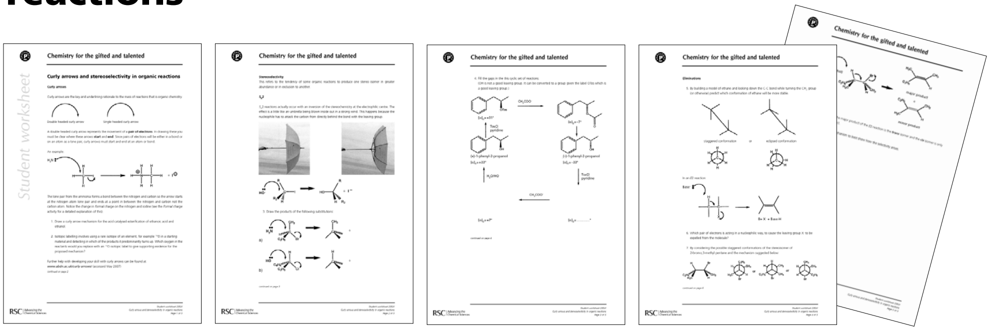
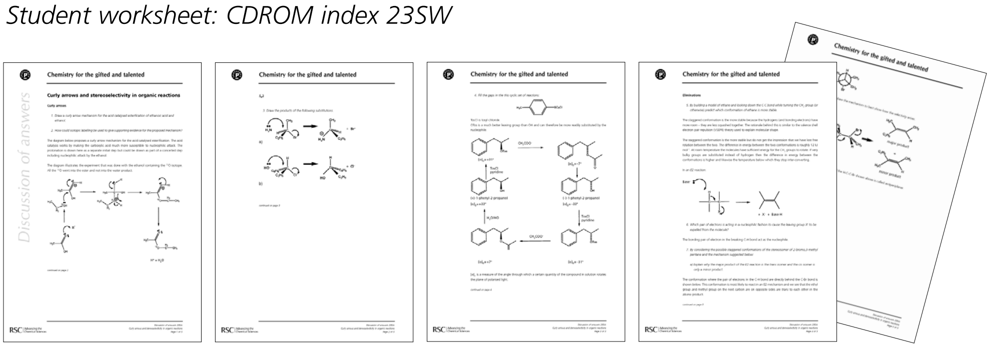
Curly arrows and stereoselectivity in organic reactions



Student worksheet: CDROM index 23SW



Discussion of answers: CDROM index 23DA

Topics

Curly arrows, the mechanism for esterification, inversion during S_N2 reactions, saw-horse representations and stereoselectivity in elimination reactions.

Level

Very able post-16 students.

Prior knowledge

Curly arrows in organic mechanisms, nucleophilic attack, electrophilic attack and optical isomerism.

Rationale

‘All practising chemists protect themselves from being crushed by the vastness of organic chemistry by moulding it and ordering it with curly arrows. Without curly arrows, chemistry is chaos, and impossible to learn. Curly arrows unify chemistry, and are essential to the solution of problems’[1].

Organic chemistry is sometimes presented to students with the emphasis on facts to recall rather than the underlying principles. Very able students tend to be interested in fundamental concepts and put off by a ‘just learn it’ approach. This activity explores some of the intellectually satisfying aspects of organic chemistry. The first part develops the use of curly arrows. If you have some very able students in a group, then there is a ready made opportunity for differentiation by giving them a chance to draw curly arrow mechanisms for whatever reactions they meet.

Evidence from the UK qualifying competition for the *International Chemistry Olympiad* suggests that even very able students get little practice in presenting the three-dimensional shapes of molecules. This activity gives the students an opportunity to develop those skills.

Use

This activity requires a good background knowledge of organic chemistry and should be used with students towards the end of their organic chemistry course. It can be given to the most able students in a group to work through independently. They should also be given the *Discussion of answers* sheet to review their progress. Students should be able to assemble simple 3D molecular models (such as Molymod®) when they are doing this activity.

[1] Clayden, Greeves, Warren and Wothers, *Organic Chemistry*, Oxford: Oxford University Press, 2001.

