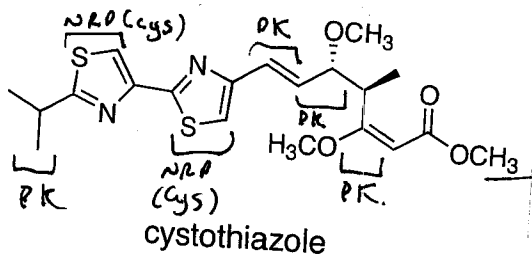
#1) See Biosci. Biotech. Biochem (2005) 69 1372-1380.

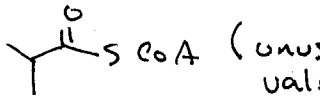
PK = polyketide
NRP = nonrib. peptide



cystothiazole

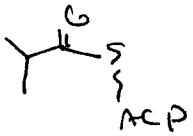
precursor is carboxylic acid. so this is last step.

start → finish.

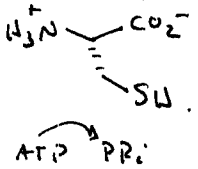


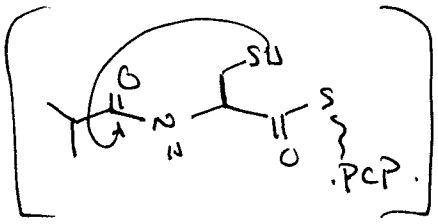
(unusual starter unit) valeryl CoA

KS AT ACP. → (KS-Q) ①

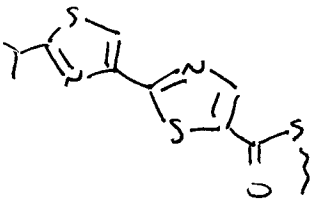


② CyOx ATP

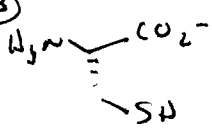




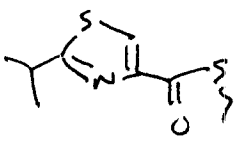
(Cy) H_2O



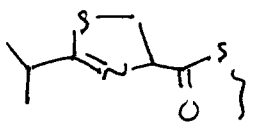
← CyOx ATP ③



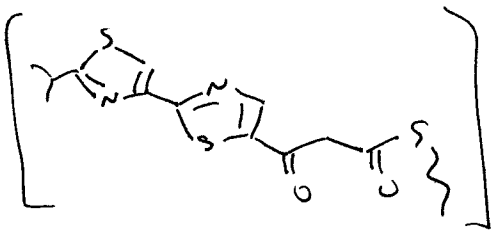
ATP → PPi



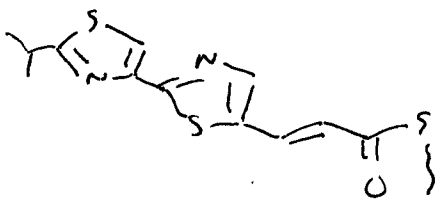
(Ox) ←



mal-CoA | KS AT KR DH ACP



(KR/DH) → H_2O.



