

**Lectures 3 and 4:** Basic thermodynamics, reaction diagrams, transition states and intermediates, kinetic vs. thermodynamic control. Hammond postulate. Reactivity: polarity in molecules, nucleophilicity & electrophilicity. Relate to FMO interactions/relative energies and electronegativity. Reactions: curly arrow rules illustrated with simple one-step processes. 'Neutralisation reactions' and non-charged counterparts. The concept of electron flow. Atoms bearing formal charges do not necessarily react according to that charge. Homing-in on reaction sites: filled and empty orbitals, HOMO & LUMO add a 3D aspect to mechanism. (Clayden chapter 13)

For a one-step process ( $A \rightarrow B$ ), no intermediates, favourable reaction ( $\Delta G$  -ve)

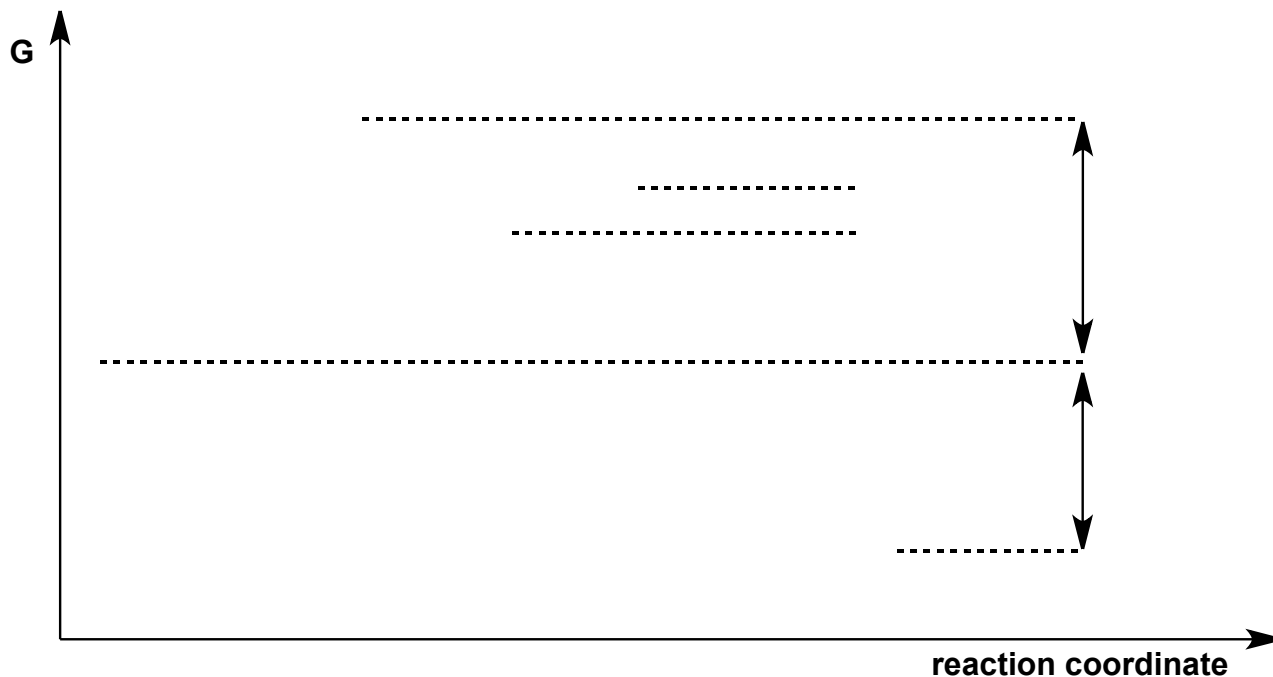


Molecules must have sufficient energy to overcome the free energy barrier ( $\Delta G^\ddagger$ , loosely the activation energy), and

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

Both enthalpy and entropy contribute to the rate of the reaction.

Compare with a simple two-step process ( $A \rightarrow B \rightarrow C$ , rate constants  $k_1$  and  $k_2$  respectively), again assuming  $\Delta G$  -ve

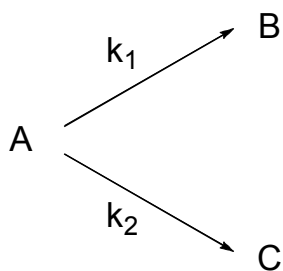


here B is an *intermediate*, a localised energy minimum;

