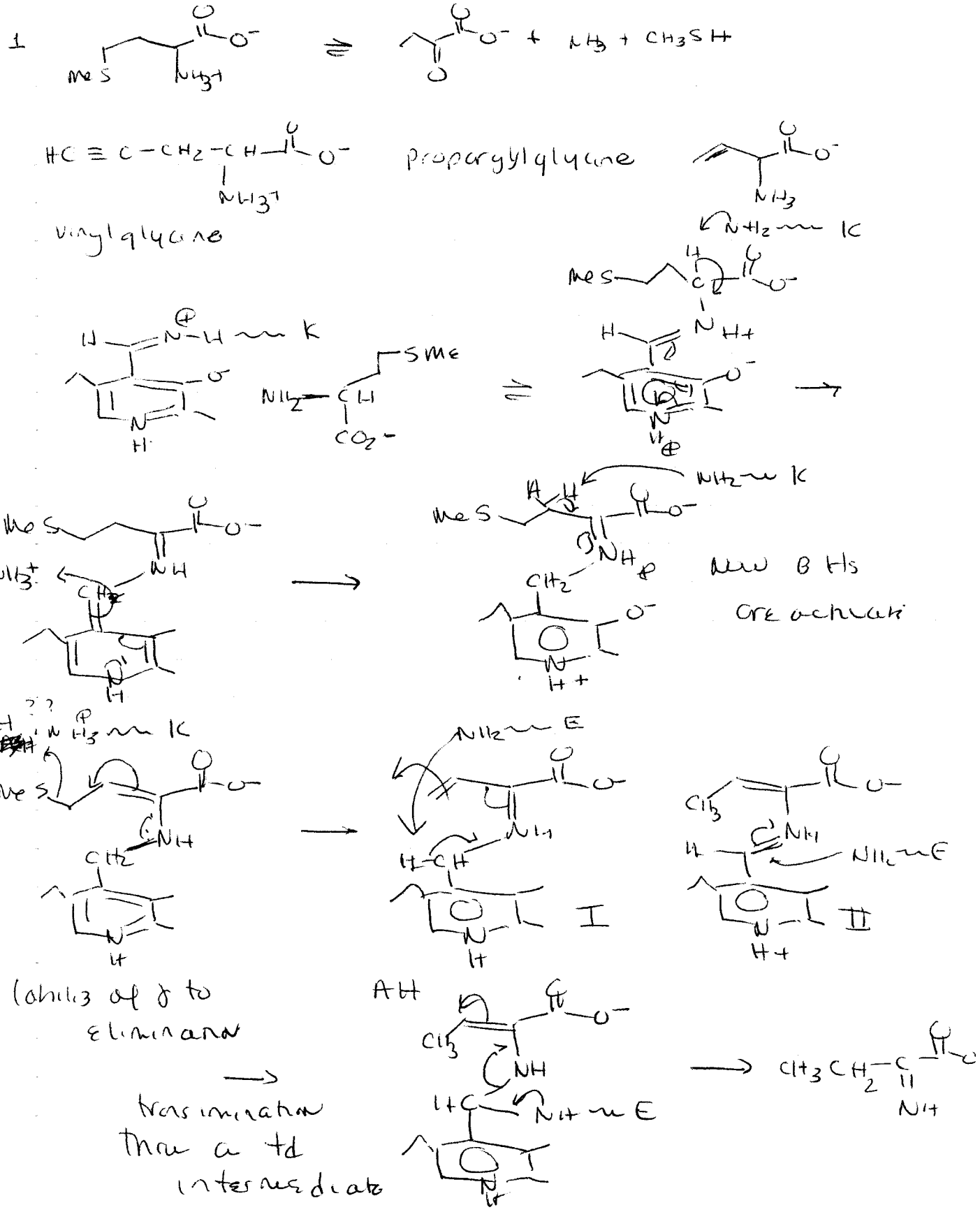
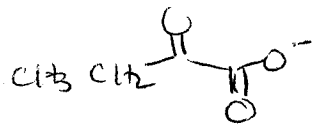
Ans Pg 7.

