CHEM95002:
Orbitals in Organic Chemistry - Stereoelectronics

LECTURE 1
Key Stereoelectronic Principles

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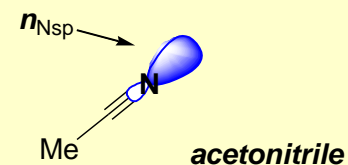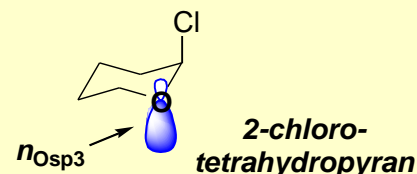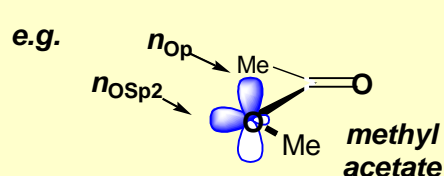# Format & scope of lecture 1

- ***Requirements for Effective Orbital Overlap***
    - Classiifcation 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:

_e.g._

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

n_{Op} → Me
n_{OSp2} → Me
methyl acetate

n_{Osp3} → **_2-chloro-tetrahydropyran_**

n_{Nsp} → N
Me
acetonitrile

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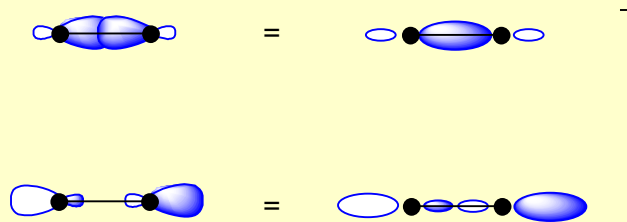
σ^* = sigma 'star' orbital;
anti-bonding orbital of a single bond
same symmetry properties as σ orbital

axis of symmetry (σ)

π = pi orbital;
bonding orbital of a double bond
comprised of two p atomic orbitals
has plane of symmetry perpendicular to bond axis
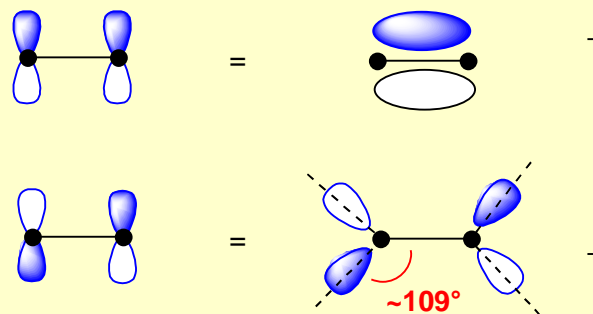
$\pi*$ = pi 'star' orbital;
anti-bonding orbital of a double bond
same symmetry properties as π orbital

~109°

plane of symmetry (π)

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

Orbital-orbital overlap

<u>INTRA</u>*MOLECULAR 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.* between NBOs vicinal to one another). This is an application of Linear Combination of Bond Orbital (LBAO) theory.
    - Brunck and Weinhold *J. Am. Chem. Soc.* **1979**, *101*, 1700 (**DOI**)

<u>INTER</u>*MOLECULAR 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 *intra*molecular NBO overlap (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:

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

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**

NB. The Klopman-Salem equation is described here for *inter*-molecular reactivity (as originally formulated). We will use it in a simplified form lacking the colulombic (=electrostatic) term (see next slides) for *intra*-molecular interactions between NBOs having a vicinal relationship

