OUT OF THE MARSH AND INTO THE SWAMP: VALIDATION OF POWDER STRUCTURES

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We have come to rely on *checkCIF* for the validation of crystal structures, but sometimes structures determined using powder data can present more challenges than the usual single crystal structure. Using *PLATON* directly (with more control over tolerances) can prove helpful, but other things can go wrong. Trirubidium citrate provides an example of traditional "Marshing"; the true space group is *Pnma*, even though the apparent space group was $Pna2_1$. Comparing the result of a Rietveld refinement to a density functional geometry optimization of the crystal structure is a powerful way of detecting errors. The original structure of paliperidone palmitate did not agree well with the DFT, providing a hint that the molecule was in the wrong conformation. A similar DFT comparison showed that for 17α-dihydroequilin, the crystal structure was solved using the wrong molecular structure. DFT calculations, like least squares refinements, find a local minimum, but provide no assurance that the global minimum has been obtained. The structure of nilotinib provides an example, in which rotation of a ring yielded a lower-energy structure with a better hydrogen bonding pattern. The DFT calculation can also be wrong; the first calculation on sitagliptin dihydrogen phosphate monohydrate was carried out using incorrect hydrogen positions. The structure of telaprevir provides an example of how a *Mogul* analysis (and many other signs) during the refinement can pont out a suspect structure.