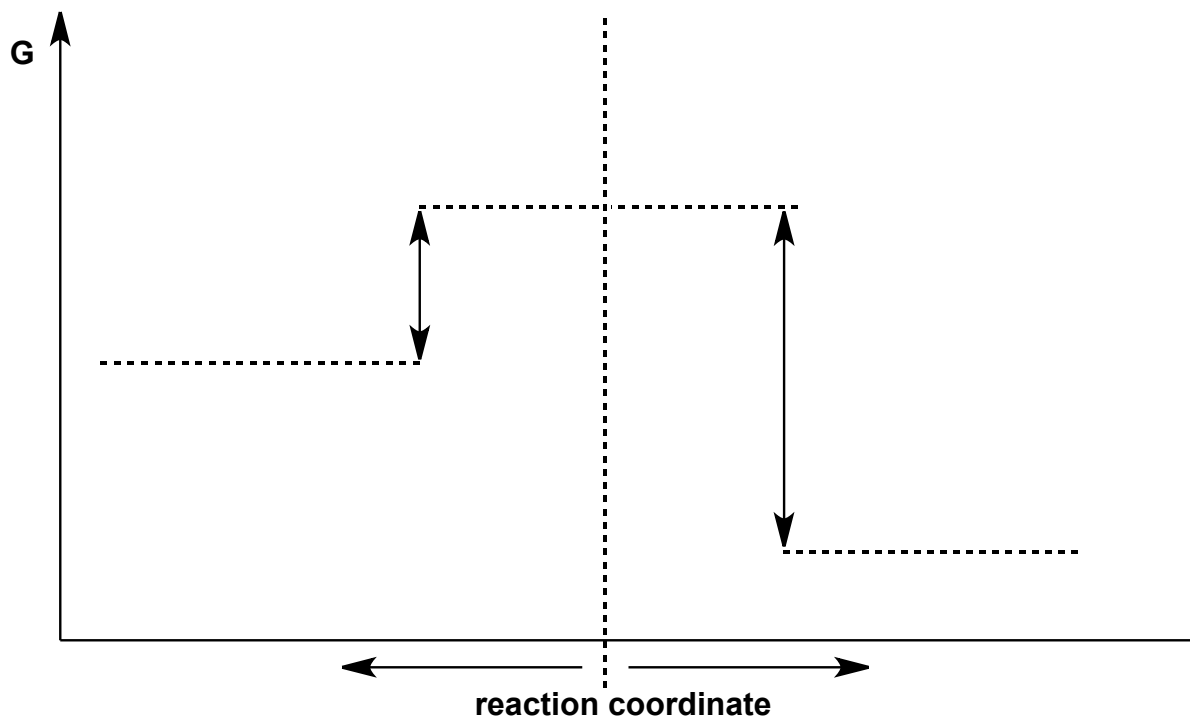
In the previous scenario, what factors influence the overall ease of the reaction  $A \rightarrow C$ ?

**Hammond postulate:** for consecutive species, close in energy implies close in structure. Here, both  $TS_1$  and  $TS_2$  are closer in (energy) structure to intermediate B than to either A or C therefore, in order to facilitate the reaction, we should consider factors that stabilise B

Now consider a divergent reaction where a starting material or an intermediate can produce two different products



If we take the case where  $\Delta G_{AB}^\ddagger < \Delta G_{AC}^\ddagger$  and  $\Delta G_{AB} < \Delta G_{AC}$ ; the reaction diagram looks like



**Under kinetic control (irreversible reaction conditions) the major product will be B**

**Under thermodynamic control (reversible conditions) the major product will be C**

Organic reactions are usually controlled by polar interactions. Reagents are routinely classified as either electrophiles or nucleophiles.

