Lecture 1

Conformational Analysis in Acyclic Systems

Learning Outcomes: by the end of this lecture and after answering the associated problems, you will be able to:

1.   use Newman and saw-horse projections as 3D representations of different conformational isomers;
2.   use the terms, staggered, eclipsed, *anti*, and *gauche* to describe different conformers;
3.   calculate the energetic costs of a range of simple eclipsing interactions;
4.   explain why different conformers have different energies;
5.   recognise a *syn* pentane interaction;
6.   calculate the equilibrium constant, and therefore the relative populations of two conformers, for a simple conformational equilibrium.

Some definitions:

conformation   conformation relates to the different spatial arrangements of the atoms in a molecule that arise through rotation about the bonds linking the atoms.

torsion or *dihedral angle*

Conformation of Alkanes

Let's consider the possible conformations of one of the simplest acyclic alkanes, ethane. We can identify two types of conformational isomer, namely staggered and eclipsed conformers.

Ethane

Rotating about the C–C bond, we see that ethane has three low-energy conformational isomers. They are identical or *degenerate* (same energy) and are described as *staggered* conformers. The H–C–C–H dihedral angle in these conformers is 60°. We can identify a second high-energy conformational isomer in which the H–C–C–H dihedral angle is 0°. For obvious reasons, this is described as an *eclipsed* conformer. Since eclipsed conformers are higher in energy than staggered conformers, there is clearly restricted rotation about the C–C single bond (although the energy barrier to rotation is relatively small).

$\theta = 0°$ $\theta = 60°$ $\theta = 120°$ $\theta = 180°$

potential energy (kcal mol^{-1})

