

Chemistry of Biomolecules 5.451

F2005

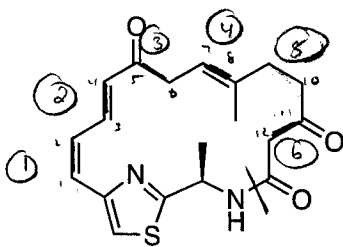
October 25, 2005

Final Exam

(do not need to repeat mechanisms)

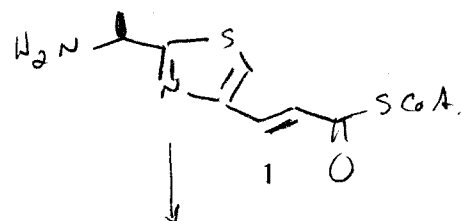
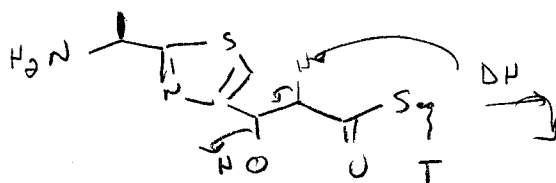
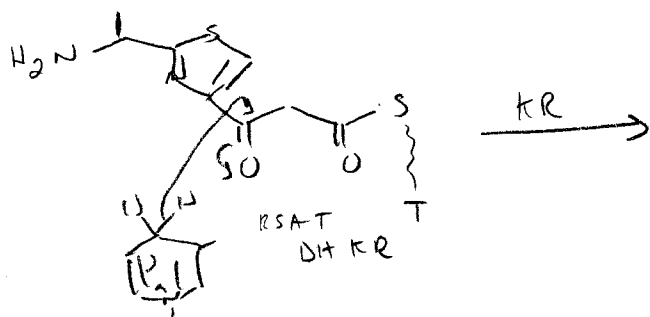
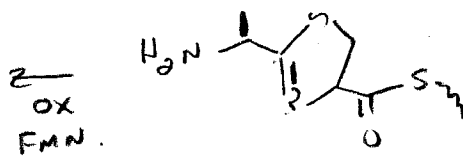
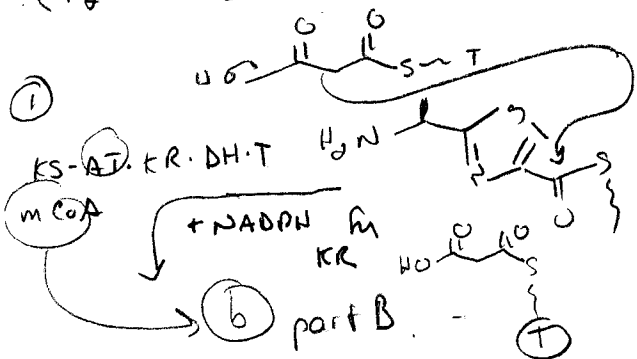
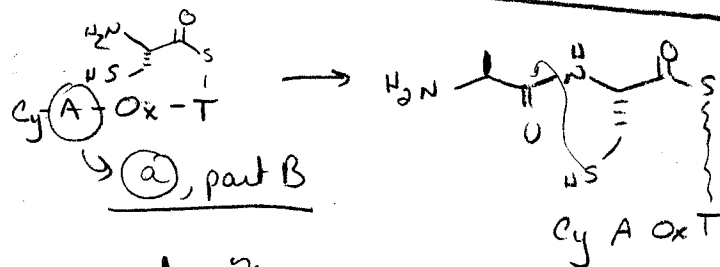
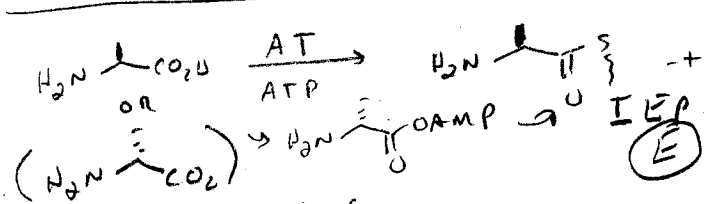
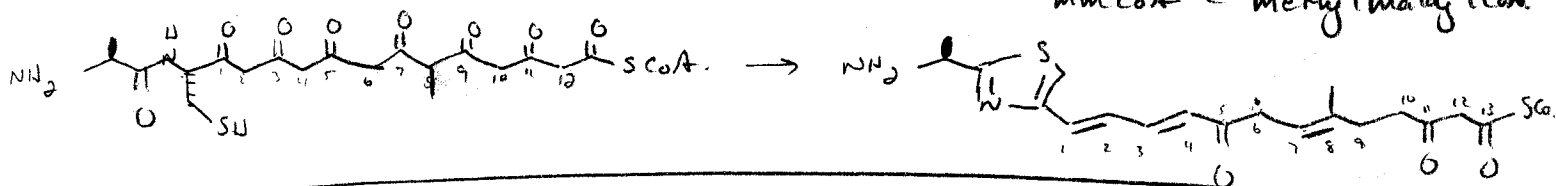
1A. (15 points) Draw a detailed, stepwise mechanism for the formation of this intermediate in leinamycin biosynthesis. Include the type of enzyme or enzyme domain being utilized in each step.

