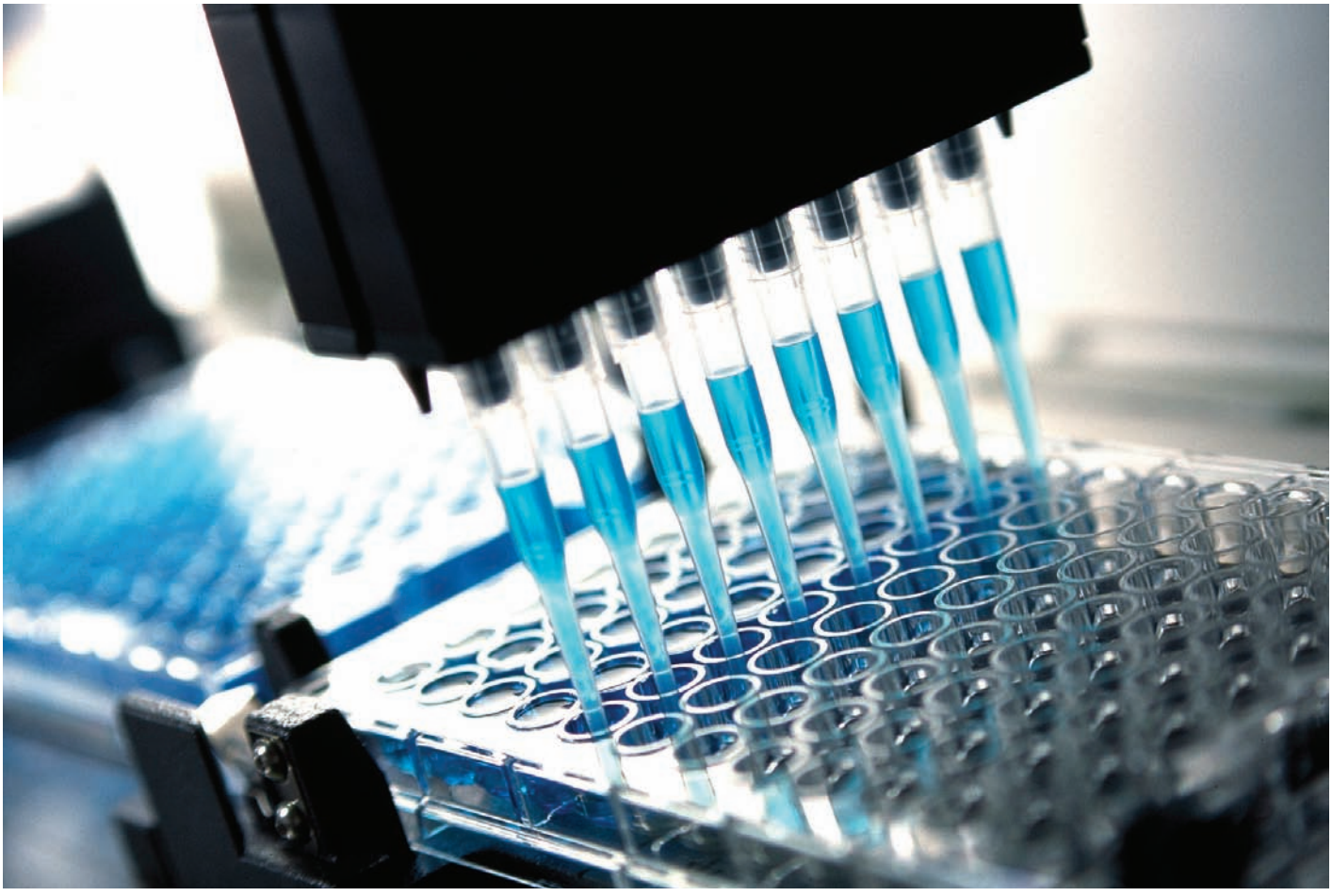
Synthesis and Analysis

Student Notes



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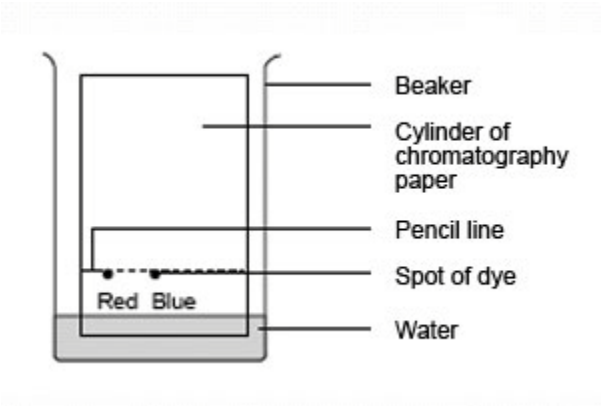
Activity 3: Chromatography of sweets

The coloured dye coating the surface is removed from M&M'S® of various colours. A spot of each is put on to a piece of chromatography paper and water is allowed to soak up the paper separating out the component dyes. The results show which dye mixtures are used to produce particular colours for the sweets.

Procedure

HEALTH & SAFETY: Students must not attempt to eat the M&M'S® or even lick them. They are for laboratory use only.

a) Place the piece of chromatography paper on a clean flat surface, with the longer side horizontal and draw a horizontal line in pencil (not biro) about 1.5 cm from the base of the paper.
b) Use the dampened paint brush to remove the colour from one of the M&M'S® and paint this colour on the line about 2 cm from one end. Small spots are best.
c) Clean the brush in fresh running water and paint the colour of another M&M® on the line about 2 cm from the first spot.
d) Repeat this until all the colours are on the paper or until you have reached the other end.
e) Use a pencil (not a biro) to write the name of the colour next to the corresponding spot.
f) Roll the paper into a cylinder and hold this in place with the paper clips. Try to avoid any overlapping of the paper when you make the cylinder.
g) Put water into the beaker up to depth of about 1 cm.
h) Lower the paper cylinder into the beaker of water thus allowing the water to rise up the paper. Ensure that the water is below the level of the spots. Try to avoid moving the paper cylinder about once it is in position.
