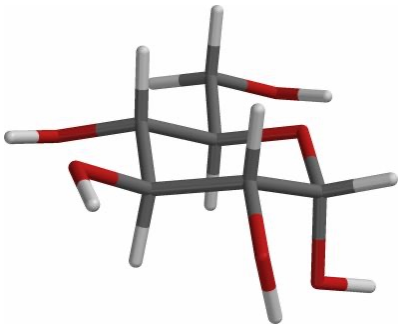

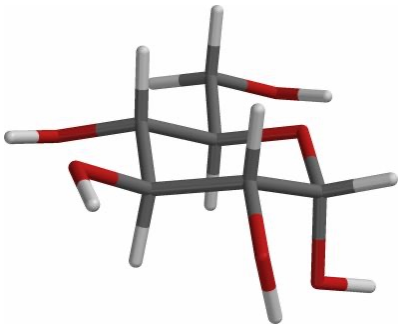

Chem 109 C
Bioorganic Compounds

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Protein Structure and Analysis (Ch 21)

structure: primary, secondary, tertiary, quaternary
parameters of alpha-helix, beta sheet, loops/coils and tertiary structures

structure determination, reagents:
$HSCH_2CH_2OH$
6M HCl

Edman's reagent
cyanogen bromide BrCN

exopeptidases: **carboxypeptidase A**
carboxypeptidase B

endopeptidases:
trypsin
chymotripsin
elastase

Catalysis (ch 22)

definition of catalyst, energy diagrams illustrating catalytic action

types of catalysis:

- acid: specific and general
- base: specific and general
- nucleophilic: stronger Nu are better catalysts
- metal-ion: types of activation

intramolecular reactions

- why are they faster? effective molarity etc...

intramolecular catalysis: examples of each class (acid, base, Nu, metal)

overview of enzyme catalyzed reactions:

- names of enzyme ("substrate" .....ase)
- lock-and-key model
- induced-fit model

examples of enzyme catalysis

- carboxypeptidase A, chymotrypsin: what is going on in the active site (what types of catalysis occur there?)

Coenzymes (ch 23)

NAD^+, $NADP^+$, NADH, NADPH (structure, redox form, reactions)
FMN, FAD, $FADH_2$ (structure, redox form, reactions)

lipoic acid (lipoate, redox forms)

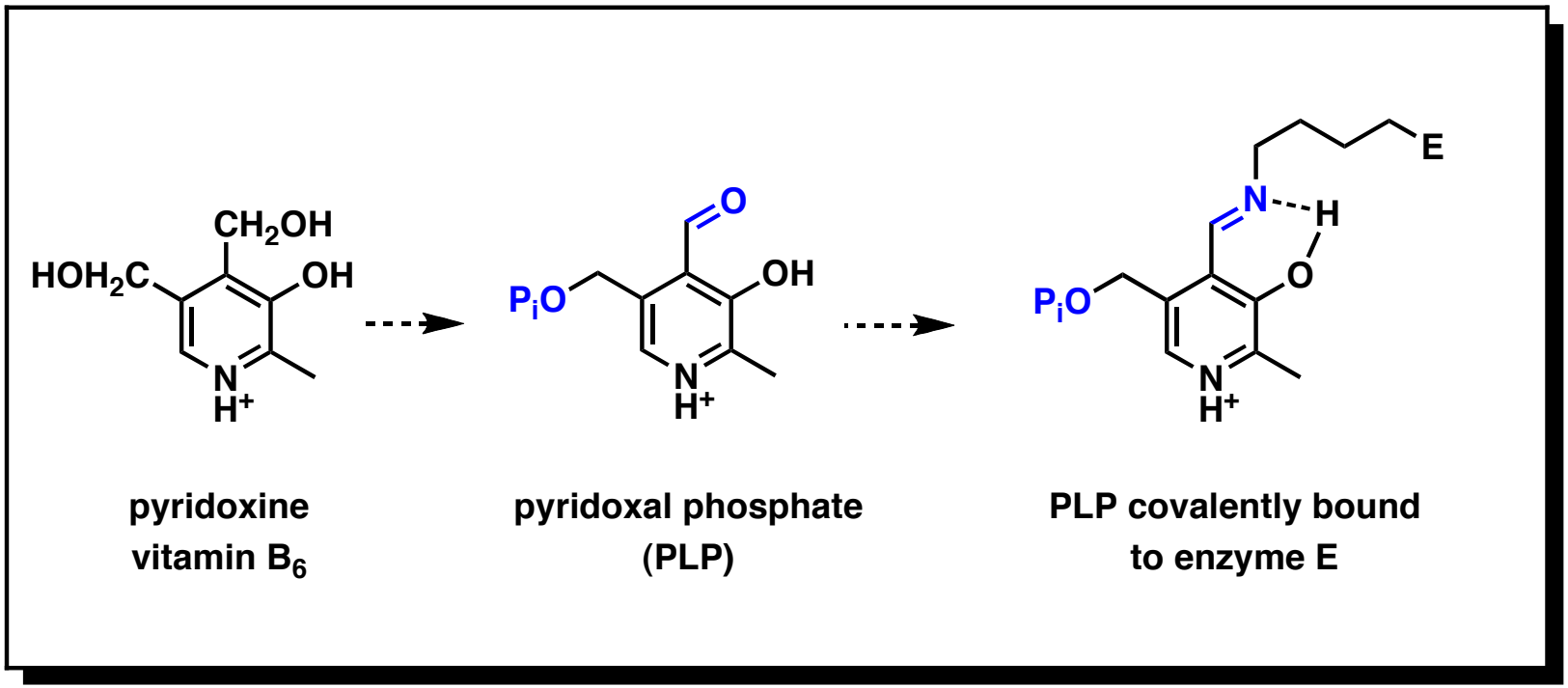
TPP (thiamine pyrophosphate, structure, ylide form, type of reactions, PD complex)

biotin (structure, type of reaction, why ATP, why Mg^{2+}?)

mechanisms

Pyridoxal (PLP)

PLP: from vitamin to active enzyme



pyridoxine
vitamin B_6

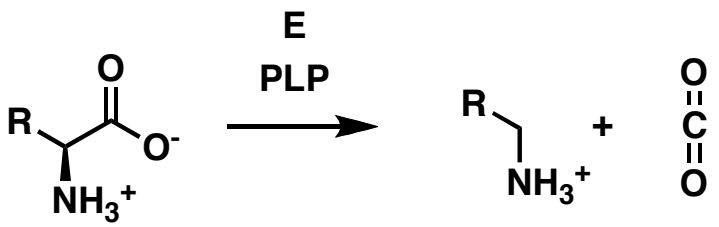
pyridoxal phosphate
(PLP)

PLP covalently bound
to enzyme E

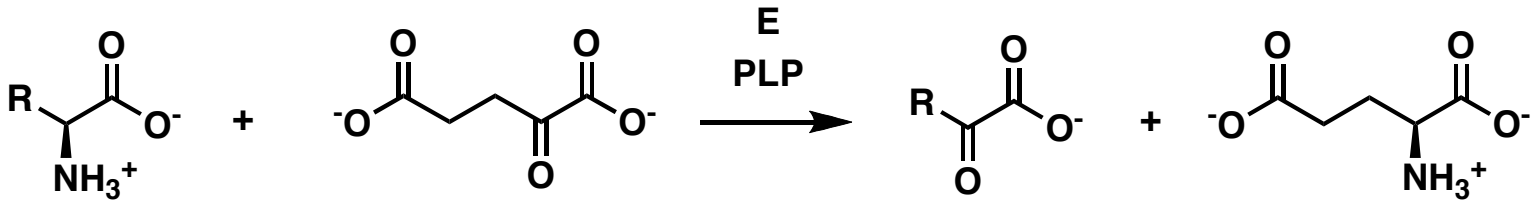
Pyridoxal (PLP)

5 reactions catalyzed by PLP

1 *decarboxylation*



2 *transamination*

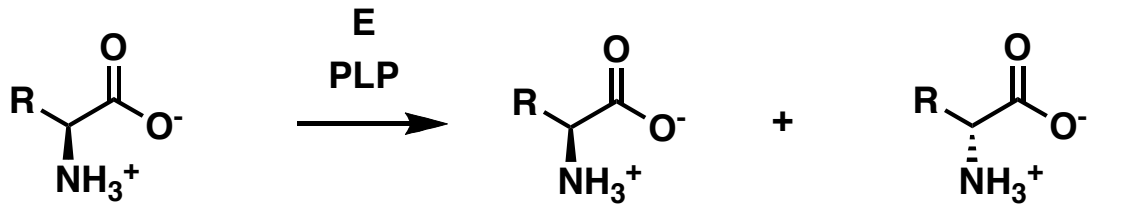


α-amino acid + α-ketoglutarate → α-keto acid + glutamate

Pyridoxal (PLP)

