The University Of Sheffield.

Department Of Chemistry.

Analysis of Aspirin

Why is aspirin important?

Aspirin is one of the most widely sold medicines in the world; being used to treat pain and inflammation, and to prevent and treat heart attacks. The active ingredient, salicylic acid, is found in the bark of willow trees and was used to treat health problems as far back as *ca*. 3000-1500 BC. However, it wasn't until the 1800s that salicylic acid was identified, extracted, and its chemical structure determined (fig. 1).

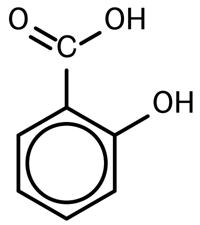
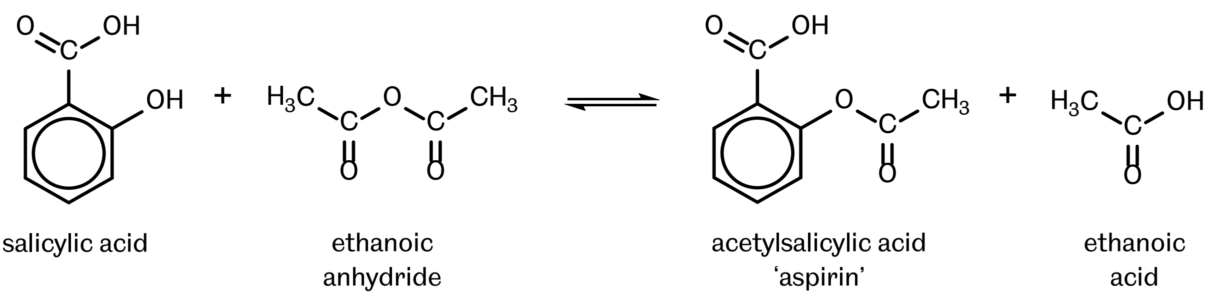


Figure 1: The chemical structure of salicylic acid

In 1897, Felix Hoffman, a chemist working for the German pharmaceutical company Bayer, found that esterifying salicylic acid to produce acetylsalicylic acid reduced the irritant properties of the drug. The company patented the commercial production of acetylsalicylic acid and named it 'aspirin'.

Making aspirin

Aspirin is an example of an ester. Esters are formed by the reaction of an alcohol with a carboxylic acid. Aspirin can be prepared by heating salicylic acid with ethanoic anhydride (scheme 1).



Scheme 1: The synthesis of aspirin (acetylsalicylic acid)

Mass Spectrometry (MS) Questions

1. The structure of aspirin and its mass spectrum is shown on page 3.
   i) Using the spectrum, state the relative molecular mass of aspirin.

   ii) State what *m/z* means on the *x* axis of the mass spectrum.

   iii) Identify the ion responsible for the peak in the mass spectrum at:
      a) *m/z* = 163