Curly arrows and stereoselectivity in organic reactions

Curly arrows

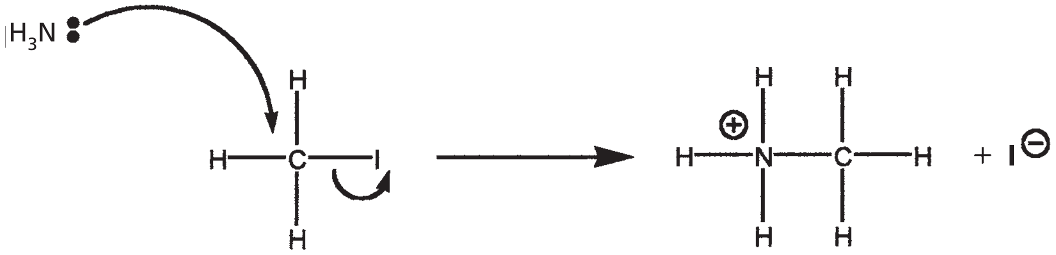
Curly arrows are the key and underlining rationale to the mass of reactions that is organic chemistry.

Double headed curly arrow

Single headed curly arrow

A double headed curly arrow represents the movement of a **pair of electrons**. In drawing these you must be clear where these arrows **start** and **end**. Since pairs of electrons will be either in a bond or on an atom as a lone pair, curly arrows must start and end at an atom or bond.

An example:



The lone pair from the ammonia forms a bond between the nitrogen and carbon so the arrow starts at the nitrogen atom lone pair and ends at a point in between the nitrogen and carbon, not at the carbon atom. Notice the change in *formal charge* on the nitrogen and iodine (see the *Formal charge* activity for a detailed explanation of this).

1. Draw a curly arrow mechanism for the acid catalysed esterification of ethanoic acid and ethanol.

2. Isotopic labelling involves using a rare isotope of an element, for example ^{18}O, in a starting material and detecting in which of the products it predominantly turns up. Which oxygen in the reactants would you replace with an ^{18}O isotopic label to give supporting evidence for the proposed mechanism?

Further help with developing your skill with curly arrows can be found at ***www.abdn.ac.uk/curly-arrows/*** (accessed May 2007).

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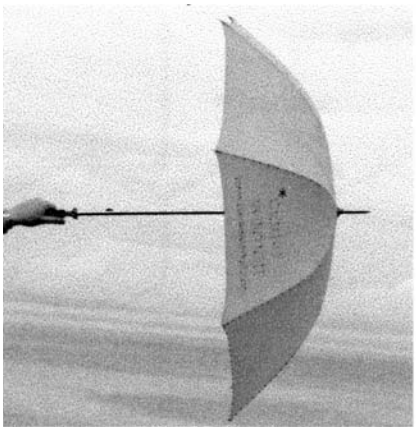
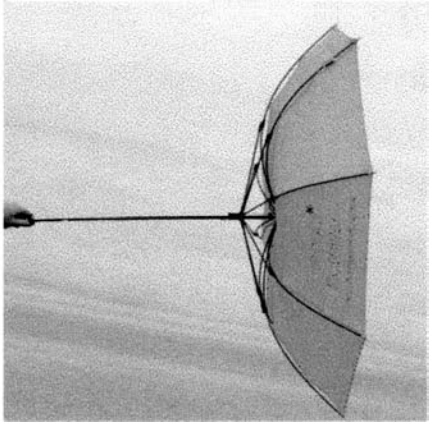
Stereoselectivity

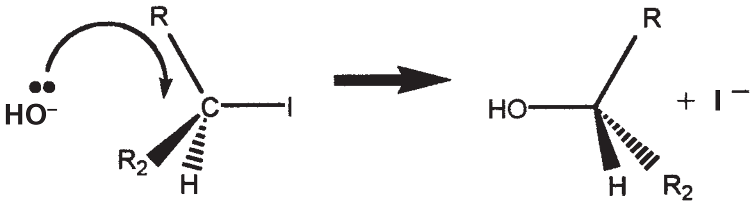
This refers to the tendency of some organic reactions to produce one stereoisomer in greater abundance or in exclusion to another.

S_N2

S_N2 reactions actually occur with an inversion of the stereochemistry at the electrophilic centre. The effect is a little like an umbrella being blown inside out in a strong wind. This happens because the nucleophile has to attack the carbon from directly behind the bond with the leaving group.