A = acylation
 T = PCP = ACP = carrier protein.
 C = condensation
 Cy = cyclization.
 Ep = epimerization

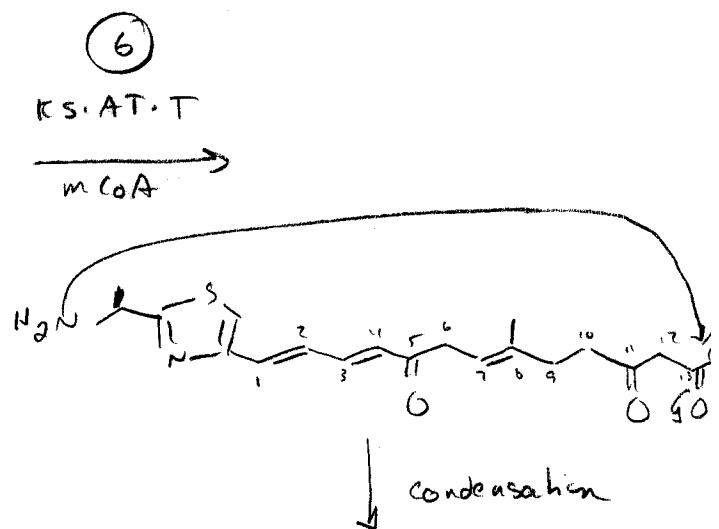
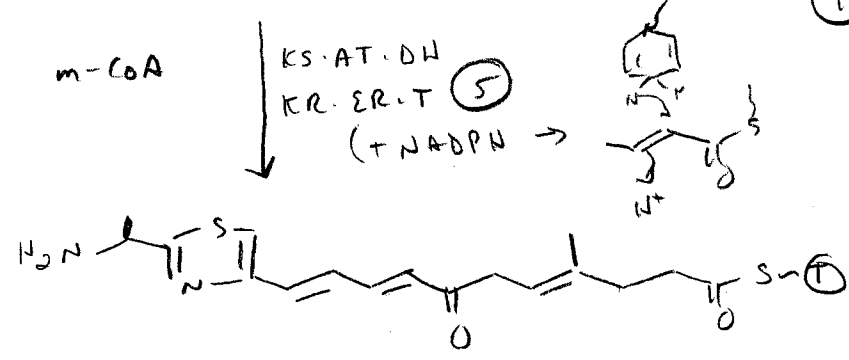
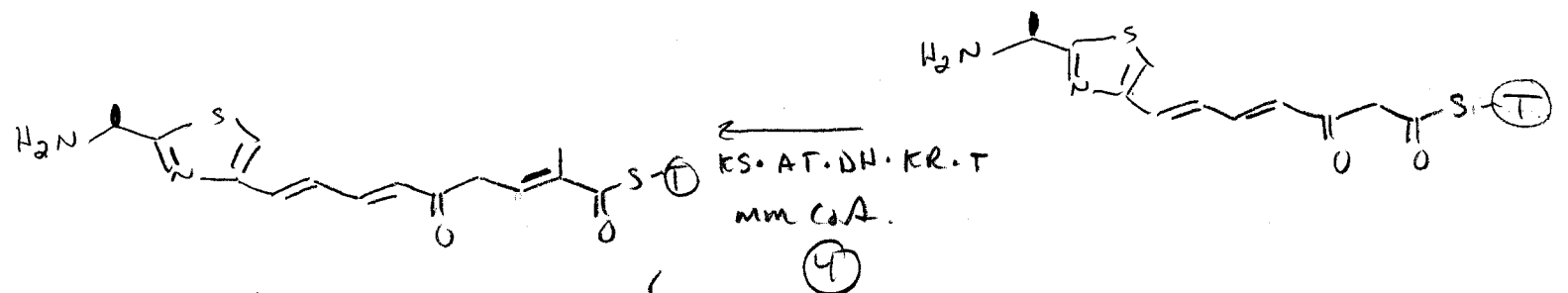
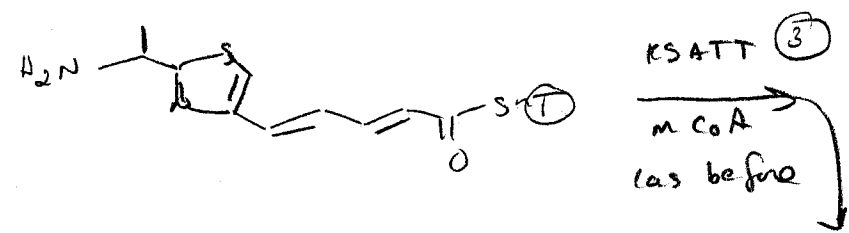


leinamycin intermediate

AT = acyl transferase
 KS = ketosynthase
 DH = dehydratase
 KR = ketoreductase
 ER = enoyl reductase
 m CoA = malonyl CoA
 mm CoA = methyl malonyl CoA

