Growing and Mounting Single Crystals Your Diffractometer Will Treasure

Welcome

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Today's Topics

- Solids and Crystals
- Growing Single Crystals
- Evaluating Crystals
- Mounting Single Crystals
- Q & A

Audience Poll 1

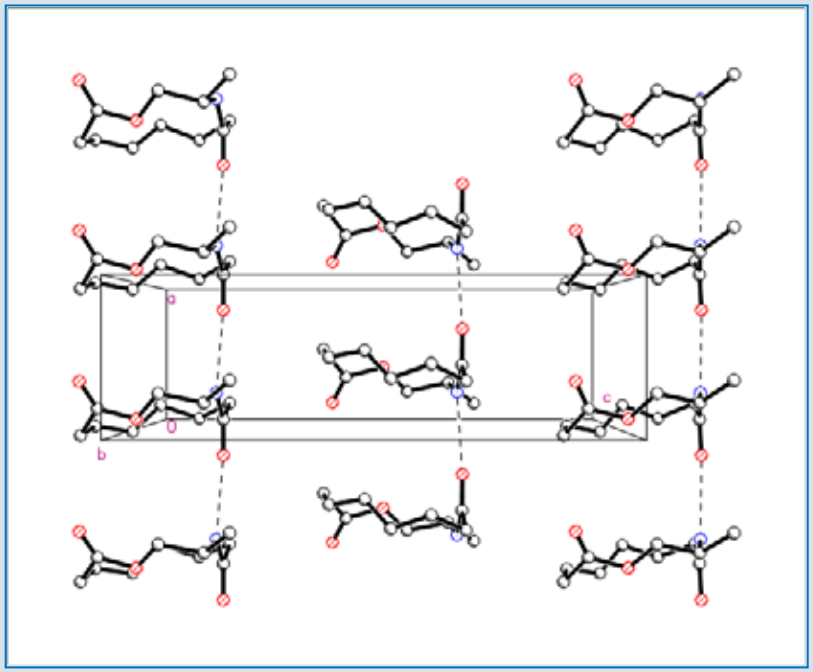
Please use your mouse to answer the question to the right of your screen:

How many different methods do you typically try to grow a crystal?

- I currently do not grow crystals
- I'm lucky – 1 method does the trick
- 2 to 3 methods
- More than 3 methods
- My crystals don't crystallize, no matter what I try!

What is a crystal structure?

- The determination of the connectivity of the atoms in a compound and the way the molecule or molecules pack to form a solid crystalline material.



Formation of a single crystal is required.

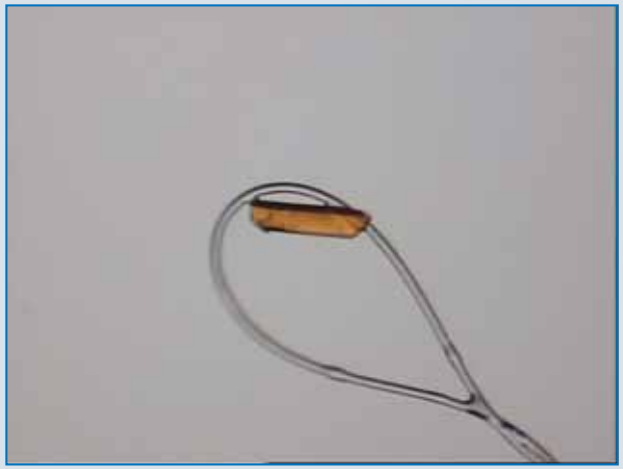
A Few References

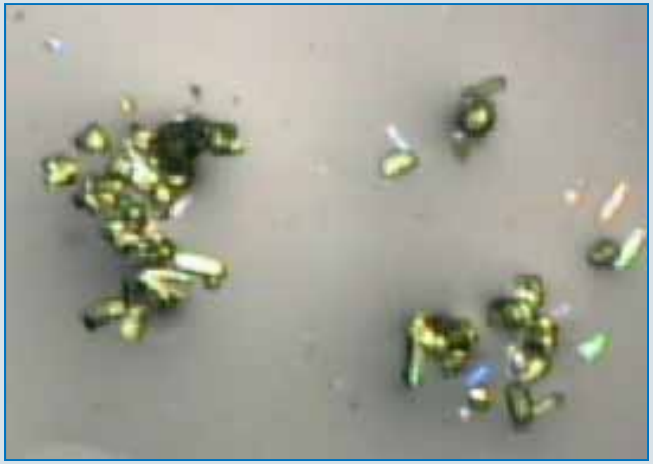
Poll 1 Results

- "Crystal Growing", Peter G. Jones, *Chemistry in Britain*, *17*(**1981**) 222-225.
- "Crystallization of Low-Molecular-Weight Organic Compounds for X-ray Crystallography"; P. Slus, A.M. Hezemans, J. Kroon, *J. Appl. Crystal.* (1989), **22**, 340-344.
- See www site by Paul D. Boyle, (2006) http://www.xray.ncsu.edu/GrowXtal.html.
- Various web sites now exist covering aspects of single crystal growth for X-ray diffraction studies.

What do I need to bring to the laboratory or instrument?

- Single crystals
- Bring what you can grow
- Chemical formula
- Compound name
- If not single, discuss re-crystallization



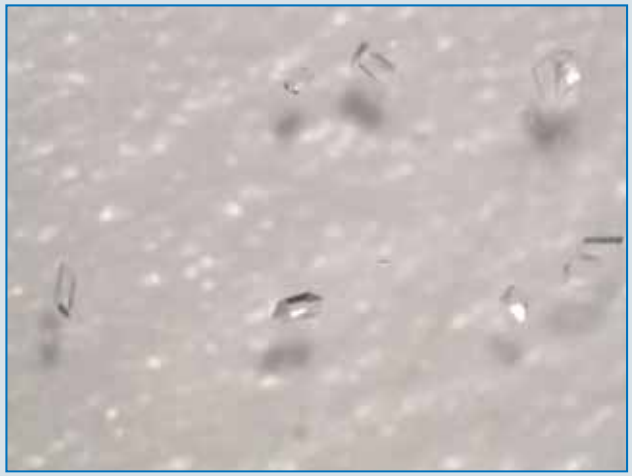


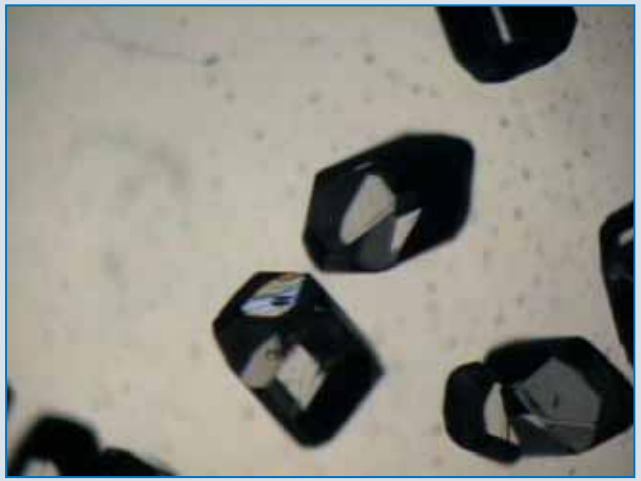
Solids and Crystals

- Solids
  - Crystalline…
    - Material which internally possesses long-range three dimensional order.
    - Examples: table salt, sugar, gems, quartz, metals
  - Non-crystalline…
    - Amorphous, short-range ordered, or random ordered materials, “super cooled liquids”
    - Examples: glass, 1 or 2D ordered solids, fibers, liquid crystals.

Crystals - Single

- Crystals
  - Single...
    - Crystal lattice is well defined with small repeating units in three dimensions.
  - Properties...
    - Extinguish on rotation of cross-plane polarized light
    - Clear, generally sparkly
    - Nice regular shape, faces and edges



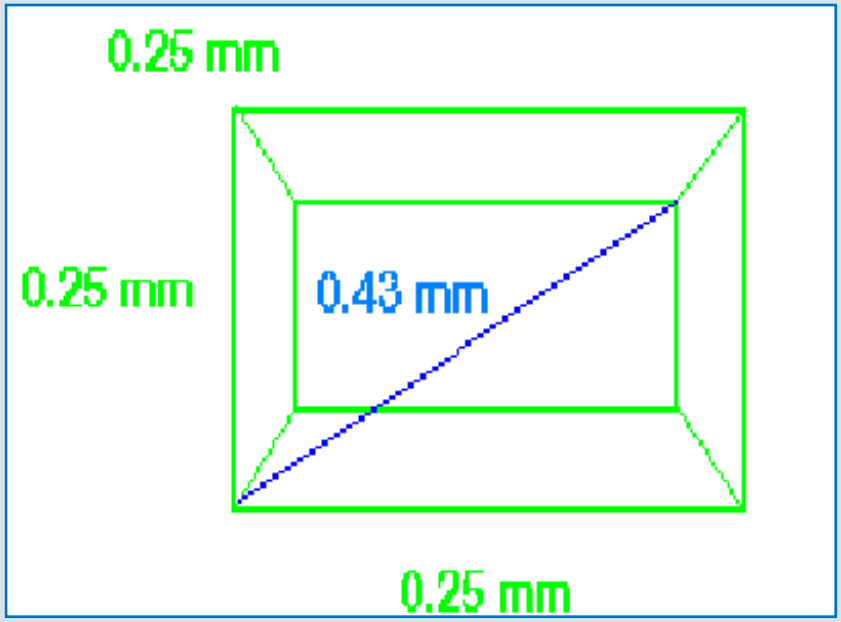


Crystals – Non-Single

- Crystals
  - Non-Single...
    - A lack of well defined repeating units, may be systematic.
  - Properties of well defined non-single crystals, twins...
    - Clear view of two extinctions under plane polarized light.
    - Symmetry related and definable operations resulting in a well defined lattice.

