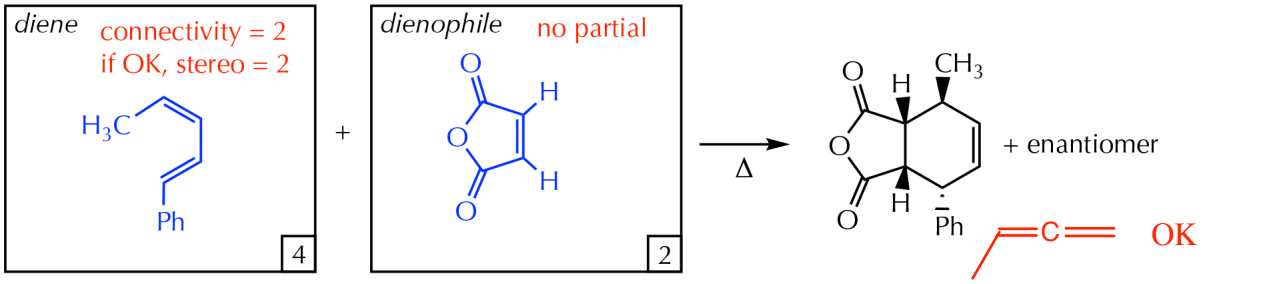
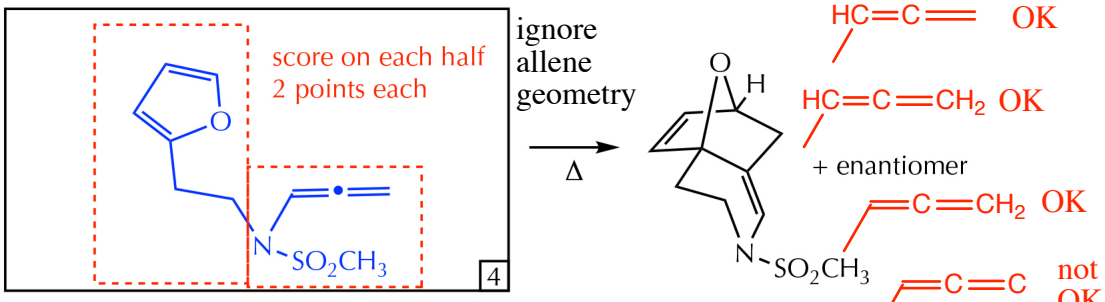
Question I (28 points) Name: _____

A. Complete the following Diels-Alder cycloaddition reactions. Assume the reactions showing any diastereoselectivity are derived from a preference for the *endo* transition state structure.

(a)



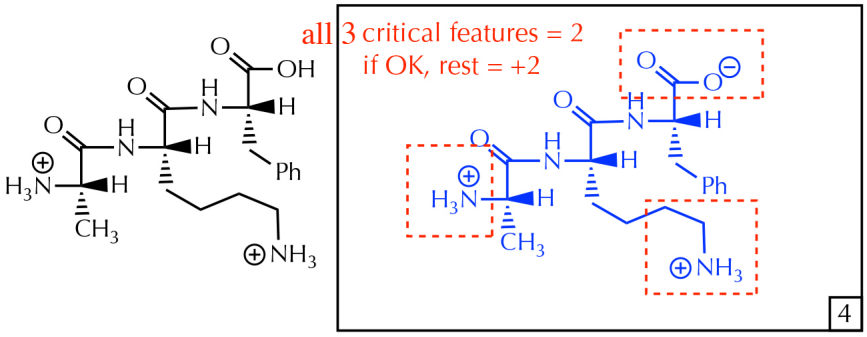
(b) among other structural features, the starting material includes an aromatic ring



=C= OK
HC=C= OK
HC=C=CH$_2$ OK
=C=CH$_2$ OK
=C=C not OK
C=C= not OK

B. The low pH (ca. pH 1) structure of a tripeptide is shown below.

(a) Using the information on the pK$_a$ table, what is the major structure in solution at pH 7.40?