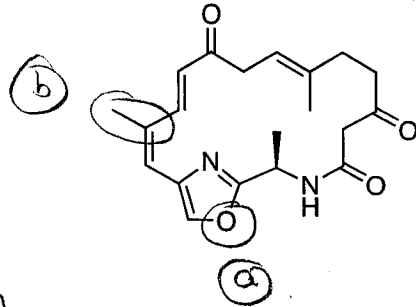


②
 KS-AT-DH-KR-T
 m CoA
 as before



product

1B. (5 points) Suggest how the following compound can be made by altering the leinamycin biosynthetic machinery. Indicate which specific enzyme domain(s) given in part A will be involved.



a) replace A domain
w/ domain specific Pn Serine vs Cysteine.
(indicate which A domain on previous page)

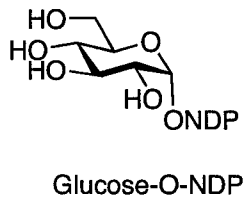
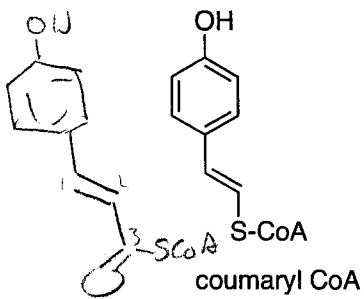
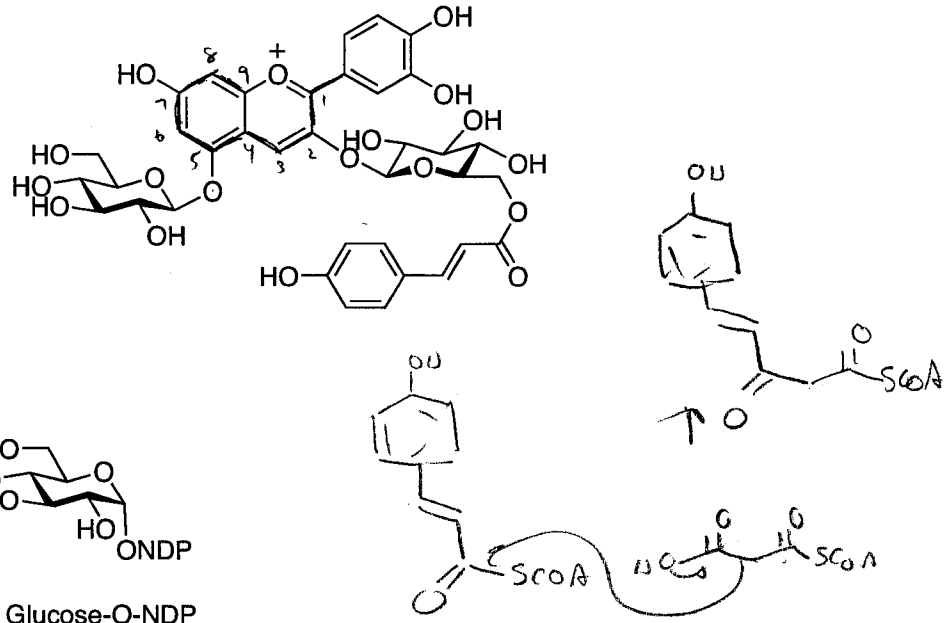
b) replace AT domain w/ domain specific
Pn mm CoA
(indicate on previous page)

- site directed mutagenesis could be used to make changes in A or AT substrate binding pocket to change specificity.

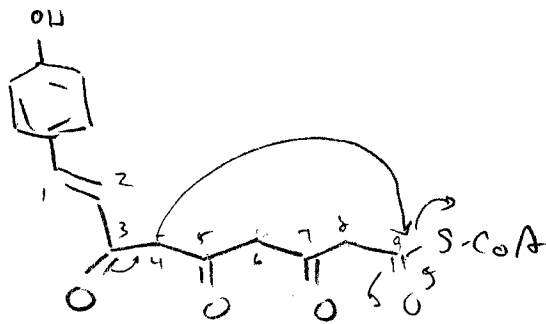
- obtain A or AT domain from other nat prod system → replace A/AT domain from leinamycin system w/ cloned A or AT domain from heterologous system