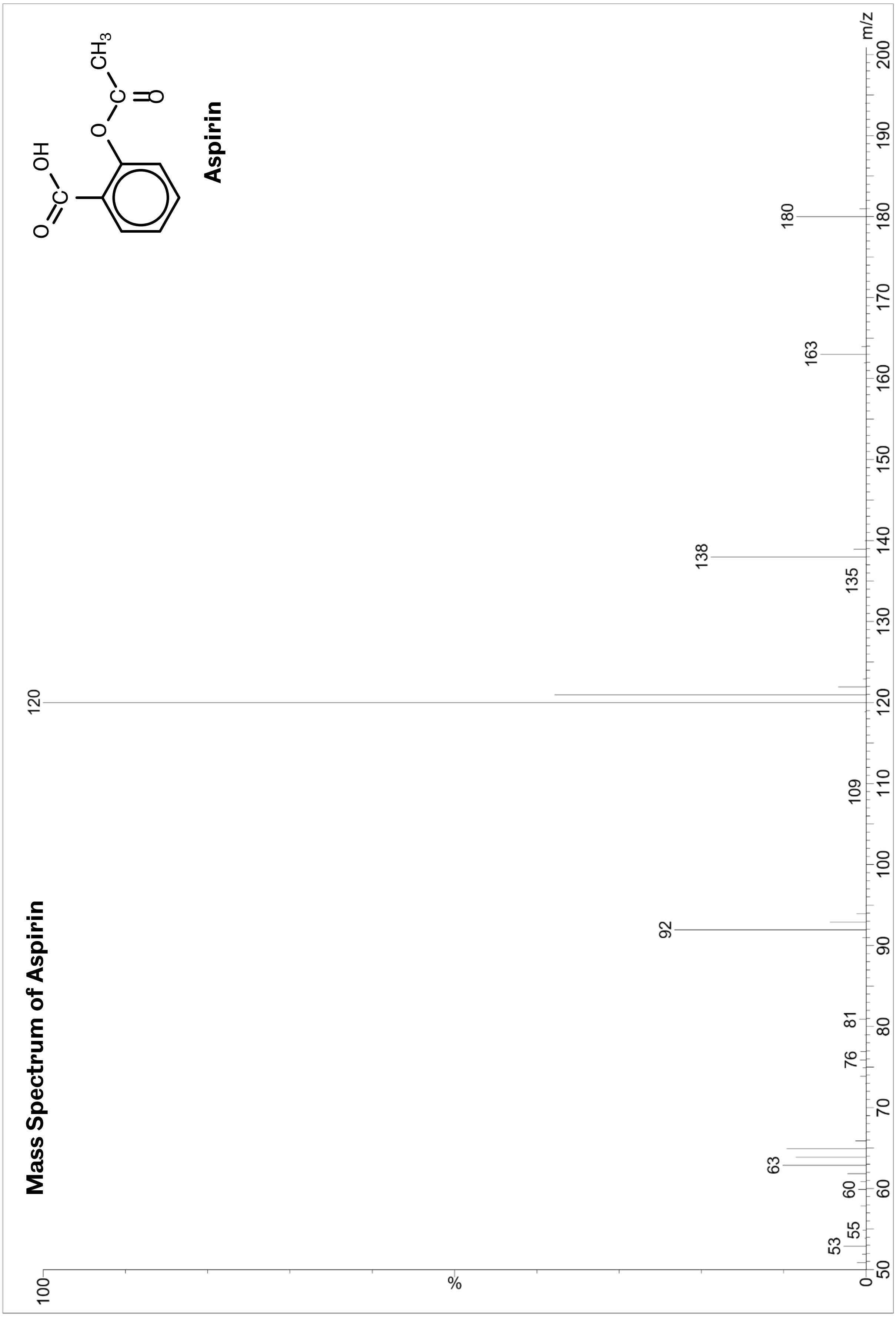
      b) *m/z* = 138

   iv) There is a small peak at *m/z* = 181. Explain the appearance of this peak in the mass spectrum for aspirin.

   v) The mass spectrum shows lines for 1^+ ions. If there were also peaks for 2^+ ions, where would you expect to find them?

2. One of the methods of ionising samples in time of flight (TOF) mass spectrometry is by electrospray ionisation. Describe the process of electrospray ionisation.

Mass Spectrum of Aspirin



Infrared (IR) Spectroscopy Questions

1. Spectrum A is an IR spectrum of just air (a background spectrum).
   i) Using your knowledge of IR spectroscopy, assign the peaks in the IR spectrum and fill in table A below.

