

CHEM60001:
An Introduction to Reaction Stereoelectronics

LECTURE 1
Recap of Key Stereoelectronic Principles

Alan C. Spivey
a.c.spivey@imperial.ac.uk

Imperial College
London

Nov 2016

Format & scope of lecture 1

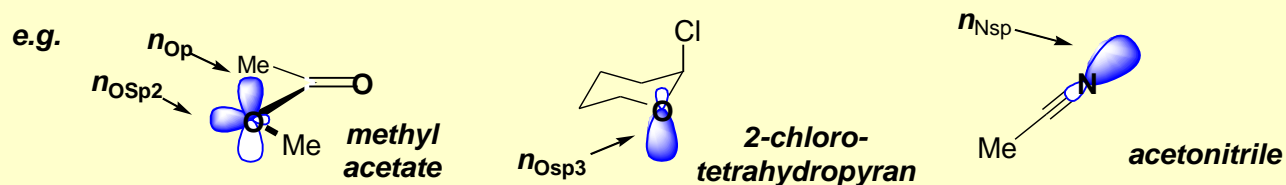
- ***Requirements for Effective Orbital Overlap***
 - Classification of orbitals and bonds – terminology
 - Natural Bond Orbital (NBO) overlap
 - Estimating interaction energies & overlap integrals
 - Kirby's theory and Deslongchamps' theory
- ***Important Interactions***
 - Resonance
 - Hyperconjugation/ σ -conjugation
 - alkene stability, carbocation stability, the Si β -effect

Classification of orbitals & bonds

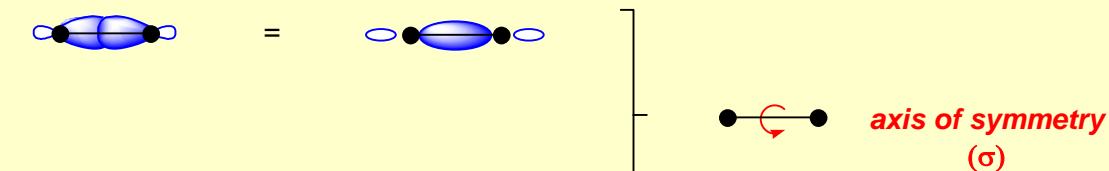
- Orbital shape is of central importance to stereoelectronic analysis**

- recall the following nomenclature from hybridisation and MO theory:

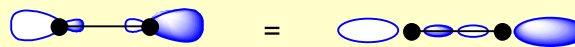
n = non-bonding orbital;
lone pair of electrons;
can be sp^3 , sp^2 , sp or p type orbital:



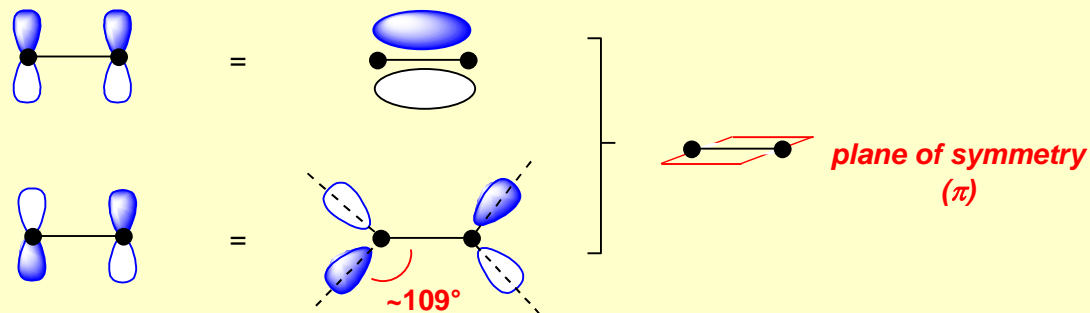
σ = sigma orbital;
bonding orbital of standard single bond
comprised of two sp^3 , sp^2 or sp hybrid atomic orbitals
has rotational symmetry along bond axis



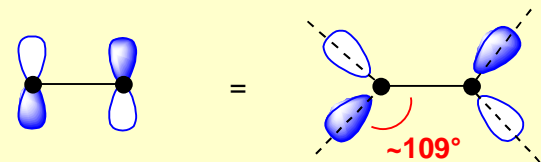
σ^* = sigma 'star' orbital;
anti-bonding orbital of a single bond
same symmetry properties as σ orbital



π = pi orbital;
bonding orbital of a double bond
comprised of two p atomic orbitals
has plane of symmetry perpendicular to bond axis



π^* = pi 'star' orbital;
anti-bonding orbital of a double bond
same symmetry properties as π orbital



- We will be referring to these 'bond-localised' molecular orbitals as Natural Bond Orbitals (NBOs)...