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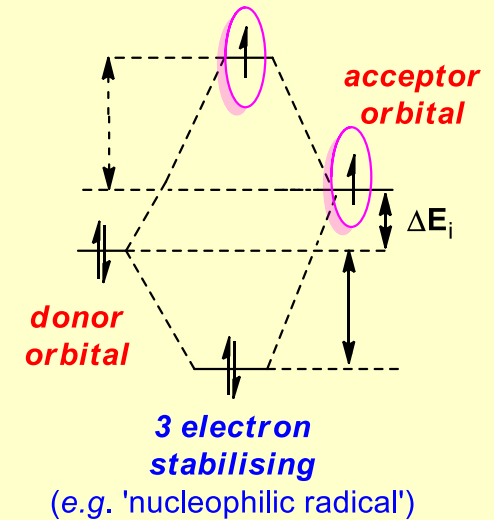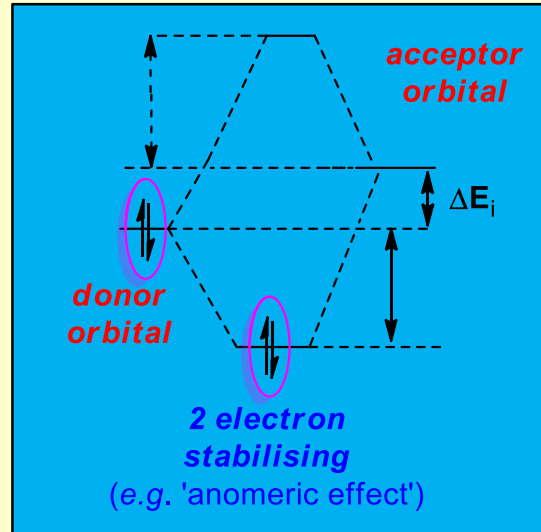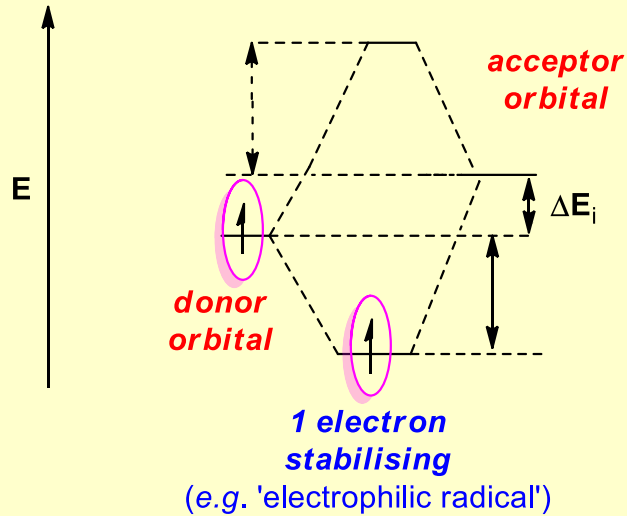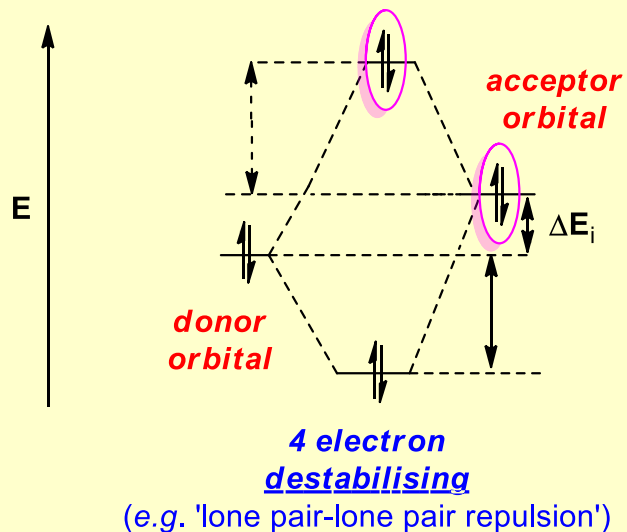
$$\Delta E = -\frac{Q_{nuc} Q_{elec}}{\varepsilon R} + \frac{2(c_{nuc}c_{elec}\beta)^2}{E_{HOMO(nuc)} - E_{LUMO(elec)}}$$

Coulombic term   **frontier orbital term**

Types of Natural Bond Orbital (NBO) overlap

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

E

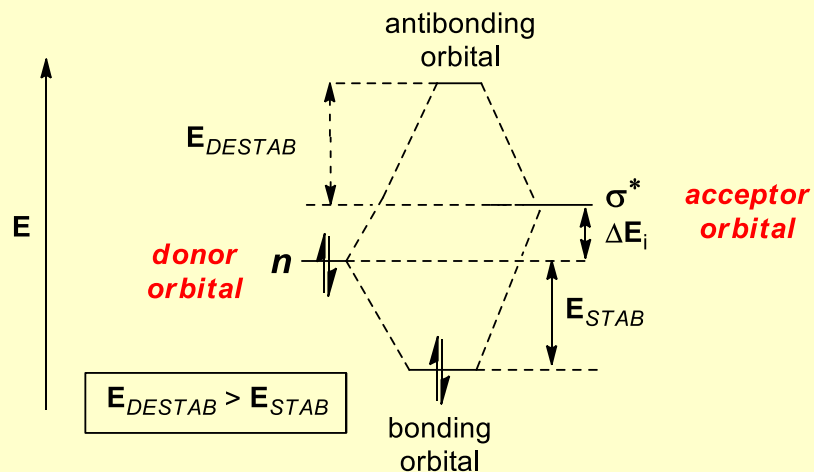acceptor orbital

ΔE_i

donor orbital

1 electron stabilising
(*e.g.* 'electrophilic radical')

acceptor orbital

ΔE_i

donor orbital

2 electron stabilising
(*e.g.* 'anomeric effect')

acceptor orbital

ΔE_i

donor orbital

3 electron stabilising
(*e.g.* 'nucleophilic radical')

