Stability Constants (K\textsubscript{stab}), haemoglobin and carbon monoxide poisoning

To succeed in this topic you will need to:
- understand the concepts of ‘dynamic equilibrium’ and Le Chatelier’s Principle
- understand the concepts of complex formation and ligand substitution in transition metal ions
- understand the concepts of entropy

After working through these notes you will be able to:
- understand the concept of stability constants and write out their mathematical expressions from balanced equations
- describe how stability constants can be used to predict the formation of a complex
- explain the biochemical importance of ligand substitution in haemoglobin involving O\textsubscript{2} and CO

What are stability constants?

Stability constants are a way of measuring the stability of transition metal ion complexes. They are an equilibrium based constant and the rules that need to be followed when dealing with them are the same as any other equilibrium constant such as K\textsubscript{c}, K\textsubscript{a} and K\textsubscript{w} and, of course, as with all equilibrium constants, they will vary with temperature.

Definition: The equilibrium constant for an equilibrium existing between a transition metal ion surrounded by water ligands and the complex formed when the same transition metal ion has undergone a ligand substitution reaction. As with any other equilibrium type constants, the value of K\textsubscript{stab} changes as temperature changes.

Ligands are substituted one at a time and so an equilibrium expression could be written for each step. However, it is more common to write an expression for the overall substitution reaction.

Example:

The stability constant for the [CoCl\textsubscript{4}]\textsuperscript{2-} complex can be expressed by considering the formation of the complex from the aqueous cobalt(II) ion

\[
[\text{Co(H}_2\text{O)}\text{6}]^{2+} \text{(aq)} + 4 \text{Cl}^{-} \text{(aq)} \rightleftharpoons [\text{CoCl}_4]^{2-} \text{(aq)} + 6 \text{H}_2\text{O (l)}
\]

\[
K_{\text{stab}} = \frac{[\text{[CoCl}_4]^{2-}]}{[[\text{Co(H}_2\text{O)}\text{6}]^{2+}][\text{Cl}^{-}]^{4}}
\]

Note: with square brackets representing concentration AND complex ions, the K\textsubscript{stab} expression has a lot of brackets! If you make the concentration square brackets slightly larger you will be able to clearly see that you have included all you need to.
As usual the $[\text{H}_2\text{O}]$ should be left out of the expression as all the species are dissolved in water and so water is in large excess. The concentration of water can be considered a constant.

**Units of $K_{\text{stab}}$**

The units for $K_{\text{stab}}$ can be determined in the same way as the units for any other equilibrium constant. Each component is in mol dm$^{-3}$ and you need to ensure that you take into account the powers to which the concentration terms are raised. Cancel out any units that you can before you express the final unit.

e.g.

$$K_{\text{stab}} = \frac{[[\text{CoCl}_4]^{2-}]}{[[\text{Co(H}_2\text{O})_6]^{2+}][\text{Cl}^-]^4} = \frac{\text{mol dm}^{-3}}{\text{mol dm}^{-3} \cdot (\text{mol dm}^{-3})^4} = \frac{1}{\text{mol}^4\text{dm}^{-12}} = \text{mol}^{-4}\text{dm}^{12}$$

[Note: some people prefer the units to be written in decreasing index order – i.e. dm$^{12}$mol$^{-4}$]

The same principles can be applied to the substitution of H$_2$O ligands by multidentate ligands such as ethane-1,2-diamine (en), ethanedioate (C$_2$O$_4^{2-}$) and EDTA$^{4-}$.

$$[\text{Cu(H}_2\text{O})_6]^{2+} \text{(aq)} + 3 \text{en (aq)} \iff [\text{Cu(en)}_3]^{2+} \text{(aq)} + 6 \text{H}_2\text{O (l)}$$

$$K_{\text{stab}} = \frac{[[\text{Cu(en)}_3]^{2+}]}{[[\text{Cu(H}_2\text{O})_6]^{2+}][\text{en}]^3} \text{mol}^{-3}\text{dm}^{9}$$

**The size of $K_{\text{stab}}$:**

The larger the value of $K_{\text{stab}}$ the further the equilibrium lies in favour of the products (i.e. the substituted complex). The more stable the complex, the higher the value of its $K_{\text{stab}}$. This means that you can compare the stability of differently substituted metal ions and predict the complex that will be more likely to form in solution.

