Module 6

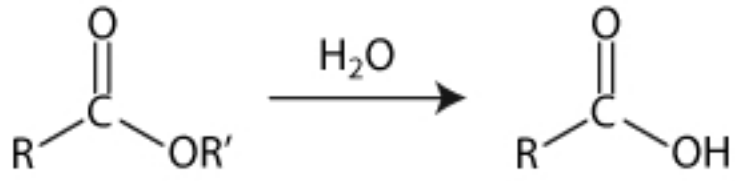
Reactions of Carboxylic Acid Derivatives

(plus extras)

Session Slides with Notes

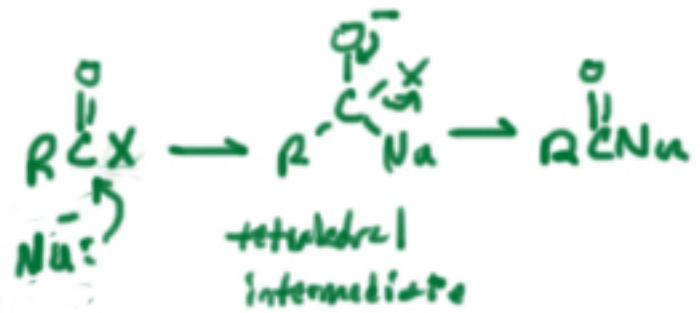
Carboxylic Acid Derivatives

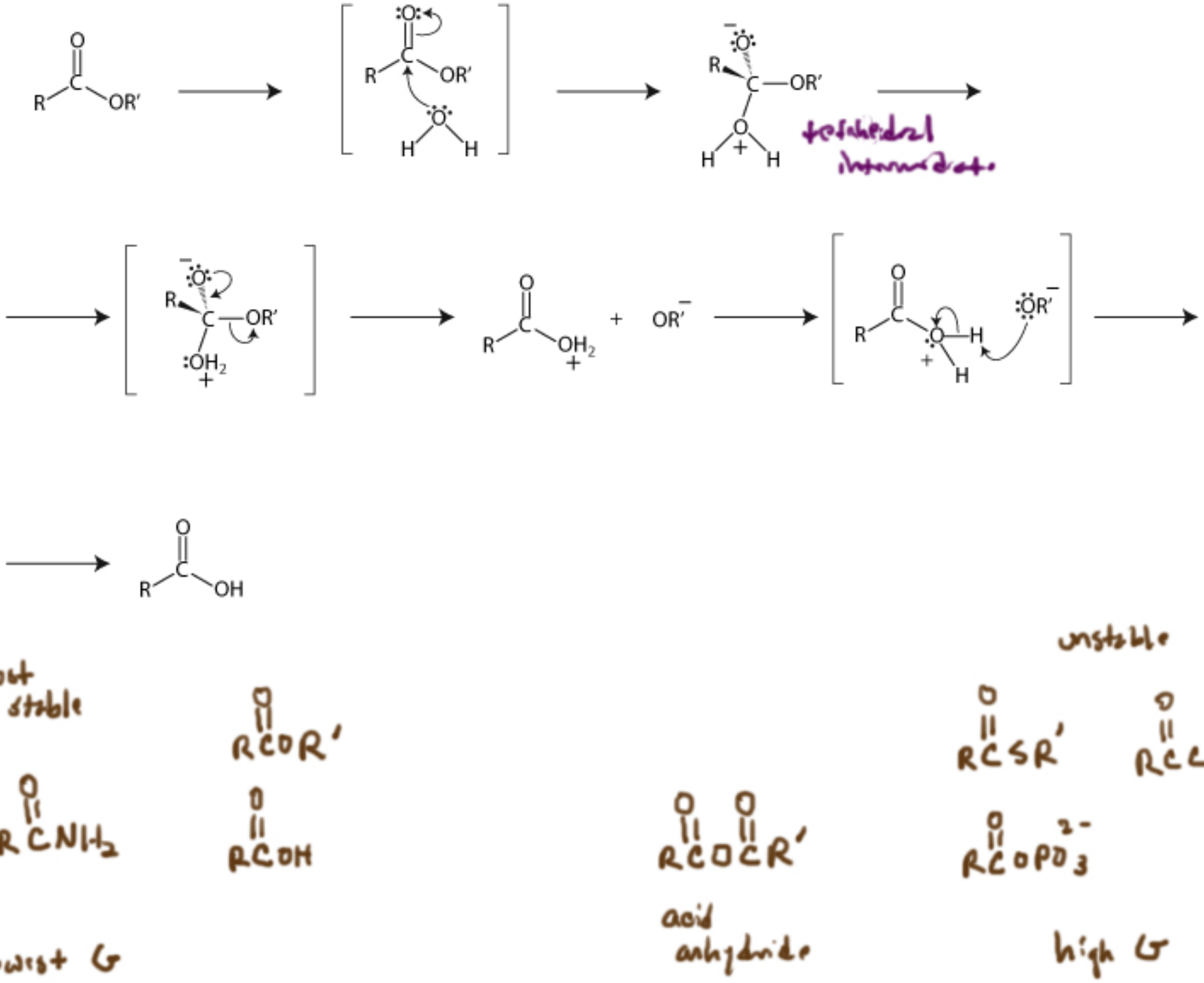
Hydrolysis of an Ester



Ester → Carboxylic Acid

Nucleophilic Acyl Substitution





Most stable

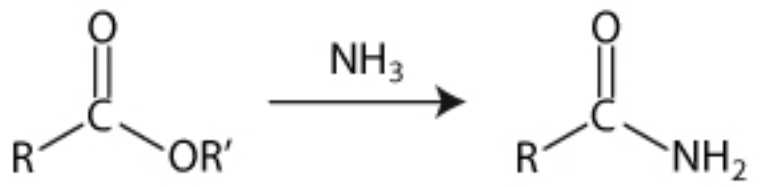
acid anhydride

unstable

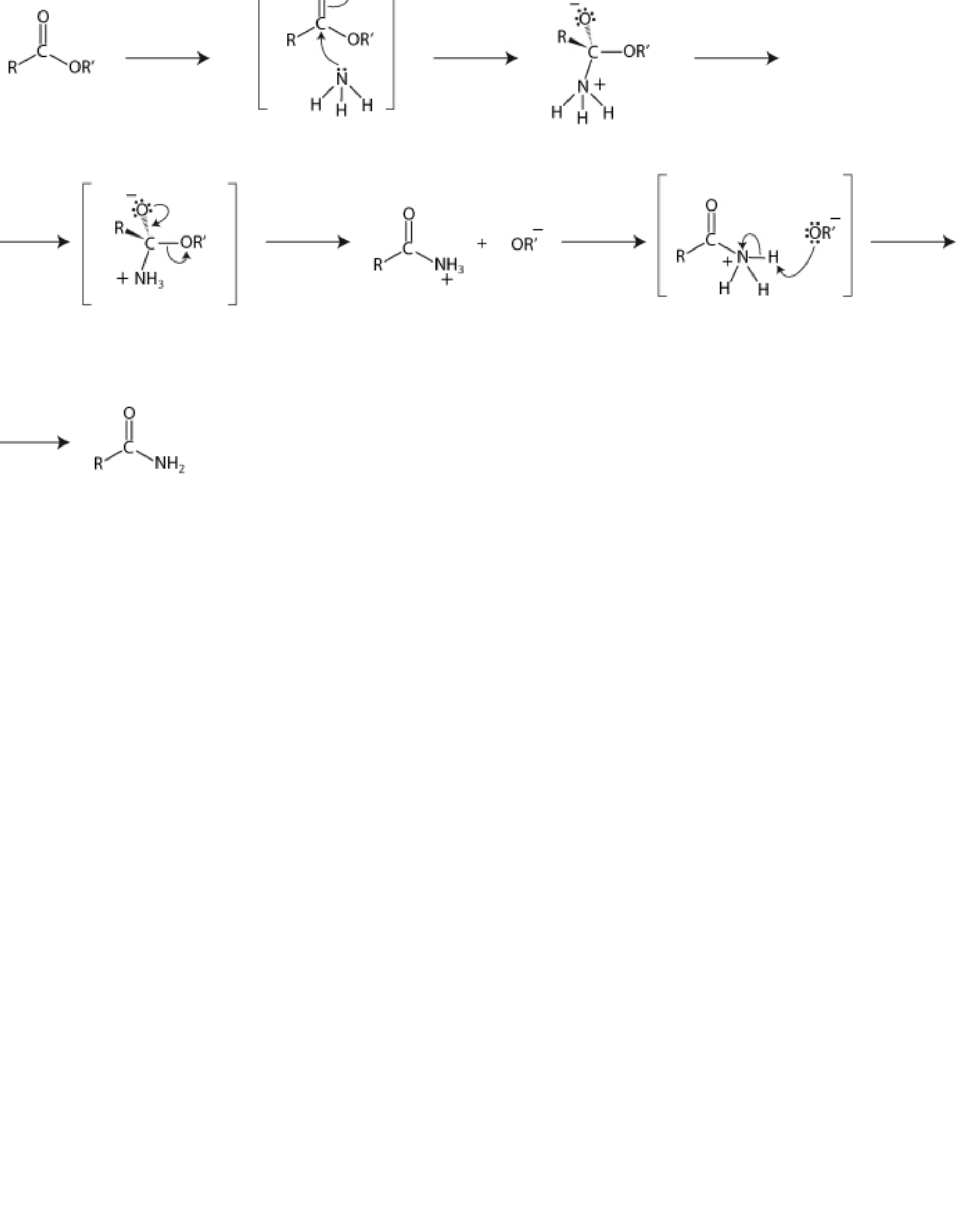
lowest G

high G

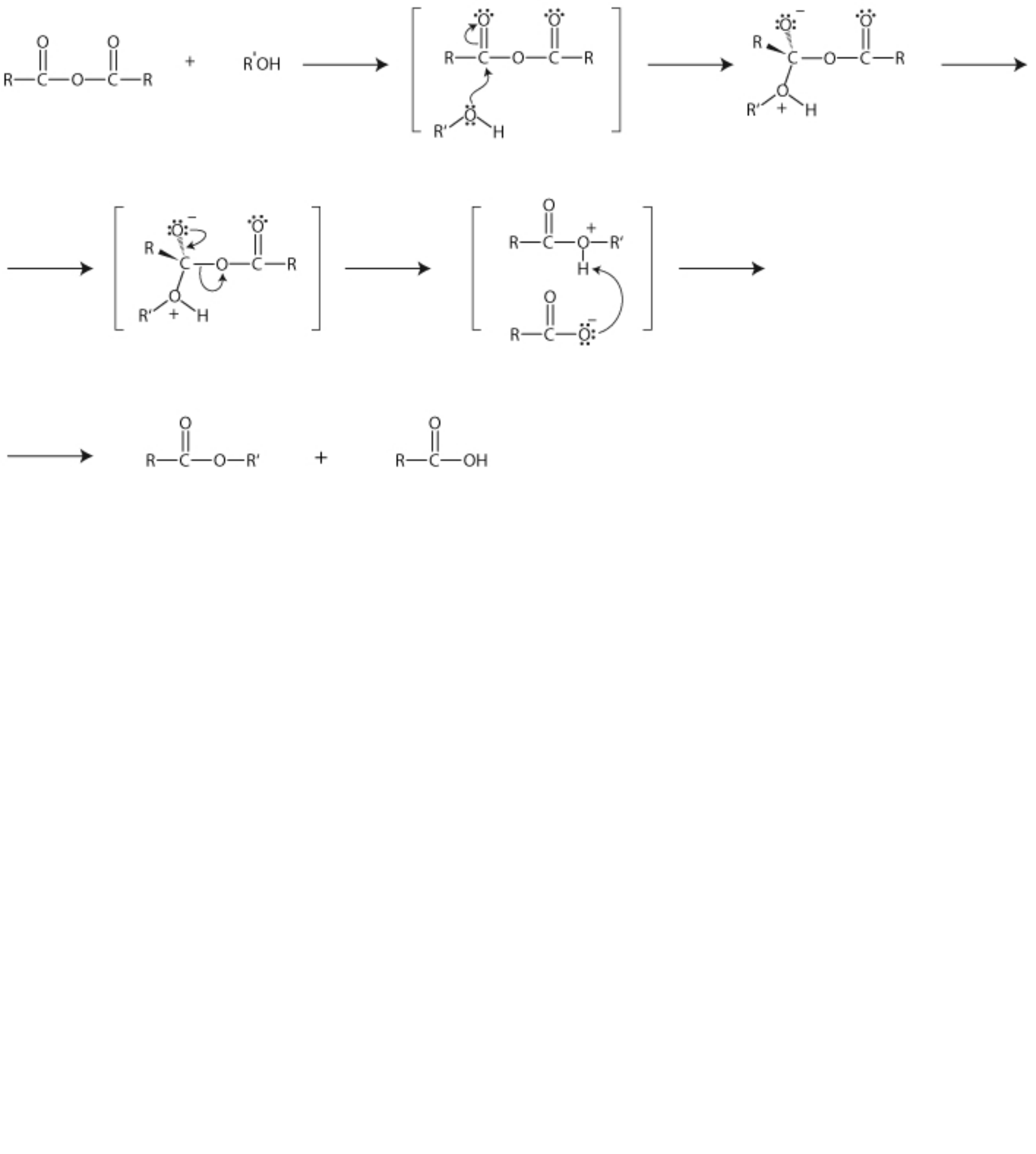