i) When the water approaches the top of the paper cylinder remove it from the water. Mark with a pencil the level of the water at the top of the filter paper.



j) Allow the paper cylinder to dry, perhaps by using a hairdryer if available or by clamping it and leaving it to dry overnight.
k) Unravel the paper cylinder and examine it carefully.

Student questions

Here are some questions for students.

a) Why do you think some dyes separate out into different colours whilst others do not ?
b) Why do you think some colours move further up the paper than others ?
c) Can you think of any way of improving the separation between the different spots ?
d) Look on the side of a M&M'S® packet for a list of the coloured dyes used. Try to identify which dyes correspond to the spots on the chromatogram.

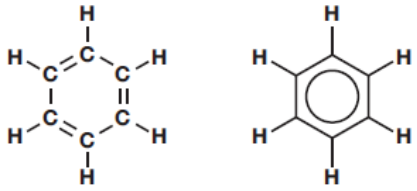
Activity 4: The Nitration of Methyl Benzoate

HEALTH & SAFETY

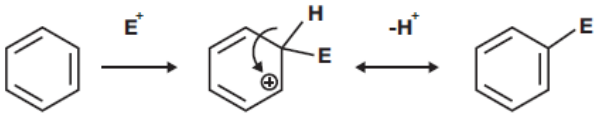
Laboratory coats, disposable nitrile gloves and safety goggles must be worn at all times. Conc. Sulfuric acid and conc. Nitric acid must be measured in a fume cupboard. No naked flames should be present while ethanol is being used.

This activity is designed to give you an insight into what organic chemists do in their day to day work.

A wide range of organic molecules, both naturally occurring and man-made, such as therapeutic medicines and dyes are aromatic compounds. The simplest aromatic compound is benzene.



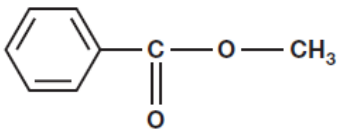
Aromatic compounds normally undergo substitution reactions – rather than addition reactions. This is because substitution reactions retain the delocalised π-electron system of the aromatic nucleus.