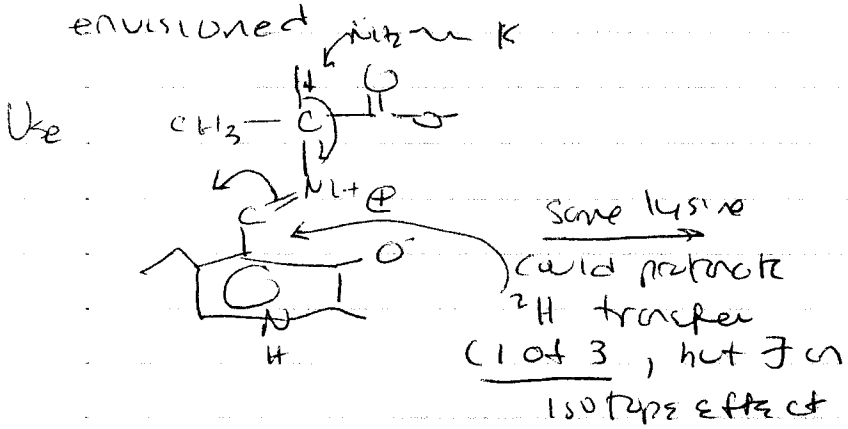

1
Me S
NH3+
+ NH3 + CH3SH
HC≡C-CH2-CH
NH3+
propargylglycine
vinylglycine
NH2 ~~ K
Me S
NH+
SMe
NH2
CH
CO2-
NH2 ~~ K
Me S
NH3+
NH
CH2
NH2 ~~ K
Me S
NH+
CH2
New β H's
are activated
AH
NH3+ ~~ K
Me S
NH
CH2
NH2 ~~ E
CH3
NH
NH2 ~~ E
I
II
Labile α to
elimination
AH
CH3
NH
H+C
NH ~~ E
CH3CH2
NH
→
transimination
thru a 1d
intermediate

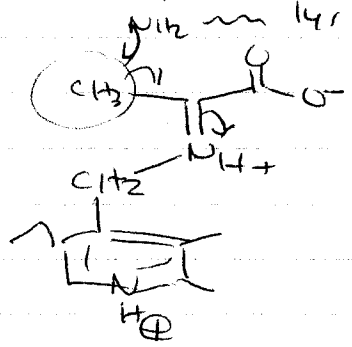
hydrolysis of Imine.



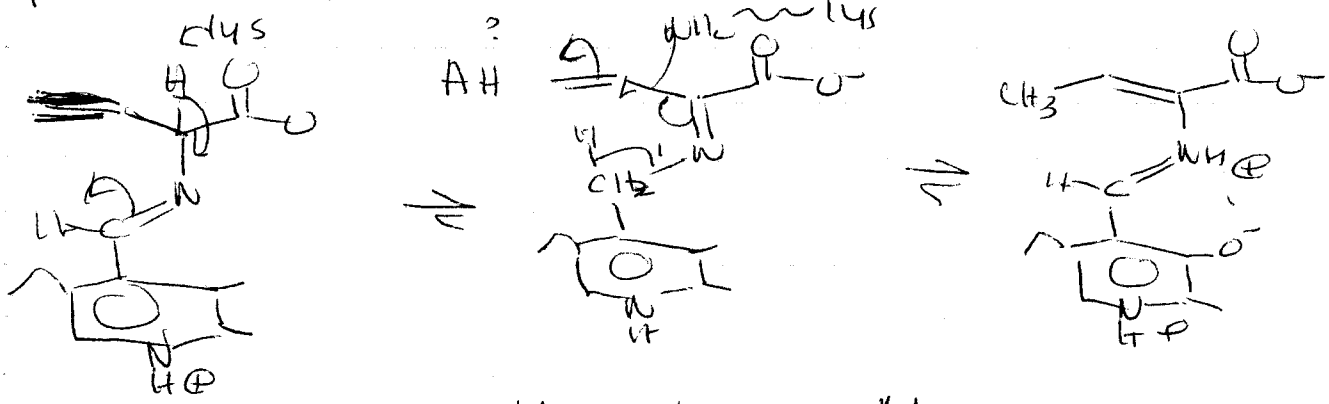
Question: What are the minimal number of acid/base catalysts to carry out this very complex set of protonation/deprotonation reactions? Can you get some insight from the structure or with mechanism based inhibitors.

Exchange rxns into both the α, β and γ positions can be envisioned





β Hs are now labile as they are adjacent to an imine and can undergo exchange. All of these rxns could potentially be carried out by the same lysine that forms the Schiff's base.

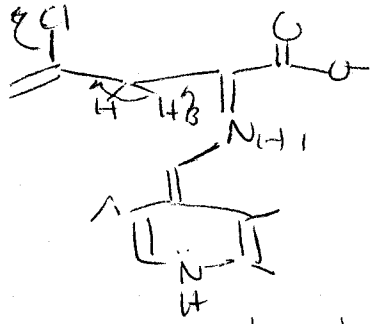


this intermediate

this intermediate are identical to I, II resp in normal pathway.

Inhibition could be envisioned thru a number of pathways and could be similar to inactivation by propargly glycine. (See attached proposed mech.