Aminolysis of Ester



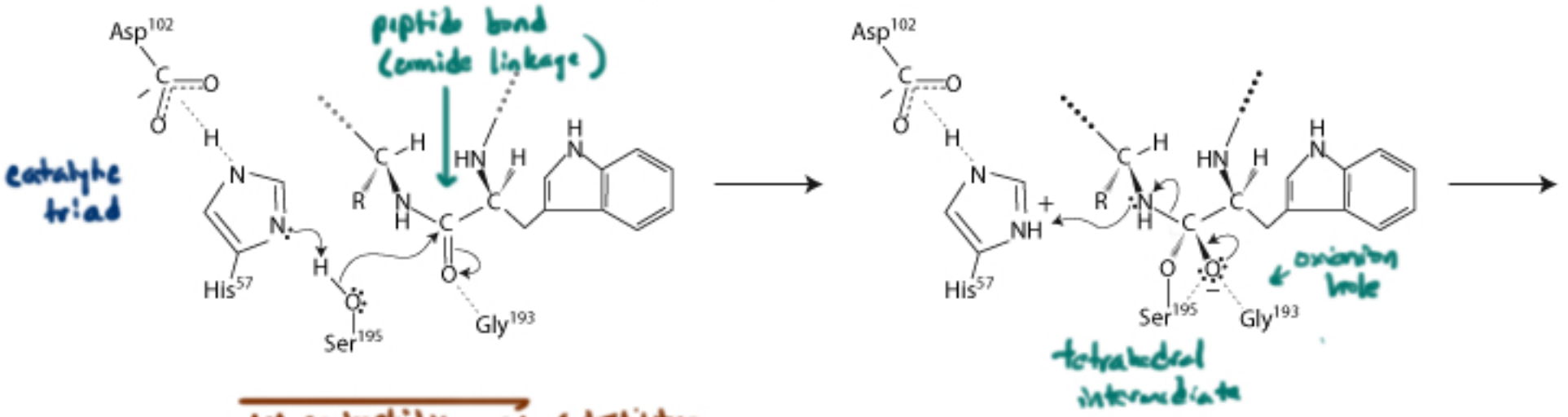
Ester → Amide



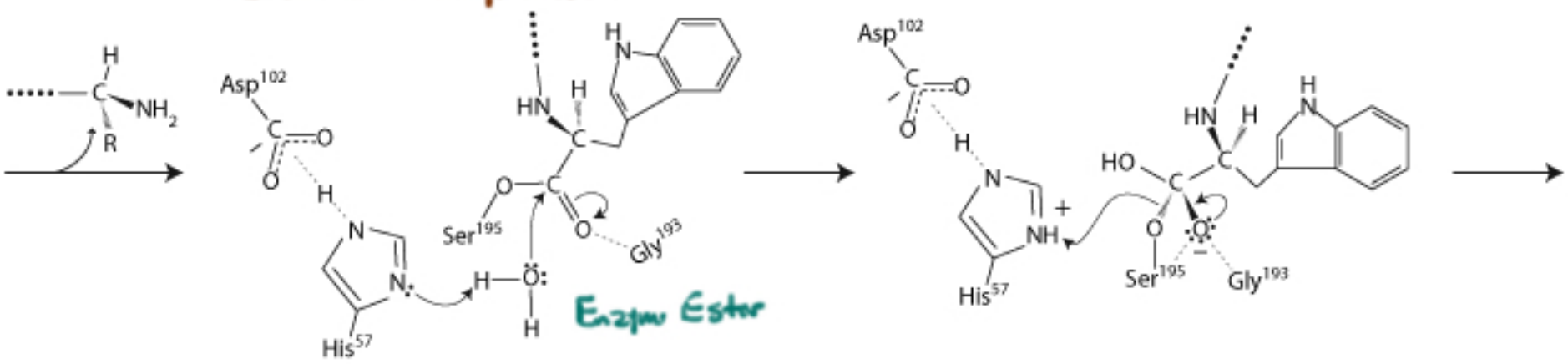
Esterification of an Anhydride



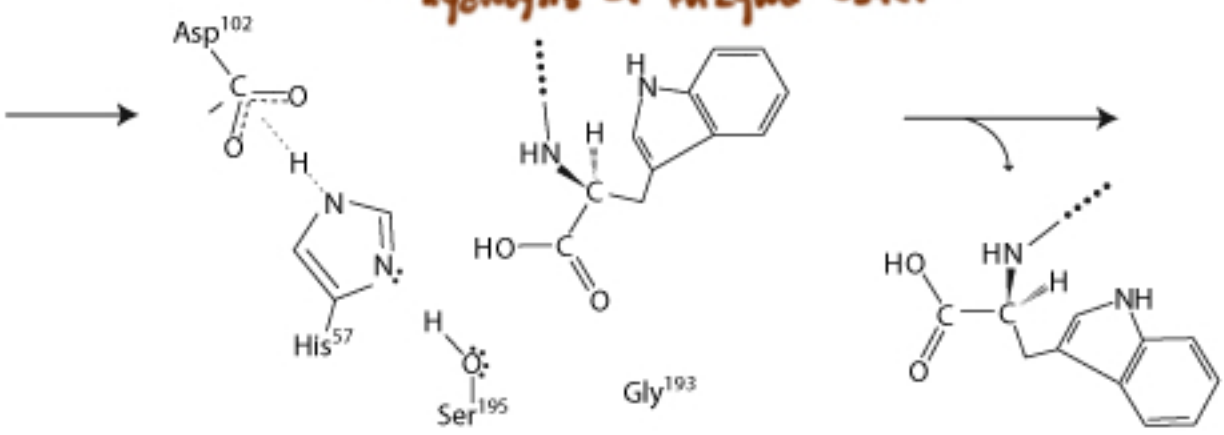
Chymotrypsin - A serine protease



1st nucleophilic acyl substitution
- formation of enzyme ester

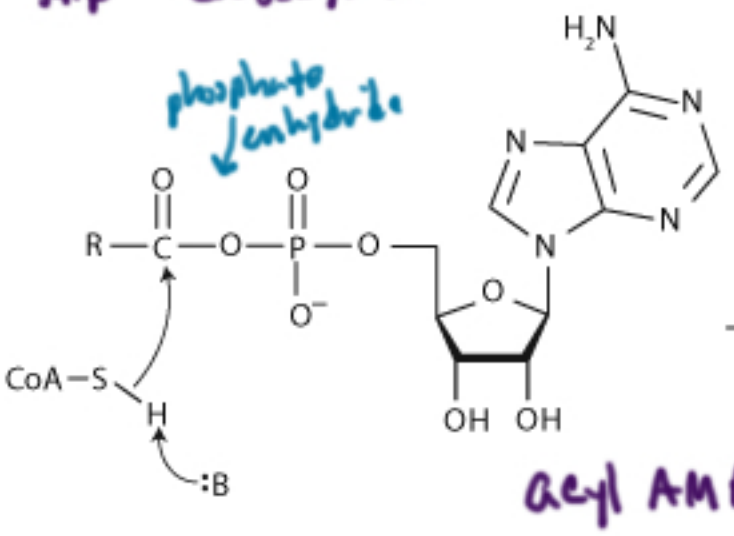


2nd acyl substitution
- hydrolysis of enzyme ester



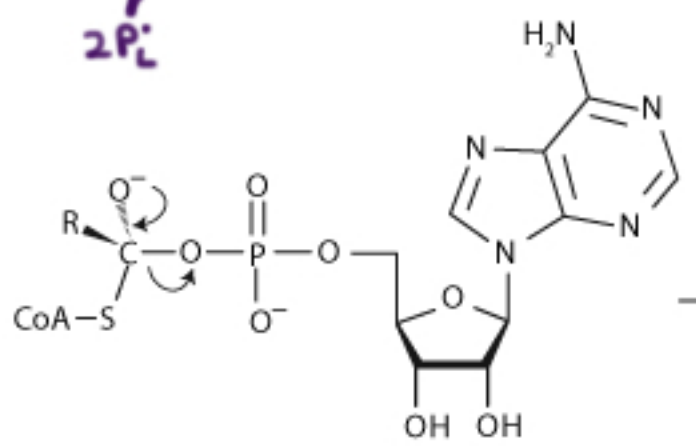
previous step : fatty acyl carboxylate + ATP → acyl AMP + PP_i → 2 P_i

