BIOCHEMISTRY

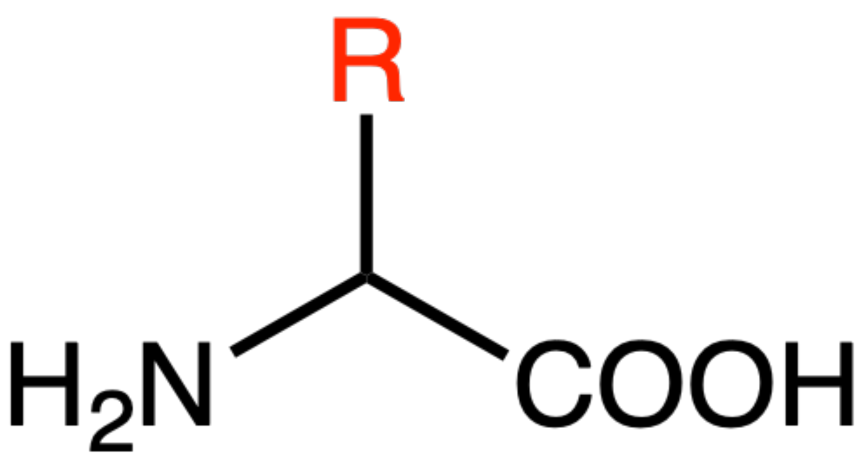
INTRODUCTION: AMINO ACIDS

CHEMISTRY 165 // SPRING 2020

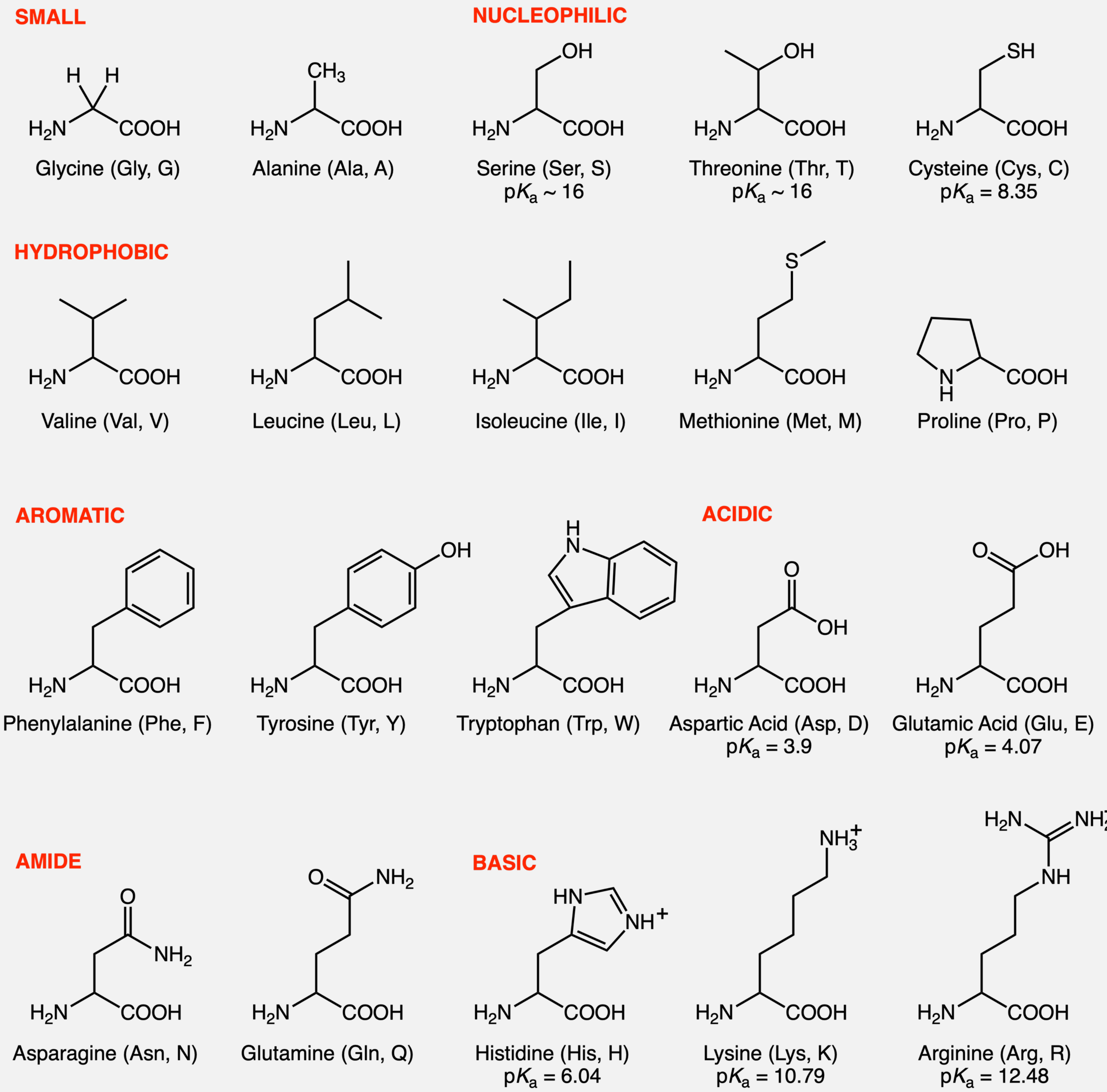
DR. MIOY T. HUYNH | 2020

The amino acids

In biochemistry, we are most interested in 20 amino acids (drawn and named to the right) with the general formula $H_2NCHRCOOH$ and the structure:



The R **group** is called the **sidechain**, and it is what gives each amino each acid its overall character (small, nucleophilic, hydrophobic, aromatic, acidic, amide, or basic).

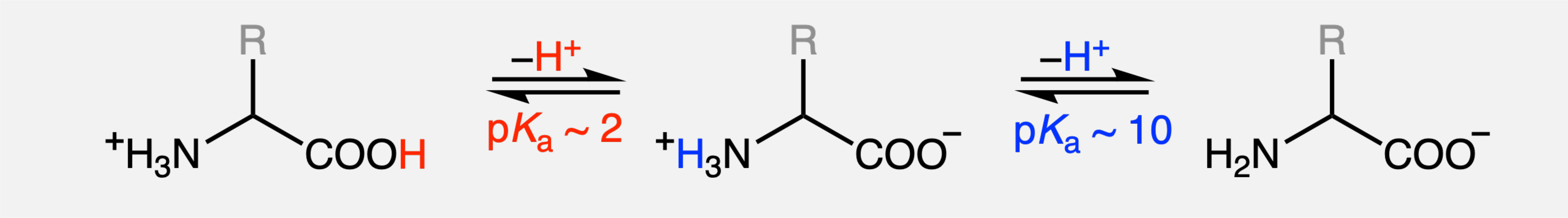


