

CEM 852 Exam-1

February 21, 2022

Please put away all notes and phones. *Use of cell phones for any reason is prohibited.* This exam consists of 5 pages. Make certain that your exam has all five 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 with actual chemical examples (15 pts)

1. The difference between a stereoselective and a stereospecific reaction.
2. The difference between a synthon and a synthetic equivalent to a synthon.
3. The difference between an A(1,3) interaction and an A(1,2) interaction.
4. The difference between the Felkin-Ahn model and the chelation controlled Felkin-Ahn model.
5. The difference between a disrotatory 8π -electron cyclization & a conrotatory 8π -electron cyclization.

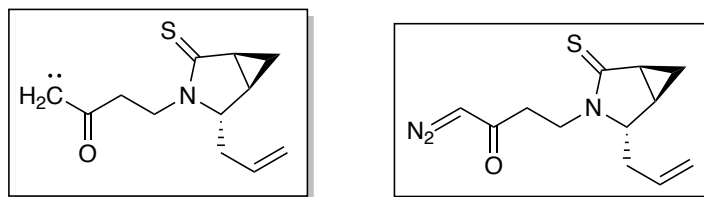
ELECTROCYCLIC REACTIONS

Reaction	Electrons	Thermal	Photochemical	Examples
	4 $4n$	conrotation	disrotation	005, 006, 025
	6 $4n+2$	disrotation	conrotation	004, 016, 026
	8 $4n$	conrotation	disrotation	017
	4 $4n$	conrotation	disrotation	
	6 $4n+2$	disrotation	conrotation	
	2 $4n+2$	disrotation	conrotation	033
	4 $4n$	conrotation	disrotation	

II. In Wittig olefinations, unstabilized ylides typically afford the E or Z alkene? (2 pts)

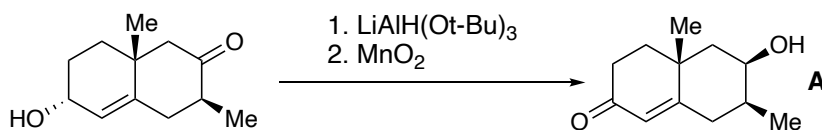
III. Sharpless' asymmetric dihydroxylation "Super" AD-mix β consists of the following reagents: $K_3Fe(CN)_6$, K_2CO_3 , (DHQD) $_2$ PHAL, and $K_2OsO_2(OH)_4$. Which of these are (a) the source of asymmetry (DHQD) $_2$ PHAL and (b) the stoichiometric oxidant $K_3Fe(CN)_6$ (2 pts).

IV. What starting material would you react with $\text{Rh}(\text{OAc})_2$ to generate the carbene shown below? (2 pts)

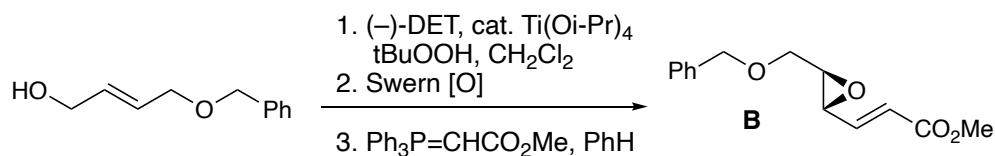


V. Provide the product or products of the reactions below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, indicate the major and minor species. (27 pts)

