27.3
Acid-Base Behavior of Amino Acids

Recall

While their name implies that amino acids are compounds that contain an —NH_2 group and a —CO_2H group, these groups are actually present as —NH_3^+ and —CO_2^- respectively.

How do we know this?

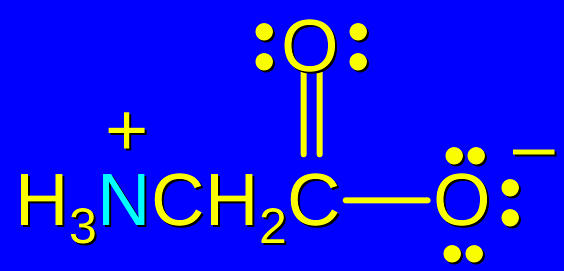
Properties of Glycine

The properties of glycine:

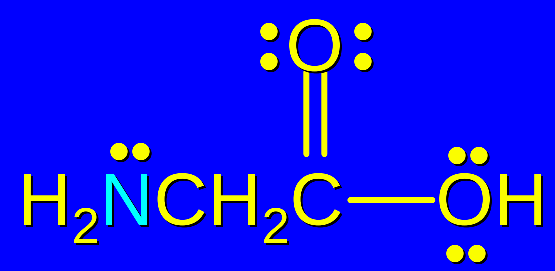
high melting point (when heated to 233°C it decomposes before it melts)

solubility: soluble in water; not soluble in nonpolar solvent

more consistent with this



than this



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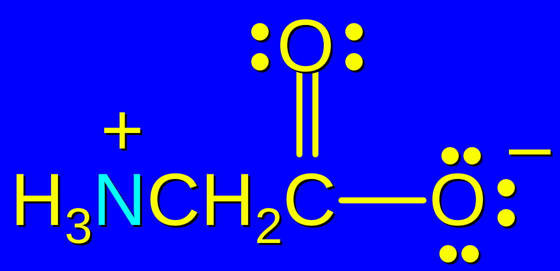

called a *zwitterion* or *dipolar ion*

Acid-Base Properties of Glycine

The zwitterionic structure of glycine also follows from considering its acid-base properties.

A good way to think about this is to start with the structure of glycine in strongly acidic solution, say pH = 1.

At pH = 1, glycine exists in its protonated form (a monocation).

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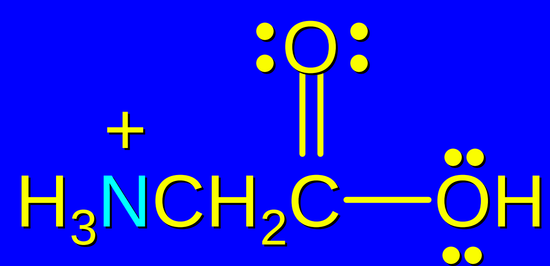
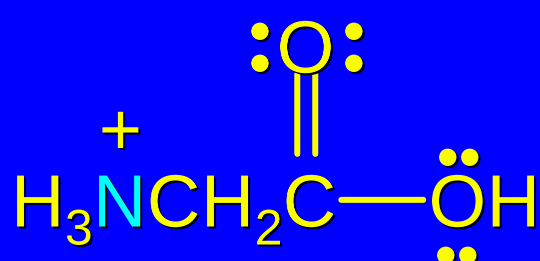


Acid-Base Properties of Glycine

Now ask yourself "As the pH is raised, which is the first proton to be removed? Is it the proton attached to the positively charged nitrogen, or is it the proton of the carboxyl group?"

You can choose between them by estimating their respective pK_as.



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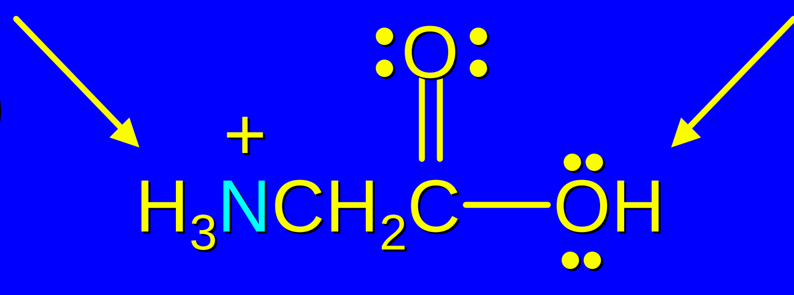
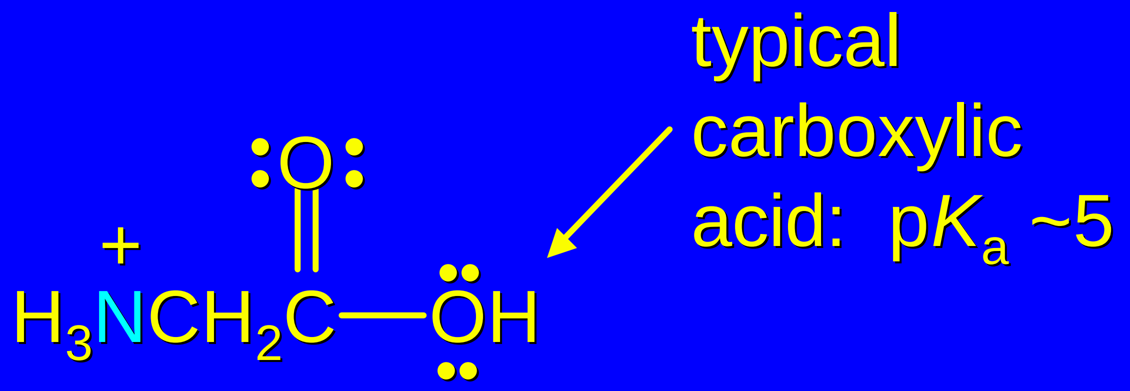
typical ammonium ion: pK_a ~9