KR KS AT ACP → mmCoA

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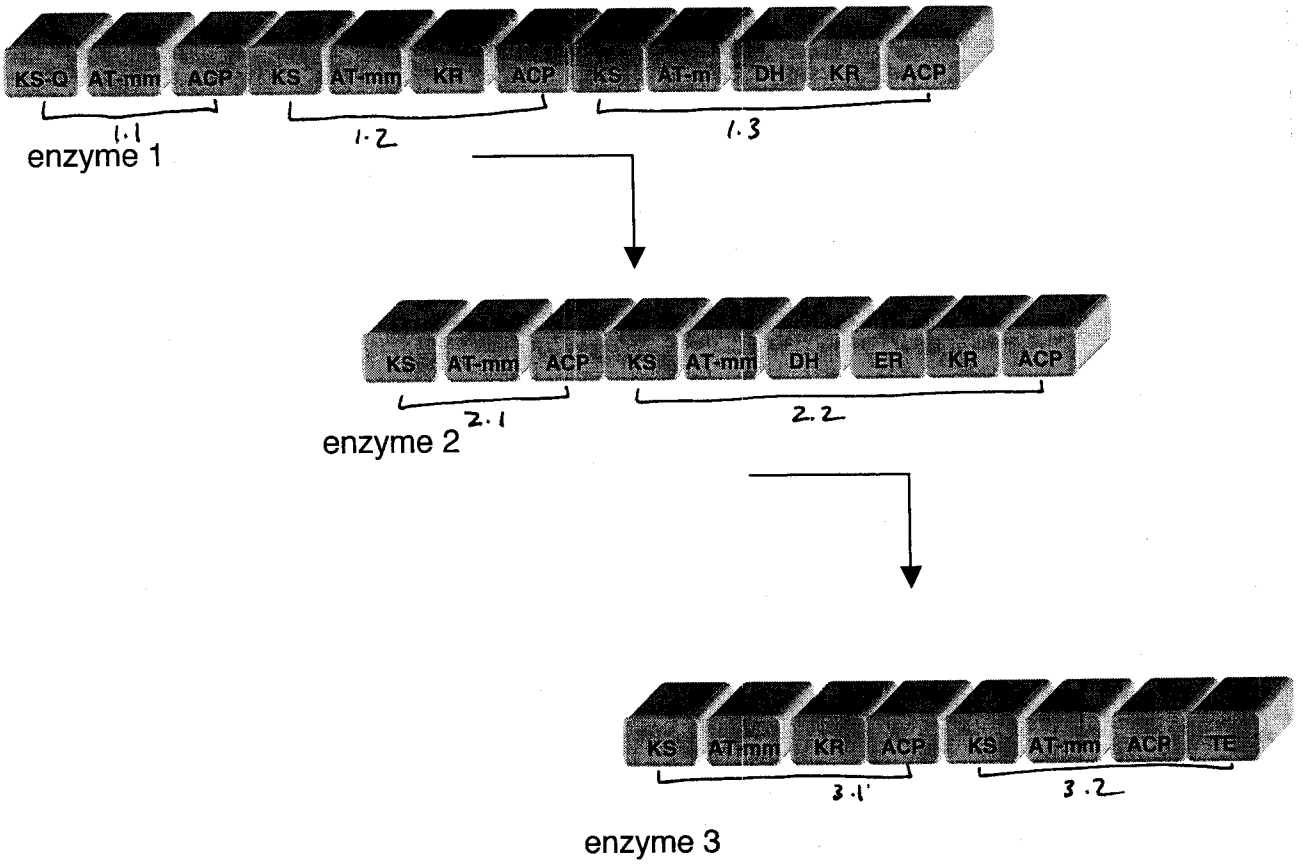
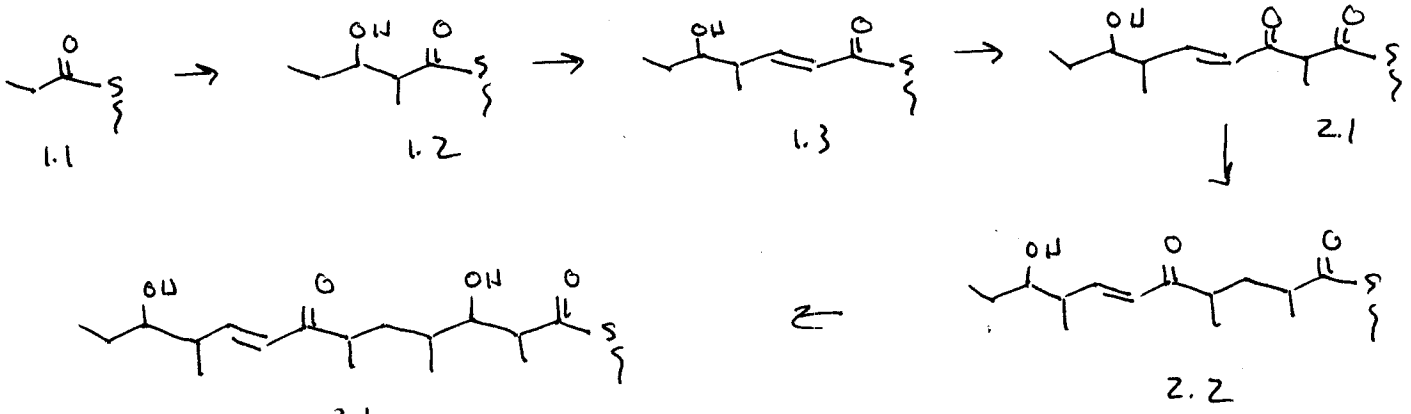
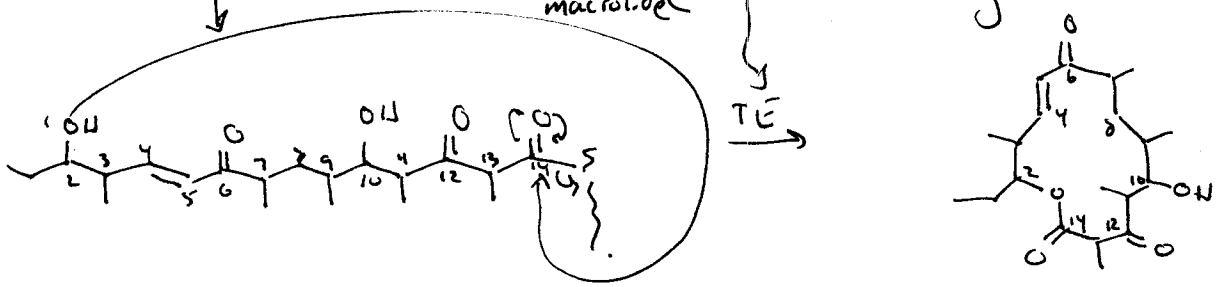
(#2) See for example Chem Rev (2005) 105 543-558





