Option D: Medicinal Chemistry

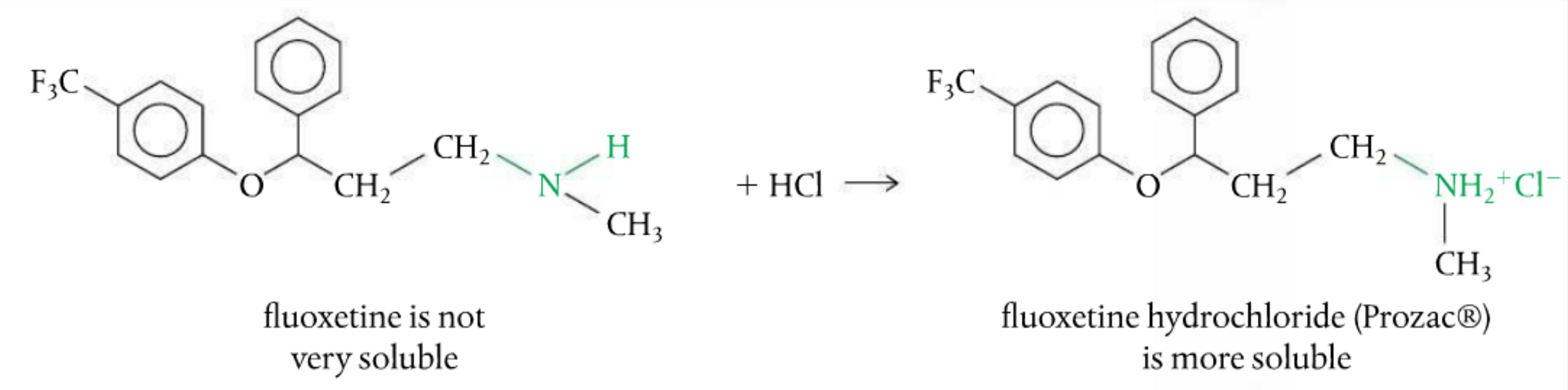
Part D.9

D.9 Drug Detection and Analysis

- When synthesizing drugs, they end up as a mixture of many different solvents and need to be separated
  - physical properties will help
    - solubility difference
    - volatility difference

Structure and Solubility

- "like dissolves like"
  - most organic compounds are non-polar and dissolve best in non-polar solvents
  - sometimes modified (like aspirin) to reach their target better



D.9 Drug Detection and Analysis

Solubility

- In order to separate:
  - choose a solvent that will selectively dissolve a drug component - **extraction**
  - if two solvents are immiscible, the component will dissolve in one and not the other

Solvent Extraction

- product mixture (aq) contains desired product X (X has solubility in hexane)
- add mixture to separating funnel + mix
- allow contents to settle/separate
- X has dissolved in the hexane more than the water
- X can be recovered by evaporating hexane