0   60   120   180 θ
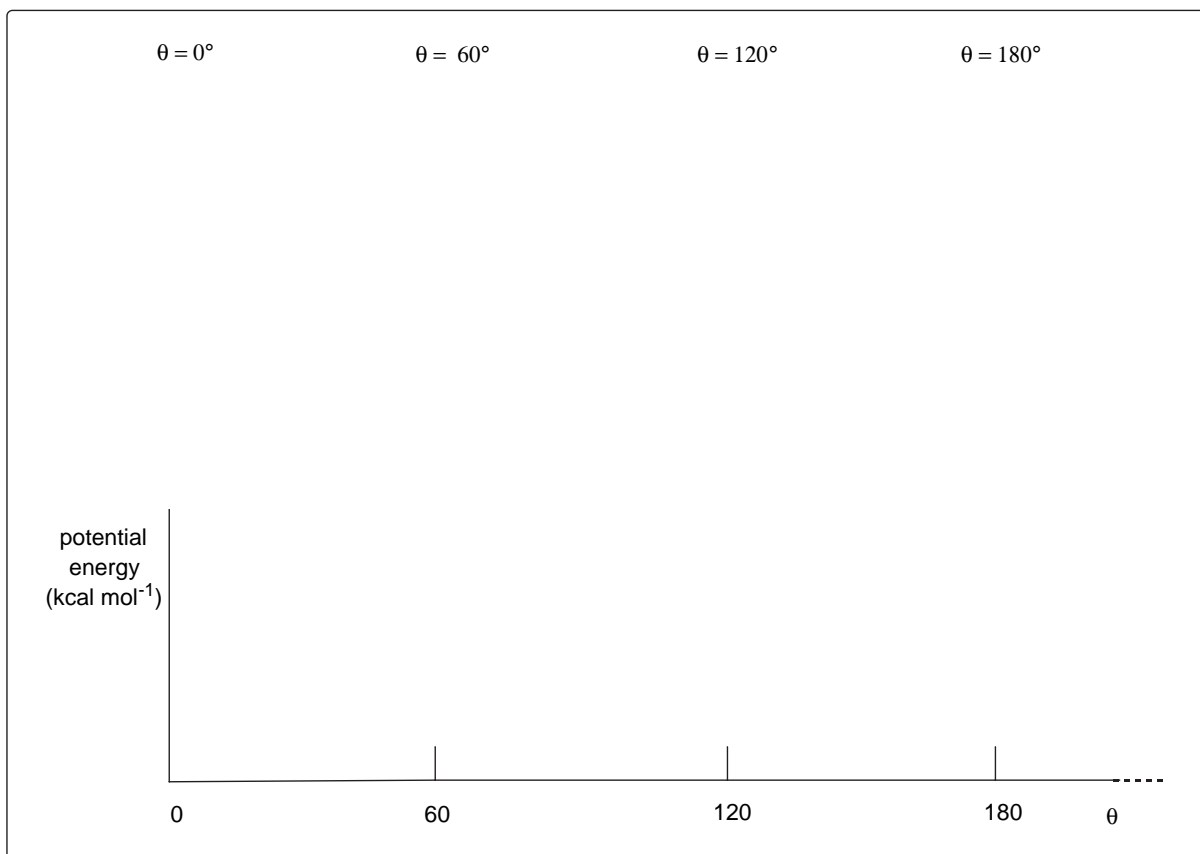
If we know the difference in energy between the two conformers, we can estimate the energetic cost of a single C–H / C–H eclipsing interaction:
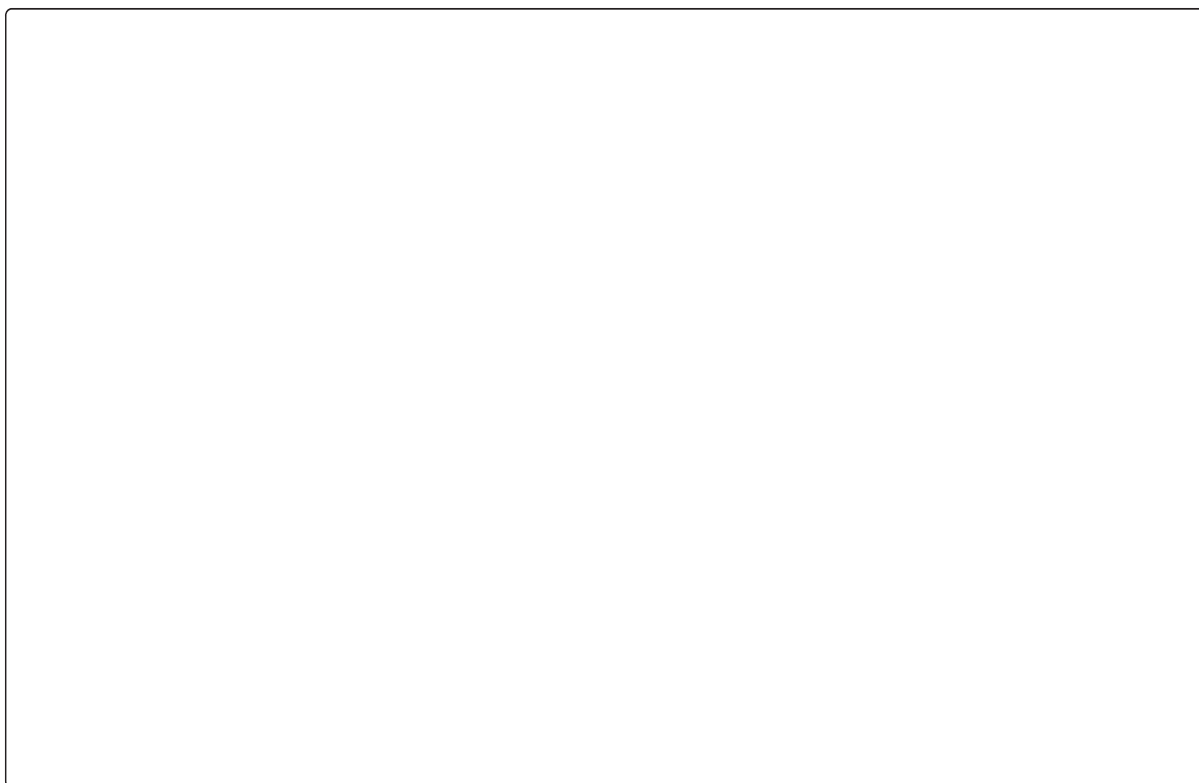
## What are the Origins of this Barrier to Rotation?

1.   *electrostatics*

Since Carbon and Hydrogen have very similar electronegativities, the C–H bond is not strongly polarised. Electrostatics are therefore NOT important in this case.