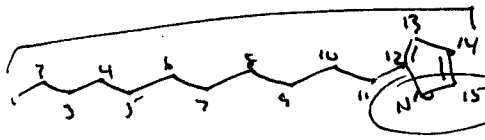
not common w/ PKS macrolide

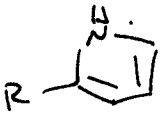
could also get hydrolysis or 6 mem. ring (not common w/ PKS TE)



can't predict stereochem from protein sequence — see ref for actual stereocenters

#3 See reference Chem Biol (2001) 8 817-829 for further discussion.

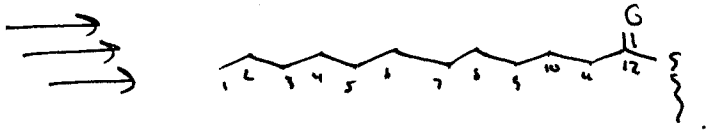
A. 

≡ 

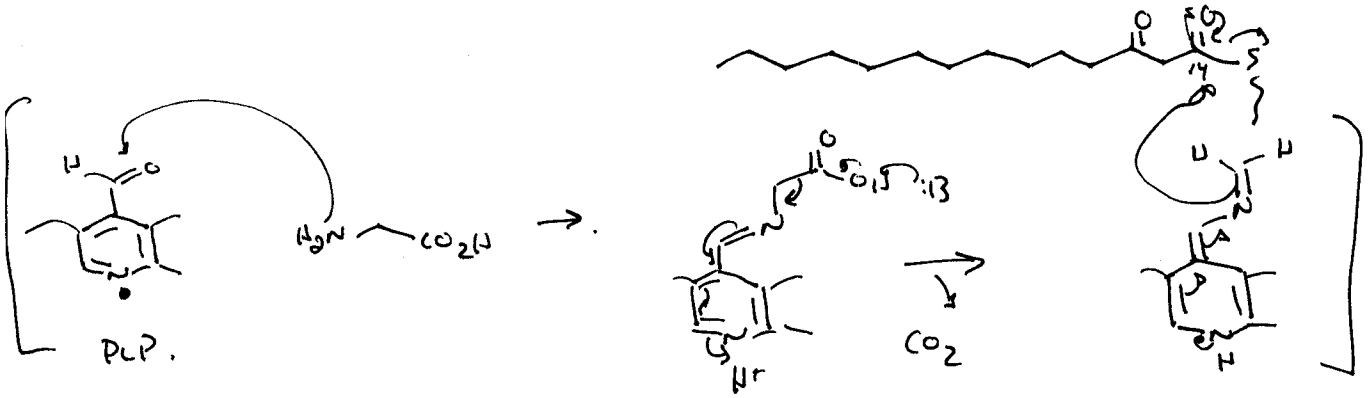