Orbital-orbital overlap

INTRAMOLECULAR ORBITAL-ORBITAL OVERLAP:

- **‘Primary orbital overlap’ → valence bonds:**
 - Valence bond MOs, or as we will be referring to them ‘Natural Bond Orbitals’ (NBOs) result from ‘primary orbital overlap’ between Atomic (often hybridised) Orbitals (AOs) on adjacent atoms within a molecule. This is an application of Linear Combination of Atomic Orbital (LCAO) theory (e.g. previous slide)
- **‘Secondary orbital overlap’ → stereoelectronic interactions:**
 - Stereoelectronic effects arise as the result of ‘secondary orbital overlap’ of NBOs on adjacent atoms (i.e. vicinal orbital interactions). This is an application of Linear Combination of Bond Orbital (LBAO) theory.
 - Brunck and Weinhold *J. Am. Chem. Soc.* **1979**, *101*, 1700 ([DOI](#))

INTERMOLECULAR ORBITAL-ORBITAL OVERLAP:

- **‘Intermolecular orbital overlap’ → intermolecular reactivity:**
 - ‘Perturbation theory’ and Frontier Molecular Orbital (FMO) theory use similar principles to extrapolate the above to inter-molecular situations. A key feature of this approach is the Klopman-Salem equation which relates the energy gained or lost when orbitals overlap .
 - We will use a simplified form of this equation to also understand *intramolecular* NBO overlap (e.g. next slides).
 - Klopman *J. Am. Chem. Soc.* **1968**, *90*, 223 ([DOI](#)); Salem *J. Am. Chem. Soc.* **1968**, *90*, 543 & 553 ([DOI](#))
 - Fleming, *Molecular Orbitals and Organic Chemical Reactions – Reference Edition* Wiley, **2010**, pp 138

Klopman-Salem

AN EQUATION FOR ESTIMATING CHEMICAL REACTIVITY

The energy (ΔE) gained and lost when the orbitals of one reactant overlap with those of another can be expressed in the following equation, developed by Klopman and Salem using Perturbation Theory:

$$\Delta E = -\sum (q_a + q_b) \beta_{ab} S_{ab} + \sum_{k < l} \frac{Q_k Q_l}{\epsilon R_{kl}} + \sum_r^{\text{occ.}} \sum_s^{\text{unocc.}} - \sum_s^{\text{occ.}} \sum_r^{\text{unocc.}} \frac{2(\sum_{ab} c_{ra} c_{sb} \beta_{ab})^2}{E_r - E_s}$$

where q_a and q_b are the electron populations in the atomic orbitals **a** and **b**

β and S are resonance and overlap integrals

Q_k and Q_l are the total charges on atoms **k** and **l**

ϵ is the local dielectric constant

R_{kl} is the distance between the atoms **k** and **l**

c_{ra} is the coefficient of atomic orbital **a** in molecular orbital **r**, where **r** refers to the molecular orbitals on one molecule

and **s** refers to those on the other

E_r is the energy of molecular orbital **r**

A SIMPLIFIED EQUATION FOR CHEMICAL REACTIVITY

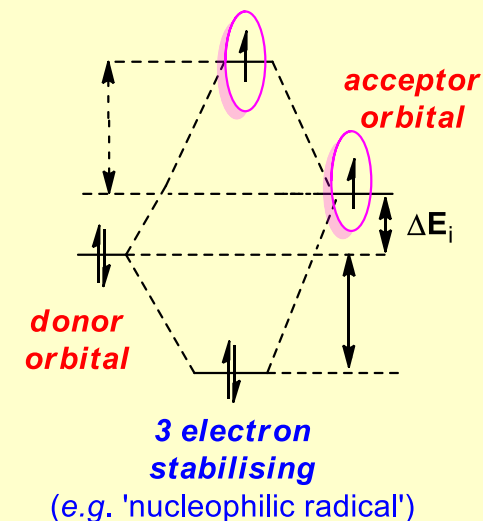
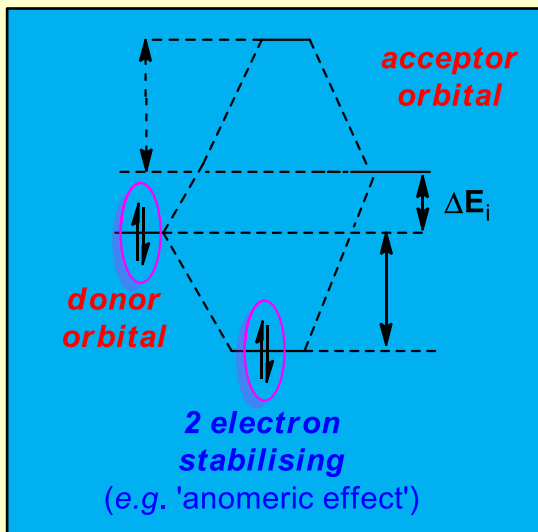
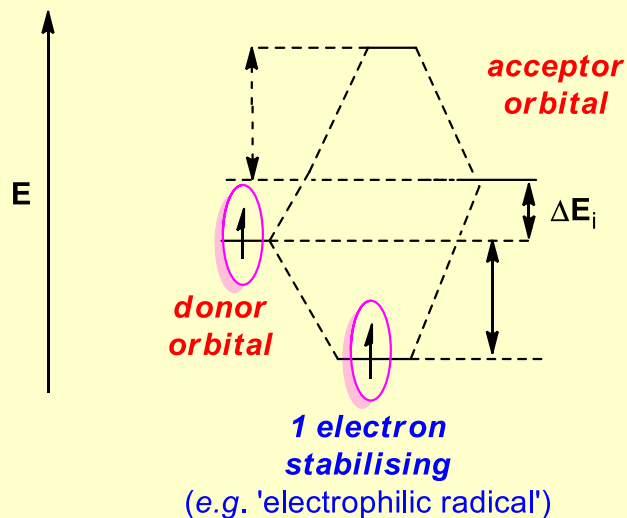
Since the interactions of all other orbitals have much larger ($E_r - E_s$) values, we can simplify the above equation by using only the **HOMO** of a nucleophile and the **LUMO** of an electrophile:

$$\Delta E = - \frac{Q_{nuc} Q_{elec}}{\epsilon R} + \frac{2(c_{nuc} c_{elec} \beta)^2}{E_{HOMO(nuc)} - E_{LUMO(elec)}}$$