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

E

acceptor orbital

ΔE_i

donor orbital

4 electron destabilising
(*e.g.* 'lone pair–lone pair repulsion')

The energetics of NBO overlap

- *Stereoelectronic effects arise as the result of 'secondary orbital overlap' of NBOs on adjacent (vicinal) atoms*
- *The Klopman-Salem equation allows us to estimate the energy gained or lost when orbitals overlap – and we can ignore the electrostatic term for these intra-molecular cases*
- *We will concentrate here on stereoelectronic effects that arise from attractive, 2-electron interactions:*

antibonding orbital

E_{DESTAB}

σ^*
ΔE_i

acceptor orbital

E

donor orbital n

E_{STAB}

$\boxed{E_{DESTAB} > E_{STAB}}$

bonding orbital

Klopman-Salem

$$E_{STAB} \; \alpha \; \frac{S^2}{\Delta E_i}$$
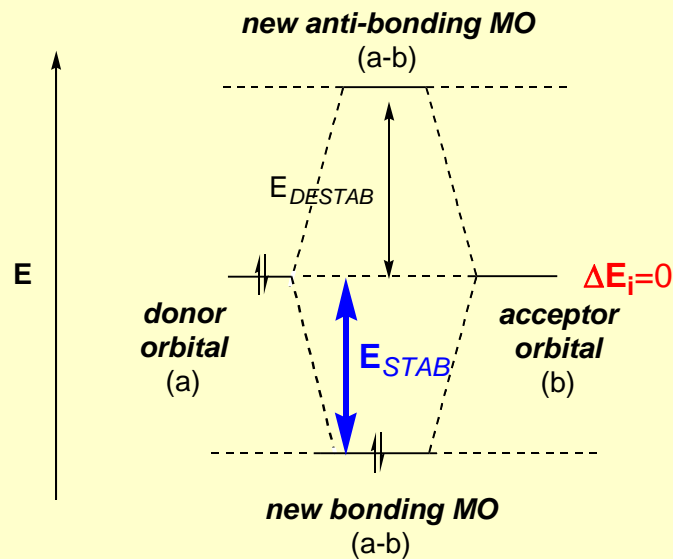
S^2 = overlap integral
E_{STAB} = stabilisation energy
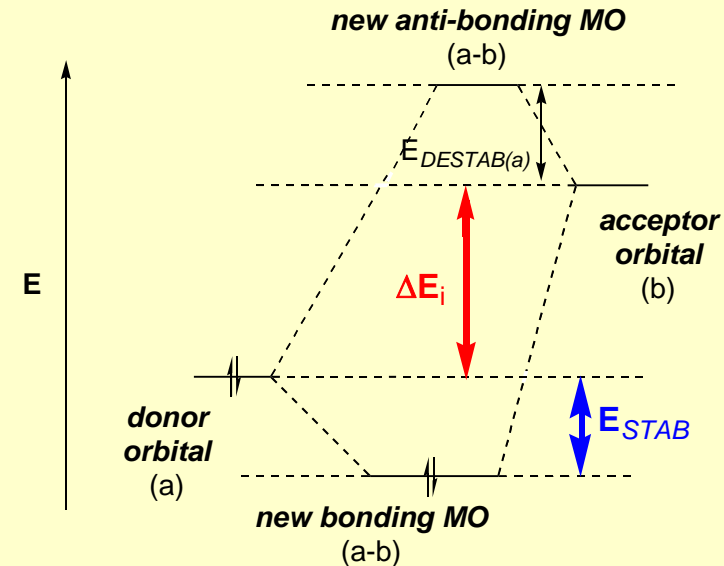ΔE_i = interaction energy

- *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*

new anti-bonding MO
(a-b)

E_{DESTAB}

E

donor orbital (a) E_{STAB} *acceptor orbital (b)* $\Delta E_i = 0$

new bonding MO (a-b)

Most favourable case -
both orbitals have ~ the same energy
ΔE_i = small -> E_{STAB} = big

new anti-bonding MO
(a-b)

