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These Crystals Will Make Your Crystallographer Happy

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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

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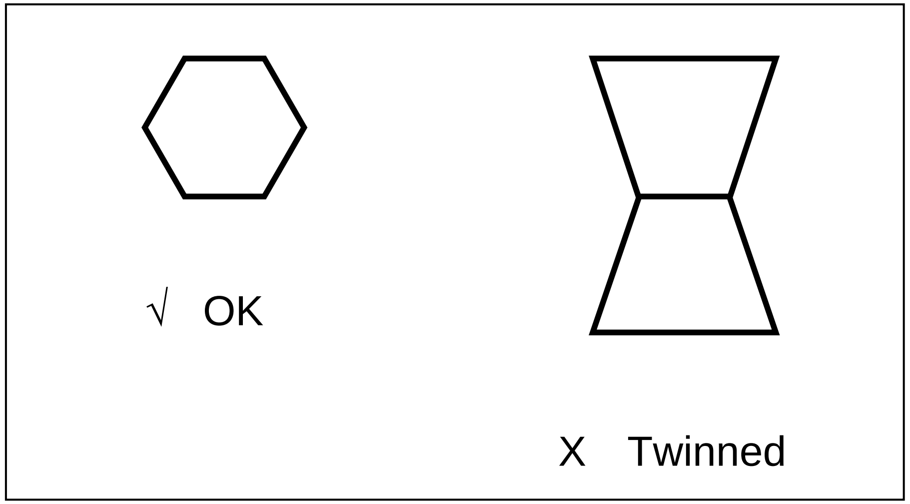
Considerations when growing a crystal

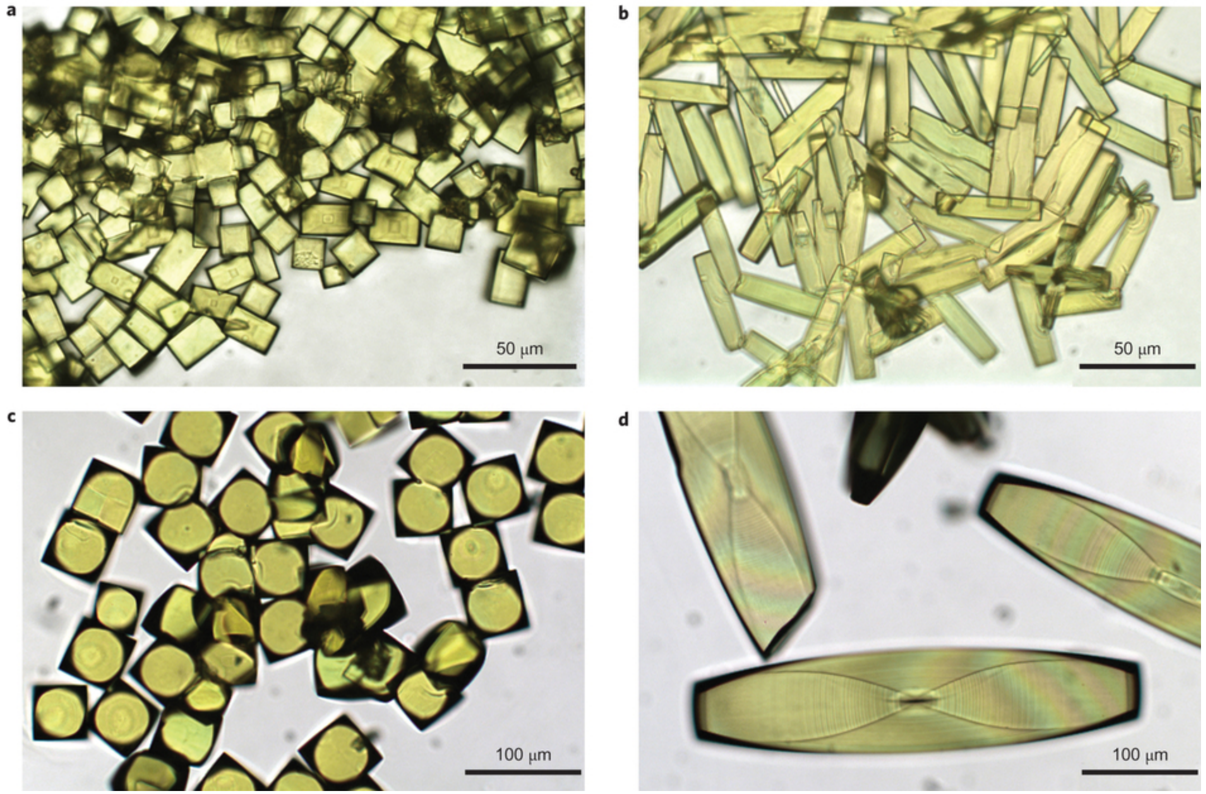
- Solubility of compound
- Amount of compound needed to grow a crystal
- Location and conditions of crystal growth
- Size of crystal required for diffraction analysis
- It is not an exact science – may need to try many methods/conditions

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

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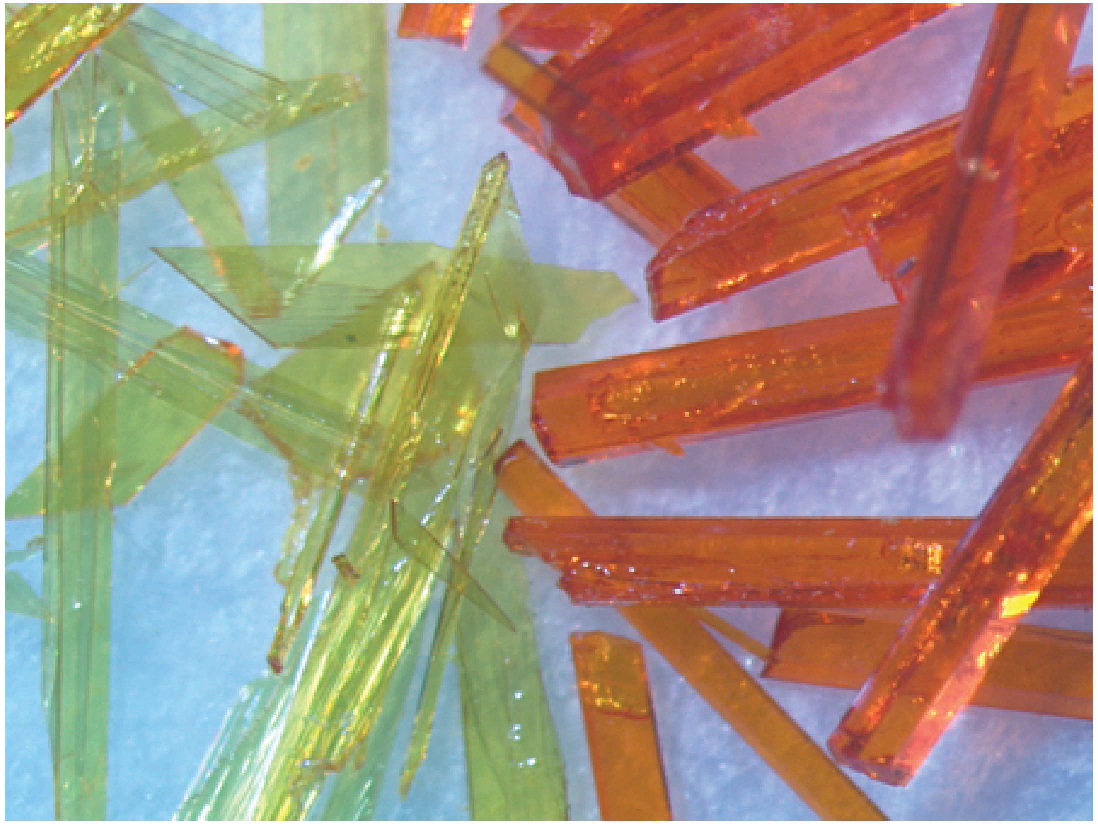
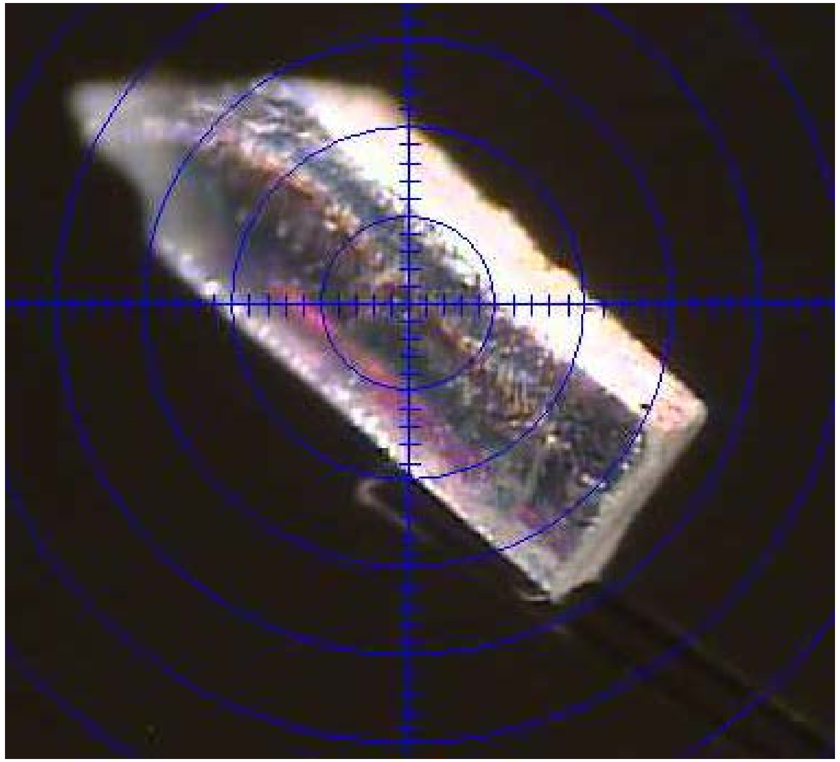
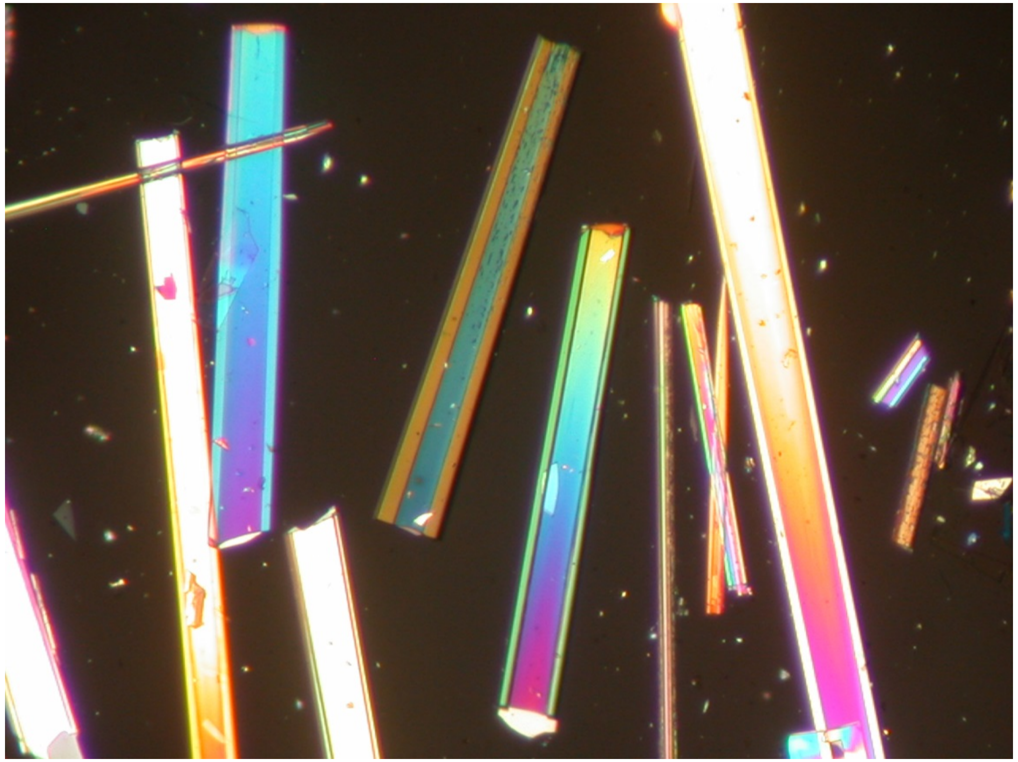