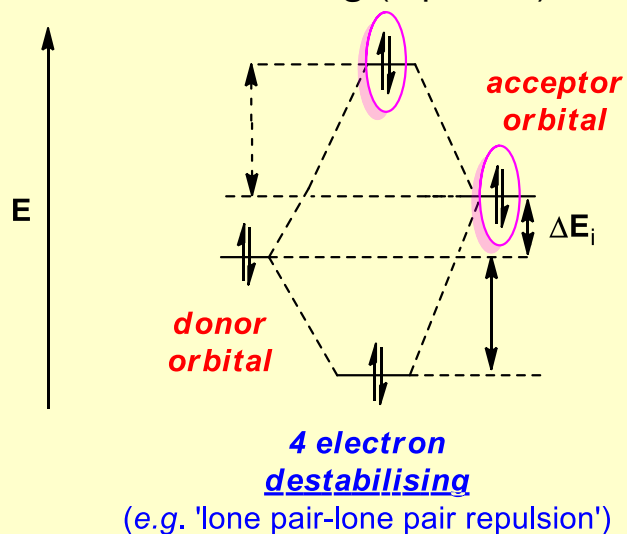
Coulombic term **frontier orbital term**

Types of Natural Bond Orbital (NBO) overlap

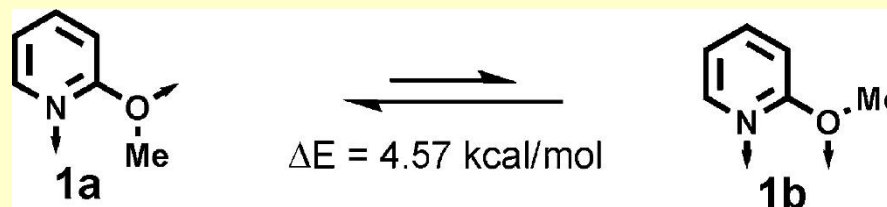
- **Stabilising** (attractive) interactions result from 1, 2 & 3 electron interactions



- **Destabilising** (repulsive) interactions result from 4 electron interactions

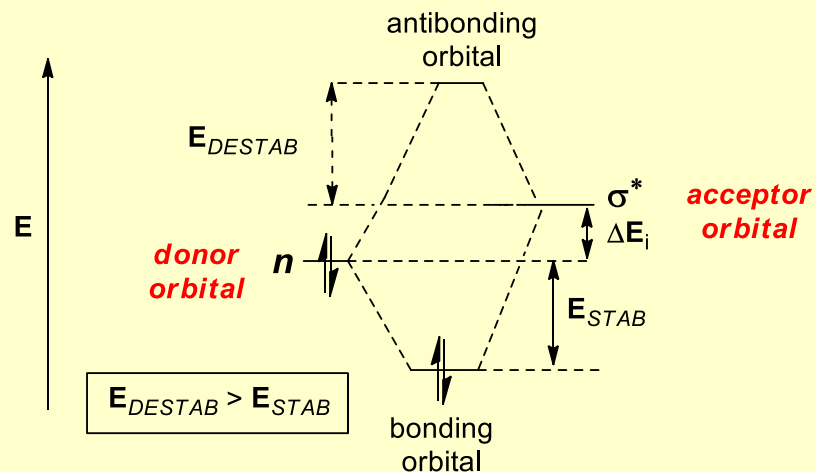


- Revise these from Prof Rzepa's Wiki:
<http://www.ch.ic.ac.uk/local/organic/conf/>
- e.g. Conformation of 2-methoxypyridine
- Corey *Org. Lett.* **2010**, 12, 132 ([DOI](#))



The energetics of NBO overlap

- **Stereoelectronic effects arise as the result of ‘secondary orbital overlap’ of NBOs on adjacent atoms**
- **The Klopman-Salem equation defines the relationship between the energy gained or lost when orbitals overlap.**
- **We will concentrate here on stereoelectronic effects that arise from attractive, 2-electron interactions:**



