Growing X-ray Quality Crystals

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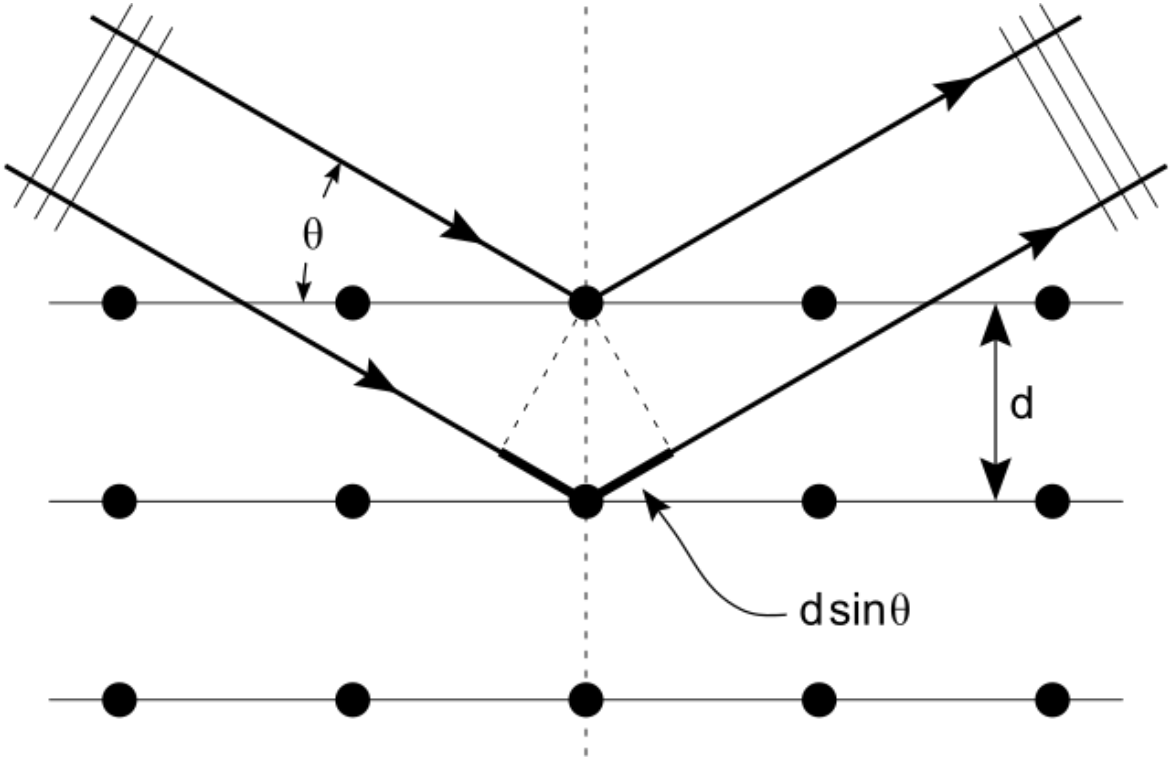
Outline

- X-ray crystallography
- Crystals
  - Quality of crystals
  - Growing crystals
    - General considerations
    - Factors affecting crystal growth
    - Techniques in growing crystals
- Example

X-ray Crystallography

- **X-ray crystallography** is a method of determining the arrangement of atoms within a crystal, in which a beam of X-rays strikes a crystal and causes the beam of light to diffract or spread into many specific directions.