2.   *orbital overlap* (most important for simple alkanes)

Overlap between two filled molecular orbitals (*e.g.* a σ_{C-H} bonding MOs) is an energetically unfavourable process. The effect is most severe when the orbitals being optimally aligned *i.e.* when the molecule adopts an eclipsed conformation. We can represent this in the form of a molecular orbital diagram:
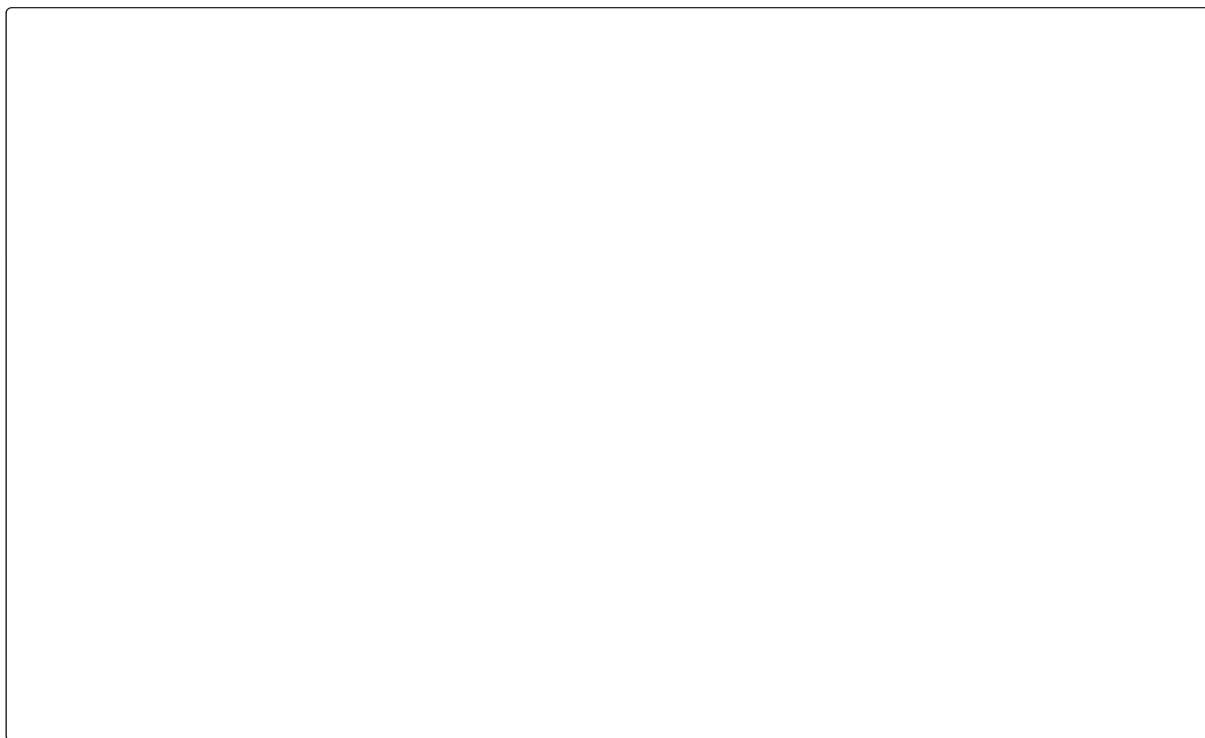
In contrast, when a filled molecular orbital overlaps with an unfilled molecular orbital this is an energetically favourable process. This is most efficient when the molecule adopts a staggered conformation. We can see this by constructing a molecular orbital diagram:
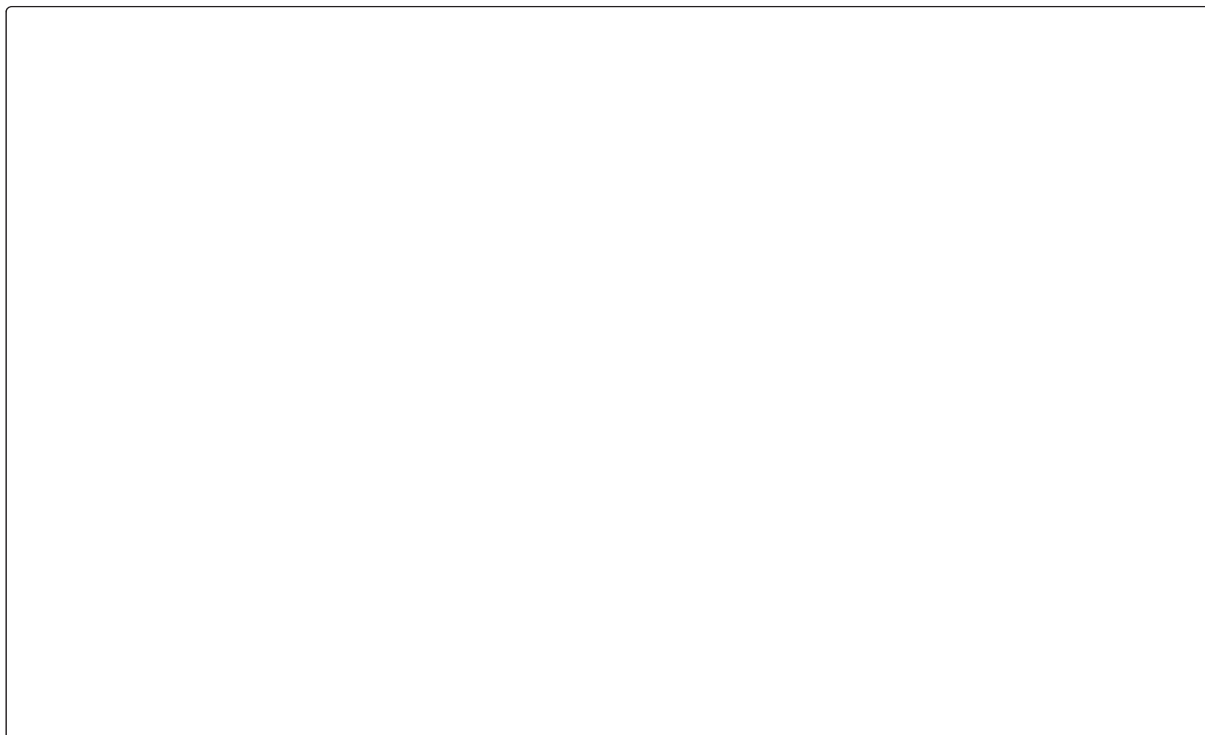
3.   *sterics*   (Van der Waals interactions)

