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Combined Vibrational Circular Dichroism and X-ray Powder Diffraction to Establish Absolute Stereochemistry and Structures of Small Molecules. Gregory A. Stephenson, Krishna Chavali, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285.

Computational chemistry has had a dramatic influence on the way that small-molecule organic research is being conducted. Application of density field theory to the determination of gas phase molecular conformations often serves as the starting point in understanding three dimensional organic structures. Molecular packing arrangements within the crystalline solids can be determined through use of simulated annealing or genetic algorithms for deriving atomic models used for comparison of calculated and observed powder diffraction patterns. Similarly, vibrational circular dichroism (VCD) uses computationally derived conformations to simulate spectra that are compared to experimental spectra and may be used to determine the absolute stereochemistry of molecules. While the role of single crystal diffraction for the determination of high resolution structure remains the undisputed favorite for organic chemists, the combination of powder diffraction and VCD techniques can be used as alternative methodologies for gaining much of the information that has traditionally been available only through single crystal diffraction. This talk will examine a number of examples of where these methods were employed to gain structural information in lieu of single crystal data and demonstrates the complimentary aspects of the combination of techniques.