typical carboxylic acid: pK_a ~5

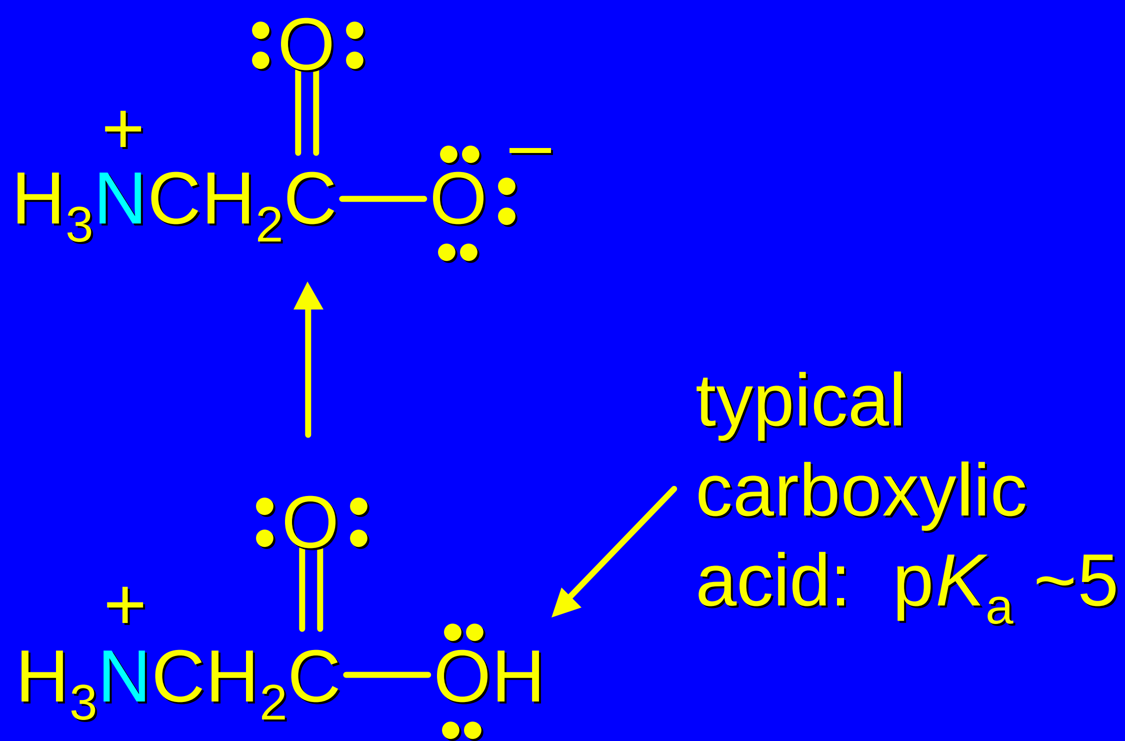
Acid-Base Properties of Glycine

The more acidic proton belongs to the CO_2H group. It is the first one removed as the pH is raised.



Acid-Base Properties of Glycine

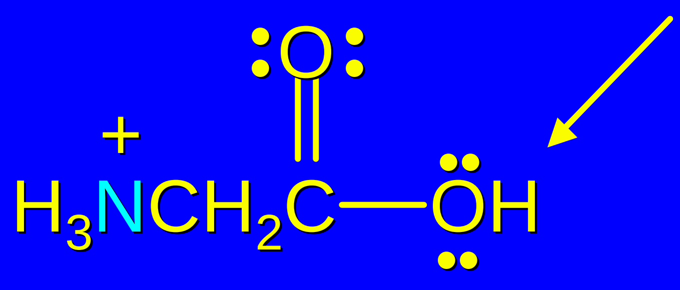
Therefore, the more stable neutral form of glycine is the zwitterion.



Acid-Base Properties of Glycine

The measured pK_a of glycine is 2.34.