Klopman-Salem

$$E_{STAB} \propto \frac{S^2}{\Delta E_i}$$

S^2 = overlap integral

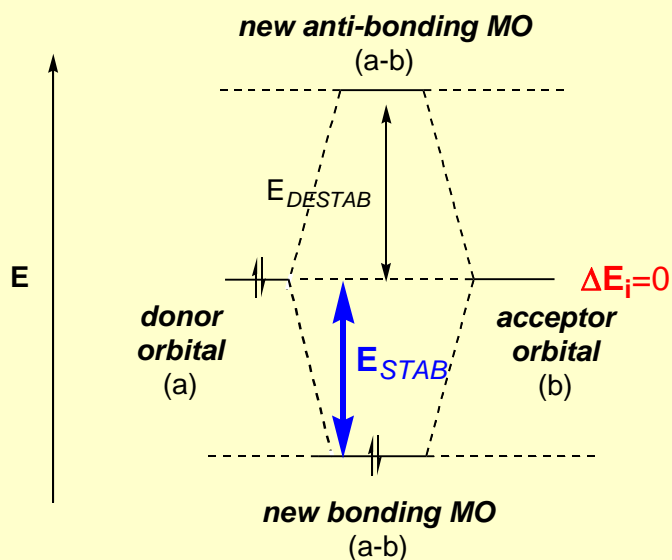
E_{STAB} = stabilisation energy

ΔE_i = interaction energy

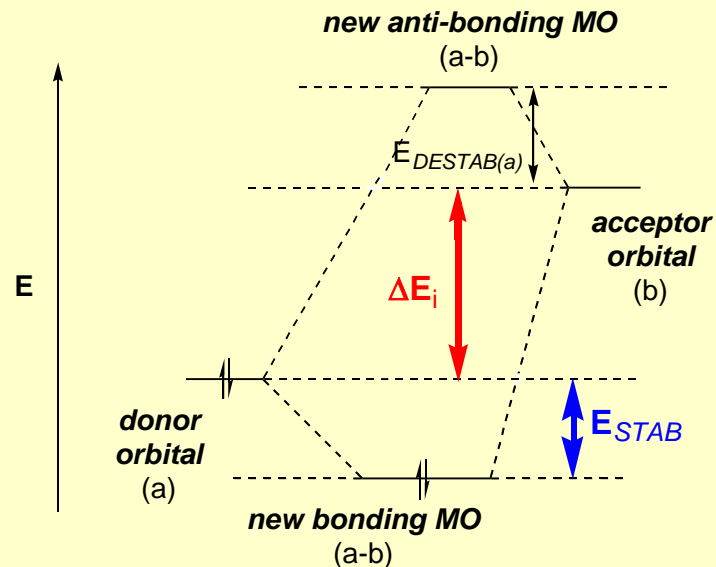
- **For maximum E_{STAB} (i.e. large ‘effect’) we need:**
 - INTERACTION ENERGY, ΔE_i (i.e. difference in energy between orbitals) = **Small**
 - OVERLAP INTEGRAL, S = **Large**

Dependence on the interaction energy (ΔE_i)

- The closer in energy the two interacting NBOs the more significant the energy gain



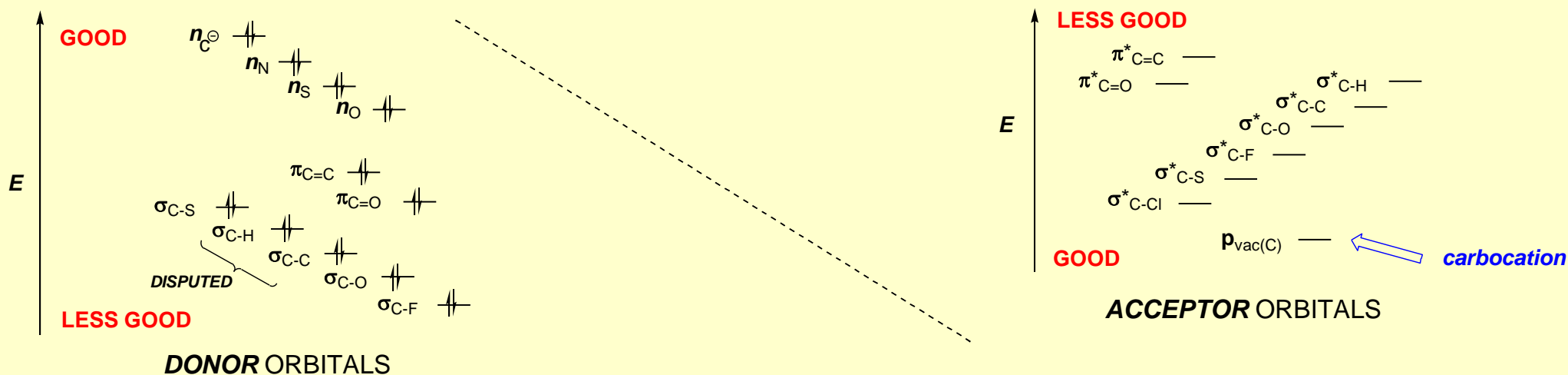
Most favourable case -
 both orbitals have ~ the same energy
 $\Delta E_i = \text{small} \rightarrow E_{STAB} = \text{big}$



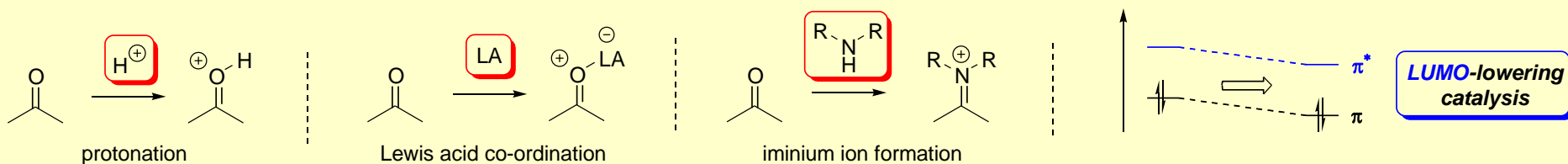
Less favourable case -
 orbitals are of significantly different energy
 $\Delta E_i = \text{big} \rightarrow E_{STAB} = \text{small}$