don't need to show mechanism of linear intermediate synthesis

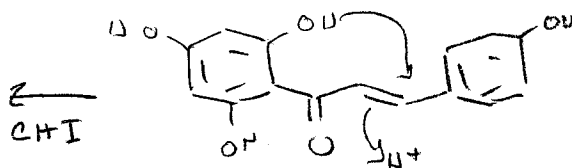
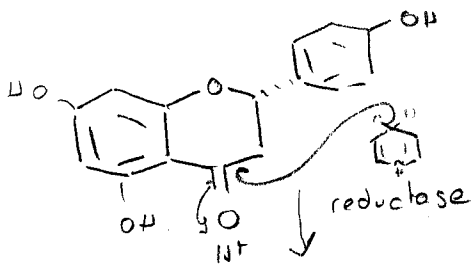
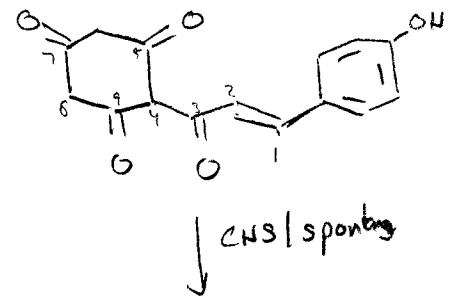
2. (20 points) Draw a detailed, stepwise mechanism for the biosynthesis of the following anthocyanin compound from coumaryl-CoA, malonyl-CoA and glucose-ONDP building blocks. Include the type of enzyme or enzyme domain being utilized in each step.



chalcone synthase will catalyze synthesis of linear intermediate



CHS
(KCS-like)
↓
HS-CoA



no linear precursor. → or isoprene bb.

3A. (15 points) Provide a detailed mechanism for the biosynthesis of the following compound. Note that the cyclase involved has a DDXXD and a DXDDT amino acid sequence motif. (2D drawing ok). ionize (2) protonate (1)

B. (5 points) Draw the reaction pathway in a conformation that results in the shown stereochemistry. Assume the enzyme templates the structure in a chair boat conformation.

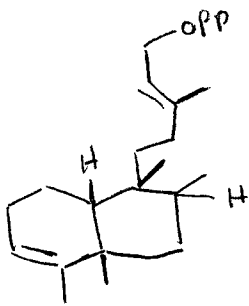
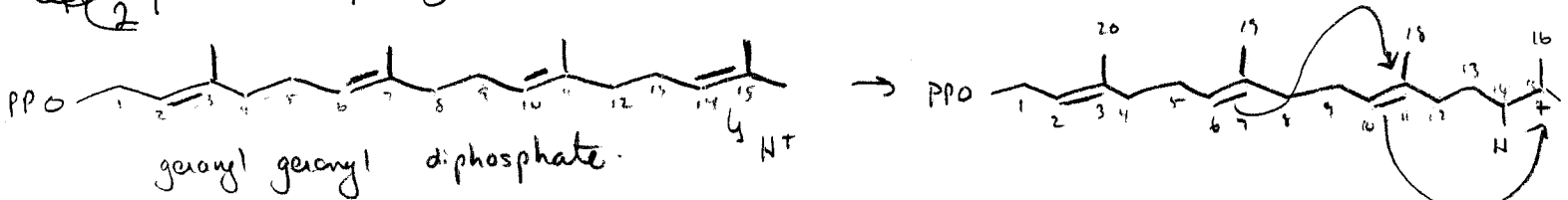
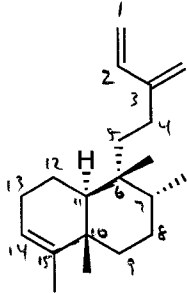
4 pts for precursor

• 2pt diterpene

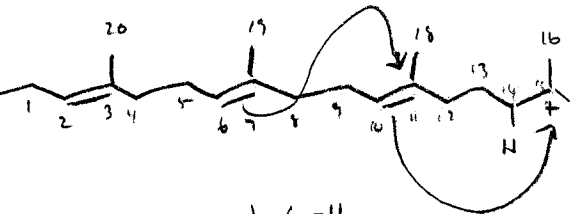
• 4pt if draw

11 pts cyclization → +3 for eliminations.