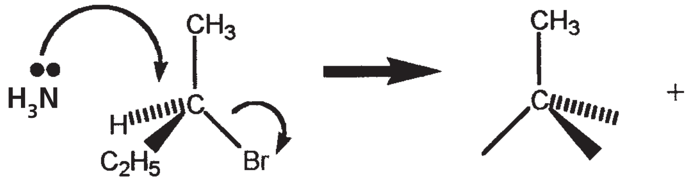




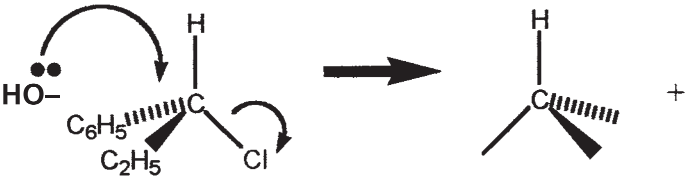


3. Draw the products of the following substitutions:

a)



b)



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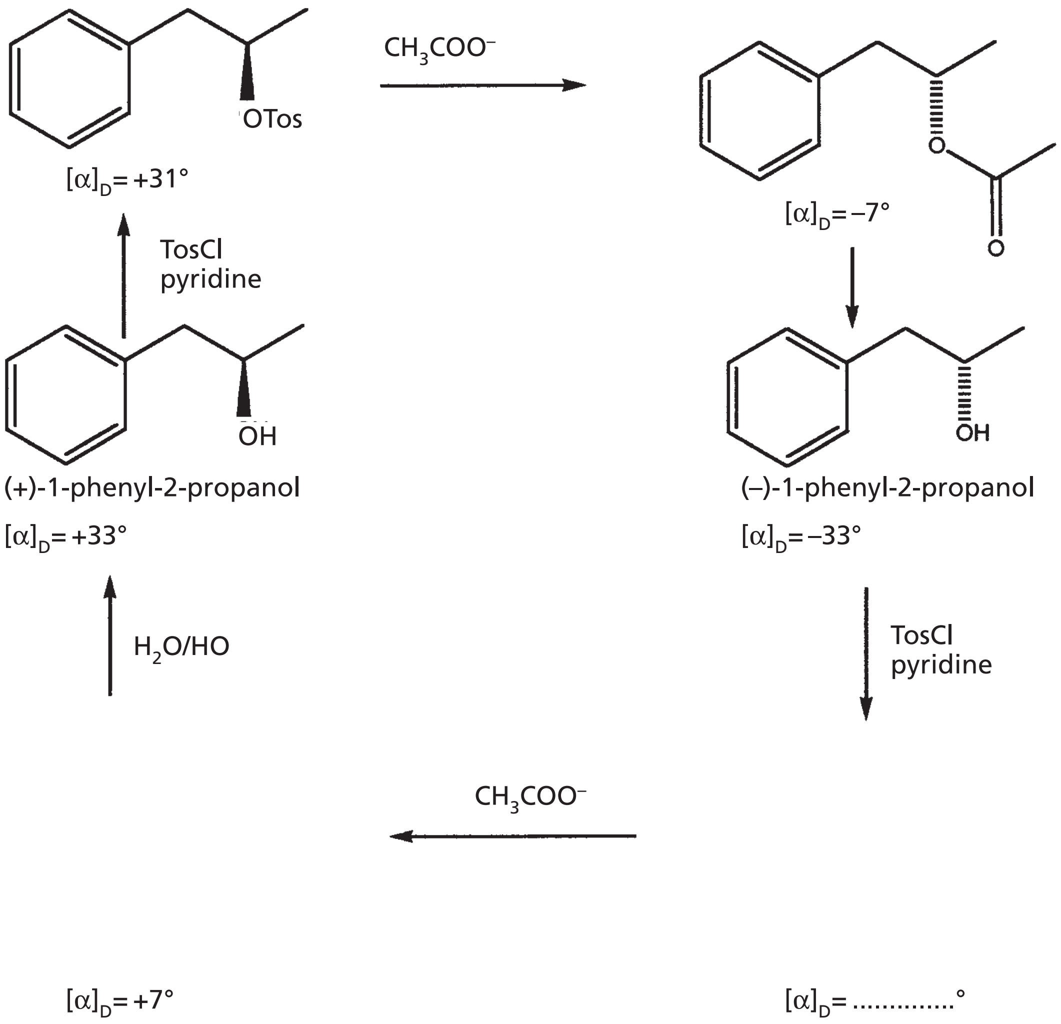
4. Fill the gaps in this cyclic set of reactions:
   (OH is not a good leaving group. It can be converted to a group given the label OTos which is a good leaving group.)