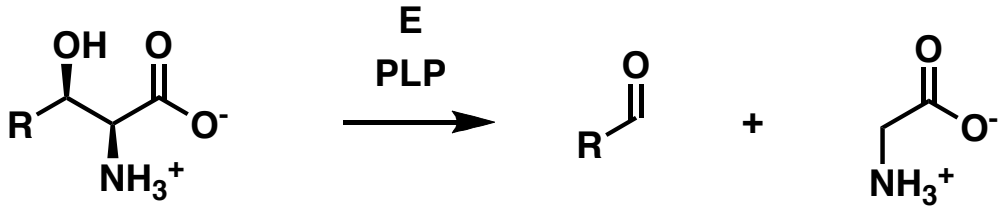
5 reactions catalyzed by PLP

3 *racemization*

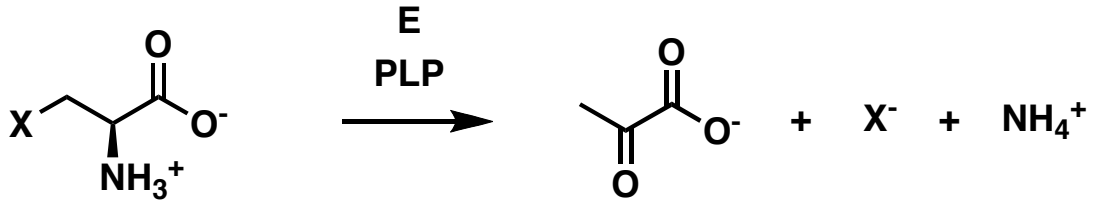


L-α-amino acid → L-α-amino acid + D-α-amino acid

4 *C_α-C_β bond cleavage*



5 *α,β–elimination*

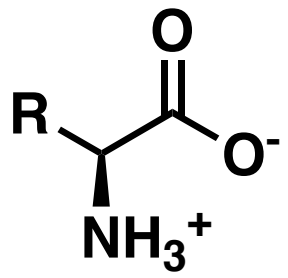


L-α-amino acid → pyruvate + X^- + NH_4^+

Pyridoxal (PLP)

common themes in all reactions with PLP

1. amino acid is the substrate



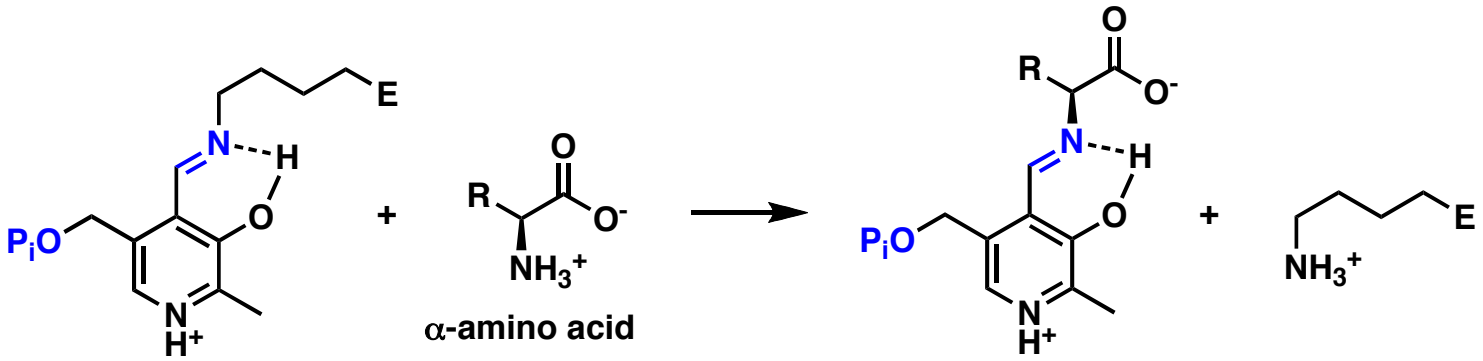
α-amino acid

all reactions take place at the α-carbon, with different bonds involved

Pyridoxal (PLP)

common themes in all reactions with PLP

2. attachment of substrate by transimination:

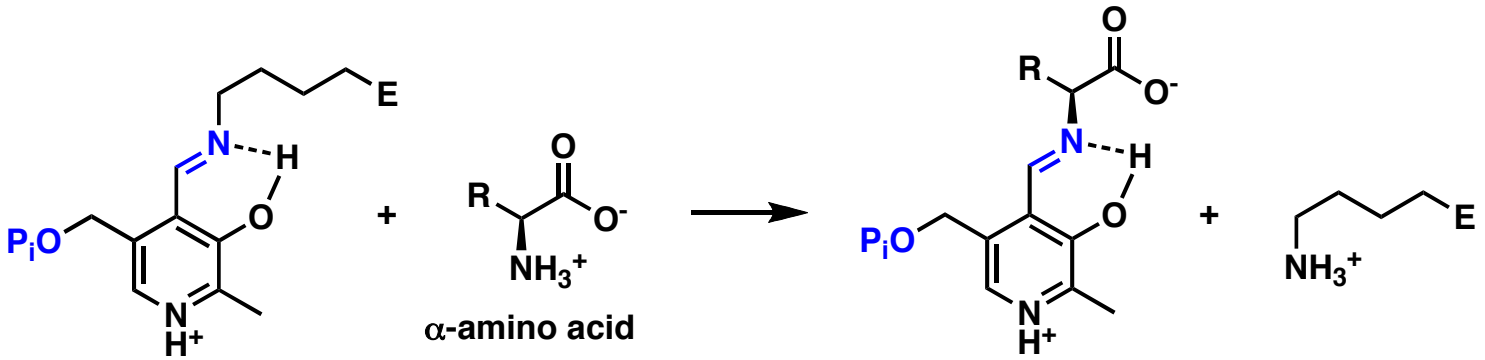


PLP covalently bound to enzyme E

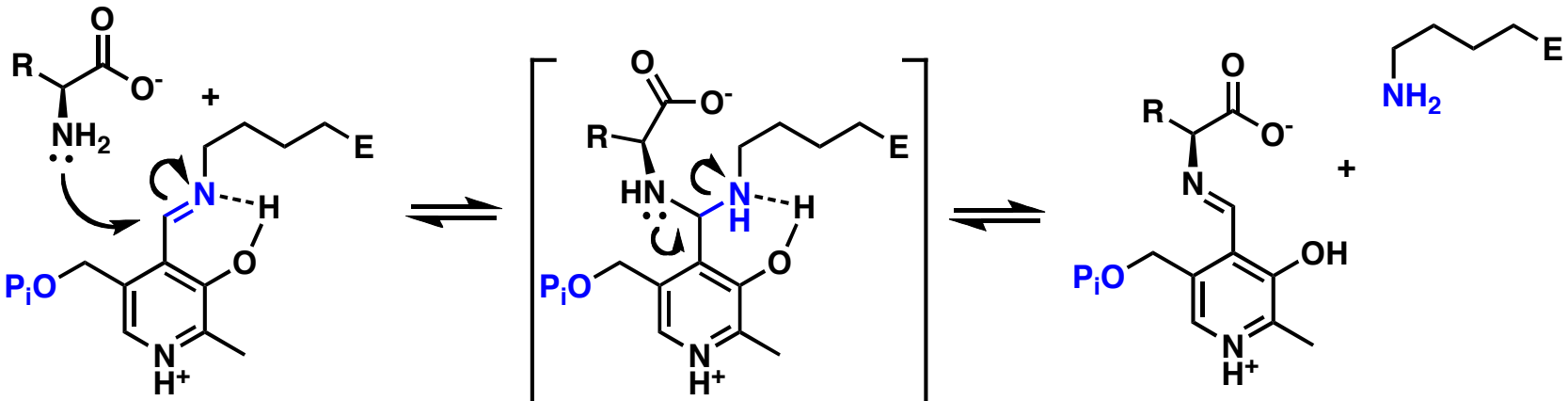
Pyridoxal (PLP)

common themes in all reactions with PLP

2. attachment of substrate by transimination:



PLP covalently bound to enzyme E



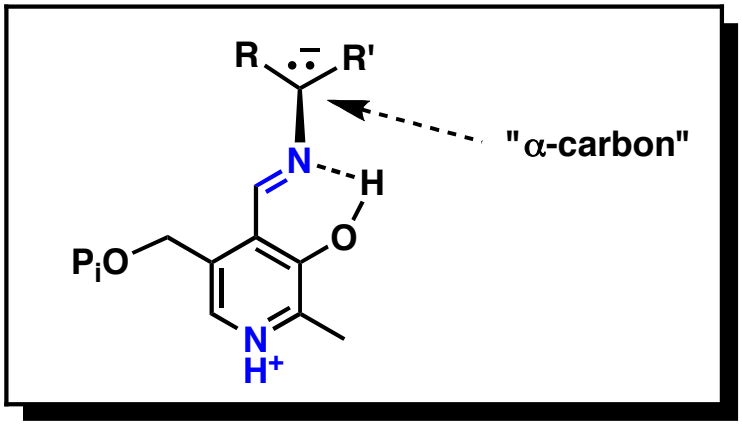
PLP covalently bound to enzyme E

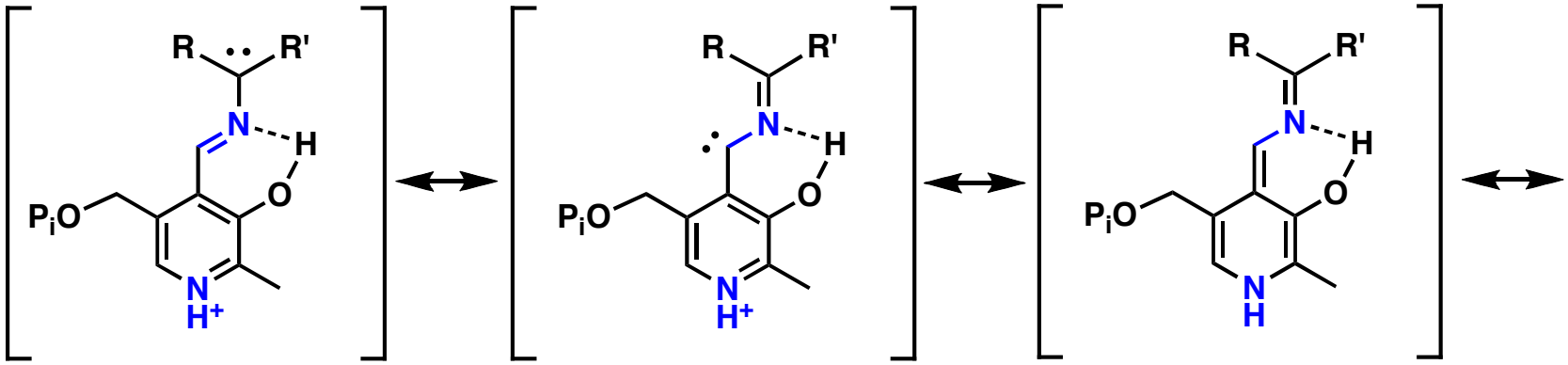
PLP covalently bound to amino acid

Pyridoxal (PLP)

common themes in all reactions with PLP

3. stabilization of negative charge at the α-carbon:

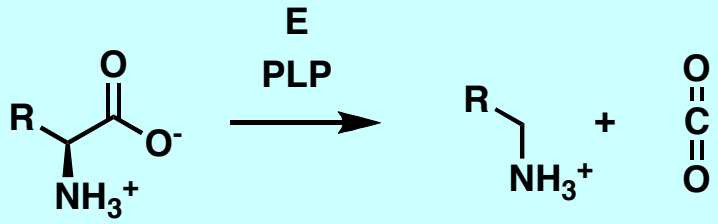


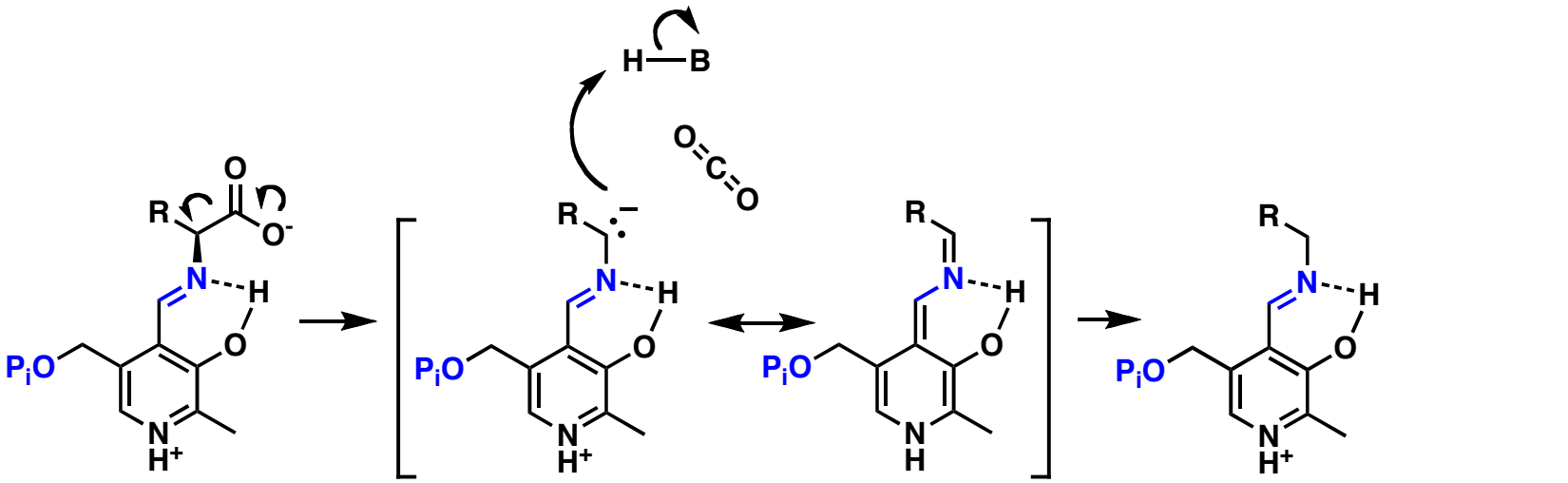


- stabilization through resonance/conjugation

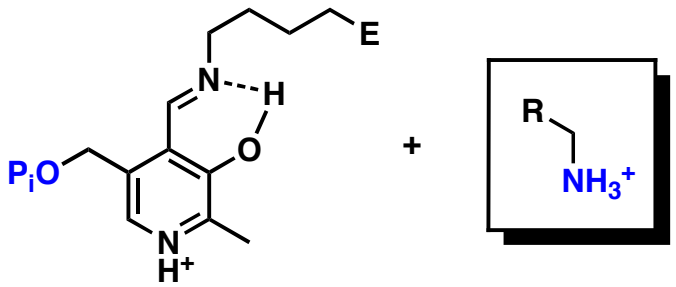
Pyridoxal (PLP)

decarboxylation



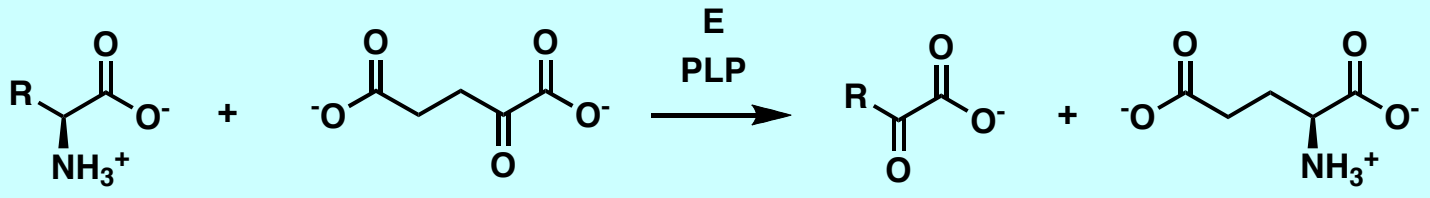


transimination
with E-$(CH_2)_4NH_3^+$



Pyridoxal (PLP)