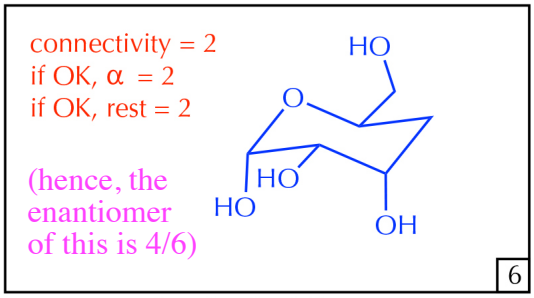


(b) Using the information on the pK$_a$ table, what is the value of its isoelectric point (provide the number with one decimal point accuracy; e.g, 16.7).

no partial
10.2
2

C. Allose is the C-3 epimer of glucose. Deoxy sugars lack a hydroxyl group at the indicated position.

(a) Draw the most stable chair conformation for α-L-4-deoxyallopyranose.



(b) When α-L-4 deoxyallopyranose is treated under the following reaction conditions, mark what is true, if any, about the reaction outcome.

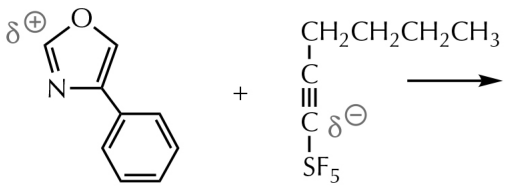
(i) $NaBH_4/CH_3OH$ no partial	(ii) KCN/H_2O no partial	(iii) Ag_2O/NH_3 no partial
☐ a racemic mixture	☐ a racemic mixture	☐ a racemic mixture
☐ a mixture of epimers 2	X a mixture of epimers 2	☐ a mixture of epimers 2

A		/10
B		/06
C		/12
		/28

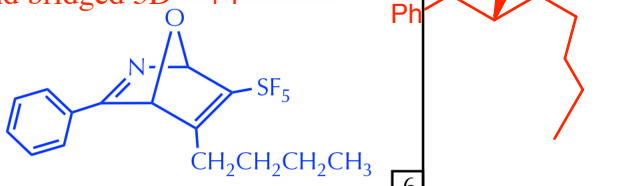
Question II (22 points) Name: _____

A. In the following hetero-Diels-Alder reaction, the regioselectivity is consistent with the partial charges shown on the two starting materials.

(a) Provide one of the enantiomers of the bridged bicyclic product using a 3D (bridged) drawing (*Org Lett*, **2006**, *24*, 5573).



regio OK regardless of bridged form = 2
if OK, wedge/dash 3D = +2
and bridged 3D = +4

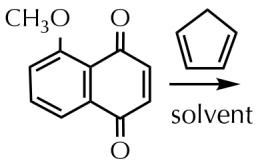


6

(b) Stereospecificity from which of the reacting partners is going to be experimentally observable?

circle one: (the diene only) the dienophile only both of them neither of them 2

B. In 1994, the rate of the following reaction was measured in hexane as a solvent and in water as a solvent (*J Org Chem*, **1994**, *59*, 5372). The reaction was 12,820 times faster in one case relative to the other. The hydrophobic effect was used to explain the faster reaction. Mark which of the statements is/are consistent with that explanation.