$E_{DESTAB(a)}$

E

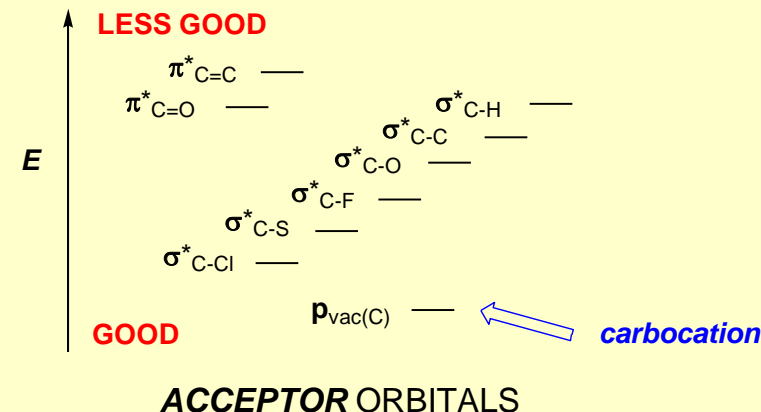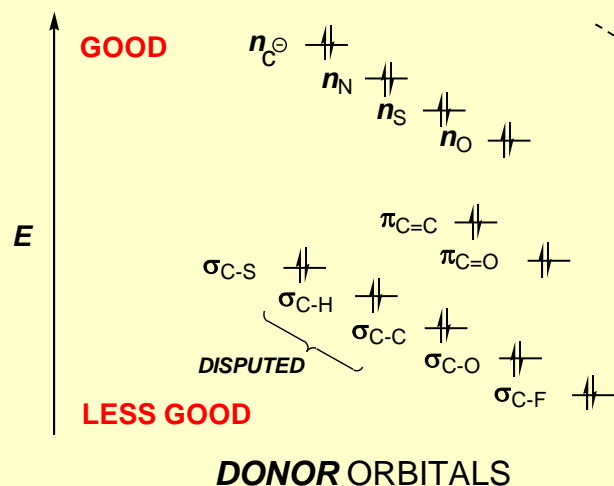*donor orbital (a)* ΔE_i *acceptor orbital (b)* E_{STAB}

new bonding MO (a-b)

Less favourable case -
orbitals are of significantly different energy
ΔE_i = big -> E_{STAB} = 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, $\sigma_{C\text{-}X}$ & $\pi_{C=X}$ orbitals:*   X = EWG (electronegative) $\rightarrow$ **LOWERS** the energy of $n/\sigma/\pi$ & σ^*/π^*

                                              X = EDG (electropositive) $\rightarrow$ **RAISES** the energy of $n/\sigma/\pi$ & σ^*/π^*

DONOR ORBITALS (left diagram): GOOD (high), $n_{C^\ominus}$, n_N, n_S, n_O, $\pi_{C=C}$, $\pi_{C=O}$, $\sigma_{C\text{-}S}$, $\sigma_{C\text{-}H}$, DISPUTED, $\sigma_{C\text{-}C}$, $\sigma_{C\text{-}O}$, $\sigma_{C\text{-}F}$, LESS GOOD (low). **DONOR ORBITALS**

ACCEPTOR ORBITALS (right diagram): LESS GOOD (high), $\pi^*_{C=C}$, $\pi^*_{C=O}$, $\sigma^*_{C\text{-}H}$, $\sigma^*_{C\text{-}C}$, $\sigma^*_{C\text{-}O}$, $\sigma^*_{C\text{-}F}$, $\sigma^*_{C\text{-}S}$, $\sigma^*_{C\text{-}Cl}$, $p_{vac(C)}$, GOOD (low) $\Leftarrow$ *carbocation*. **ACCEPTOR ORBITALS**

  - 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 $\rightarrow$ LOWERS the energy of σ/π & σ^*/π^***

protonation   Lewis acid co-ordination   iminium ion formation   *LUMO-lowering catalysis*
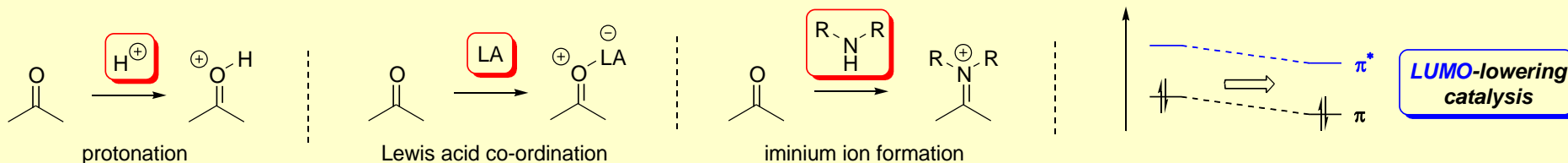
Effect of substituents on alkene frontier orbitals

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

NB. For a good explanation of the reason for the reduction in the energy gap between HOMO and LUMO with increasing conjugation see: https://chemistry.stackexchange.com/questions/8910/why-does-the-energy-gap-for-%CF%80-%CF%80-transitions-shrink-with-the-size-of-the-pi-co

Estimating the overlap integral (S)

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

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

        - *anti*-periplanar (**app**) / periplanar (**pp**) = **GOOD**
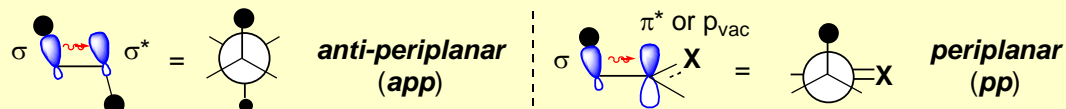
   - *syn*-periplanar (**spp**) = **OK**