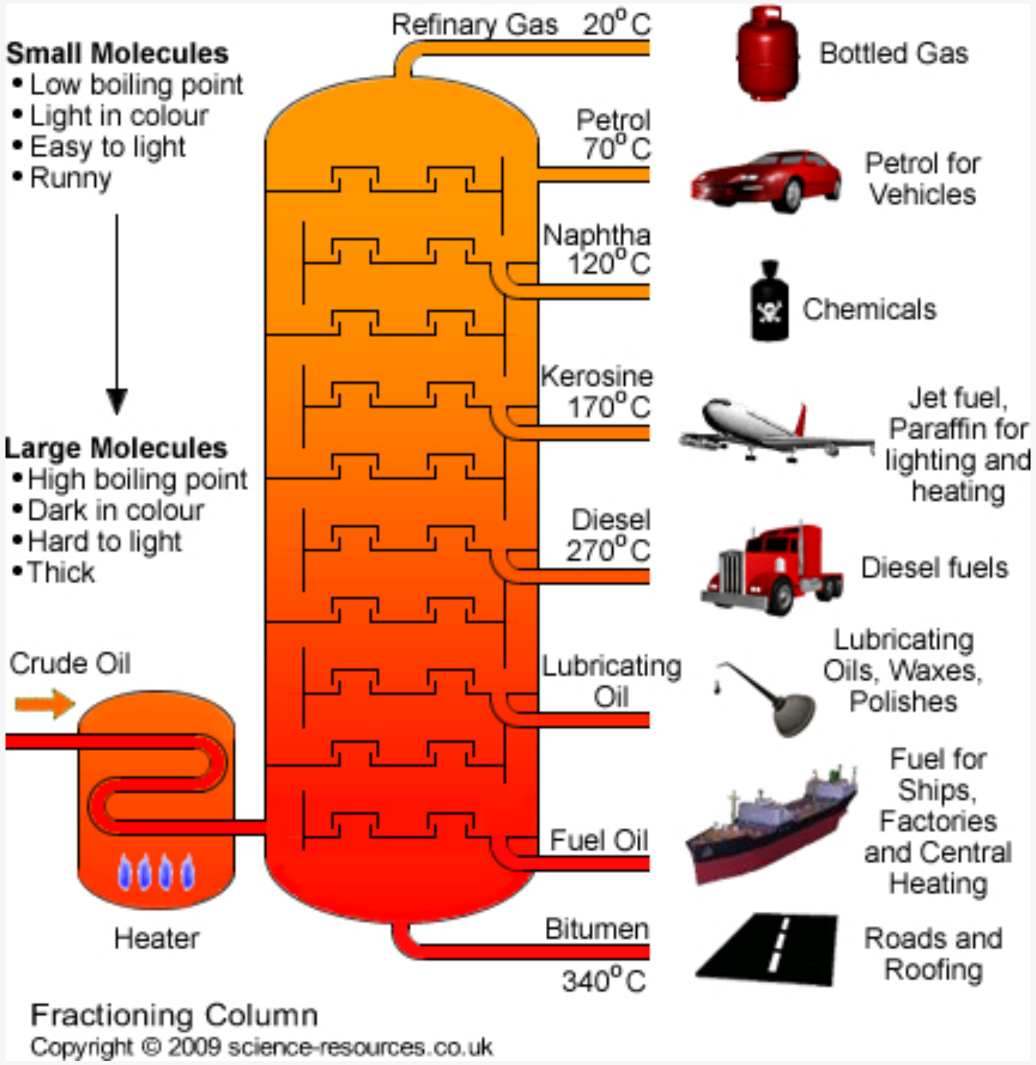
D.9 Drug Detection and Analysis

Structure and Volatility

- Molecular Size vs Polarity
- London Dispersion Forces (VDW) - size matters
    - bigger molecules have greater IMFs
- Dipole-Dipole - polarity of molecule
    - functional groups!!
    - amide>carboxyl>hydroxyl>ketone>aldehyde>amino>ester>ether
- Fractional Distillation!!

Fractional Distillation

- Remember hydrocarbons?
- evaporation and condensation
  - used in the isolation of drug products from liquid mixtures
  - Also used in reacquiring chemical stock substances from the reaction (phenols and toluene) used in production of drugs



D.9 Drug Detection and Analysis

- Mole Fraction
- Stupid equation in book...

$$\chi_A = \frac{n(A)}{n(A)+n(B)} \quad \text{and} \quad \chi_B = \frac{n(B)}{n(A)+n(B)}$$

The sum of the mole fractions is:

$$\chi_A + \chi_B = \frac{n(A)}{n(A)+n(B)} + \frac{n(B)}{n(A)+n(B)} = 1$$

- part (fraction) /whole(total moles)
- duh

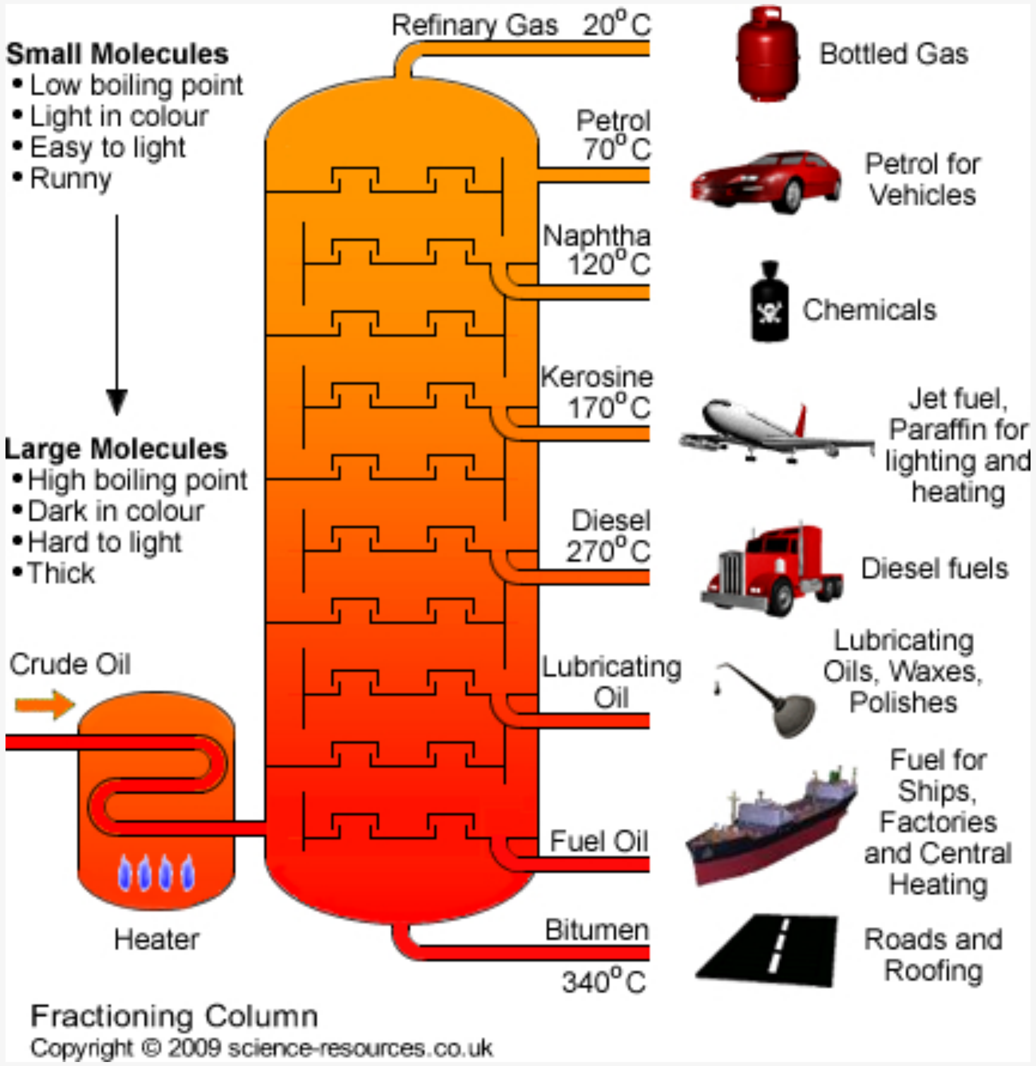
D.9 Drug Detection and Analysis

Vapor Pressure

- $P_{total} = P_A + P_B$ - for two liquids, A and B
- v.p. (A, in mixture) = v.p. (pure) x mole fraction
- so…
  - P_{total} = v.p. A (pure) x χ_A + v.p. B (pure) x χ_B
  - Works for solvents that are completely dissolved in one another

Separations

- Using different vapor pressures, one may separate molecules with different attractions
- The fractional distillation column will separate these liquids by different boiling points
- The higher the liquid travels in the column, the lower the boiling point



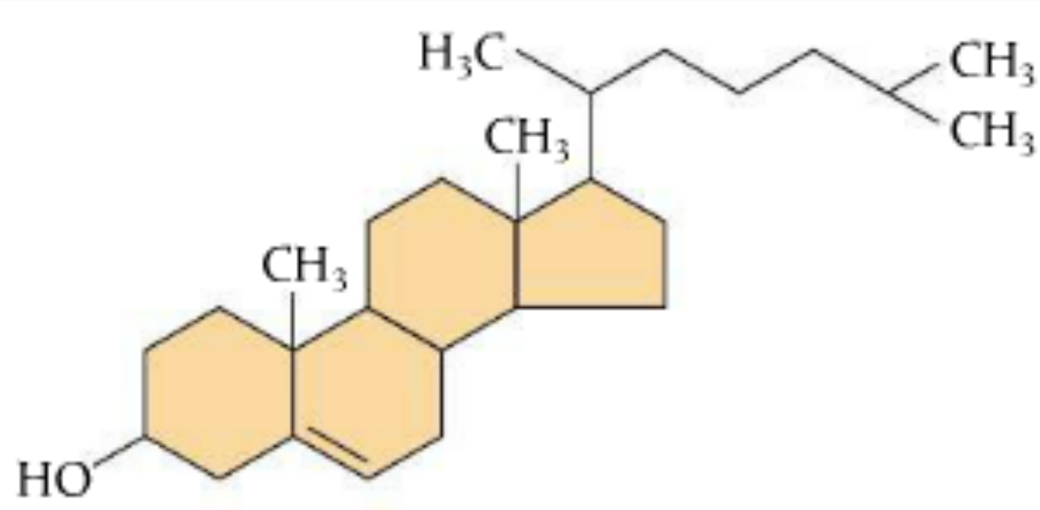
D.9 Drug Detection and Analysis

Drug Detection

- Most common types include:
  - PED - abuse in sports
  - Drinking and driving
- laws and governing bodies have surveillance methods dedicated to checking for presence and concentration of drugs