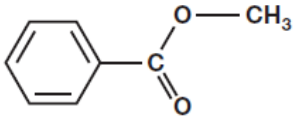


One of the most important substitution reactions of aromatic compounds is nitration – *ie* the addition of an NO_2 group.

The experiment

In this experiment you will nitrate methyl benzoate, which is a relatively simple non-toxic derivative of benzene. You will use a mixture of nitric acid and sulfuric acid to carry out the nitration and then purify the product by recrystallisation.





Finally you will determine the structure of the nitro compound that you have made. How many nitro groups you have added to the ring, and where? You will use a range of spectroscopic techniques – mass spectrometry (MS), infrared (IR) spectroscopy and nuclear magnetic resonance (NMR) spectroscopy – to work out the answer.

The procedure

1. Measure 2.5 cm^3 of methyl benzoate into a small conical flask and then dissolve it in 5 cm^3 of concentrated sulfuric acid. When the liquid has dissolved, cool the mixture in ice.

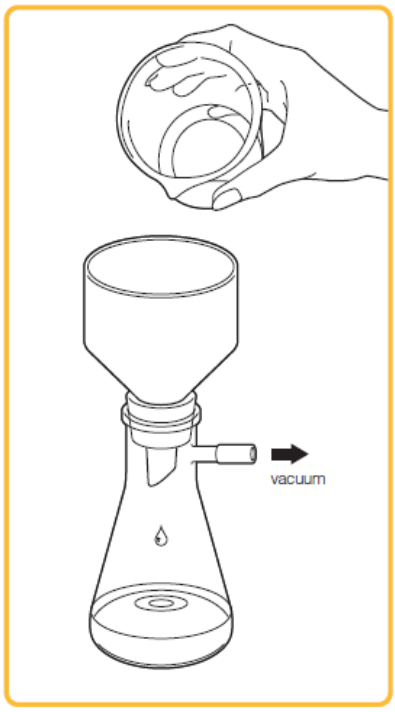
2. Prepare the nitrating mixture by carefully adding 2 cm^3 of concentrated

sulfuric acid to 2 cm³ of concentrated nitric acid. Cool this mixture in ice.

5 Add the nitrating mixture – drop by drop from a teat pipette – to the solution of methyl benzoate. (NB: Do not allow the nitrating mixture to get into the rubber teat.) Stir the mixture with a glass rod and keep the temperature below 10 °C. When you have completed the addition, leave the mixture to stand at room temperature for another 15 minutes.

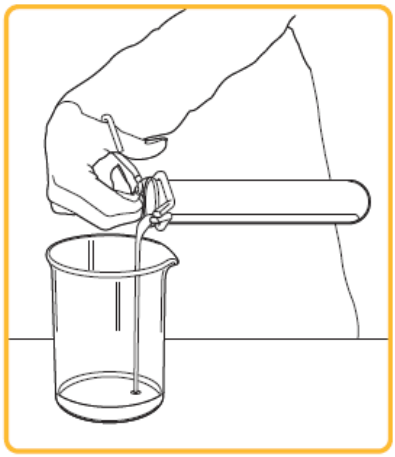
6 After 15 minutes, pour the reaction mixture on to about 25 g of crushed ice and stir until all the ice has melted and the crystalline nitro derivative forms.

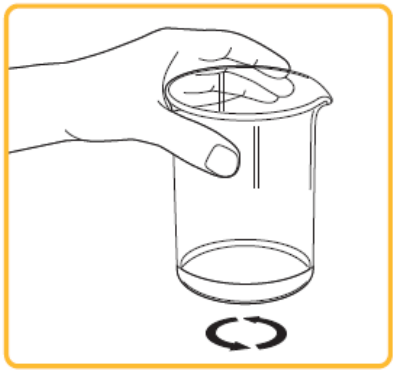
7 Filter the crystals using a Buchner funnel, wash thoroughly with cold water and then transfer to a small beaker.

