These crystals will make your crystallographer happy

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These Crystals Will Make Your Crystallographer Happy

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LOUGHBOURGH UNIVERSITY
Overview

- Roles
- Crystals - Desirable features
- Methods of Crystallisation
- Case Studies.
What’s Your Role?

- Synthetic Chemist
- Synthetic Chemist/Crystallographer
- Crystallographer advising synthetic Chemists
Crystal growth

Work with nature – but stack the odds in your favour.

Crystallisation occurs in two steps:
  • Nucleation
  • Growth

Nucleation can occur at:
  • A seed crystal
  • Particle of dust
  • Imperfection in the vessel
Considerations when growing a crystal

• Solubility of compound
• Amount of compound needed to grow a crystal
• Location and conditions of crystal growth
• Size of crystal required for diffraction analysis
• It is not an exact science – may need to try many methods/conditions
Desirable Crystal Features

- Flat faces
- Straight edges
- Sharp vertices
- Optical clarity
- No re-entrant angles
- Extinguish plane polarised light.
Some Decent crystals

http://www.nature.com/nchem/journal/v5/n10/images/nchem.1730-f2.jpg
Some Decent crystals

http://www.nature.com/nmat/journal/v7/n7/images/nmat2211-f1.jpg
Some Decent crystals

Optical Inspection – Take a proper look

- Every lab should have a jewellers lupe for initial inspection. 20-30X magnification.
- Then check under a polarising microscope.
Polarising Microscope
Desirable Crystals

- The large flat crystal shows well defined, faces with minimal imperfections.
- When rotated 90° under polarised light, the crystal extinguishes the light.
- This is a preliminary indication that a crystal is of good quality.
Crystal rotated under polarised light
Undesirable Crystals

- Crystals grown via the evaporation method:
- The crystals are of decent quality, however they’re covered in a fine crust, a result of the evaporation process.
- Also dust and a fibre have contaminated the sample due to the open lid setup.
Glassware

Want a small number of large crystals not many small ones.

- Crystals have flat faces, so use glassware with flat surfaces.
- A round-bottomed flask/Schlenk tube is not the best choice unless sample is unstable.
- Sample vials have flat bottoms – a better choice if air stable.
- Rinse sample vials before use – the cardboard boxes they come in can shed paper fibres which act as nucleation sites.
- Use new or annealed glassware, not vessels that have been washed up many times and have micro-scratches which also act as nucleation sites.
- Silicone coatings can be applied to reduce nucleation sites.
Solvent choice

- Use pure solvents, not mixtures like ‘40-60 petrol’.

- Evaporation and slow cooling may be the only choices for compounds soluble only in non-polar solvents.

- Solvents with H-bonding ability may promote crystallisation of compounds with H-bond donors/acceptors by solvate formation.

- Avoid solvents with very long alkyl chains.
Amount of compound required

- Typically 5-20mg

- An NMR sample is a great place to start:
  - It is the best solution you’re likely to prepare
  - NEVER throw away your NMR sample if you may need the crystal structure

- NMR solution preparation:
  1. Use high purity solvent (right)
  2. Filter solution to remove impurities
  3. Use new/clean glassware

  e.g. 99.5% purity Acetone
Crystal growth conditions

Create an environment which changes very slowly over time

Factors affecting size and quality of crystals obtained:
• Solvents/solutions
• Method
• Nucleation sites available
• Vibrational disturbances
• Temperature and light conditions/ variations
• Rate of change of conditions
Common crystallisation techniques

- Slow evaporation
- Vapour diffusion
- Liquid diffusion
- Liquid diffusion (H-tube)
- Very slow cooling
- Sublimation

See also Peter Müllers article: Crystallography Reviews, (2009), 15, 57-83.
Slow evaporation

Evaporation of solvent

Crystal Formation
Slow evaporation
Slow evaporation Pros and Cons

Pros:
- Easy to set up
- Often works

Cons:
- Volume of solution decreases, so crystals can dry out, form crusts or desolvate
Vapour diffusion

Air tight lid

Outer Container

Inner Container

Anti-Solvent

Solution

Solvent diffusion

Crystal Formation at Solvent Interface
Vapour diffusion
Vapour diffusion Pros and Cons

Pros:
• Volume increases so crystals don’t dry out, form crusts, or desolvate

Cons:
• None
Liquid diffusion

Air tight lid

Container

2\textsuperscript{nd} Solution/Antisolvent

Solution 1

Crystal Formation at Solvent Interface
Liquid diffusion

Put a lid on!
Case Study 1 – An Arene-Ru salt.

\[ [(\eta^6-p-cy)\text{Ru}(\eta^6:\eta^6-C_{16}H_{16})\text{Ru}(\eta^6-C_6\text{Me}_6)][\text{BF}_4]_4 \] - No decent crystals.

All-in-One Liquid diffusion/Ion Exchange/Crystallisation with NaBPh₄ gave:

\[ [(\eta^6-p-cy)\text{Ru}(\eta^6:\eta^6-C_{16}H_{16})\text{Ru}(\eta^6-C_6\text{Me}_6)][\text{BF}_4]_3[\text{BPh}_4] \]
Case Study 1 – An Arene-Ru salt.

\[ [(\eta^6-p\text{-cy})\text{Ru}(\eta^6:\eta^6 - \text{C}_{16}\text{H}_{16})\text{Ru}(\eta^6-\text{C}_6\text{Me}_6)]\text{[BF}_4\text{]}_3\text{[BPh}_4\text{]} \]
Liquid diffusion (H-Tube)

- Air tight lid
- H-tube
- Solution Mixing
- Solvent Bridge for Diffusion

Solution 1

Solution 2

Crystal Formation at Interface
Liquid diffusion (H-Tube) Pros and Cons

Pros:
• Ideal for growing crystals that are very insoluble i.e. can’t be recrystallized.
• Diffusion dictates that reaction/crystallisation will be slow (a good thing)

Cons:
• None
Liquid diffusion (H-Tube)

Put Parafilm over the tops
Very slow cooling

- Air Tight Lid
- Sample Tube
- Warm Saturated Solution
- Hot Water
- Dewar Flask
- Aluminium Foil
Schlenk tube with cold finger for sublimation crystallisation.
Case Study 2. A pyrene.

A good example to illustrate problems and routes to improvement.

Optically imperfect.
Some hairline cracks.
Striations under polarised light.
Turns out to be twinned.
Case Study 2. A pyrene.

The structure was determined.

By-product

Hexane of crystallisation - at least a pure solvent was used.
Case Study 2. A pyrene.

What advice can we give to avoid the twinning & improve the result?

Need to change something/anything.
1. Run a column to remove the by-product impurity.
2. Switch from hexane (C$_6$) to pentane (C$_5$) or heptane (C$_7$), etc.
Other crystallisation techniques

• Thermal gradient
• Counterions or ionisation
• Co-crystals and clathrate
• Reactant diffusion
• Melting and recrystallization
• Similar crystal seeding
• Gel crystallisation
• Parr bomb for MOFs etc.
Be aware of the factors that govern crystallisation.

Use knowledge of the compound to guide choice of crystallisation method and conditions.

Try as many methods as possible.

Learn from imperfect results to achieve better outcomes.
Summary

- Be aware of the factors that govern crystallisation.
- Use knowledge of the compound to guide choice of crystallisation method and conditions.
- Try as many methods as possible.
- Learn from imperfect results to achieve better outcomes.
- If all else fails - grow a beard!

From: A Book of BEARDS By Justin James Muir