D.9 Drug Detection and Analysis

Steroid Detection



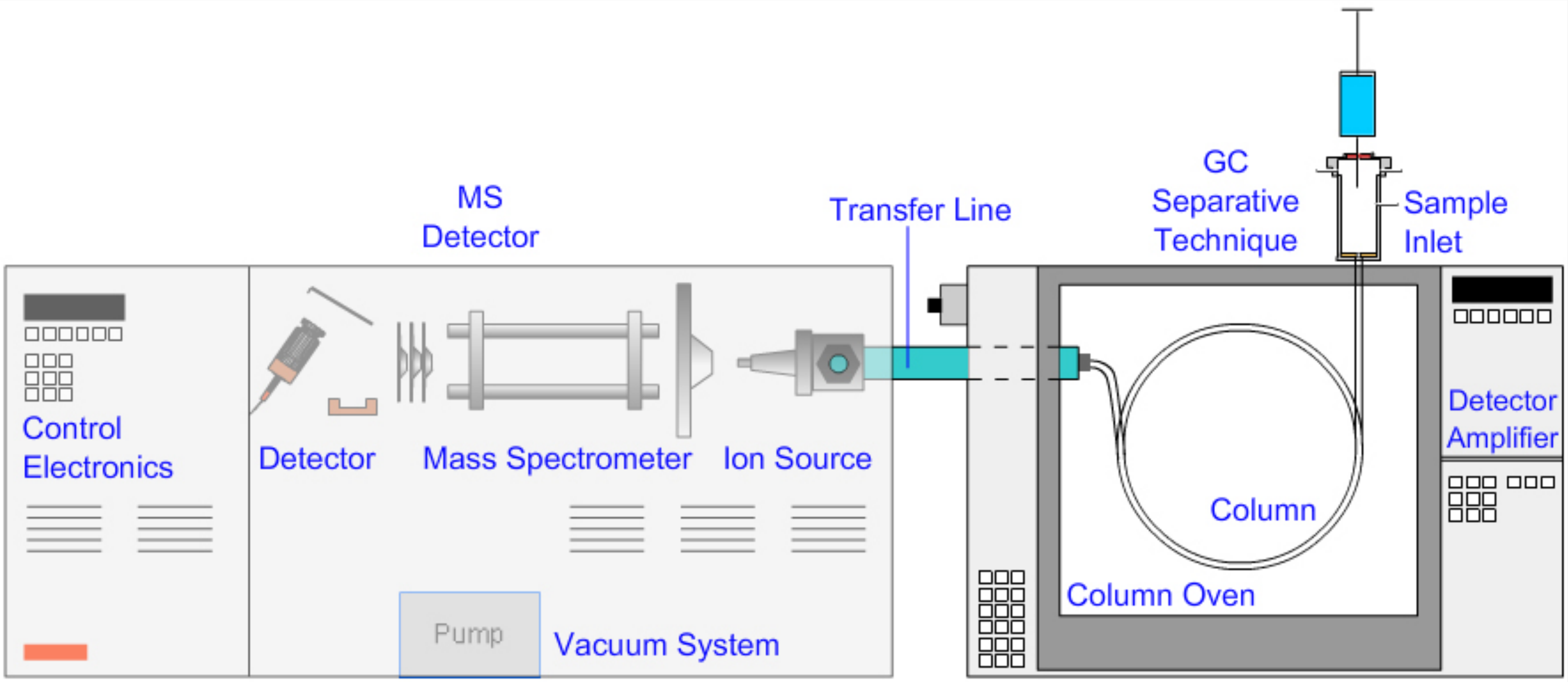
Cholesterol

structure on table 34 of data booklet

- 4 fused rings - steroidal backbone
- found in hormones (mainly sex hormones)
- testosterone - anabolic steroid
  - muscle growth
- more anabolic steroids are synthesized from testosterone