Fatty Acid Activation



Acyl AMP

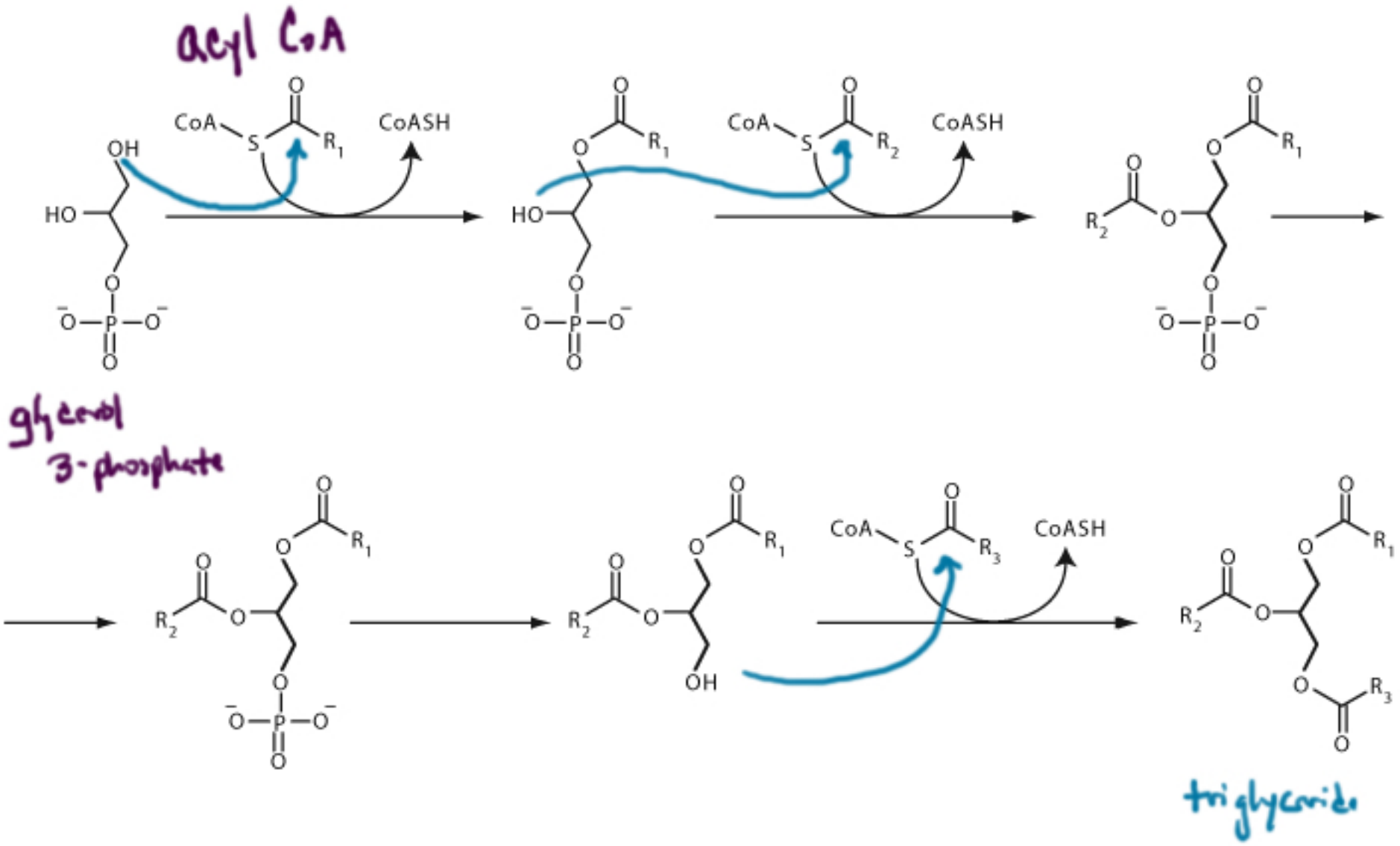
Acyl Coa synthetase →



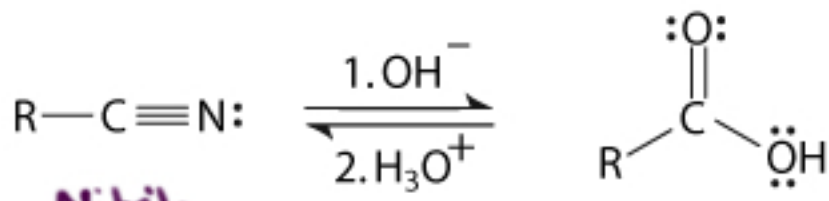
Acyl Coa synthetase →

Acyl Coa synthetase →

Fatty Acyl CoA


acyl CoA
CoA
S
R1
CoASH
OH
HO
O
P
O
glycerol
3-phosphate
R2
R3
triglyceride

Nitrile Hydrolysis

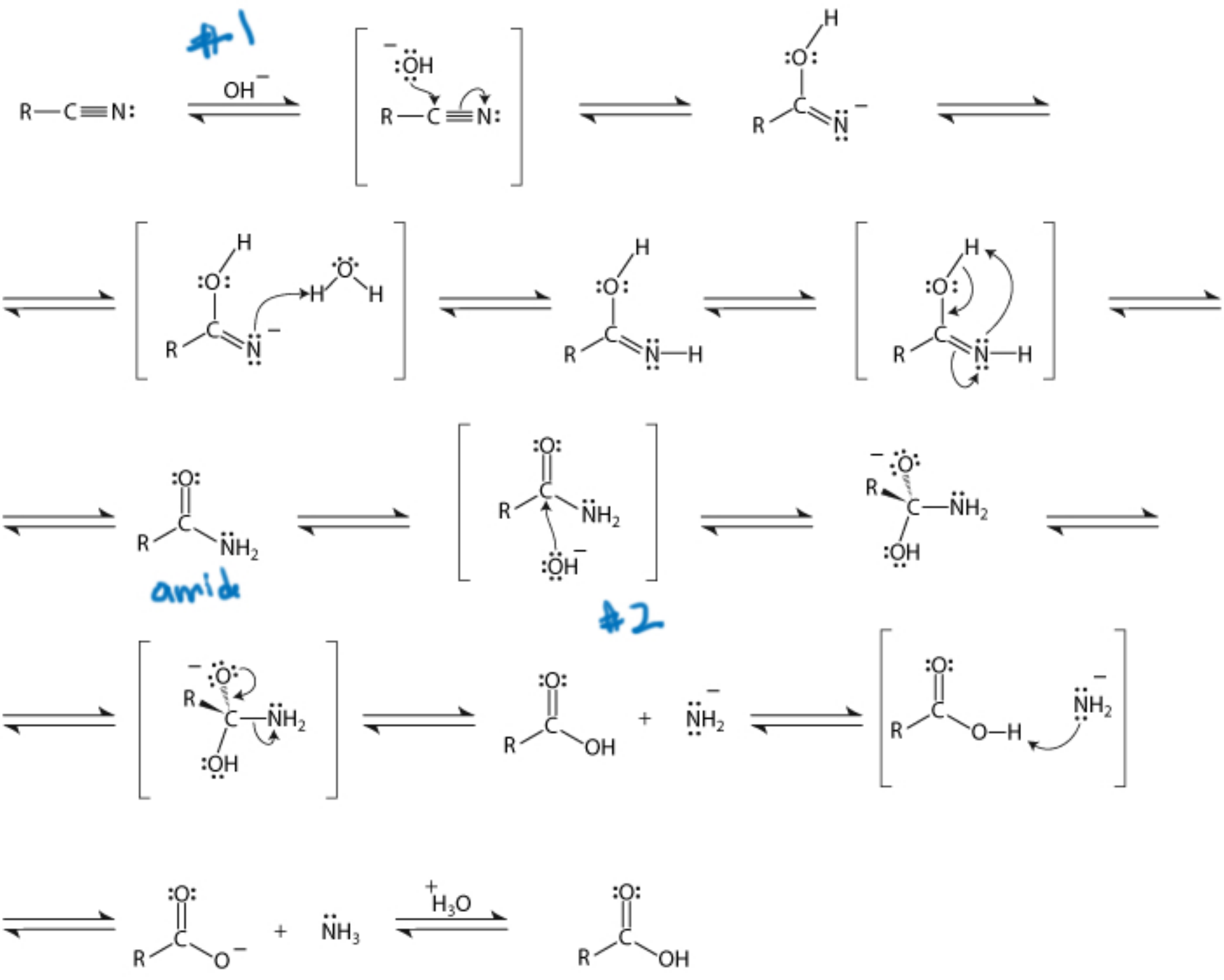


Nitrile

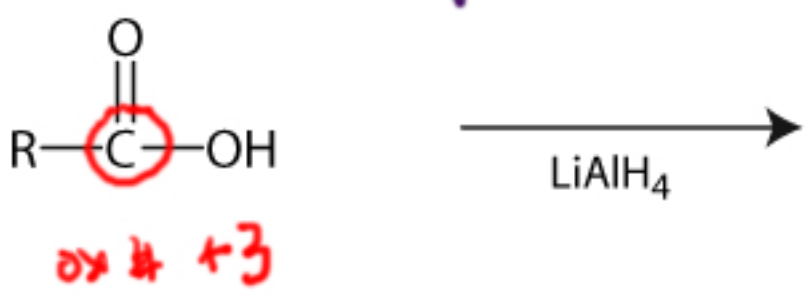
R-C≡N
| 2 H₂O
| (or OH)