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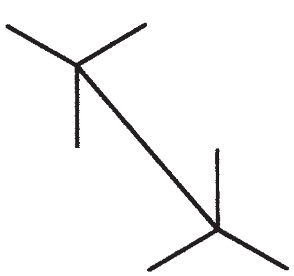
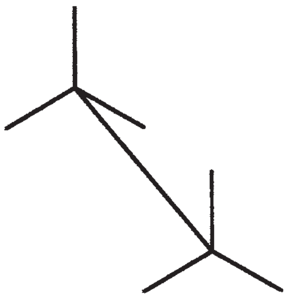
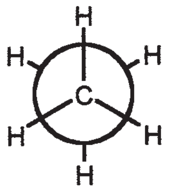
Eliminations

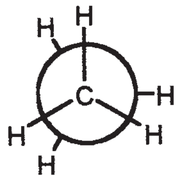
5. By building a model of ethane and looking down the C-C bond while turning the CH_3 group (or otherwise), predict which conformation of ethane will be more stable. State your reasons why.



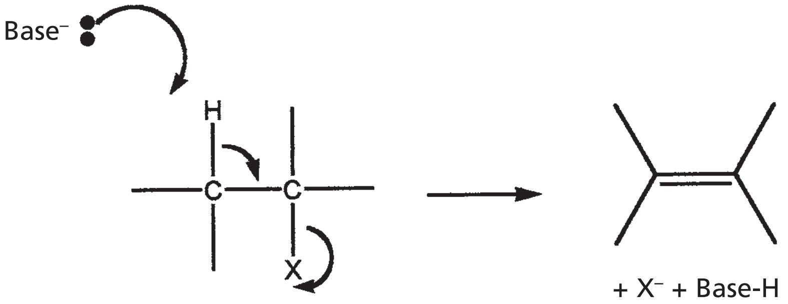


staggered conformation or eclipsed conformation



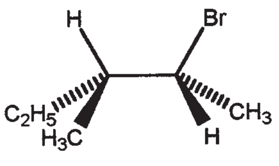


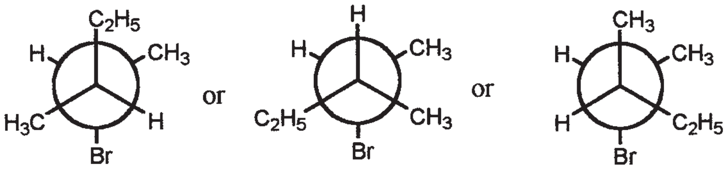
In an *E*2 reaction:



6. Which pair of electrons is acting in a nucleophilic fashion to cause the leaving group X^- to be expelled from the molecule?

7. By considering the possible staggered conformations of the stereoisomer of 2-bromo,3-methyl pentane and the mechanism suggested below:





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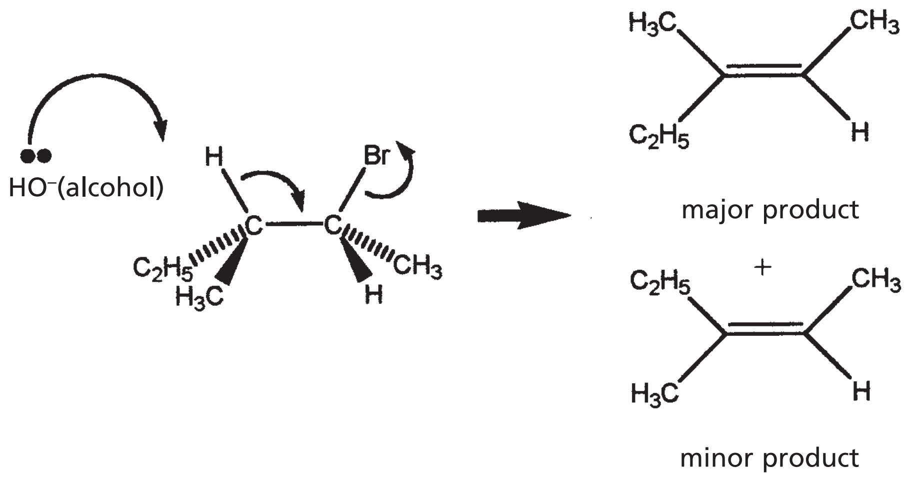


a) Explain why the major product of the *E*2 reaction is the ***trans*** isomer and the ***cis*** isomer is only a minor product.

b) Re-draw the mechanism to best show how the selectivity arises.