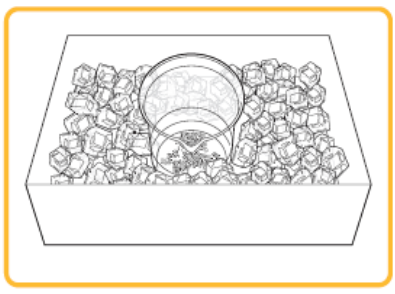


8 Recrystallise the product from hot ethanol. The idea of recrystallisation is to dissolve the impure product in the minimum possible volume of hot solvent. When you cool the solution, the product that you want crystallises out of solution. This is because there is not enough solvent to dissolve it all at the lower temperature. However, the impurities stay behind in solution, because there are less of these impurities there is enough solvent to keep them dissolved. You then filter off the crystals of the product from the remaining solution.

9 Put 15 cm³ of ethanol in a boiling tube. Warm it to about 50 °C on the steam bath. Dissolve all the crystals in the minimum possible volume of this hot ethanol. Allow the solution to cool to room temperature, then immerse the beaker in ice to complete the crystallisation.







10 Filter the crystals and dry them between filter paper. If there is time, measure the melting point of the crystals.

Activity 5: Aspirin

HEALTH & SAFETY

Wear goggles (not safety spectacles). Handle ethanoic anhydride in a fume cupboard.

aspirin the wonder medicine

Nearly all of us have used aspirin at some time in our lives, but not many people know that for hundreds of years a related compound from willow bark was used to relieve pain and treat fevers. Ancient Asian records show it was used 2400 years ago.

In the 1890s Felix Hoffman of the Bayer Company in Germany made aspirin, which was found to have good medicinal properties. In 1898 aspirin was sent for clinical trials and Bayer patented the process. In 1915 during World War One the British very much wanted aspirin and the British government offered a substantial reward to anyone who could develop a manufacturing process. A Melbourne pharmacist, George Nicholas, did just that.

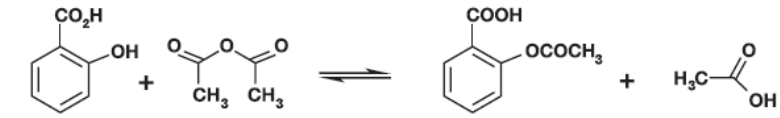
Approximately 35,000 metric tonnes are produced and consumed annually, enough to make over 100 billion standard aspirin tablets every year. Nowadays aspirin is not only used as a pain killer but has also been proposed as effective in reducing the incidence of heart disease.

This practical session aims:

- to introduce you to the synthesis of one of the oldest medicines, aspirin
- to analyse the purity of your aspirin using techniques you will not have used in school.

Synthesising aspirin

Aspirin is a relatively simple molecule containing an ethylated phenol group and a carboxylic acid group. In your experiment you will make aspirin from an acid called 2-hydroxybenzoic acid by esterification with ethanoic anhydride under acid catalysed conditions. Ethanoic anhydride is an 'activated' form of ethanoic acid which most of you will have encountered in its dilute form as the vinegar you put on fish and chips. Using ethanoic anhydride ensures that the esterification reaction goes to completion much more quickly than if you use ethanoic acid. Why is ethanoic anhydride more effective than ethanoic acid? Also, why is H^+ added? Once you've made the aspirin you'll then need to purify it by recrystallisation from a suitable solvent.



2-hydroxybenzoic acid | Ethanoic anhydride | 2-Ethanoyloxybenzene carboxylic acid (aspirin) | Ethanoic acid

Materials that are made for human consumption must be checked thoroughly to ensure that:

- the material is the correct product; and
- it is highly pure.