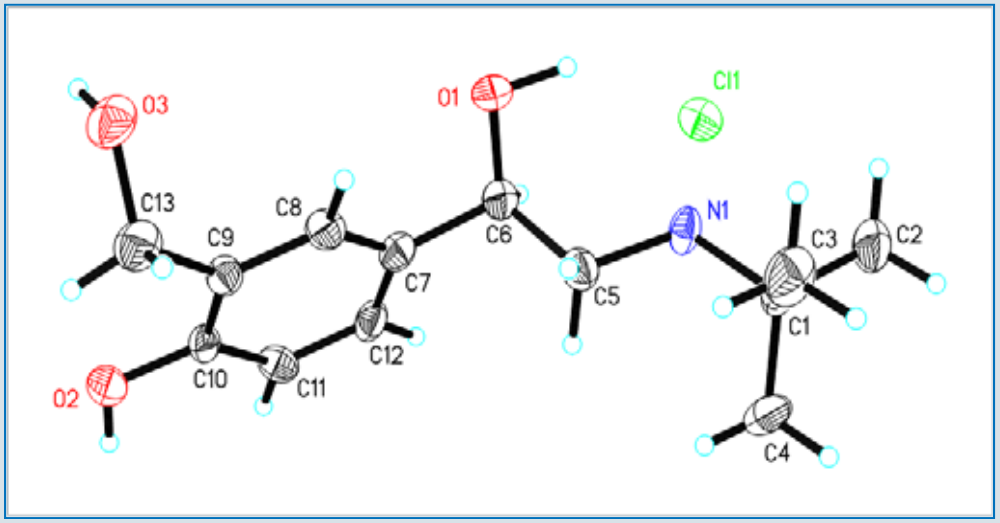
Crystal Size

- Based on a 0.5 mm beam size.
- Size should be 0.25 x 0.25 x 0.25 mm perfect.
- Gives 0.43 mm diagonal. Smaller can use smaller beam size.
- Smaller crystals are very possible!
- Larger crystals can be cut!



Where do I start?

- Simple re-crystallization.
- During purification, did you create crystalline material?
- Are these crystals big enough?



These crystals were 0.05 x 0.025 x 0.002 mm
Collected on an APEX, sealed tube, Mo system

How much material do I need?

- Depends on the vessel you are going to use to grow the crystals. (I like to use about 10-15 mg in each trial.)
- Depends on solubility of sample in the solvent.
- NMR sample – Generally a good concentration level.

How much material is in a single crystal?

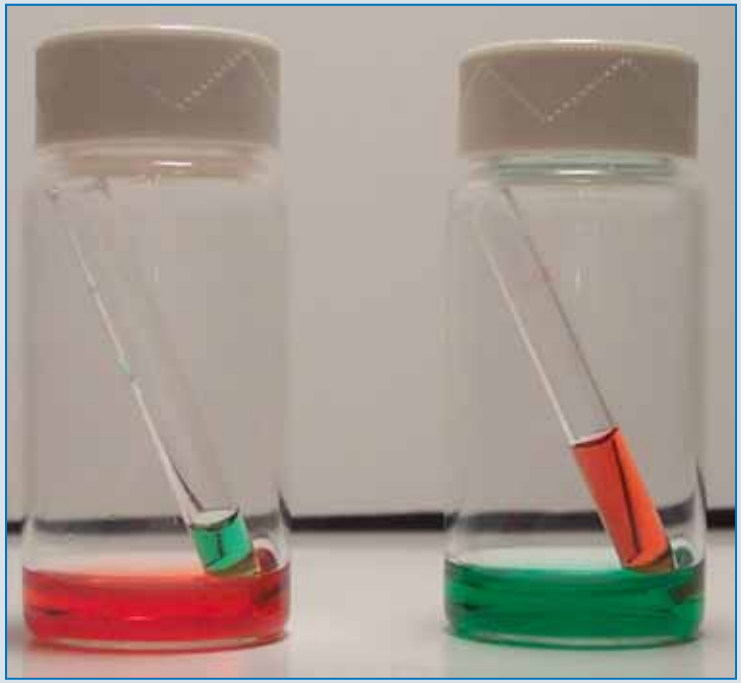
- If the crystal for X-ray diffraction is to be 0.3 x 0.3 x 0.3 mm, volume = 0.027 mm^3
- Typical unit cell is 12 x 12 x 12 Å, volume = 1728 $Å^3$
- Å = 10^{-10} meters = 10^{-8} cm = 100 pm (picometers)
- Therefore, in a typical crystal there are 1.6 x 10^{16} unit cells
- 1.3 x 10^{17} molecules for 8 molecules per cell.
  - MW = 206.2 then only 2.49 x 10^{-7} moles in the cell. 5.1 x 10^{-5} g, **0.051 mg**
- Unfortunately, more than one crystal grows in the vessel so more material is needed.
- ONLY ONE CRYSTAL OF THE BULK

What is the goal?

- To create a single crystal which diffracts on the instrument such that an analysis can be accomplished.
- Generally this means to get the material to go from solution to a solid very slowly.
- Create an environment that slowly changes over time to cause crystallization.

What do I grow the crystals in?

- Clean glassware, most of the time.
- Consider location.
- Consider volume needed to grow the crystal.
- Usually, clean new vials that fit inside one another work well.

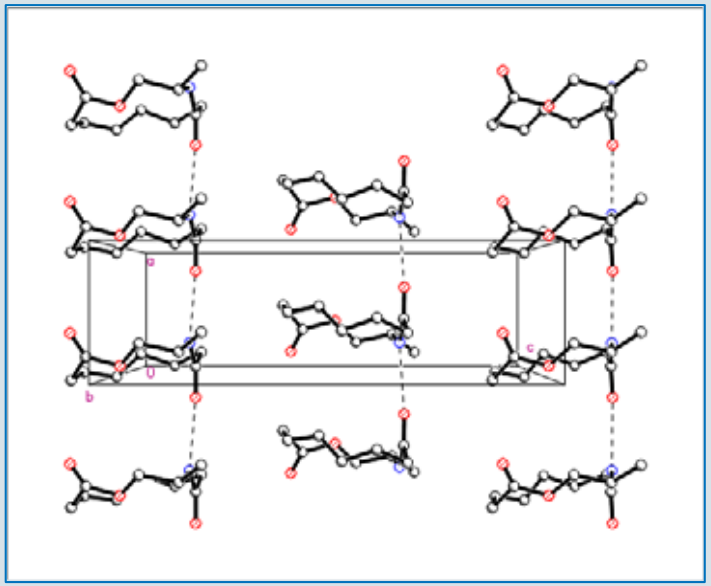


Solvent Choice

- Polar – polar solvent layered with a non-polar solvent
- Non-polar – non-polar solvent, evaporation or layer with polar solvent, harder.

Hydrogen Bonding

- Hydrogen bonding is very important in the crystallization process.
- Consider whether hydrogen bonding solvent might help or hinder crystallization.
- Amides generally do better with hydrogen bonding solvents.



Solvents to Use and NOT to Use

- Do use benzene*! Seems to be a magic solvent. It has been seen that toluene can do the same sort of thing.
- Aromatic rings seem to help fill holes in lattice as well.
- Ethyl acetate works for a lot of compounds.

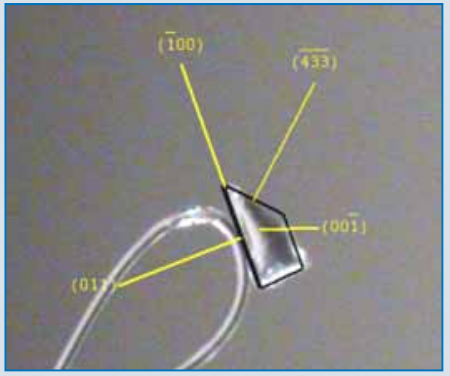
The Crystallographer would like you to:

- Avoid volatile solvents such as CH_2Cl_2, Diethyl Ether and long alkyl chains. These can create disorder and make final solution more complex.

