Synthesis and Sustainable Chemistry

Considering % yield and % Atom Economy:

- high % yield means very efficient conversion from reactants to products
- increasing % yield means more efficient use of starting materials
- increasing % atom economy means reducing the amount of waste products, which improves the sustainability of the process.

Calculating Atom Economy

The atom economy tells us how much waste there will be – for sustainable chemistry we minimise this by using atom economy to help select between different possible reactions to create the product we want.

$$\% \text{ atom economy} = \frac{\text{mass of the atoms in the product(s) we want}}{\text{mass of all the atoms in the products (or reactants)}} \times 100$$

Note:

- *Any reaction which only produces one product has 100% atom economy! This means that* ***addition reactions*** *have 100% atom economy.*
- *If you can use the other products, they are not necessarily waste. You may be able to improve atom economy by better use of the reaction products.*

Application:

Hydrogen can be manufactured by reacting methane (natural gas) with steam. Calculate the atom economy of this reaction.

$$CH_4(g) + 2H_2O(g) \rightarrow CO_2(g) + 4H_2(g)$$

$$\% \text{ atom economy} = \frac{4 \times 2}{(12 + 16 + 16) + (4 \times 2)} \times 100$$

= **15.4%** which is not very good at all !

Check your understanding:

i) Hydrogen can also be produced by cracking ethane. Calculate the atom economy of this reaction.

$$C_2H_6(g) \rightarrow C_2H_4(g) + H_2(g)$$

ii) Comment on the sustainability of this process compared to the manufacture of hydrogen from methane and suggest a reason why cracking may be chosen rather than the previous reaction.

Calculating % yield

Another consideration is how much of the product you will actually be able to obtain. There are a number of reasons why all the reactants may not be collected as finished products.

- impure reactants
- losses when purifying products and removing from reaction vessels
- other side reactions making unwanted products
- incomplete reaction of products e.g. when equilibria are set up

The % yield is used to compare how much product we actually made (the yield) to how much we could have made in theory (a mole calculation).

$$\% \text{ yield} = \frac{\text{mass of product obtained}}{\text{theoretical mass of product}} \times 100 \quad \text{or} \quad \frac{\text{moles of product obtained}}{\text{theoretical moles of product}} \times 100$$

For example: Methane can react with bromine when exposed to uv light, forming bromomethane. If 1.6g of methane reacted with excess bromine and 6.0g of bromomethane were formed, what was the % yield ?

$$CH_4(g) + Br_2(g) \rightarrow CH_3Br(g) + HBr(g)$$

Step 1: do a mole calculation to find out how many moles of CH_3Br would be made if all the methane formed bromomethane.

- Moles of CH_4 = mass ÷ RFM = 1.6 ÷ 16 = 0.1 moles
- Mole ratio from equation is 1:1 so 0.1 moles of methane makes 0.1 moles of CH_3Br
- Mass of CH_3Br = moles x RFM = 0.1 x (12 + 3 + 79.9) = 9.49g

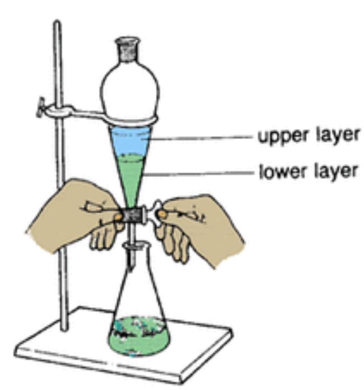
Step 2: work out % yield

$$\% \text{ yield} = \frac{6.0}{9.49} \times 100 = \mathbf{63.22\%}$$

Check your understanding:

iii) Methane can also react with chlorine when exposed to uv light, forming chloromethane. If 1.6g of methane reacted with excess chlorine and 4.0g of chloromethane were formed, what was the % yield ?