Estimating the interaction energy (ΔE_i)

- **Assessment of the INTERACTION ENERGY (ΔE_i):**
 - Filled orbitals (donors) will be lower in energy than the empty orbitals (acceptors) (~Aufbau principle)
 - The smallest ΔE_i will be between the HOMO (donor) & the LUMO (acceptor)
 - For n_X , σ_{C-X} & $\pi_{C=X}$ orbitals:
 - X = EWG (electronegative) → **LOWERS** the energy of $n/\sigma/\pi$ & σ^*/π^*
 - X = EDG (electropositive) → **RAISES** the energy of $n/\sigma/\pi$ & σ^*/π^*



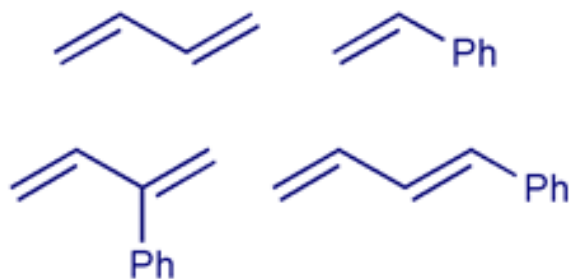
- I.V. Alabugin and T.A. Zeidan *J. Am. Chem. Soc.* **2002**, 124, 3175 ([DOI](#))
- **Protonation & Lewis Acid co-ordination to X & iminium ion formation** → **LOWERS** the energy of σ/π & σ^*/π^*



Effect of substituents on alkene frontier orbitals

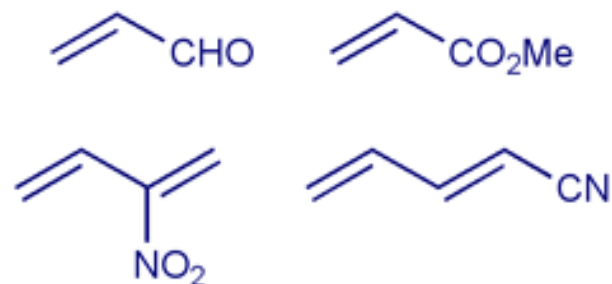
Conjugating groups

- higher HOMO energy
- lower LUMO energy



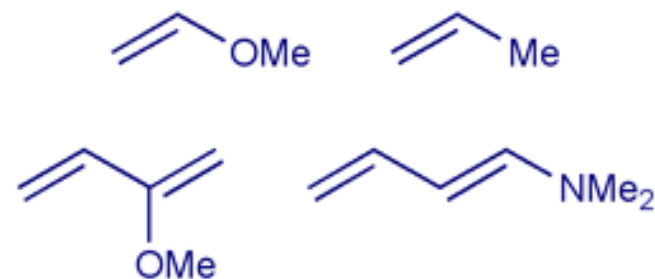
Electron-accepting groups

- lower HOMO energy
- lower LUMO energy



Electron-donating groups

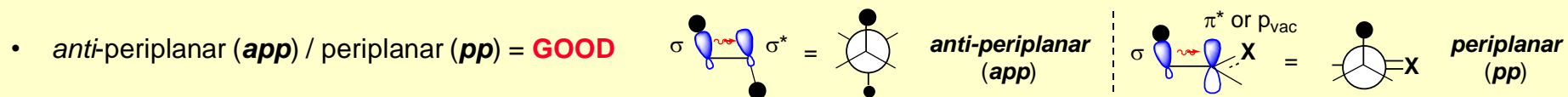
- higher HOMO energy
- higher LUMO energy



Estimating the overlap integral (S)

- The **OVERLAP INTEGRAL (S)** is strongly dependent of two factors:

- (1) **Relative orientation of interacting orbitals:**



- *syn*-periplanar (**spp**) = **OK**



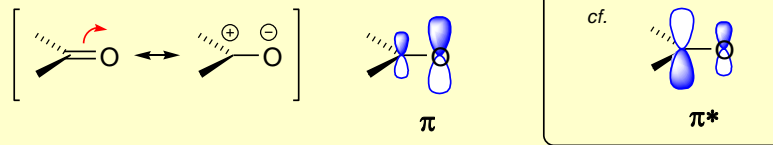
BUT: note that this is an **eclipsed** conformation which suffers from a 4 electron, repulsive NBO overlap stereoelectronic interaction between the three pairs of σ orbitals. See: <http://www.ch.ic.ac.uk/local/organic/conf/>

- anything else = **BAD**

- (2) **The co-efficients (i.e. sizes) of interacting orbitals:**

- orbitals of matched size, e.g. between orbitals on elements in same row of Periodic Table: N \leftrightarrow O \leftrightarrow C = **GOOD**
- orbitals of mismatched sizes, e.g. between orbitals on elements in different rows of Periodic Table: S \leftrightarrow C = **BAD**
- **NB.** relative sizes of orbital co-efficients in NBOs of polarised systems can be estimated from consideration of charge distribution (*i.e.* resonance forms):
 - e.g. π & π^* NBOs of a **carbonyl group**