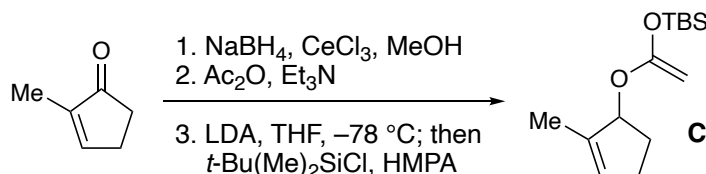
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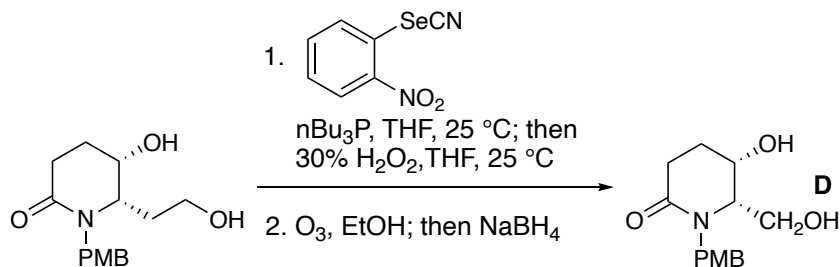
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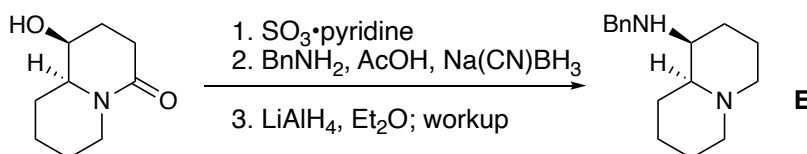
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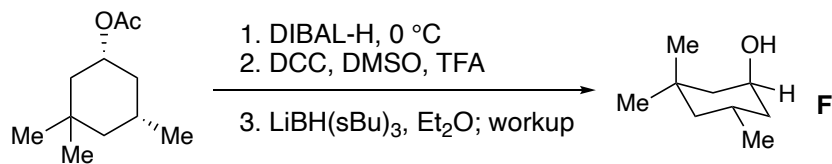
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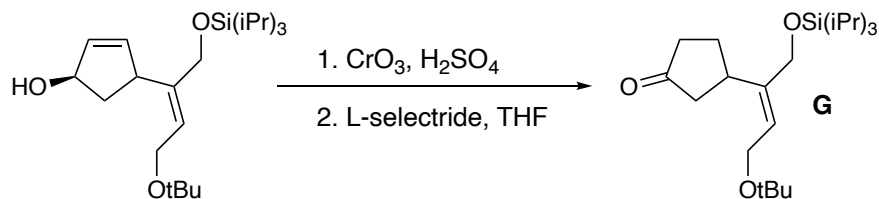
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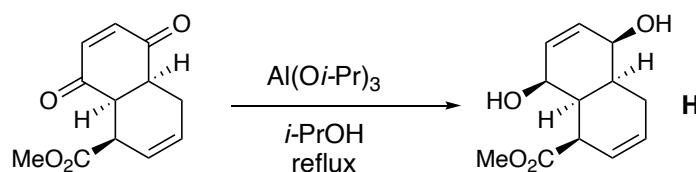
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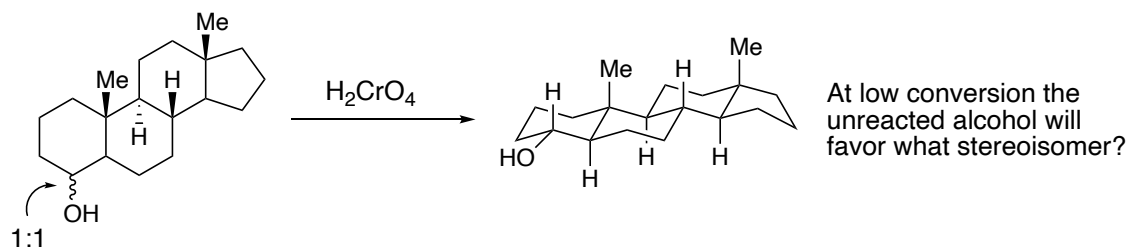
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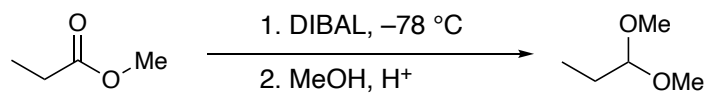