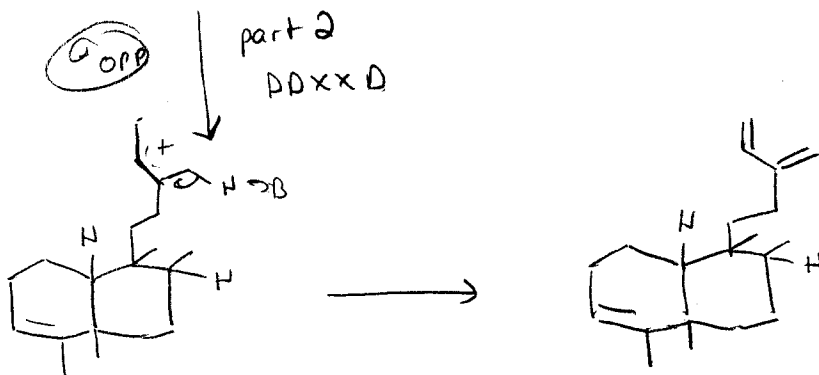
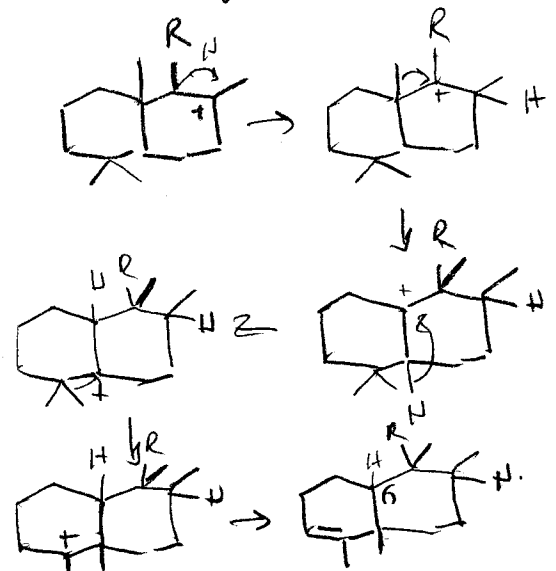
~~2~~ 2 pts if specify prot/ionize.

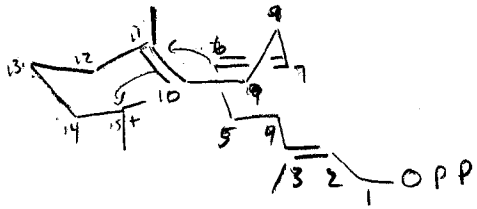
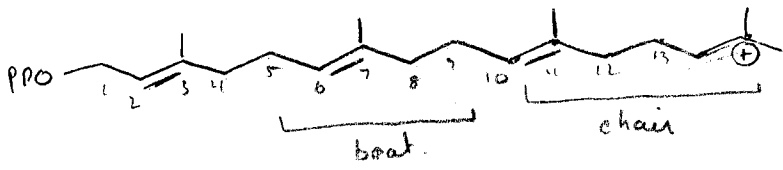


C6-H → C7
 C18 → C6
 C10-H → C11
 C16/17 → C10
 eliminate C14-H

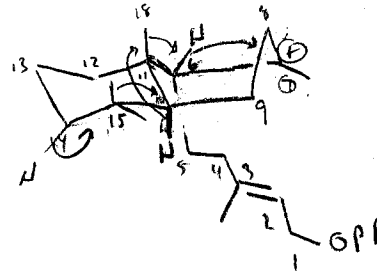


step wise

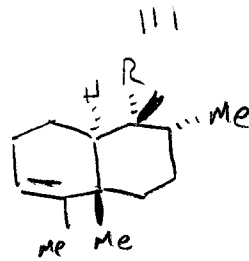




C10-15
 \longrightarrow
 C6-C11



\downarrow C6H - C7
 C18 - C6
 \downarrow C10H - C11
 C16/17 - C10.