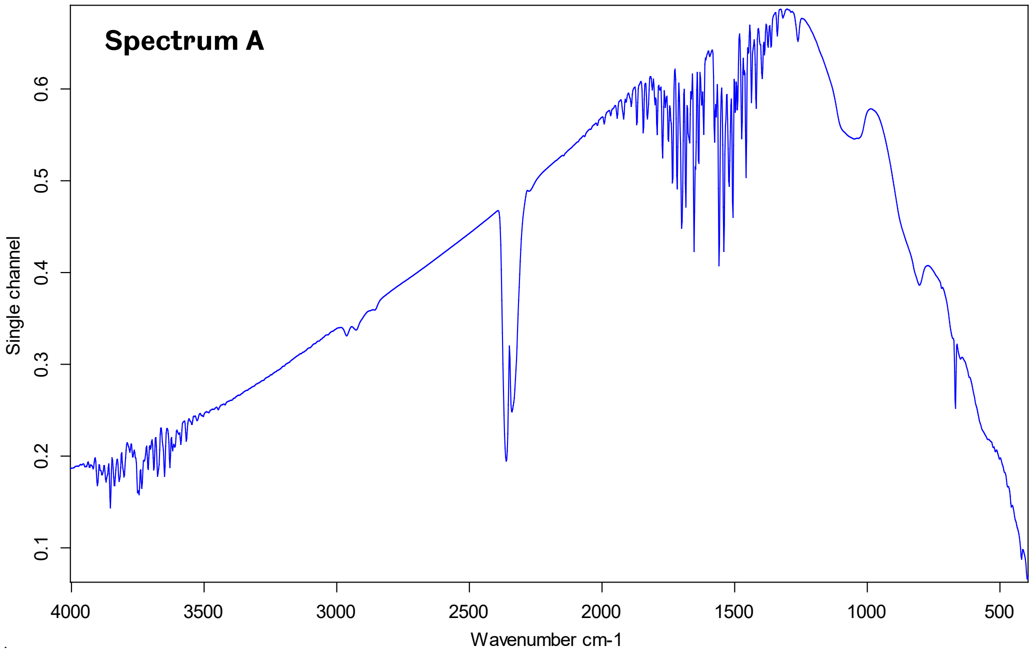


Table A

Wavenumber / cm^{-1}				
Bond				

   ii) Explain why we do not see a peak for oxygen or nitrogen in the IR spectrum of air.

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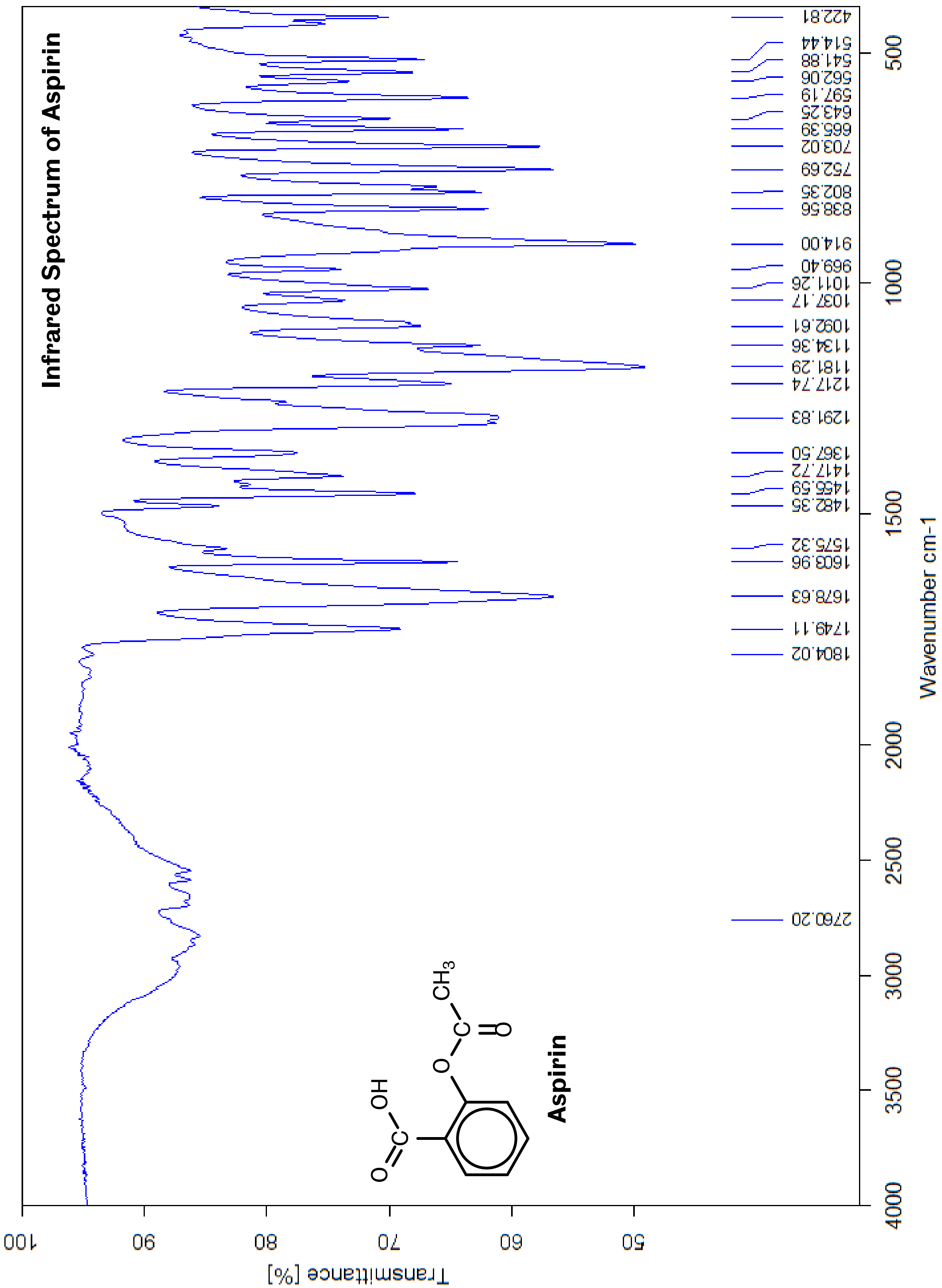
2. The structure of aspirin and its IR spectrum is shown on page 5. Using the correlation table below, assign all of the peaks in the IR spectrum of aspirin and fill in the blank column.

