These crystals will make your crystallographer happy

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These Crystals Will Make Your Crystallographer Happy

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LOUGHBOROUGH 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.

√ OK

X Twinned
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

Loose fitting lid

Container

Solution

Evaporation of solvent

Crystal Formation
Slow evaporation
**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

Solvent diffusion

Outer Container

Inner Container

Anti-Solvent

Solution

Crystal Formation at Solvent Interface

BC A 2016
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\(^{nd}\) Solution/Antisolvent → Solution 1 → Crystal Formation at Solvent Interface
Liquid diffusion

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

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

All-in-One Liquid diffusion/Ion Exchange/Crystallisation with NaBPh$_4$ gave:

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

\[ ((\eta^6-p\text{-cy})\text{Ru}(\eta^6:\eta^6 - C_{16}H_{16})\text{Ru}(\eta^6-C_{6}Me_{6}))][BF_4]_3[BPh_4] \]
Liquid diffusion (H-Tube)

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

Solution Mixing

Solution 1

Solution 2

Crystal Formation at Interface

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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
Sublimation

Cold Finger

Schlenk Tube

Cold Water In
Water Out
Vacuum

Crystal Formation on Surface of Cold Finger

Dry Compound

Water/Oil Bath for Heating
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.
Tums 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 (C₆) to pentane (C₅) or heptane (C₇), etc.

Asymmetric unit.
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.
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.
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