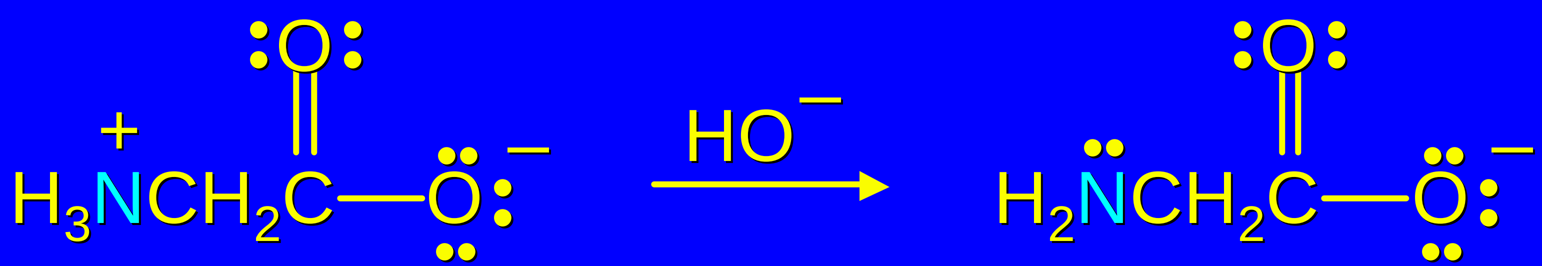
Glycine is stronger than a typical carboxylic acid because the positively charged N acts as an electron-withdrawing, acid-strengthening substituent on the α carbon.



typical carboxylic acid: pK_a ~5

Acid-Base Properties of Glycine

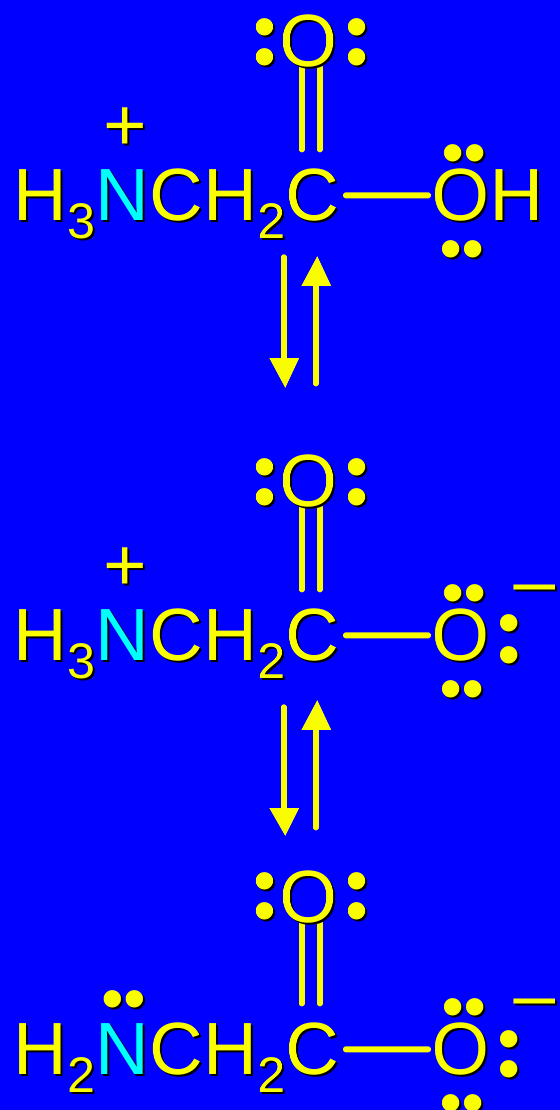
A proton attached to N in the zwitterionic form of nitrogen can be removed as the pH is increased further.



The pK_a for removal of this proton is 9.60.
This value is about the same as that for NH_4^+ (9.3).

*Isoelectric Point p*I

$pK_a = 2.34$



$pK_a = 9.60$

The pH at which the concentration of the zwitterion is a maximum is called the *isoelectric point*. Its numerical value is the average of the two pK_as.

The p*I* of glycine is 5.97.

Acid-Base Properties of Amino Acids

One way in which amino acids differ is in respect to their acid-base properties. This is the basis for certain experimental methods for separating and identifying them.

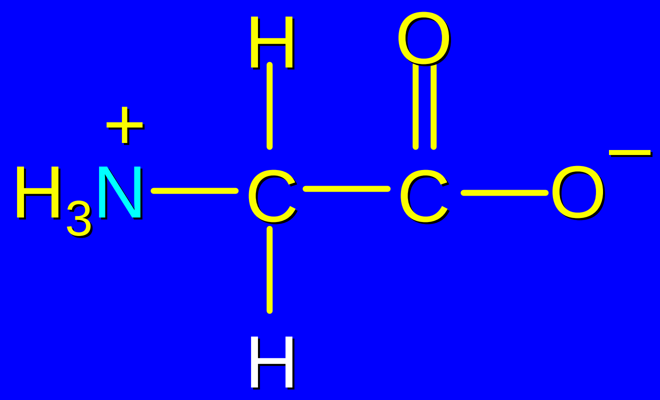
Just as important, the difference in acid-base properties among various side chains affects the properties of the proteins that contain them.