http://www.nature.com/nmat/journal/v7/n7/images/nmat2211-f1.jpg

Some Decent crystals



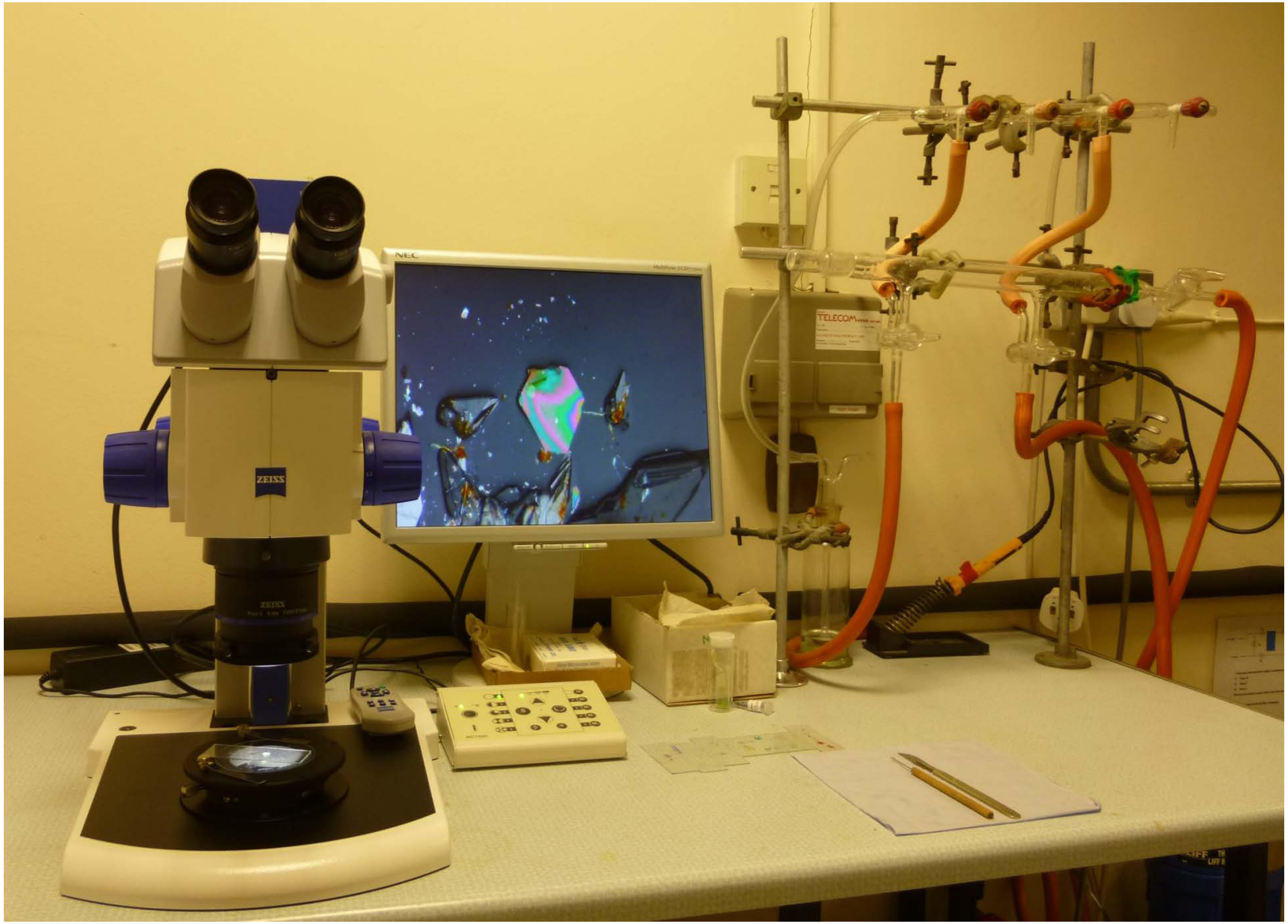


http://college.wfu.edu/chemistry/research/xray/wp-content/uploads/DSCN2917.jpg

Optical Inspection – Take a proper look

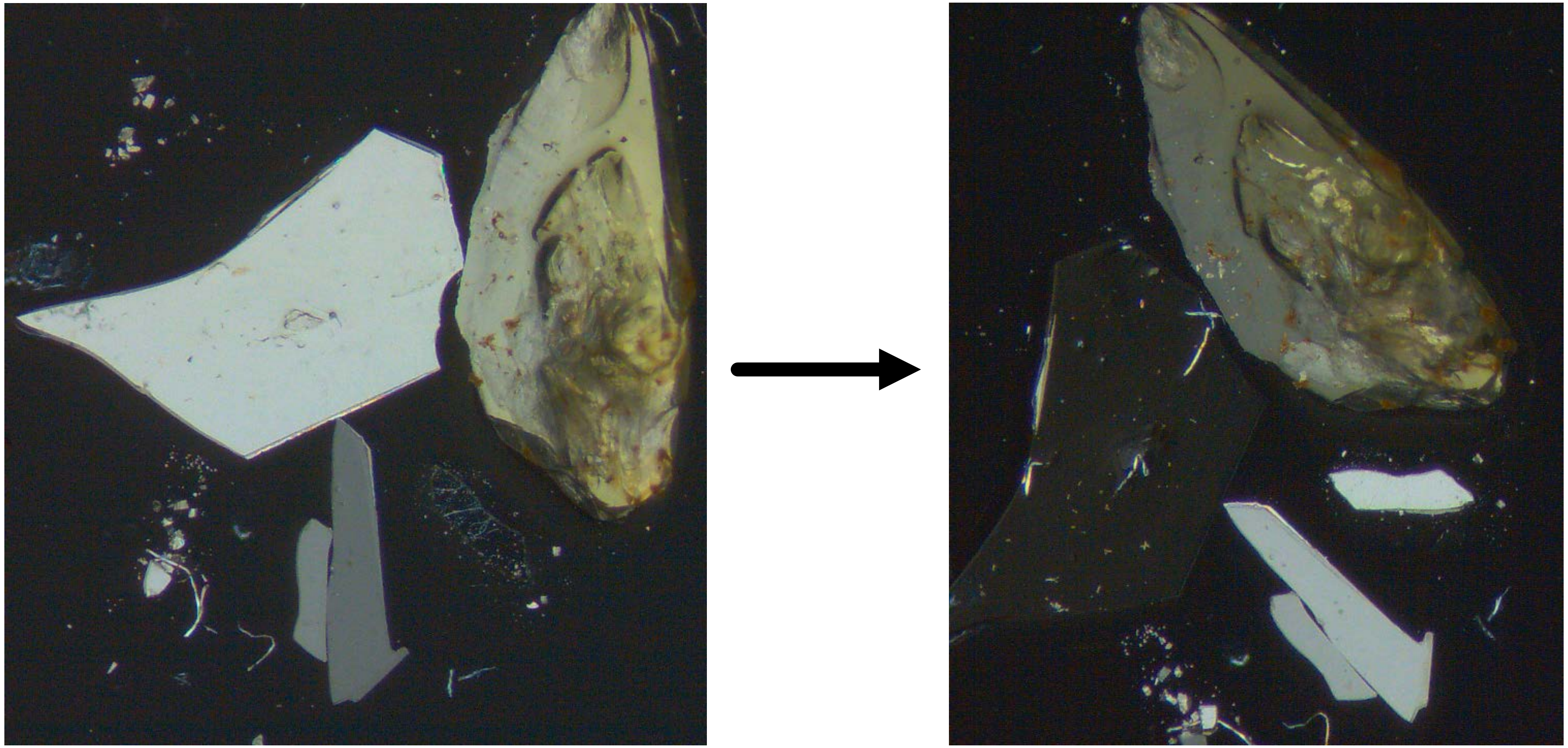
- Every lab should have a jewellers lupe for initial inspection. 20-30X magnification.
- Then check under a polarising microscope.

