

Introduction to Reactions and Mechanisms

Reaction the transformation of one or more substances (reactants) into different substances (products).

Mechanism the events that take place on a molecular level as reactants become products. *Mechanism is the movement of electrons.*

The most important mechanistic concept is **electronegativity**. This simple idea helps us decide where the electrons are coming from, and where they go to during the course of a reaction.

Here's the reaction of hydroxide ion with an alkyl halide.

The reverse reaction doesn't happen, because Br is more stable as Br⁻ than OH is as OH⁻

And notice the stereochemistry – according to this mechanism, we expect a reversal of chirality as the (S) –2-bromobutane flips inside out during the addition of OH⁻.

Categories of Organic Reactions

Substitution

General Case

Specific Example

In a substitution reaction, one group replaces another.

Addition

General Case

Specific Example

In an addition reaction, all parts of the adding reactant appear in the product.

Elimination

General Case

Specific Example

In an elimination reaction the reactant loses the elements of a small molecule. Elimination is the opposite of addition. If $X = H$ and $Y = OH$ the reaction is a **dehydration**. If $X = H$ and $Y =$ a halogen, the reaction is a **dehydrohalogenation**.

Rearrangement

General Case

Specific Example

A rearrangement occurs if a molecule reorganizes its framework during the reaction.

Acid-Base Reactions – The Simplest Reactions

Now would be a really good time to review your general chemistry of acids, bases, conjugate acids and conjugate bases.

Here's the familiar **Lowry-Brønsted** definition:

an acid is a proton donor

a base is a proton acceptor

Why?

A proton is H^+ . It is strongly electronegative (don't get confused with the atom H, which is electropositive). Bases are electron-rich atoms/ions/molecules

So a base can supply the electrons that a proton so badly needs

So this business of proton donation/acceptance is just a special case of electronegativity. Electropositive ions/atoms/molecules are strongly attracted to (and may bond with) electronegative ions/atoms/molecules. This leads to a more general, "non-protoncentric" definition of acids and bases.

The **Lewis** definition:

an acid is an electron pair acceptor

a base is an electron pair donor

According to this broader definition, any electron-deficient atom/ion/molecule can act as a Lewis acid. This is much more useful for organic chemistry than being stuck with protons.

For example the atoms of group 3A (aluminum, boron) have a sextet of electrons in their outer shells. This electron deficiency makes them strong Lewis acids.

Also Zn^{2+} and Fe^{3+} salts. Zn^{2+} has an unoccupied 4s shell just waiting for a pair of electrons...

There are also organic Lewis acids and bases

Carbon Lewis Acids and Bases

Carbocation. **Cations** migrate to the **cathode** of an electrochemical cell, so they have **positive** charge. A carbocation has 6 electrons in its outer shell, so is electron deficient. A carbocation is a **Lewis acid**. It is an **electrophile**.

Carbanion. **Anions** migrate to the **anode** of an electrochemical cell, so they have **negative** charge. A carbanion has a surplus of electrons. A carbanion is a **Lewis base**. It is a **nucleophile**.

Acids, Bases and Curly Arrows

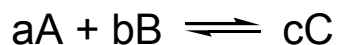
Curly arrows (with a whole arrow head, not half an arrow head) show where an electron pair has come from (a covalent bond or a lone pair, for example) and points to the electron-deficient part of the molecule where they will go.

As an exercise, label the conjugate acids and the conjugate bases.

Acids and Bases. K_a and pK_a

Another good time to review your General Chemistry notes!

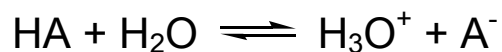
For any equilibrium process



The equilibrium constant is defined as

$$K =$$

For the ionization of any protic acid



The acidity constant is defined as

$$K_a =$$

A large value of K_a indicates a strong acid, a small value of K_a indicates a weak acid. Formic acid is a weak acid with $K_a = 1.77 \times 10^{-4}$. What is the concentration of formate ion in a 0.1 M aqueous solution of formic acid?

K_a can have values from 0.000001 (or less) to 10,000,000 (or more). This isn't very convenient, so we use pK_a instead.

$$\text{pK}_a = -\log_{10}K_a$$

So if K_a = 0.000001, pK_a = 6 (a very weak acid, eg H₂CO₃). If K_a = 10,000,000 pK_a = -7, (a very strong acid, eg HCl). **Low (and -ve) pK_a = strong acid. High pK_a = weak acid.**

Also notice that because of the relationship $\Delta G^\circ = -RT\ln K$, **pK_a \propto ΔG° !**

Strong and Weak Bases

Use your knowledge of the acid to predict the strength of a base.

eg HCl is a strong acid (pK_a = -7) – what does that say about Cl⁻, its conjugate base?

H₂O is a very weak acid (pK_a = 15.7) – what does that say about OH⁻, its conjugate base?

Amines are bases that are commonly encountered in organic chemistry. The simplest example is ammonia.

Ammonium ion is the conjugate acid of ammonia. The pK_a of the ammonium ion is 9.2.

Compare methylamine.

The pK_a of the methylammonium ion is 10.6. So the ammonium ion is a stronger acid than the methylammonium ion, hence methylamine is the stronger base.

In the recrystallization lab you might have used 4-chloroaniline.

The pKa of 4-chloroanilinium is 3.98. Is it a stronger or a weaker base than methylamine?

Acid-Base Reactions

Acid-base reactions always favor the weaker acid and the weaker base.

This often results in the formation of water-soluble salts

Structure and Acidity

Electronegativity

General Chemistry – acidity increases with increasing electronegativity of the counterion.

Look at the first row of the periodic table:

Hybridization

More s-character in a hybrid orbital bond means that electrons in that orbital will have lower energies than those in orbitals with more p-character. This is because s-orbitals hold electrons closer to the nucleus.

If we pull a proton off ethyne, the remaining pair of electrons occupies an sp orbital with 50% s-character. If we do the same to ethene, the electrons are left behind in an sp² orbital which has 33% s-character.

Remember that a more stable anion means a freer proton, hence a stronger acid.

Ethyne is more acidic than ethene, which is more acidic than ethane.

And as we expect, the reverse trend is seen with the basicity of the carbanions

Inductive Effects

Consider *tert*-butanol ($pK_a = 18$) and methanol ($pK_a = 15.2$)

Methanol is the stronger acid. This is because the three methyl groups of $(CH_3)_3CO^-$ can supply negative charge through their σ -bonds to the electronegative oxygen atom, effectively increasing its charge density compared to CH_3O^- . The oxygen atom in methoxide has less negative charge density than the oxygen in *tert*-butoxide, so it holds its proton less strongly. A freer proton is a stronger acid.

As we expect, *tert*-butoxide is a stronger base than methoxide.

Alkyl groups are said to be **inductively donating**.

Resonance Effects

Consider methanol ($pK_a = 15.2$) and phenol ($pK_a = 9.9$).

Phenol is the stronger acid. We can draw 5 resonance structures for the phenolate anion. Three of these place the electrons at locations other than the oxygen.

Remember that more resonance structures equals more stability, so the phenolate anion is **resonance stabilized**, and has less need of the proton to stabilize it than methanol.