Acid-base properties

Let's ignore the R group for now and look just at the amine ($-NH_2$) and carboxylic acid ($-COOH$) groups.

For all of the amino acids, the general acid-base properties are:

- The $-COOH$ group is a weak acid with a $pK_a \sim 2$
- The $-NH_3^+$ group is a weak base with a $pK_a \sim 10$



Isoelectric point (pI) & the zwitterion

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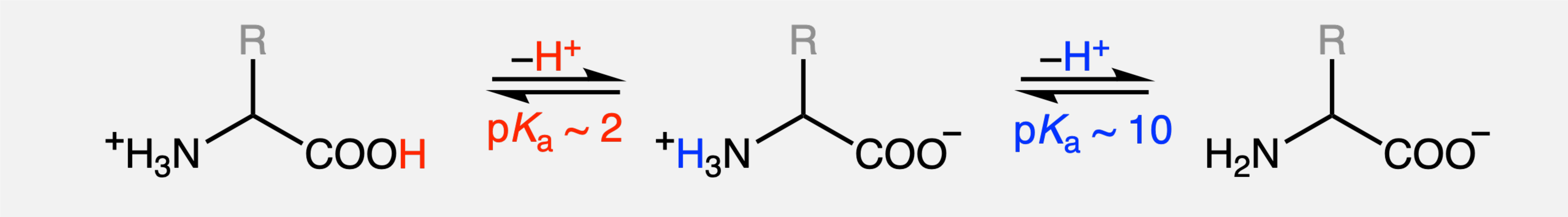


The **zwitterion** is the **neutral ion** shown in the middle, where there are multiple charged groups: $-COO^-$ and $-NH_3^+$.