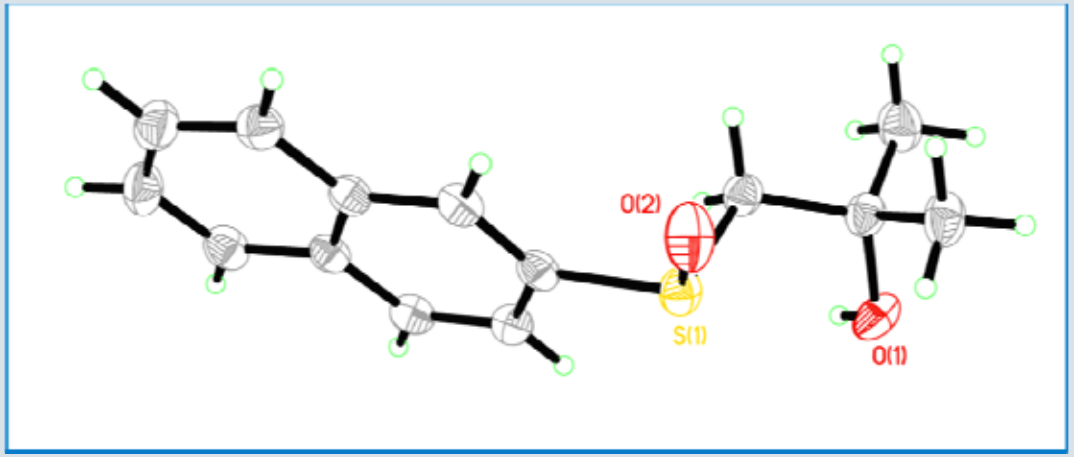
* Caution: benzene is a known cancer hazard.

Solvent Layering

- Layering must be very careful.
- Place a solvent between the two layers.
- Do **not** disturb the vessel.
- Set it so you can view it without moving it.



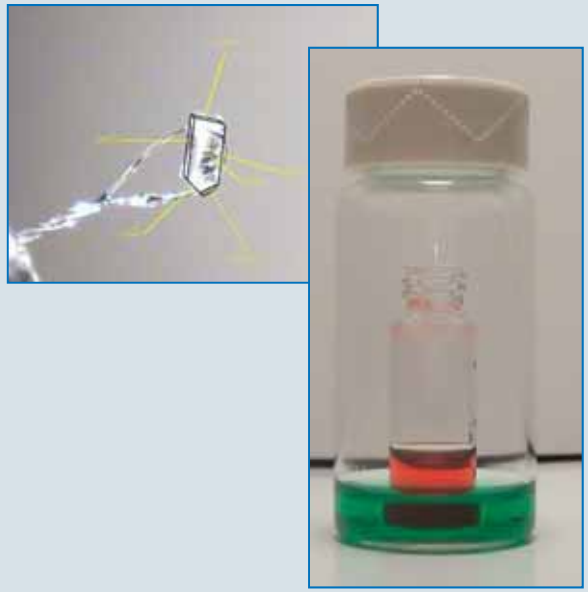
- Grown by layering a solution of methylene chloride with hexanes and a drop of benzene.

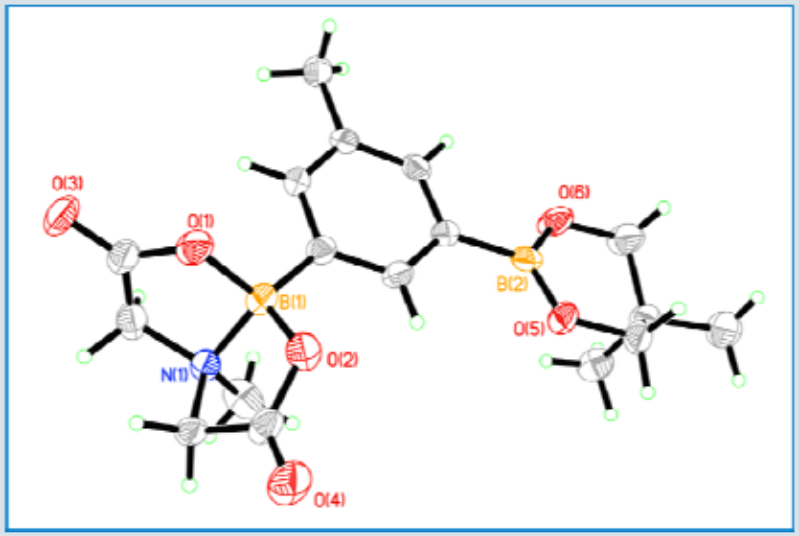


Borhan, Anyilca, Staples, MSU.

Vapor Diffusion

- Good for milligram amounts.
- Volatile solvents.
- Slowly create a less desirable solvent.
- Need to be aware of vapor pressures of solvents.





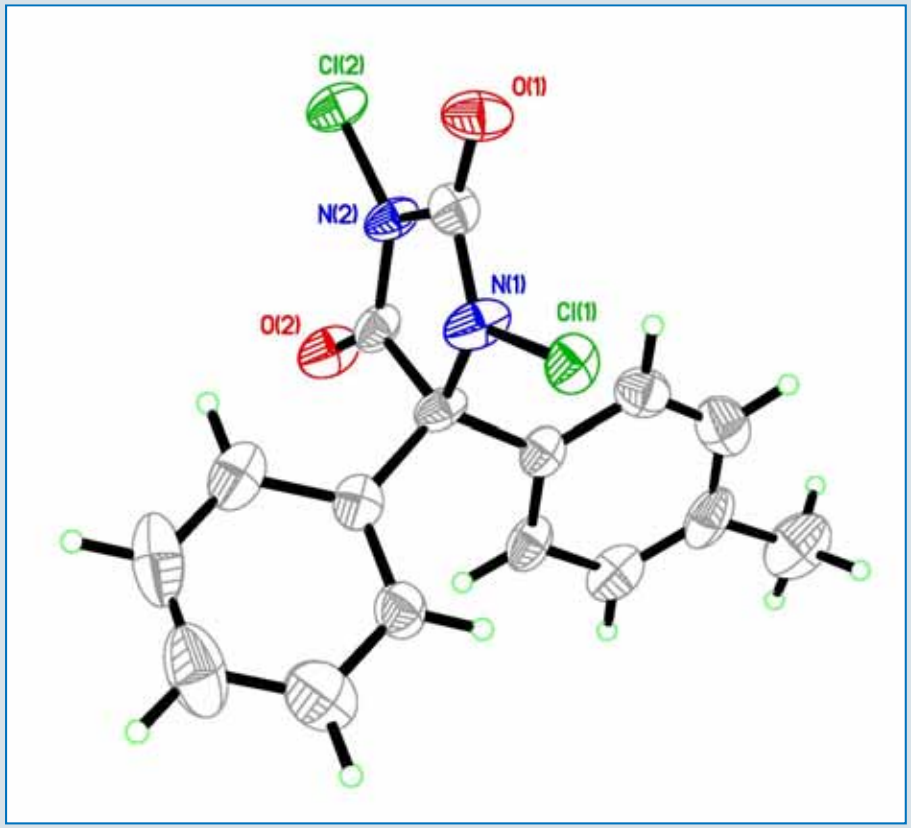
Smith, Bala, Staples, MSU

- Used a diffusion chamber with compound in the Acetonitrile and then Ethyl Ether in the outside chamber.

Slow Evaporation

- Allow the material to crystallize out as the solvent evaporates.
- Keep the solution clean and covered to avoid dust particles.

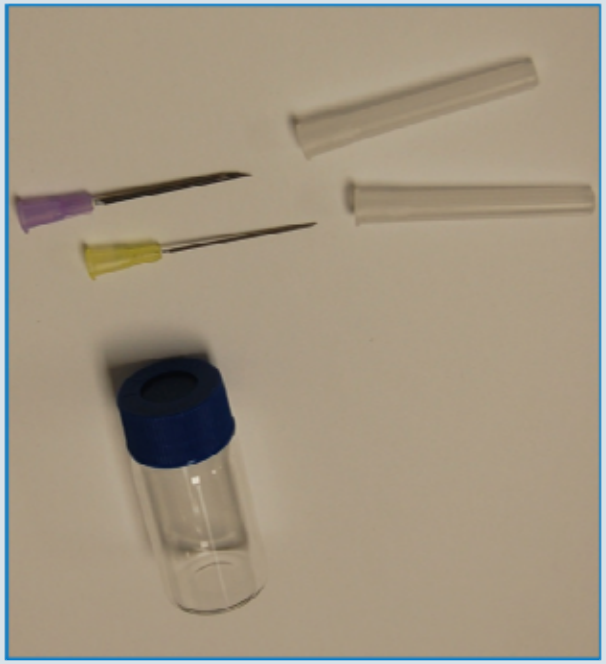
D.C. Whitehead, R.J. Staples, B. Borhan
Tetrahedron Let. 50 (2009) 656-658.