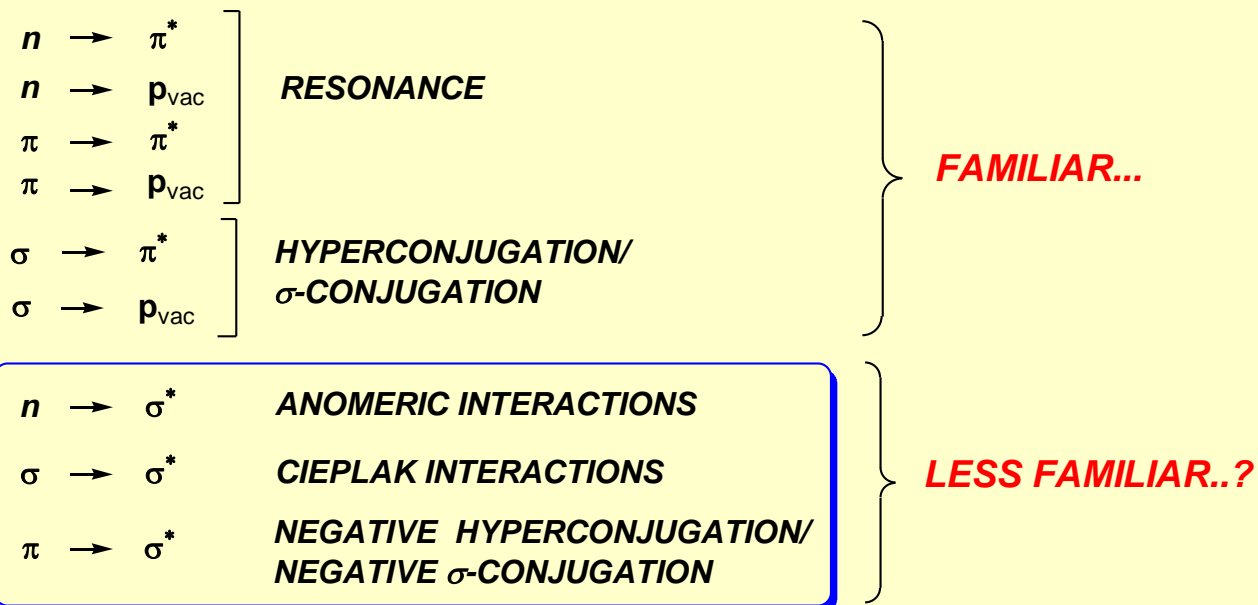
NB. the 'intuitive' polarisation is that of the π -bonding orbital...the anti-bonding π^* orbital shows the 'opposite' polarisation. (This holds true for σ and σ^* too).



Important interactions - *summary*

- **KIRBY'S THEORY**: “There is a stereoelectronic preference for conformations in which the best donor lone pair or bond is anti-periplanar to the best acceptor bond or orbital”
- **DESLONGCHAMPS' THEORY**: “Two stereoelectronic interactions are better than one!”
 - **BUT** beware, *a molecule can only adopt one conformation at any one instant in time* and so multiple **stereoelectronic effects are only additive in a single conformation**. If two competing stereoelectronic interactions require two different conformations then, all other factors being equal (e.g. steric effects, dipole effects *etc.*), the molecule will adopt the conformation which allows the more stabilising interaction to occur

Significant interactions are:

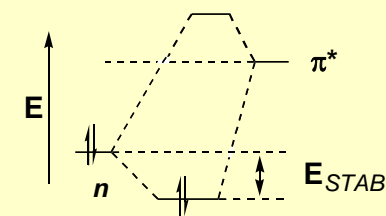
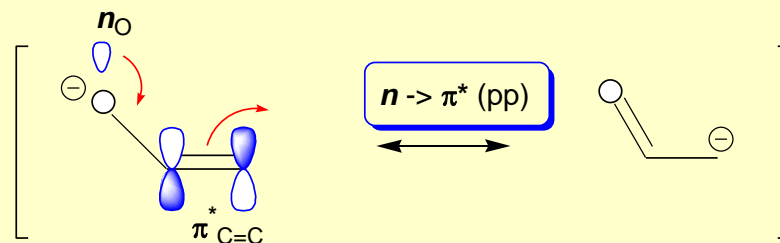


Resonance

- Resonance stabilisation (NB. geometric implications):**

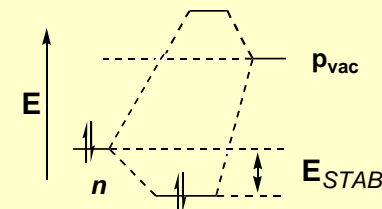
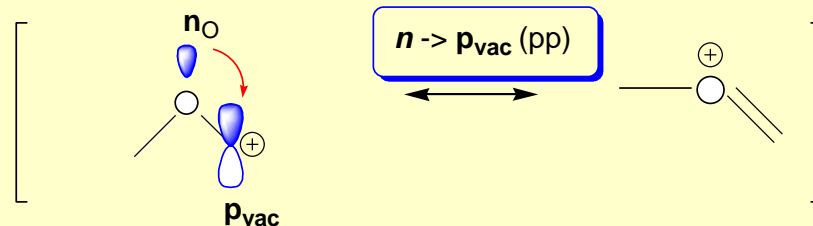
Resonance