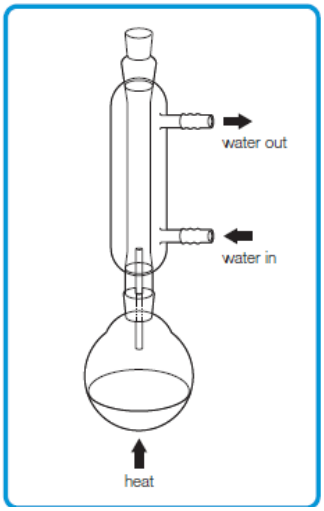
Checking the purity of a sample can be done in a variety of ways and you will be using traditional 'wet' chemistry techniques as well as more advanced spectroscopic techniques to determine the purity of your sample.

The experiment

1. Collect a 250 cm^3 round bottom flask containing ethanoic anhydride (8.0g) and concentrated sulfuric acid (3 drops).

2. Collect 5 g of 2-hydroxybenzoic acid. Add the 2-hydroxybenzoic acid in small portions to the ethanoic anhydride/concentrated

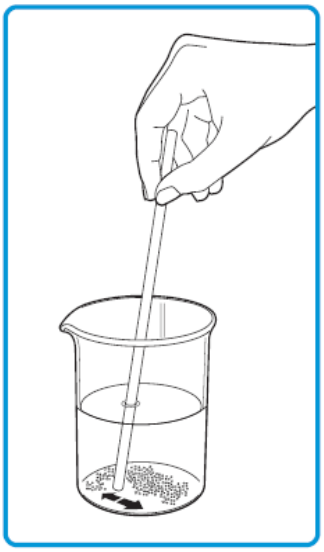
sulfuric acid mixture. Gently swirl the flask after each addition of 2-hydroxybenzoic acid so that it is mixed with, and dissolves in, the ethanoic anhydride. When all the 2-hydroxybenzoic acid is added there may be some solid which will not dissolve – do not worry as this is normal.



3. Connect a reflux condenser to the round bottom flask and heat the reaction mixture under reflux in a water bath for 15 minutes.

4. Then add water (60 cm^3) and swirl the reaction mixture to ensure complete mixing.

5. Leave the reaction mixture to cool for about 10 minutes. The crude aspirin should crystallise from solution at this stage. If you do not have a solid, do not panic this can happen to even the most experienced organic chemists! The problem can be overcome by 'scratching' the reaction flask with a glass rod – one of the demonstrators will show you how to do this.



6. Filter off the white, crude aspirin solid under vacuum using a Buchner flask and funnel, wash the product with ice cold water (20 cm^3) and then leave the solid to suck as dry as possible.

7. Save a small portion of the crude aspirin (about 0.1 g).

8. Recrystallise the rest of the product as follows.

9. Carefully transfer your crude aspirin into a round bottom flask then connect the condenser. Gradually, add ethanol and heat the mixture under reflux using a water bath until the solid dissolves. This should require approximately 15-20 cm^3 of ethanol.

10. Transfer the solution to a 250 cm^3 beaker and leave the clear, colourless solution to cool to room temperature slowly, during which time crystallisation of aspirin should begin.

11. Collect the recrystallised aspirin, which should be white, using the Buchner flask and funnel.

12. Use the filtrate to transfer any remaining crystals from the beaker to the funnel.

13. When all of the solid has been carefully collected in the Buchner funnel, wash the crystals with ice cold ethanol (10 cm^3) and allow the solid to suck as dry as possible for about five minutes.

14. Transfer the crystals to a watch glass and allow to air dry for at least 15 minutes.

15. Weigh the dry, purified aspirin product.

16. Measure the melting range of your dried product.

SAFETY

The reaction should be done in a fume cupboard.

The results

Weight of recrystallised product = _____ g

Melting point range = _____ - _____ °C

Literature m.p. = 138-140 °C

Theory and percentage yield of product

An organic chemist always calculates the % yield of the product obtained using the following procedure.

1. The number of moles of each reagent used in the reaction is worked out.

2. The limiting reagent, the reagent that is present in the lowest number of moles, is identified.

3. We then assume that if every single molecule of this reagent was converted to the product this is the maximum amount of product that could be obtained. This is known as the 100% or theoretical yield.