Table 27.2 gives pK_a and pI values for amino acids with neutral side chains.

Table 27.2

Amino Acids with Neutral Side Chains

Glycine



pK_{a1} = 2.34

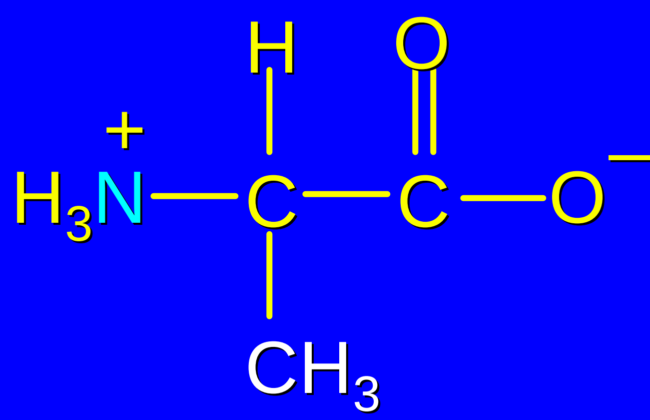
pK_{a2} = 9.60

pI = 5.97

Table 27.2

Amino Acids with Neutral Side Chains

Alanine



pK_{a1} = 2.34

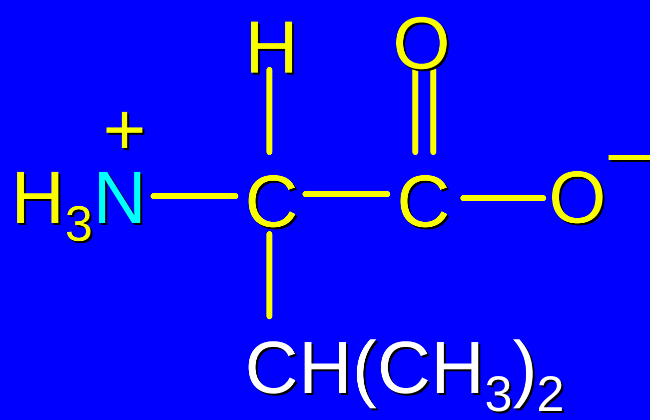
pK_{a2} = 9.69

p*I* = 6.00

Table 27.2

Amino Acids with Neutral Side Chains

Valine



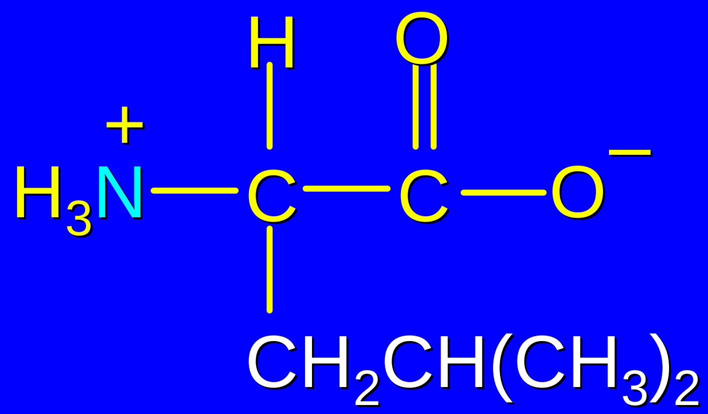
pK_{a1} = 2.32

pK_{a2} = 9.62

p*I* = 5.96

Table 27.2
Amino Acids with Neutral Side Chains

