Structure Determination
How to determine the structures of molecules?

- Probe physical properties
- Elemental Analysis
  - atomic composition (relative ratios)
  - empirical formula
- Mass Spectrometry
  - molecular formula
  - element identification (isotopes)
  - connectivity
Mass Spectrometer

- Sample inlet
- Heated filament
- Ionizing electron beam
- Slit
- Ions deflected according to $m/z$
- Detector
- CRT display
- Magnet
Electromagnetic Spectrum

The Electromagnetic Spectrum is a range of wavelengths of electromagnetic radiation, which includes radio waves, microwaves, infrared, visible light, ultraviolet, X-rays, and gamma rays. Each type of radiation has a specific wavelength and frequency, and they are ordered by increasing wavelength and decreasing energy. Visible light, which is a small portion of the spectrum, is further divided into colors based on wavelength: red, orange, yellow, green, blue, and violet. These colors correspond to wavelengths from 700 nm to 400 nm, with red having the longest wavelength and violet having the shortest.
Electronic (UV-VIS) Spectroscopy

- Energy to excite an electron to a higher excited state
- More conjugation, lower energy

![NMR spectrum images with wavelengths 220 nm, 258 nm, and 455 nm]
How to determine the structure of molecules?

- Vibrational (Infrared) Spectroscopy

- functional groups

![Molecular diagrams showing various types of vibrations and bends.](image)
How to determine the structure of molecules?

- X-Ray Crystallography
- 3D positions of atoms
NMR Spectroscopy

- Atom Connectivity
- Functional Group Identification
- Stereochemistry
- Higher Order Structure
A spinning charged particle generates a magnetic field. A nucleus with a spin angular momentum will generate a magnetic moment (m).

When placed in a magnetic field ($B_0$), they will adopt two different states - one aligned with the field and one aligned against the field.

Energy difference between the states at a particular magnet strength. In the $R_f$ range of the EM Spectrum.
- NMR is the basis for MRI
- Difficult - Carbon 13 only 1.1% of all carbon.
- Number of different carbons
- Functional Group Regions
Proton NMR Scale

- Range 0-10 ppm
Identification of a Natural Product

- **High Res. Mass Spectrometry**
  
  210.0764 4.4% \(\text{C}_{11}\text{H}_{13}\text{N}_{2}\text{Cl}^{37}\)
  
  208.0769 15.5% \(\text{C}_{11}\text{H}_{13}\text{N}_{2}\text{Cl}^{35}\)

- **UV Spectroscopy**
  
  217 nm and 250-280 nm indicates pyridine ring

- **IR Spectroscopy**
  
  1428 and 1112 cm\(^{-1}\) suggests a pyridine ring

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**Epibatidine**


Isolated from the Ecuadorian tree frog - *Epibatis Tricolor*

Analgesic activity 500 times greater than morphine.
Epibatidine
Epibatidine
Mass Spectrometry

- A GAS PHASE Technique
- Ionization
  - Electron Impact, electrospray, FAB, maldi
- Mass Selection
  - Curved magnet, quadrupole, time of flight
- Detection
Mass Spectrometry - electron impact ionization

- High energy
- Radical Cations
- Ionized molecules fragment apart
Mass Spectrometry - electrospray ionization

Diagram showing the process of electrospray ionization (ESI). The sample solution is introduced into a high-voltage environment, creating charged droplets. These droplets then enter a vacuum interface and are introduced into a mass spectrometer for analysis.
Mass Spectrometry - fast atom bombardment

- Ionized sample is bombarded with large atoms (Xe) to dislodge them and get them into the gas phase
- Can vaporize very large biomolecule
Matrix Assisted Laser Desorption Ionization
Mass Spectrometer - Quadrupole Mass Selection
Mass Spectrometer - Time of Flight Mass Selection

- **UV Laser**
  - Matrix containing sample

- **High Voltage Ion Accelerating Grids**
  - All ions are formed during laser pulse impact

- **Drift Tube (1-2 meters)**
  - Ions spread out
    - Lighter = Faster
    - Heavier = Slower

- **High and Low Mass Ion Detector**
  - Signal Out
- Molecular Mass of our analyte
  - Information about molecular formula
- Fragments provide information about structure
- Isotopic information