Lecture 8: Conjugation

Objectives:

By the end of this lecture you will be able to:

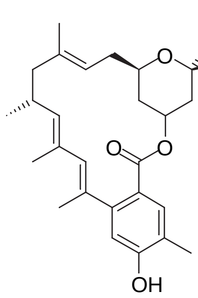
- recognise conjugation in molecules;
- understand how conjugation affects the HOMO-LUMO energy gap and therefore UV spectra of molecules;
- understand why α,β-unsaturated carbonyl compounds are ambident electrophiles;
- draw the mechanism of a conjugate reaction.

Introduction

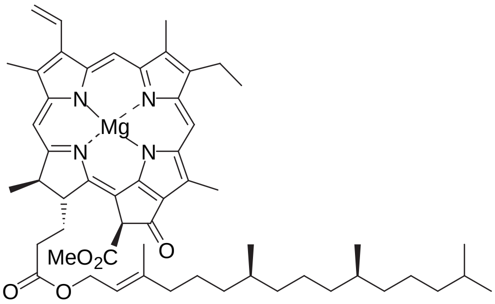
Two double bonds in a diene are *conjugated* when they are i) separated from one another by a single bond *and* ii) the π-MOs in each double bond can overlap. *Both* conditions must be met for the diene to be conjugated.

All types of functional group that possess a degree of *unsaturation* can form a conjugated system. Functional groups commonly found include double bonds, triple bonds, aromatic groups, carbonyl groups, nitro and nitrile groups *etc*.

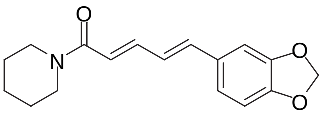
Conjugation is also very common in Nature:



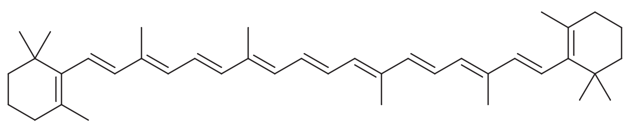
milbemycin β_3



chlorophyll a



piperine (from black pepper)



β-carotene

Conjugation affects both the physical and the chemical properties of the functional group, and therefore the molecule. Let us consider one of the simplest conjugated systems, buta-1,3-diene and use a molecular orbital approach to show that the diene behaves not as two separate double bonds, but rather as a single entity.

Each carbon atom is sp^2-hybridised. The sp^2-HAOs are used, as normal, to construct the σ-bonds in the molecule; the remaining p AOs overlap to form the π-system. When we consider the structure of a double bond we use two p AOs to form two MOs, namely the π-bonding MO and the π^*-antibonding MO.

We now have four p AOs, one from each carbon atom, which are all in the same plane and which can therefore all overlap. From the Conservation of Orbitals, if we start with *four* AOs, when we allow these orbitals to *mix*, we will generate *four* new MOs.

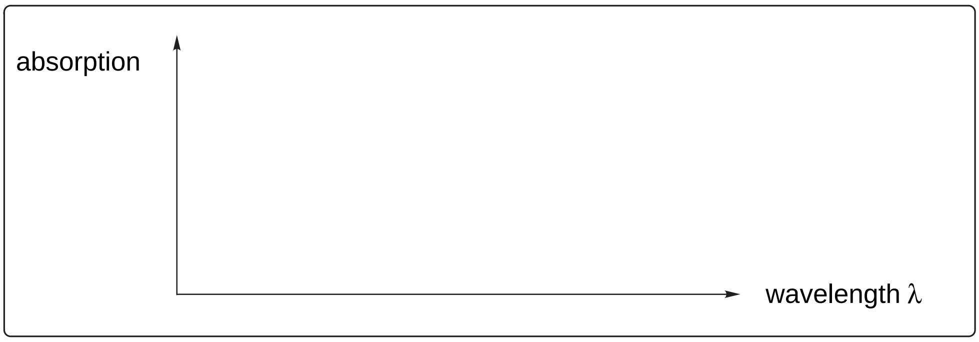
Since the two double bonds are separated by a single bond the MOs can mix further. We can do this by *adding* and *subtracting* the two π-MOs (this will generate two new MOs), and then doing the same for the two π^* MOs (to generate two more MOs):

So we have now satisfied the Conservation of Orbitals rule. We can now fill the four new MOs with the four electrons, one from each carbon atom. Filling the lowest energy MO first, we can fully occupy Ψ^1 and Ψ^2.

When we put the four new MOs on to an energy diagram along with the two separate π-MOs we see that the HOMO has been raised in energy and the LUMO lowered in energy.

UV-Spectra

We have seen that the energy associated with molecular vibrations is in the IR region of the electromagnetic spectrum. The energy associated with promotion of an electron from the HOMO to the LUMO in a π-bond is in the UV-Visible region of the electromagnetic spectrum. For an isolated olefin the energy of this transition lies in the UV region, hence molecules containing isolated double bonds are generally not coloured. However we have seen that in a conjugated diene the HOMO-LUMO gap is reduced. Therefore the band corresponding to this transition is shifted to lower energy *i.e.* longer wavelength and therefore further into the visible region. As a consequence molecules that have a high degree of conjugation tend to be highly coloured (*e.g.* β-carotene which is one of the chemicals responsible for the orange colour of carrots).