Curly arrows and stereoselectivity in organic reactions

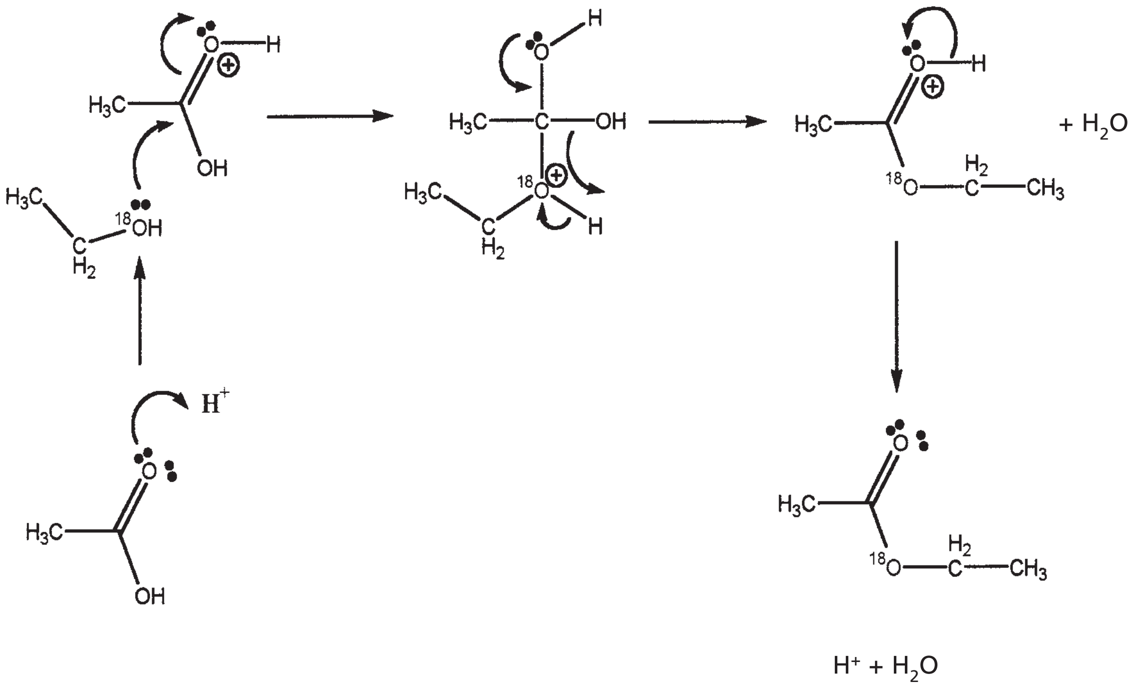
Curly arrows

1. *Draw a curly arrow mechanism for the acid catalysed esterification of ethanoic acid and ethanol.*

2. *How could isotopic labelling be used to give supporting evidence for the proposed mechanism?*

The diagram below proposes a curly arrow mechanism for the acid catalysed esterification. The acid catalysis works by making the carboxylic acid much more susceptible to nucleophilic attack. The protonation is drawn here as a separate initial step, but could be drawn as part of a concerted step including nucleophilic attack by the ethanol.

The diagram illustrates the experiment that was done with ethanol containing the ^{18}O isotope. All the ^{18}O went into the ester and not into the water product.