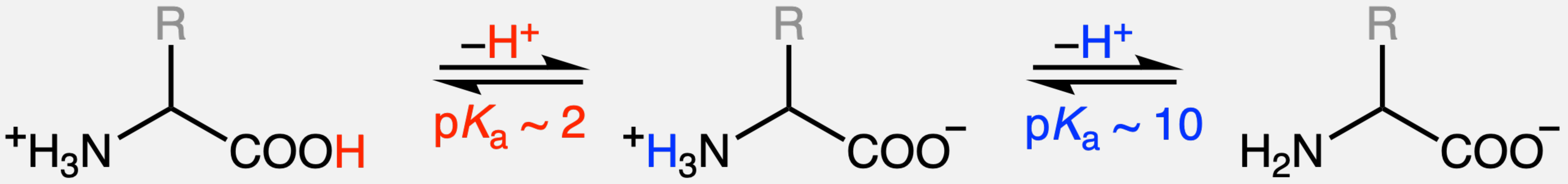
The pH at which the zwitterion exists in solution is called the **isoelectric point** (pI):

$$\mathrm{pI} = \frac{\mathrm{p}K_{a,1} + \mathrm{p}K_{a,2}}{2}$$

Charges on amino acids

The polyprotic acid-base properties of amino acids also lend them different charges in solutions of different pH.

Consider, again, the following generic example:



The pH at which the neutral zwitterion exists in solution is called the <u>isoelectric point</u> (pI):

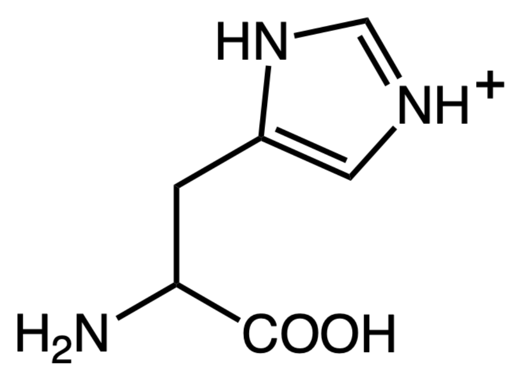
$$\mathrm{pI} = \frac{\mathrm{p}K_{\mathrm{a},1} + \mathrm{p}K_{\mathrm{a},2}}{2} \approx \frac{2 + 10}{2} \approx 6$$

For this general amino acid, where the pI = 6:

- In acidic medium (pH < pI), it mostly exists as the **cation** $[^{+}H_3NCHRCOOH]^{+}$ with an overall **+1 charge.**
- At a pH ~ pI, it mostly exists as the **neutral zwitterion** $[^{+}H_3NCHRCOO^{-}]^{0}$ with an overall **0 charge.**
- In basic medium (pH > pI), it mostly exists as the **anion** $[H_2NCHRCOO^{-}]^{-}$ with an overall **–1 charge.**

PRACTICE PROBLEM 1

Estimate the isoelectric point (pI) for histidine if the sidechain (R) group has a pK_a = 6.04.



Histidine (His, H)
pK_a = 6.04

— answer —

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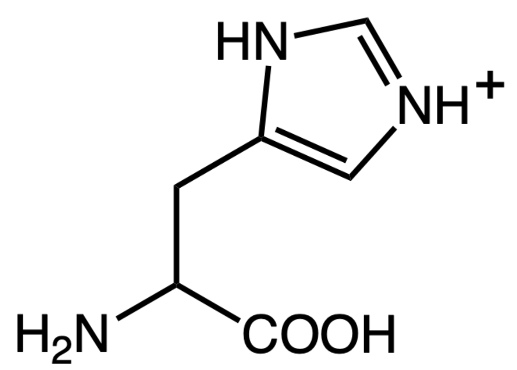
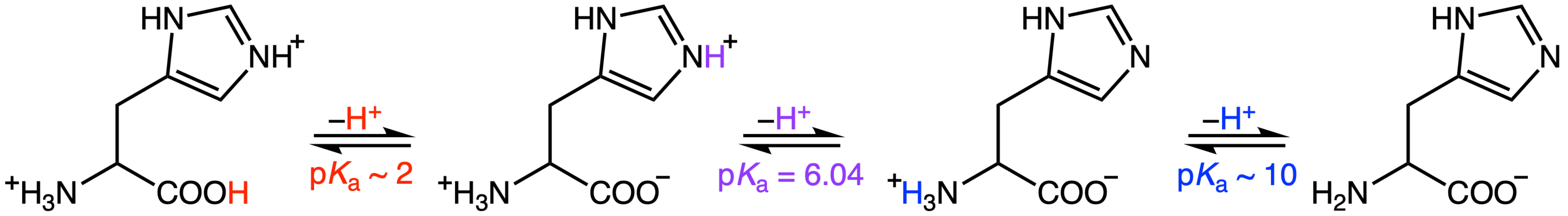


Histidine (His, H)
pK_a = 6.04

— answer —

First, write out the following acid-base dissociation equilibria that would exist for histidine.