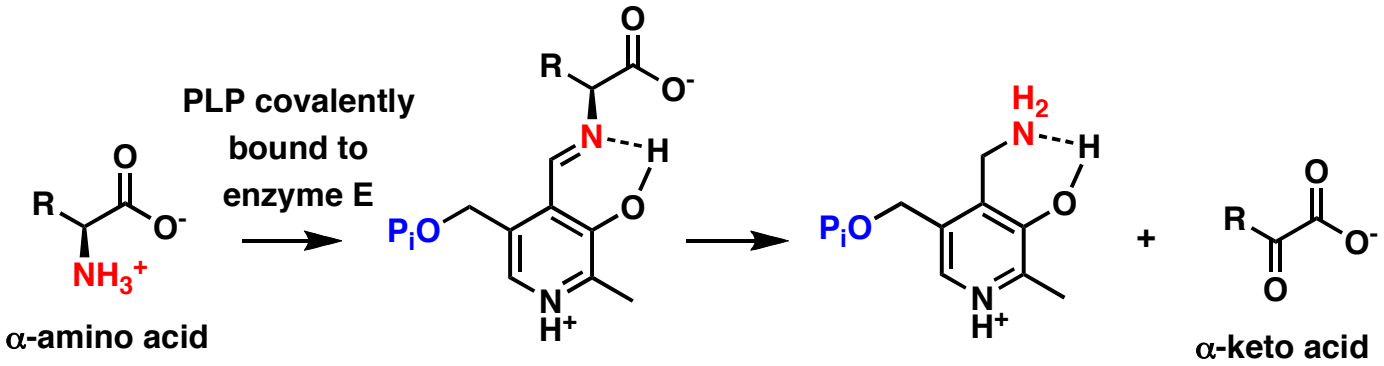
transamination



α-amino acid + α-ketoglutarate → α-keto acid + glutamate

summary of the mechanism:

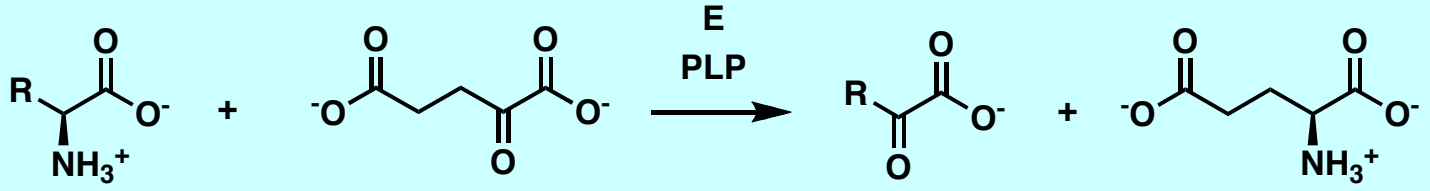
stage 1:



α-amino acid → α-keto acid

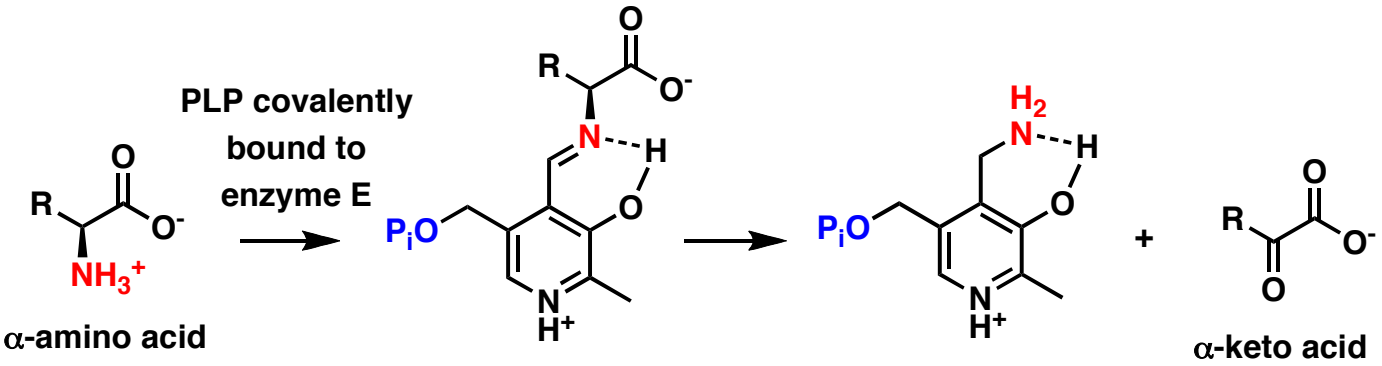
Pyridoxal (PLP)

transamination

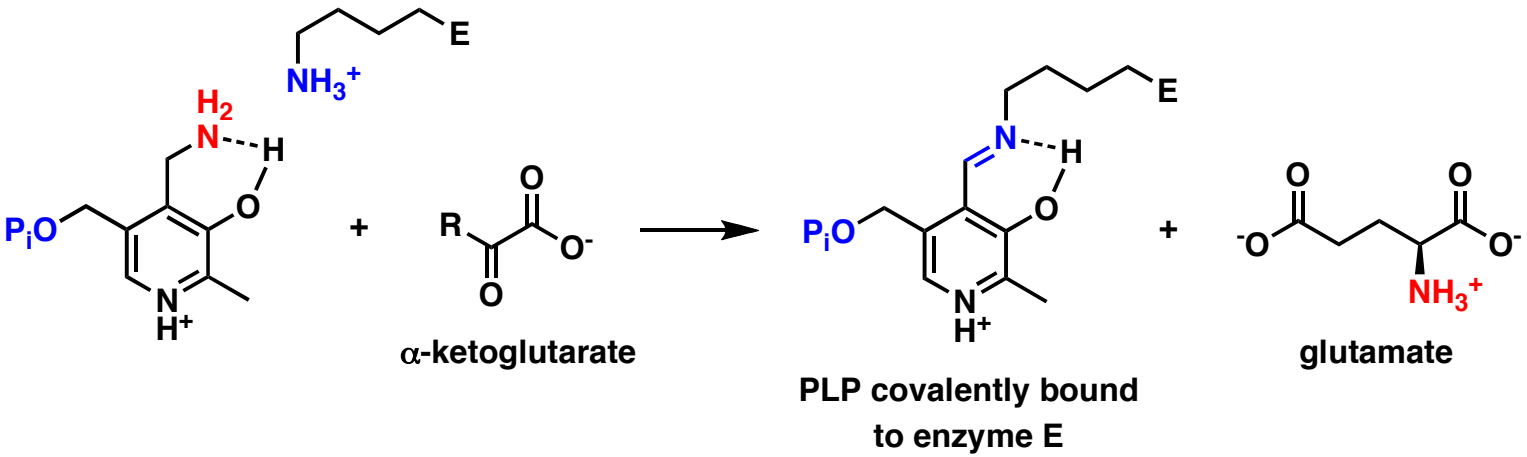


summary of the mechanism:

stage 1:

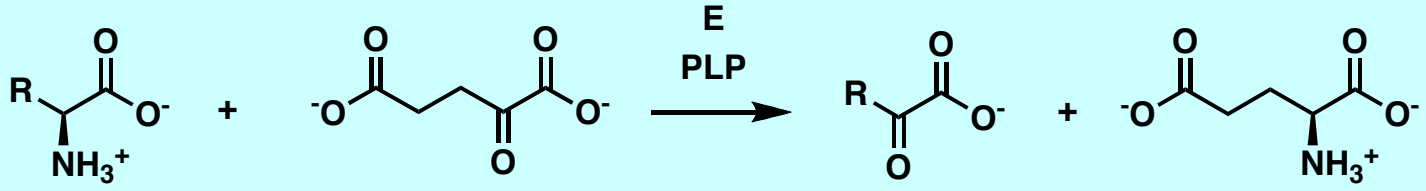


stage 2:

