A Day in the life of a Scientist



I'd like to explore this topic as a possible future reality, rather than try to describe what for me was a typical day.

I was never a particle characterisation analyst so I've never operated a laser particle size instrument, an X-ray diffractometer, an electron microscope, nor most of the 50 analytical techniques listed on the PCIG website. Incidentally, the committee will continue to update the list as other techniques are developed and hopefully include hyper-links to supporting articles with lots more operational detail.

What I have experienced are the challenges presented by particles with the wrong or poor characteristics, and my imagined future is a world where particles with the right properties can be created routinely and consistently.

I have some very fond memories from my life as a scientist. One I remember very vividly was a bromination of an acetophenone in glacial acetic acid. This was easily monitored as the brown colour of the solution by adding bromine dropwise would initially disappear rapidly, and only remain once the reaction was complete. I then added an equal volume of water and within minutes a white crystalline product was formed. This was filtered, washed and dried, and the process proved suitable for further scale-up.

However, there wasn't anything I did which directed either formation of the form (polymorph) or habit (shape) of the crystals, though maybe the choice of the solvent, anti-solvent and (room) temperature was exactly right. Who knows!

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I recall another compound I worked on which was a variable hydrate. The X-ray crystallography revealed fixed locations for water molecules, though in reality the water content of the crystals varied with relative humidity. It was also a nuisance that the predominant habit was needle-like and the right particle size range had to be achieved by micronisation. A more tabular habit which flowed well would have been preferred.

Particle shape can also be affected by how the material is handled. Small scale batches of a few grams are easily filtered and dried without agitation by sucking air through the product, or vacuum tray drying. As the batch size is increased to multi-kilogram and perhaps tonne scale, mechanical handling becomes essential and this can significantly and sometimes disastrously impact particle shape and properties.

I recall a visit to a factory in Scotland where an operator was “working the cake” to ensure that the thin layer of maybe 20kg of an intermediate on a cloth filter bag was washed effectively. The crystals had a long fibrous shape and formed a dense mat. The activity took hours and was very labour intensive.

I recall another factory visit, this time in the USA, where a similar problem was encountered, though being in a high-containment facility the operator needed an air-suit and the filtration was in an enclosed filter. In this case washing wasn’t initially effective, some acidity remained, and the batch had to be reworked to meet the specification.

How much easier will the life of a scientist (in this case a development chemist) be if we have the skills, knowledge, insights and understanding to create the desired form and habit by first intent?

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Molecules will crystallise in different configurations, so finding the lowest energy polymorph would seem the highest priority. Factors to be considered would include solvent, temperature and agitation. Kinetic versus thermodynamic control may be another factor. Beware the “disappearing polymorph” - a form of a crystal structure that can’t be reproduced.

We can characterise each type of crystal (prismatic, tabular, acicular, etc.), but can we direct which one is created?

Chemists have tended to screen a small group of bulk solvents for both form and habit. Perhaps screening should be extended to include more exotic or unusual solvents such as acetals, perfluorinated solvents, ionic liquids, etc. Once the thermodynamically most stable polymorph has been identified, maybe there’s a possibility of using these seeds in other solvents to see if different habits can be found.

Perhaps in the future there is a world where particles with the right properties can be created routinely and consistently!

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