

The Role of NMR Crystallography in Structure Verification of Organic Solids

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Solid-state NMR spectra are sensitive to small differences in local structure, but could traditionally only be used as a “fingerprint” for distinct solid forms e.g. polymorphs. The advent of efficient DFT-based codes for computing NMR parameters in crystalline solid has provided a direct link between crystal structure and NMR observables. Prompted by the case of two CSD structures differing only in the position of an OH hydrogen, but which have distinct computed ^{13}C NMR spectra[1], we have undertaken a systematic survey of the CSD. Having identified ca. 4200 repeat determinations of the same solid form, we have assessed the potential of NMR crystallography for identifying the “correct” structure. In most cases, the differences resolve when the structures are “geometry optimized” using DFT calculations. In a significant fraction of cases, however, alternative structures relax to different energy minima. The differences typically involve H positions (such as a recent example involving the drug furosemide[2]) which would be difficult to resolve by XRD. Functionalities where NMR crystallography is most informative are identified, allowing a clear role for NMR in the verification of organic crystal structures to be proposed.

NMR has a particularly important role to play in structure verification when confronted by disorder is involved. Using the example of co-crystal structures of furosemide, we show how straightforward solid-state NMR experiments can characterize dynamic disorder, and distinguish between different structural models that are equally plausible outcomes of Bragg diffraction studies[3].

1. R. K. Harris, P. Hodgkinson, V. Zorin, J.-N. Dumez, B. Elena, L. Emsley, E. Salager and R. Stein, *Magn. Reson. Chem.* **48** (2010) S103.
2. C.M. Widdifield, H. Robson and P. Hodgkinson, *Chem. Commun.* **52** (2016) 6685.
3. H. E. Kerr, L. K. Softley, K. Suresh, A. Nangia, P. Hodgkinson and I. R. Evans, *CrystEngComm* **17** (2015) 6707.