- N-MT 3

- P450 3

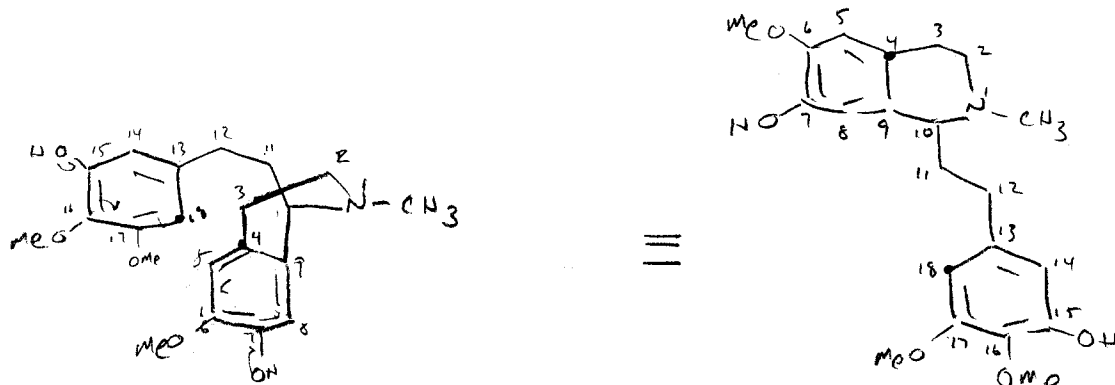
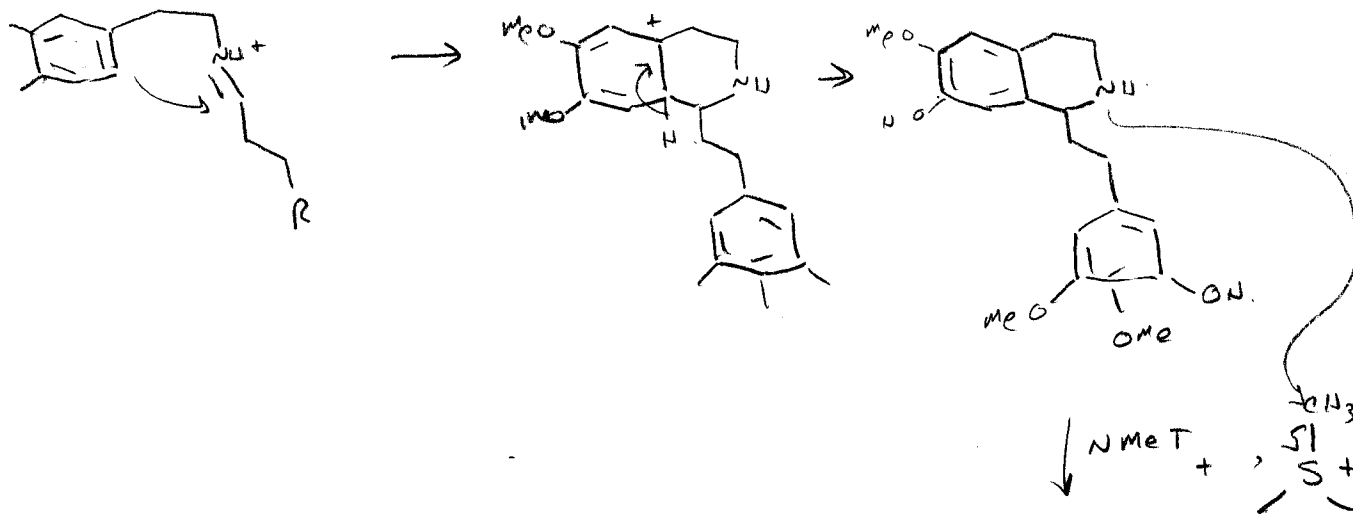
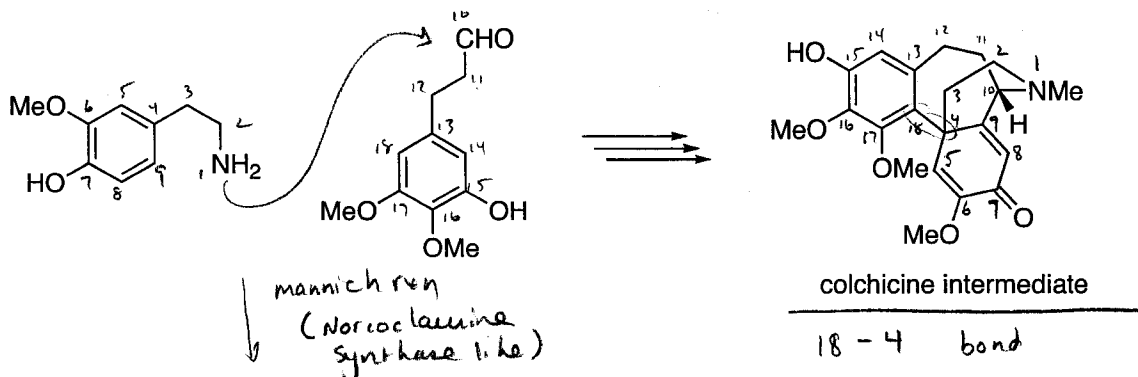
- Piet Spenger 6
imine, cyclizations.

- right regioselect 3

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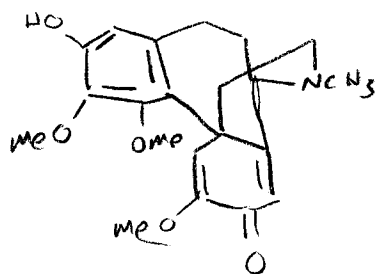
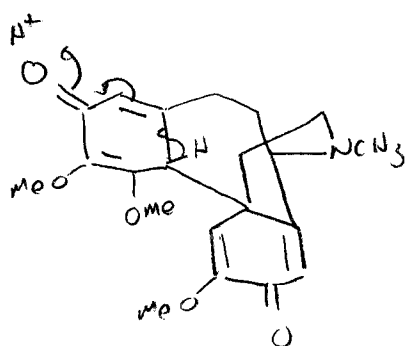
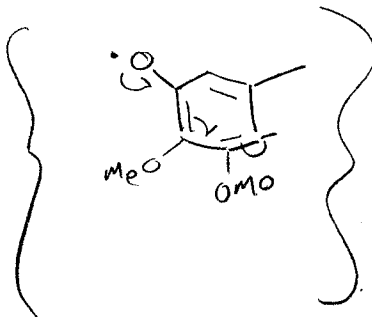
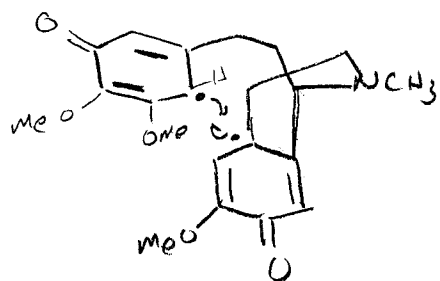
p. 2979