Polarising Microscope

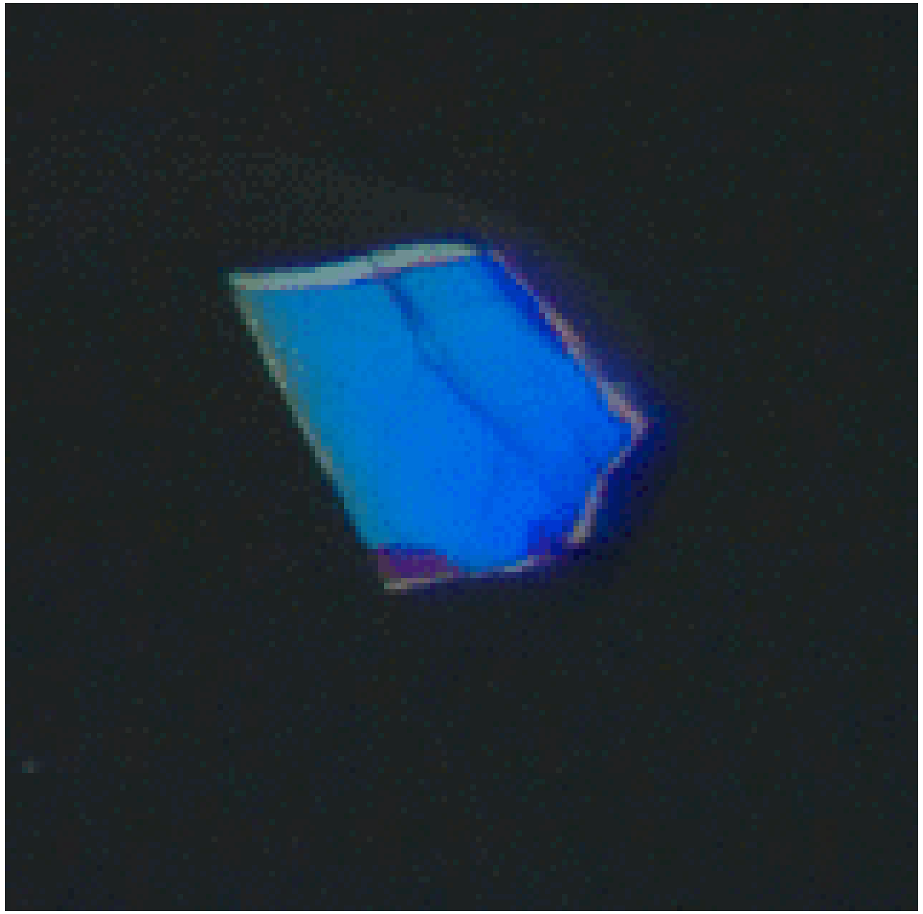


Desirable Crystals

- 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

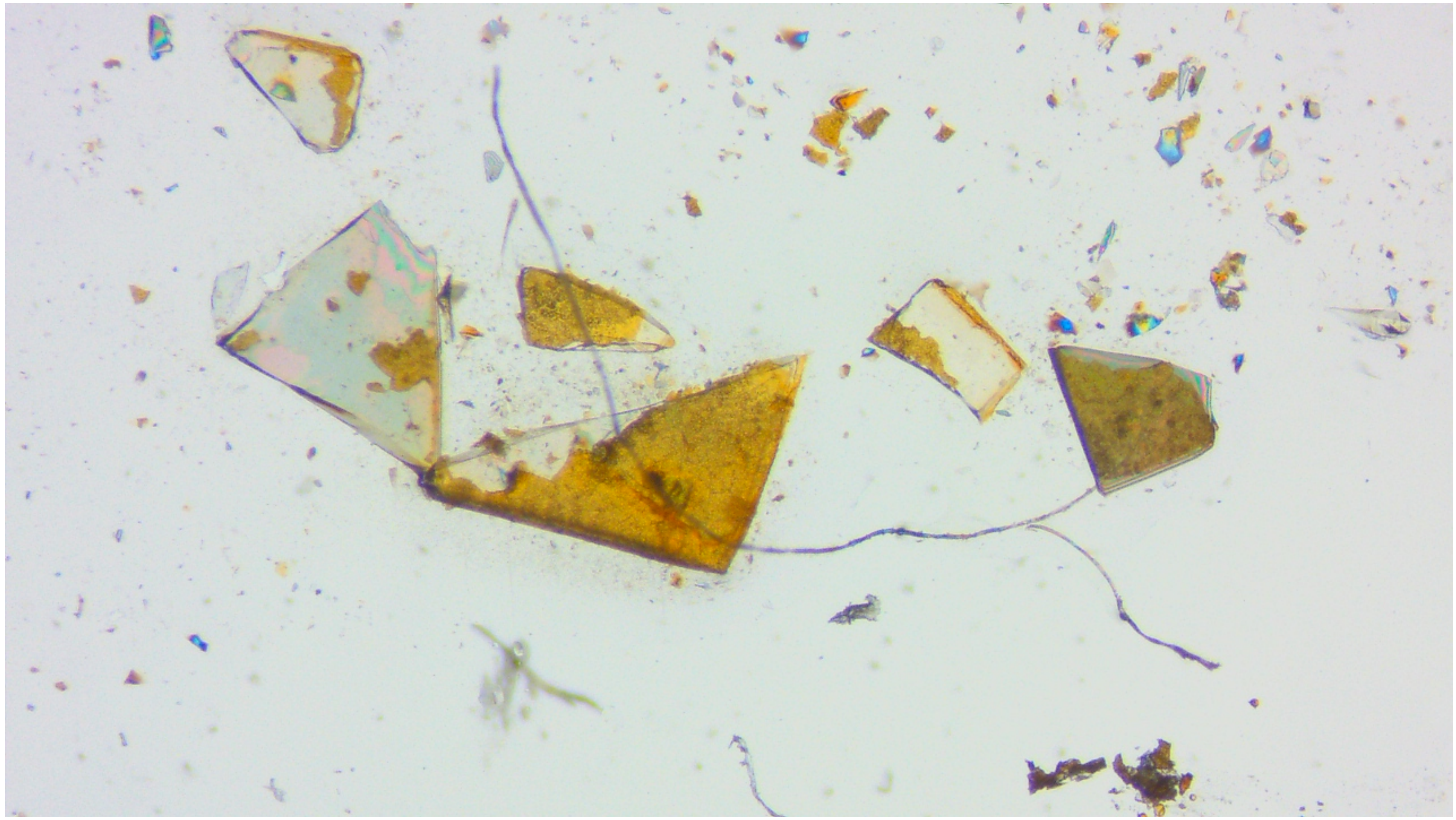


Undesirable Crystals

- 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

Crystal growth conditions

Create an environment which changes very slowly over time

Factors affecting size and quality of crystals obtained:

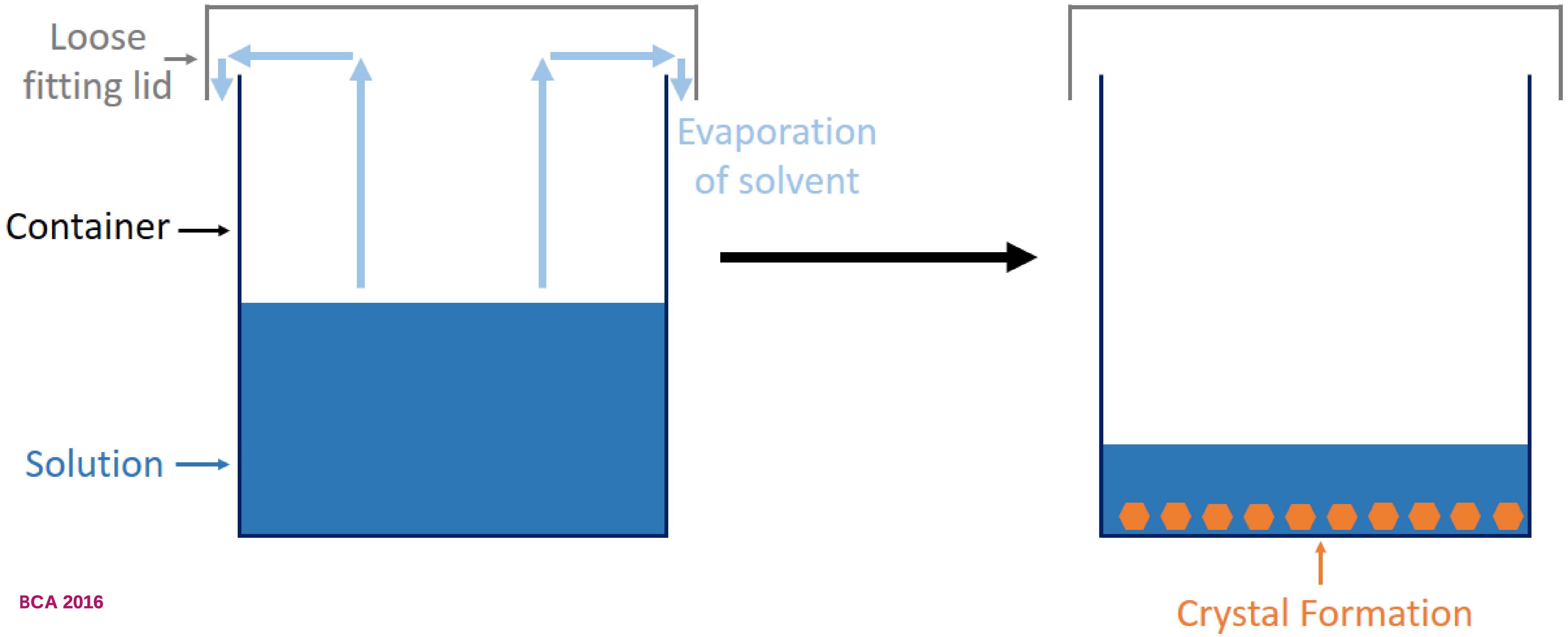
- Solvents/solutions
- Method
- Nucleation sites available
- Vibrational disturbances
- Temperature and light conditions/variations
- Rate of change of conditions

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



Slow evaporation

Slow evaporation Pros and Cons

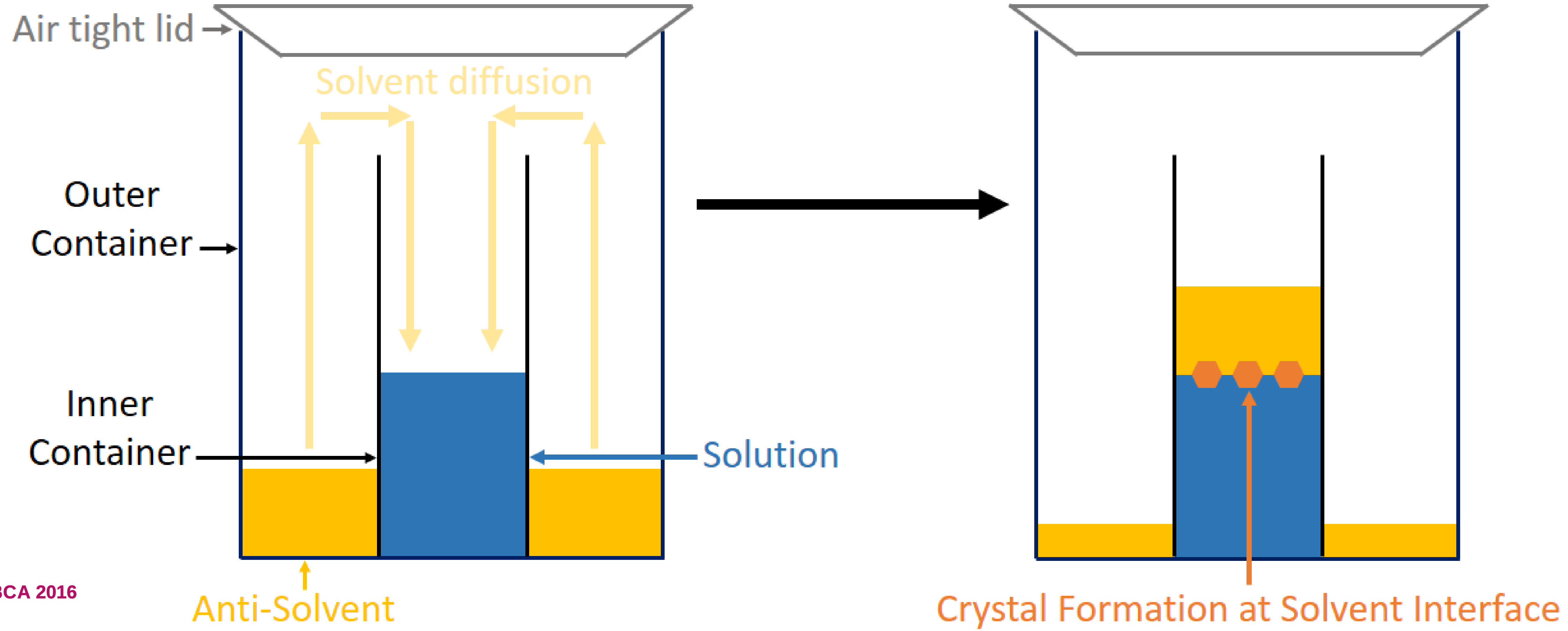
Pros:

- Easy to set up
- Often works

Cons:

- Volume of solution decreases, so crystals can dry out, form crusts or desolvate

Vapour diffusion



Vapour diffusion

Vapour diffusion Pros and Cons

Pros:

- Volume increases so crystals don’t dry out, form crusts, or desolvate

Cons:

- None

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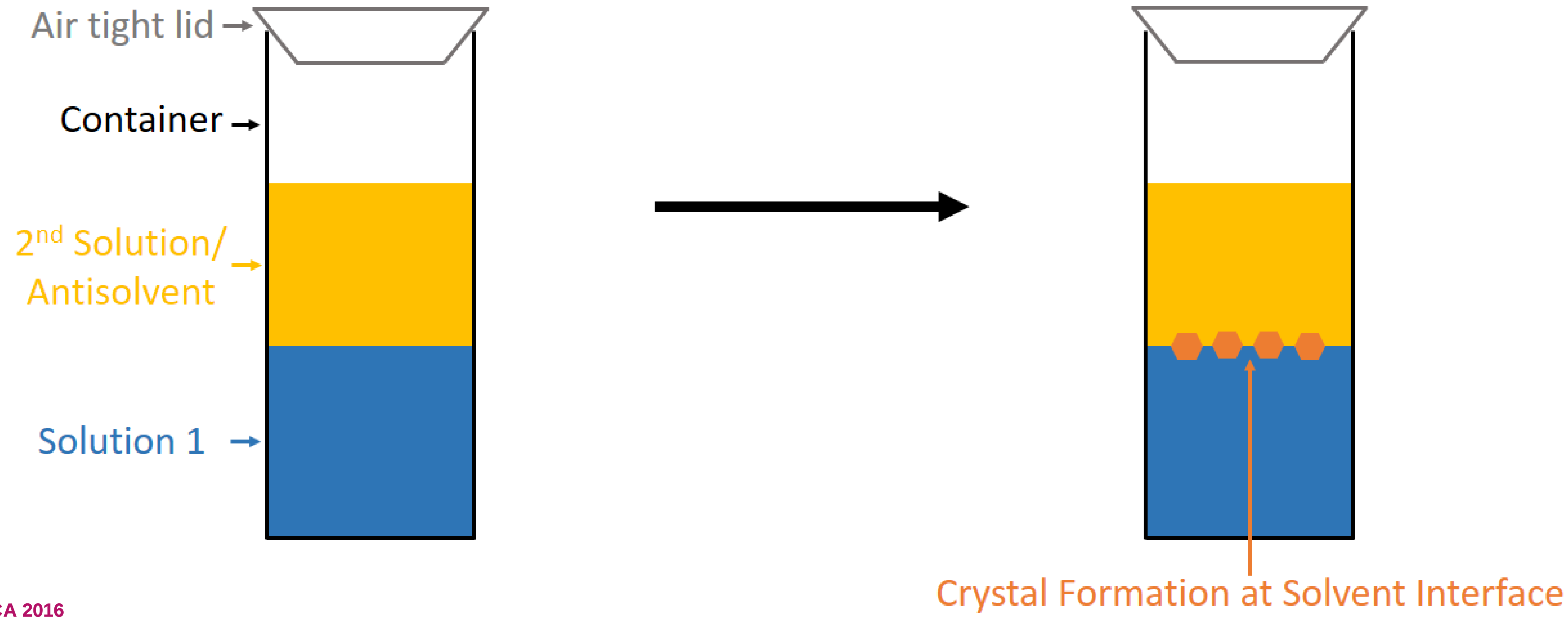
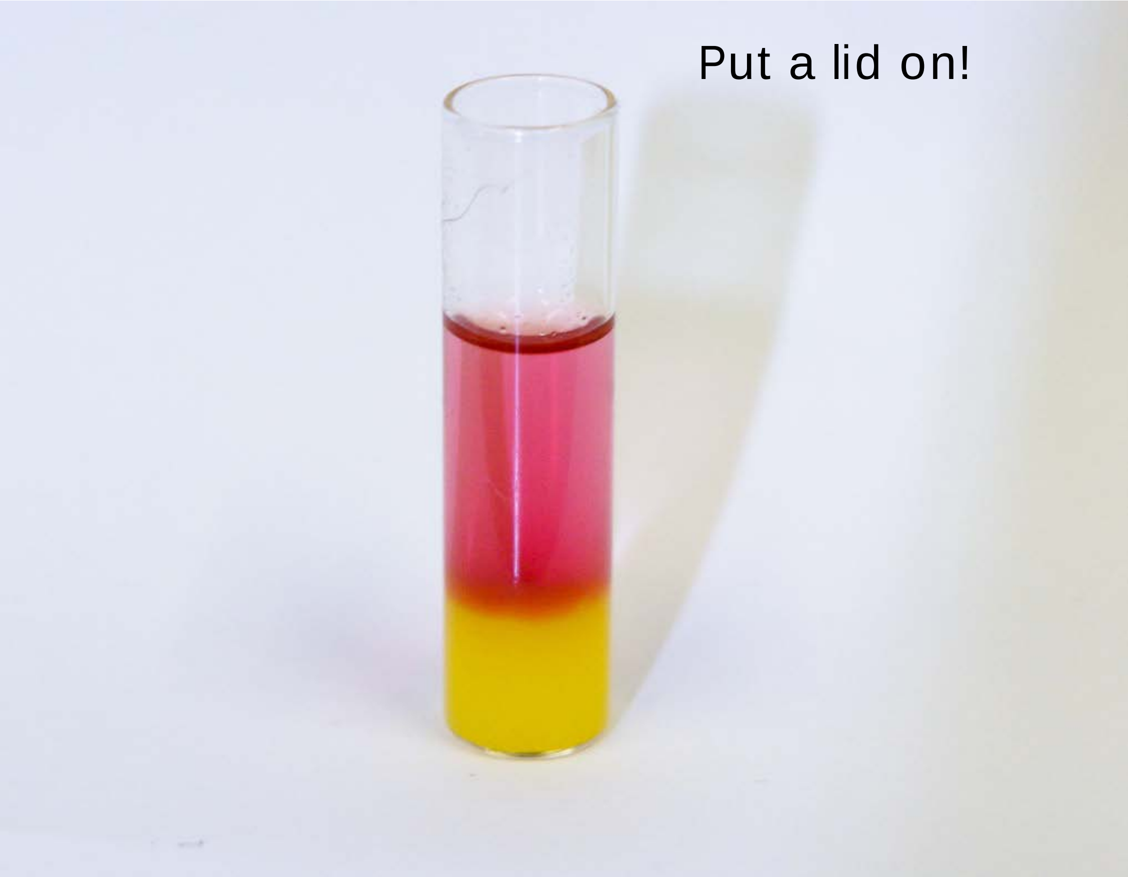
Liquid diffusion



Liquid diffusion



Put a lid on!

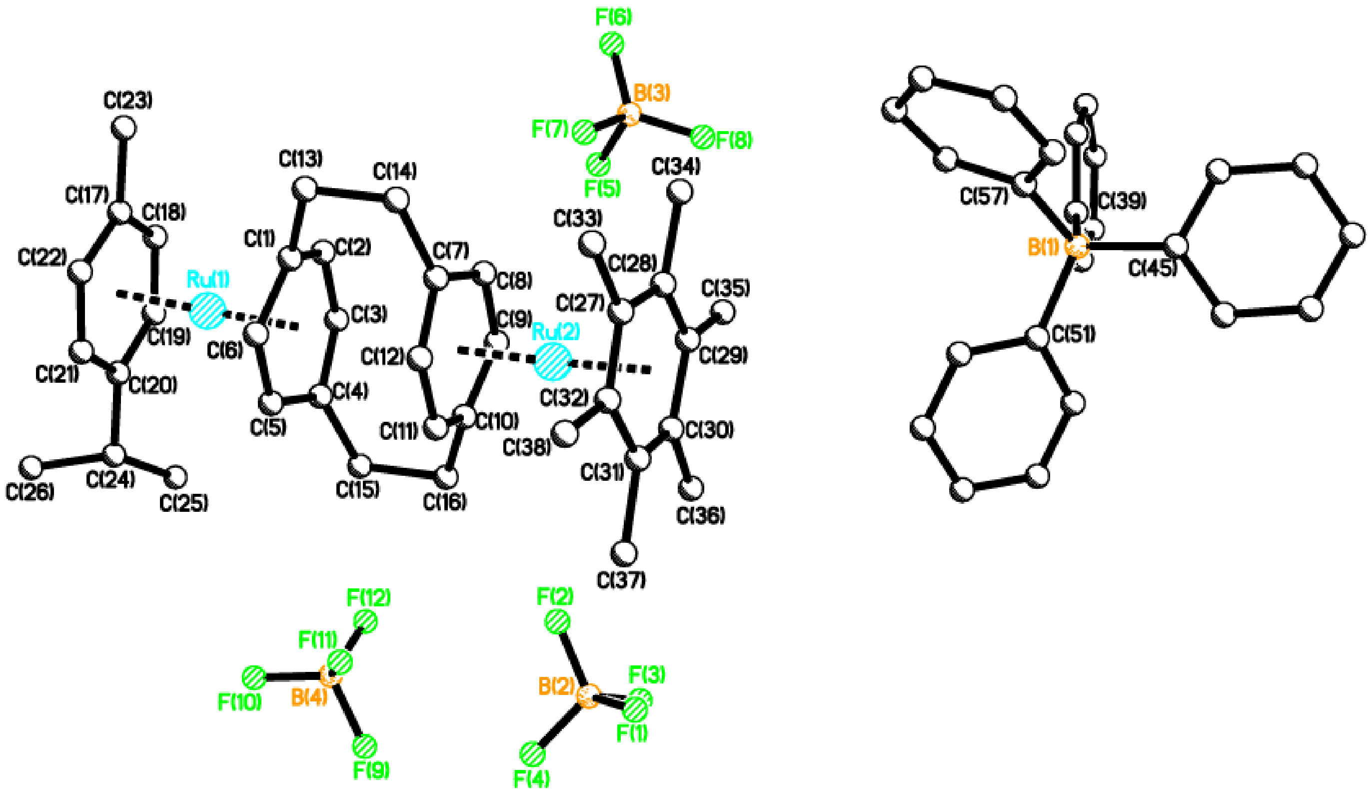
Case Study 1 – An Arene-Ru salt.

[(η^6-*p*-cy)Ru(η^6:η^6-$C_{16}H_{16}$)Ru(η^6-C_6Me_6)][BF_4]$_4$ - No decent crystals.