4. The actual % yield is calculated.

The following steps are followed to obtain the required information:

Molecular formula of ethanoic anhydride = $C_4H_6O_3$

Molecular weight of ethanoic anhydride = (4 x) + (6 x) + (3 x)

Number of moles of ethanoic anhydride = weight of ethanoic anhydride used ÷ molecular weight of ethanoic anhydride

Number of moles of ethanoic anhydride = _____ mol

Molecular formula of 2-hydroxybenzoic acid = _____

Molecular weight of 2-hydroxybenzoic acid = _____

Number of moles of 2-hydroxybenzoic acid = _____

The limiting reagent = _____

Molecular formula of aspirin = _____

Molecular weight of aspirin = _____

Theoretical yield = no. of moles of limiting reagent * Molecular weight of the product

∴ Theoretical yield = _____ g

% yield = (actual yield/theory yield) x 100

= (/)* 100

% yield = _____

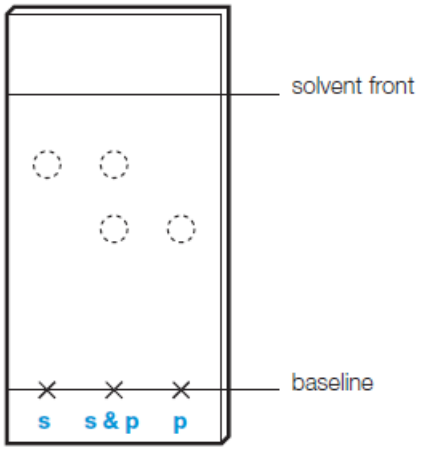
Purifying and identifying aspirin

Thin layer chromatography (tlc)

You've probably used simple chromatography as part of your earlier studies to separate the dyes in coloured ink. In this activity you investigate the purity and identity of your laboratory prepared aspirin samples using thin layer chromatography (tlc).

Thin layer chromatography is a rapid separation technique, which means that a pure substance gives 'one spot'. However, if extra spots are observed as well as the characteristic pattern of the known compound, then impurities are likely to be present in the sample. (What impurities are likely to be present in your sample?) You can also identify 'unknown' compounds by comparing their Rf values (the distance travelled by the component spot/distance travelled by the solvent front) with an authentic standard running on the same plate.

You'll see a demonstration of how to run a tlc of your product. The solvent system used to run your tlc is a mixture of acetonitrile/ethanoic acid/water (why do the different components travel different distances on the TLC plate?).



s starting point
p product

Tlc results for crude and recrystallised aspirin

TLC results for crude and recrystallised aspirin

Sample		Crude Aspirin	Recrystallised Aspirin
Number of spots observed			
Distance travelled by solvent front (mm)			
Distance travelled by UV active spots (mm)	1 2 3		
Rf Values	1 2 3		

You will also run an infrared (IR) spectrum of the product and compare it with the spectrum of pure aspirin. If they are identical your synthesis of aspirin has been successful. You will also see demonstrations of both a nuclear magnetic resonance (NMR) spectrometer and high performance liquid chromatography (HPLC).

Activity 6: Reaction mechanisms

Chemists use reaction mechanisms to show what they think might be happening as molecules interact during chemical reactions.

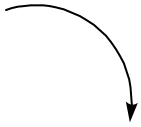
When drawing reaction mechanisms the chemist usually assumes:

1. that the reaction occurs in several distinct steps;

2. that each step can be represented as the movement of electrons; and

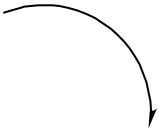
3. that sometimes electrons move as pairs, and sometimes they move individually.