e.g. enolate anion
allyl anion



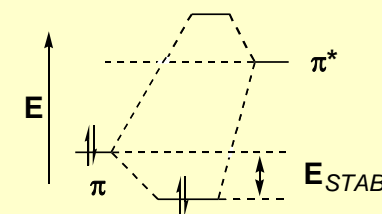
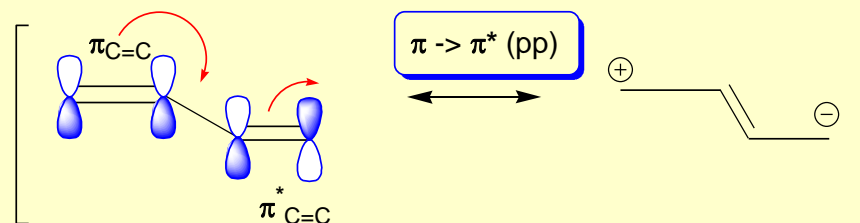
Resonance

e.g. oxonium ions



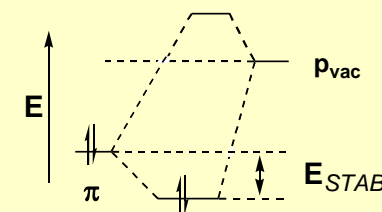
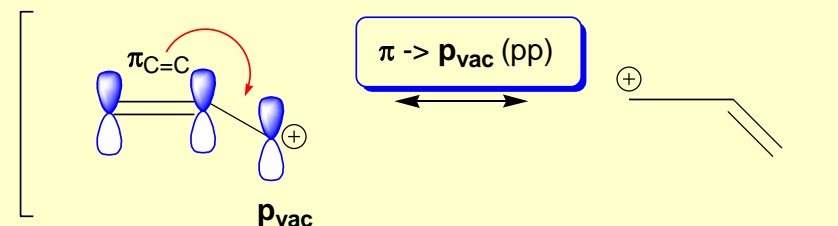
Resonance

e.g. conjugated alkenes
 α,β -unsat carbonyls



Resonance

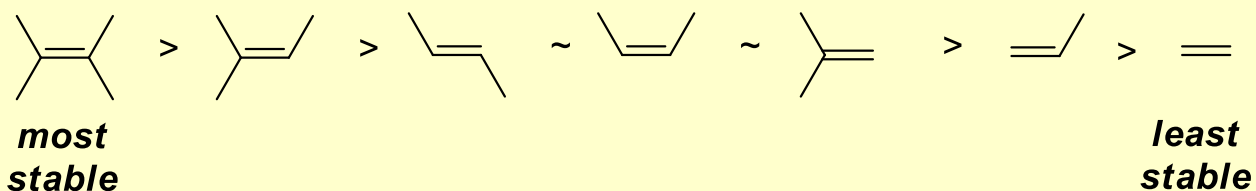
e.g. allylic cations
benzylic cations



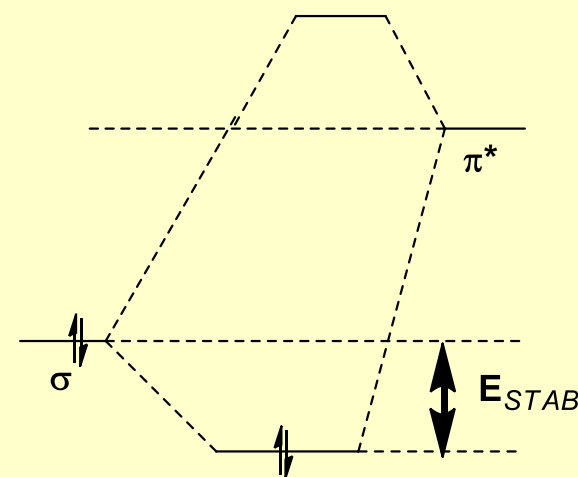
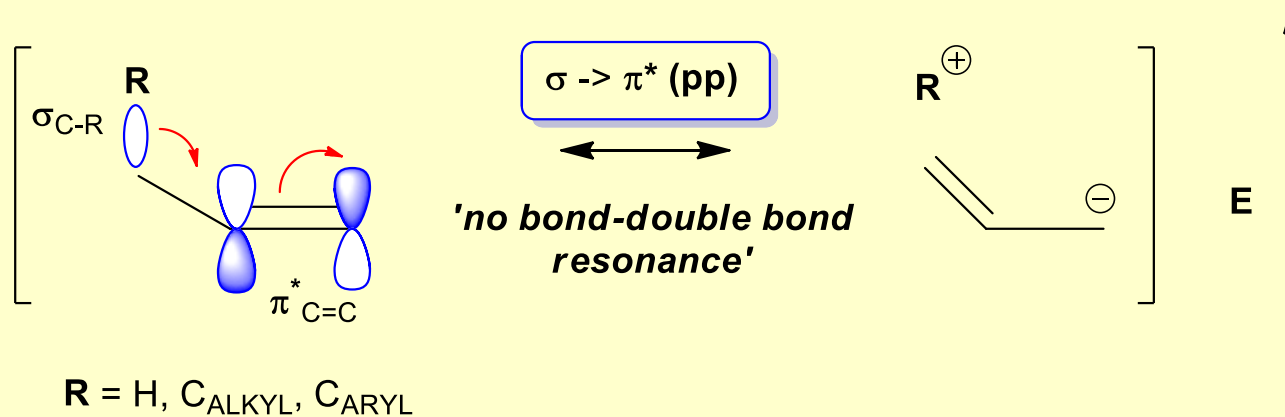
Hyperconjugation / σ -conjugation