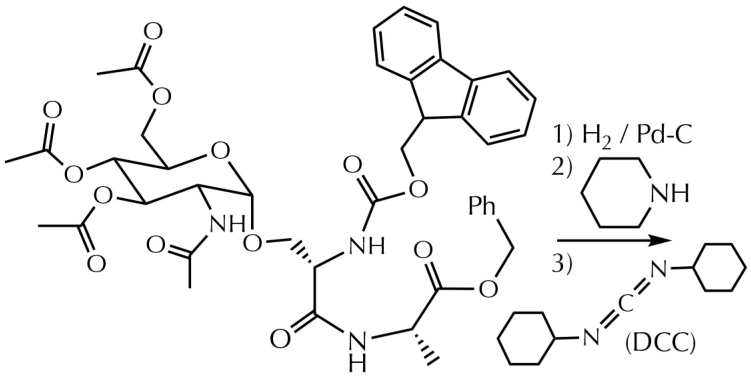


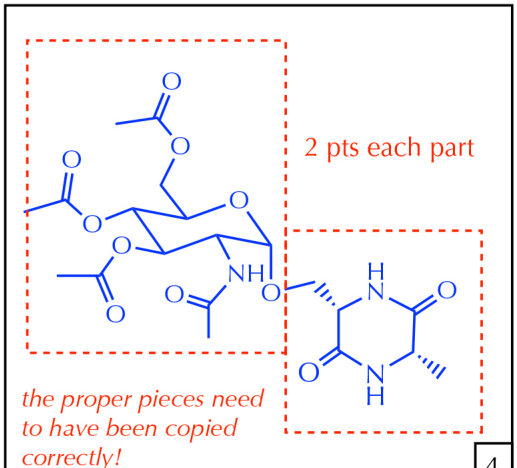
- [ ] The rate in hexane is 12,820 times faster than in water.
- [X] The rate in water is 12,820 times faster than in hexane.
- [X] Decreasing the surface contact of the reagents with water is more favorable.
- [ ] Increasing the surface contact of the reagents with water is more favorable.
- [X] In water, increasing the entropy of the solvent forces the reactants together, allowing more collisions between the reagents to occur.
- [ ] In hexane, the increased entropy of mixing allows more collisions between the reagents to occur.

1 pt per correct answer

6

C. The carbohydrate derivative (compound A) was designed to mimic the surface of cancer cells. Complete the steps used in the final stages of its synthesis.

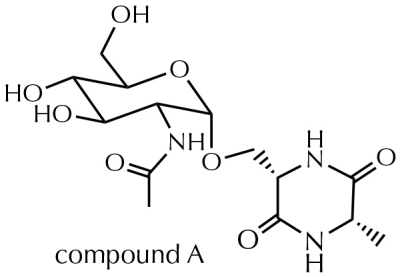




2 pts each part

the proper pieces need to have been copied correctly!

4



ignore H_3O^+ or workup step 2's

excess or 3x NH_3 (added base OK)