Diagrams showing the steps in reaction mechanisms usually show the molecules and/or ions (shown by + and –) and/or radicals (shown by •) involved, as well as arrows showing the movement of electrons. Two types of arrows are used:



curly arrow

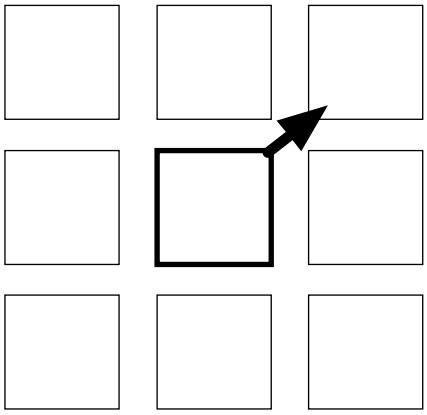
An arrow with a full head (a 'curly' arrow) represents a pair of electrons



fish-hook arrow

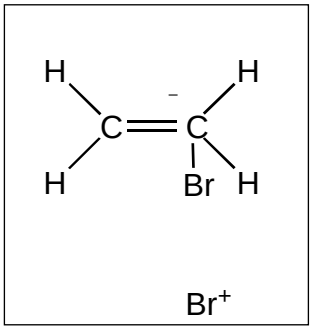
An arrow with a half head (a 'fish-hook' arrow) represents the movement of a single

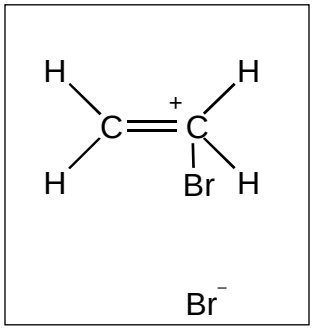
There are two questions in this exercise. The questions each consist of a central diagram showing the initial stage in a reaction mechanism, surrounded by a selection of suggestions for the result of that step. Your task in each case is to identify which of the diagrams gives the correct outcome of that reaction step. Draw a large arrow showing which diagram is correct, as in the example below.

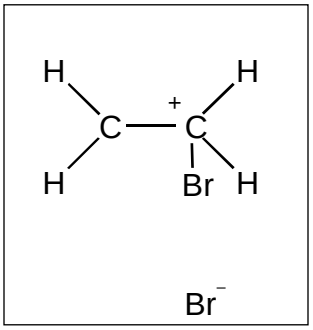


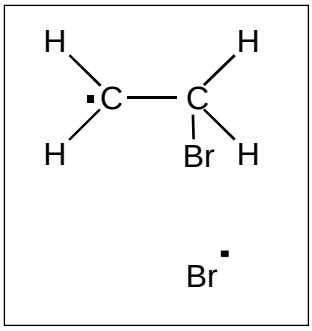
Try and explain your reason(s) for selecting the diagram you chose.