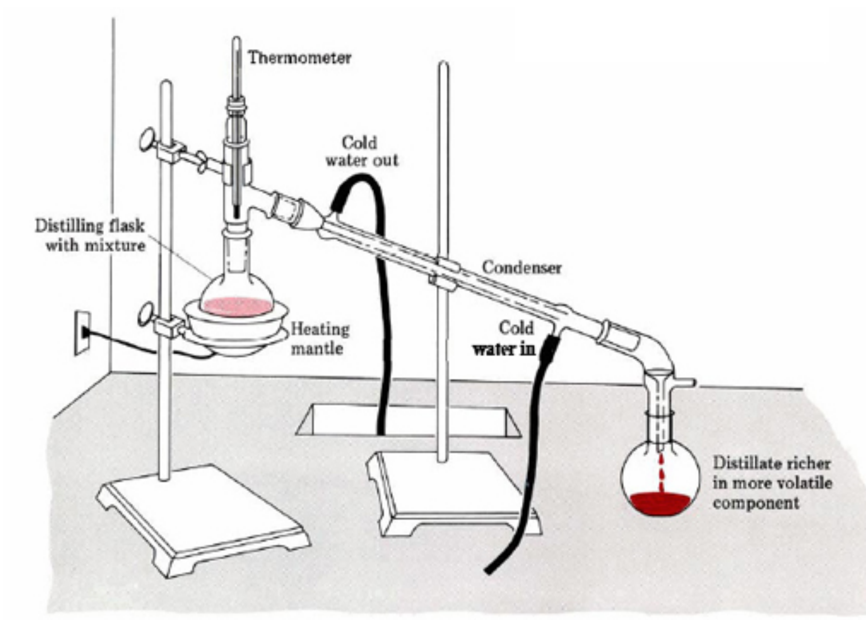
Purifying organic liquids



It is easy to see how the %yield is diminished when considering the steps that might be needed to purify an organic liquid product produced in a reaction mixture.

If the organic liquid has low solubility in water, it can be separated from impurities which are water soluble by using a **separating funnel**. Water is added to the reaction mixture and shaken in the funnel to allow the water-soluble impurities to dissolve in the water. Because they have different densities, the insoluble organic components will form a separate liquid phase, and the two phases can easily be separated by running the aqueous layer out of the funnel and discarding it. It is important to know which is the organic layer and which is the aqueous layer!

Once the organic layer has been separated from aqueous impurities it needs to be dried to remove residual water. This can be done by adding a solid anhydrous salt such as $CaCl_2$ or $MgSO_4$. These absorb the water, leaving the organic liquid dry. The solid can be removed by filtering through a cotton wool plug in a funnel. Some of the organic liquid will also be lost as it soaks into the cotton wool, however.



The dry organic liquid phase is still likely to contain a mixture of organic components e.g unreacted species and products from side-reactions. The required product can be separated from this mixture by **distillation**, collecting only the fraction that comes over around the boiling point of the required product. This will also reduce the %yield as some product will remain in the mixture in the distillation flask.

With each of these processes, the %yield decreases while the purity increases. This is a necessary compromise, which must continue until the require purity is reached.

Synthesis

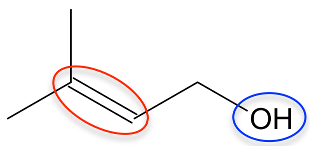
Synthesis is the choice of a sequence of reactions which can transform a starting molecule (preferably cheap, readily available, renewable) into a desired product molecule. Reactions are chosen to progressively alter the functional groups in the molecule until the required product is formed.

To design a synthesis route we need to

- Know the properties and reactions of the different functional groups
- Be able to identify the functional groups present in molecules containing several functional groups
- Be able to use information given in questions about reactions of functional groups which do not form part of the specification

Predicting properties and reactions

e.g. prenol, $(CH_3)_2C=CHCH_2OH$, is a natural compound found in many fruits and widely used in organic synthesis. If we tabulate its properties and reactions of its functional groups, we are well on the way to determining how it can be used in synthesis.



Functional group: alkene
primary alcohol

Properties	Reactions of alkene	Reactions of 1° alcohol
Soluble in water: the –OH group will form hydrogen bonds with water	→ alkane (with H_2)	→ alkene (dehydration)
	→ haloalkane (with HX or X_2)	→ haloalkane (HX in situ)
	→ alcohol (with $H_2O_{(g)}$)	→ aldehyde (H^+ and $Cr_2O_7^{2-}$)
		→ carboxylic acid (as above)

Suggesting two-step synthesis routes

The best strategy is to work from both ends of the synthesis.

- Tabulate the reactions of the functional groups in the starting molecule to see the different molecules which can be made from it using the reactions you know about.
- Tabulate all the reactions which could be used to make the desired product molecule.
- Match the two maps up to find the two reactions which could be used to turn the starting molecule into the final product.

Application:

Ethanal, CH_3CHO, can be produced from ethane in a two-stage synthesis. Write equations for the two reactions, and give the necessary reagents and conditions.

Map for ethene: C_2H_4 → C_2H_6 *hydrogenation*
→ C_2H_5X *reaction with HX*
→ $C_2H_4X_2$ *reaction with X_2*
→ C_2H_5OH *hydration with steam*