PK synthesis

KS KR DH ER AT ACP

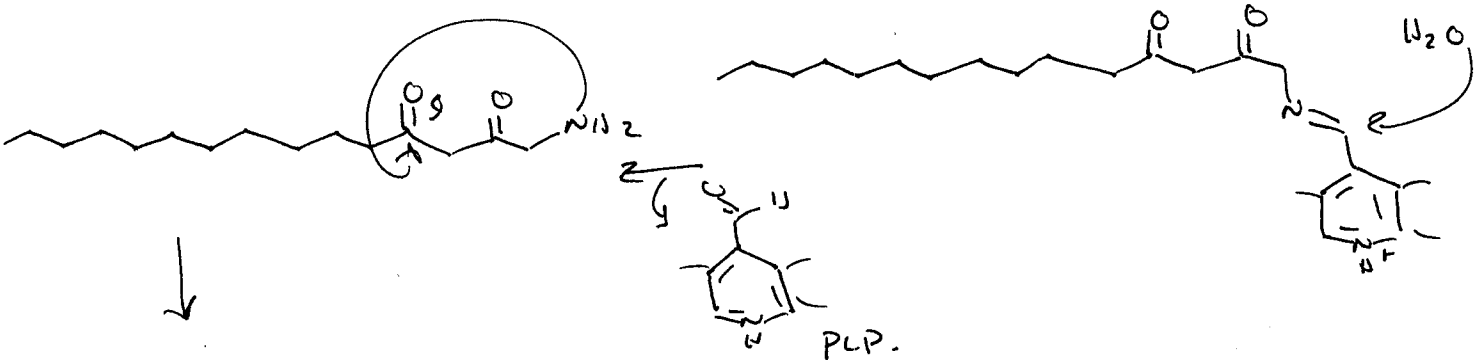
m CoA

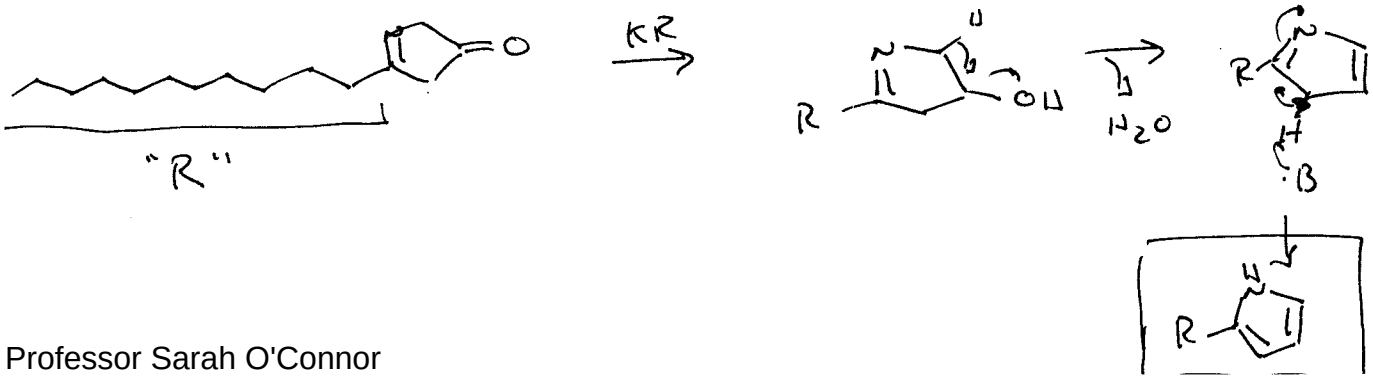


↓ KS AT ACP
m CoA



↓ ⇒ SN-ACP.





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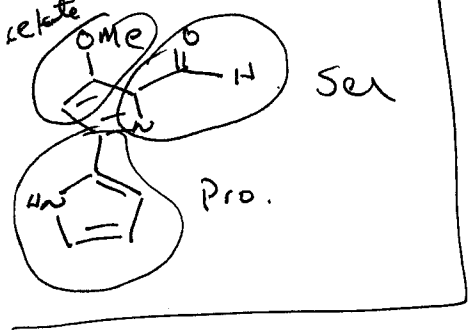
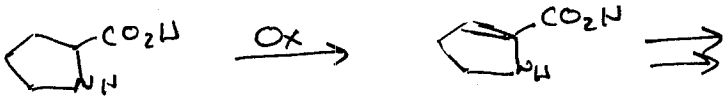
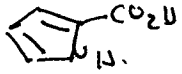
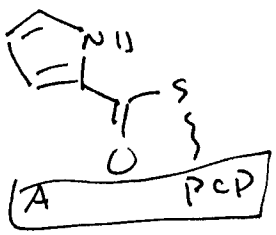
#3 con't. (B).





