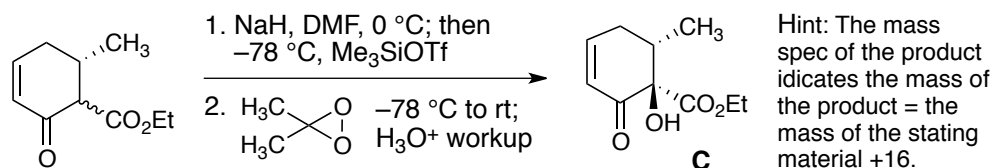
1.



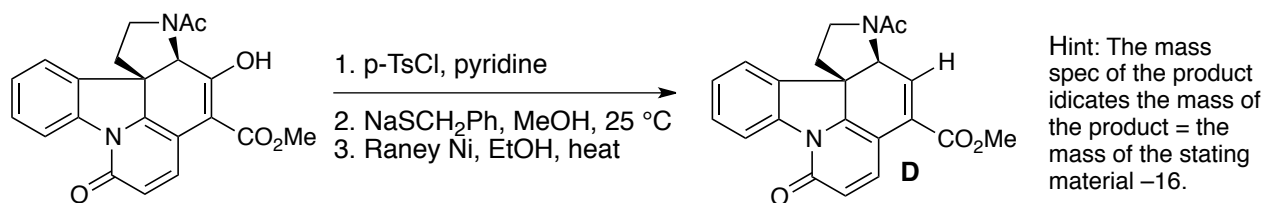
2.



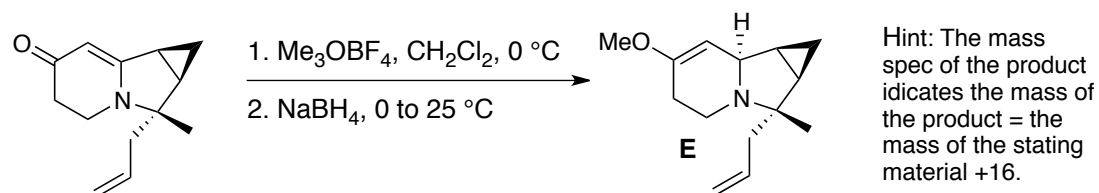
3.



4.

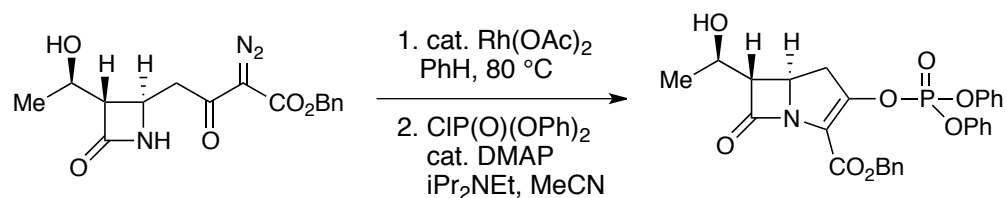


5.

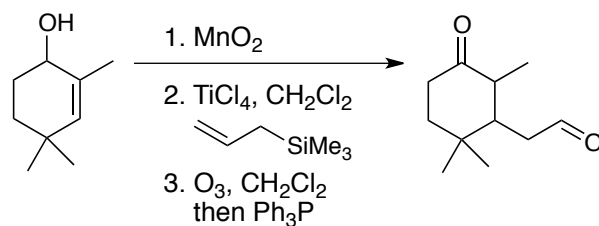


VII. Provide conditions that will afford the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (15 pts)

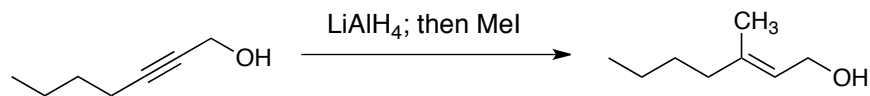
1.