All-in-One Liquid diffusion/Ion Exchange/Crystallisation with $NaBPh_4$ gave:

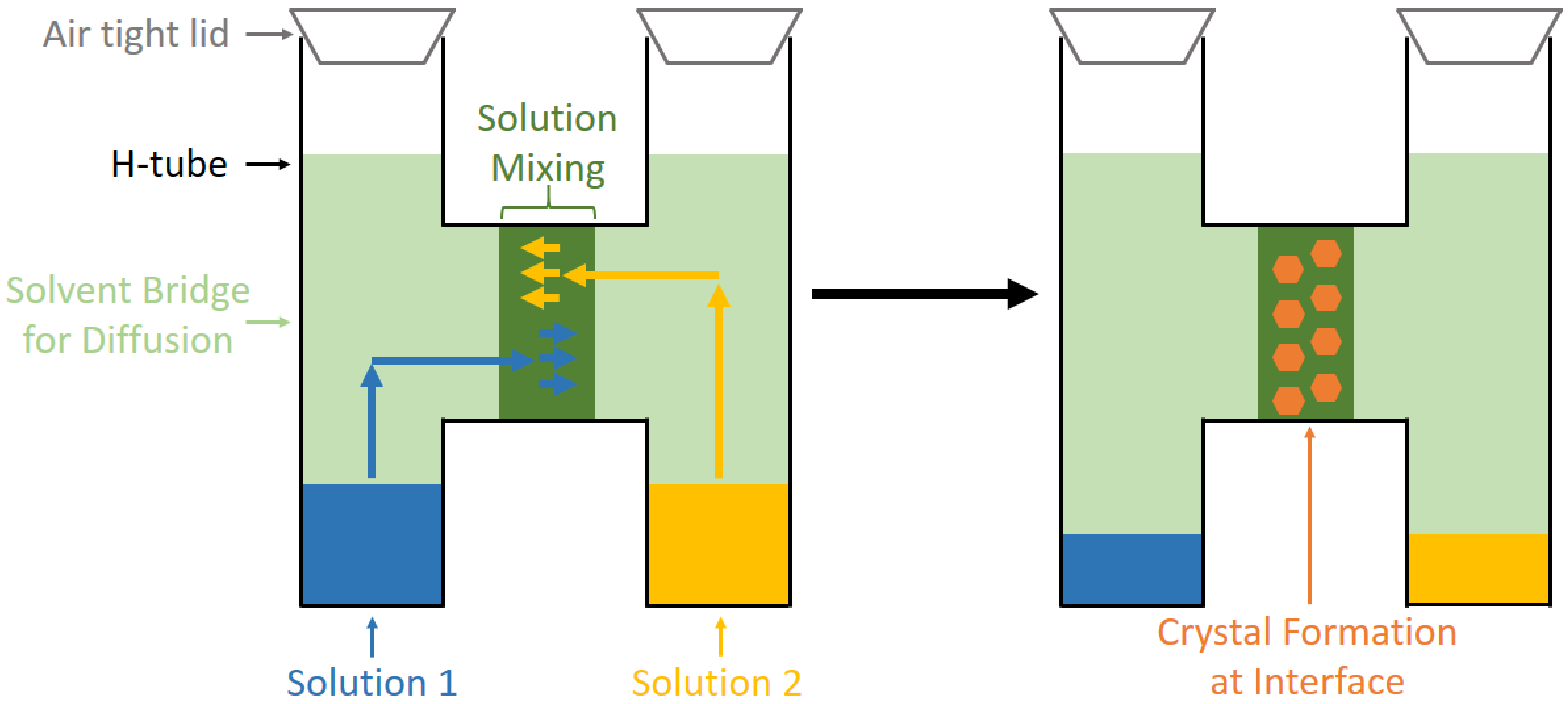
[(η^6-*p*-cy)Ru(η^6:η^6 - $C_{16}H_{16}$)Ru(η^6-C_6Me_6)][BF_4]$_3$[BPh_4]

Case Study 1 – An Arene-Ru salt.



$[(\eta^6\text{-}p\text{-cy})Ru(\eta^6{:}\eta^6 - C_{16}H_{16})Ru(\eta^6\text{-}C_6Me_6)][BF_4]_3[BPh_4]$

Liquid diffusion (H-Tube)



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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

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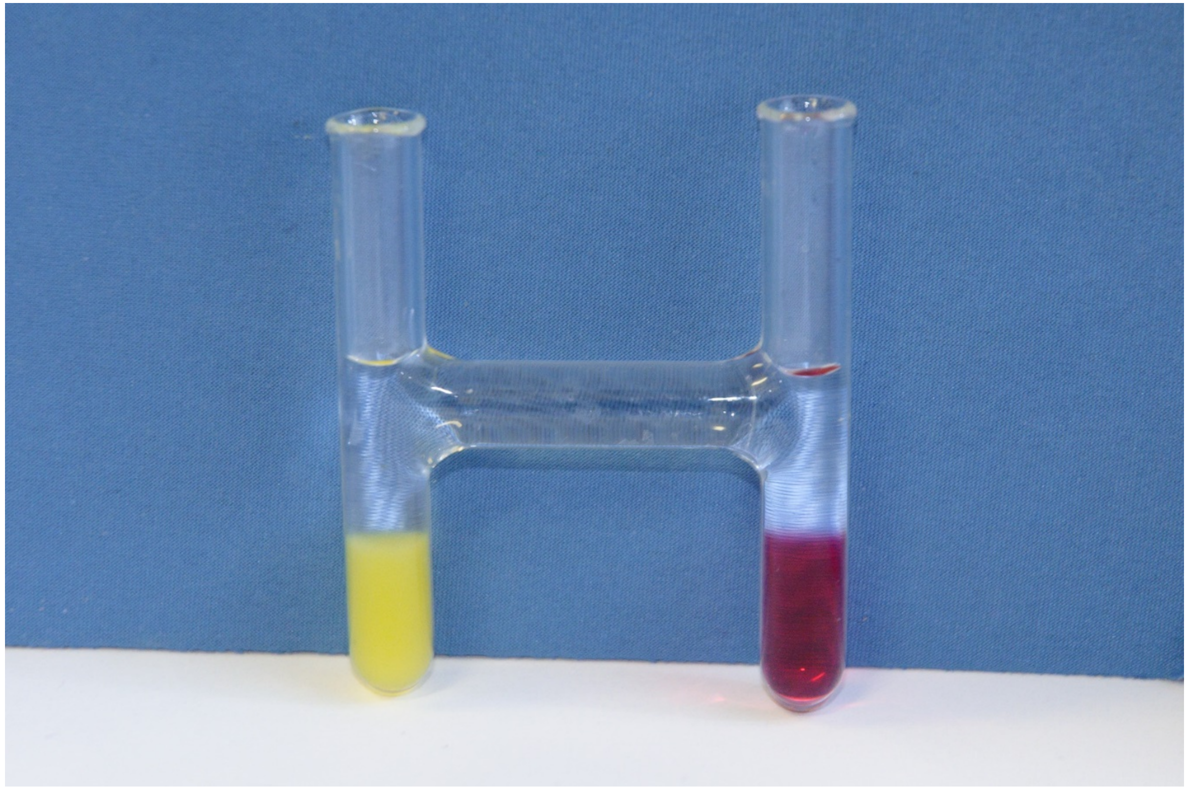
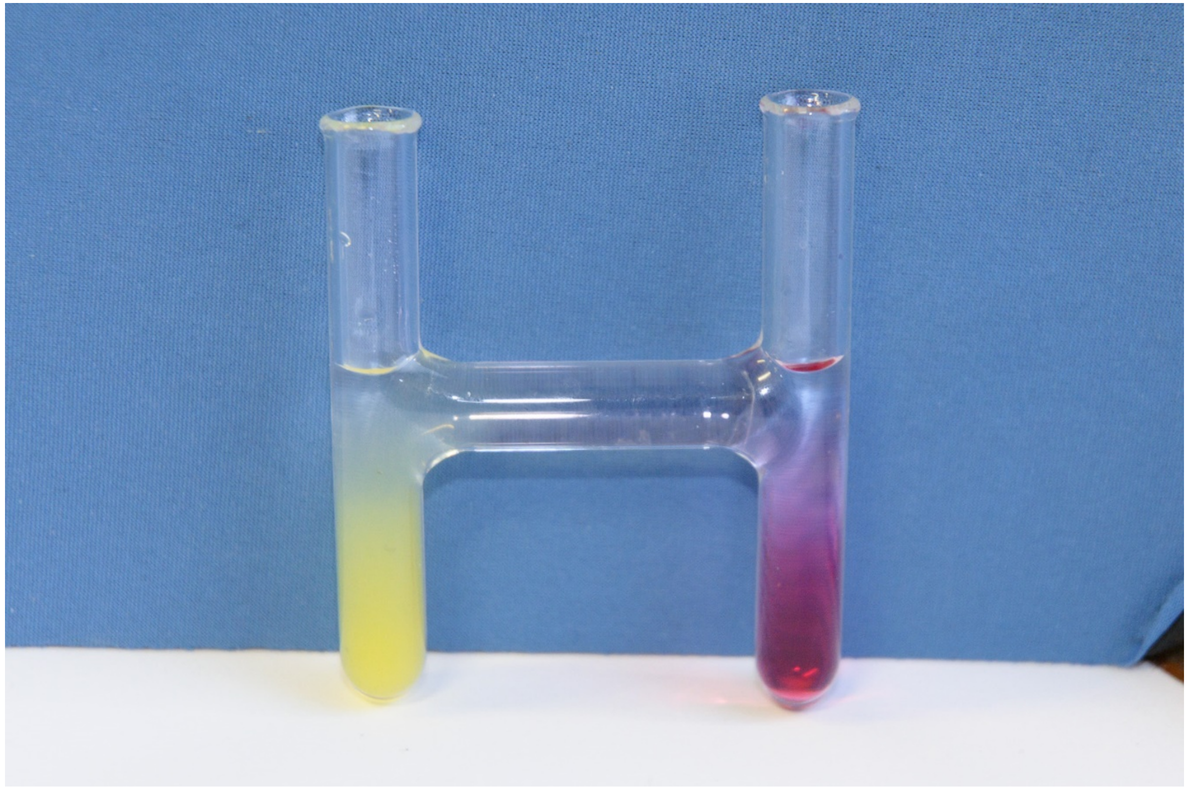
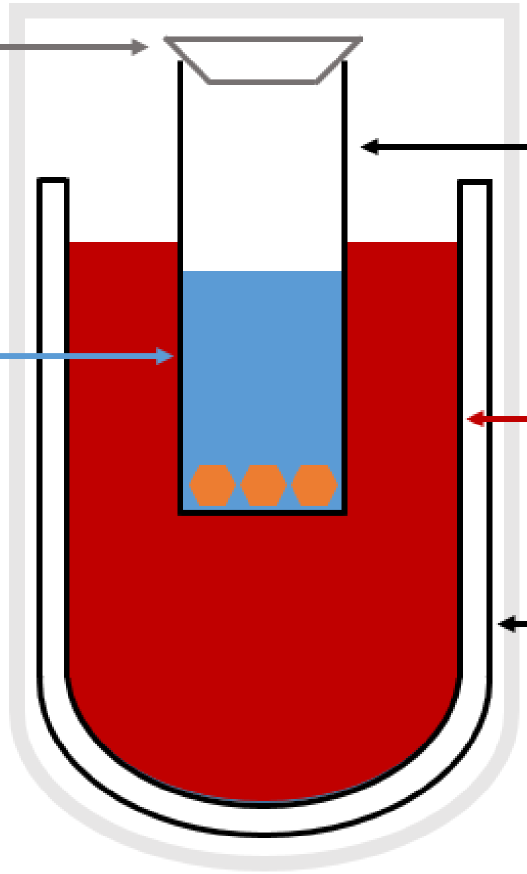
Liquid diffusion (H-Tube)