Therefore, the isoelectric point (pI) for which the neutral zwitterion (third structure) would exist is:

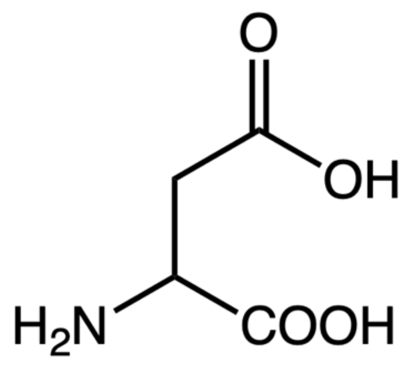
$$\mathrm{pI} = \frac{\mathrm{p}K_{\mathrm{a},1} + \mathrm{p}K_{\mathrm{a},2}}{2} \approx \frac{6.04 + 10}{2} \approx 8.02$$

PRACTICE PROBLEM 2

(a) Estimate the isoelectric point (pI) for aspartic acid if the sidechain (R) group has a pK_a = 3.9.

(b) Estimate the overall charge of aspartic acid in a solution with pH = 6.

(c) Estimate the overall charge of asparatic acid in a solution with pH = 12.



Aspartic Acid (Asp, D)
pK_a = 3.9

— *answer* —

PRACTICE PROBLEM 2

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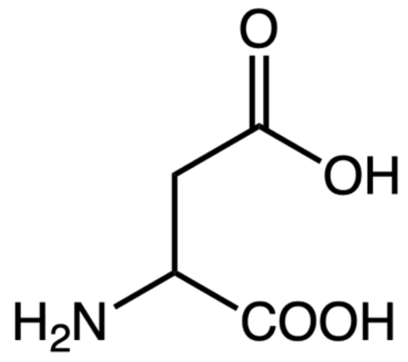
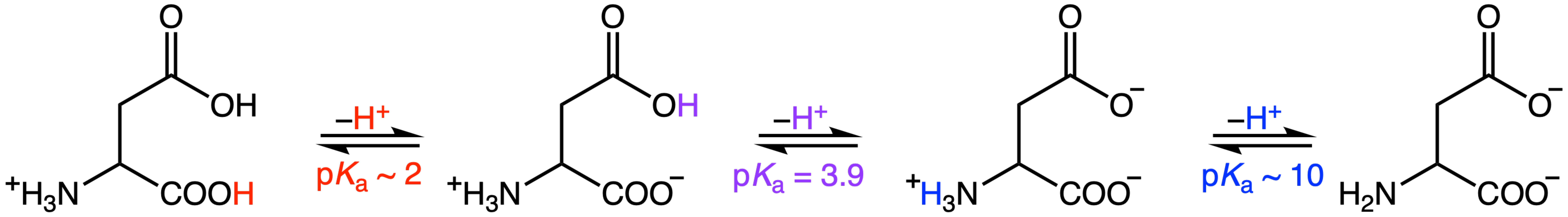


Aspartic Acid (Asp, D)
pK_a = 3.9

— answer —

(a) First, write out the following acid-base dissociation equilibria that would exist for aspartic acid.



Therefore, the isoelectric point (pI) for which the neutral zwitterion (second structure) would exist is:

$$\text{pI} = \frac{\text{p}K_{a,1} + \text{p}K_{a,2}}{2} \approx \frac{2 + 3.9}{2} \approx 2.95$$

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(a) Estimate the isoelectric point (pI) for aspartic acid if the sidechain (R) group has a pK_a = 3.9.

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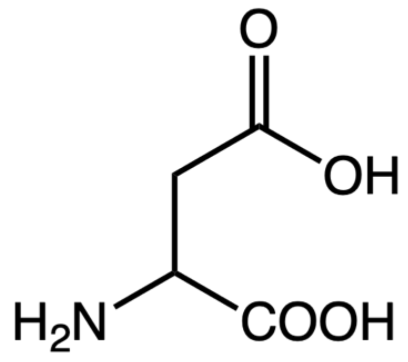
(c) Estimate the overall charge of asparatic acid in a solution with pH = 12.