Slow evaporation benzene and hexanes

Evaporation Methods

Tighten or loosen cap

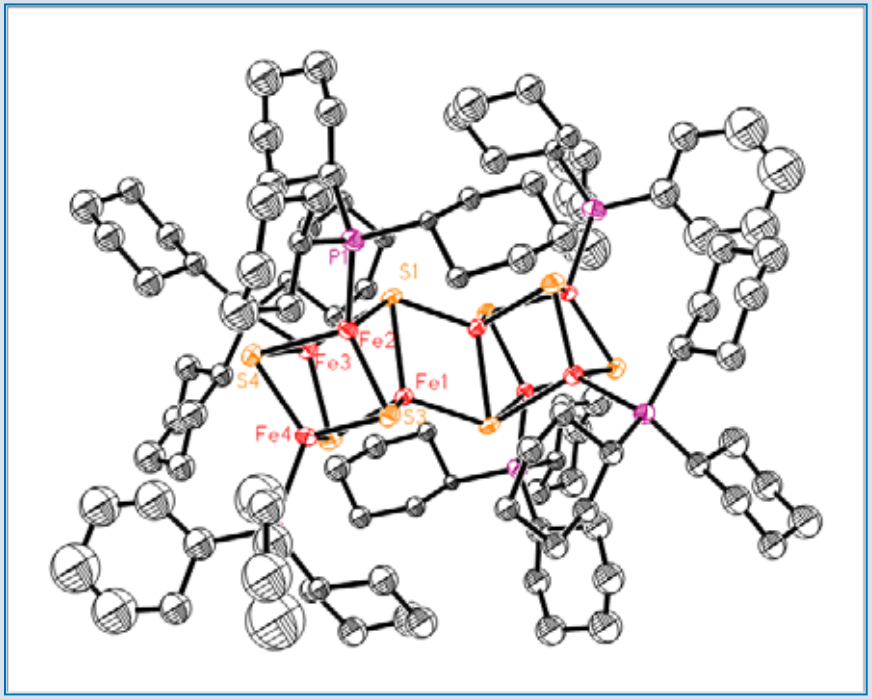


Use of needles through septa of vial governs the speed of evaporation.

Inside a desiccator with desiccant, some use a vacuum desiccator.

Use the NMR tube

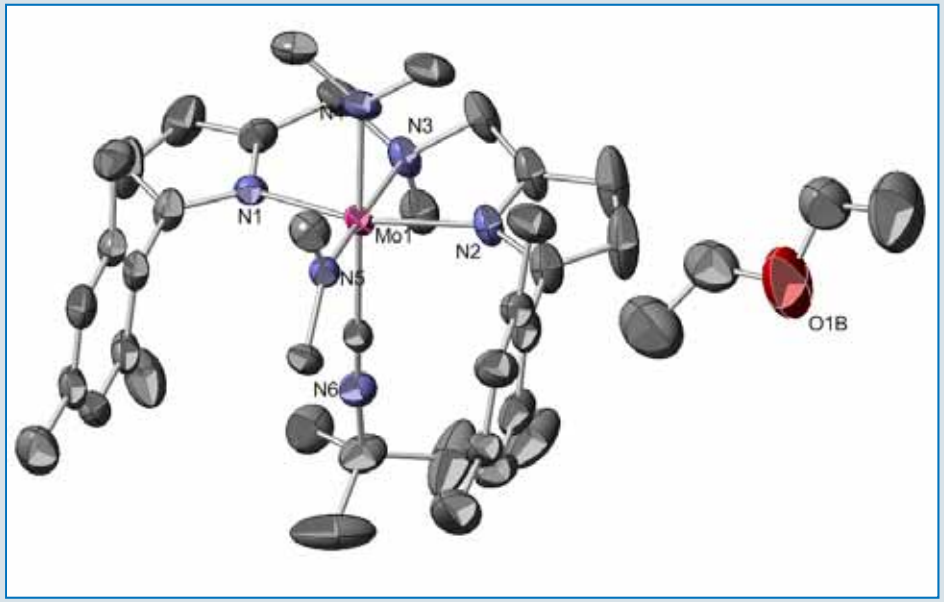
- Often crystals have been obtained by allowing the solvent to evaporate slowly from the NMR tube.
- Remember to keep the tube covered to avoid dust and dirt.



Holm's Group, left in NMR tube overnight, Benzene-d6

Slow Cooling

- Standard re-crystallization technique.
- Must perform this slowly to work well.
- Slow reduction of the temperature is best. Use freezer with vial inside of a Dewar, glass jar, insulate.



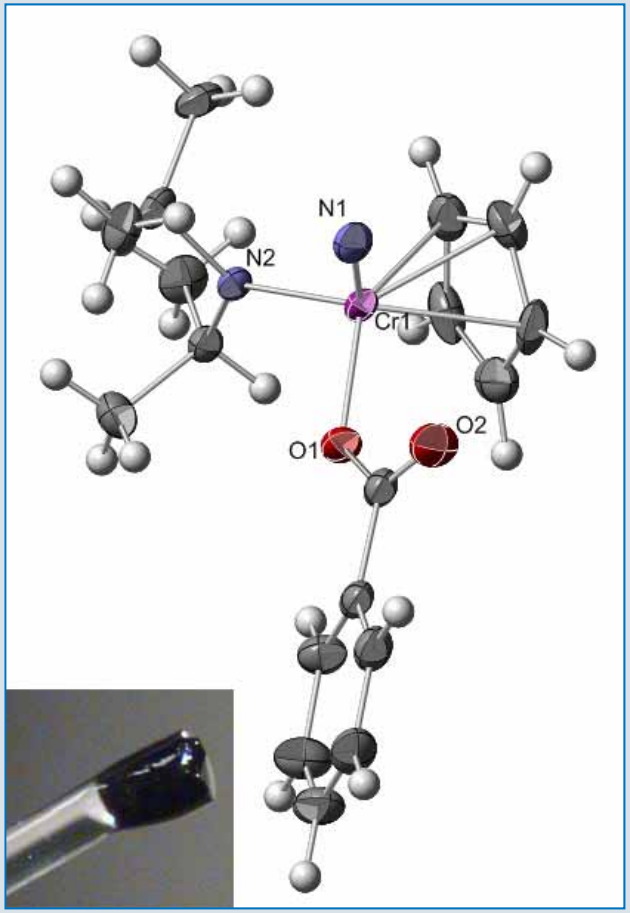
Crystallized from ether at -35ºC

S. Difranco, A.L. Odom, MSU

Combined Methods

- In some case combining techniques works well.
- We have seen many compounds crystallized vial, a soluble solvent, layered non-soluble solvent, then placed in a fridge or freezer.

Crystallized from concentrated toluene solution layered in pentane held at -35ºC



S. Difranco, A.L.Odom, MSU

Audience Poll 2

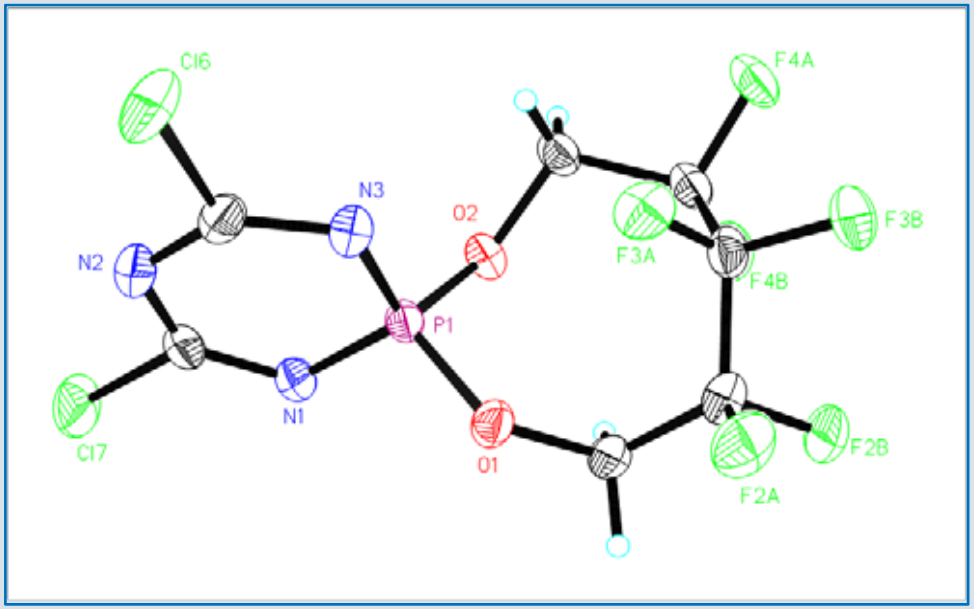
Please use your mouse to answer the question to the right of your screen:

Why might chiral compounds be more difficult?