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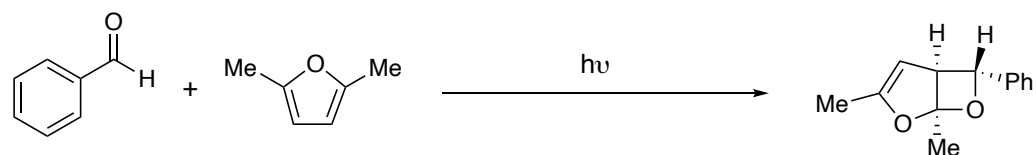


VI. Provide conditions that will affect the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (15 pts)

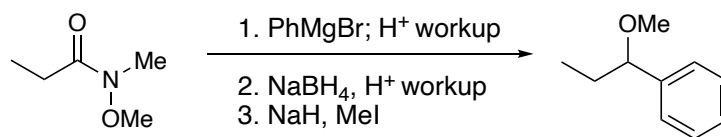
1.



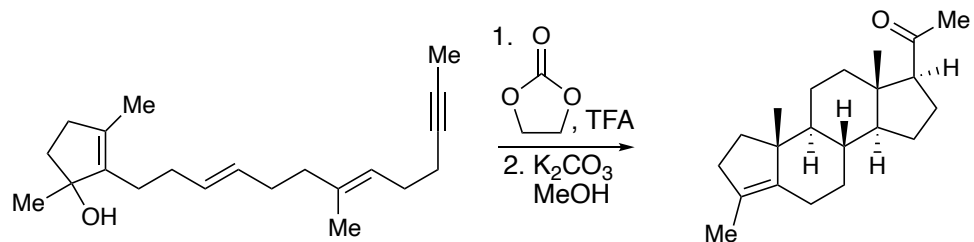
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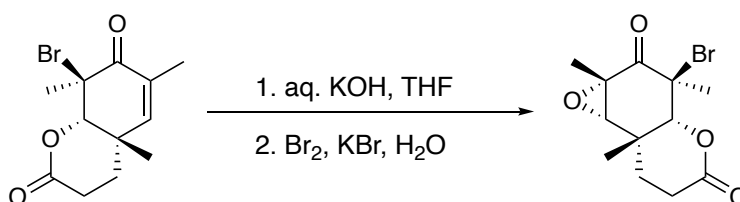