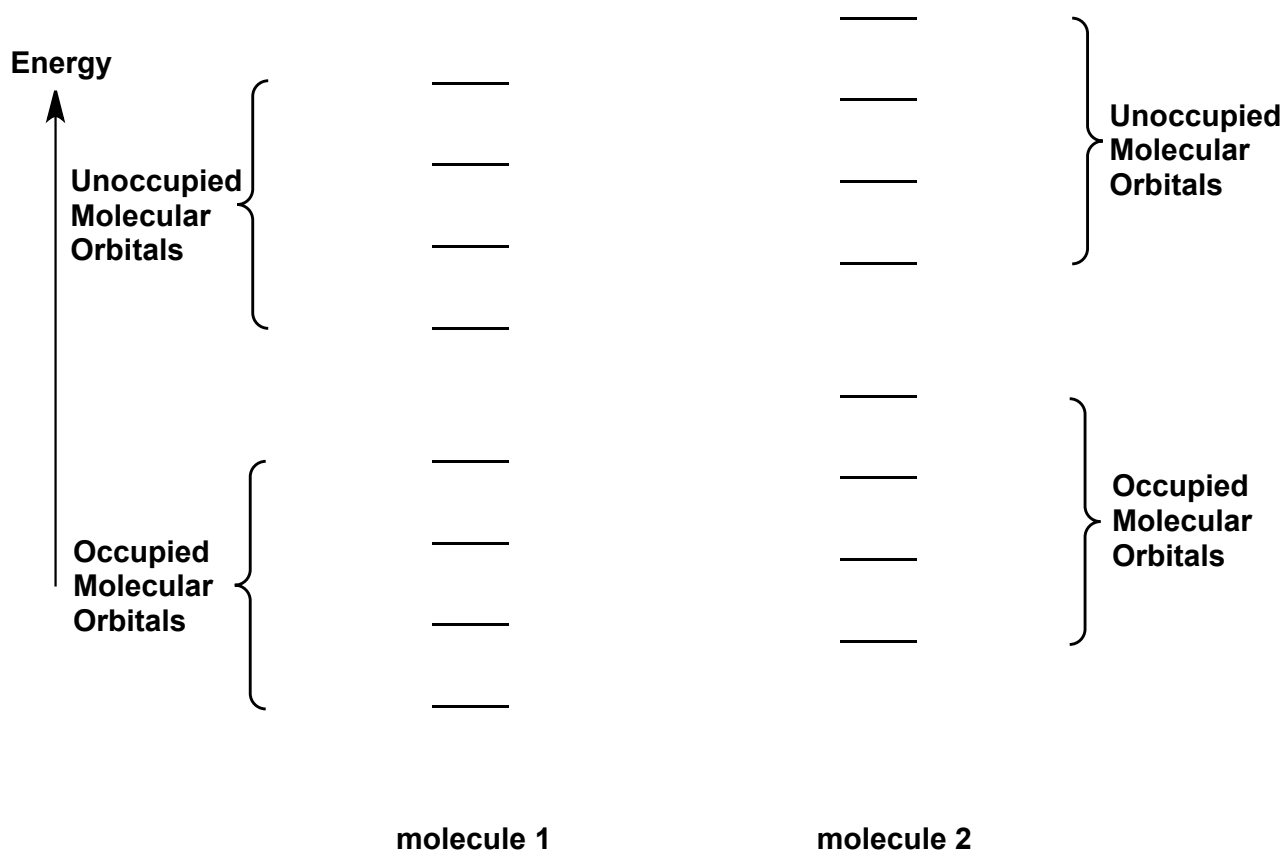
## **Nucleophiles**

## **Electrophiles**

## **Frontier Molecular Orbital (FMO) Treatment of Simple Reactions**

In molecular orbital terms, the dominant interaction is between:

The diagram below is a schematic of the general situation; here *molecule 2* has the relatively high-lying HOMO and acts as the nucleophile, *molecule 1* has the relatively low-lying LUMO and acts as the electrophile.

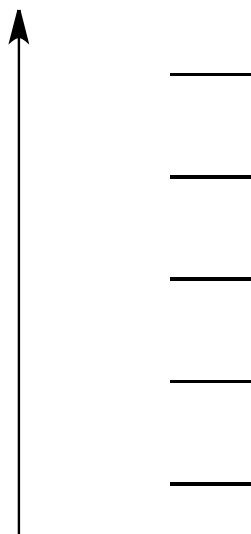


The HOMOs and LUMOs have 'shapes' (spatial probability distribution of electrons at a particular energy within a molecule). An important consequence of all this is that nucleophiles and electrophiles must approach one another so that HOMO/LUMO overlap is possible in order for bonding to occur.

Underlies *stereospecificity*: a change in the stereochemistry of the starting material leads to a corresponding change in the stereochemistry of the product as a consequence of the mechanism.

## General Relative Ordering of MO Types

Energy



## Curly Arrow Rules

Arrow comes *from* the nucleophile *to* the electrophile;

*Overall* charge is conserved in each reaction step;

The important first row atoms B, C, N & O must not have more than 8 outer shell (valence) electrons; B and C can have 6 (in  $R_3B$  and  $R_3C^+$  respectively) but N and O almost always have 8; C, N and O can have 7 valence electrons in radical species;

Only centres that have an available electron pair [lone pair ( $n$ ), double bond ( $\pi$ ), or e-rich single bond ( $\sigma$ )] can act as nucleophiles;

Watch out for sites with *formal* charges and 8 valence electrons that activate the attached atoms (e.g.  $\text{H}_4\text{B}^-$ ,  $\text{H}_3\text{O}^+$ );

**Nucleophiles:**

HOMO:  $n$  (lone pair)

HOMO:  $\pi$

HOMO:  $\sigma$

**Electrophiles:**

LUMO:  $p^0$



LUMO:  $\pi^*$

LUMO:  $\sigma^*$