4. (15 points) Using your knowledge of the morphine biosynthetic pathway, propose how the formation of this colchicine intermediate is enzymatically catalyzed.



↳ like salutaridinol
synthase.

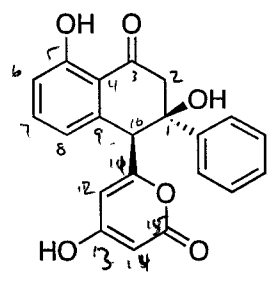
generate radical via P450



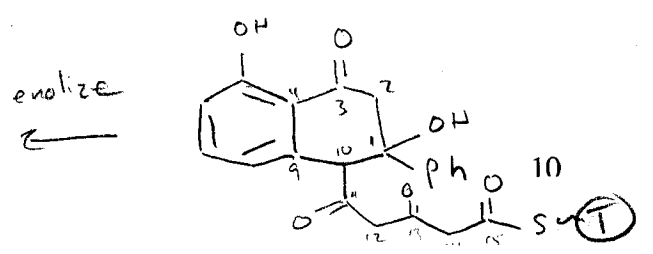
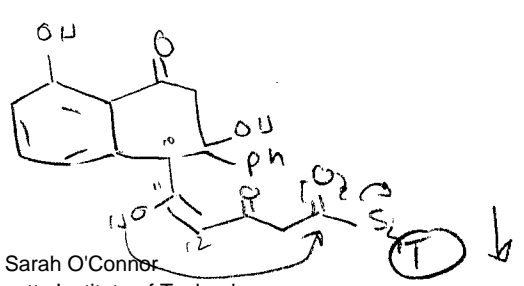
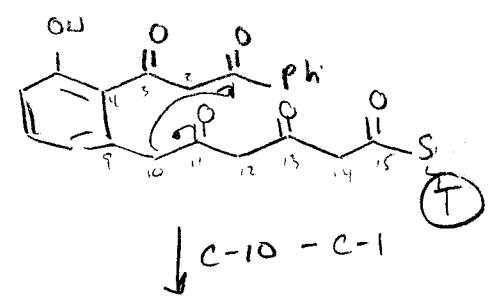
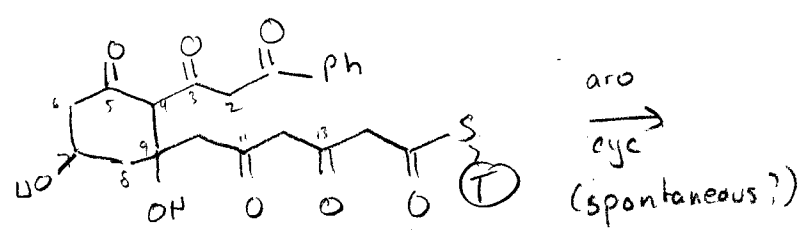
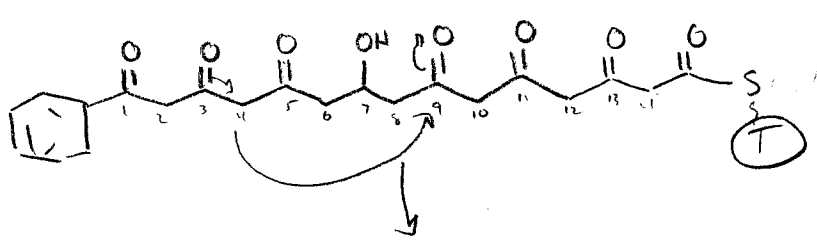
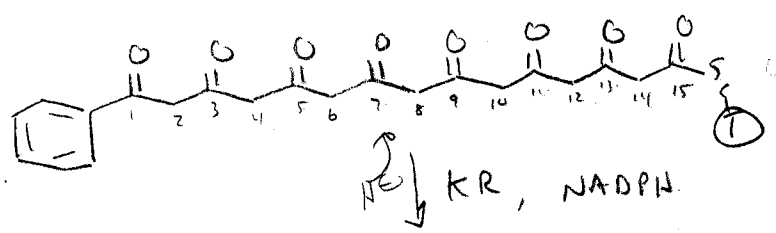
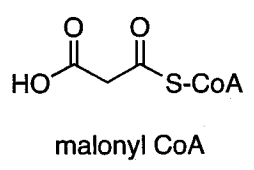
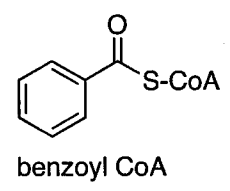
T = ACP (thiolation)

