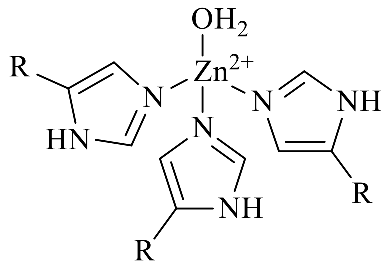
Marks 7

- The structure below represents the active site in carbonic anhydrase, which features a $Zn^{2+}$ ion bonded to 3 histidine residues and a water molecule.




The p$K_a$ of uncoordinated water is 15.7, but the p$K_a$ of the water ligand in carbonic anhydrase is around 7. Suggest an explanation for this large change.

**The high charge on the $Zn^{2+}$ ion draws electron density out of the O–H bonds in the water molecule. This weakens the O–H so the $H^+$ is more likely to leave.**

**The water in carbonic anhydrase is therefore more acidic, as shown by the large decrease in p$K_a$.**

When studying zinc-containing metalloenzymes, chemists often replace $Zn^{2+}$ with $Co^{2+}$. Using the box notation to represent atomic orbitals, work out how many unpaired electrons are present in the $Zn^{2+}$ and $Co^{2+}$ ions.

| | | | | | |
|---|---|---|---|---|---|
| **$Zn^{2+}$, $3d^{10}$** | ↑↓ | ↑↓ | ↑↓ | ↑↓ | ↑↓ |
| **$Co^{2+}$, $3d^{7}$** | ↑↓ | ↑↓ | ↑ | ↑ | ↑ |

**$Zn^{2+}$ has 0 unpaired *d* electrons, $Co^{2+}$ has 3 unpaired *d* electrons. $Co^{2+}$ is therefore paramagnetic and will be attracted by a magnetic field.**

Suggest why it is useful to replace $Zn^{2+}$ with $Co^{2+}$ when studying the nature of the active site in carbonic anhydrase.

**The ions have similar radii so the properties of natural carbonic anhydrase and the version with cobalt replacing zinc should have similar biological properties. The unpaired electrons on $Co^{2+}$ however mean that it is paramagnetic and the magnetism can be used to study the active site.**

Suggest two differences in the chemistry of $Zn^{2+}$ and $Co^{2+}$ ions that may affect the reactivity of the cobalt-containing enzyme.

**Zinc only forms +2 ions but cobalt forms +2 and +3. The cobalt-containing enzyme may be susceptible to oxidation.**

**$Zn^{2+}$ tends to form 4-coordinate tetrahedral complexes but $Co^{2+}$ is slightly larger and often forms 6-coordinate octahedral complexes. The metal ion may change its coordination by bonding extra ligands.**