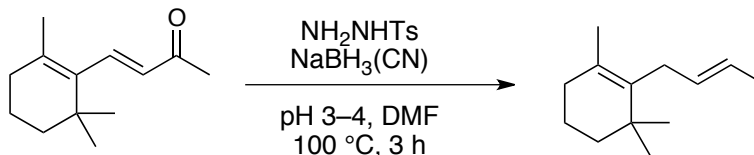
2.



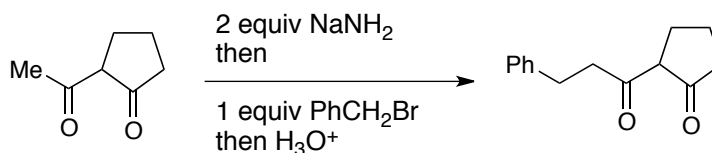
3.



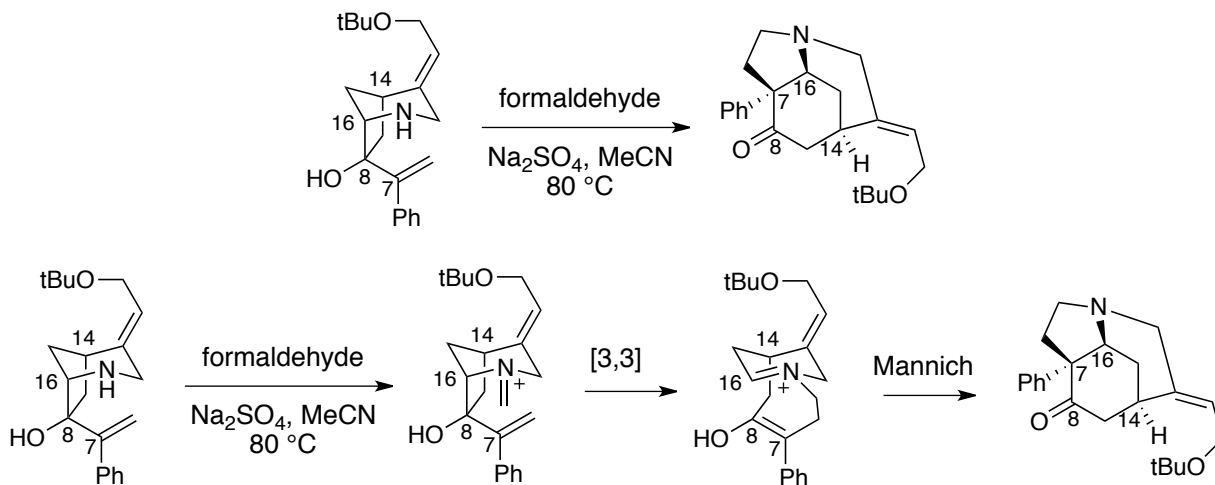
4.



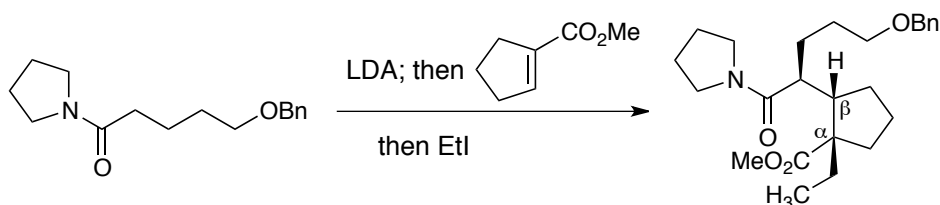
5.