Gas Chromatography-Mass Spectrometry

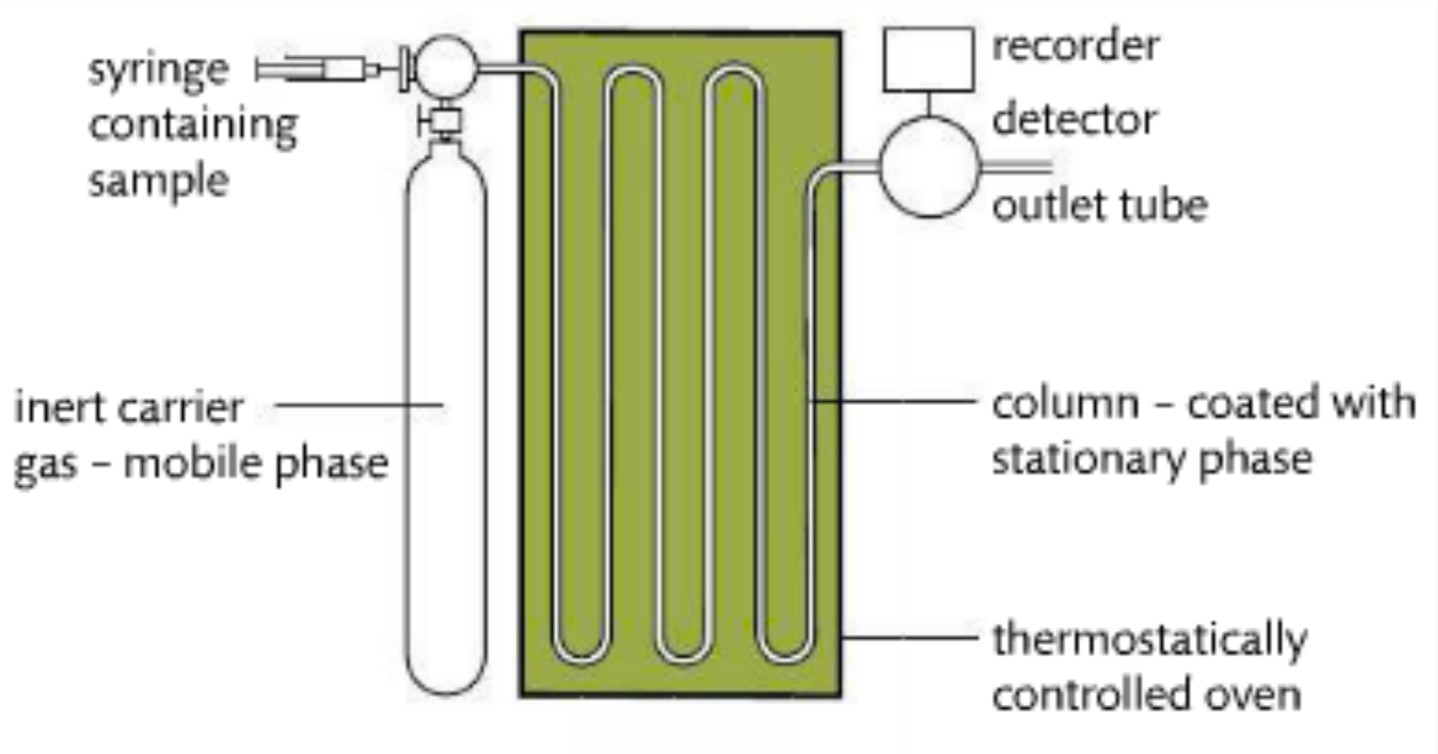
- GC-MS - most common method of detection for blood and urine
  - GC - separates the chemical mixture into pure components
  - MS - identifies and quantifies the components



D.9 Drug Detection and Analysis

Gas Chromatography

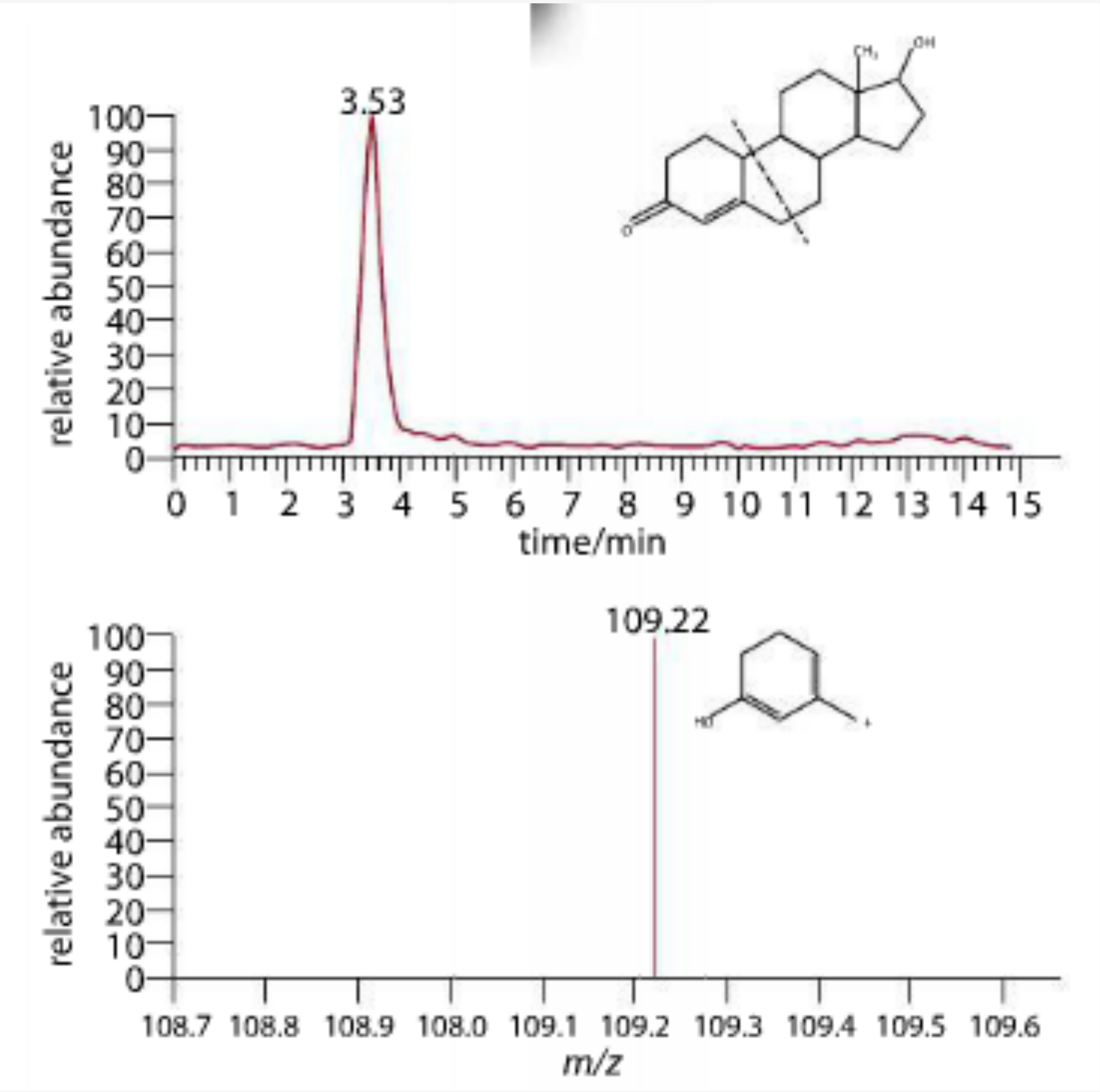
- useful for separating components of a mixture
- basic principle - components have affinity for:
  - stationary phase - microscopic layer of a non-volatile *liquid,* usually a polymer - coated on walls of inert solid
  - mobile phase - inert carrier *gas,* such as Helium