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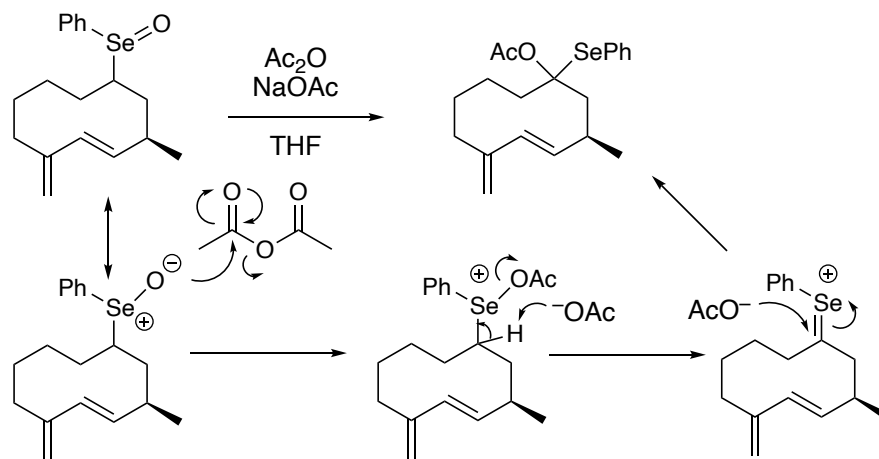
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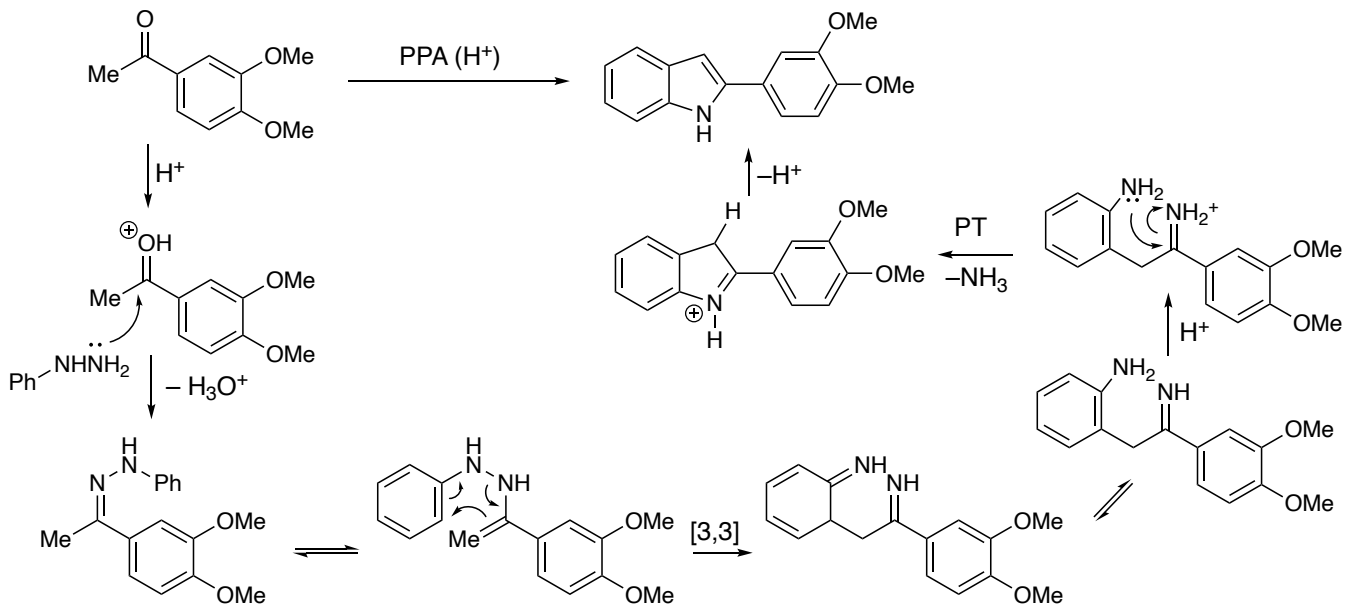
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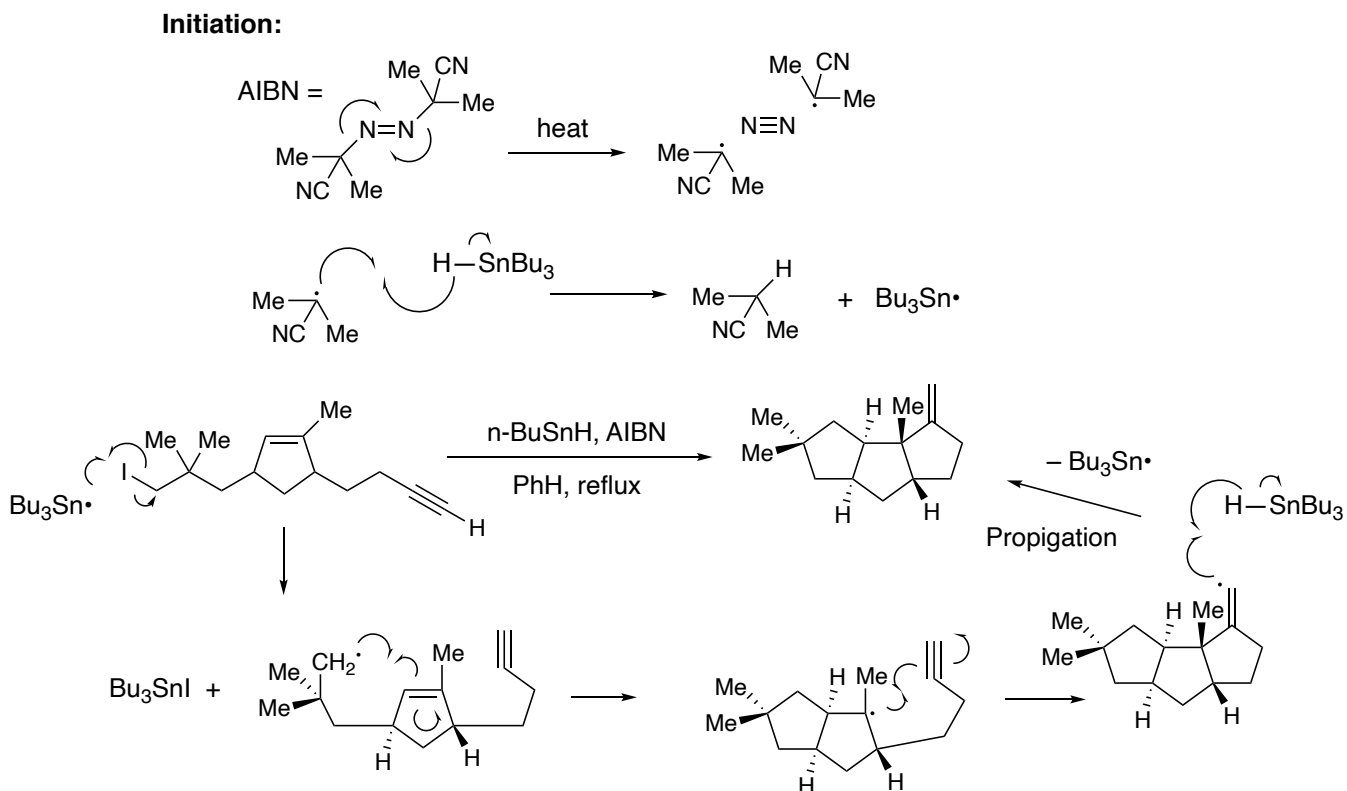
VII. Provide a detailed arrow (electron) pushing mechanism for the seleno-Pummerer reaction below. (5 pts)