Aspartic Acid (Asp, D)
pK_a = 3.9

— answer —

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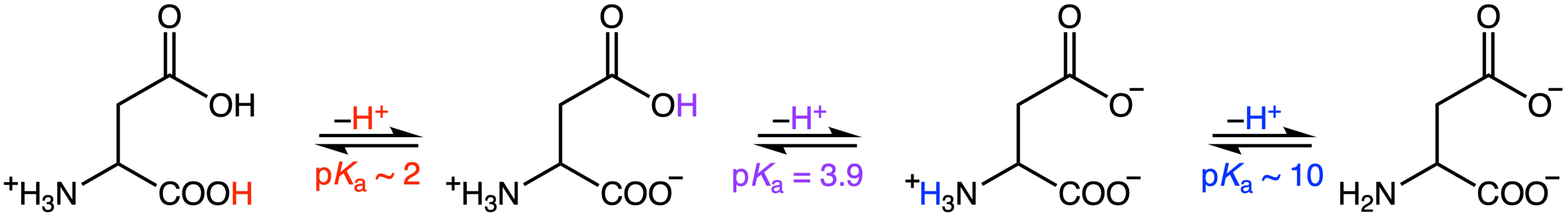

Therefore, the isoelectric point (pI) for which the neutral zwitterion (second structure) would exist is:

$$\mathrm{pI} = \frac{\mathrm{p}K_{a,1} + \mathrm{p}K_{a,2}}{2} \approx \frac{2 + 3.9}{2} \approx 2.95$$

(b) In a solution with pH = 6 (in other words, pH > pI), aspartic acid is mostly likely to exist as the anion (third structure) with an overall charge of –1.

PRACTICE PROBLEM 2

(a) Estimate the isoelectric point (pI) for aspartic acid if the sidechain (R) group has a pK_a = 3.9.

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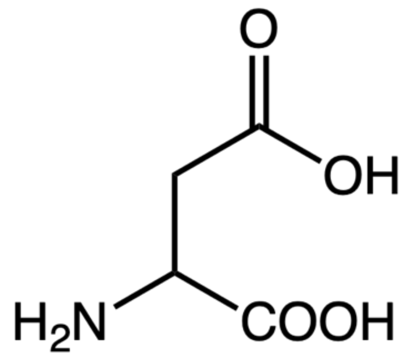
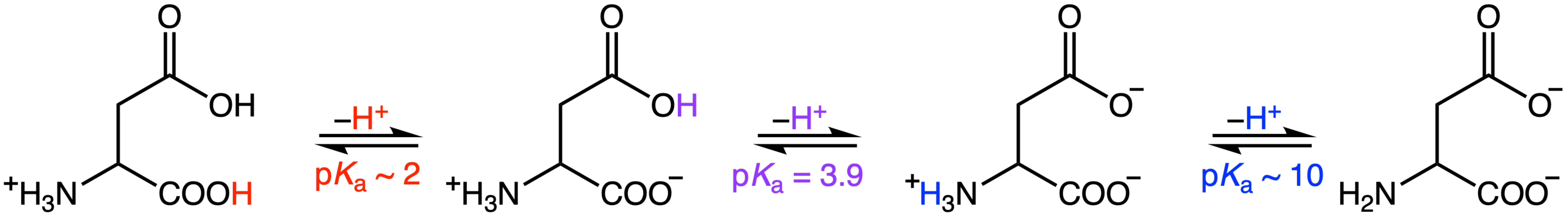


Aspartic Acid (Asp, D)
pK_a = 3.9

— answer —

(a) First, write out the following acid-base dissociation equilibria that would exist for aspartic acid.



Therefore, the isoelectric point (pI) for which the neutral zwitterion (second structure) would exist is:

$$\mathrm{pI} = \frac{\mathrm{p}K_{a,1} + \mathrm{p}K_{a,2}}{2} \approx \frac{2 + 3.9}{2} \approx 2.95$$

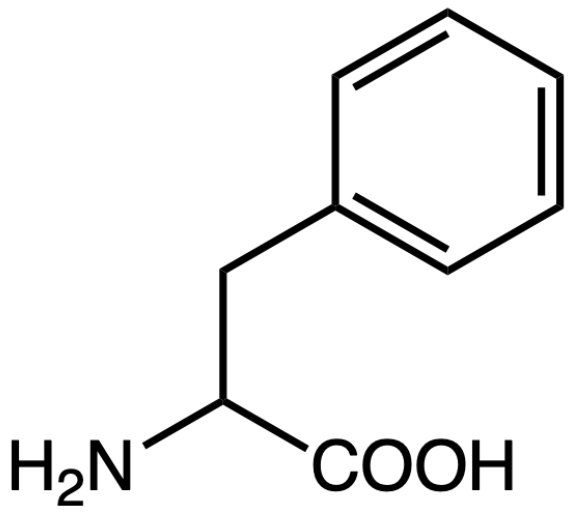
(b) In a solution with pH = 6 (in other words, pH > pI), aspartic acid is mostly likely to exist as the anion (third structure) with an overall charge of –1.