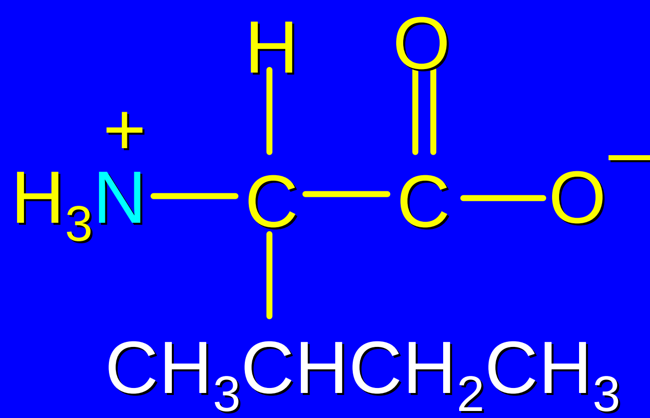
Leucine



pK_{a1} = 2.36
pK_{a2} = 9.60
p*I* = 5.98

Table 27.2
Amino Acids with Neutral Side Chains

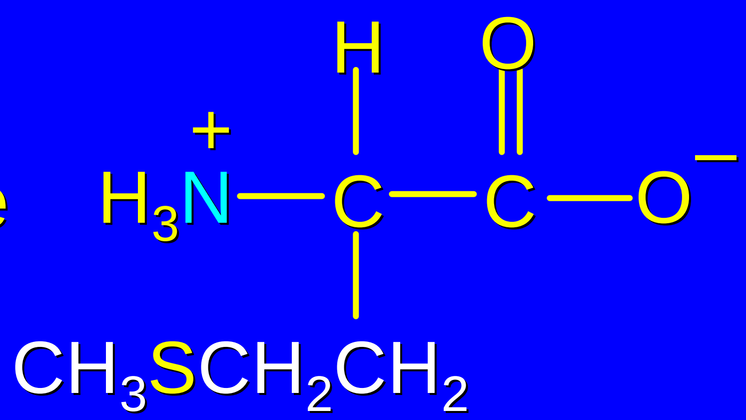
Isoleucine



pK_{a1} = 2.36
pK_{a2} = 9.60
p*I* = 5.98

Table 27.2
Amino Acids with Neutral Side Chains

Methionine

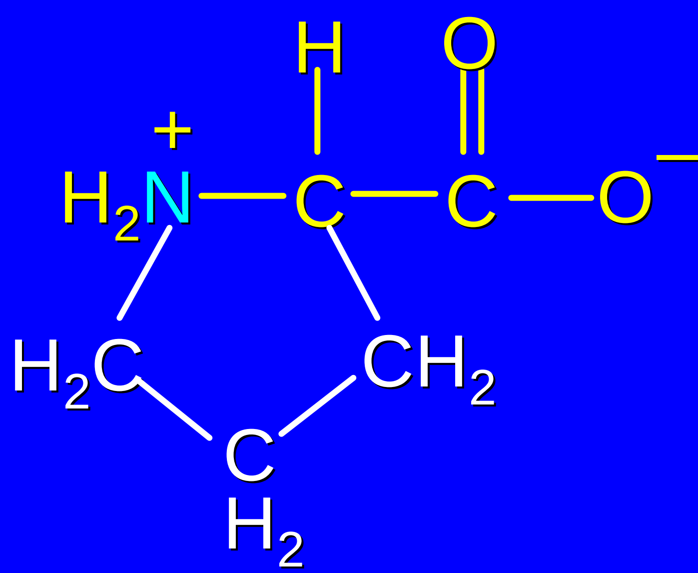


pK_{a1} = 2.28
pK_{a2} = 9.21
p*I* = 5.74

Table 27.2

Amino Acids with Neutral Side Chains

Proline



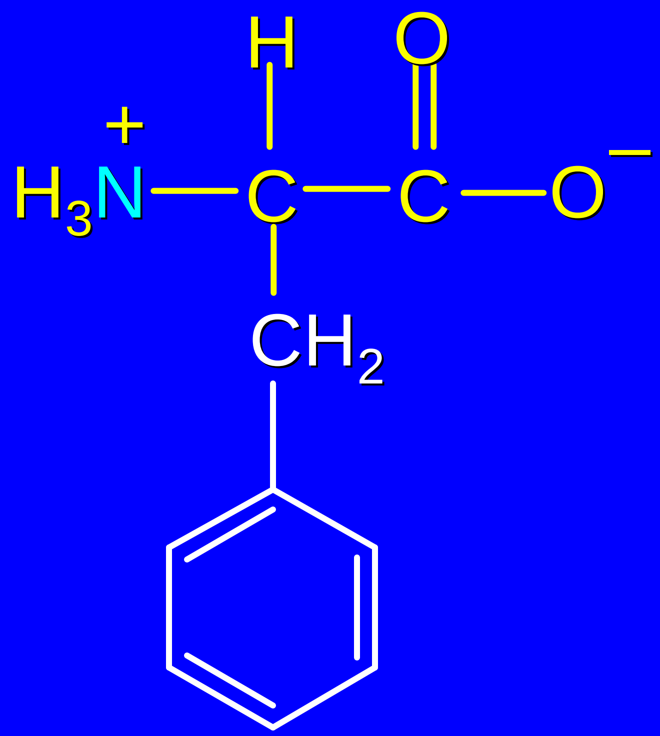
pK_{a1} = 1.99

pK_{a2} = 10.60

pI = 6.30

