

Organic and Inorganic Reactivity

Lecture 1

In the next four lectures I and Dr. Welton will be looking at the reactivity of organic and inorganic compounds respectively in an overall perspective. In particular we want to show you where the patterns of reactivity in these two areas of chemistry are similar and where they differ so that you will be able to see that, in terms of reactivity, organic and inorganic chemistry are related in spite of an historical separation.

Functional Group Approach.

Historically, the chemistry of organic compounds has been taught according to the type of functional group within the molecule. What is a functional group? If we look at 1-butanol:



We see that it has many atoms and therefore potentially many sites of attack by various reagents. However, most (but not all!!) of its chemistry is dictated by the hydroxyl group OH. Since this functions as its main site of reactivity it is termed the functional group. The advantage of teaching according to the functional group is that the chemistry of the functional group is largely (but not exclusively!!) the same irrespective of the nature of the rest of the molecule i.e. 1-butanol behaves just like ethanol, 1- or 2-propanol, 2-butanol, 1- or 2- or 3-pentanol etc. Thus we only have to learn the limited number of reactions of the functional group rather than the individual chemistries of each molecule containing that group. As a means of classification of organic compounds, the functional group approach is still very useful. However, if we look at a list of common functional groups in organic chemistry (Table 1) we see that there is still a lot of bulk learning, especially since this list is not comprehensive and there are at least 100 functional groups.

Table 1 Common Functional Groups

<u>Structure</u>	<u>Name</u>
R-F	Fluoroalkanes, Alkyl fluorides
R-Cl	Chloroalkanes, Alkyl chlorides
R-Br	Bromoalkanes, Alkyl bromides
R-I	Iodoalkanes, Alkyl iodides
R-OH	Alkanols, Alcohols
R ¹ -OR ²	Dialkyl ethers, Ethers
R-SH	Alkanethiols, Thiols
R ¹ -SR ²	Dialkyl sulphides
RSO ₃ H	Sulphonic Acids
R-NH ₂	Monoalkylamines, Primary amines
R ₂ NH	Dialkylamines, Secondary amines
R ₃ N	Trialkylamines, Tertiary amines
R ₄ N ⁺ X ⁻	Tetraalkylammonium Salts

R-NO	Nitrosoalkanes
R-NO ₂	Nitroalkanes
R-Li	Alkyllithiums
R-MgX	Alkylmagnesium halides, Grignards
R-H	Alkanes (Paraffins)
R ₂ C=CR ₂	Alkenes (Olefins)
RC≡CR	Alkynes (Acetylenes)
PhH, ArH	Benzenes, Arenes
RCH=O	Alkanals, Aldehydes
R ¹ R ² C=O	Alkanones, Ketones
R-CN	Alkanonitriles, Alkyl Cyanides
RC(=O)OH	Alkanoic acids, Carboxylic acids
RC(=O)Cl	Acyl chlorides, Acid chlorides
R ¹ C(=O)OR ²	Esters
R ¹ C(=O)NR ² ₂	Amides
RC(=O)OC(=O)R	Anhydrides

In inorganic chemistry the same functional groups occur but it is the elements themselves which tend to dominate the chemistry and the functional groups perform a more moderating function.

Mechanism Approach

In an effort to overcome the problem of the multitude of functional groups, organic chemists in the 1930s began to consider classifying organic compounds according to reactivity, that is according to the mechanisms of the reactions of each functional group since each of these mechanisms might encompass a number of functional groups. What is a mechanism? A mechanism is simply a description of what happens to the bonds during a reaction i.e. which ones are broken and which are made and in which sequence that occurs. Since bonds are comprised of electrons, a mechanism is really a description of what happens to electrons during a reaction. Hence the introduction of the term “Electronic Theory of Organic Reactions” for mechanisms in the 1930s by the founder of much organic mechanistic detail, C. K. Ingold.

When we do this with the large number of functional groups in organic chemistry we find that there are only 10 major reaction types (table 2). Within each of these reaction types there may be more than one mechanism but the total does still not number greater than approximately 30.