        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 ↔ O ↔ C = **GOOD**

        - orbitals of mismatched sizes, *e.g.* between orbitals on elements in differrent rows of Periodic Table: S ↔ 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):
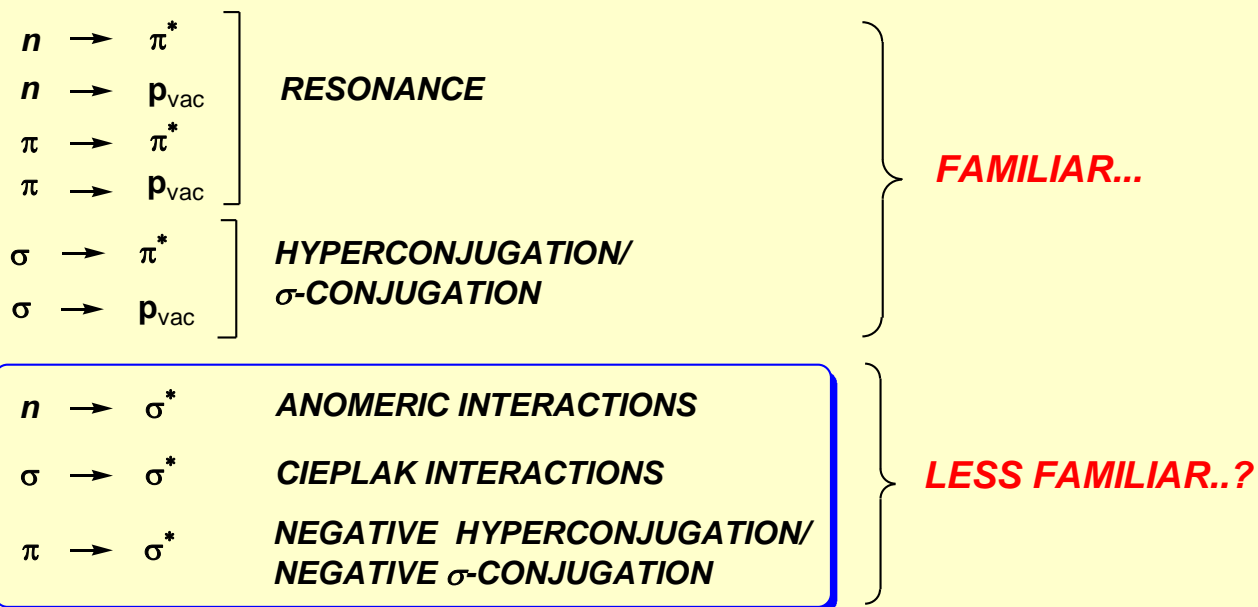   - *e.g.* π & π* NBOs of a **carbonyl group**

    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).
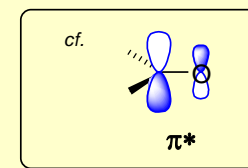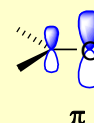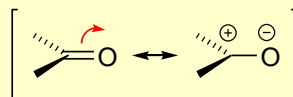
Important interactions - *summary*

- **<u>KIRBY'S THEORY</u>**: *"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"*

- **<u>DESLONGCHAMPS' THEORY</u>**: *"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
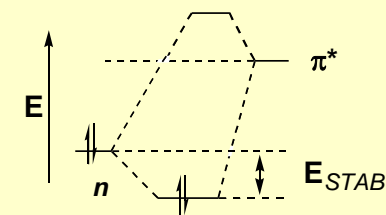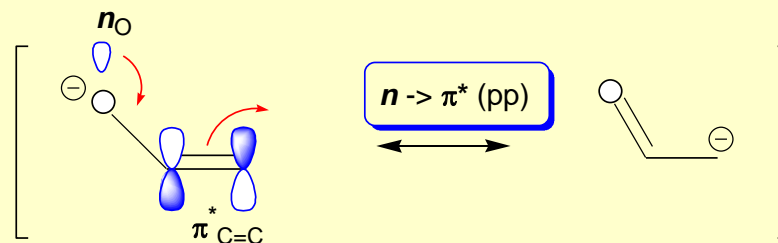
Significant interactions are:

$n \rightarrow \pi^*$

$n \rightarrow p_{vac}$ **RESONANCE**

$\pi \rightarrow \pi^*$

$\pi \rightarrow p_{vac}$

$\sigma \rightarrow \pi^*$ **HYPERCONJUGATION/**

$\sigma \rightarrow p_{vac}$ **σ-CONJUGATION**

FAMILIAR...