- each component passes the detector, and time eluted is recorded - known as retention time

Mass Spectrometry

- used after gas chromatography to analyze a sample



D.9 Drug Detection and Analysis

Ethanol Detection

- Alcohol has a polar -OH group that makes it very soluble in water - passes into your blood stream quickly - high bioavailability
- BAC - measured in mg ethanol / cm^3 of blood
- Roadside analyzers use the oxidation of ethanol to ethanal and ethanoic acid to measure the concentration
- acidified $K_2Cr_2O_7$ (orange to green) is the oxidizing agent
  - orange to green color change
  - concentration measured by photocell

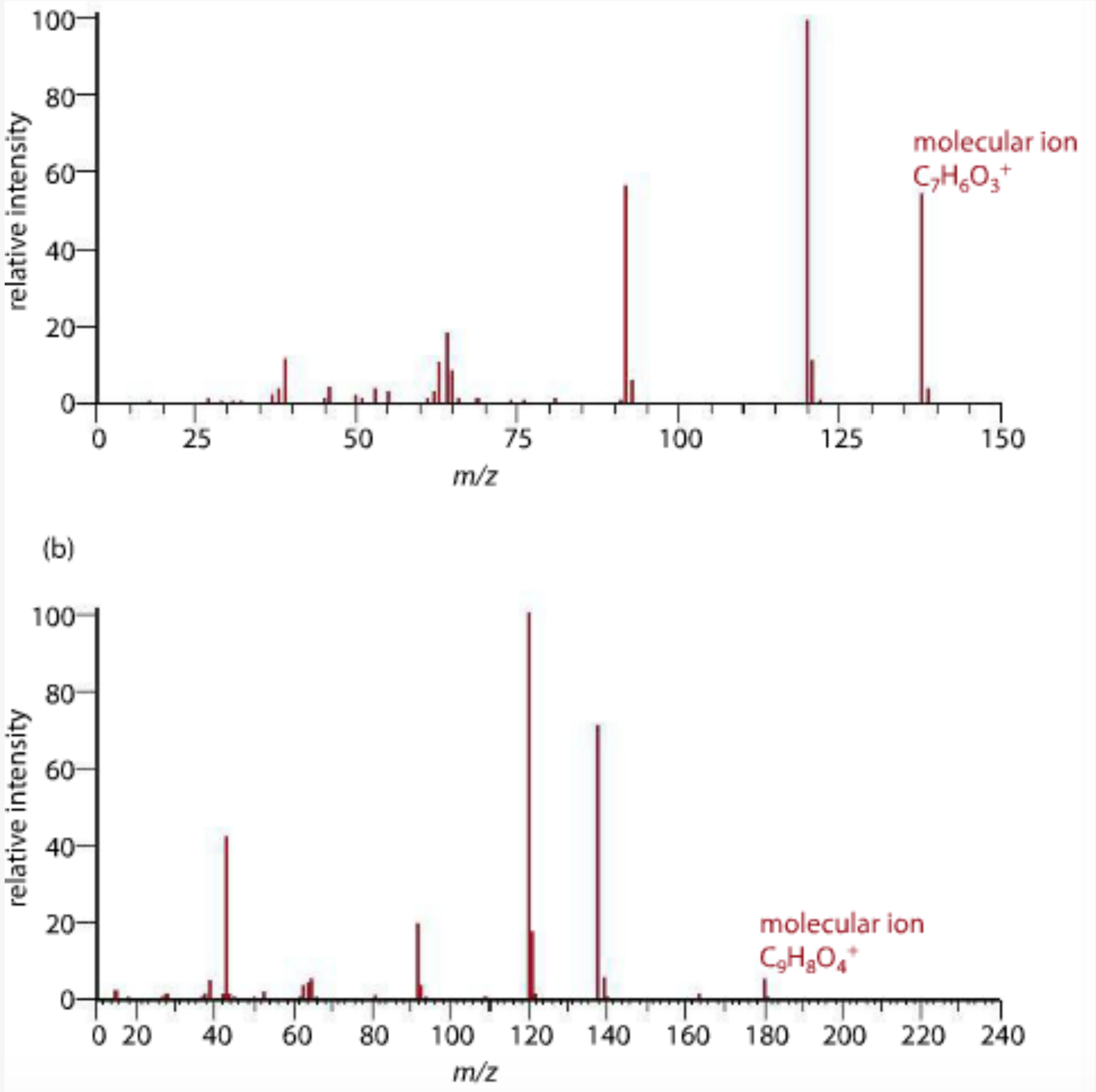
Ethanol Detection