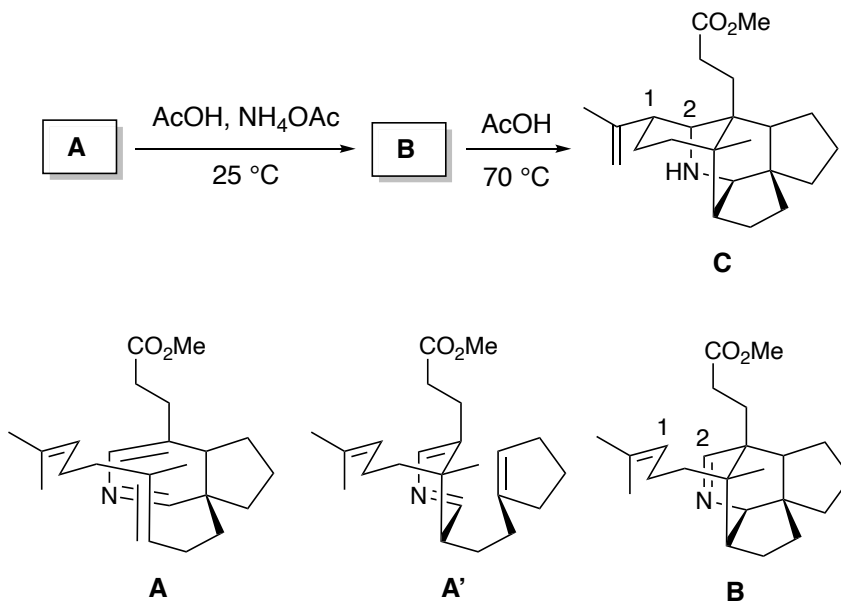
VIII. Provide a detailed arrow (electron) pushing mechanism for Fisher Indole reaction below. (5 pts)



IX. (a) Provide a detailed arrow (electron) pushing mechanism for the radical reaction shown below, being sure to include the initiation and propagation steps. (5 pts)



- X. Treatment of **A** with acetic acid at rt triggers a [4+2] cycloaddition between a hetero diene and a trisubstituted dienophile to form an iminium containing six membered ring **B**. Heating **B** in acetic acid then triggers an aza-prins reaction that forms the C–C bond between carbons 1 and 2 indicated in structure **C**. Provide structures for **A** and **B**. (8 pts)