[Note: sometimes the values are quoted as log $K_{\text{stab}}$ to make the numbers easier to handle]
Questions:

1) Give the expression for the $K_{\text{stab}}$ for the complex $[\text{Ni(NH}_3\text{)}_6]^{2+}$ and give the units.

2) Consider the data below. Rank the complex ions in order of increasing stability?

\[
\begin{align*}
[\text{Cu(NH}_3\text{)}_4(\text{H}_2\text{O})_2]^{2+} & \quad K_{\text{stab}} = 1 \times 10^{13} \text{ mol}^{-4} \text{dm}^{12} \\
[\text{Co(NH}_3\text{)}_6]^{2+} & \quad K_{\text{stab}} = 2 \times 10^{4} \text{ mol}^{-6} \text{dm}^{18} \\
[\text{Ni(NH}_3\text{)}_6]^{2+} & \quad K_{\text{stab}} = 1 \times 10^{8} \text{ mol}^{-6} \text{dm}^{18}
\end{align*}
\]

3) An aqueous solution containing 1.0 mol dm\(^{-3}\) of $[\text{CuCl}_4]^{2-}$ and 0.5 mol dm\(^{-3}\) Cl\(^-\) ions was at equilibrium.

Calculate the concentration of $[\text{Cu(H}_2\text{O})_6]^{2+}$ present given the $K_{\text{stab}} = 4.17 \times 10^5$ mol\(^{-4}\) dm\(^{12}\)

Stability of multidentate ligand complexes:

The stability constants for complexes with multidentate ligands show that multidentate complexes are often more stable than complexes containing monodentate ligands.

The diagram below shows three complexes of nickel (II) ion. The values of $K_{\text{stab}}$ for each complex are given below. You can see by looking at the $K_{\text{stab}}$ values that the complex containing the bidentate ligand, en, is more stable than the one containing the monodentate ligand. Similarly, the complex containing the hexadentate ligand, EDTA, is more stable still.

\[
\begin{align*}
[\text{Ni(NH}_3\text{)}_6]^{2+} & \quad 5 \times 10^7 \text{ mol}^{-6} \text{dm}^{18} \\
[\text{Ni(en)}_3]^{2+} & \quad 2 \times 10^{18} \text{ mol}^{-3} \text{dm}^{9} \\
[\text{Ni(EDTA)}]^{2-} & \quad 1 \times 10^{13} \text{ mol}^{-1} \text{dm}^{3}
\end{align*}
\]

This also means that, since the $K_{\text{stab}}$ for the EDTA complex is greater than the other complexes, that EDTA will substitute for the other ligands.

e.g.

\[
[\text{Ni(NH}_3\text{)}_6]^{2+} (aq) + \text{EDTA}^{4+} (aq) \rightleftharpoons [\text{Ni(EDTA)}]^{2-} (aq) + 6 \text{NH}_3 (aq)
\]
This is called the chelate effect. A chelate is a complex ion that contains a multidentate ligand. A chelating agent is any multidentate ligand that will substitute for monodentate ligands.

[Note: chelate comes from the Greek word meaning ‘claw’.]

Explaining the chelate effect.

Whichever example you consider, you will always find that a chelate is more stable than an ion with only monodentate ligands. To explain this, you have to consider the substitution equilibrium and the entropy change that occurs.

Let’s take the equilibrium for the substitution of NH₃ ligands by EDTA shown above.

We can predict the entropy change for the reaction to be high. Remember that entropy is a measure of disorder – the more disorder, the higher the entropy. Reactions tend to favour an increase in entropy. This is not always the case, as enthalpy has a part to play in reaction predictions too, but in this case, the enthalpy change is fairly small.