- ❍ They're generally not as pure
- ❍ Nature prefers symmetry in crystals
- ❍ People in Texas prefer larger crystals
- ❍ Solubility is less well determined

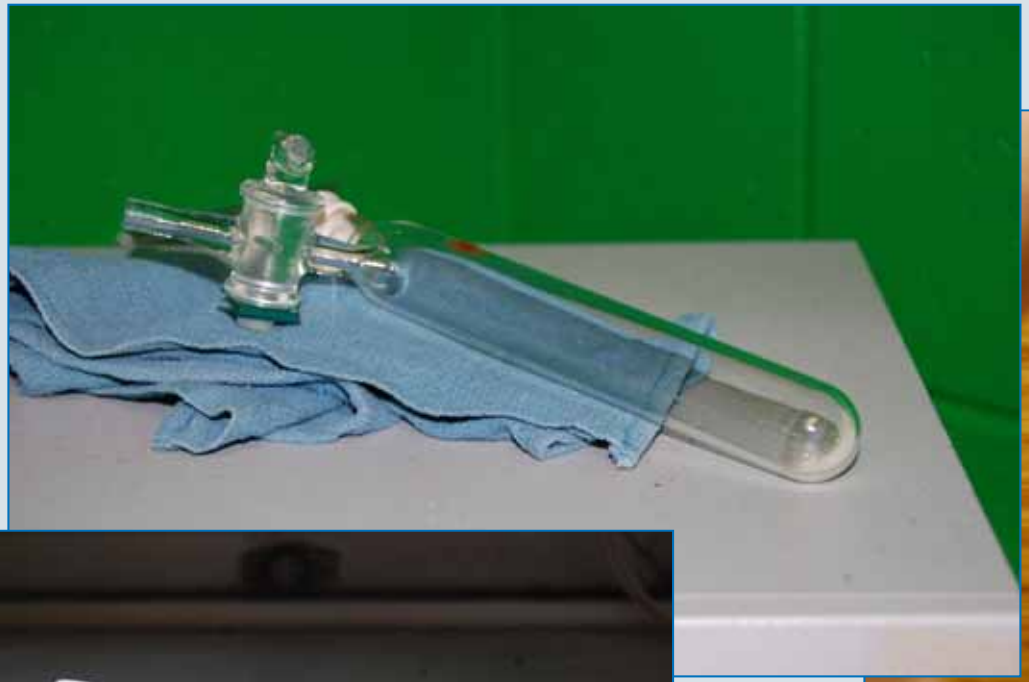
Sublimation

- Works extremely well when it can be done.
- Must be performed slowly to achieve good size crystals.



Vij, Elias, Kirchmeier, Shreeve, *Inorg. Chem.* 1997, *36*, 2730-2745.

Sublimation Techniques

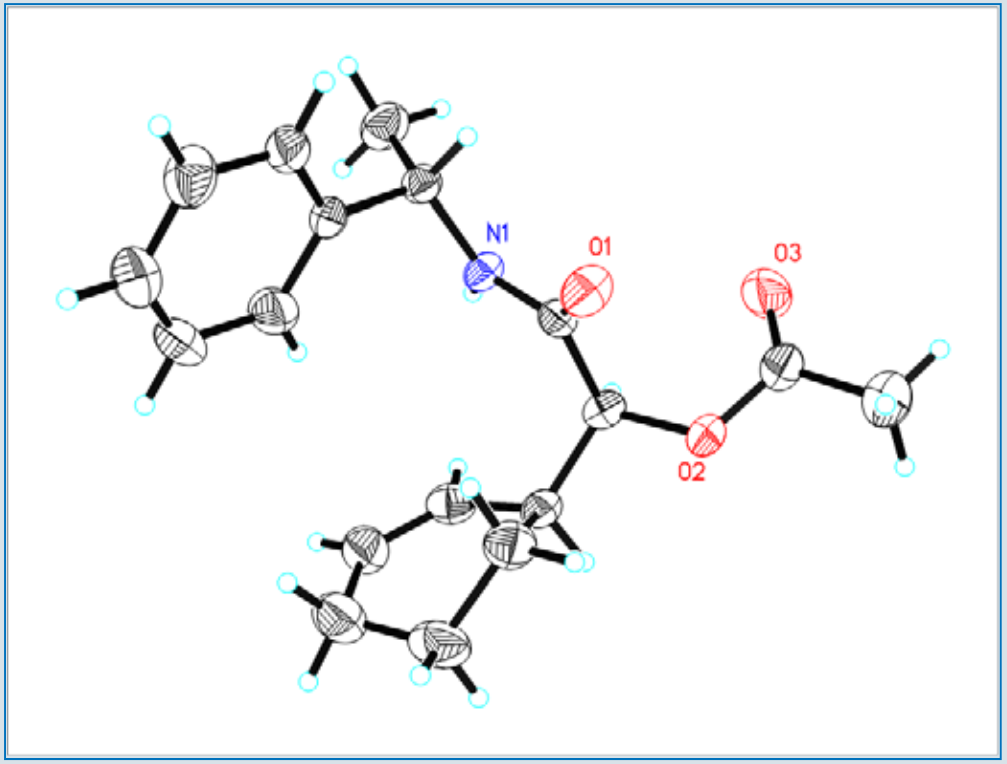


Perform under vacuum. Vacuum can be lousy to great, depending on compound.

Chiral Compounds

Poll 2 Results

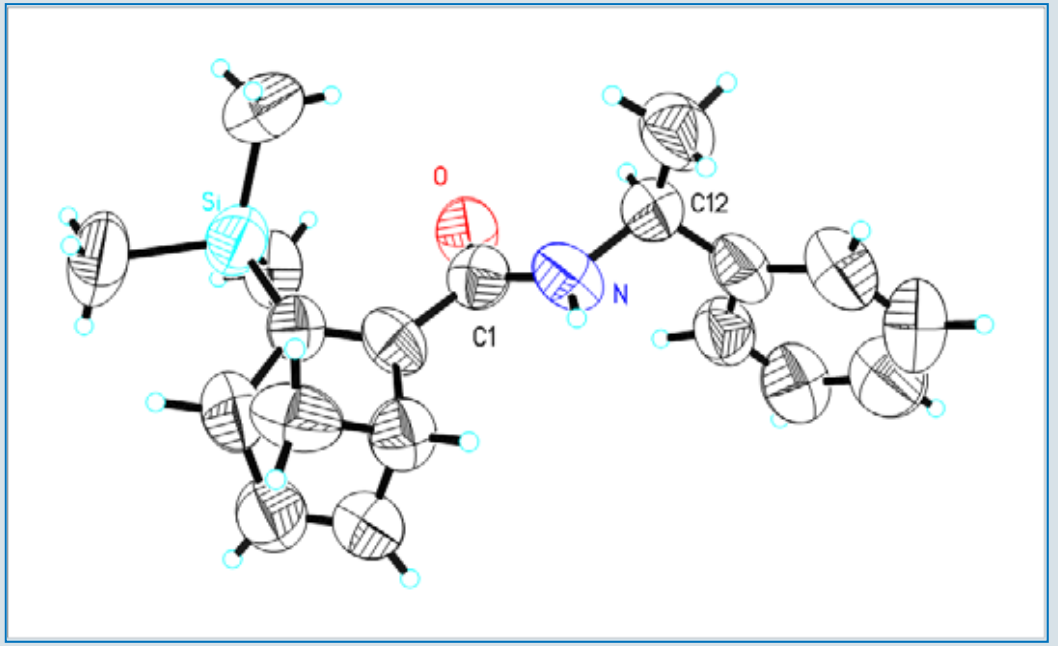
- These tend to be more difficult.
- Try to make derivatives which will improve packing, e.g. phenyl rings.
- Have atoms heavier than carbon.



Evans's group, CH_2Cl_2/hexane

S-alpha-methylbenzylamine

- Use with carboxcylic acids, could be generated from alcohol or aldehydes.
- Cheap and usually easily crystallized.

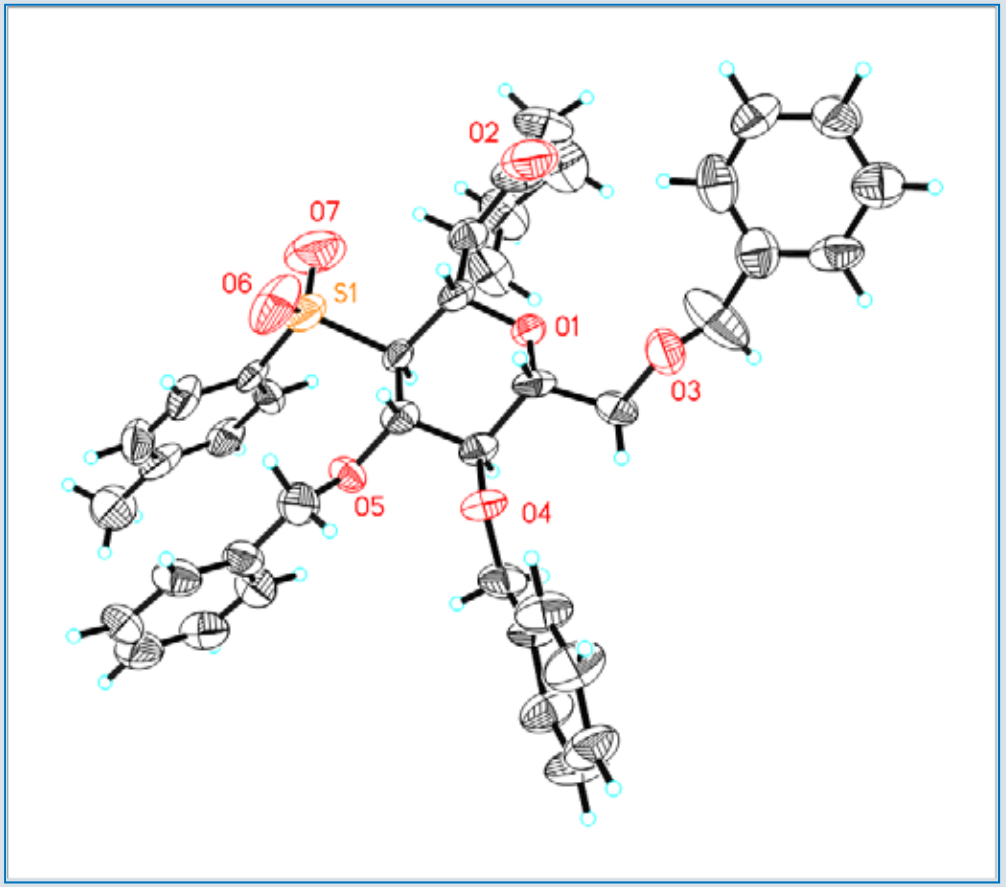


Aldehyde converted to acid then to the amide.
Corey, Lee. *Tetrahedron Lett.* 1997, *38*, 5755.