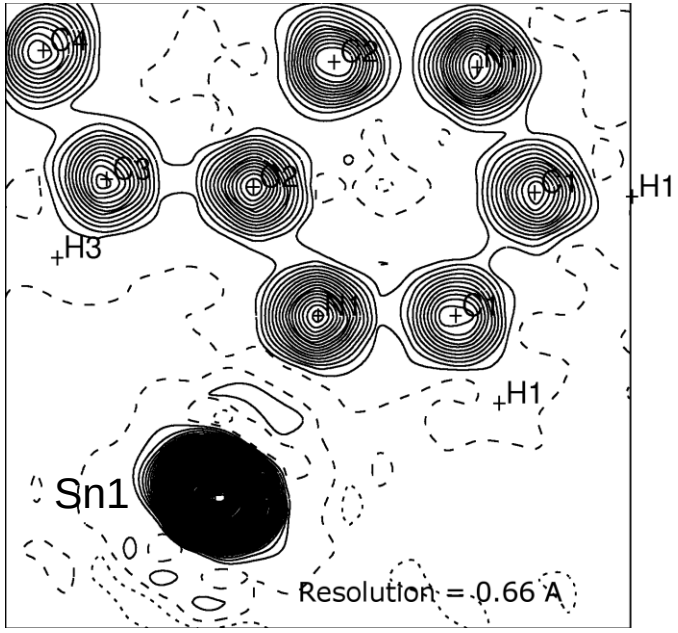


Bragg's Law

$2d\sin\theta = n\lambda$

X-ray Crystallography

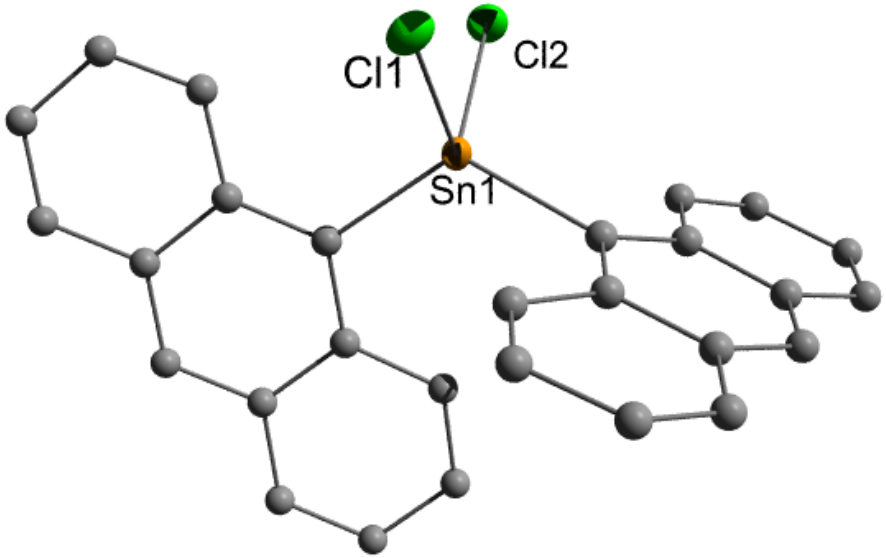
- **X-ray crystallography** is a method of determining the arrangement of atoms within a crystal, in which a beam of X-rays strikes a crystal and causes the beam of light to diffract or spread into many specific directions.
- From the angles and intensities of these diffracted beams, the density of electrons within the crystal can be mapped.