In the forward reaction, you can see that 2 species react to form 7 species. You can get more disorder from 7 species than 2 so there will be a significant increase in entropy (ΔS will be positive). The reverse reaction would involve a significant decrease in entropy (ΔS will be negative) and so the reaction is unlikely to happen unless there is a large negative change in enthalpy (ΔH needs to be negative). This means that the chelate is very stable.

[Note: There is unlikely to be a significant change in enthalpy in these ligand substitution reactions since the number and type of bonds broken and made in the reaction is similar.]

Questions:

4) The $K_{\text{stab}}$ values for two cobalt(II) complexes are shown below.

\[
\begin{align*}
[\text{Co(NH}_3)_6]^2^+ & \quad 2.5 \times 10^4 \text{ mol}^{-6}\text{dm}^{18} \\
[\text{Co(EDTA)}]^2^- & \quad 2.0 \times 10^{16} \text{ mol}^{-1}\text{ dm}^{3}
\end{align*}
\]

a) Write the equations for the formation of these complexes from the hexaaquacobalt(II) ion, $[\text{Co(H}_2\text{O})_6]^2^+$

b) Write expressions for the stability constants for these complexes and give the units.

c) Explain why the stability constant of the $[\text{Co(EDTA)}]^2^-$ complex is much greater than that of the $[\text{Co(NH}_3)_6]^2^+$ complex
Haemoglobin and stability constants.

Haemoglobin is a protein in red blood cells that transports oxygen from the lungs to the tissues. The haem group in the haemoglobin molecule is a non-polypeptide co-factor that consists of a central Fe$^{2+}$ ion coordinately bonded to a porphyrin ring. The porphyrin ring can be described as a tetradeutate ligand since it forms 4 coordinate bonds to the central Fe$^{2+}$ ion.

One of the other coordinate bonds to the Fe$^{2+}$ ion is responsible for attaching the haem group to the polypeptide chain and the other is where the oxygen molecule is attached. When oxygen is not being carried, a water ligand is usually present instead.

There are 4 haem groups per haemoglobin molecule.

Deoxygenated haemoglobin (deoxyhaemoglobin) can be represented as Hb(H$_2$O)$_4$  
Oxygenated haemoglobin (oxyhaemoglobin) can be represented as Hb(O$_2$)$_4$

Consequently when deoxygenated blood reaches the lungs a ligand substitution reaction occurs.

\[
\text{Hb}(H_2O)_4 + 4 O_2 \xrightleftharpoons{\text{lungs}}^{\text{tissues}} \text{Hb}(O_2)_4 + 4 H_2O
\]

Of course, in the tissues, the reverse reaction takes place and oxygen is released to be used by the cells for respiration.

[Note: Le Chatelier’s Principle can be applied here to describe how under conditions of high oxygen concentration (i.e. the lungs) the forward reaction is favoured and oxygen is picked up by haemoglobin and under conditions of low oxygen concentration (i.e. the tissues) the reverse reaction is favoured and oxygen is released.]
The formation of oxyhaemoglobin falls precisely into the type of reactions for which we can describe a stability constant.

\[
K_{\text{stab}} = \frac{[\text{Hb}(\text{O}_2)_4]}{[\text{Hb}(\text{H}_2\text{O})_4][\text{O}_2]^4}
\]

Carbon monoxide poisoning

Carbon monoxide also bonds to the Fe\(^{2+}\) ion in haemoglobin to form carboxyhaemoglobin, Hb(CO)\(_4\).