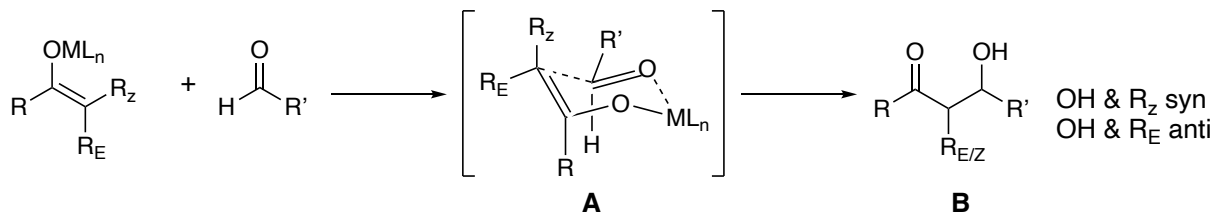
- XI. Provide conditions to safely work up a LiAlH_4 reduction. (4 pts)

- To work up a reaction containing x g lithium aluminum hydride
 1. Dilute with ether and cool to 0°C
 2. Slowly add x mL water
 3. Add x mL 15 % aqueous sodium hydroxide
 4. Add 3x mL water
 5. Warm to RT and stir 15 min
 6. Add some anhydrous magnesium sulfate
 7. Stir 15 min and filter to remove salts

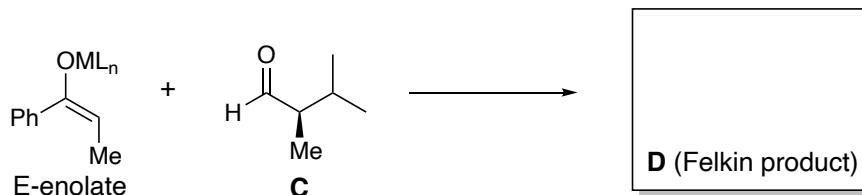
Fieser, L. F.; Fieser, M. Reagents for Organic Synthesis 1967, 581–595.

For an excellent review of LAH chemistry see:
<https://onlinelibrary.wiley.com/doi/10.1002/047084289X.rl036.pub2>

XII. Aldol reactions of metal enolates often proceed via a Zimmerman-Traxler closed transition structure (**A**), where the geometry of the metal enolate dictates the *relative* stereochemistry of the product (**B**), i.e. the *E*-metal enolate favors the anti-product and the *Z*-metal enolate favors the syn product.

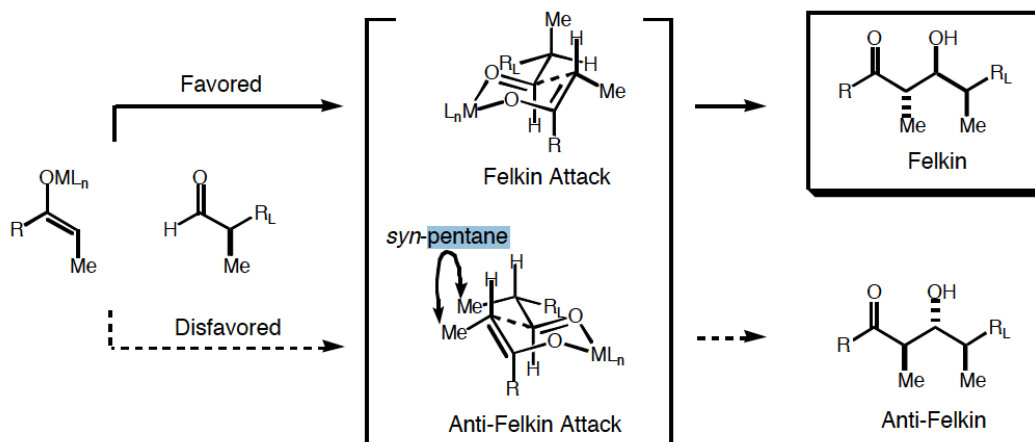


If the aldehyde partner in the aldol has a set stereochemistry at the α -carbon, one would think that the *absolute* chemistry could be predicted by an application of the Felkin-Ahn model. Indeed, this is true for the reaction of aldehyde **C** and the *E*-metal enolate, which favors Felkin product **D**. Provide the structure of **D**. (5 pts)