Heavy atoms = more electrons = areas of higher electron density

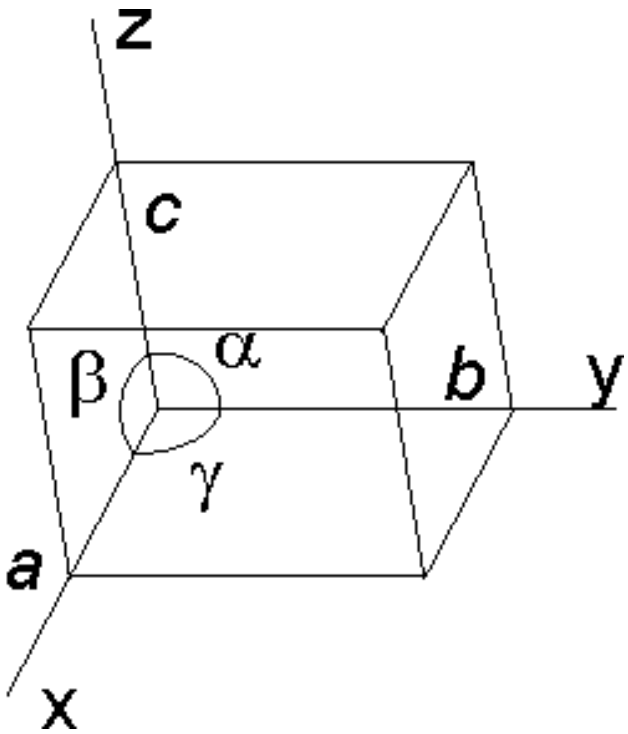
X-ray Crystallography

- From electron density maps, the mean positions of the atoms in the crystal can be determined, allowing for the elucidation of a three-dimensional picture of chemical structures.
- Chemical bond distances, angles between atoms, inter- and intramolecular interactions, dimensionality, pore sizes, and other information can also be determined.



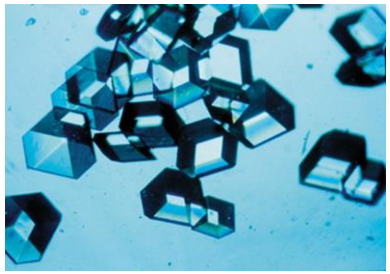
Crystals

- Crystals are three dimensional ordered structures than can be described as a repetition of identical unit cells.
- The unit cell is made up of the smallest possible volume that when repeated, is representative of the entire crystal.



Unit cells are unique for each compound!!

Quality of Crystals



- Good crystals :
  - 0.1 mm to 0.4 mm in size (at least two dimensions)
  - Clear and uniform in color
    - Grow from clear not cloudy solutions
  - Well defined faces and edges
    - Maintain integrity after cutting to an appropriate size
  - Refract polarized light (prism)
    - Shine in direct light
    - Flashlight test
  - Diffract X-rays
    - Discrete spots, well spaced apart, and move with each new frame

Growing Crystals

- Growing crystals is an “art”
  - Time
    - Longer crystallization times improve crystal quality.
  - Trial and error
    - Different techniques must be employed in order to obtain the best quality sample.
      - Crystallization, data collection, and solving
  - Patience
    - Great care and attention must be taken in order to achieve success.
    - Crystalline material will not always be obtained easily!!!!

General Considerations

- Purity of compound
- Solubility of compound
- Physical properties of compound
- Concentration of solution

General Considerations

- Purity of compound
  - Purify your compound before trying to crystallize
    - Precipitation
    - Filtering
    - Recrystallization
  - Recrystallizations should be performed using pure sample
    - Characterized by NMR or IR
  - Recrystallizations should be performed in neat solvents
    - Any impurity in the solvent will affect crystal growth
      - Side products
      - Moisture

General Considerations

- Solubility of compound
  - Understand the solubility properties of your compound
    - Is the compound itself polar or non-polar?
  - Determine a solubility profile for your compound
    - Solubility vs. insolubility in either polar or non-polar compounds
  - Solubility properties of compounds directly affect the crystallization technique that will be employed

General Considerations

- Physical properties of compound :
  - Air and moisture sensitivity
  - Light sensitive
  - Temperature (decomposition upon melting)
- Concentration of solution :
  - Dilute solutions do not crystallize
    - A fair amount of compound is necessary for crystal growth.
  - Supersaturation leads to poor quality crystals
    - Crystals should always be kept in the solution they grew from.
    - Solvents can become trapped in the crystal; if removed, integrity of crystal is compromised.
    - Avoid “drying” the crystals out!!!!!!!!!

Factors Affecting Crystal Growth

- Solvent Choice
- Nucleation Sites
- Mechanics
- Time

Factors Affecting Crystal Growth

- Solvent Choice :
  - "Like dissolves like"
  - Moderate solubility is best
    - Gentle heating can be used to fully dissolve a compound in a solvent
  - Avoid highly volatile solvents
  - Choose solvents with rigid geometries
    - Benzene, toluene
  - Choose solvents that can aid in stabilizing interatomic forces necessary for crystallization
    - H_2O and alcohol – hydrogen bonding

Factors Affecting Crystal Growth

- Commonly used solvents :
  - Water
  - Diethyl ether
  - THF
  - Methanol
  - Ethanol
  - Dichloromethane
  - Acetonitrile
  - Ethyl acetate
  - Acetone
  - Pyridine
  - DMF
  - DMSO
  - Toluene
  - Benzene
  - Pentane
  - Hexane
  - Heptane
  - Cyclohexane
- All have inherent advantages and disadvantages
- Trial and error!!!!