Improve heavy atom and crystallization

- Have heavy atom present.
- Alcohols and amines make derivative with

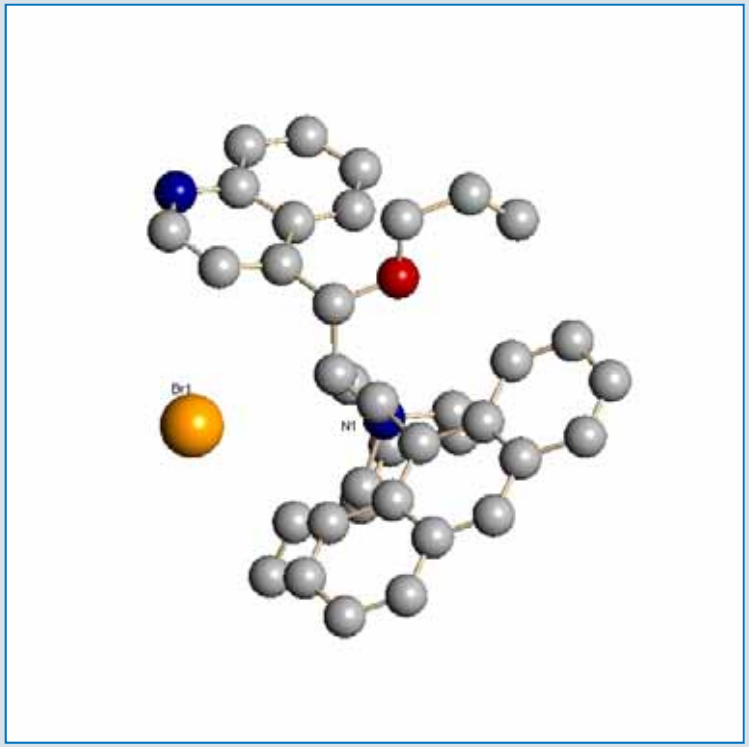
  p-Bromobenzoate
- Include aromatic components in derivative.



Crystal was 0.1 x 0.05 x 0.05 mm, grown benzene layered with hexane.

Heavy Atom Present

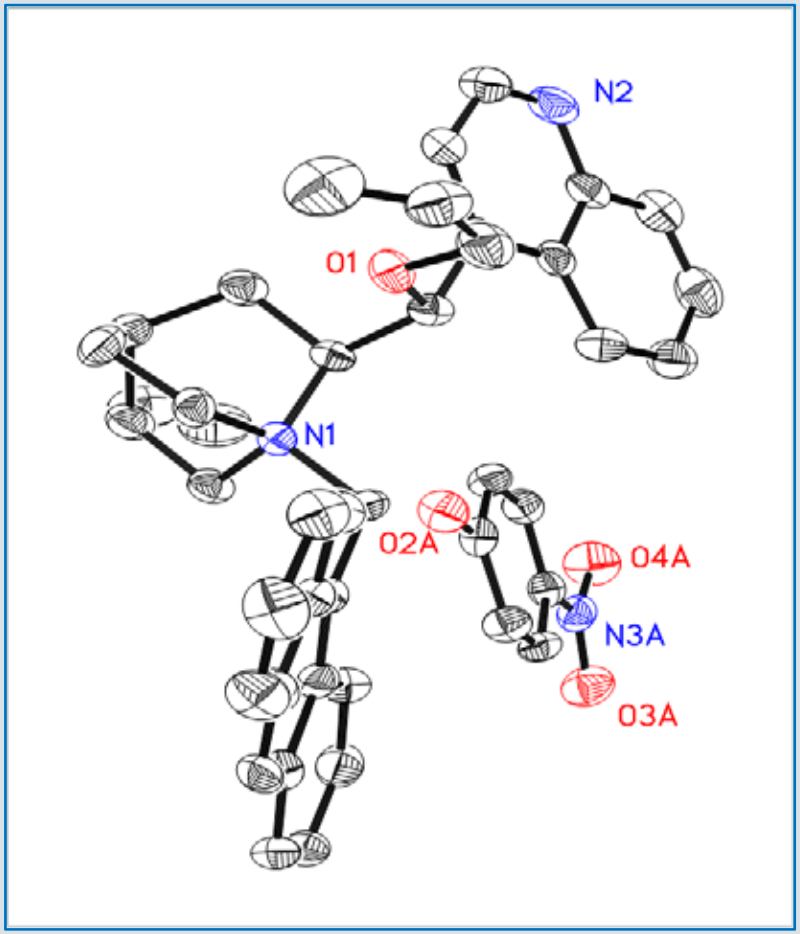
- In some cases you can make a salt and have the heavy atom be the anion or cation.



Corey, Xu, Noe *J. Am. Chem. Soc.* 1997, *119*, 12414-12415.

Counterions or Ionization

- Change a counterion in the complex.
- Ions of the same size tend to pack well.
- If neutral compound does not crystallize or is liquid, create an ion.
  - Deprotonation or protonation.
  - Good to confirm the identity of the material.



Corey, Xu, Feng, Noe *JACS* 1997, *119*, 1214

Reactant Diffusion

- Perform the reaction on a small scale compared to surface area.
- Layer one reactant on top of the other reactant and allow diffusion to control reaction rate and crystal formation.
- Good when product formed is highly insoluble.

Odd Methods

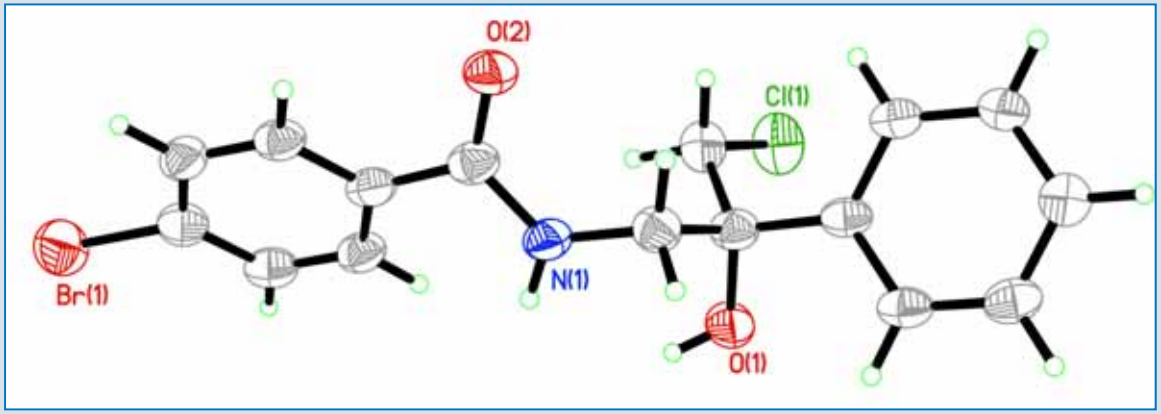
- Melting the compound and letting it re-crystallize!
- Seeding a solution with similar crystallized material.
- Reports of seeding with stir bar or boiling chips.

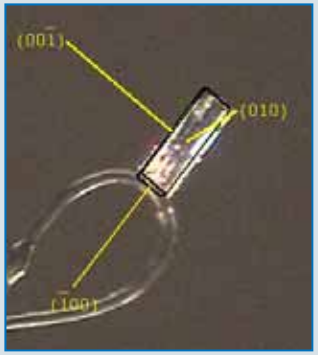
Vary the Vial or Glassware

We have been trying siliconized vials.

After weeks and several attempts in standard new vials, original solvent system in Si vial produced good single crystals.

DCM, $CHCl_3$, Hexanes





A. Jaganathan, A. Garzan, D. C. Whitehead, R.J. Staples and B. Borhan, MSU

More Variations in Vials or Glassware

- Scratchy round bottom, flask or scratch a vial.
- Smaller vial, more concentric or larger flat area.
- Size difference, give rise to difference in concentration levels.

Learning

- Chemist is often in the best position to grow single crystal.
- Compound properties, solubility, and reactivity.
- Type of crystal grown can lead to understanding of possible changes needed to get better crystals.