- More accurate test - alcosensor - uses the electrochemical processes in a fuel cell
  - two platinum electrodes with acid electrolyte in between
  - exhaled air passed over the cell and ethanol is oxidized to ethanoic acid at the anode
    - $C_2H_5OH_{(g)} + H_2O_{(l)} \longrightarrow CH_3COOH_{(l)} + 4H^+_{(aq)} + 4e^-$
    - then… $O_{2(g)} + 4H^+_{(aq)} + 4e^- \longrightarrow 2H_2O_{(l)}$
    - electric current produced is measured by a computer to calculate BAC - accurate portable and widely used

D.9 Drug Detection and Analysis

Structure Analysis and Identification

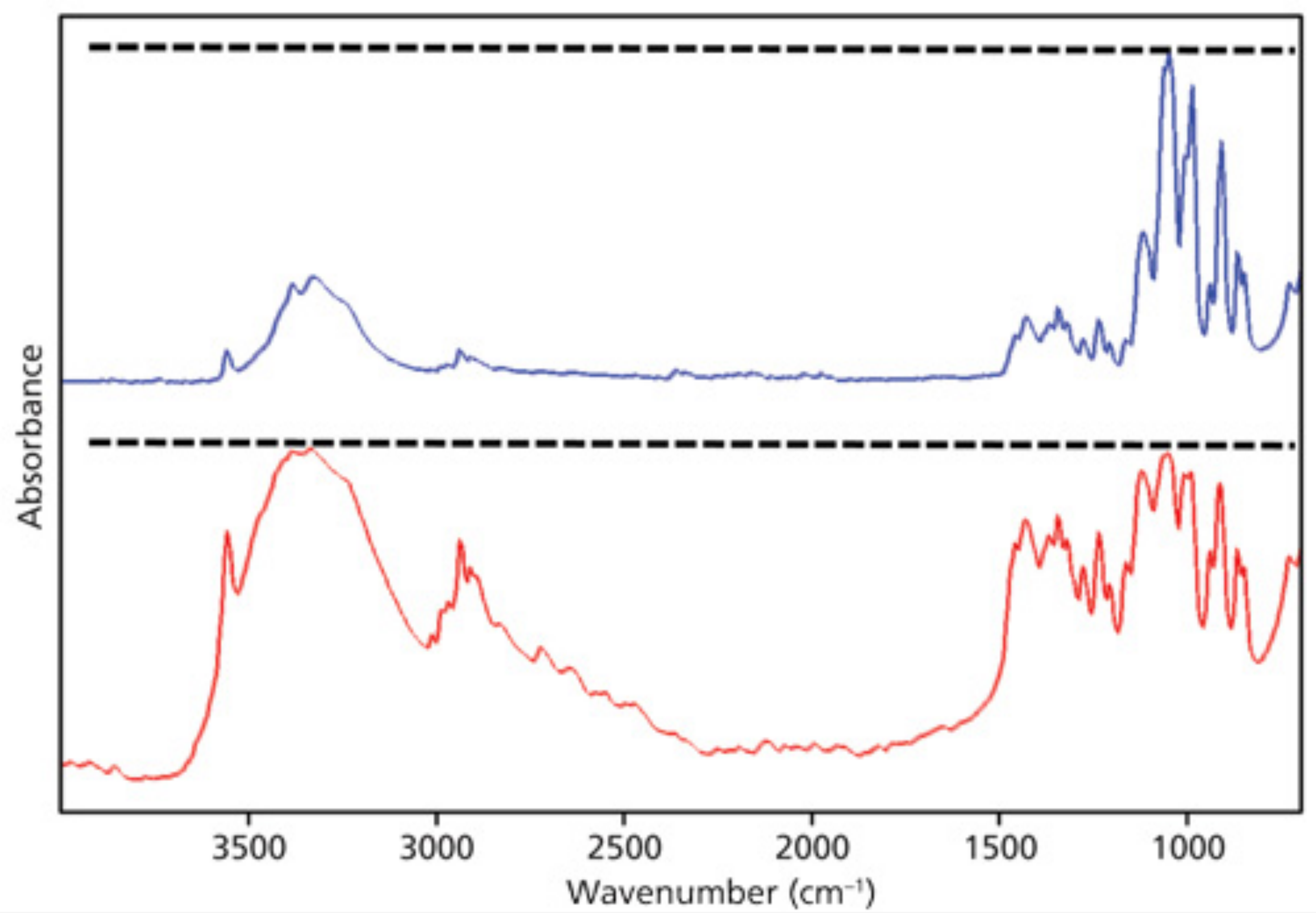
- Mass Spec. - identifies parts of the structure, but can't tell purity
- peak @ 138 in bottom picture (aspirin) is unreacted salycilic acid