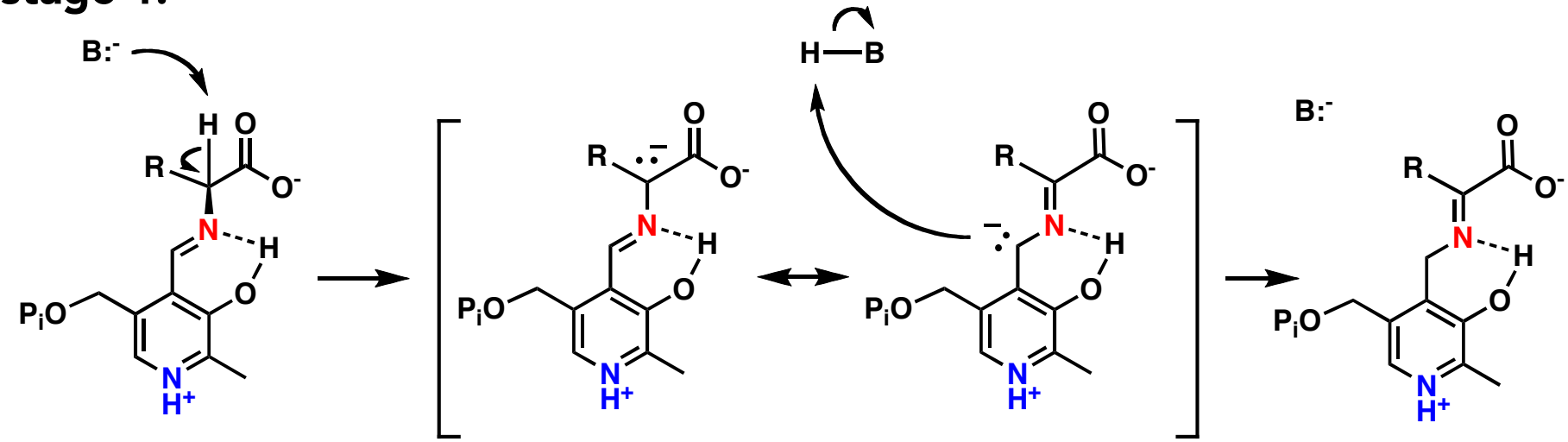


Pyridoxal (PLP)

transamination

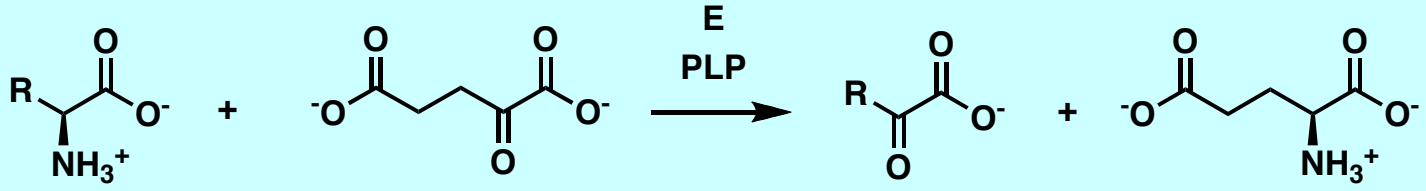


stage 1:

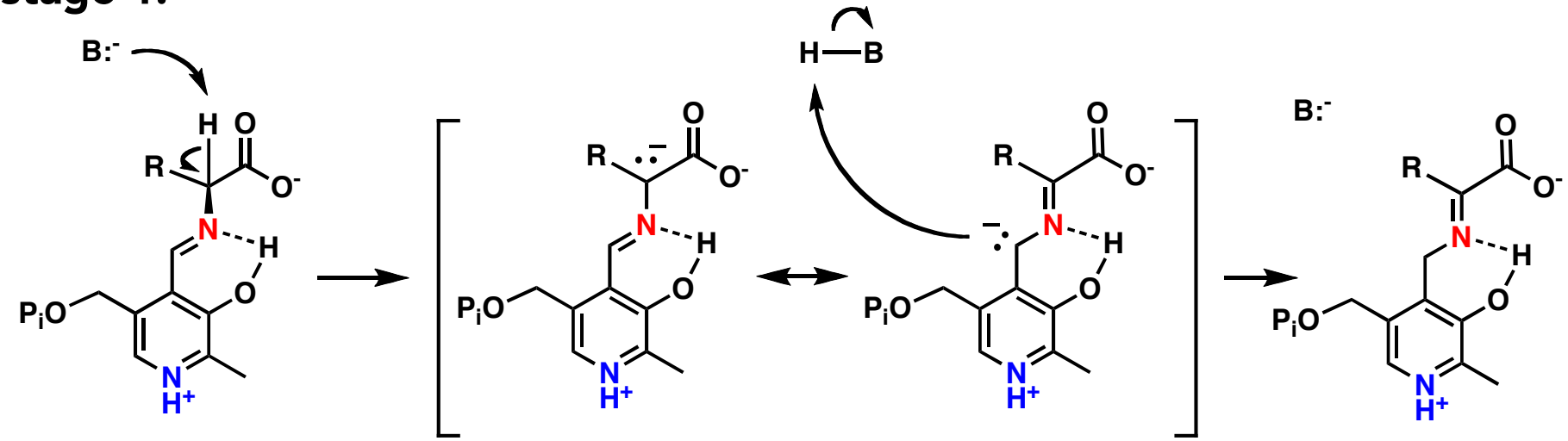


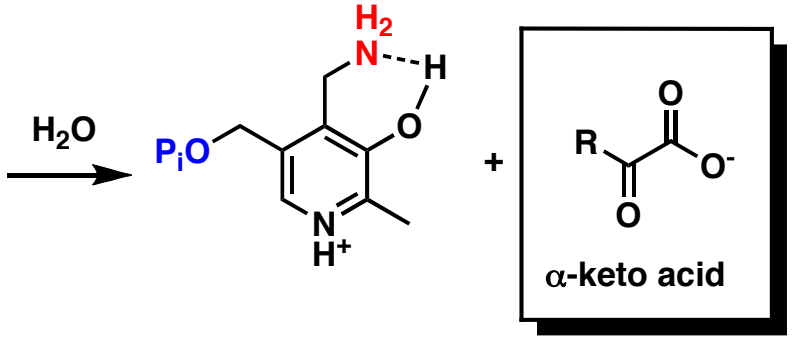
Pyridoxal (PLP)

transamination



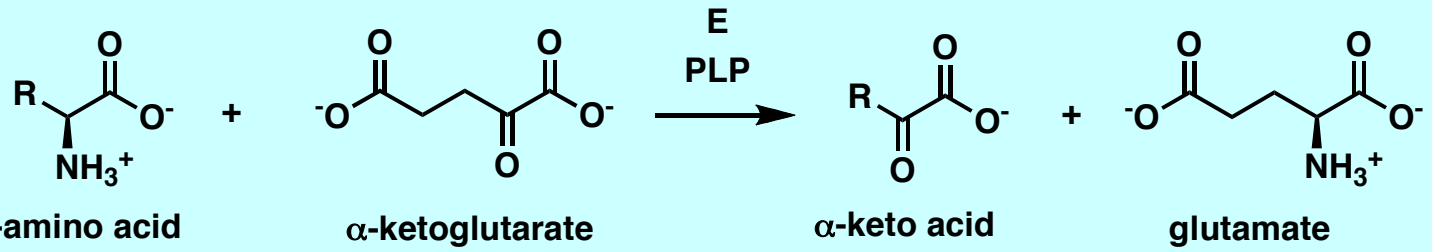
stage 1:





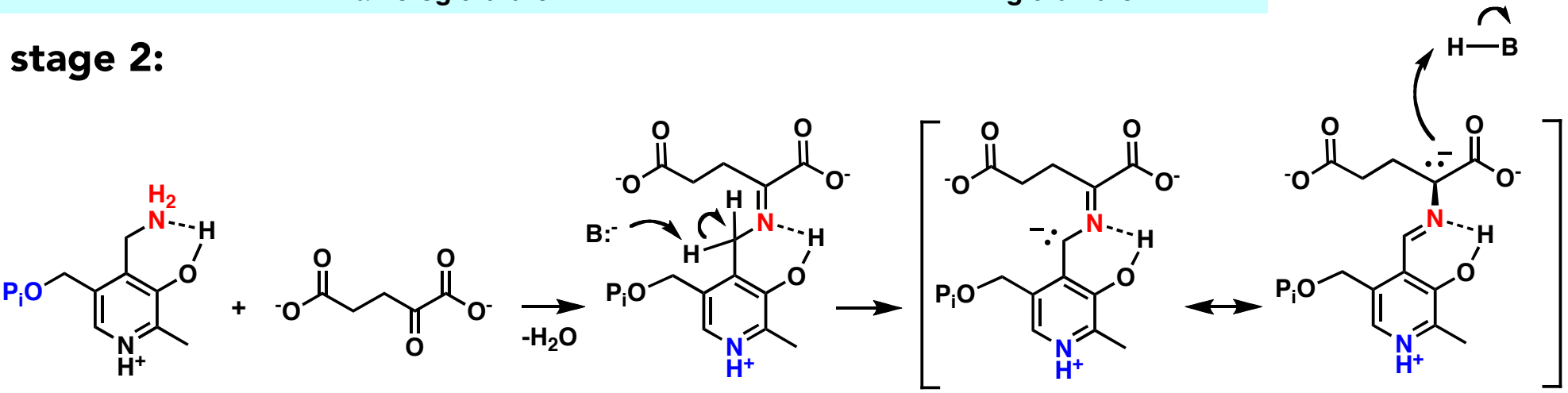
Pyridoxal (PLP)