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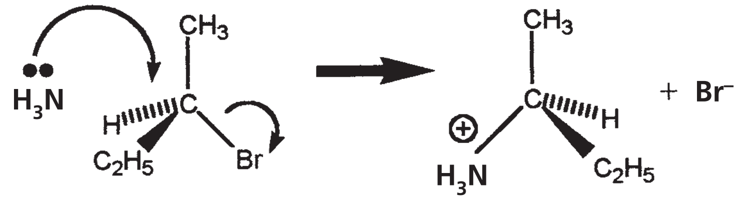
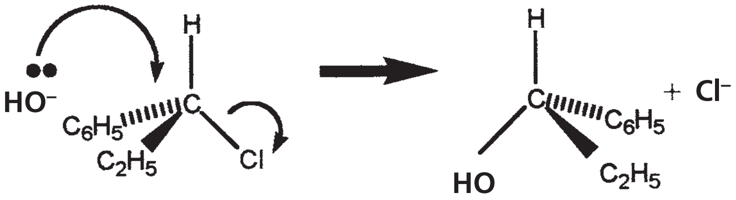
S_N2

3. *Draw the products of the following substitutions.*

a)



b)



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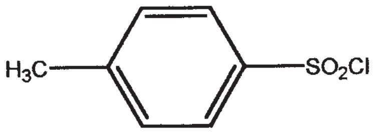
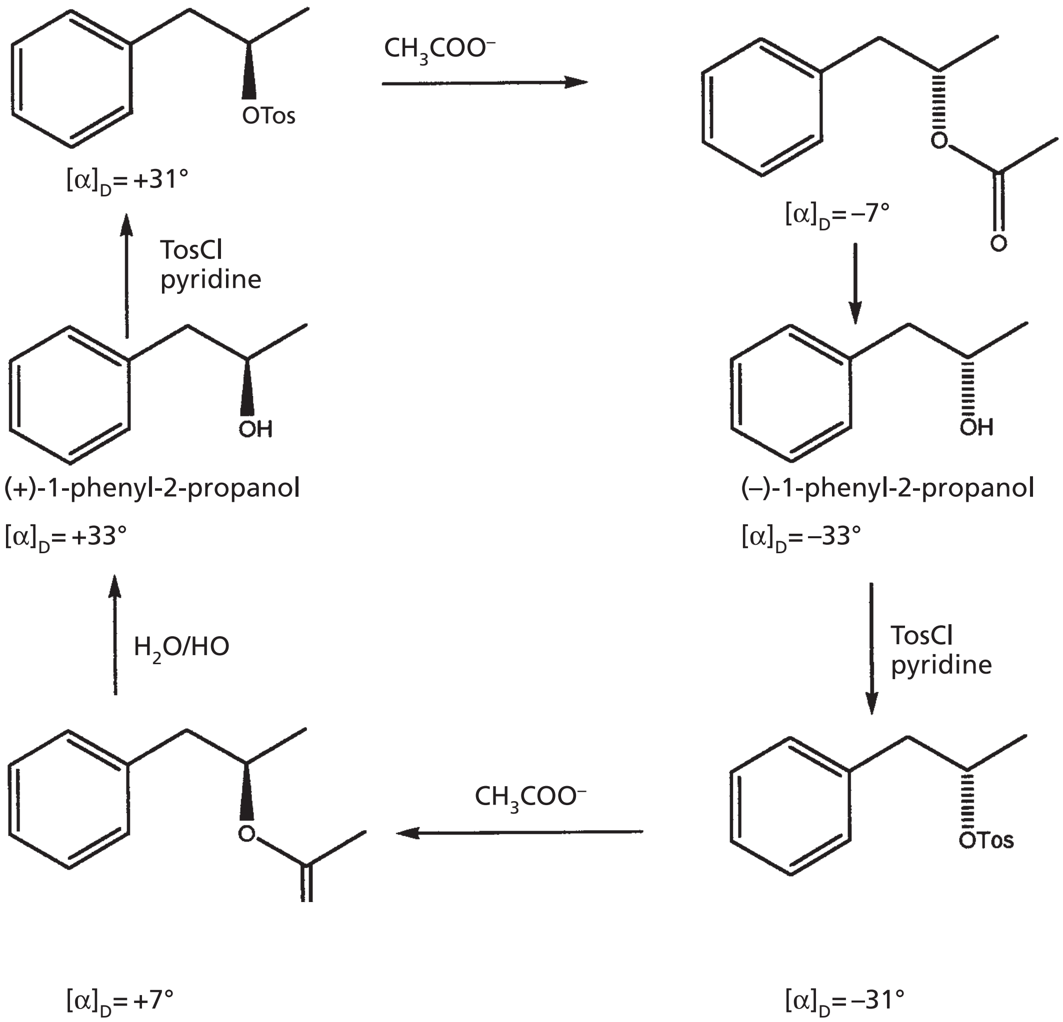
4. Fill the gaps in this cyclic set of reactions:



TosCl

TosCl is tosyl chloride.