(c) In a solution with pH = 6 (in other words, pH > pI and pH > pK_a [-NH_3^+]), aspartic acid is mostly likely to exist as the dianion (fourth structure) with an overall charge of –2.

PRACTICE PROBLEM 3

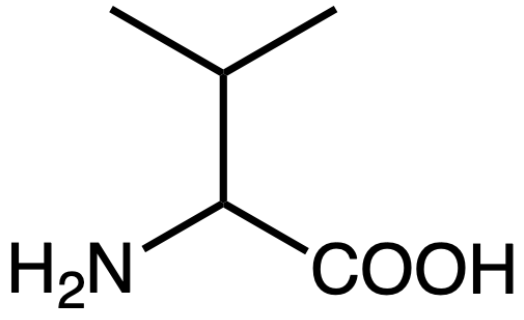
Label each of the following amino acids (A–F) as acidic, basic, or neutral.

— answer —



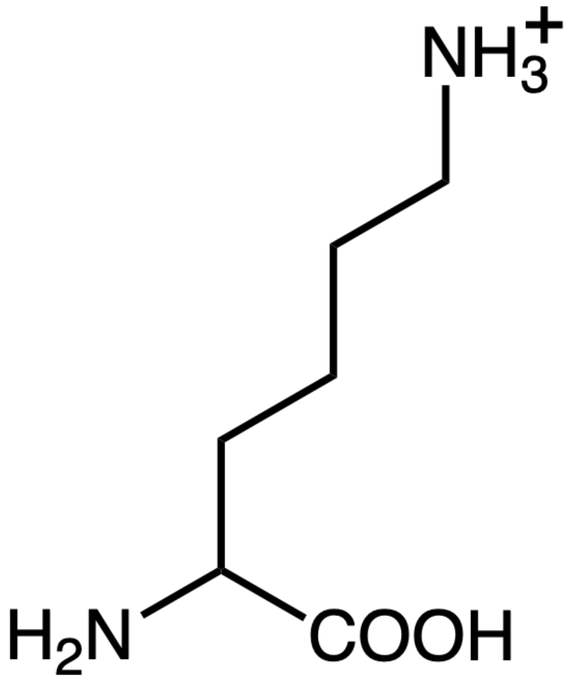
Phenylalanine (Phe, F)

A



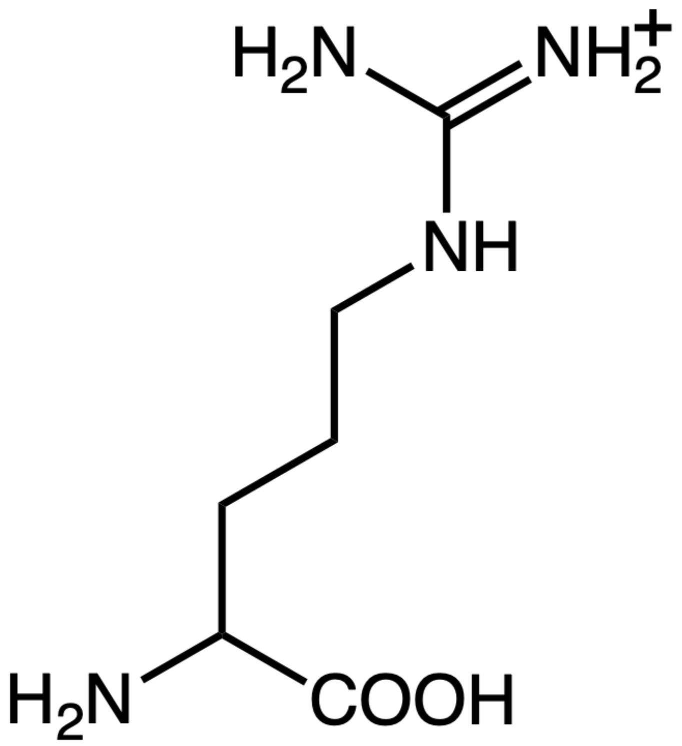
Valine (Val, V)