R-C(=O)-OH

#1



Reduction of Carboxylic Acid



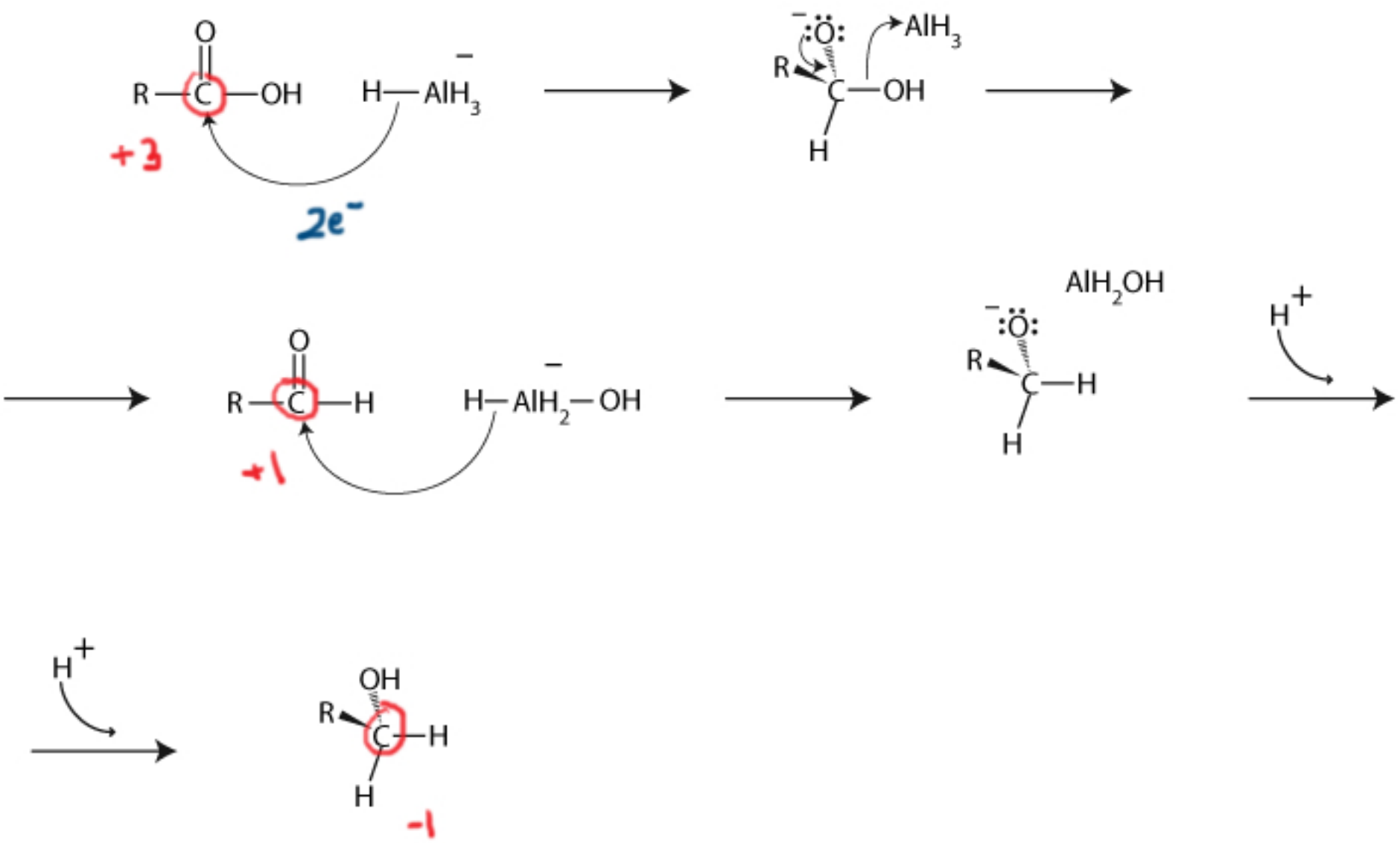
ox # +3

ox # -1

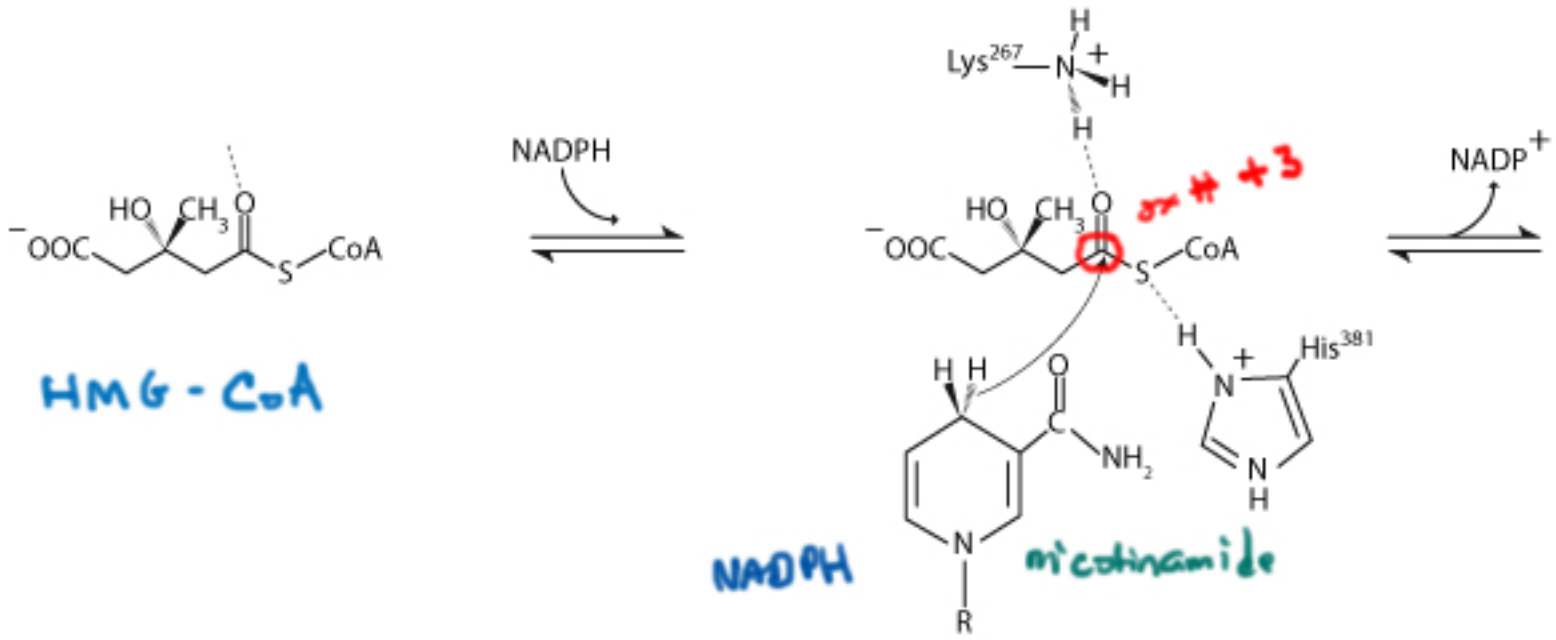
ROH most reduced

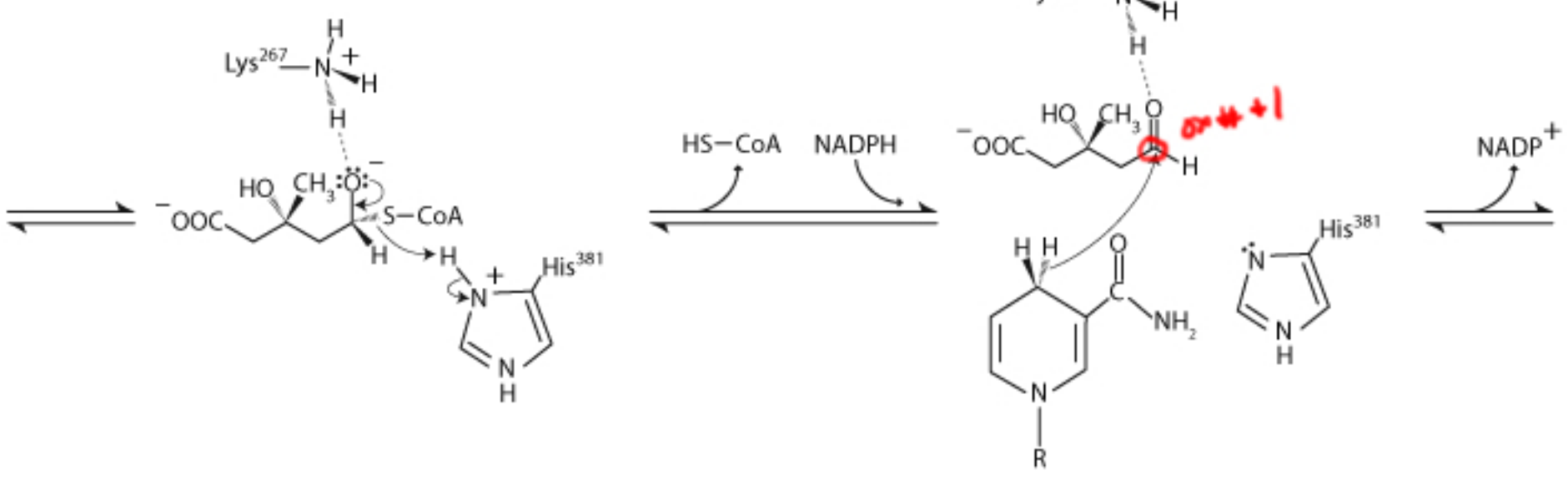
RCH

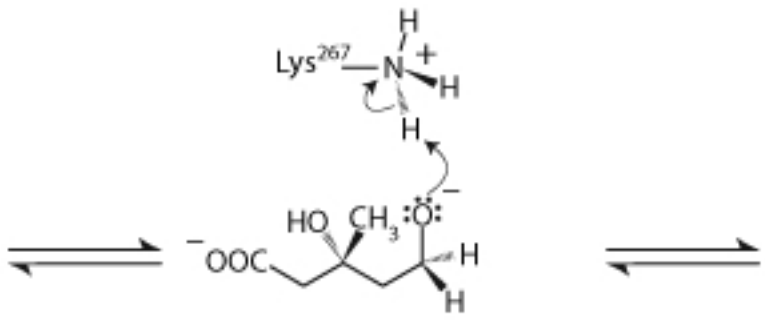
RCOH most oxidized



HMG-CoA Reductase







mevalonate

↓

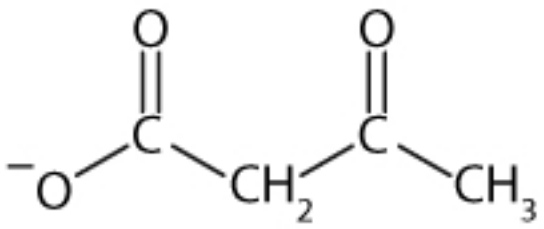
isopentyl pyrophosphate

↓

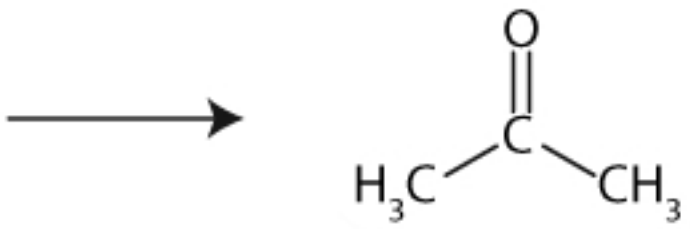
isoprenoid lipids + cholesterol ad steroids

β Keto Acids Decarboxylate Easily

β Keto Acid

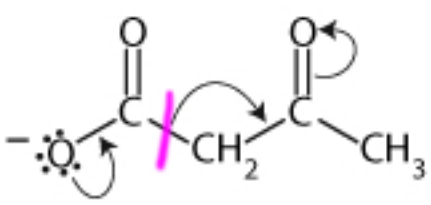


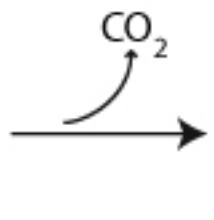
acetoacetate (ketone body)