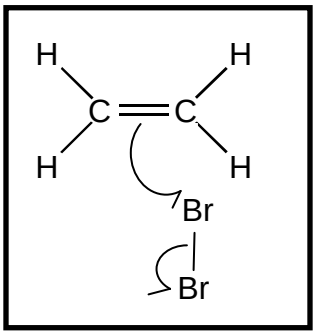
Reaction mechanism 1

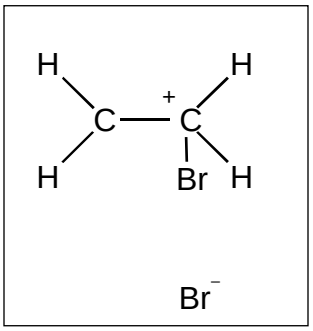


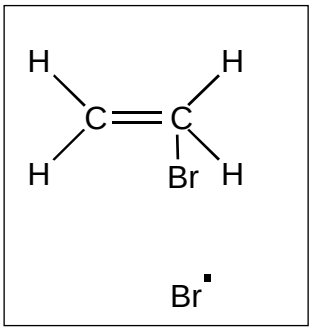


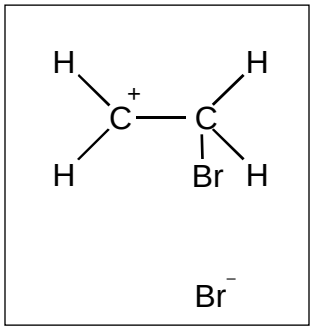


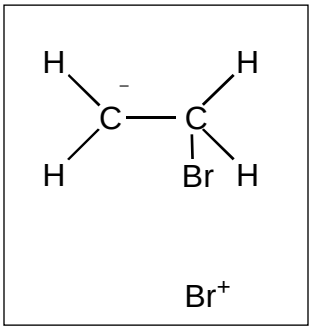












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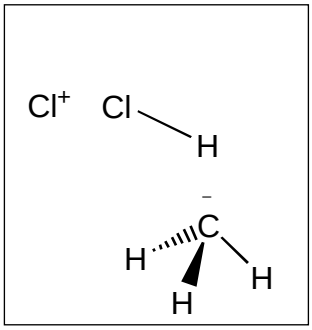
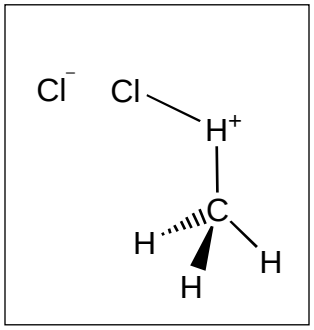
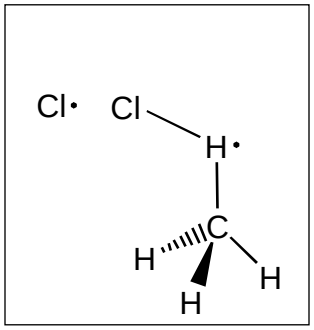
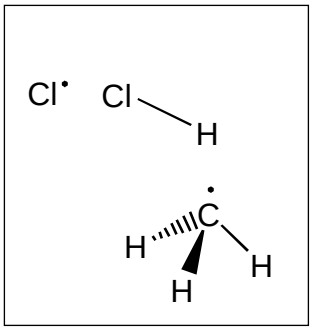
I selected this diagram because:

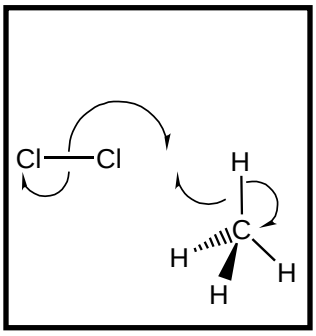
Reaction mechanism 2

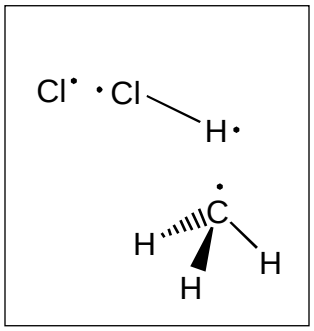


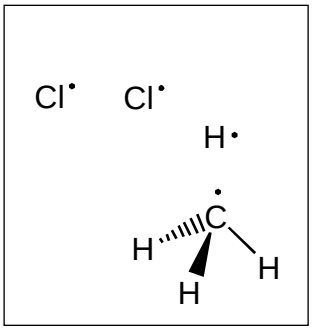


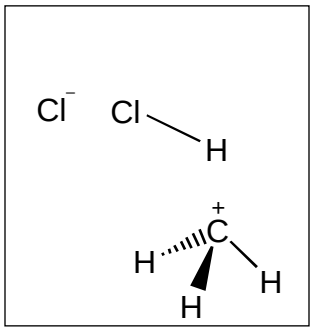


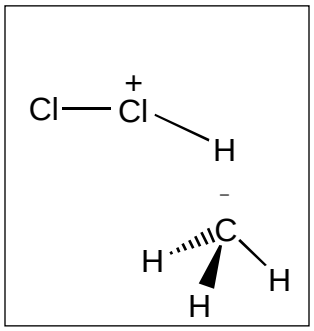












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THE WOLFSON FOUNDATION

I selected this diagram because:

Glossary

adsorption	The adhesion of atoms or molecules to a surface.
affinity	The attraction of an analyte to a stationary phase.
analyte	The analyte is the substance to be separated during chromatography.
aromatic	Aromatic compounds are ring structures containing unsaturated bonds.
elutant	The solvent that carries the analyte.
ionisation	The process of conversion of an atom or molecule into an ion.
partition	The degree of separation of the components under chromatography.

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