B



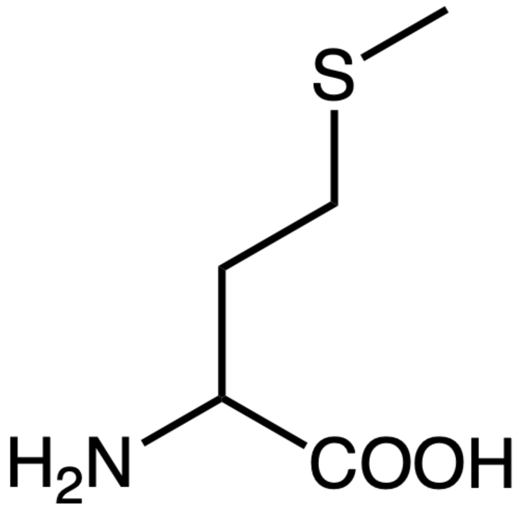
Lysine (Lys, K)
pK_a = 10.79

C



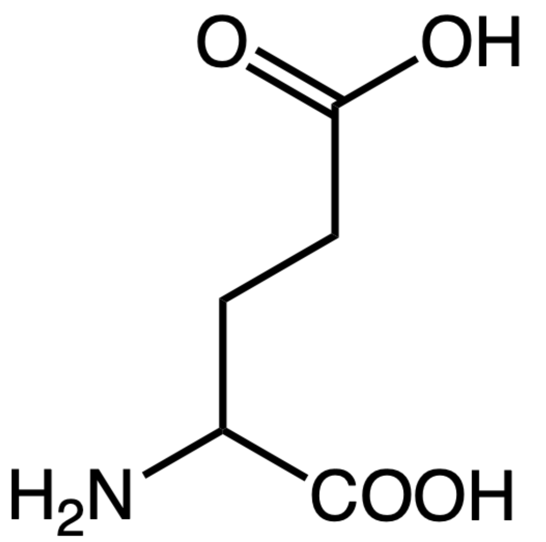
Arginine (Arg, R)
pK_a = 12.48

D



Methionine (Met, M)

E



Glutamic Acid (Glu, E)
pK_a = 4.07

F

PRACTICE PROBLEM 3

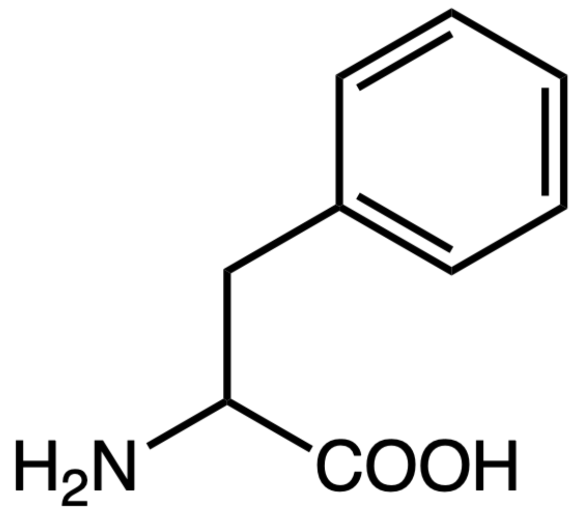
Label each of the following amino acids (A–F) as acidic, basic, or neutral.

— answer —

Because amino acids A, B, and E have sidechains (R groups) that do not have ionizable protons (hint: no reported side chain pK_a values), these will be neutral amino acids with a pI ~ 6.

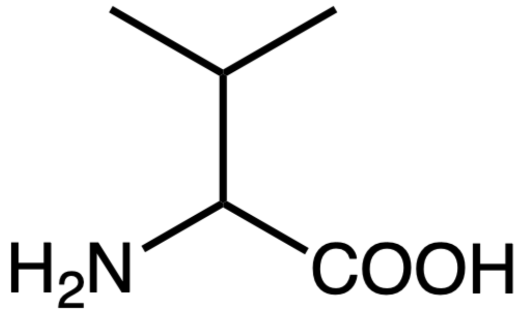
Amino acids C and D have sidechains (R groups) that have ionizable protons with a reported pK_a > 7; these are basic amino acids with a pI > 6.

Amino acid F has a sidechain (R group) that has an ionizable proton with a reported pK_a < 7; this is an acidic amino acid with a pI < 6.



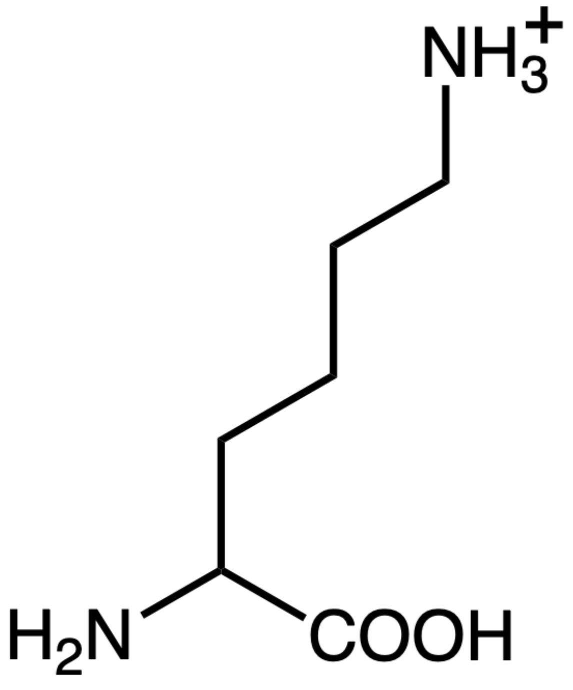
Phenylalanine (Phe, F)