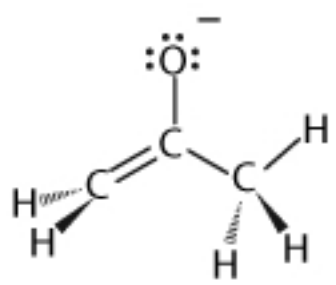


Acetone

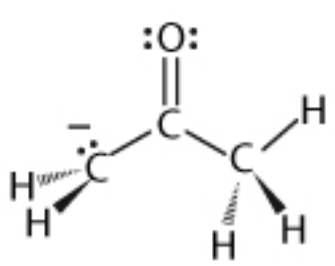
+ CO_2

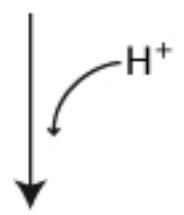


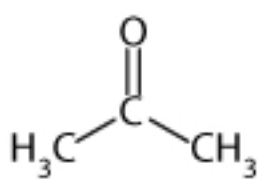


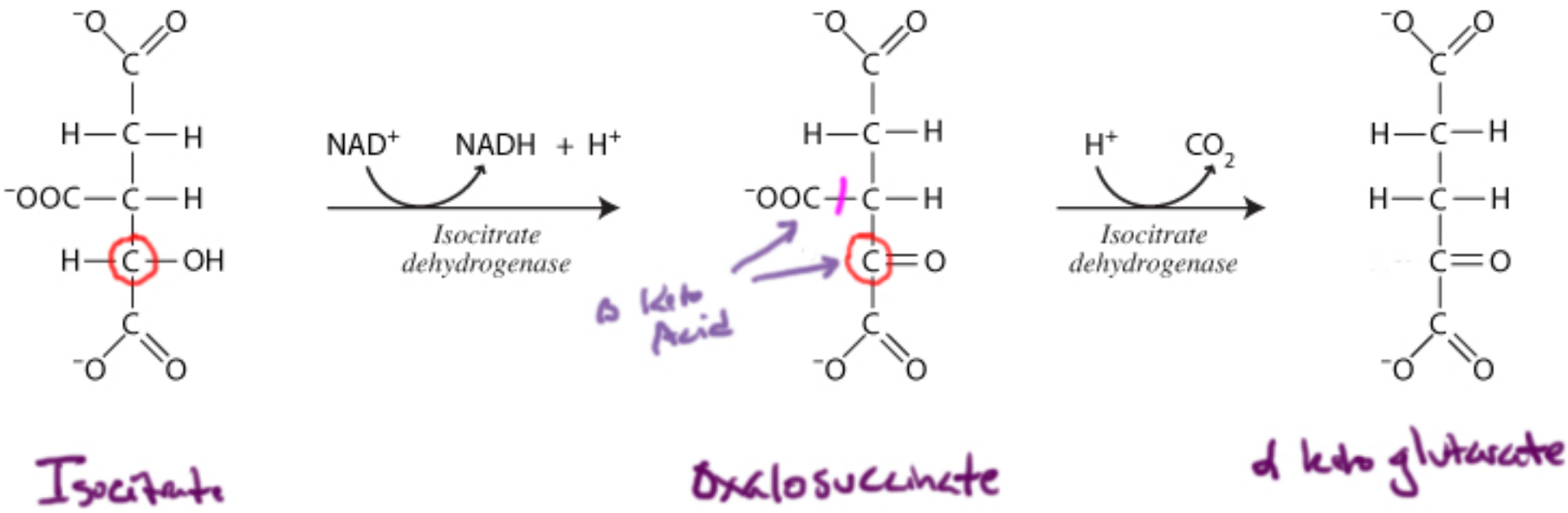


Resonance Stabilized Enolate







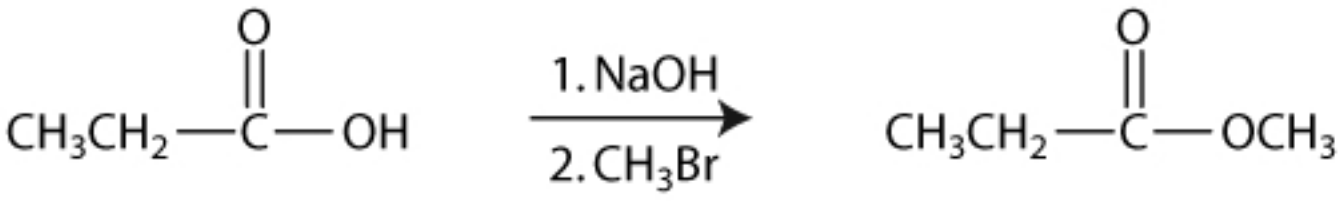


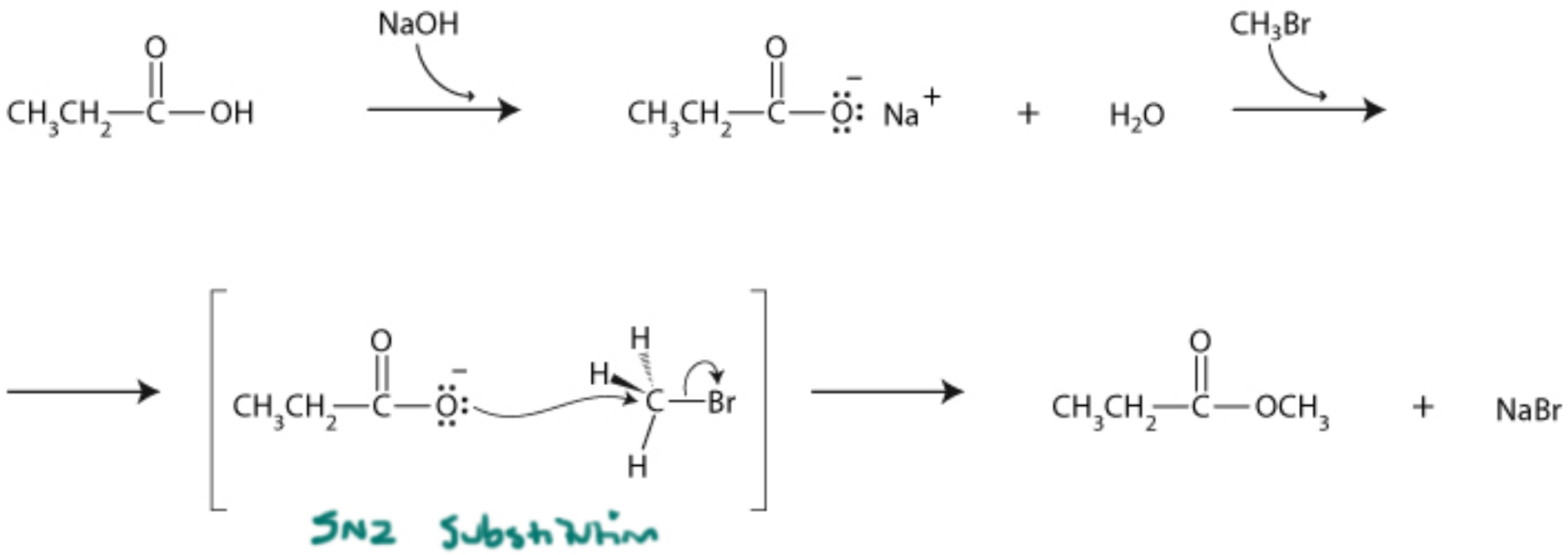
Isocitrate

Oxalosuccinate

