Crystal Structure Prediction with Quadrupolar NMR Crystallography (QNMRX-CSP)

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Crystal structure prediction (CSP) is a growing set of methodologies for the prediction of crystal structures from first principles.[1,2] CSP methods can be assisted by key experimental data; as such, NMR crystallography (NMRX), which uses data from solid-state NMR (ssNMR) spectroscopy, powder X-ray diffraction (pXRD), and quantum chemical calculations of NMR parameters and static lattice energies, is emerging as an important technique for the prediction, refinement, and validation of crystal structures. Most modern NMRX studies rely upon the calculation of chemical shifts,[3-6] with recent efforts featuring machine learning algorithms pushing the bounds of NMRX-CSP even further.[7-8] To date, NMRX-CSP methods involving quadrupolar nuclides (spin > ½) have been only sparingly reported,[9,10] despite the sensitivity of electric field gradient (EFG) tensors to the surrounding electronic environments (including hydrogen bonding interactions), and the rapidity with which EFG tensors can be calculated from first principles (in comparison to chemical shifts).[11] I will describe the design and application of our new *Quadrupolar NMR Crystallography Crystal Structure Prediction* (**QNMRX-CSP**) protocol, which to date focuses on the use of experimental and theoretical ^{35}Cl EFG tensor parameters for the prediction, refinement, and validation of crystal structures of organic HCl salts. The protocol has three modules: (1) selection of molecular fragments, (2) crystal structure packing using Monte-Carlo simulating annealing, and (3) dispersion corrected plane-wave DFT calculations of structures and ^{35}Cl EFG tensor parameters. I will discuss (i) benchmarking of the QNMRX-CSP protocol using five simple organic HCl salts; (ii) the prediction and refinement of two "blind" structures without the aid of single-crystal XRD; (iii) thoughts on procedures for predicting the uncertainty of atomic positions; (iv) potential extensions to other quadrupolar nuclides, including ^{14}N, ^{17}O, and ^{23}Na; and (v) the great potential of this protocol as both a standalone technique and a complementary technique to other NMRX-CSP and Rietveld refinement protocols. Future applications to a wide range of pharmaceutical solids will also be considered.

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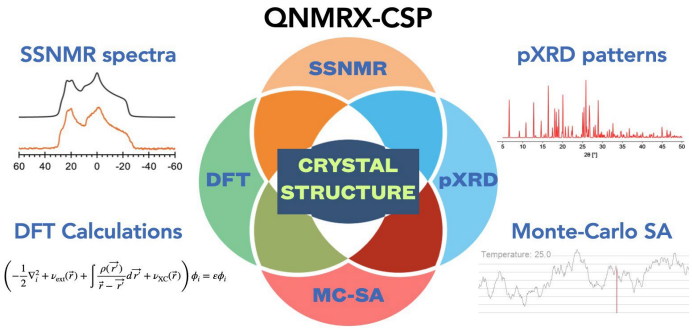

Figure 1