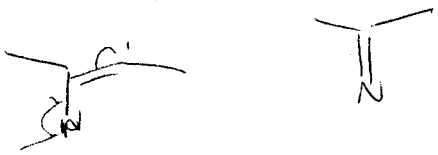
In intermediate II



→ III

intermediate III

II could come off the protein by denaturation as the imine would be hydrolyzed

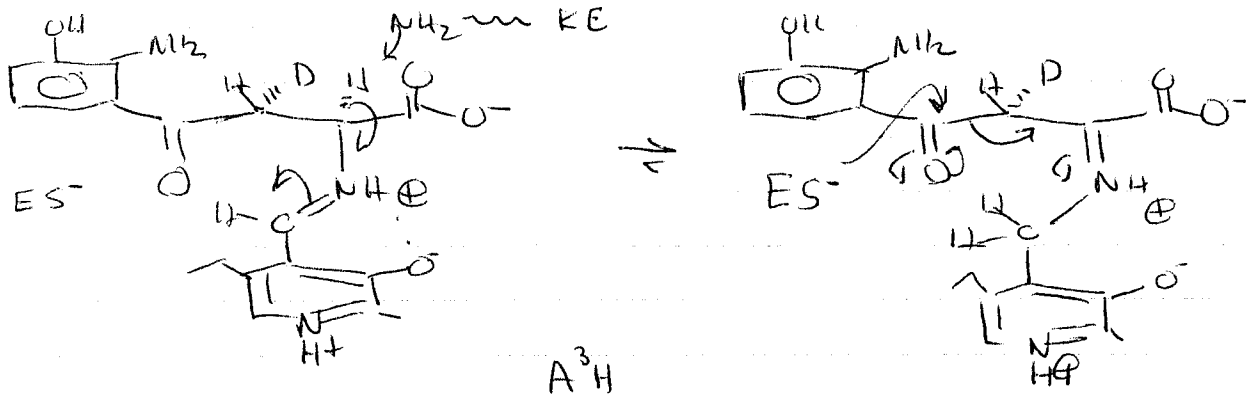


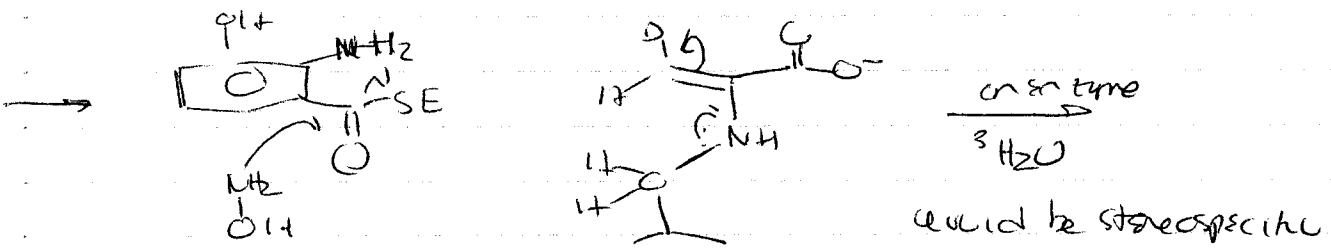
→ could also hydrolyze but O, S nucleophile would give a stable linkage.

Active Site Structure:

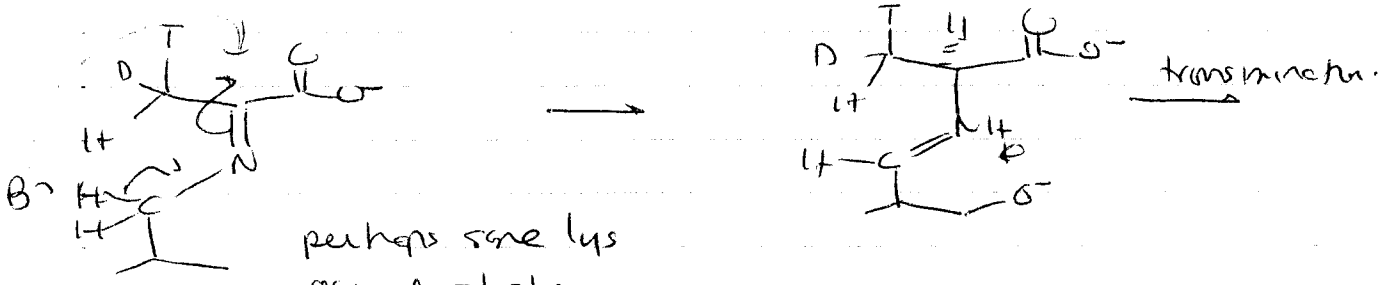
Key residues K209
Y111
and D84 that position the pyridine of PLP

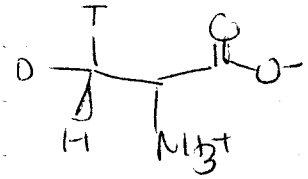
2. Proposed Mechanism: First step is transamination
This RXN is a Claisen RXN in reverse





observed product





Need to convert alanine to acetate w/o modifying the integrity of the methyl group