α keto glutarate

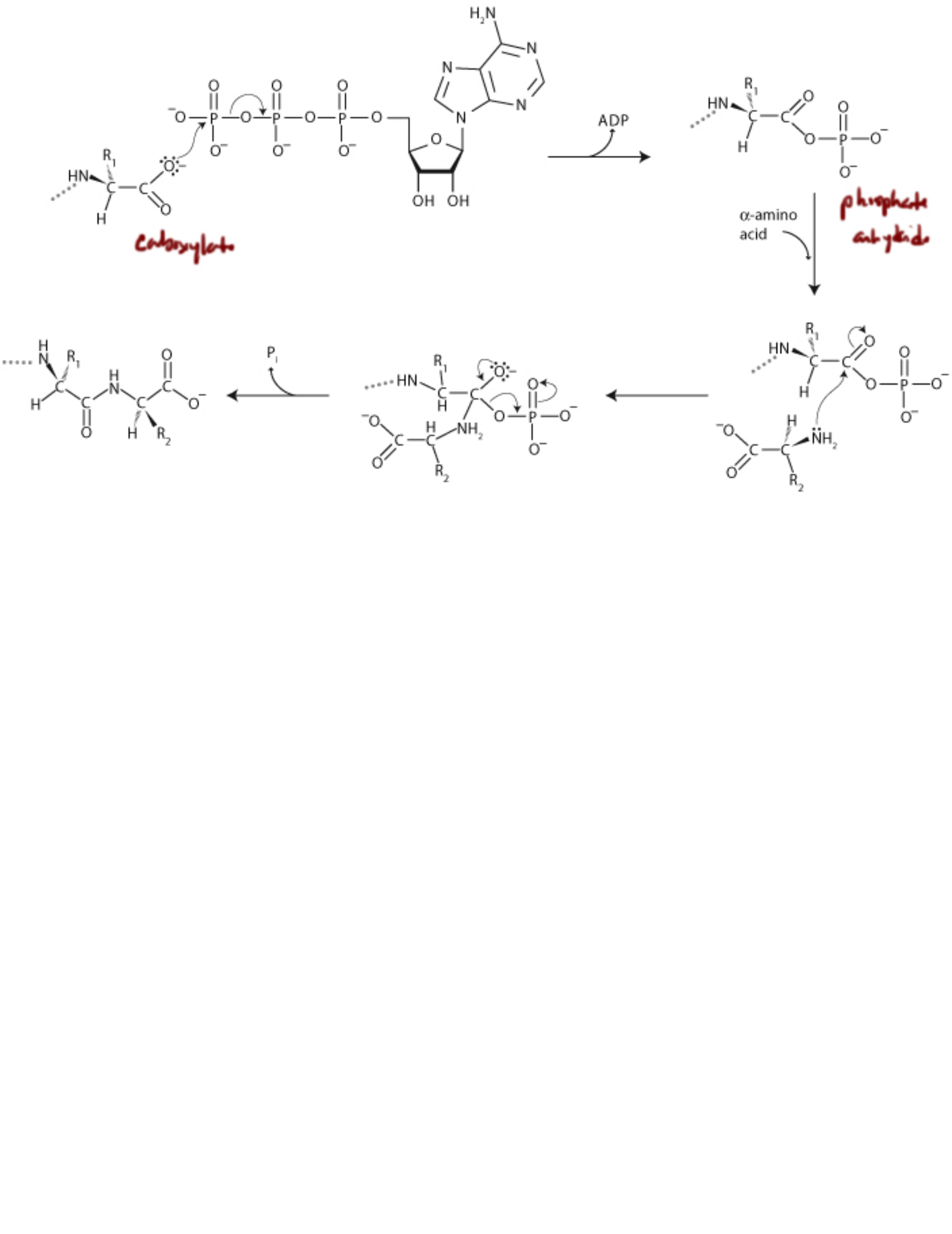
Use of Carboxylate Nucleophile

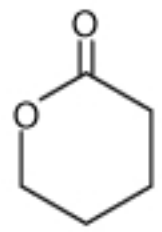




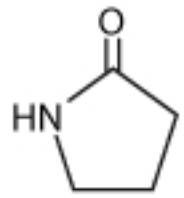
SN2 Substitution

Abiotic Peptide Bond Formation





Lactone



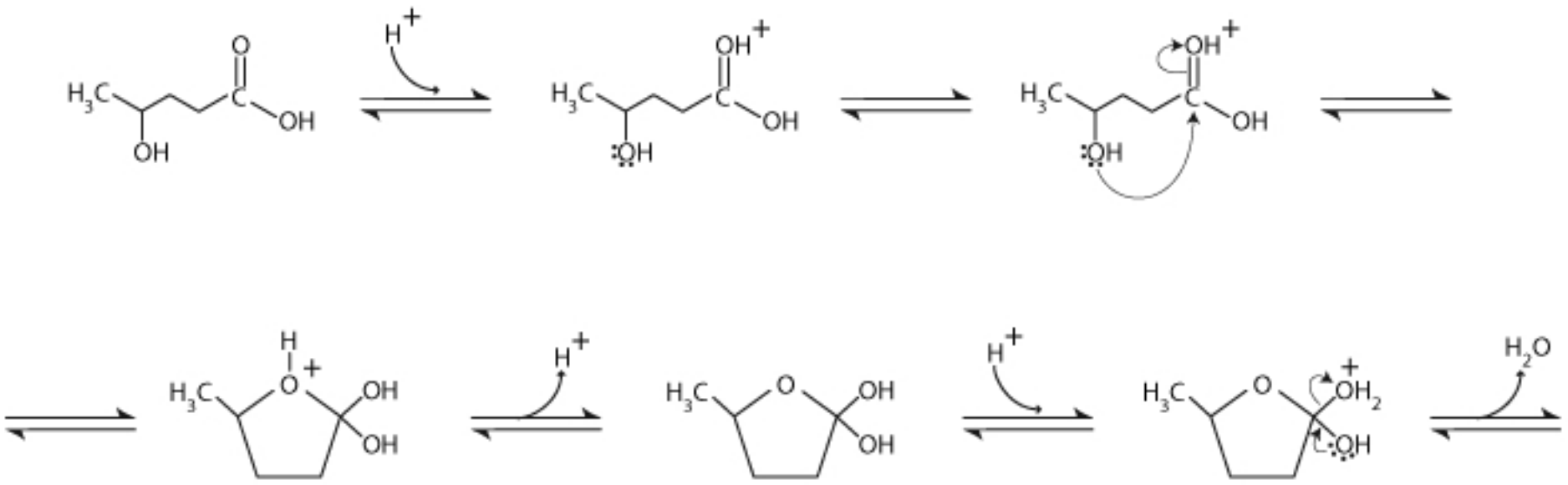
Lactam

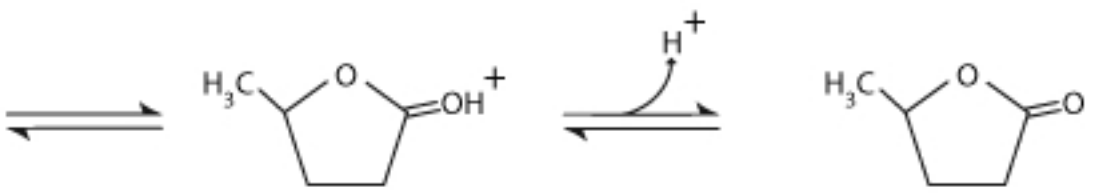
β - 4 membered

γ - 5 membered

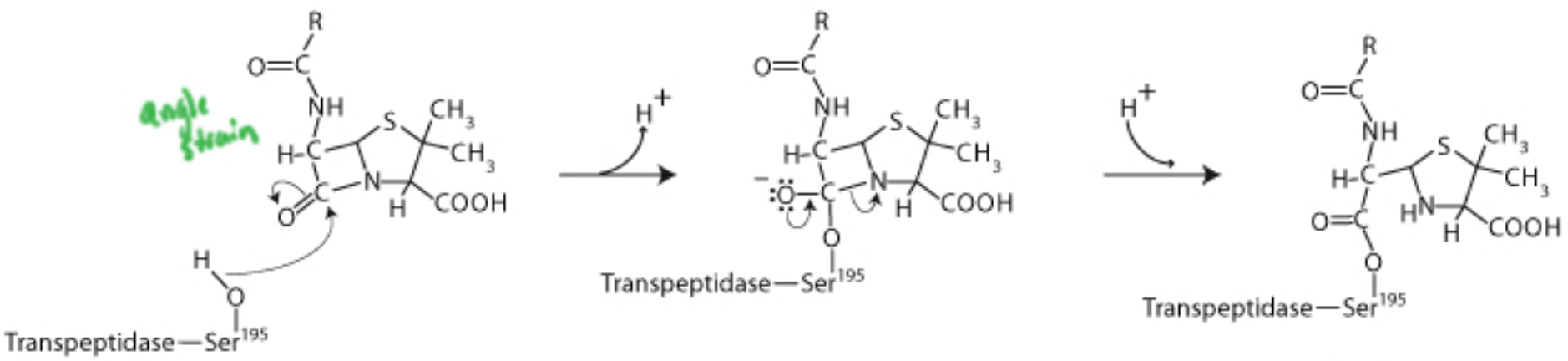