transamination



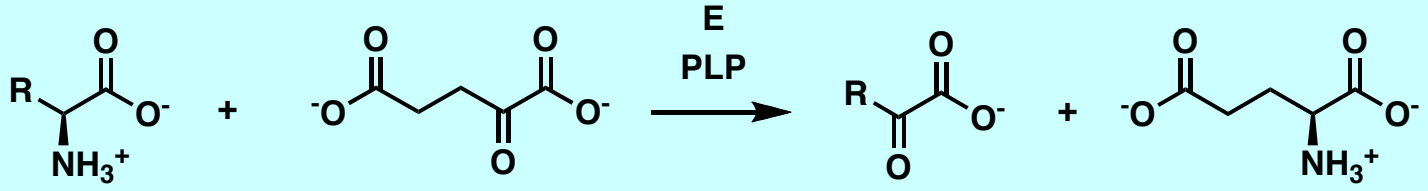
α-amino acid α-ketoglutarate α-keto acid glutamate

stage 2:

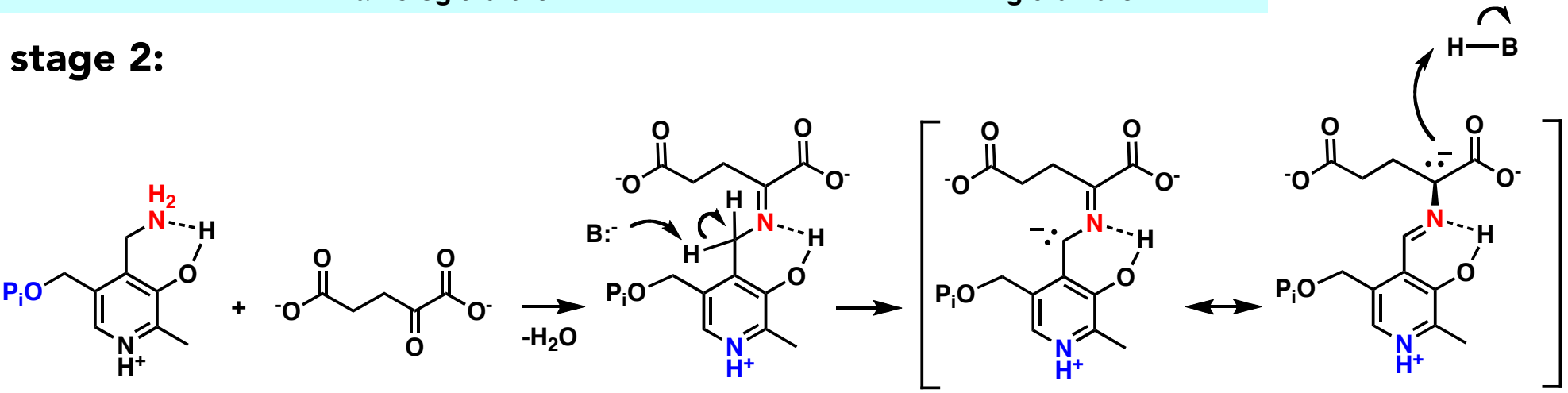


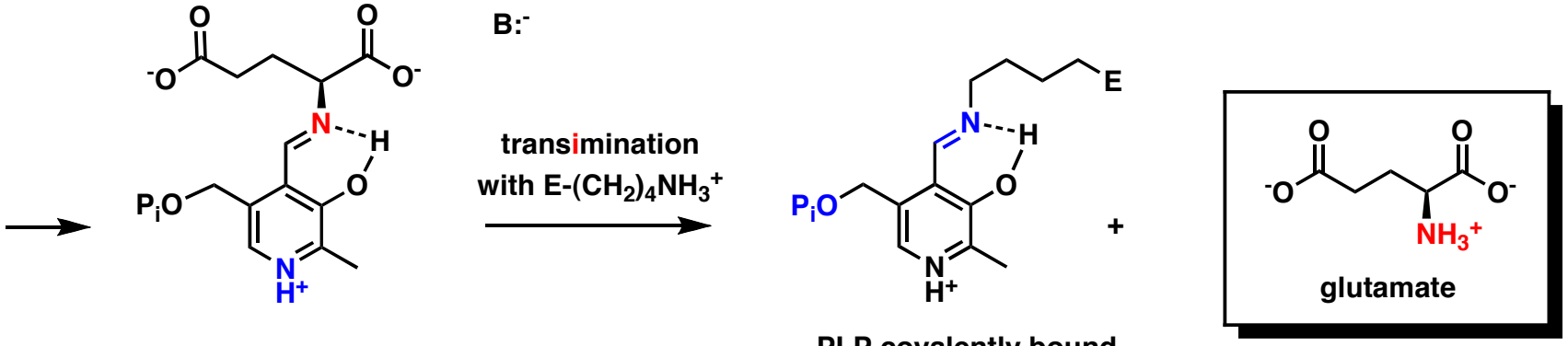
Pyridoxal (PLP)

transamination



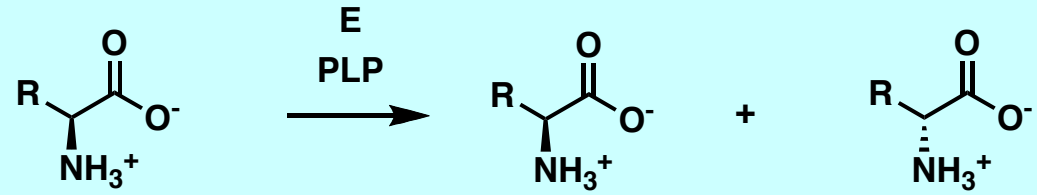
stage 2:



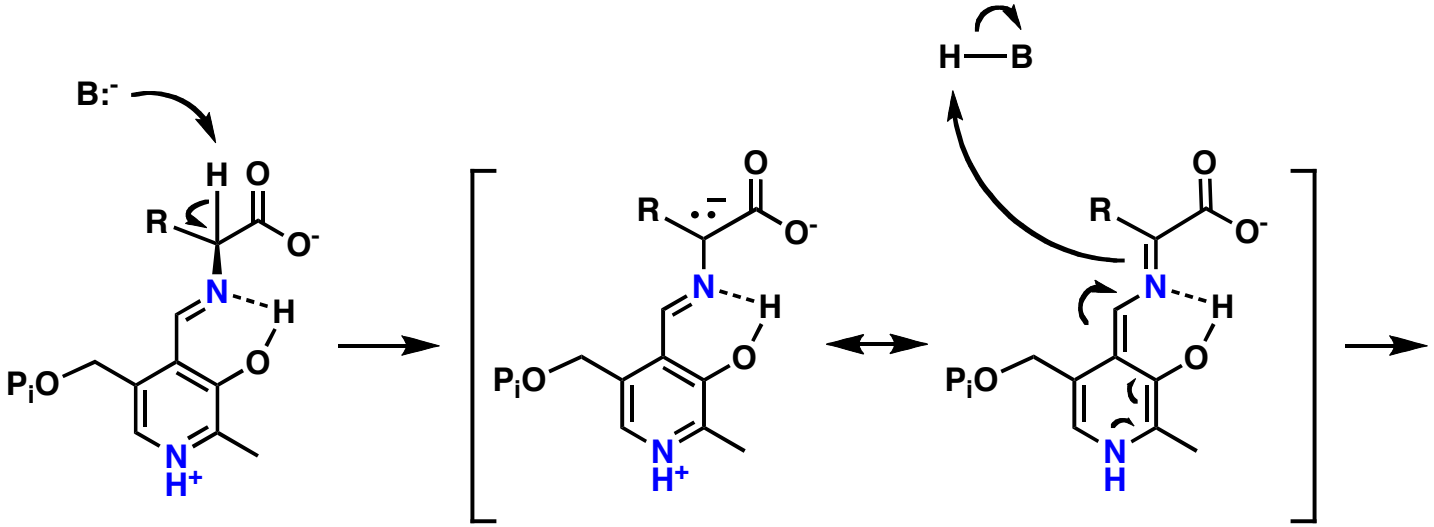


Pyridoxal (PLP)