Since the H atoms are barely within van der Waals distance this effect is not very important in this case (estimate that sterics contribute to 10% of the energy barrier in this instance).
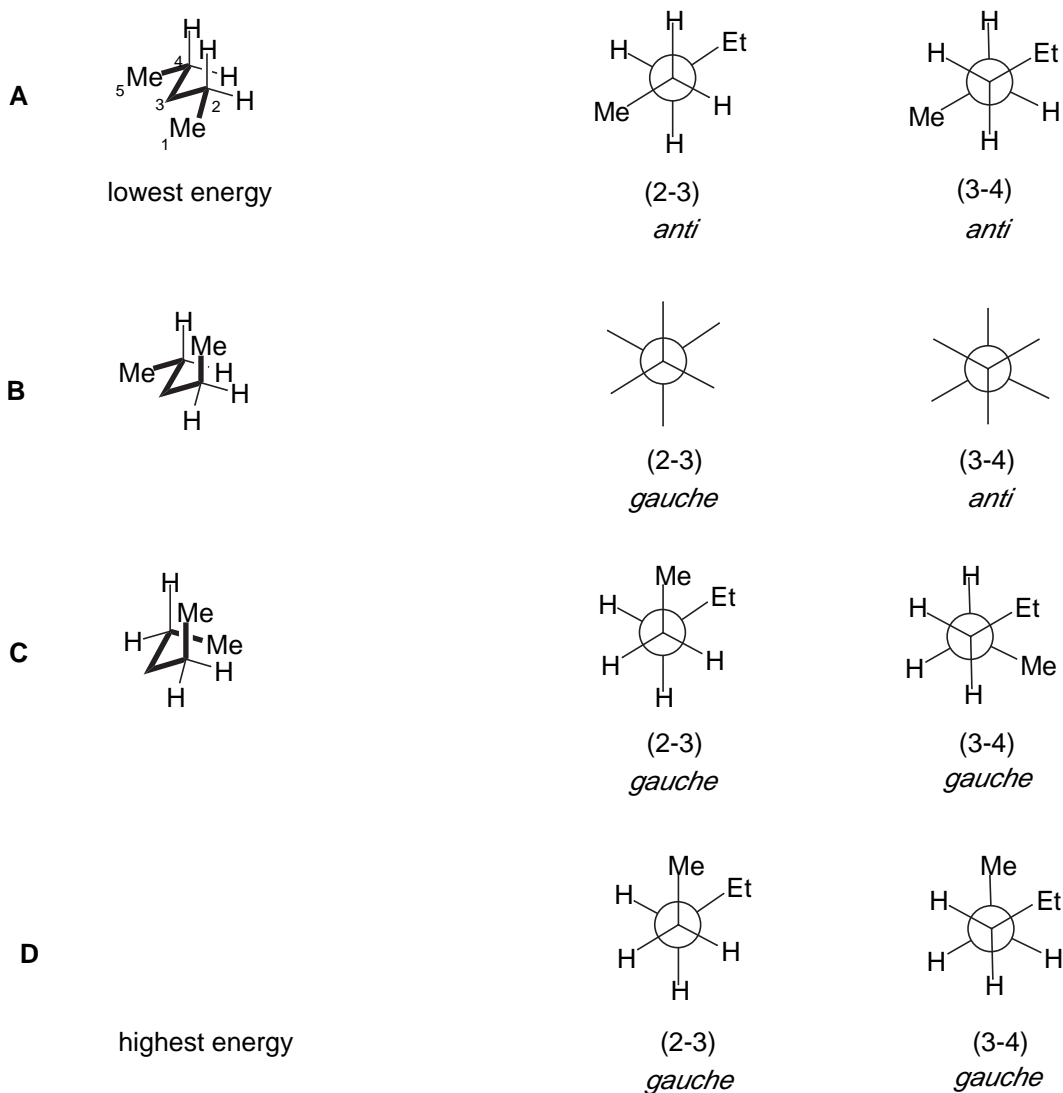
Note