δ - 6 membered

supplemental (Intramolecular acyl substitution)





Penicillin



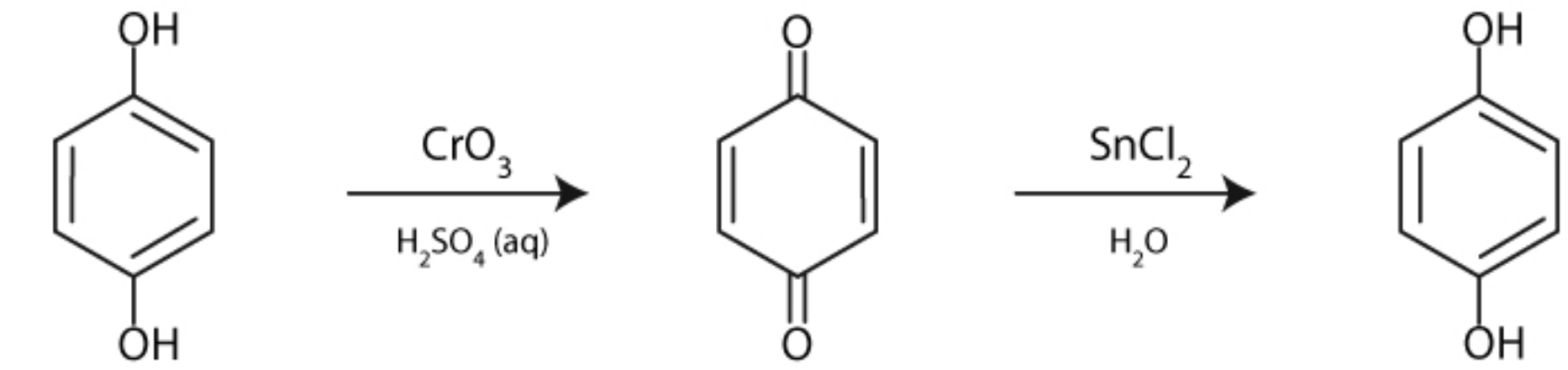
suicide inhibition

Bacterial cell wall -

comprised of peptidoglycan

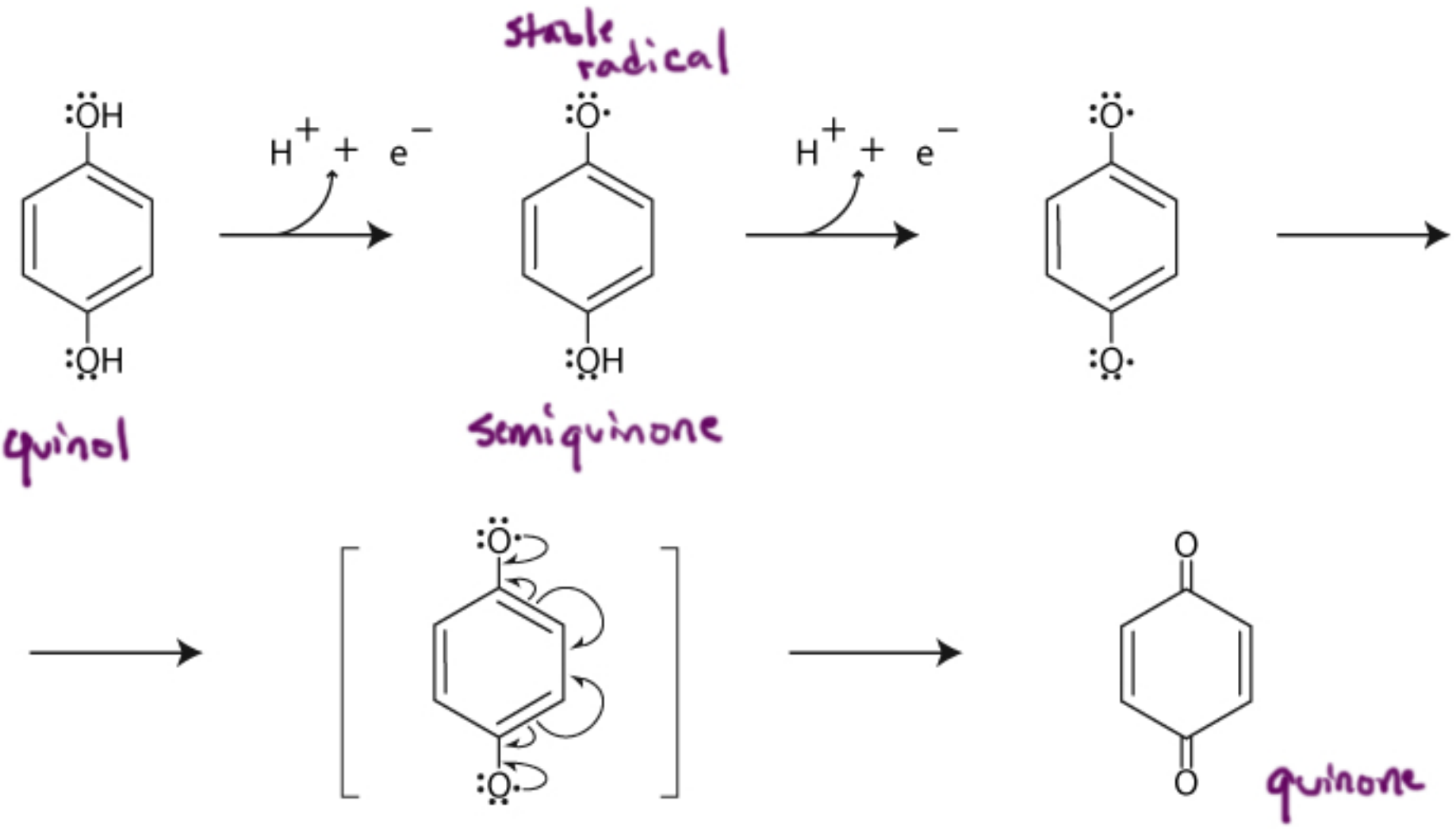
- long chains of NAG (N-acetyl glucosamine)
  NAM (N-acetyl muramic acid)
- with peptide crosslinks formed by transpeptidase