D.9 Drug Detection and Analysis

Structure Analysis and Identification - cont’d

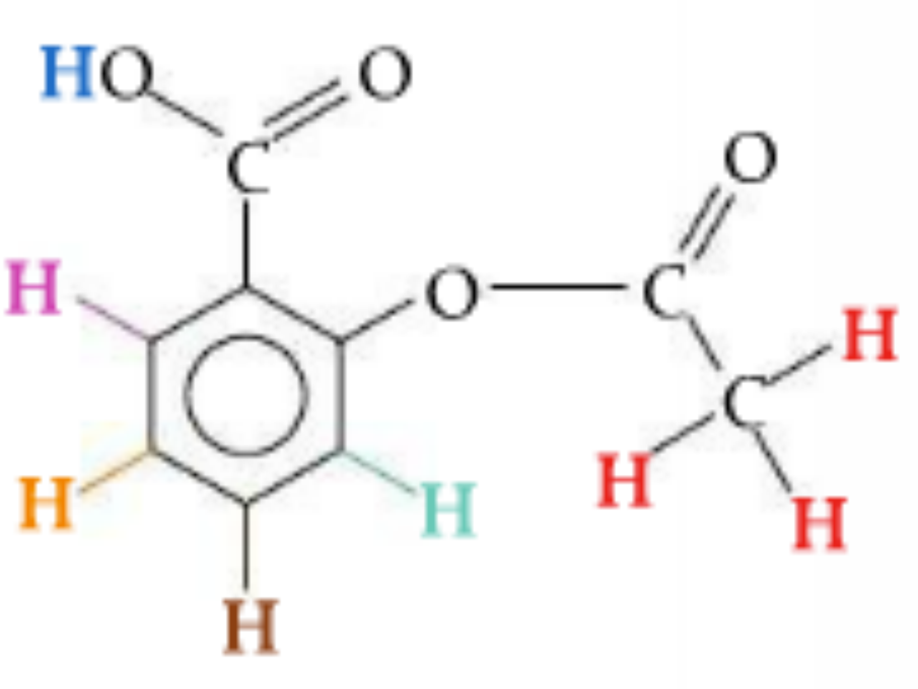
- Infrared - can act as a fingerprint for certain functional groups
- Can identify unknown compounds by comparing to known pure samples



D.9 Drug Detection and Analysis

Proton NMR

- sensitive! - enables chemists to check identity using chemical shifts, number of peaks as well as area and splitting patterns



Peak	Chemical shift / ppm	Type of proton	Splitting pattern
1	2.3	3 equivalent protons on the $-CH_3$ group in the ester group	singlet
2	range 7–8	4 protons attached within the aromatic ring, each in slightly different chemical environments	doublet
3			triplet
4			triplet
5			doublet
6	11	–OH of carboxylic acid; but the peak is so broad that it is almost not visible	singlet