

# **SOLVING CRYSTAL STRUCTURES WITH MOLECULAR ORIENTATIONAL DISORDER USING XRPD AND SIMULATED ANNEALING METHODS**

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Molecular orientational disorder is fairly prevalent in drug crystal structures. Until now such disordered structures have been solved only when single crystals of these drugs could be synthesized. However, many pharmaceutical compounds are available only as microcrystalline powders. Recent advances in crystallographic computing and availability of high-resolution diffraction data have made it relatively easy to solve crystal structures from powders that would have traditionally required single crystal samples. The success of direct space methods depends heavily on starting with an accurate molecular model. In this paper we address the applicability of using these methods in finding subtleties such as disorder in the molecular conformation that might not be known *a priori*. We use ranitidine HCl form 2 as our test sample as it is known to have a conformational disorder from single crystal structural work. We re-determine the structure from powder data using simulated annealing and show that the conformational disorder is clearly revealed by this method.