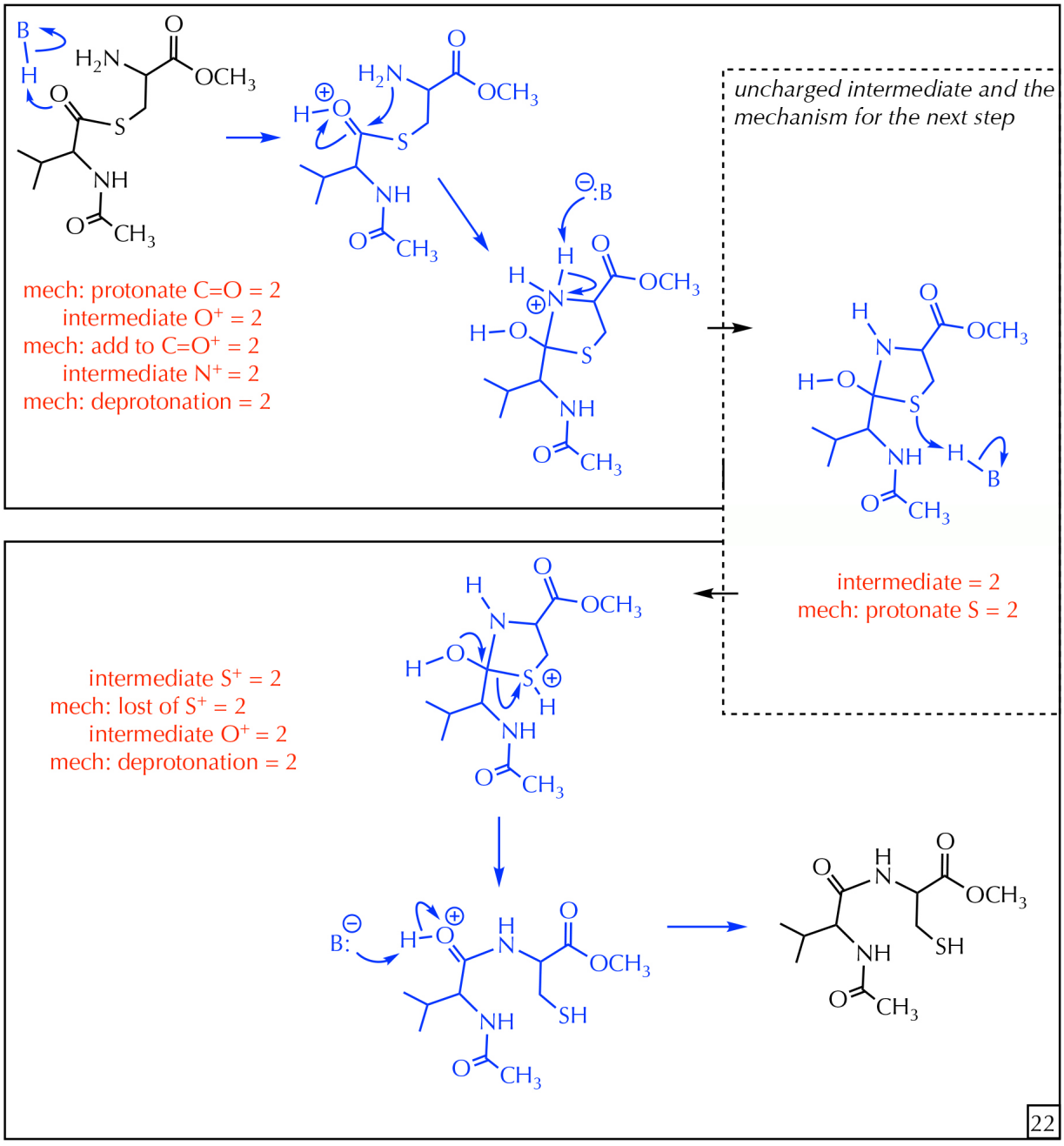
NH_3 = 3
excess or 3x = 1

4

Aa		/06
Ab		/02
B		/06
C		08
		/22

Question III (22 points) Name: _____

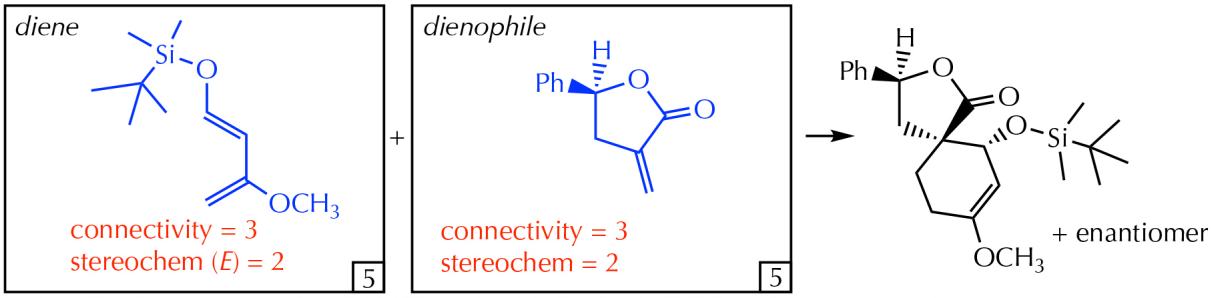
The following isomerization reaction takes place under acid catalyzed conditions, starting with protonation of carbonyl group. Draw the stepwise mechanism for this transformation. Note that there is a single, uncharged intermediate along the mechanistic pathway, and this should be drawn in the space indicated for it. You may use HB as a Brønsted acid and B:⊖as its conjugate base (or HB⊕ and B:, if you prefer, just be consistent!).