Put Parafilm over the tops

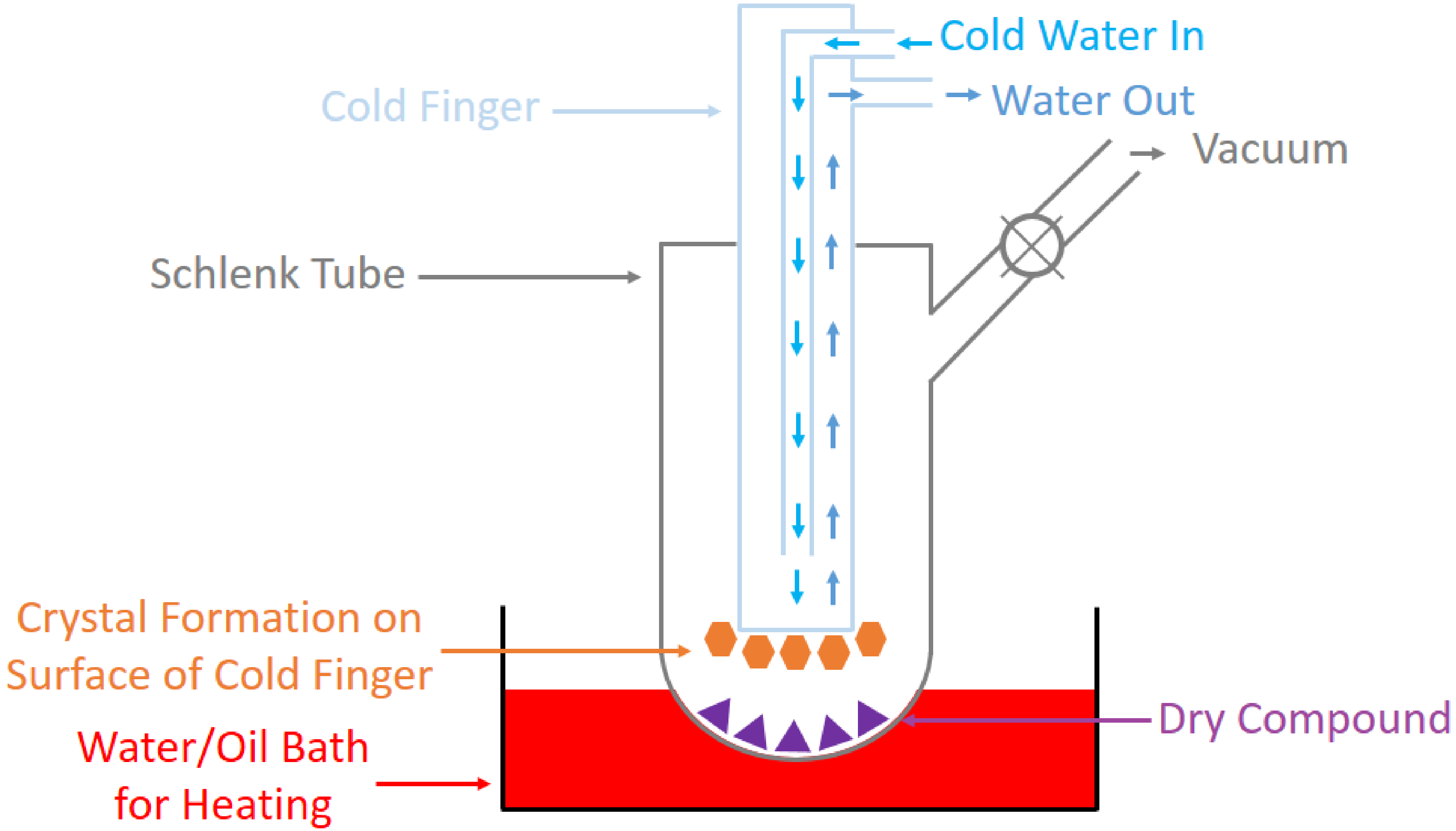




Very slow cooling



Sublimation



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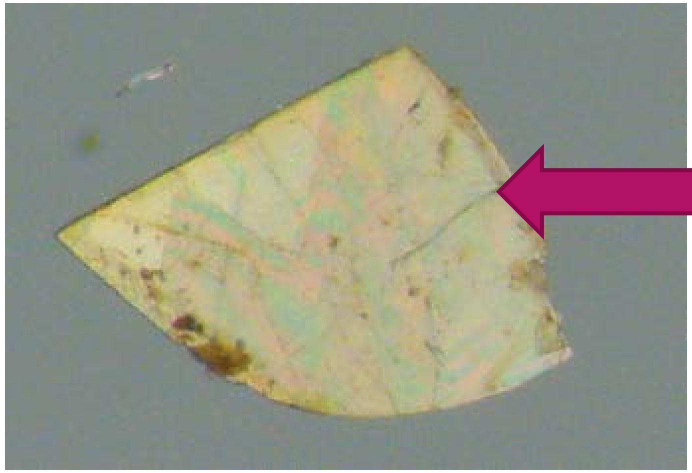
Schlenk tube with cold finger for sublimation crystallisation.

Case Study 2. A pyrene.

A good example to illustrate problems and routes to improvement.

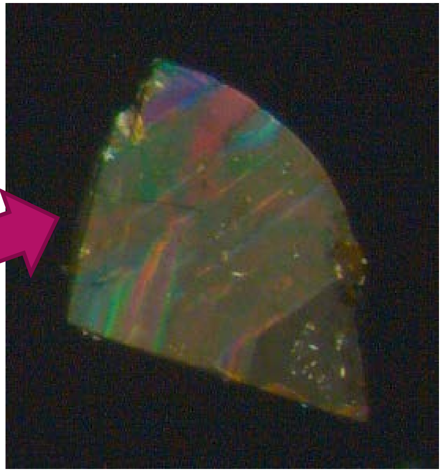


Optically imperfect.