A



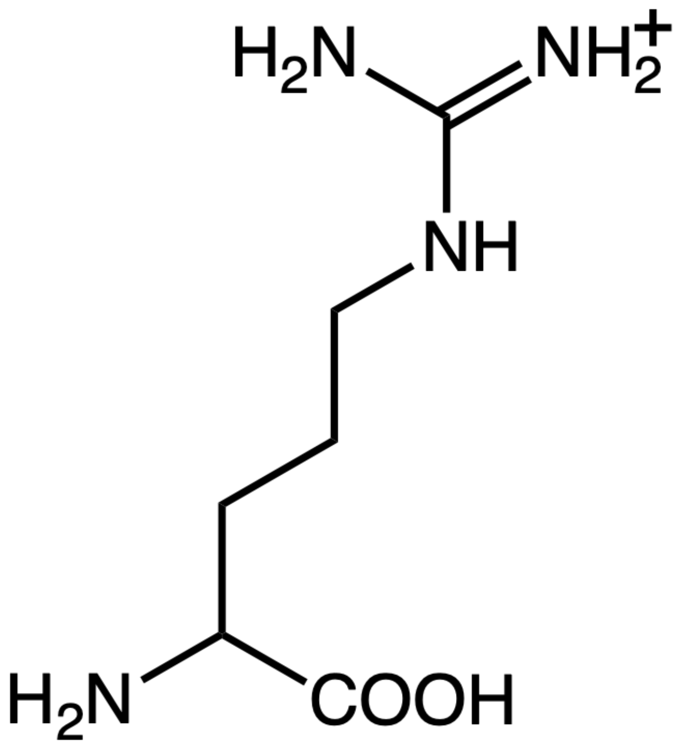
Valine (Val, V)

B



Lysine (Lys, K)
pK_a = 10.79

C



Arginine (Arg, R)
pK_a = 12.48

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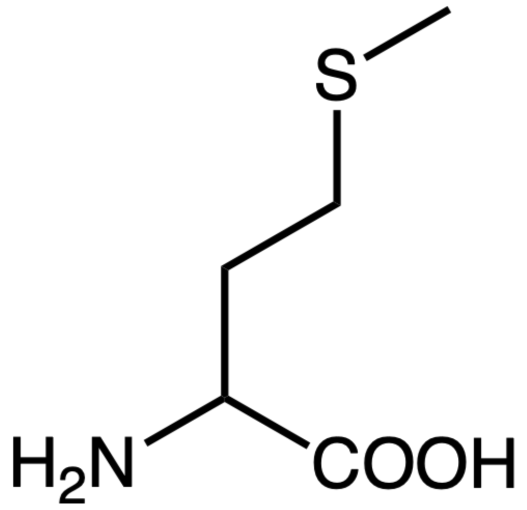
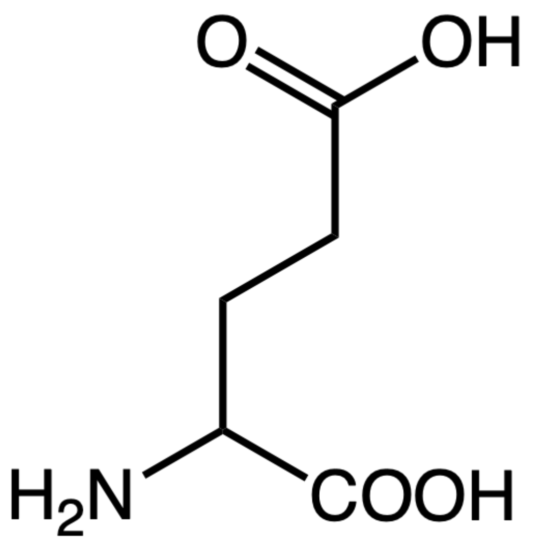


Methionine (Met, M)

E



Glutamic Acid (Glu, E)
pK_a = 4.07

F