$n \rightarrow \sigma^*$ **ANOMERIC INTERACTIONS**

$\sigma \rightarrow \sigma^*$ **CIEPLAK INTERACTIONS**

$\pi \rightarrow \sigma^*$ **NEGATIVE HYPERCONJUGATION/ NEGATIVE σ-CONJUGATION**

LESS FAMILIAR..?

Resonance

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

Resonance

e.g. enolate anion
allyl anion

n_O

$n \to \pi^*$ (pp)
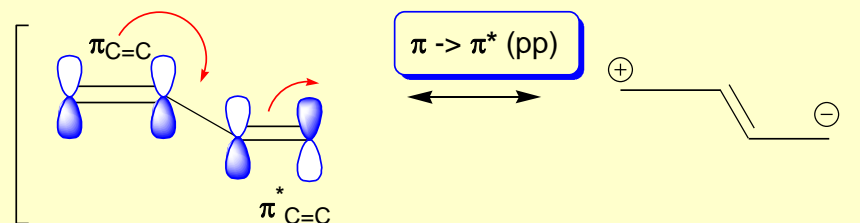
$\pi^*_{C=C}$

E

π^*

n

E_{STAB}

Resonance

e.g. oxonium ions

n_O

$n \to p_{vac}$ (pp)

p_{vac}

E

p_{vac}

n

E_{STAB}
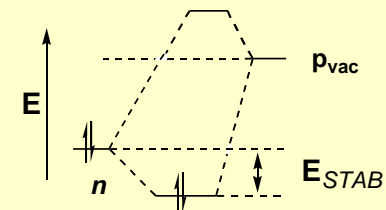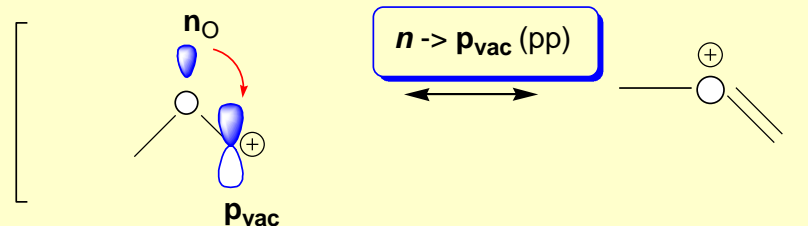
Resonance

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

$\pi_{C=C}$

$\pi \to \pi^*$ (pp)

$\pi^*_{C=C}$

E

π^*

π

E_{STAB}
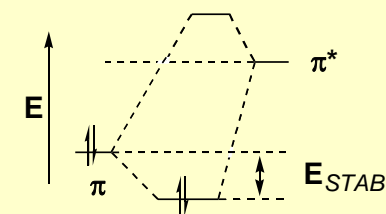
Resonance

e.g. allylic cations
benzylic cations

$\pi_{C=C}$

$\pi \to p_{vac}$ (pp)

p_{vac}

E

p_{vac}

π

E_{STAB}
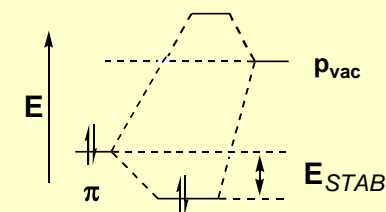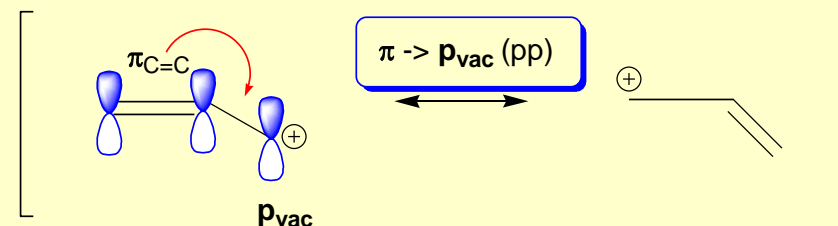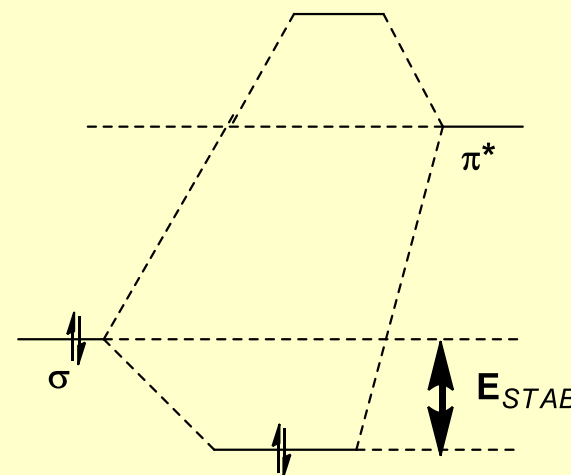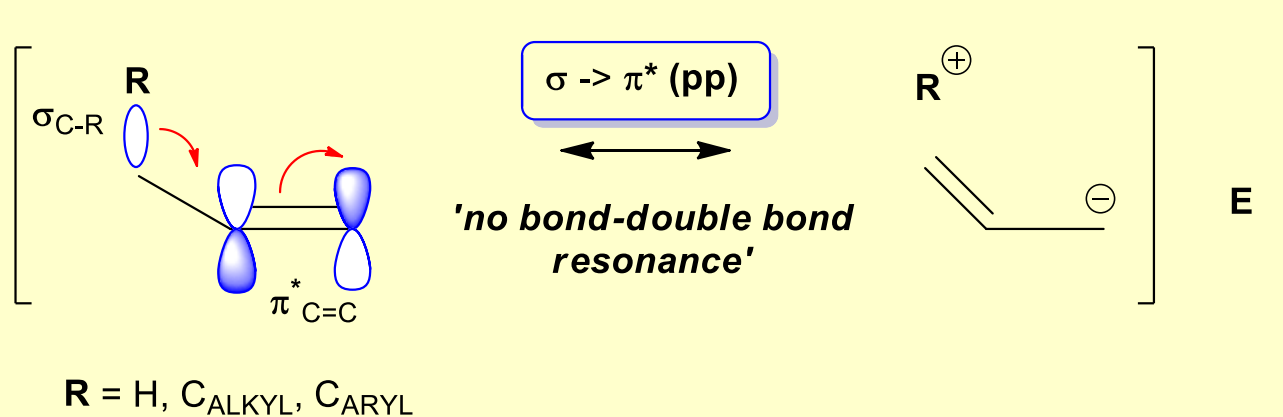
Hyperconjugation / σ-conjugation