Van der Waals' repulsions become much more significant contributors to the energy barrier when the substituents on the carbon atoms are large, *e.g.* in hexachloroethane.
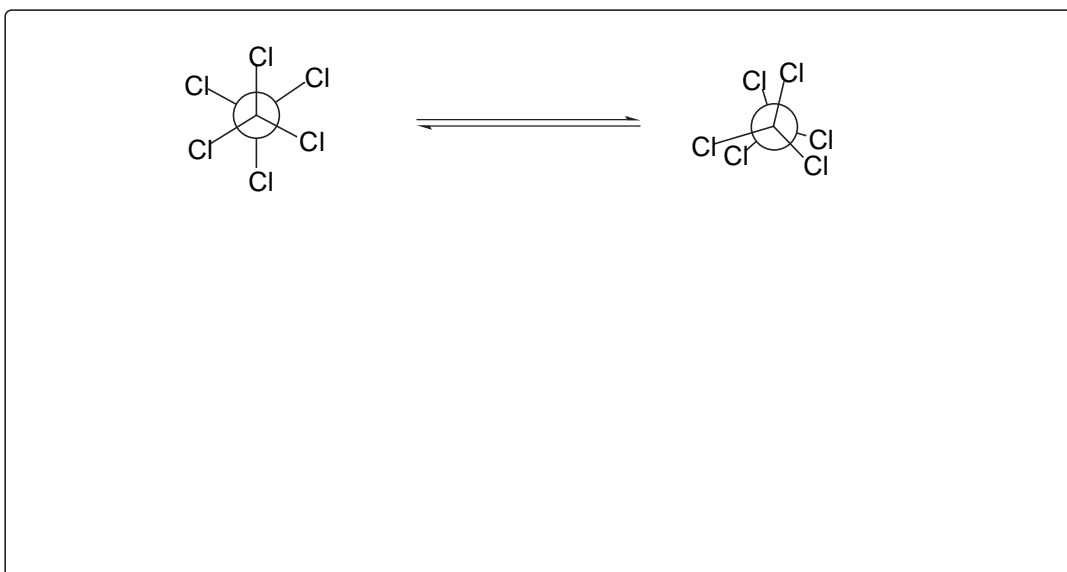
Pentane