Table 27.2
Amino Acids with Neutral Side Chains

Phenylalanine



pK_{a1} = 1.83

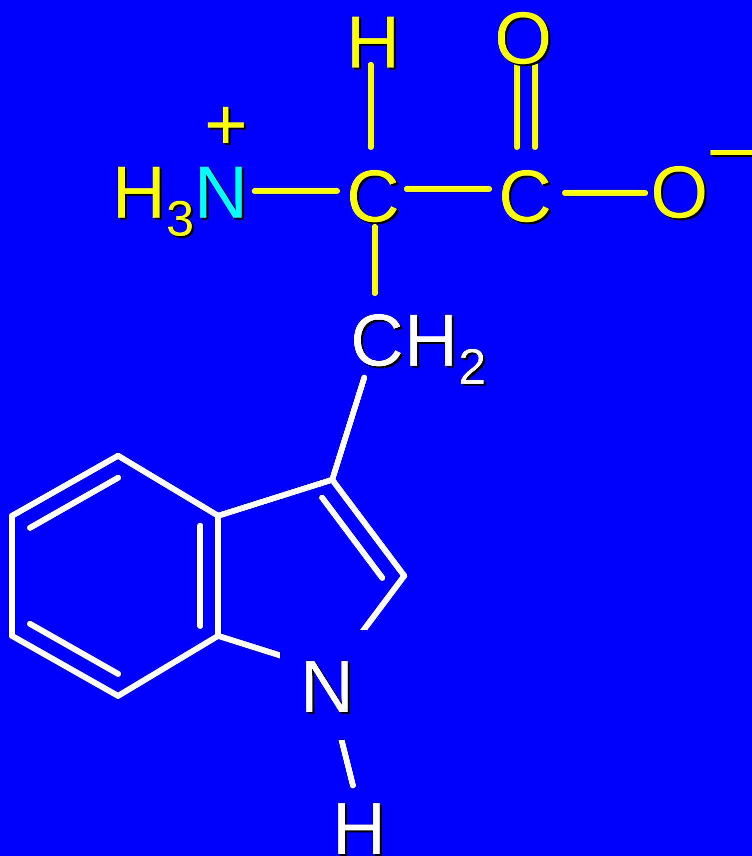
pK_{a2} = 9.13

pI = 5.48

Table 27.2

Amino Acids with Neutral Side Chains

Tryptophan



pK_{a1} = 2.83

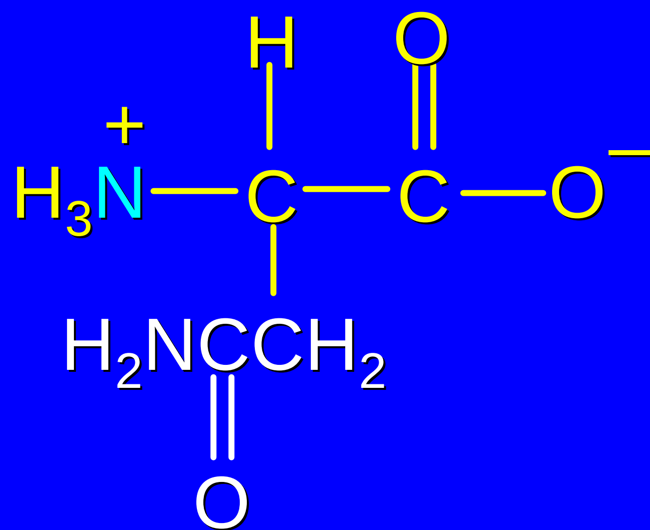
pK_{a2} = 9.39

pI = 5.89

Table 27.2

Amino Acids with Neutral Side Chains

Asparagine



pK_{a1} = 2.02

pK_{a2} = 8.80

pI = 5.41

Table 27.2
Amino Acids with Neutral Side Chains

Glutamine

$pK_{a1} = 2.17$

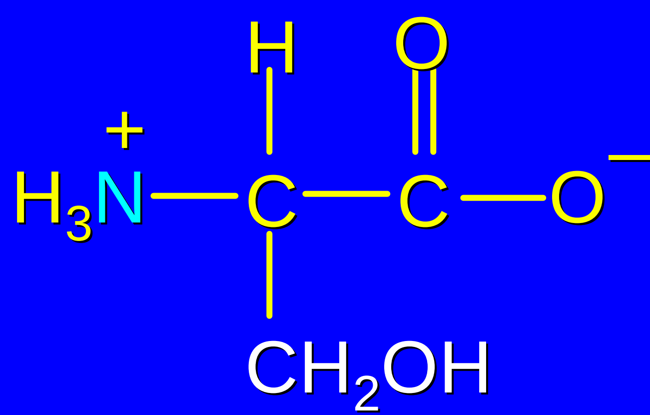
$pK_{a2} = 9.13$