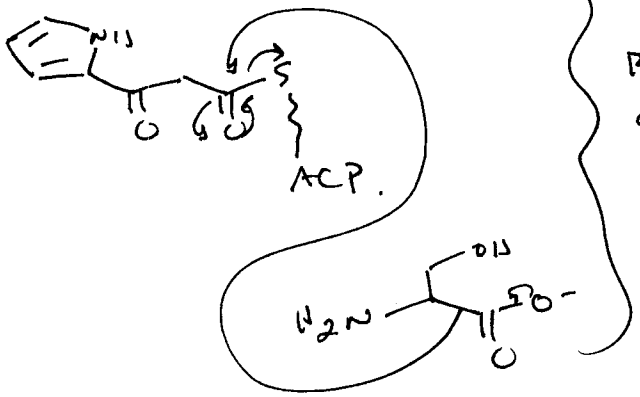


oxidation to pyrrole is believed to occur off PCP OK if shown on PCP in prob. set.

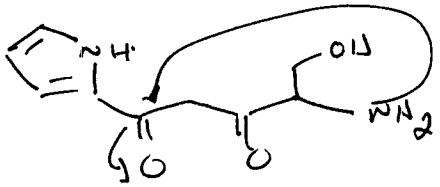


mCoA

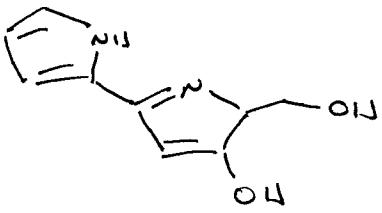
KSAT ACP.

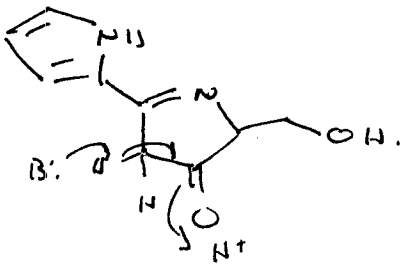


PCP-mediated decarbox as on previous page.

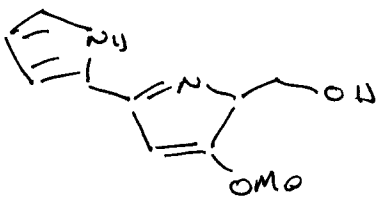


$\downarrow N_2O$





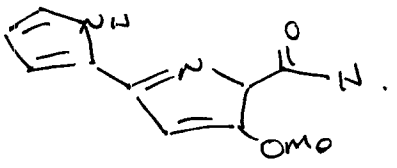
OMT + SAM



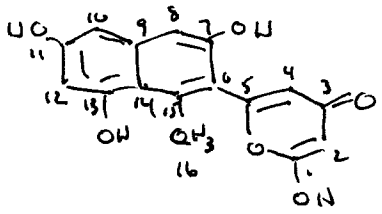
Ox

NAD^+

↳ similar to cholesterol dehydrogenase.