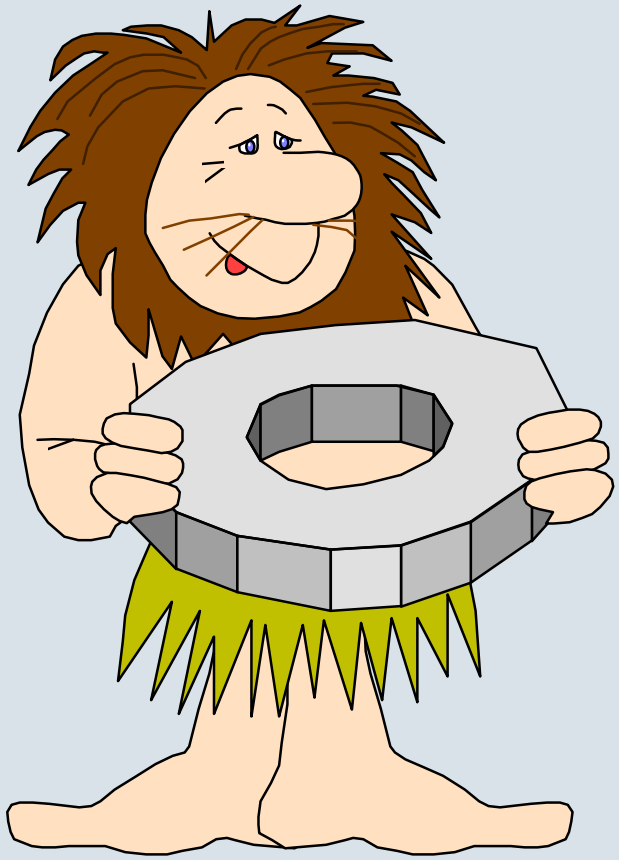
Solidified oil

Dendritic

Microcrystalline

Powder

Key Factors to Good Crystals



- Solvent
- Nucleation
- Mechanics
- Time

- Patience, Patience
- Art Form

- Patience, Patience

Crystal Evaluation

- Evaluation starts at the microscope. Do they look crystalline and single under cross polarized light?
- Are all the crystals uniform in shape?
- Do they become less defined over time, loss of solvent?
- Mount and evaluate the crystal on the diffractometer. Requires about 20 - 30 minutes, less if it does not diffract at all.

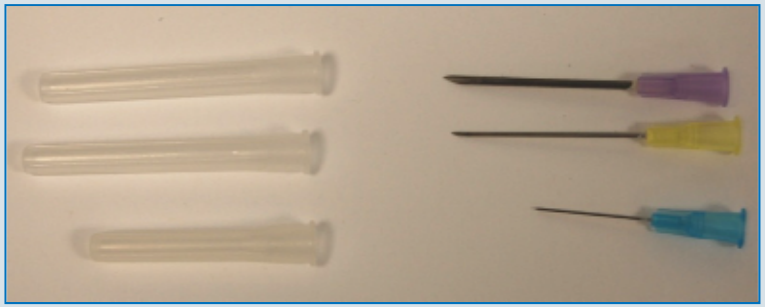
Manipulation Tools for Crystals

- Varies with crystallographer and type of crystals.
- Have a variety of tools so you can choose the appropriate one for the occasion.

You can purchase expensive tools to do the job.

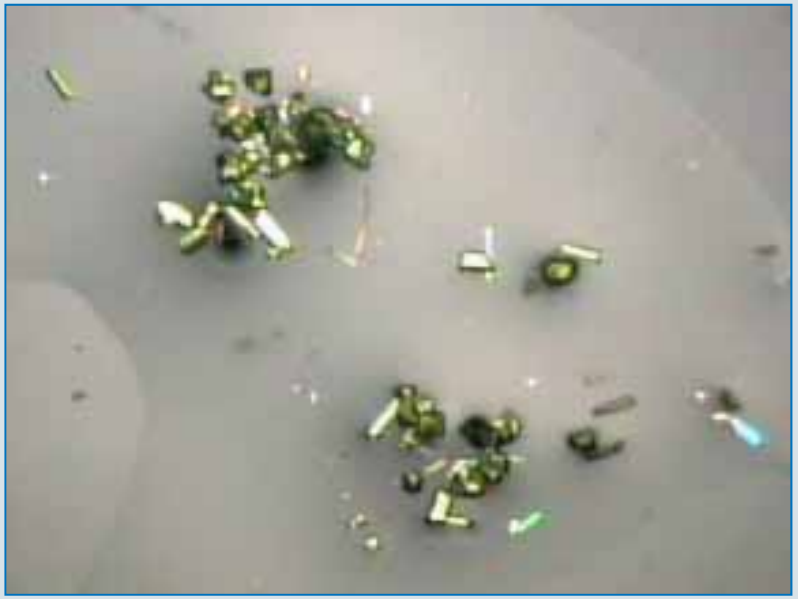
Manipulation Tools – Common

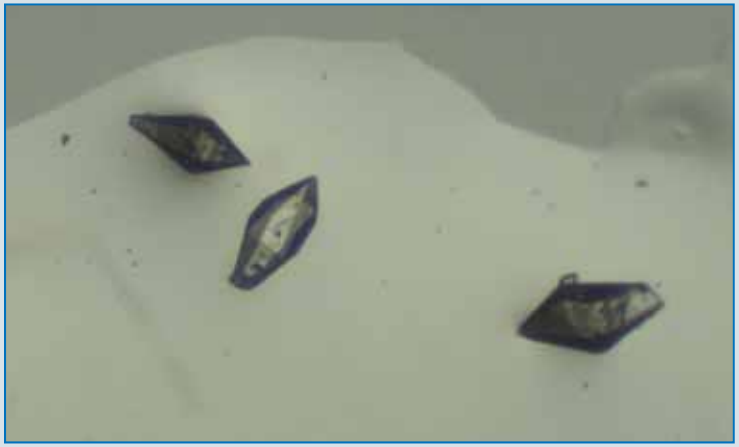
- Good standard probe tools from biology work well.
- Some like to use dental tools, can get them free after the dentist is done with them.
- Some use glass fibers or needles.



What is a good crystal?

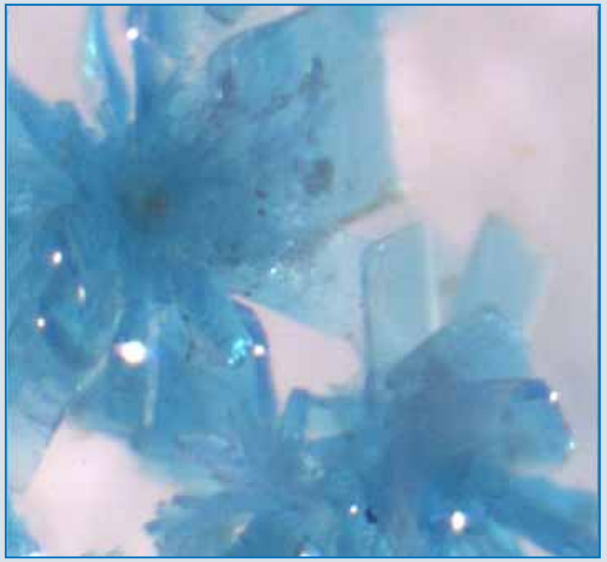
- Well defined crystalline shape often results in good crystals.
- Free of cracks, other crystal fragments or other observable defects.
- Sparkle or clear
- Uniform in color
- One that works!
- Gives good spots and spot shapes.





Manipulating and Cutting Crystals

- Cut the crystals to size. Use a new blade, nice sharp edge.
- When cutting, if they crumble, they are not likely single.
- Use of a scalpel or X-Acto knife works well.
- Razor blades are some people's preference.
- ❖ A Sapphire knife is expensive, but works really well for small or fragile crystals.



Where to Manipulate the Crystal

Often done in an oil or the solvent it was grown in.

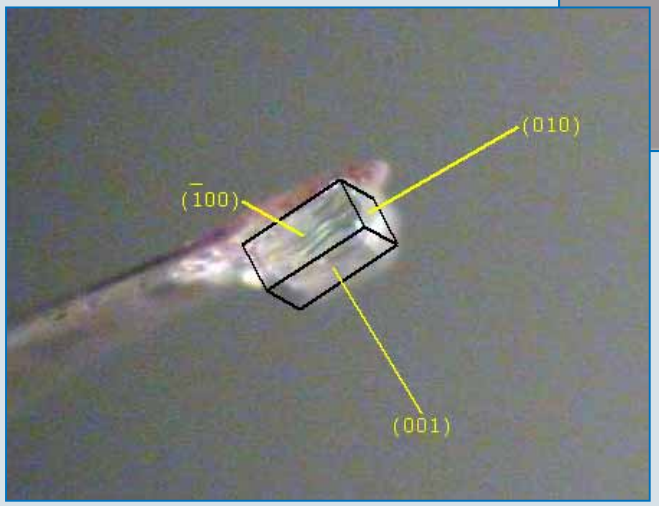
- Paratone oil
- Mineral oil
- Greases, normal and fluorinated
- UV curable epoxy

Considerations for choice

- Are you running low temperature?
- Does the compound dissolve?
- Radiation using?
- Do you need to cut the crystals?
- Does the crystal degrade, or is it air sensitive?

