These crystals will make your crystallographer happy

This item was submitted to Loughborough University's Institutional Repository by the/an author.

**Citation:** ELSEGOOD, M. and CARPENTER-WARREN, C., 2016. These crystals will make your crystallographer happy. IN: 2016 BCA Spring Meeting, University of Nottingham, Nottingham, Great Britain, 4-7 April 2016.

**Additional Information:**
- This item is a conference presentation.

**Metadata Record:** [https://dspace.lboro.ac.uk/2134/21243](https://dspace.lboro.ac.uk/2134/21243)

**Version:** Accepted for publication

**Publisher:** British Crystallographic Association

**Rights:** This work is made available according to the conditions of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) licence. Full details of this licence are available at: [https://creativecommons.org/licenses/by-nc-nd/4.0/](https://creativecommons.org/licenses/by-nc-nd/4.0/)

Please cite the published version.
These Crystals Will Make Your Crystallographer Happy

Dr. Mark R. J. ELSEGOOD and Cameron L. CARPENTER-WARREN

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 samples 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
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

Container → Solution

Loose fitting lid

Evaporation of solvent

Crystal Formation

BCA 2016
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

Solvent diffusion

Solution

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

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

\[(\eta^6\text{-p-cy})\text{Ru}(\eta^6\text{-}C_{16}H_{16})\text{Ru}(\eta^6\text{-}C_6\text{Me}_6)][BF_4]_4\] - No decent crystals.

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

\[
\[(\eta^6\text{-p-cy})\text{Ru}(\eta^6\text{-}C_{16}H_{16})\text{Ru}(\eta^6\text{-}C_6\text{Me}_6)][BF_4]_3[BPh_4]\]
Case Study 1 – An Arene-Ru salt.

$$\left[(\eta^6-p\text{-cy})\text{Ru}(\eta^6:\eta^6 - C_{16}H_{16})\text{Ru}(\eta^6-C_6\text{Me}_6)\right][\text{BF}_4]_3[\text{BPh}_4]$$
Liquid diffusion (H-Tube)

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

Dewar Flask

Hot Water

Aluminium Foil
Sublimation

- Schlenk Tube
- Cold Finger
- 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.
- 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 (C₆) to pentane (C₅) or heptane (C₇), 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.
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