racemization

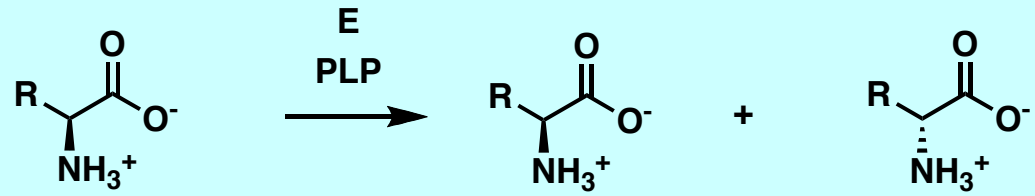


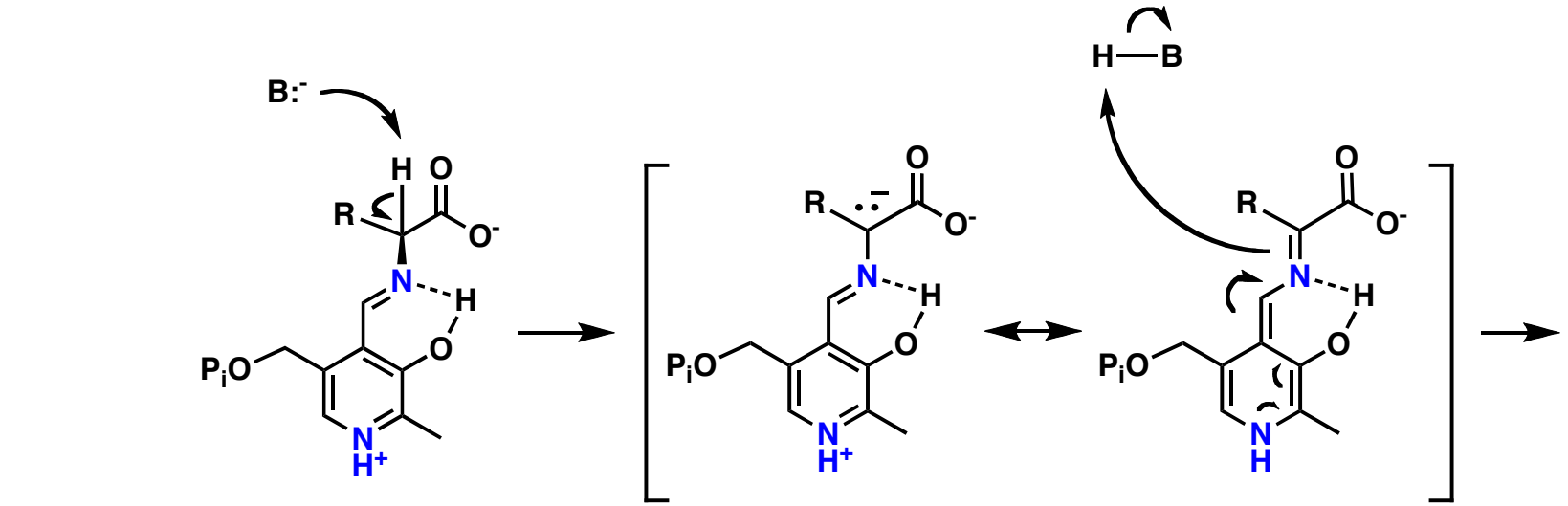
L-α-amino acid L-α-amino acid D-α-amino acid

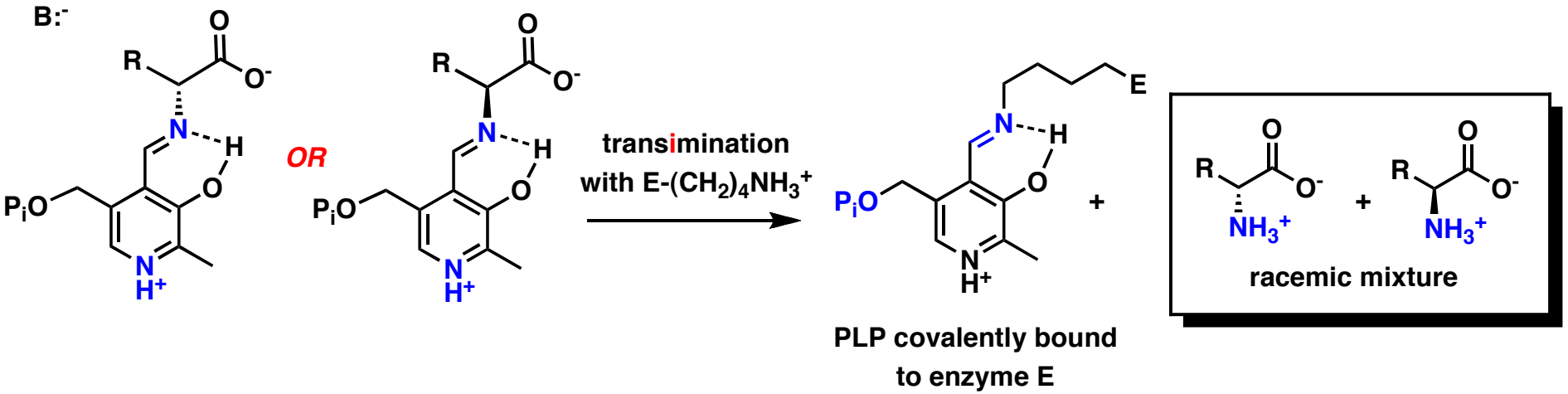


Pyridoxal (PLP)

racemization

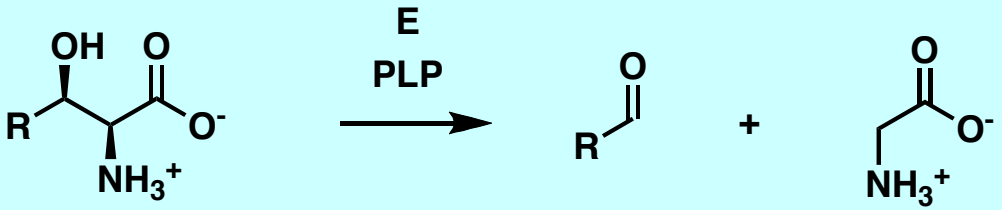






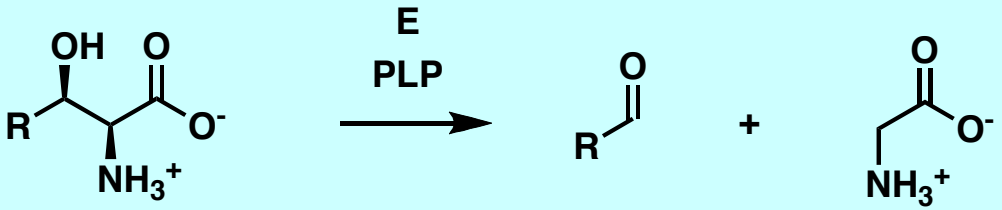
Pyridoxal (PLP)