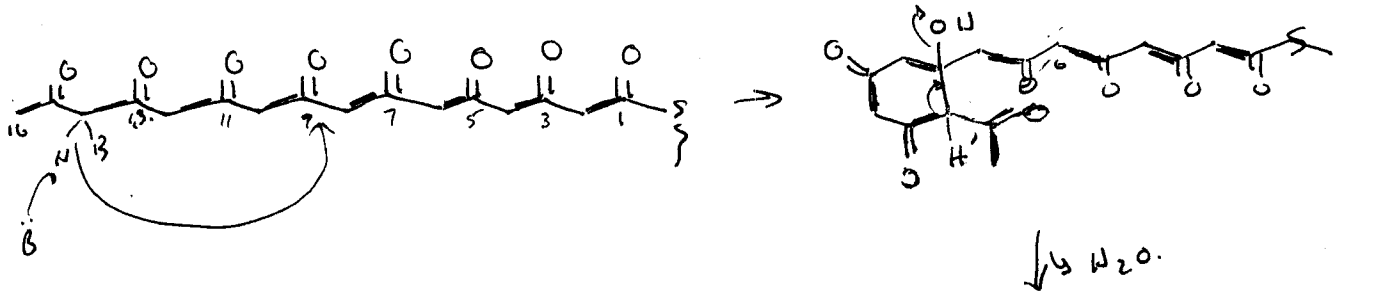


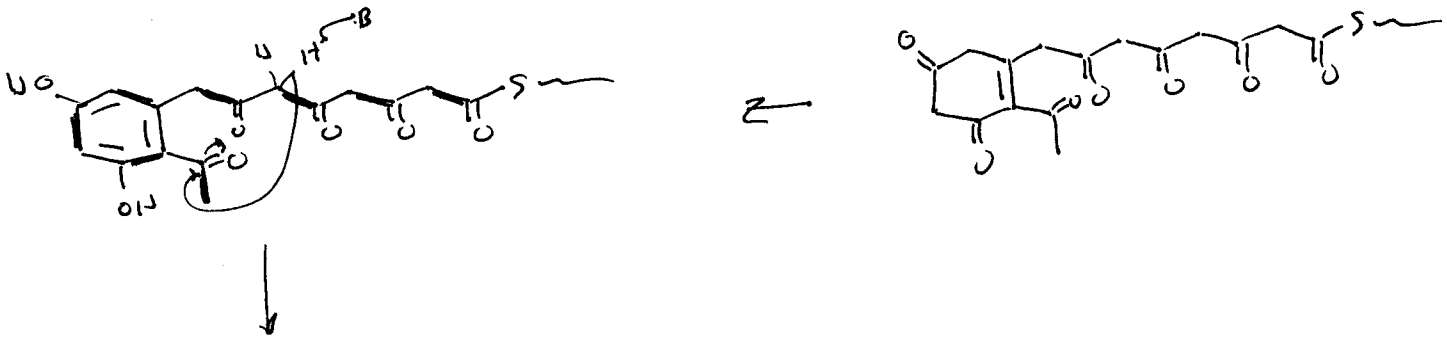
(#4) See JACS (1995) 117 6811-6821

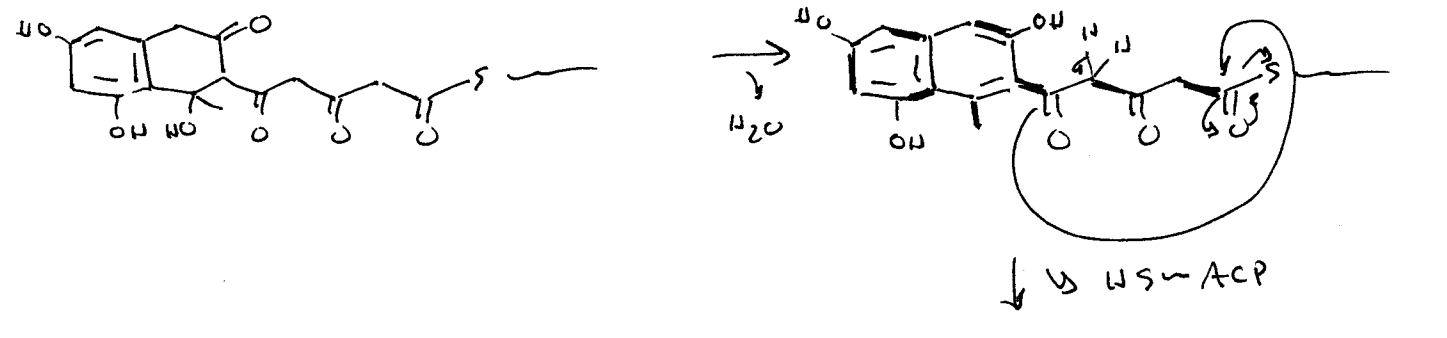


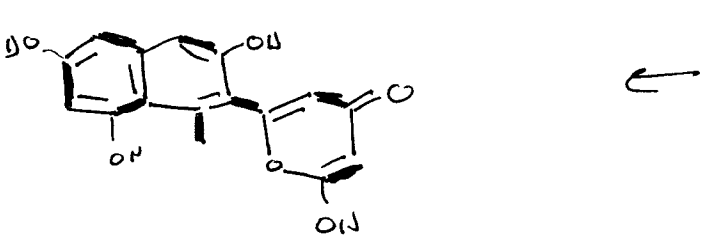
16 carbons

bonds 9-14
15-6
O-5