Some hairline cracks.

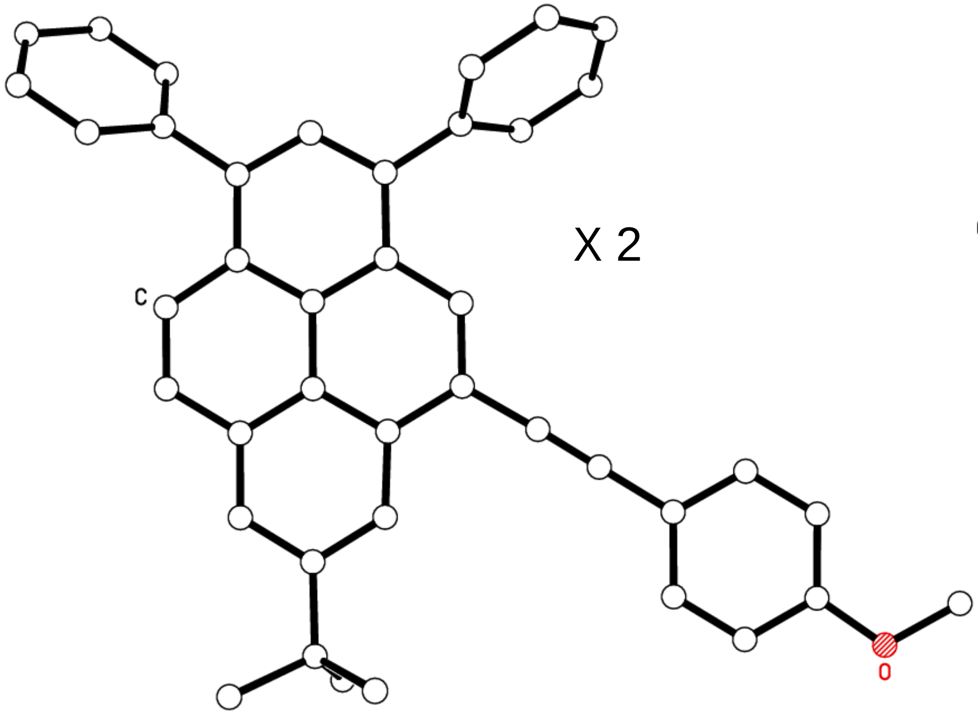
Striations under polarised light.

Turns out to be twinned.

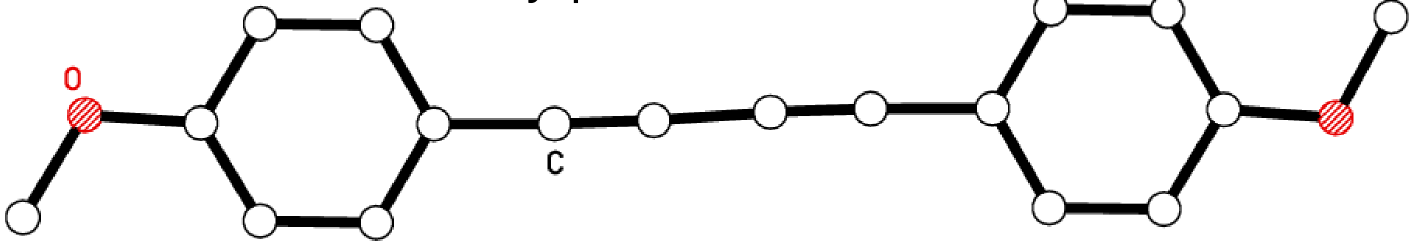


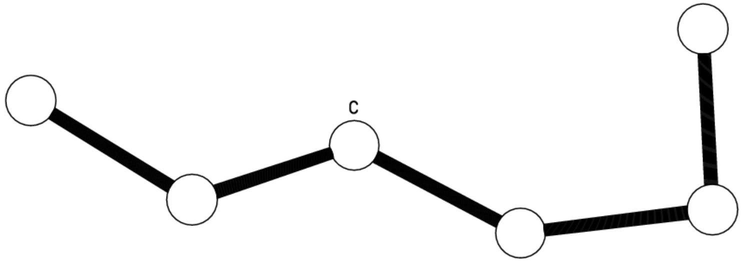
Case Study 2. A pyrene.

The structure was determined.



By-product





Hexane of crystallisation – at least a pure solvent was used.

Case Study 2. A pyrene.

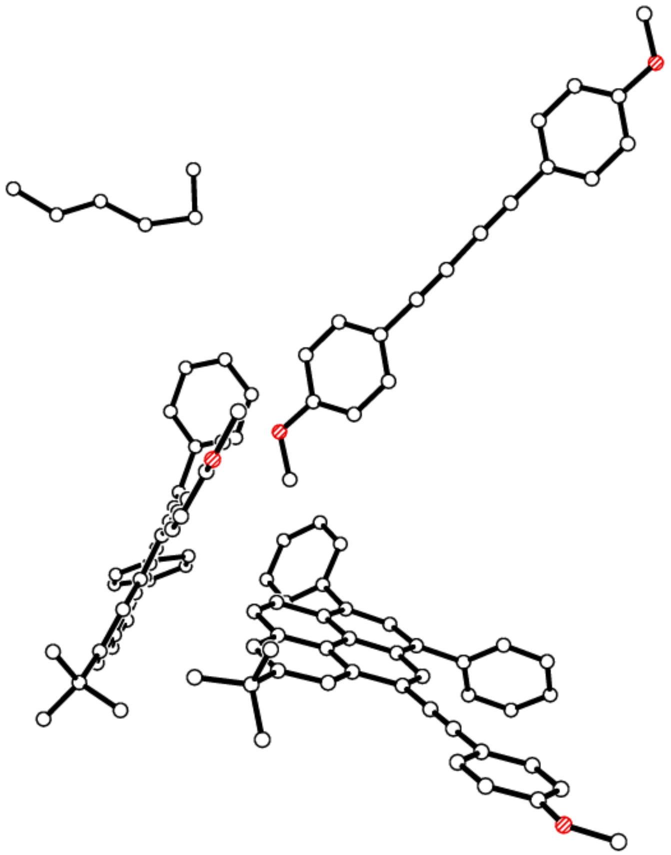
What advice can we give to avoid the twinning & improve the result?

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.

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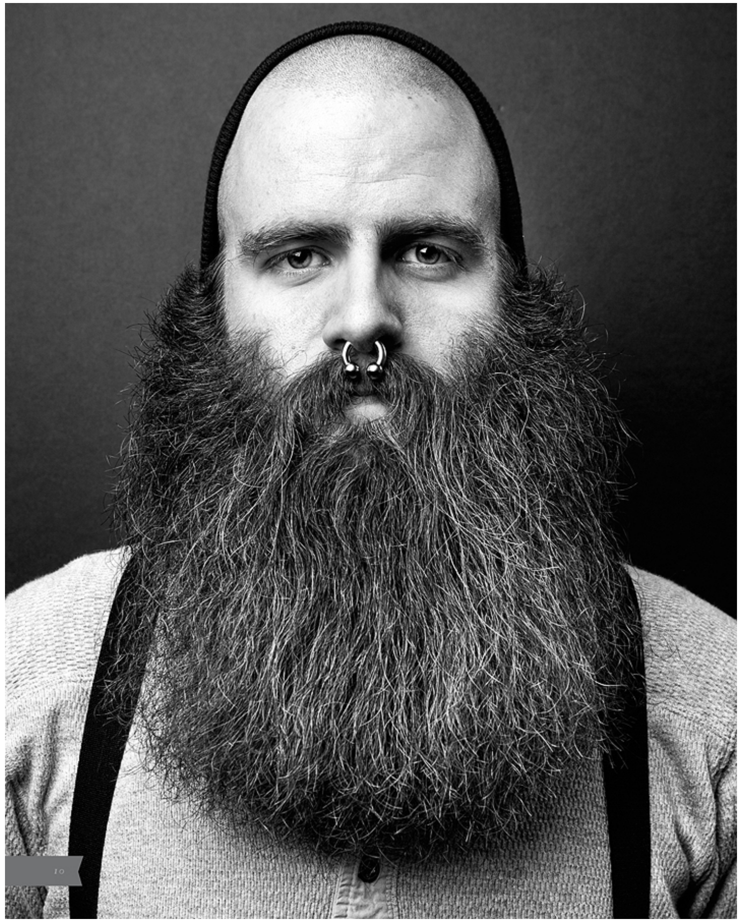
- Be aware of the factors that govern crystallisation.
- Use knowledge of the compound to guide choice of crystallisation method and conditions.
- Try as many methods as possible.
- Learn from imperfect results to achieve better outcomes.
- If all else fails – grow a beard!



From: A Book of BEARDS By Justin James Muir