$pI = 5.65$

Table 27.2

Amino Acids with Neutral Side Chains

Serine



pK_{a1} = 2.21

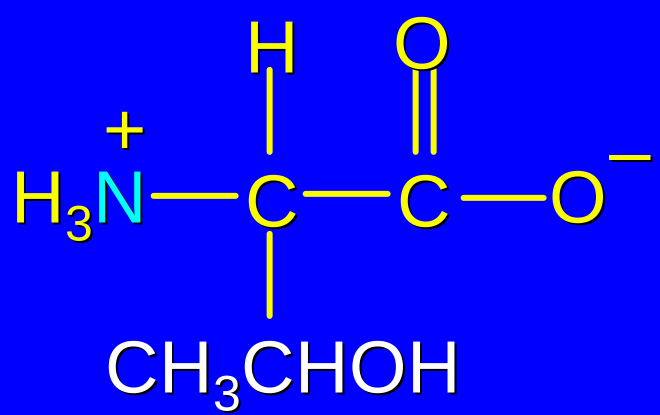
pK_{a2} = 9.15

p*I* = 5.68

Table 27.2

Amino Acids with Neutral Side Chains

Threonine



pK_{a1} = 2.09

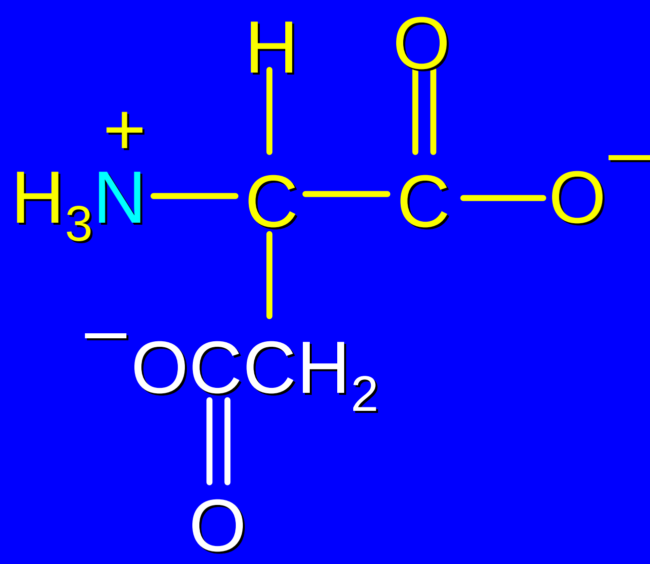
pK_{a2} = 9.10

pI = 5.60

Table 27.3

Amino Acids with Ionizable Side Chains

Aspartic acid



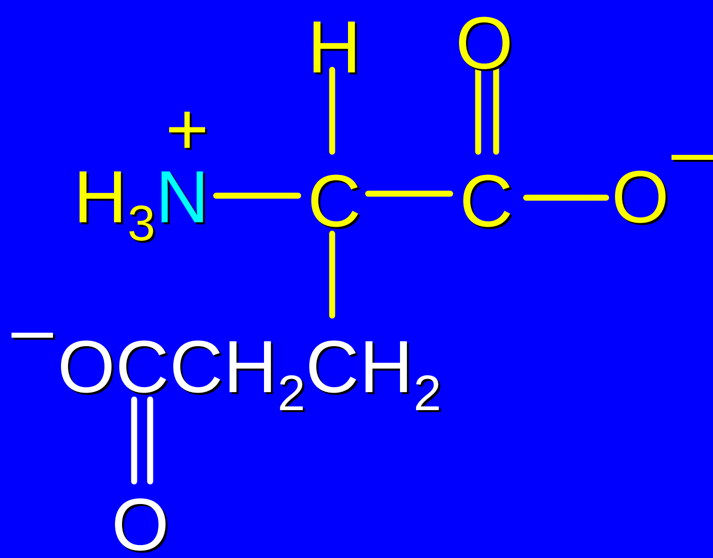
pK_{a1} = 1.88
pK_{a2} = 3.65
pK_{a3} = 9.60
pI = 2.77

For amino acids with acidic side chains, pI is the average of pK_{a1} and pK_{a2}.