- Enhanced thermodynamic stability of more substituted alkenes:

approximate order of stability (from thermochemical data):

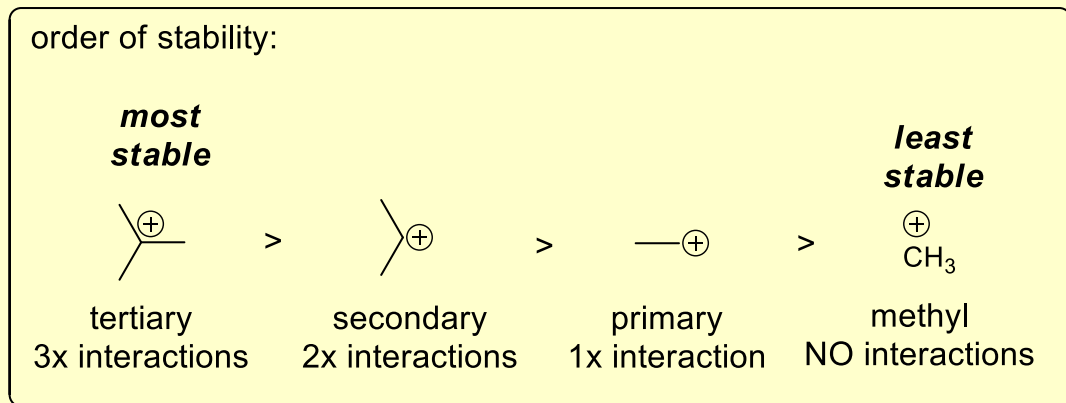


NB. This is an example of **Deslongchamps' theory** that 'two stereoelectronic interactions are better than one'.

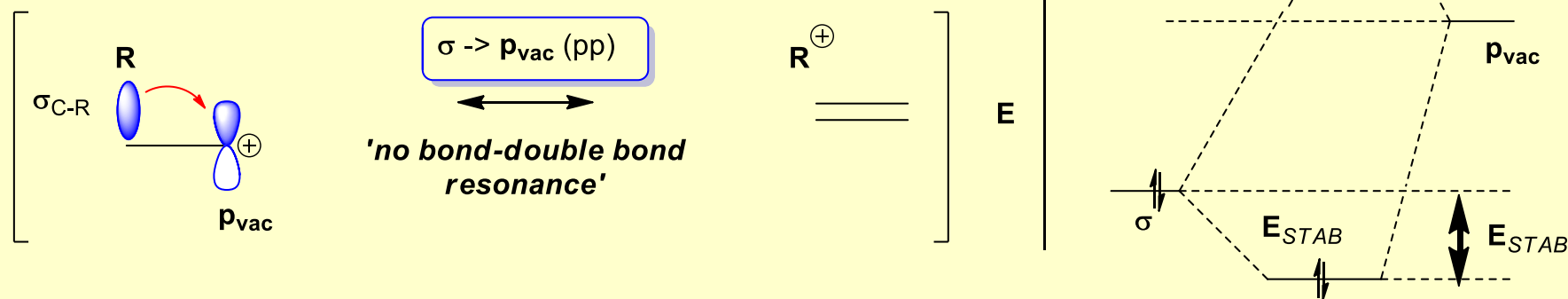


Hyperconjugation / σ -conjugation cont.

- Enhanced stability of more highly substituted carbocations:



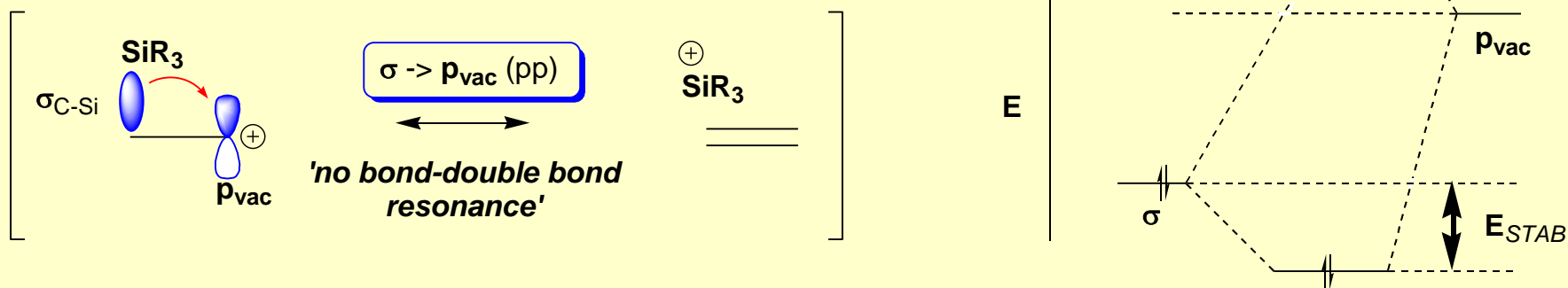
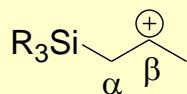
NB. Another example of *Deslongchamps' theory* i.e. 'two stereoelectronic interactions are better than one'.



Hyperconjugation / σ -conjugation cont.

- The silicon β -effect :**

carbocations β to Si are particularly stable and therefore easily formed:



NB. Si is highly electropositive so the $\sigma_{\text{C-Si}}$ bond is a good donor (*i.e.* is high in energy)