Table 2 Reaction Types

<u>Reaction Type</u>	<u>Seen in the Chemistry of</u>
1. Nucleophilic Substitution	Alkyl Halides
2. Electrophilic Substitution	Alkyl Metals
3. Radical Substitution	Alkanes

4.	Nucleophilic Addition	Aldehydes, Ketones, Nitriles
5.	Electrophilic Addition	Alkenes, Alkynes
6.	Radical Addition	Alkenes, Alkynes
7.	Nucleophilic Addition – Elimination	Carboxylic Acid Derivatives
8.	Electrophilic Addition – Elimination	Arenes
9.	Elimination	Alkyl Halides
10.	Pericyclic	1,3-Dienes

Note that electrophilic addition-elimination reactions of arenes (entry 8)(benzene and its derivatives) are often called electrophilic substitution because that is the overall result – please note, however, that it is a combination of two reactions and is not the same as the true electrophilic substitution of alkyl metals (entry 2). Note, also, that oxidation and reduction are not included in the table. This is because many oxidation and reduction reactions are actually described by some of the reactions 1 – 10. **This is not true in inorganic chemistry where processes of electron transfer occur which are fairly rare in organic chemistry.** I will deal with oxidation and reduction at the end of the lectures. In the meantime we will run through each of the 10 basic reaction types and compare them with their inorganic counterparts.

In order to show how electrons are moving in organic reactions, organic chemists use a technique known as Arrow-Pushing. Inorganic chemists tend not to do this to any great extent. As I run through these reactions I will be drawing the arrow-pushing; this will be covered again in a workshop.

We have noted that mechanistic chemistry is about the electrons in the molecule. In organic molecules there are three environments for electrons, namely;

- Single bond = σ -electrons
- Multiple bond = π -electrons
- Lone pairs of electrons

In inorganic chemistry we have additionally the electrons in the d- (and sometimes f-) orbitals on the metal.

Before we discuss each reaction we need a few definitions:

- Nucleophile(literally nucleus seeking; often denoted by Nu): A species which is electron rich and whose electrons are available to make bonds with electrophiles
- Electrophile (literally electron seeking; often denoted by E): A species which is electron poor and is able to accept electrons to make bonds from nucleophiles.
- Radical (often denoted R): A species with a single electron rather than an electron pair which wishes to pair up its single electron.
- Substitution: Replacement of one functional group by another
- Addition: Combination of one molecule with another
- Elimination: Cleavage of one molecule from another (the opposite of addition)
- Pericyclic: Involves a movement of electrons in a cyclic manner.

We will now look at each reaction keeping these definitions and the three electron environments in mind.

Nucleophilic Substitution

This is characteristic of alkyl halides. If we study an alkyl halide in detail:



We see that we have two of the types of electron environments mentioned above, namely, σ -electrons and lone pairs. The halogens are very electronegative elements i.e. they attract electrons towards themselves. This has two consequences for alkyl halides:

- The lone pair electrons are generally not available to make bonds
- The σ -electrons are closer to the halogen atom than to the carbon atom thus creating a permanent dipole moment in the C-X bond.

The resultant slight positive charge on the carbon atom makes it susceptible to attack by nucleophiles e.g.



This process may occur by two mechanisms which you may have covered at school, $\text{S}_{\text{N}}1$ (substitution, nucleophilic, unimolecular) and $\text{S}_{\text{N}}2$ (substitution, nucleophilic, bimolecular). In inorganic chemistry the same mechanisms may occur but $\text{S}_{\text{N}}1$ is called “dissociative” and $\text{S}_{\text{N}}2$ is called “interchange”. In addition there is a third mechanism in inorganic chemistry called “associative” for which there is no counterpart in organic. Thus, silicon is in the same group as carbon so we might expect similar mechanisms to accrue for halosilanes, R_3SiX . However, the $\text{S}_{\text{N}}1$ mechanism is almost unknown in silicon chemistry and the chemistry is dominated by both interchange and associative mechanisms.

If the nucleophile is the solvent then the substitution process is called a solvolysis:



Electrophilic and Radical Substitution Reactions

These do not have a ready counterpart in inorganic chemistry

Alkyl metals e.g. Grignard reagents, RMgBr , have very electropositive elements attached to carbon which repel σ -electrons thus setting up an opposite polarisation in the metal-carbon bond compared to alkyl halides i.e. the carbon is now slightly negatively charged and attracts electrophiles e.g.



Note that as far as the metal is concerned this reaction is another nucleophilic substitution since the counter-anion, X^- , of the acid HX interchanges with the organic group R . It may also be considered a metathesis.

Radical substitution tends to occur mainly in the chemistry of alkanes. Alkanes have neither strongly electronegative elements nor strongly electropositive elements

attached to carbon. Hence they do not suffer nucleophilic or electrophilic attack. They do, however, have a lot of electrons associated with the C-H bonds and these can be used to pair up with the single electrons of the radicals e.g.