Conjugation and Chemical Reactivity

Conjugation affects the chemical reactivity of molecules. α-β-Unsaturated carbonyl compounds can be represented in two *resonance forms* as a result of the olefin and the carbonyl group being conjugated:

Using this valence bond representation, we can see that the conjugated double bond is also polarised with the β–carbon atom, *i.e.* that furthest away from the carbonyl group, being polarised with a formal δ+ charge.

The polarised double bond in an α,β-unsaturated carbonyl system is also readily observable in the ^{13}C-NMR and IR spectra of these molecules:

α,β-Unsaturated carbonyl groups are **AMBIDENT ELECTROPHILES** in that a nucleophile can attack at *more* than one site, in this case, at the carbonyl carbon or at the β-carbon.

We have seen that when a nucleophile reacts with a carbonyl group in the standard way, the important molecular orbital interaction is that between the HOMO of the nucleophile and the LUMO of the carbonyl group, namely the π*-antibonding MO. It is this interaction that is primarily responsible for forming the new bond.

The same frontier orbital interaction is going to be important in the reaction between a nucleophile and an α,β-unsaturated carbonyl group. In this case the LUMO of the electrophile is very similar to the Ψ^3 molecular orbital of a simple 1,3-diene.

We have seen how replacing an olefin in a diene, for a carbonyl group polarises the remaining olefin. This polarisation is also reflected in the size of the lobes of the orbitals making up the LUMO. Remember that the size of the lobes in a MO provides an indication of where electron density would reside if the orbital were to be populated. A large lobe will also better interact with the HOMO (source of electron density) of an approaching nucleophile.

The LUMO (Ψ^3) of an α,β-unsaturated carbonyl group clearly shows large lobes on the carbonyl carbon and the β-carbon. So just by examining this frontier molecular orbital we would also expect the nucleophile to react at these sites in an α,β-unsaturated system.

Conjugate Addition

When the nucleophile reacts at the β-carbon in an α,β-unsaturated carbonyl group, the reaction is described as a *conjugate addition* or a *Michael addition* or a *1,4-addition*. You will see all three reaction descriptors used; they all mean the same thing (although strictly the Michael addition refers to the use of a specific type of nucleophile in a conjugate addition reaction).

Mechanism

- In the first step, the nucleophile attacks at the β-carbon; electron density is pushed on to the electronegative oxygen.
- The negatively charged intermediate is called an *enolate*. You will learn a lot more about this species next year.
- The enolate can be trapped with an electrophile in a variety of ways. We will just consider the reaction where the electrophile is a proton. In this case the carbonyl group is regenerated.

Some Examples

1. Cyanide addition

- We have already seen that the cyanide anion reacts with carbonyl groups to form cyanohydrins. This 1,2-addition reaction is reversible.
- Conjugate addition is slower since it is attacking at the β-carbon which is less electron deficient, and therefore less electrophilic, than the carbonyl carbon. However it provides the *thermodyamic product* and is essentially irreversible (it is better to retain the strong C=O bond than the weaker C=C bond).

2. Sulfide and amine addition

Thiolates and primary and secondary amines are also good nucleophiles for conjugate addition reactions:

Note that if the β-carbon is asymmetrically substituted, a new stereogenic centre is also produced in the reaction.

3. Carbon nucleophiles

We have seen that organolithium reagents and Grignard reagents react readily with most carbonyl compounds. In the case of α,β-unsaturated carbonyl compounds the nucleophile can attack at two sites.

IN GENERAL: 'hard' nucleophiles react in a 1,2-fashion whilst 'soft' nucleophiles react in a 1,4-fashion.

Organolithium and Grignard reagents are hard nucleophiles and provide the 1,2-addition product.

Copper reagents are soft carbon nucleophiles and react in a 1,4-fashion with α,β-unsaturated carbonyl compounds.

Summary

Conjugation is an important phenomenon in organic chemistry; it occurs whenever two unsaturated functional groups are separated by a single bond and whose π-molecular orbitals can overlap.

Conjugation affects the physical properties of a molecule:

It causes a raising of the HOMO and lowering of the LUMO in the π-system leading to a shift in the band that results from promotion of an electron from the HOMO into the LUMO to longer wavelength (lower energy). Conjugated molecules are often coloured.

α,β-Unsaturated carbonyl compounds also exhibit characteristic changes in their IR and ^{13}C-NMR spectra:

- strong C=C stretching band around 1620 cm^{-1} (double bond now has a permanent dipole moment).
- a downfield shift in the resonance for the β-carbon in ^{13}C-NMR spectra reflecting the increased electron deficiency at this carbon centre.

Conjugation also affects the chemical properties of molecules.

α,β-Unsaturated carbonyl compounds behave as *ambident electrophiles*: a nucleophile can attack at two sites, namely at the carbonyl carbon and at the β-carbon centre.

Attack at the β-carbon centre is called conjugate or Michael or 1,4-addition and generally provides the thermodynamic product.

Soft nucleophiles tend to react preferentially in a conjugate fashion. Good examples of soft nucleophiles are thiolates and organocopper species.

If the addition reaction is reversible then the thermodynamic product is often obtained (*e.g.* cyanide addition).