Bond	**Wavenumber / cm^{-1}**	**Spectrum peak / cm^{-1}**
C-H stretch (alkane)	2850 - 3000	
C-H stretch (arene)	3000 - 3150	
O-H stretch (acid)	2500 - 3300 (very broad peak)	
C=O stretch (acid)	1660 - 1760	
C=O stretch (ester)	1735 - 1750	
C-C (in-ring) stretch (arene)	1585 - 1615	
C-O stretch (ester and acid)	1000 - 1300 (large peak)	


Infrared Spectrum of Aspirin
Transmittance [%]
100
90
80
70
60
50
Wavenumber cm-1
500
1000
1500
2000
2500
3000
3500
4000
422.81
514.44
541.88
562.06
597.19
643.25
665.39
703.02
752.69
802.35
838.56
914.00
969.40
1011.26
1037.17
1092.61
1134.36
1181.29
1217.74
1291.83
1367.50
1417.72
1456.59
1482.35
1575.32
1603.96
1678.63
1749.11
1804.02
2760.20
Aspirin

Nuclear Magnetic Resonance (NMR) Questions

1. The structure of aspirin and its ^{1}H NMR spectrum is shown on page 7.
   i) Using this structure and the ^{1}H NMR spectrum, fill in the table below.

∂ / ppm	2.2	7.2	7.4	7.6	7.9
Integration ratio					
Spin-spin splitting pattern					
Proton assignment					

   ii) Determine the number of peaks in a ^{13}C NMR spectrum of aspirin.

   ____

2. The solvent used to record the ^{1}H NMR spectrum is deuterated dimethylsulfoxide (DMSO).

   i) Explain why deuterated solvent is needed to record the ^{1}H NMR spectrum.

   ____

   ii) Make a suggestion as to what might lead to the appearance of the singlet peak at ∂ = 2.5 ppm in the ^{1}H NMR spectrum.

   ____

   iii) Make a suggestion as to what might lead to the appearance of the broad peak between ∂ = 3.0-4.0 ppm in the ^{1}H NMR spectrum.

   ____

3. The non-toxic, inert substance TMS is used as a standard in recording both ^{1}H and ^{13}C NMR spectra. Give two other reasons why TMS is used as a standard in recording NMR spectra.

1.

2.

^{1}H NMR Spectrum of Aspirin