A ligand substitution equilibrium for the reaction in which carbon monoxide replaces the water ligands can be written

\[
\text{Hb}(\text{H}_2\text{O})_4 + 4 \text{CO} \rightleftharpoons \text{Hb}(\text{CO})_4 + 4 \text{H}_2\text{O}
\]

The stability constant for carboxyhaemoglobin is much greater than for oxyhaemoglobin. This means that carboxyhaemoglobin is more stable than oxyhaemoglobin. Therefore carbon monoxide binds in preference to oxygen and forms a stronger coordinate bond to the iron. Consequently if oxyhaemoglobin is exposed to carbon monoxide, the oxygen molecules will be substituted for carbon monoxide.

\[
\text{Hb}(\text{O}_2)_4 + 4 \text{CO} \rightleftharpoons \text{Hb}(\text{CO})_4 + 4 \text{O}_2
\]

The equilibrium lies heavily towards the right hand side.

Of course, treatment of carbon monoxide poisoning involves breathing air containing high levels of oxygen. Le Chatelier’s Principle can be seen to be applied here as increasing oxygen concentration will encourage the equilibrium to move to the left hand side causing the carbon monoxide to be released.

Questions

5) Using ligand substitution reactions, explain how haemoglobin can transport oxygen in the blood

6) Carbon monoxide binds to haemoglobin in preference to oxygen. Explain in terms of stability constants and bond strengths why this is the case.
Answers

1) \[ K_{stab} = \frac{[\text{Ni(NH}_3\text{)}_6]^{2+}}{[\text{Ni(H}_2\text{O})_6]^{2+}} \cdot [\text{NH}_3]^6 \text{ mol}^{-6}\text{dm}^{18} \]

2) lowest stability: \([\text{Co(NH}_3\text{)}_6]^{2+}\)

highest stability: \([\text{Cu(NH}_3\text{)}_4(H}_2\text{O)}_2]^{2+}\)

[note: remember as the stability constant increases, the stability of the complex increases]

3) Substituting the data in the question into the expression for \(K_{stab}\) and rearranging gives

\[
\frac{1.0}{((4.17 \times 10^5) \times 0.5^4)} = 3.84 \times 10^{-5} \text{ mol dm}^{-3}
\]

[note: remember to raise the concentration of Cl\(^-\) ions to the power 4]

4a) \([\text{Co(H}_2\text{O})_6]^{2+} (\text{aq}) + 6 \text{ NH}_3 (\text{aq}) \rightleftharpoons [\text{Co(NH}_3\text{)}_6]^{2+} (\text{aq}) + 6 \text{ H}_2\text{O (l)} \]

\([\text{Co(H}_2\text{O})_6]^{2+} (\text{aq}) + \text{EDTA}^{4-} (\text{aq}) \rightleftharpoons [\text{Co(EDTA)}]^{2-} (\text{aq}) + 6 \text{ H}_2\text{O (l)} \]

4b) \[ K_{stab} = \frac{[[\text{Co(NH}_3\text{)}_6]^{2+}]}{[[\text{Co(H}_2\text{O})_6]^{2+}].[\text{NH}_3]^6} \text{ mol}^{-6}\text{dm}^{18} \]

\[ K_{stab} = \frac{[[\text{Co(EDTA)}]^{2-}]}{[[\text{Co(H}_2\text{O})_6]^{2+}].[\text{EDTA}]} \text{ mol}^{-4}\text{dm}^{3} \]

4c) The EDTA complex is more stable than the NH\(_3\) complex because when the EDTA complex is formed there is a large increase in entropy (7 species formed from 2 species). In the formation of the NH\(_3\) complex, there is very little entropy change (7 species formed from 7 species). This effect is called the chelating effect.

5) In the lungs, an oxygen molecule binds to the Fe\(^{2+}\) ion in the haem group of the haemoglobin molecule substituting a water molecule. As the blood circulates through the body, the bond between the oxygen molecule and the Fe\(^{2+}\) ion is broken and oxygen is released into the tissues.

6) \(K_{stab}\) for carboxyhaemoglobin is greater than for oxyhaemoglobin. This means that carboxyhaemoglobin is more stable than oxyhaemoglobin. The coordinate bond that is formed between the CO molecule and the Fe\(^{2+}\) ion is stronger than the bond between the oxygen molecule and the Fe\(^{2+}\) ion.