Chiral Aldehyde Aldol Reactions— α -Chiral Aldehydes

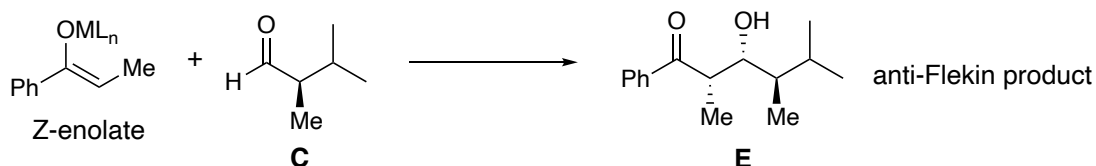
■ (*E*) Enolates Give the Felkin Product



Evans *Topics in Stereochemistry*, **1982**, *13*, 1-115
Roush *J. Org. Chem.* **1991**, *56*, 4151

Image taken from https://macmillan.princeton.edu/wp-content/uploads/Northrup_aldol.pdf

In contrast, reaction of the Z-metal enolate with **C** favors the anti-Felkin product **E**. This result has been rationalized by an unfavorable syn-pentane interaction in the combined Zimmerman-Traxler Felkin transition structure. Illustrate that transition structure, highlighting that unfavorable syn-pentane interaction. (5 pts)



■ Stereochemical Model:

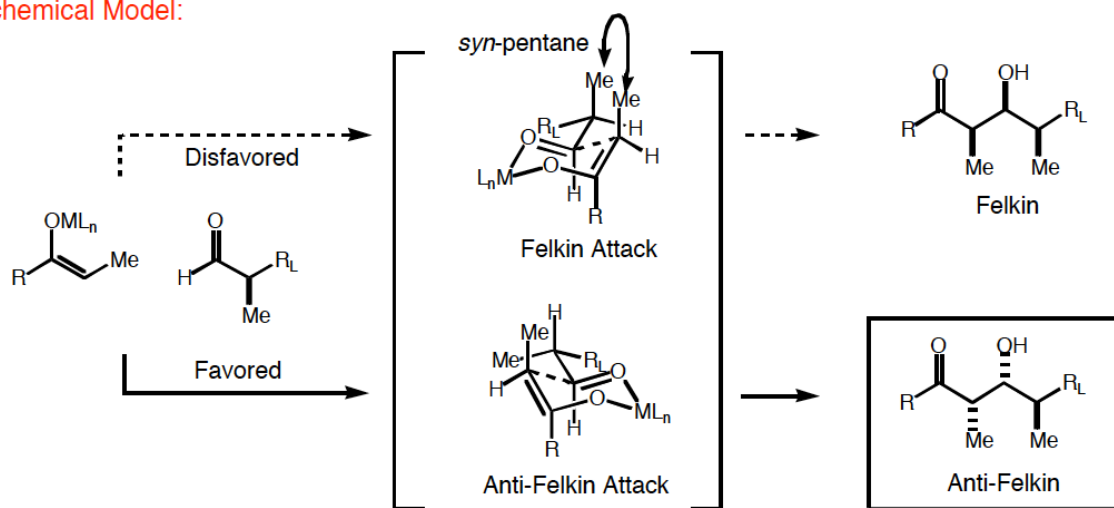


Image taken from https://macmillan.princeton.edu/wp-content/uploads/Northrup_aldol.pdf

Bonus Question: Yesterday the 2022 Beijing Winter Olympics came to a close. Among the most talked about Olympians was Russian figure skater Kamila Valieva, who had tested positive for the banned compound trimetazidine. What's the structure of trimetazidine (**A**)? (2 pts)