- ***Enhanced thermodynamic stability of more substituted alkenes:***

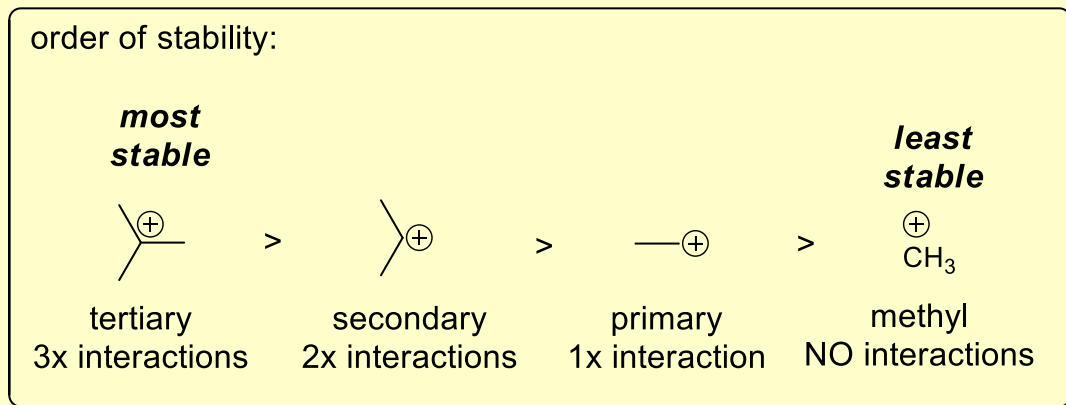approximate order of stability (from thermochemical data):

most stable

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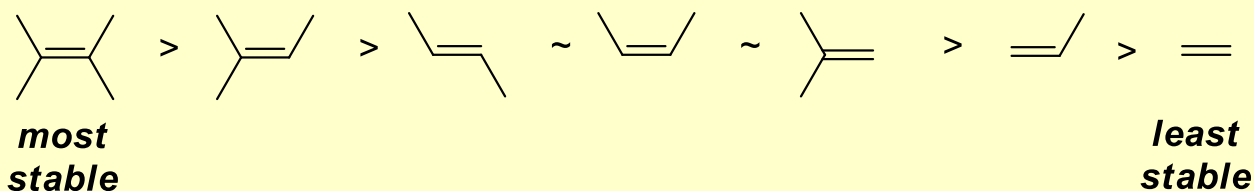
NB. This is an example of ***Deslongchamps' theory*** that 'two stereoelectronic interactions are better than one'.