With this longer chain alkane, we now need to consider rotation about TWO CH_2-CH_2 bonds. This additional conformational flexibility gives rise to NINE possible staggered conformations (some of which are enantiomeric):

A

lowest energy

(2-3)
anti

(3-4)
anti

B

(2-3)
gauche

(3-4)
anti

C

(2-3)
gauche

(3-4)
gauche

D

highest energy

(2-3)
gauche

(3-4)
gauche

Conformation **D** is the highest energy staggered conformation and is effectively unpopulated at room temperature. The additional destabilising 1,3-interaction is known as a **double *gauche* pentane** or, more commonly, a *syn* **pentane interaction**.

Calculating the Populations of Different Conformers

Consider the two staggered conformers of butane:
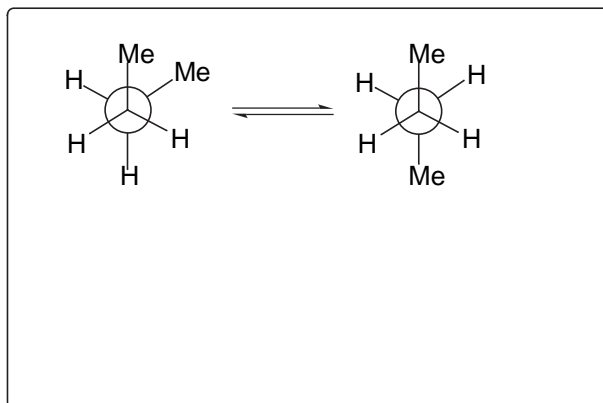
Recall that the equilibrium constant, K, is related to the Gibb's free energy according to the following equation:
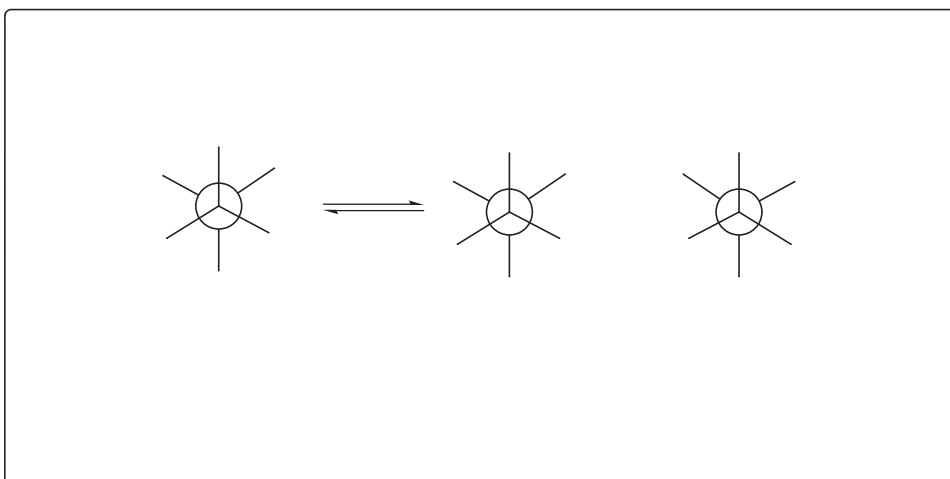
$$$$
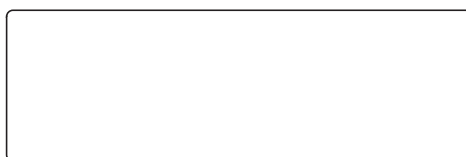
and

$$$$

We know that $\Delta H° =$ kcal mol^{-1}

Thus to evaluate $\Delta G°$, and therefore the equilibrium constant, K, we need to incorporate an entropy contribution. Since there are *two* enantiomeric *gauche* conformers and only one *anti* conformer.

⇨ ΔS° = -R ln2 (R = gas constant; 1.9872×10^{-3} kcal K^{-1}mol^{-1})

Substituting this information into equation 2 (see above),

⇨ ΔG° = -0.9-(−RT ln2).