Oxidation of Dihydroxybenzene

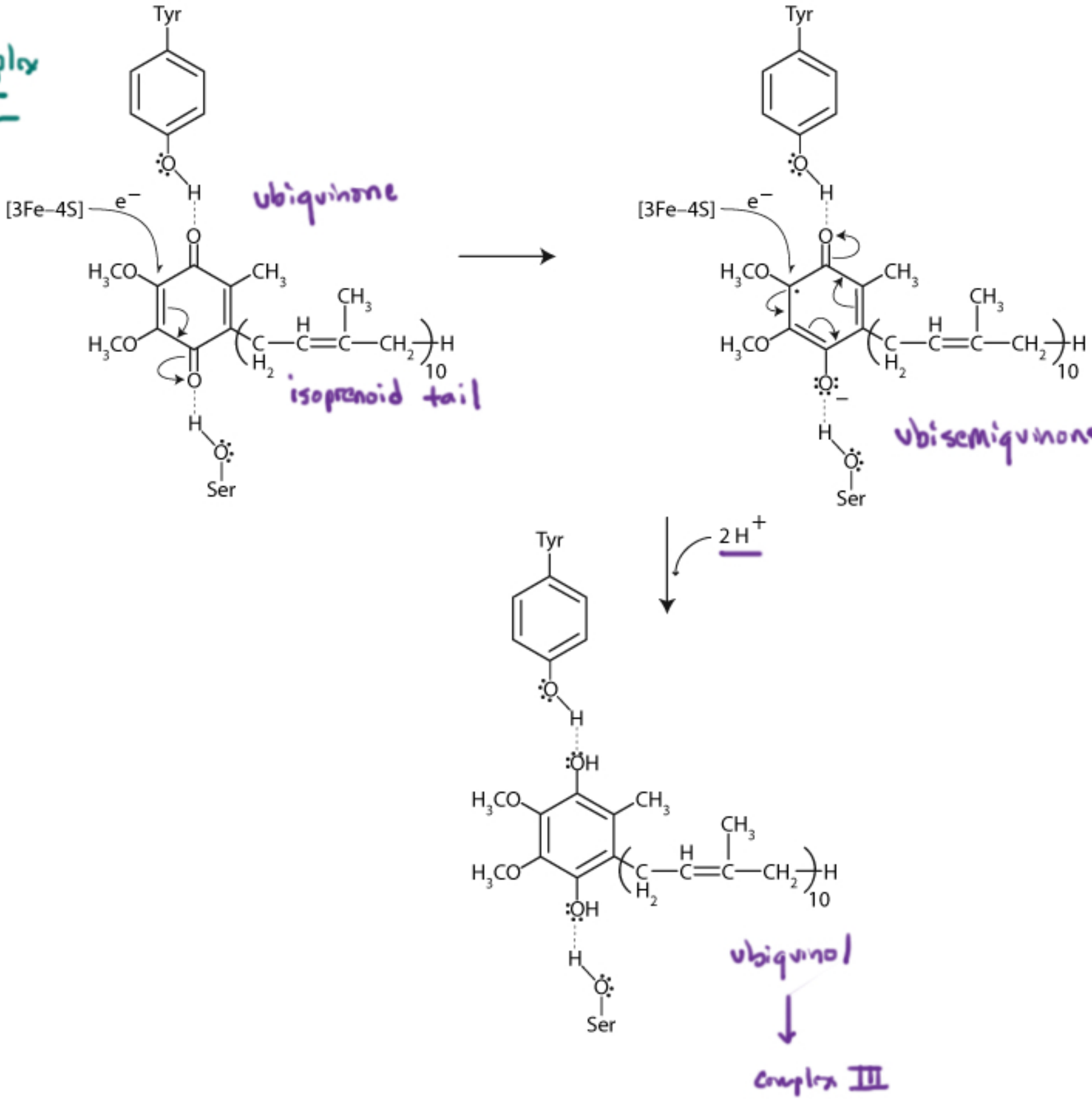


Dihydroxybenzene

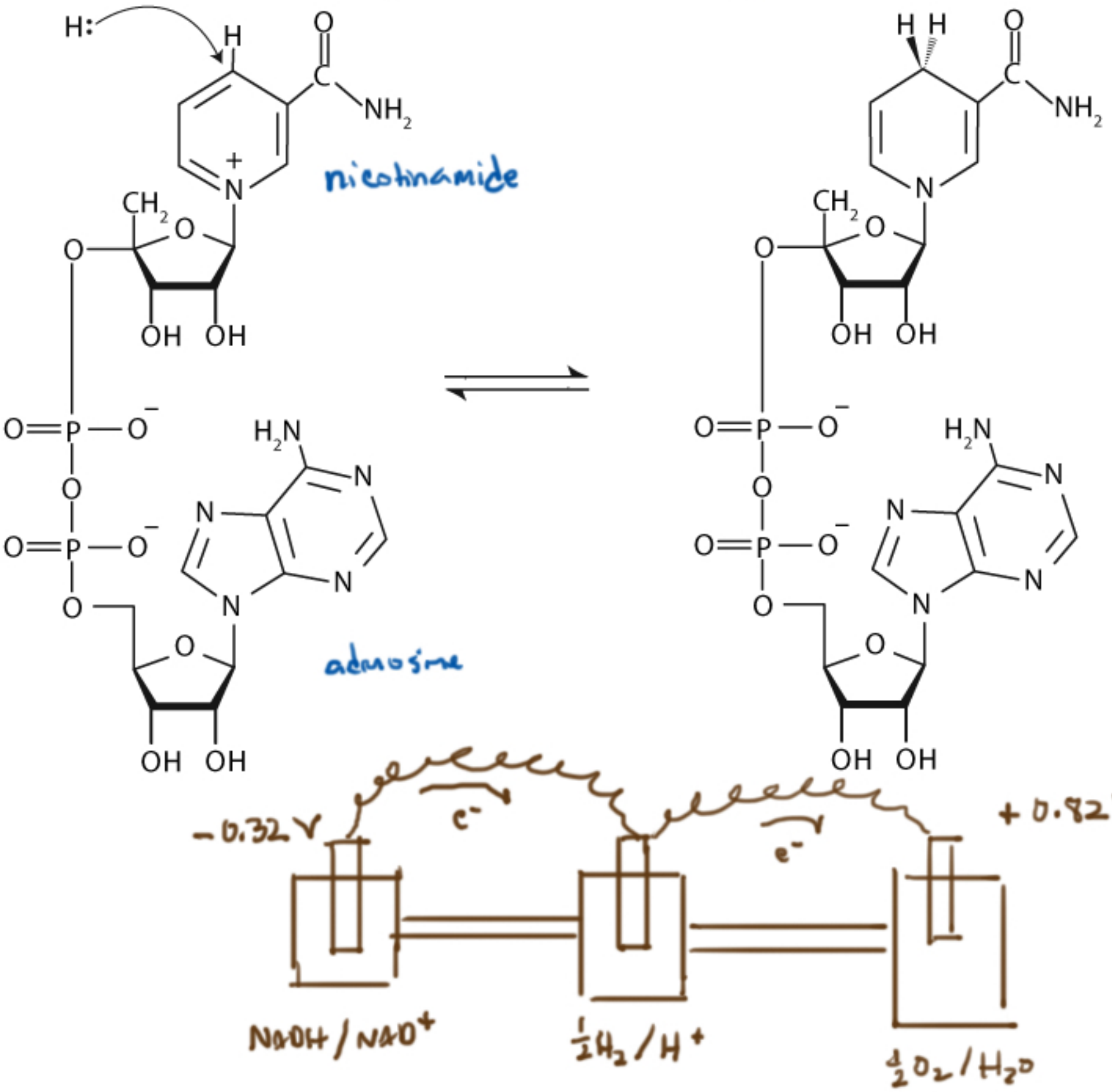
Benzoquinone



Complex II


Tyr
[3Fe–4S]
e⁻
ubiquinone
isoprenoid tail
Ser
ubisemiquinone
2 H⁺
ubiquinol
Complex III

Reduction of NADH



$$E_{cell} = E^{\circ}_{cathode} - E^{\circ}_{anode}$$

$$= 0.92\,V - (-0.32\,V) = 1.14\,V$$

Flavin (isoNoxazine ring)