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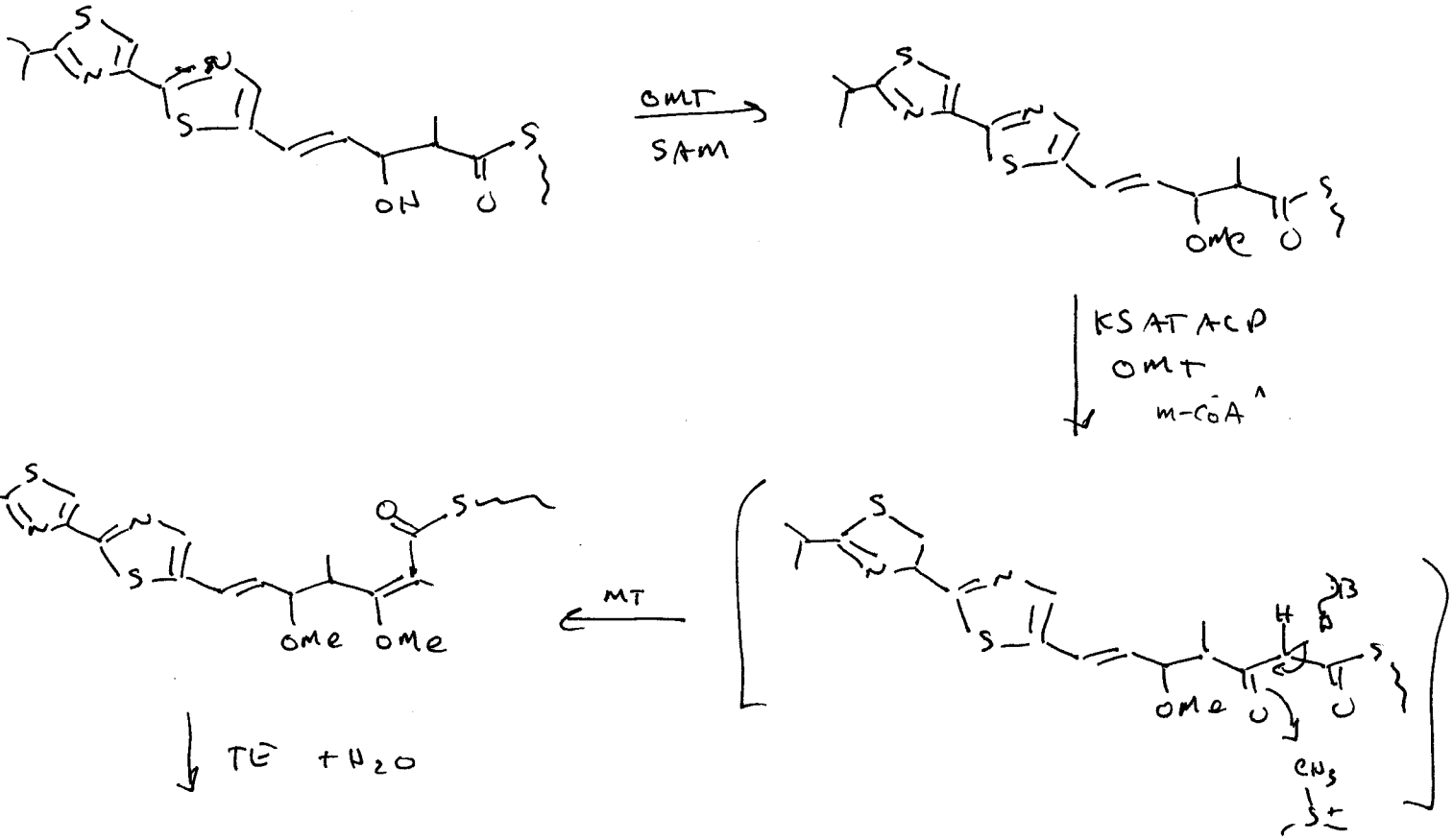
4) (con't)



→ in actuality, an additional Glycine is added, oxidatively cleaved to yield an amide, hydrolyzed to the acid + then methylated.

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