Physicochemical aspects of polymorph prediction

Hans-Beat Bürgi, Laboratory of Crystallography, University of Bern, Bern, Switzerland

The practical importance of the phenomenon of polymorphism need not be elaborated here. It must be pointed out, however, that a scientific understanding of the formation and properties of polymorphs is still a formidable scientific challenge, because the prediction of polymorphs, especially of organic compounds, has seen not only significant successes, but also notable failures. On one hand elaborate computer codes for generating sets of energetically and geometrically reasonable crystal structures have proven very helpful in characterizing materials for which diffraction information is limited (poorly crystalline materials, powder data or both). On the other hand none of these schemes has succeeded in consistently identifying from such sets the polymorph appearing under defined condition of crystallization. Some of the reasons for this limitation and attempts to improve our understanding of the crystallization process will be discussed: accuracy in the parameterisation of intermolecular interaction energies; simple models for describing crystal dynamics (enthalpy and entropy contributions to crystal free energy); our understanding of the early and intermediate stages of crystallization (crystal nuclei and their phase transitions, growth mechanisms and disorder). All of these topics are ideal themes for fundamental research and, in parallel with improved understanding, will lead to improved tools for predicting crystal structures and properties in an industrial environment. Facing this challenge in Academia becomes increasingly difficult, as crystallography (except for structure determination of biomolecules) tends to disappear from University curricula and basic research.