Map for ethanal: C_2H_5OH → CH_3CHO *only reaction we know*

i) The first stage is convertion of ethene to ethanol, reacting the ethene with steam in the presence of a phosphoric acid catalyst:

$$C_2H_{4(g)} + H_2O_{(g)} \rightarrow CH_3CH_2OH_{(g)}$$

ii) The second stage is partial oxidation of the ethanol to ethanal by warming with acidified sodium dichromate(VI) and distilling the product as it forms:

$$CH_3CH_2OH + [O] \rightarrow CH_3CHO + H_2O$$

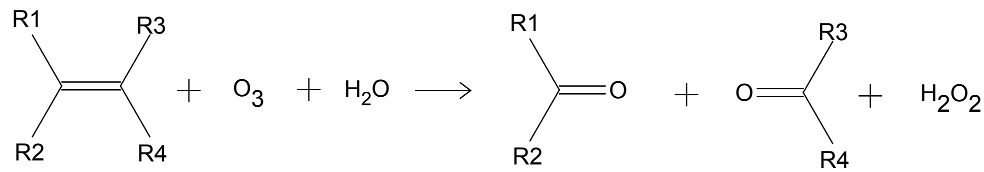
Working with unfamiliar reactions

It is important to appreciate that reactions which work on a functional group in one molecule can be applied to the same functional group in other molecules. We can be shown an example of an unfamiliar reaction and expected to use it on different molecules which contain the same functional group.

Application:

Reaction with ozone can be used to break open C=C bonds, resulting in the formation of aldehydes or ketones.

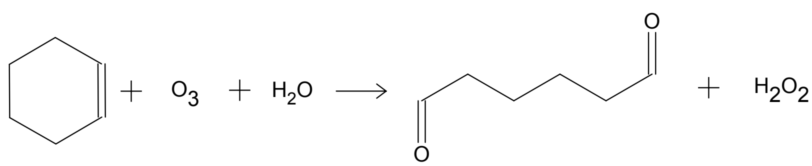
In general:



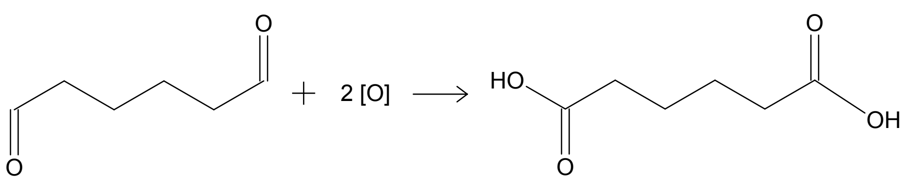
…where R1-R4 are alkyl groups or hydrogen atoms

Show how this reaction can be part of a two stage synthesis to produce hexanedioic acid starting with cyclohexene.

Step 1: Use the reaction above to break open the double bond in cyclohexene, forming a chain with aldehyde groups at each end:



Step 2: Reflux with acidified sodium dichromate(VI) to convert the aldehyde groups to carboxylic acid groups:



Check your Understanding:

iv) Write the equations for two synthesis steps that could be used to produce 1-bromo-3-methylbutane from prenol, $(CH_3)_2C{=}CHCH_2OH$.

Answers

i) Hydrogen can also be produced by cracking ethane. $C_2H_6(g) \rightarrow C_2H_4(g) + H_2(g)$
Calculate the atom economy of this reaction.

$$\% \text{ atom economy} = \frac{2}{28 + 2} \times 100 \qquad \mathbf{= 6.7\%}$$

ii) The % atom economy is even lower, so this appears to be a les sustainable process, however:

- ethene is itself a useful product, if used rather than wasted the %Atom Economy would be 100%

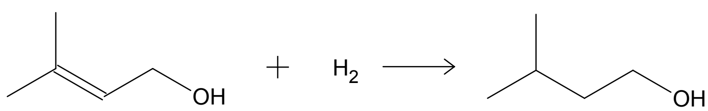
- the energy costs, or the raw materials may be cheaper/more readily available

iii) Methane can also react with chlorine when exposed to uv light, forming chloromethane. If 1.6g of methane reacted with excess chlorine and 4.0g of chloromethane were formed, what was the % yield ?

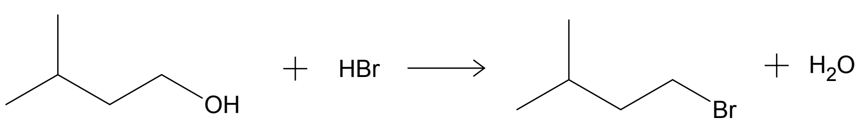
- Moles of CH_4 = mass ÷ RFM = 1.6 ÷ 16 = 0.1 moles
- Mole ratio from equation is 1:1 so 0.1 moles of methane makes 0.1 moles of CH_3Cl
- Mass of CH_3Br = moles x RFM = 0.1 x (12 + 3 + 35.5) = 5.05g

% yield = (4.0 / 5.05) x 100 **= 79.2%**

iv) The first step is hydrogenation of the alkene group using H_2 and a Ni catalyst at 150°C.



The second step is substitution of the –OH group by –Br by refluxing with sodium bromide and sulphuric acid, to produce HBr in-situ.



Note that even though the two steps work on different functional groups, they need to be done in this order, otherwise the HBr will react with both the alkene group and the –OH group, forming a dibromoalkane.