VIII. Provide a detailed arrow pushing mechanism for the reaction shown below. Hint: The transformation involves as [3,3]-sigmatropic rearrangement and a Mannich reaction. (8 pts)

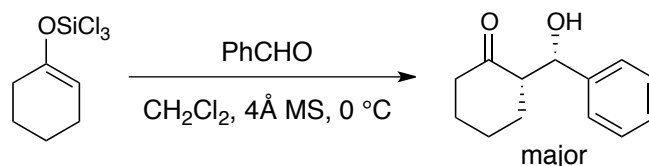


IX. Provide a detailed arrow pushing mechanism for the sequence shown below, being sure to explain the observed stereochemistry at the α & β carbons of the product. (8 pts)

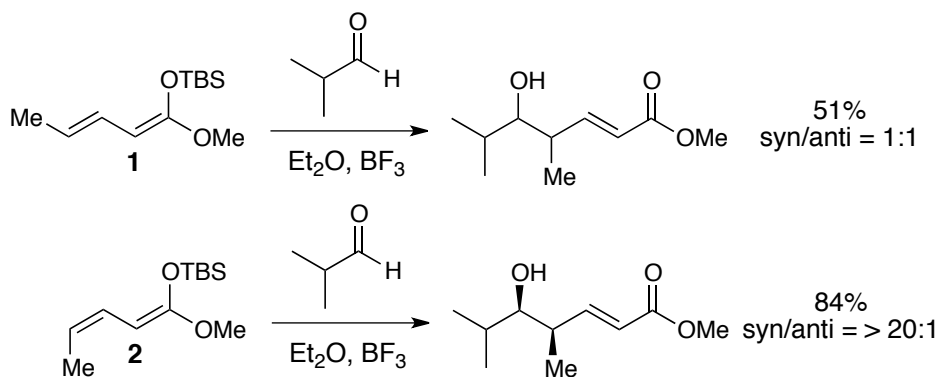


See Morgan's Classics presentation

- X. Reactions with trichlorsilylenol ethers such as that illustrated below have been shown to proceed through a closed transition structure and to very efficient and stereoselective.



- (a) Based on the description above, why is the observed stereoselectivity unusual. **E-enolates in a usual chair-like Zimmerman-Traxler transition structure should give the anti-product** (2 pt)
- (b) Provide an explanation for the observed stereoselectivity that is consistent with the description above. (2 pts) **Boat-like Zimmerman-Traxler transition structure**
- (c) This is the work of the Denmark group. What did they add to the reaction conditions to reverse the stereochemical outcome? **Added a Lewis base that promotes a chair-like Zimmerman-Traxler transition structure** (2 pts)
- XI. Ketene acetals 3,4-*Z* (**1**) and the 3,4-*E* (**2**) can be made to undergo vinyllogous Mukaiyama aldol reactions with isobutyraldehyde. Interestingly, the *E*-configured ketene acetal (**2**) gave a *low yield and poor syn/anti-selectivity*. In contrast, *Z*-ketene acetal **1** gave *high yields and was > 20:1 syn selective*. Provide an argument for the observations. (Hint: Both **1** and **2** react with isobutyraldehyde via open transition structures, however in these reactions steric interactions between the Lewis acid and the substituents on **1** and **2** are less disruptive than steric interactions between the isopropyl group on the aldehyde and the substituents on **1** and **2**). (10 pts)



- XI. Ketene acetals 3,4-*Z* (**1**) and the 3,4-*E* (**2**) can be made to undergo vinylogous Mukaiyama aldol reactions with isobutyraldehyde. Interestingly, the *E*-configured ketene acetal (**2**) gave a *low yield and poor syn/anti-selectivity*. In contrast, *Z*-ketene acetal **1** gave *high yields and was > 20:1 syn selective*. Provide an argument for the observations. (Hint: Both **1** and **2** react with isobutyraldehyde via open transition structures, however in these reactions steric interactions between the Lewis acid and the substituents on **1** and **2** are less disruptive than steric interactions between the isopropyl group on the aldehyde and the substituents on **1** and **2**). (10 pts)