OTos is a much better leaving group than OH and can therefore be more readily substituted by the nucleophile.



$[\alpha]_D$ is a measure of the angle through which a certain quantity of the compound in solution rotates the plane of polarised light.

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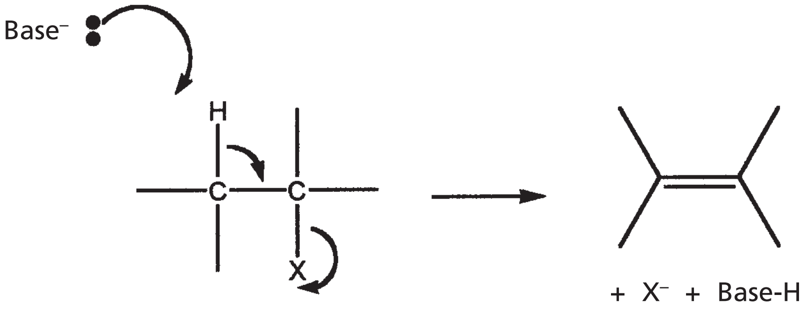
Eliminations

5. *By building a model of ethane and looking down the C-C bond while turning the CH_3 group (or otherwise), predict which conformation of ethane is more stable. State your reasons why.*

The staggered conformation is the more stable because the hydrogens (and bonding electrons) have more room - they are less squashed together. The rationale behind this is similar to the valence shell electron pair repulsion (VSEPR) theory used to explain molecular shape.

Although the staggered conformation is the more stable, do not get the impression that we have lost free rotation between the two. The difference in energy between the two conformations is roughly 12 kJ mol^{-1}. At room temperature the molecules have sufficient energy for the CH_3 groups to rotate. If very bulky groups are substituted instead of hydrogen then the difference in energy between the conformations is higher and likewise the temperature below which they stop inter-converting.

In an *E2* reaction:



6. *Which pair of electrons is acting in a nucleophilic fashion to cause the leaving group X^- to be expelled from the molecule?*

The bonding pair of electrons in the breaking C-H bond act as the nucleophile.

7. *By considering the possible staggered conformations of the stereoisomer of 2-bromo,3-methyl pentane and the mechanism suggested below:*

   a) *Explain why the major product of the E2 reaction is the* **trans** *isomer and the* **cis** *isomer is only a minor product.*

The conformation where the pair of electrons in the C-H bond are directly behind the C-Br bond is shown on the next page. This conformation is most likely to react in an E2 mechanism and we see that the ethyl group and methyl group on the next carbon are on opposite sides and so are *trans* to each other in the alkene product.

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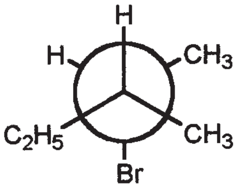
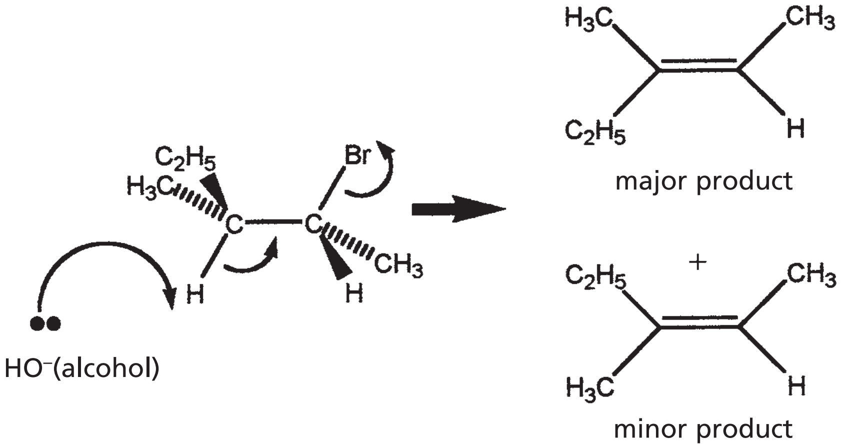


b) Re-draw the mechanism to best show how the selectivity arises.



The relative orientation of the H-C-C-Br shown above is called antiperiplanar.