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Powder Crystallography by Combining NMR and Crystal Structure Predictions

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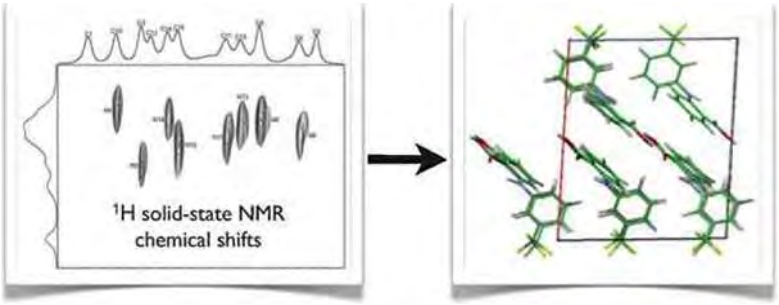
State-of-the-art work in the field of NMR crystallography for molecular systems at natural abundance has recently focused on the accurate measurement of 1H chemical shift values. We will show how when coupled with crystal structure prediction (CSP) methods, this protocol is well-suited for solving the crystal structures of small to medium sized organic molecules, including cocaine and the de-novo structure determination of AZD8329.[1,2] As complementary 1D and 2D NMR experiments are needed for the 1H assignment process, other information, such as isotropic 13C chemical shift values (δiso) are measured. Unfortunately, 13C chemical shifts are not generally useful for structure determination. Additional NMR parameters that are sensitive to structure would ensure that the structure determination procedure is robust, and would provide more accurate refinements when studying larger or more challenging systems. Here, we measure 13C chemical shift tensors for a variety of prototypical organic pharmaceuticals and use density functional theory computations under the gauge-including projector augmented-wave (GIPAW) formalism to probe whether these parameters may be discriminatory for unit cell determinations and structure determination (notably when added to the CSP + 1H chemical shifts protocol).

[1] *Baias, M., Widdifield, C. M.; Dumez, J.-N.; et al. Phys. Chem. Chem. Phys., 2013, 15, 8069.,* ***[2]*** *Baias, M.; Dumez, J.-N.; Svensson, P. H.; et al. J. Am. Chem. Soc., 2013, 135, 17501*



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