Crystal Structure Prediction and NMR Powder Crystallography

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Structure activity relationships are the basis of development in modern chemical sciences, which depends on the capacity for atomic-level characterization. While it is straightforward to determine structures from single crystals, when the sample is a powdered solid, in many cases structure determination is difficult if not impossible. This is a major handicap in the development of complex materials. For example, the drug delivery properties of a pharmaceutical compounds are governed by the three-dimensional packing in the crystal structure, and the overall architecture of the formulation.

Over the past few decades computational crystal structure prediction (CSP) methods have seen great improvement and have been successfully used to predict and confirm single and multicomponent systems [1]. Recently they have been combined with solid-state NMR and DFT chemical shift calculations to provide a tool for structure determination in powders [2-4]. The main bottleneck for these methods today is the computational cost that grows sharply as the systems get bigger and more complex.

We present how solid state NMR measurements can be used to accelerate CSP. As an example we correctly determine the crystal structure of the medium-sized organic molecule ampicillin, where the ordinary approach fails to determine the correct structure.

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