Table 27.3

Amino Acids with Ionizable Side Chains

Glutamic acid



pK_{a1} = 2.19

pK_{a2} = 4.25

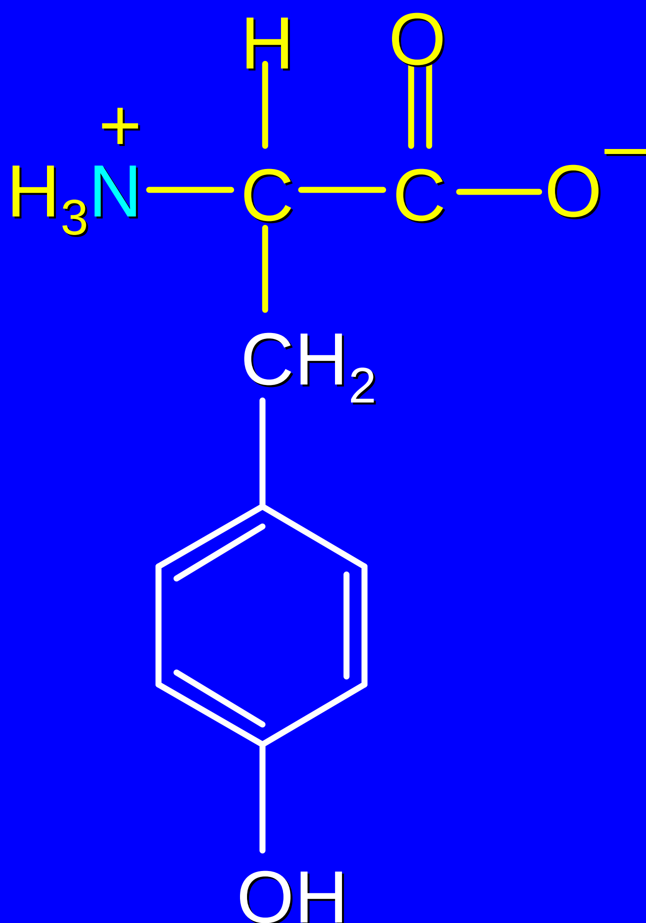
pK_{a3} = 9.67

p*I* = 3.22

Table 27.3

Amino Acids with Ionizable Side Chains

Tyrosine



pK_{a1} = 2.20

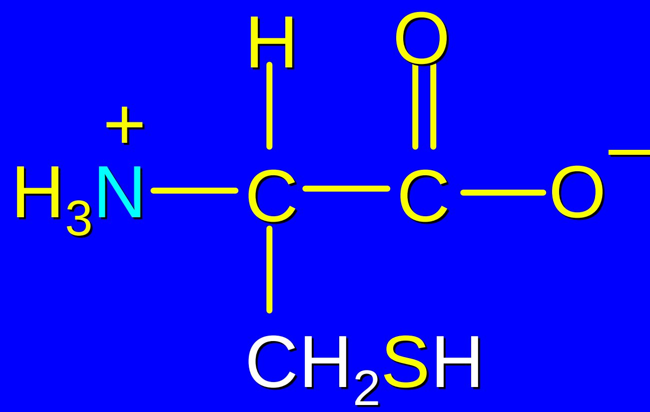
pK_{a2} = 9.11

pK_{a3} = 10.07

pI = 5.66

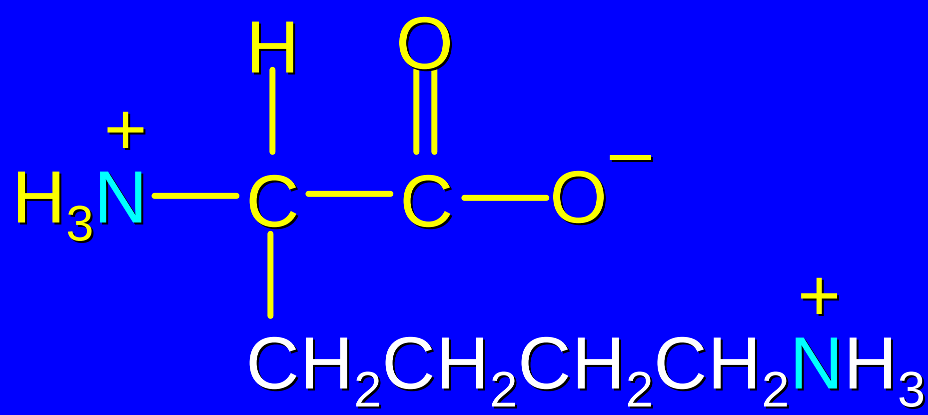
Table 27.3
Amino Acids with Ionizable Side Chains

Cysteine



pK_{a1} = 1.96
pK_{a2} = 8.18
pK_{a3} = 10.28
p*I* = 5.07

Table 27.3
Amino Acids with Ionizable Side Chains



Lysine

pK_{a1} = 2.18
pK_{a2} = 8.95
pK_{a3} = 10.53
p*I* = 9.74

For amino acids with basic side chains, pI is the average of pK_{a2} and pK_{a3}.

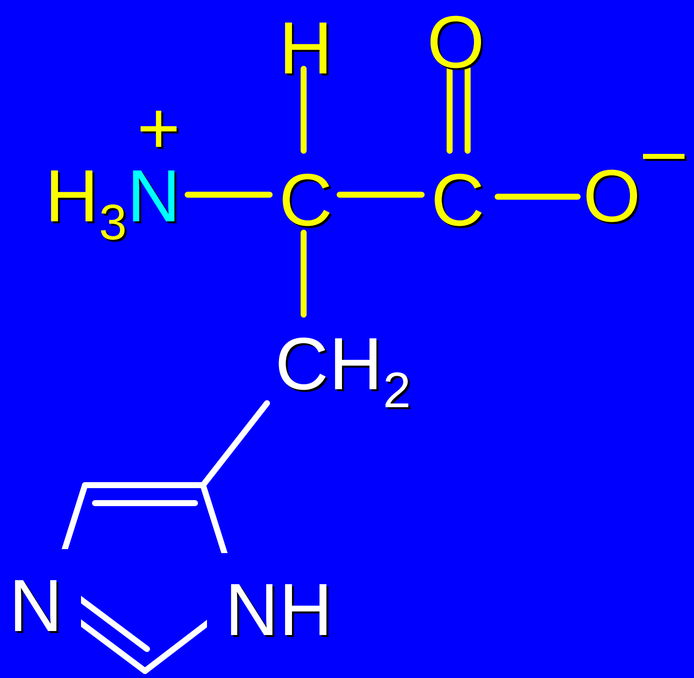
Table 27.3
Amino Acids with Ionizable Side Chains

Arginine

pK_{a1} = 2.17
pK_{a2} = 9.04
pK_{a3} = 12.48
p*I* = 10.76

Table 27.3
Amino Acids with Ionizable Side Chains

Histidine



pK_{a1} = 1.82
pK_{a2} = 6.00
pK_{a3} = 9.17
p*I* = 7.59