Suggestions for Mounting

- Try not to create flags with fibers.
- Micro Mounts – place on inner curved side (a must for SMART X2S system).
- Use as little grease, oil, or glue as possible.
- Try not to orient in direction of mount.



Mounts and Goniometers

Various mount types depend on the instrument and goniometer you are using.

Gluing for Room Temperature

- Super Glue – Caution: acetone soluble compounds. Need to work quickly.
- Epoxy: 3-5 minute epoxy, good for air sensitive compounds, generally higher background.
- Bruker AXS new UV glue: Low background, does not adhere till UV, but water soluble compounds can be problematic.

↗ Can do this for Low Temperature Collection, but cleavage can occur.

Audience Poll 3

Please use your mouse to answer the question to the right of your screen:

The most important factor in single crystal growth is:

- Solvent
- Nucleation
- Patience
- Tools
- Good looks

Getting Crystal on Fiber or Loop

All crystallographers have their own method to accomplish this task. Some methods may work well for you and others may not work as well. The following two methods work for most students at Michigan State University, running low temperature data collections.

- **Slide method**
  Place the crystals in a small amount of Paratone oil. Slide the crystal out of the oil until the crystal prefers to stay on the fiber. This is used well for large crystals mounted on fibers.

- **Pick up method**
  Try and put enough oil on the fiber that the crystal comes with the oil. This method means you should try to remove excess oil before placing on diffractometer. Good for loops. Slide method also works for loops with small crystals.

Poll 3 Results

Mounting to Loop in Solvent

Mounting on a Fiber

Mounting UV Curable

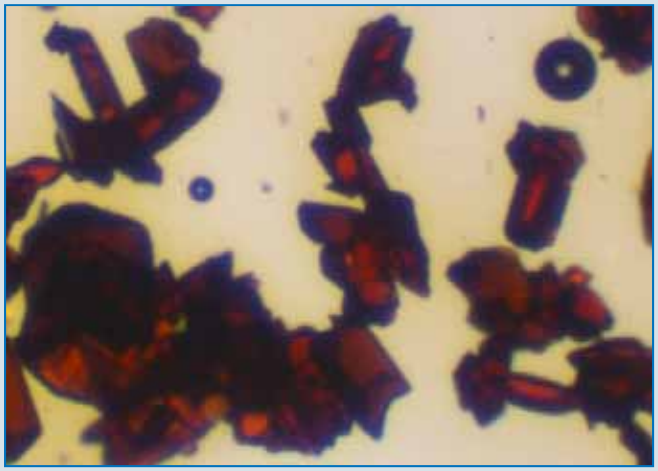
Limitations to Crystallography

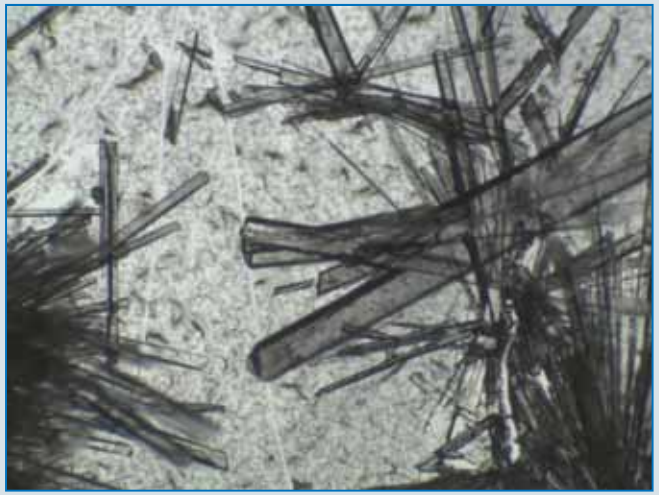
- Requires single crystals.
- Crystal quality governs quality of results obtained.
- Only one crystal of the bulk material.
- Crystallographer to handle non-routine crystals (twinned, non-commensurate, etc.) and difficult solutions.

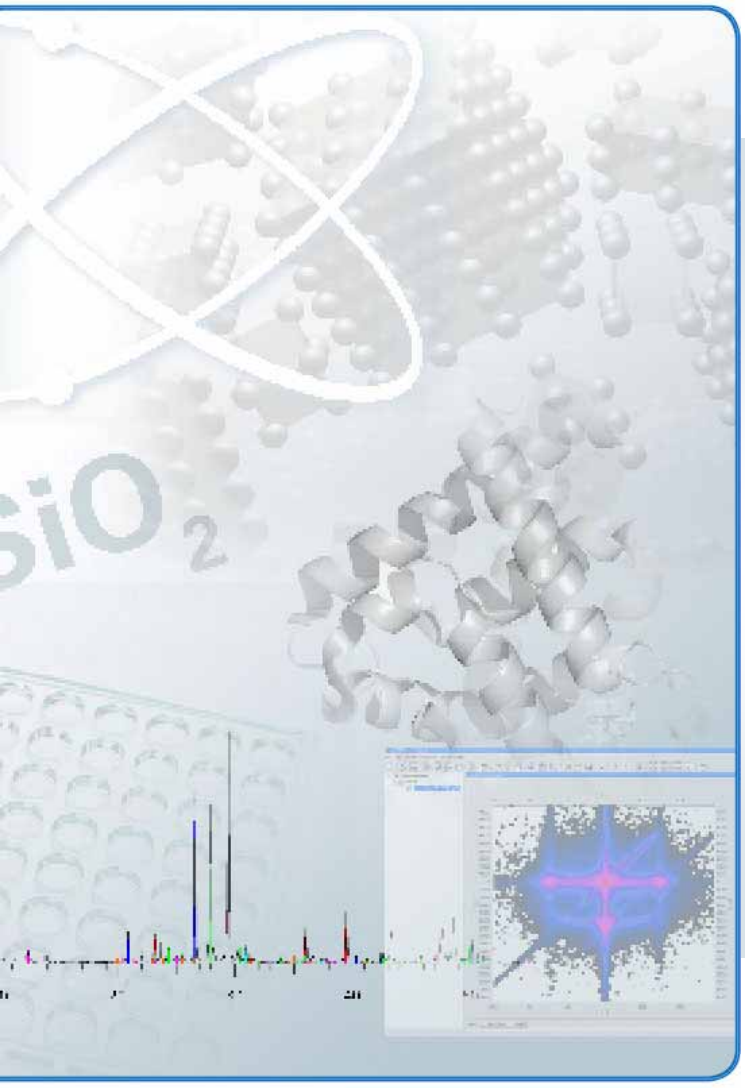
Acknowledgements

- All Chemists and Crystallographers I have known and worked with over the last 25 years.

- Particular Crystallographers who influenced my decision to be a crystallographer:
  - Prof. Alan Pinkerton
  - Dr. Larry Favello
  - Dr. Joe Reibenspies
  - Dr. Lee Daniels



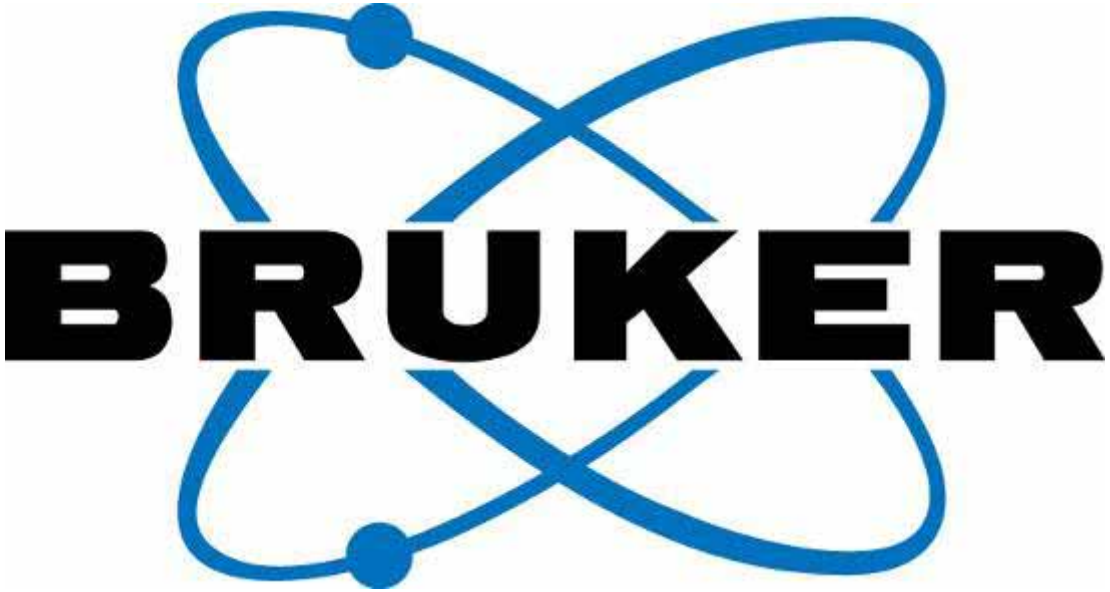




Any Questions?

Please type any questions you may have in the Q&A panel and then

click Send.



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