Thus at 298 K, ΔG° = -0.9 + 0.41 = -0.49 kcal mol^{-1}

but from equation 1, ΔG° = -RT lnK

⇨ K =   = 2.3

This corresponds to a distribution of 70% *anti* and 30% *gauche* conformers.

Conformation of Saturated Acyclic Molecules with Polar Substituents / Chains

When polar substituents are introduced into a molecule, electrostatic effects become much more important for governing the relative energies of different conformers. Different conformations will have different dipole moments, which will also have an impact on the solvation energy; thus solvent will now also be more important in affecting the position of a conformational equilibrium.

1,2-Dihaloethanes

We can draw two staggered conformations (*c.f.* butane) - *anti* and *gauche* - for these molecules. Evidence for the adoption of both conformations comes from the IR spectrum of this class of molecules. If the *anti* conformation was adopted exclusively, the molecule would have no dipole moment and therefore would be only weakly IR active. The presence of significant bands in the IR spectrum of 1,2-dichloroethane shows that other conformations are also significantly populated; *i.e.* we also need to consider the population of the *gauche* staggered conformation.
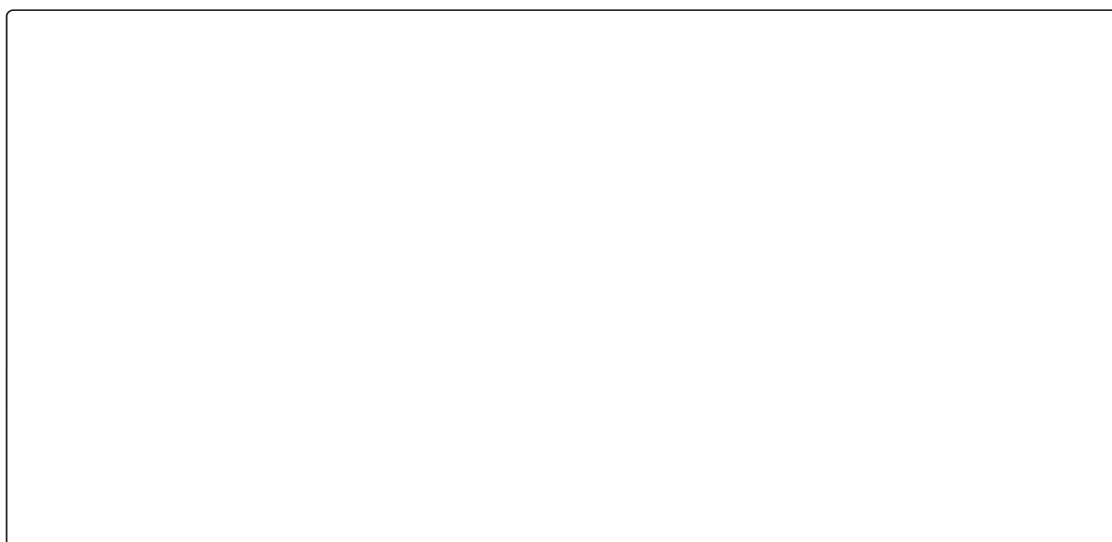
In the gas-phase, dipole-dipole repulsion is significant ⇨ *gauche* conformer is disfavoured.

In solution, the polarity of the solvent is important and must be considered. In polar solvents, the conformer with the higher dipole moment will benefit from increased energy of solvation. This results in an increase in the population of the *gauche* conformer.

As the polarity (which correlates with the dielectric constant) of the solvent increases, the energy difference between the *gauche* and *anti* conformers decreases.