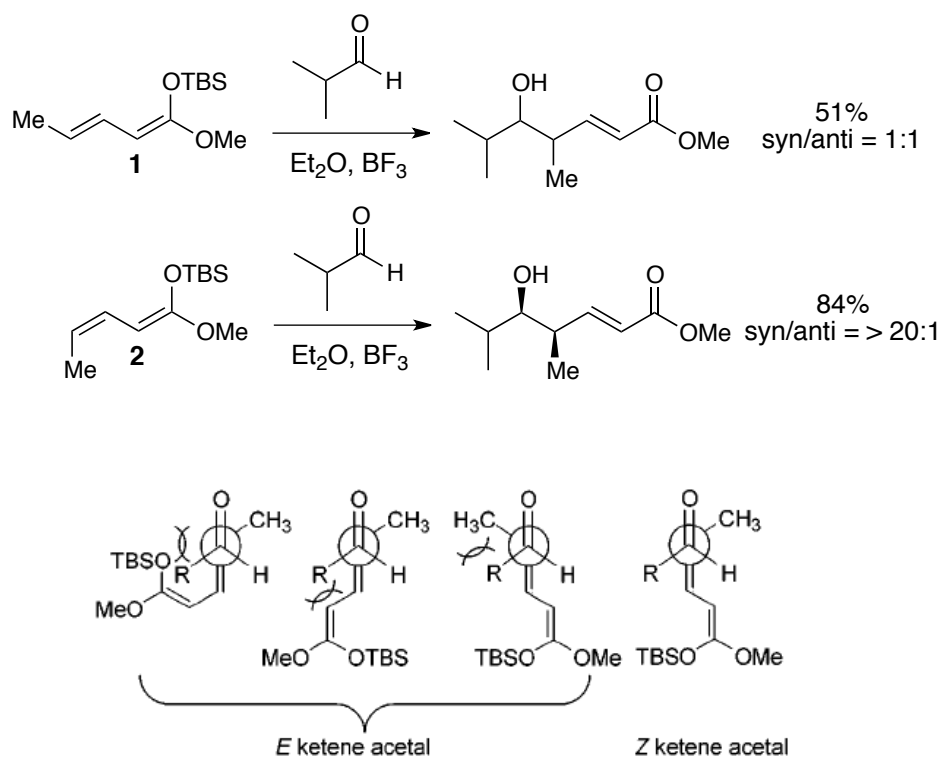
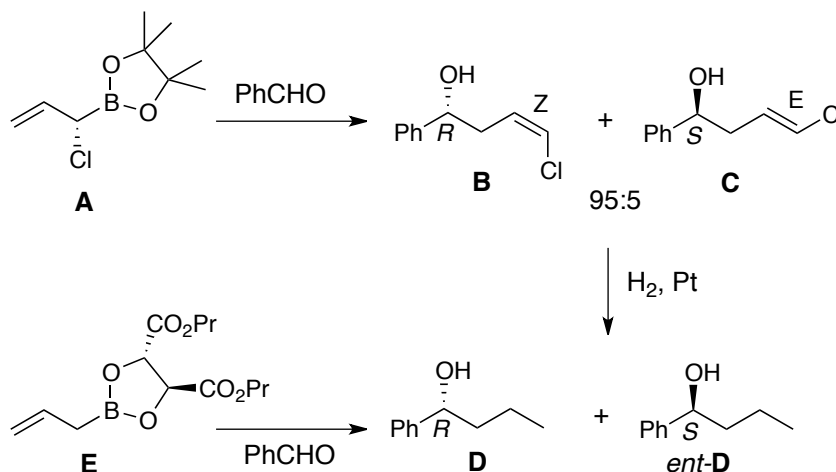


Figure 1. Proposed transition states for the nucleophilic attack of both ketene acetals.

See: Hassfeld, J.; Christmann, M.; Kalesse, M. *Org. Lett.* 2001, 3, 3561–3564.

XII. The reaction shown below of optically active **A** with benzaldehyde affords (*R*)-**B** and (*S*)-**C** in a ratio of 95:5.