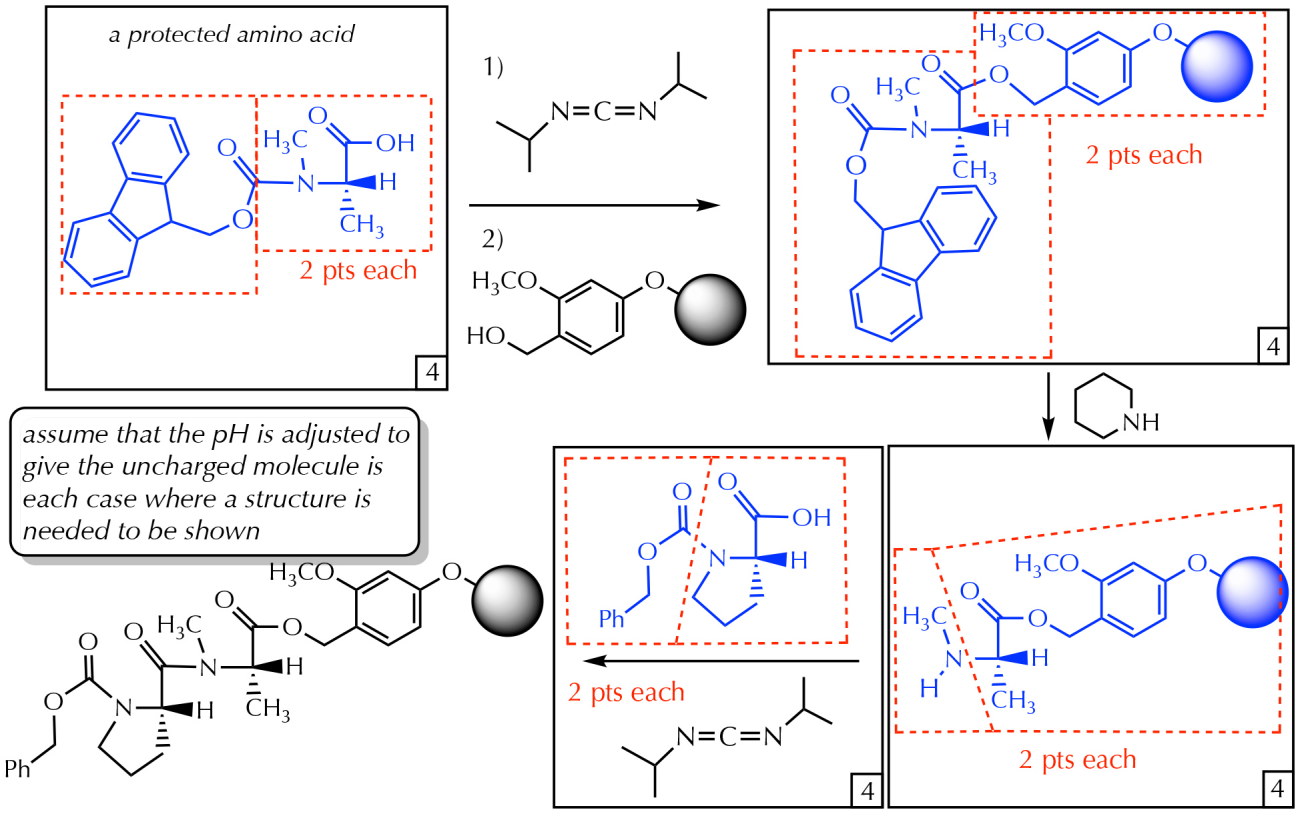
/22

Question IV (30 points) Name: _____

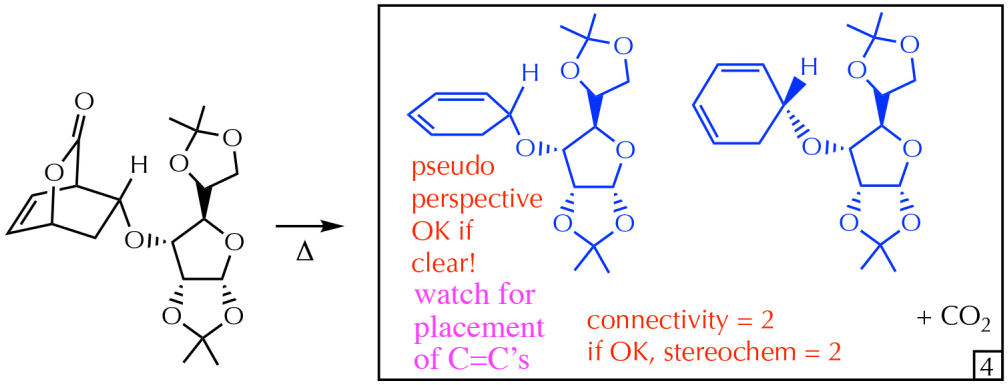
A. In the following reaction, an unexpected outcome was observed. Rather than the typical stereoselectivity favoring the *endo* transition state product, the *exo* product was favored. Complete the following (*Org Lett*, **2022**, *24*, 2242).