σ_{C-R}

R

$\pi^*_{C=C}$

σ -> π* (pp)

'no bond-double bond resonance'

$R^{\oplus}$

$\ominus$
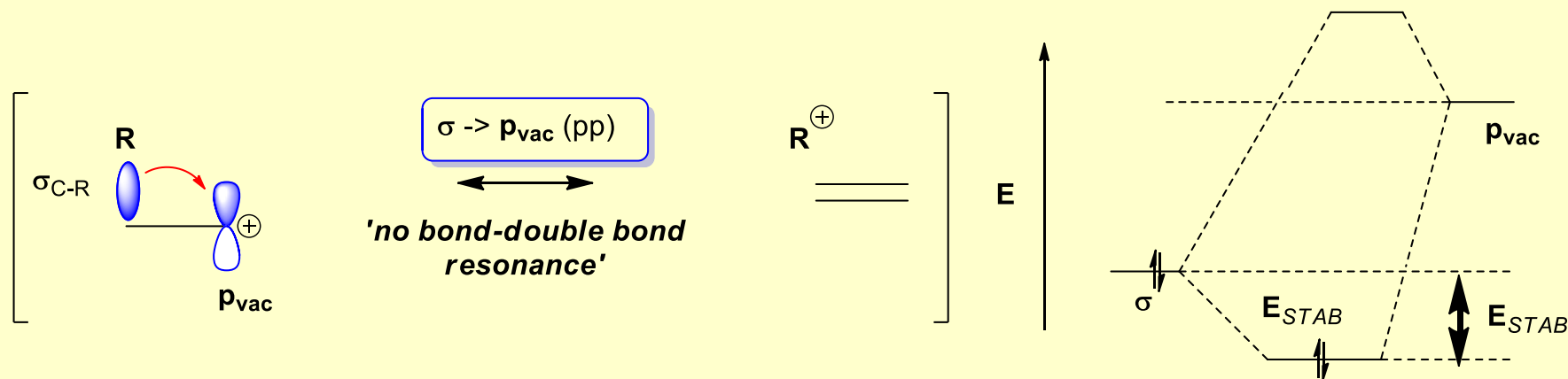
R = H, C_{ALKYL}, C_{ARYL}

E

π*

σ

E_{STAB}

Hyperconjugation / σ-conjugation cont.

- **Enhanced stability of more highly substituted carbocations:**

order of stability:

most stable   *least stable*

tertiary	secondary	primary	methyl
3x interactions	2x interactions	1x interaction	NO interactions

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

$\sigma \to p_{vac}$ (pp)

'no bond-double bond resonance'

σ_{C-R} R p_{vac}

$R^{\oplus}$

E p_{vac}

σ E_{STAB} E_{STAB}

Hyperconjugation / σ-conjugation cont.

- ***The silicon β-effect :***

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

R_3Si —— $\overset{\oplus}{\underset{\alpha \quad \beta}{}}$

SiR$_3$

$\sigma_{C\text{-Si}}$

σ -> **p$_{vac}$** (pp)

p$_{vac}$

'no bond-double bond resonance'

$\overset{\oplus}{\text{SiR}_3}$

E

p$_{vac}$

σ

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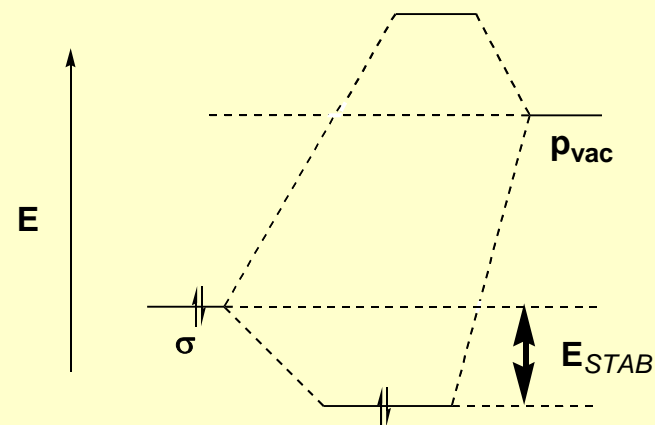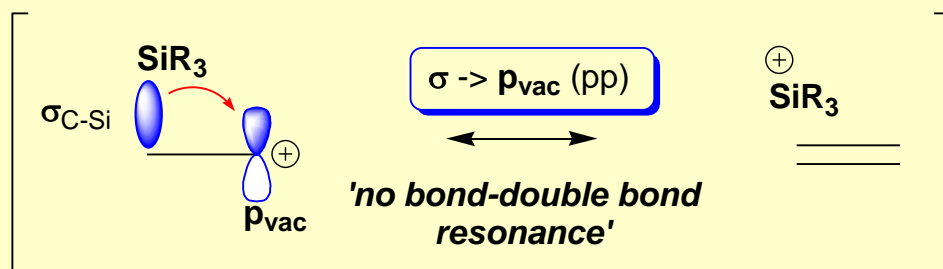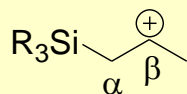
NB. Si is highly electropositive so the $\sigma_{C\text{-Si}}$ bond is a good donor (*i.e.* is high in energy)