Factors Affecting Crystal Growth

- Nucleation Sites:
  - Crystals initially form via “nucleating events”.
    - This a thermodynamical process.
  - Once a crystallite has nucleated it can grow.
    - Addition of seed crystals can aid in this process.
  - Excess nucleation sites cause smaller average crystal size.
    - Stir bars
    - Insoluble precipitate
    - Ambient dust
    - Filter paper fibers
    - Broken off pipette pieces
  - Make sure that crystals have a clean neat solution to grow in.

Factors Affecting Crystal Growth

- Mechanics :
  - Crystals grow by the ordered deposition of the solute molecules onto the surface of a pre-existing crystallite.
  - Crystal growth is facilitated by the environment changing slowly over time.
    - Solvent evaporation – solution concentration
    - Change in temperature
  - Keep crystal growth vessel away from sources of mechanical agitation (e.g. vibrations).
  - Do not shake or move the sample excessively.
    - Do not check crystals daily.
  - Leave samples alone!!

Factors Affecting Crystal Growth

- Time :
  - Crystals need time to grow in near equilibrium conditions.
  - Crystals that deposit rapidly out of solution are most likely poor formed and thus poor quality.
  - It is in your best interest to grow crystals throughout a long period of time.
  - Leave samples alone!!

Techniques in Growing Crystals

- Reduce Temperature:
  - Dissolve sample in solvent
  - Cool down slowly
    - RT – Fridge - Freezer
  - Allow sample to remain at a certain temperature range for some time before continuing to cool down
  - In some instances, it is necessary to warm up the solution in order to solubilize the sample.
    - Allow warm solution to come to RT and then continue to slowly cool down the sample
  - If cooling occurs too quickly, small and poor quality crystals will form.

Techniques in Growing Crystals

- Slow Evaporation (air stable)
  - Dissolve sample in solvent, and allow solvent to evaporate. This results in a slowly saturating solution and allowing crystal growth.
    - Example:
      - Put sample in a vial, cover the opening with parafilm and poke small holes to allow evaporation
      - Leave sample in an NMR tube
  - Do NOT let the sample dry out!!!!

Techniques in Growing Crystals

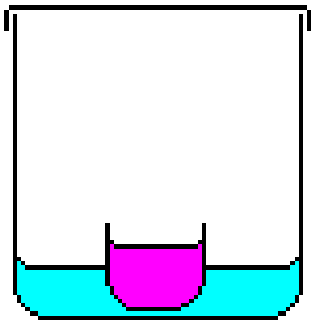
- Reduce Volume (air sensitive):
  - Pull slight vacuum on Schlenk flask in order to reduce volume of solvent.
  - Immediately stop applying vacuum if precipitate appears on sides of Schlenk flask.
  - Allow precipitate to go back into solution.
  - If it does not go back into solution, apply moderate heat or add more solvent.
  - Allow to recrystallize.
  - Do NOT remove all of the solvent!!!!

Techniques in Growing Crystals

- Solvent Layering :
  - Dissolve sample in a solvent.
  - Slowly pipette or syringe a small amount of solvent with opposite polarity creating layers.
  - Stop adding once two visible layers can be seen or interface between layers becomes cloudy.
  - Allow crystals to grow.

Techniques in Growing Crystals

- Vapor Diffusion:
  - Dissolve sample in a solvent.
  - Place inside a beaker containing a solvent in which the compound is insoluble in
  - Cover and allow for diffusion of the outer solvent into your sample.
  - Sample solution will become saturated and crystals will precipitate.



Conclusions

- The quality and meaningfulness of your results is directly dependent on the quality of your sample crystal.

Garbage in = Garbage out

- You can get information from a bad crystal structure, but it will be difficult to publish.
- Spend the time and effort to determine the best method of crystallization.
- There are many solvents and crystal growing techniques available – try everything.

References

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