Energy difference between *gauche* and *anti* conformers of 1,2-dichloroethane:

phase	dielectric constant ε	energy difference (kcal mol^{-1})

1,2-Difluoroethane

1,2-Difluoroethane seems anomalous; the *gauche* conformer is favoured even in the gas phase.
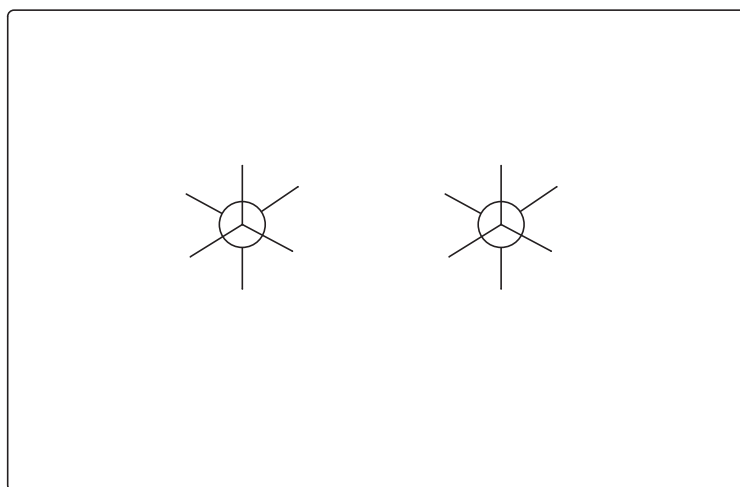

To rationalise this observation we need to consider:

1. *statistical factors* (*i.e.* an entropic contribution to ΔG° (remember there are two degenerate *gauche* conformers, whereas only one *anti* conformer).

2. *dipole-dipole interactions* - these are repulsive and will be high in the *gauche* conformer especially in the gas phase.

3. *van der Waals repulsions* (steric effects) - the small size of the F atom (van der Waals radius = 1.5 - 1.6 Å) means that this not too important; (this factor is very important for 1,2-dichloroethane, and even more so for 1,2-dibromoethane).

4. *stereoelectronic* or *hyperconjugative effects*. In the *gauche* conformer, both C−F bonds can benefit from the most favourable σ → σ* orbital overlap (most compatible HOMO-LUMO set). [Remember that a filled MO interacting with an unfilled MO leads to an energetically favourable interaction.]
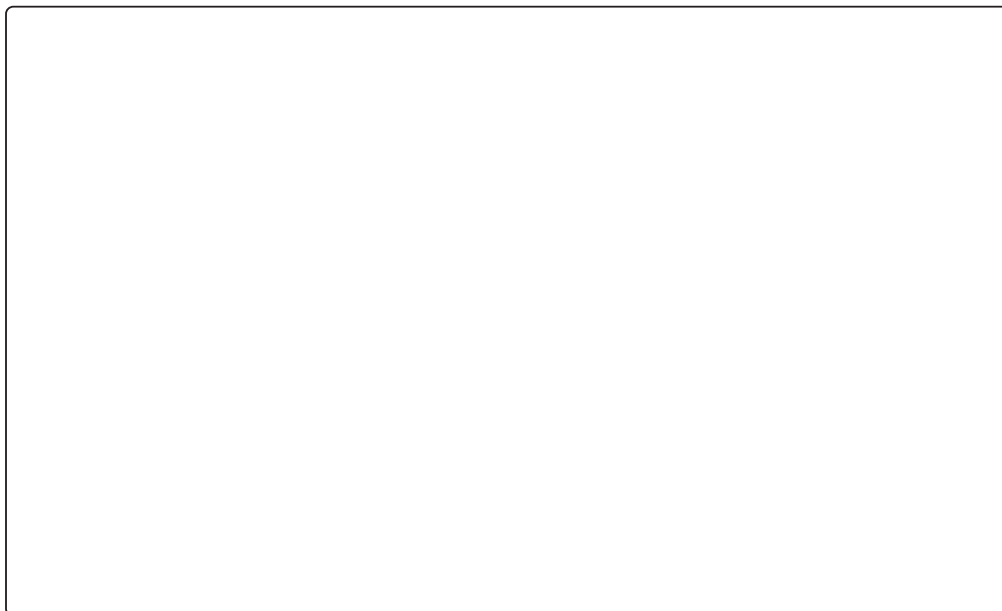
Summary

Acyclic molecules tend to be conformationally relatively flexible. Nevertheless, there is rarely *free* rotation about a single bond; rather we can identify low energy *staggered* conformers and high energy *eclipsed* conformers. A number of factors account for the difference in energy between these conformers. These include entropic, electrostatic, steric and stereoelectronic effects. All contribute to varying degrees depending on the substituents and local environment (*e.g.* solvent).