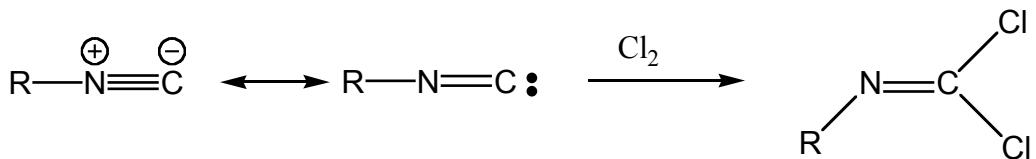


“ α -Addition”

The generic equation for this process is:



This process corresponds to oxidative addition in inorganic chemistry. It is very rare in organic chemistry because carbon does not have a variable oxidation state but it does occur during the addition to isonitriles (also called isocyanides) which formally can be considered as derivatives of carbon(II):



The corresponding addition to carbon monoxide is an example of a reaction called Insertion in inorganic chemistry.

“ β -Addition”

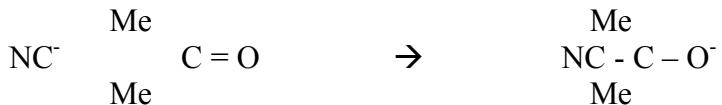
The generic equation for this process involves the addition of one molecule to another containing a multiple bond:



In inorganic chemistry the reaction where XY is the inorganic component is quite rare because of the rarity of multiple bonds in inorganic compounds.

The alternative where AB is the inorganic component adding to an organic compound XY is much more common and is again called Insertion

In organic chemistry multiple bonds abound, both C – C and C – X bonds. For C – X bonds the addition is mechanistically nucleophilic addition. In order to get a nucleophilic addition we need a multiple bond with the same polarisation as the single bond of the alkyl halides. Just such is available in the carbonyl group because oxygen is also fairly electronegative (although less so than the halogens) and attracts electrons to itself e.g.



For C – C bonds the addition is mechanistically electrophilic or radical addition.

Typical substrates for both these mechanisms are the alkenes and alkynes. The multiple bonds in these are not polarised in any powerful way (so the electrophile or

radical may attack either end in an unsymmetrical alkene or alkyne) but the π -electrons are further removed from the nucleus than are σ -electrons and therefore are more readily available to make bonds e.g.

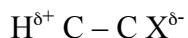


β -Elimination

We saw in alkyl halides that the electronegativity of the halogen polarised the C-X bond strongly:



This is sufficiently strong that some of the polarisation extends further along the chain to the C-H bonds on an adjacent (β) carbon:



These hydrogen atoms are thus susceptible to attack by bases resulting in the elimination (called β -elimination) of the elements of HX from the alkyl halide e.g.



In inorganic chemistry β -elimination refers to the reverse of β -Addition above i.e. where an inorganic compound A-B is eliminated from A-X-Y-B. This is often also called an Extrusion which is different from an extrusion in organic chemistry (see below).

α -Elimination

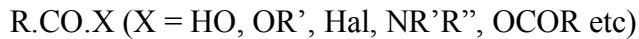
If there are no hydrogens on the adjacent carbon or no adjacent carbon, very occasionally α -elimination occurs. e.g. :



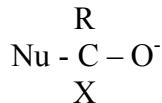
This results in a very reactive, six-electron, divalent carbon species known as a carbene. **The reaction is equivalent to the reductive elimination of inorganic chemistry.**

Nucleophilic Addition – Elimination

These mechanisms are characteristic of acid derivatives such as carboxylic acid themselves, esters, acid halides, amides, acid anhydrides etc. all of which may be represented by the generic formula:



The first step in these mechanisms is the same as the nucleophilic addition to aldehydes and ketones to give the tetrahedral intermediate:



But now we have a group attached to the original carbonyl carbon which is capable of leaving the molecule, i.e. X^- is a reasonably stable entity, so we can eliminate X^- :

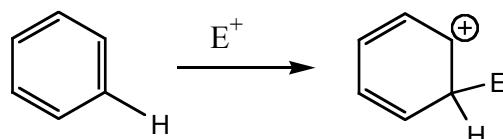


The overall combination looks like a nucleophilic substitution but it almost always proceeds through the two steps e.g.:

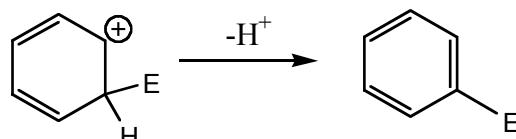


Electrophilic Addition – Elimination

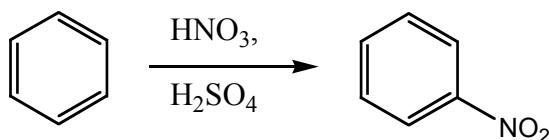
This mechanism occurs in arenes such as benzene. As you know, benzene does not have simple double bonds but rather a delocalised system of three π -bonds in conjugation. Nevertheless in the first step of this mechanism the electrophile attacks the arene as if it contained a simple double bond as in an alkene or alkyne:



Because of the stability of delocalised systems this intermediate has a strong desire to return to an aromatic system. It can do this by losing an electrophile, usually (but not always) a proton, attached to the carbon attacked by the original electrophile:



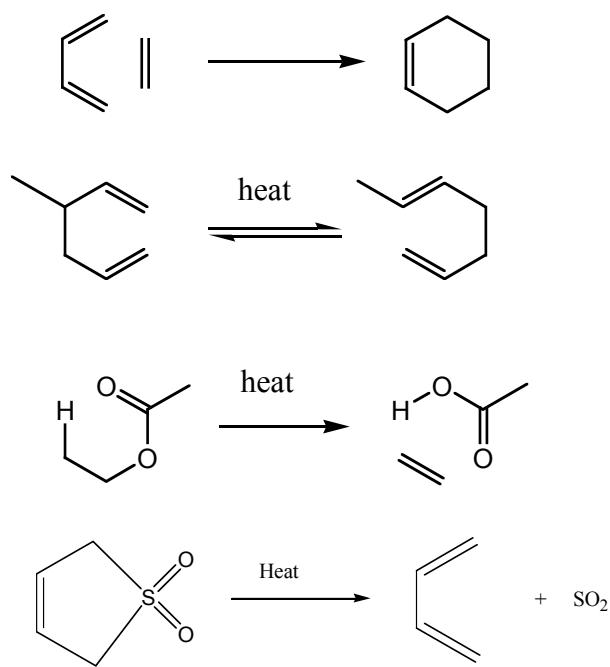
The overall result is an apparent substitution of H by E but this reaction always proceeds through two steps e.g.:



Direct analogues of the benzene ring where other elements take the place of carbon e.g. borazines and cyclophosphazenes are not common and the mechanisms of their reactions do not suggest any great degree of aromaticity.

Pericyclic

There are many reactions using this type of mechanism. They were originally called “no-mechanism” reactions because they did not fit into the categories nucleophilic, electrophilic or radical. We now know that they are controlled by molecular orbitals about which you will learn a little this year and a lot next. They are spread throughout functional group chemistry so I shall only give you four examples, one cyclo-addition, one rearrangement, one β -cyclo-elimination and one δ -cyclo-elimination (also known by organic chemists as an Extrusion):



In all cases a cycle of six electrons is involved and, although six is not the only number of electrons which may be represented in pericyclic reactions, all these reactions go through a cyclic transition state. **Some pericyclic reactions also occur in inorganic chemistry.**

Oxidation and Reduction

Many organic oxidations and reductions proceed through variations of the basic mechanisms given above. Some examples are:

Reductions:

- Nucleophilic addition (LiAlH_4)

- Pericyclic ($\text{AlO}i\text{Pr}_3$)

Oxidations:

- β -Elimination/Pericyclic (CrO_3)
- Nucleophilic Substitution (H_2O_2)

Electron transfer mechanisms, **common in inorganic chemistry**, are less frequently seen in organic chemistry. Examples in first year organic chemistry are dissolving metal reductions of alkynes and carbonyls.

Finer Details

I have just given you an overview of mechanisms. As your degree progresses you will see that some finer points will emerge concerning each mechanistic type. Although these will add to the complexity of their respective mechanisms, they will not change the gross nature of them.

For example you will learn

- Why alkyl fluorides are inert towards nucleophilic substitution and elimination whereas the other halides are reactive
- Why electrophilic addition of bromine to alkenes goes by a well-defined stereochemistry whereas the same addition of chlorine is not so well behaved
- Why aldehydes are generally more reactive than ketones in nucleophilic additions
- That the order of reactivity in nucleophilic addition-eliminations is acid halides > esters > amides
- How the substituent already on a benzene ring influences both the rate and site of attack by an electrophile in electrophilic addition – elimination.