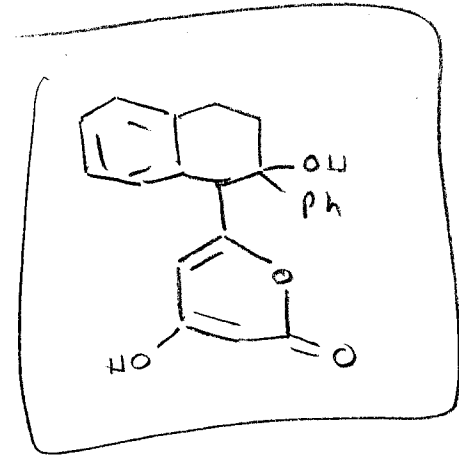
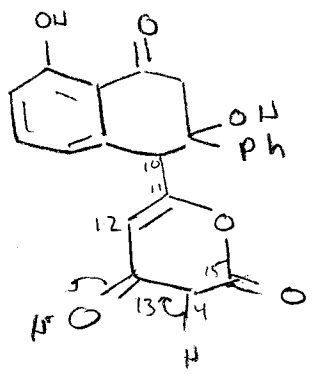
5. (15 points) Draw the mechanism of biosynthesis for the following polyketide product starting from malonyl CoA units and benzoyl-CoA (the starter unit). Indicate the general type of enzyme used in the steps. *not necessary to rationalize S.C.*

Show
linear
chem

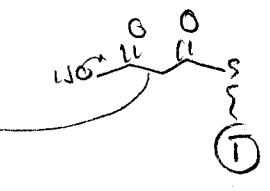
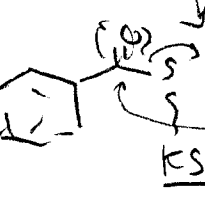
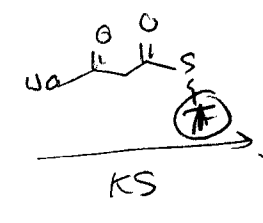
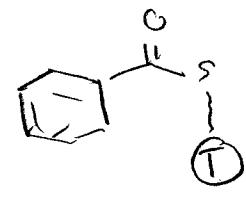
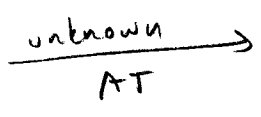
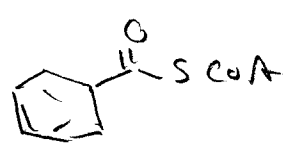


4-9
1-10
15-0
reduce at C7

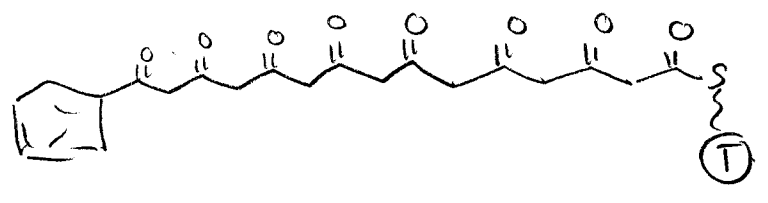
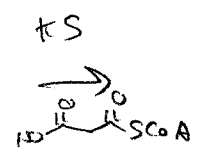
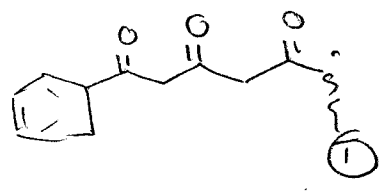
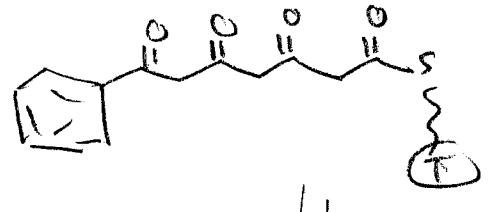
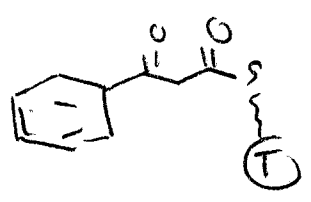




Linear chain



repeat
w/ SAME
KS/T.



6. (10 points) Draw a mechanism for the biosynthesis of the following dideoxysugar from the glucose nucleotide diphosphate. A mechanism for the C3 deoxygenation is not required, but indicate the required cofactor.