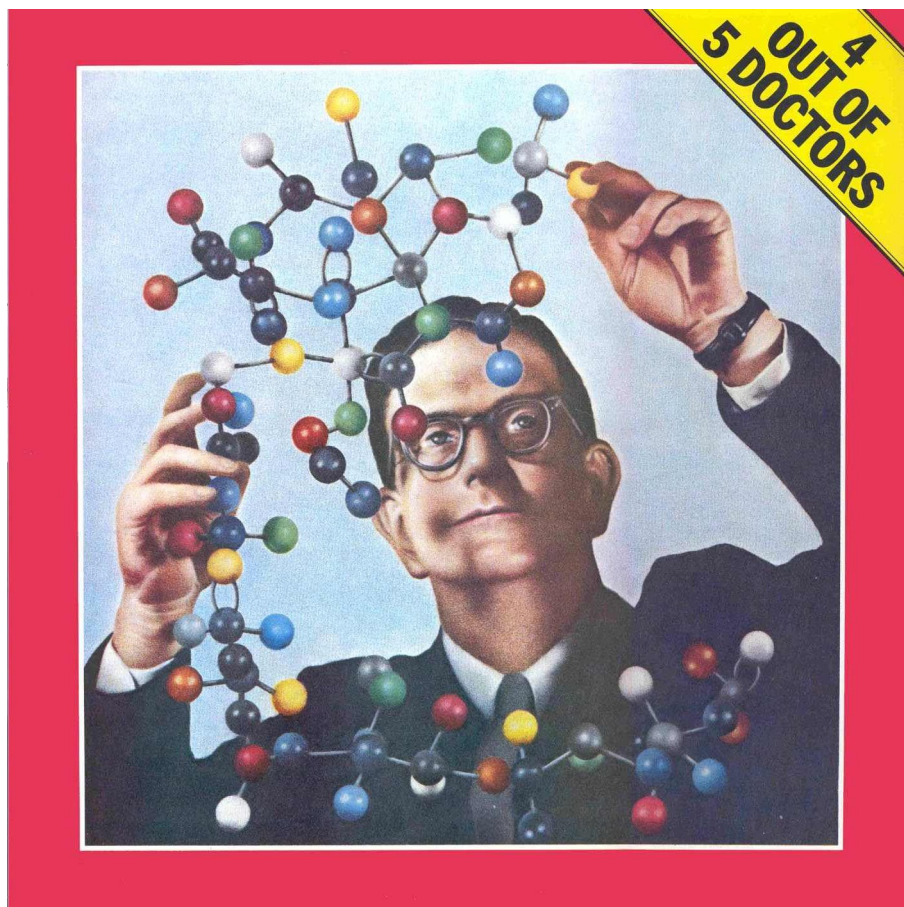


Hydrogenation of **B** affords **D**, while hydrogenation of **C** affords its enantiomer. Allylation of benzaldehyde with optically active **E** directly affords **D** and *ent*-**D** with **D** being the major enantiomer formed. *Both allylations proceed with the same level of enantioselectivity*, yet the two-step process (starting with **A**) can afford **D** in greater enantiomeric excess than the one-step process (starting with **E**). Explain (3 pts). (Hint: Don't overthink this question as it is only worth 3 pts!) **B** and **C** are not enantiomers. They are different geometric isomers and different geometric isomers are separable by any number of methods. Thus hydrogenation can be done on only **C**. **D** and *ent*-**D** will not be easily separable. See Hoffmann, R. W.; Landmann, B. *Angew. Chem. Int. Ed. Engl.* 1984, 23, 437–438.

Bonus Question: Yesterday evening the Women in Chemistry hosted virtual musical bingo. Understandably (and rightly) you probably missed the event owing to today's exam. To give you a little taste of what you missed, what Nobel prize winning organic chemist was featured on the cover of an album by the band "4 out of 5 doctors"? (2 pts)

- E.J. Corey
- Ei-ichi Negishi
- K. Barry Sharpless
- Bob Woodward
- Alexander Borodin

Bonus Question: Yesterday evening the Women in Chemistry hosted virtual musical bingo. Understandably (and rightly) you probably missed the event owing to today's exam. To give you a little taste of what you missed, what Nobel prize winning organic chemist was featured on the cover of an album by the band "4 out of 5 doctors"? (2 pts)



Bob Woodward