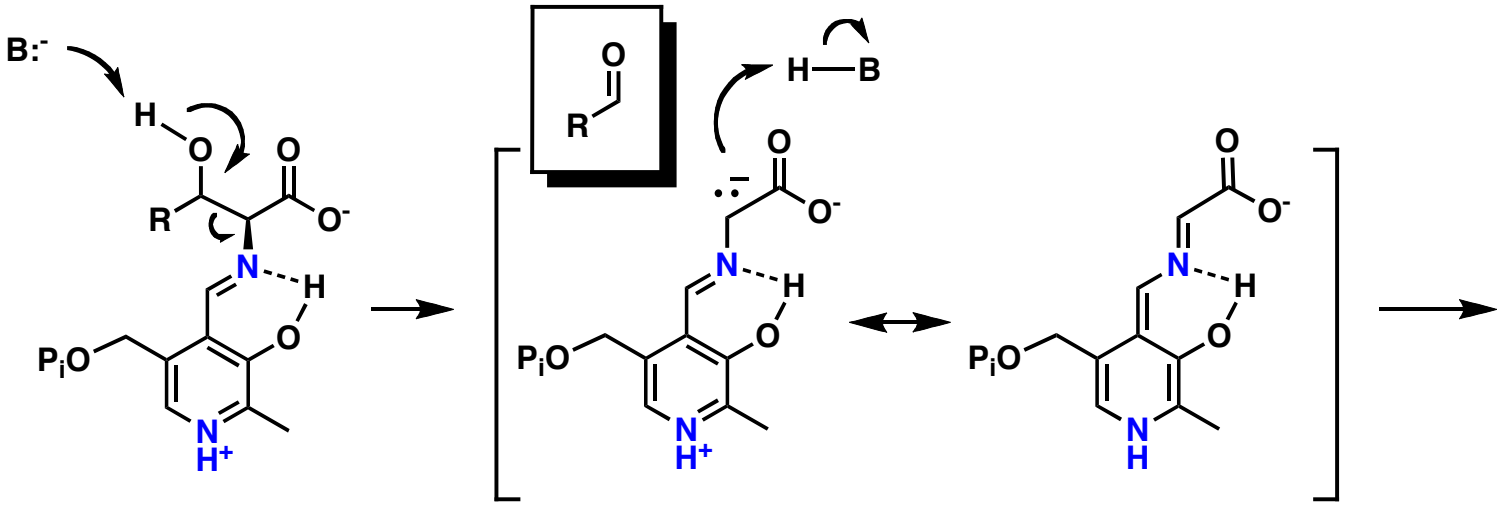
C_α-C_β bond cleavage



Pyridoxal (PLP)

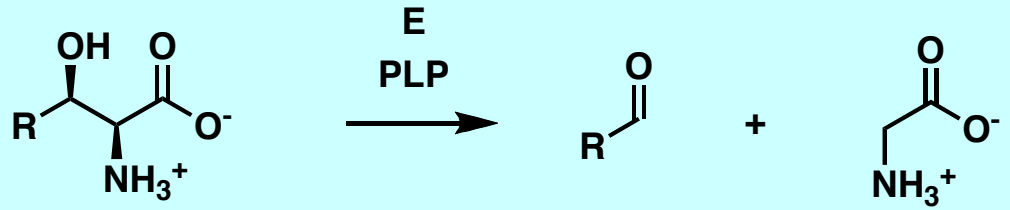
C_α-C_β bond cleavage

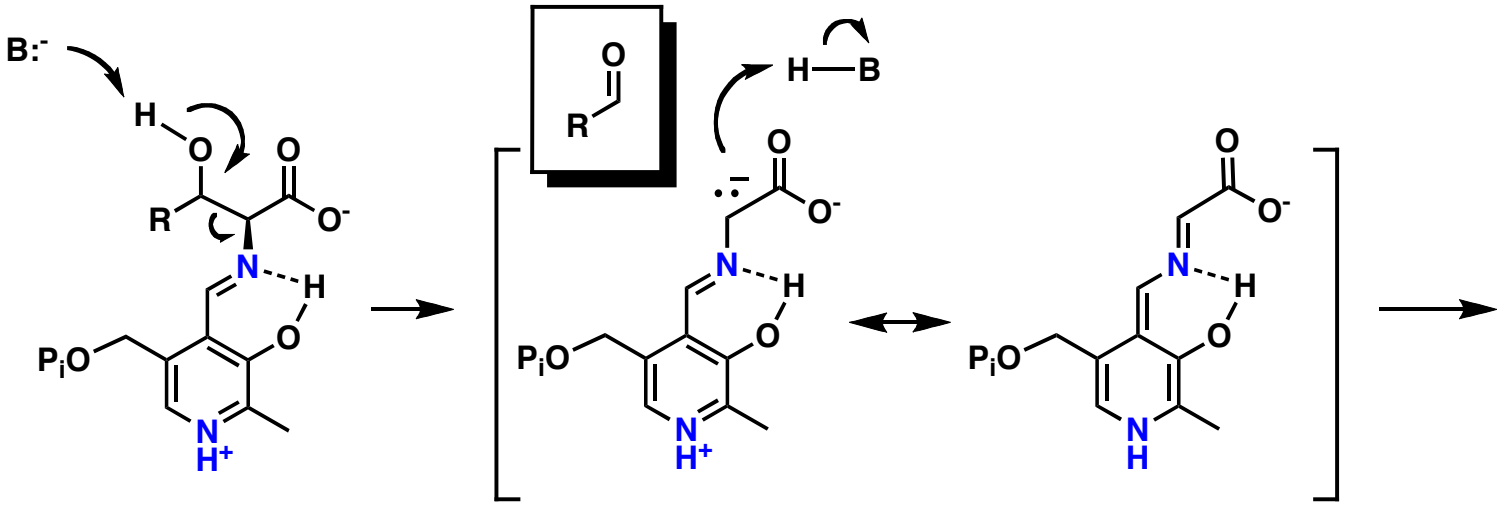


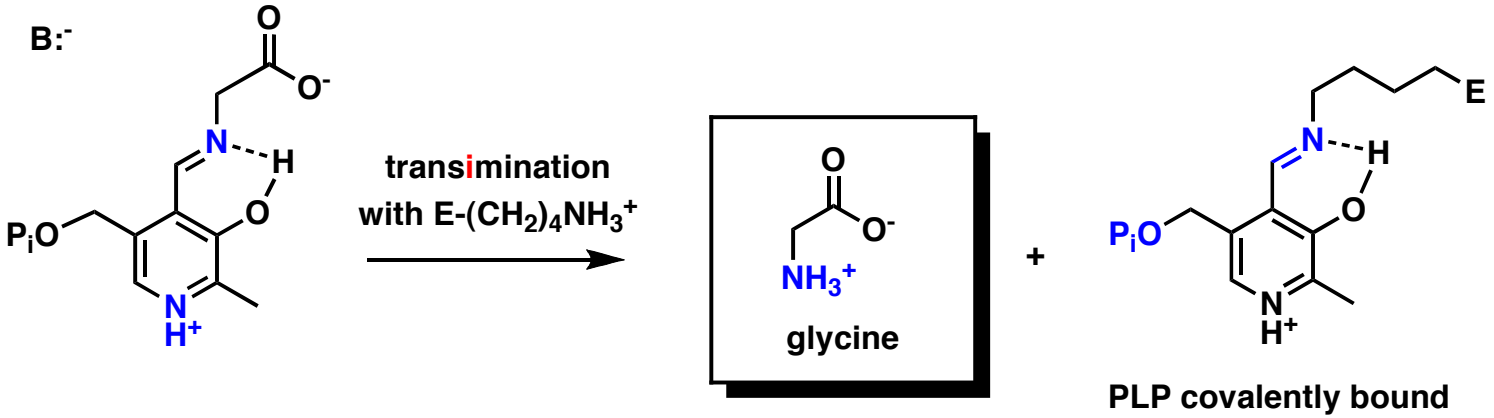


Pyridoxal (PLP)

C_α-C_β bond cleavage





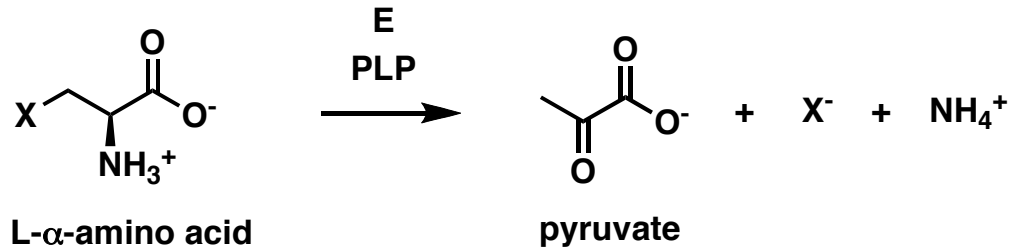


PLP covalently bound to enzyme E

PRACTICE PROBLEM 18

Propose a mechanism for PLP-catalyzed α,β–elimination?

α,β–elimination



L-α-amino acid pyruvate

also, see related problem 34

Pyridoxal (PLP)

PRACTICE PROBLEM 15, 16

Explain why the ability of PLP to catalyze its reactions is greatly reduced if they are carried out at a pH at which the pyridine nitrogen is not protonated.

Explain why the ability of PLP to catalyze an amino acid transformation is greatly reduced if the OH group of pyridoxal phosphate is replaced by OCH_3?