B. In the following transformation, Solid Phase Peptide Synthesis (SPPS) methods were used (the shaded shape corresponds to the polymer bead/support); *Org Lett*, **2018**, *20*, 788. Provide complete structures (no abbreviations).



C. When heated, the following compound undergoes a retro-hetero-Diels-Alder reaction in which carbon dioxide is released as one of the two products (*Org Lett*, **2010**, *12*, 5564). Draw the product, including any stereochemistry.

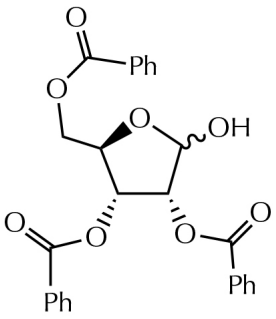


A		/10
B		/16
C		/04
		/30

Question V (18 points)

Name: _____

The following transformations were used to synthesize thionucleotides used as potential anticancer drug candidates (*Org Biomol Chem*, **2022**, *20*, 1401). Provide the missing intermediates or reagents from each step, as called for. Include stereochemistry, and assume that the pH has been adjusted to give uncharged organic molecules in each case where a structure is called for.

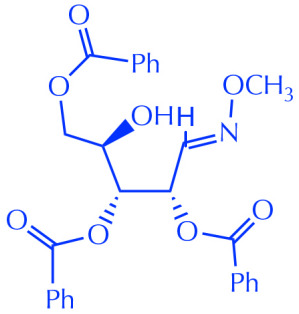


$H_2N{-}OCH_3$

pH 6.5

CH_3OH

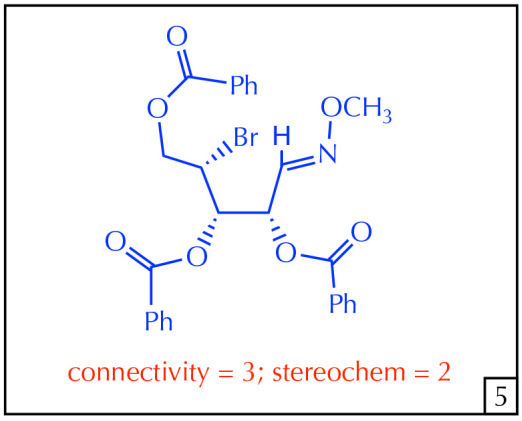
open chain form; (*E*)-diastereomer



connectivity = 3; stereochem = 2 [5]

1) CH_3SO_2Cl / $(CH_3CH_2)_3N$

2) LiBr

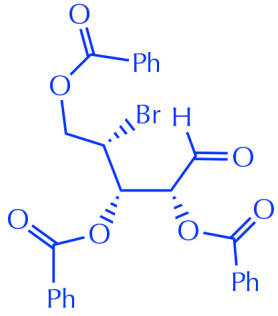


connectivity = 3; stereochem = 2 [5]

H_2O

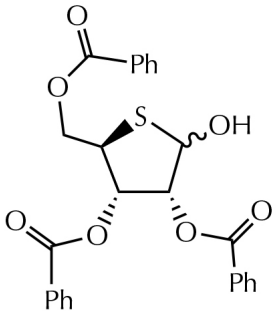
HCl

open chain form; plus $CH_3\overset{\oplus}{O}NH_3\ \overset{\ominus}{Cl}$



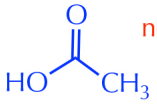
connectivity = 3; stereochem = 2 [5]

NaSH



carried out under S_N1 conditions to give the diastereomer shown

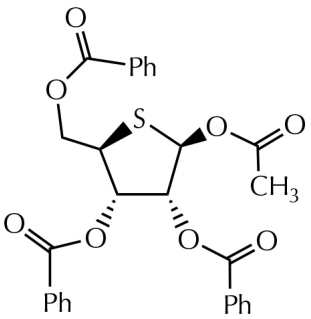
key feature = the acid:



no partial

added acid catalysts eg, TsOH, H_2SO_4, HCl optional

OK if H_2O or H_3O^+ present. [3]



acylation with acid halide, etc not OK. Not S_N1, would give the stereomixture.

/18