CALORIMETRY IN ACTION: POLYMORPHISM AND SIZE EFFECTS IN CRYSTALLINE SOLIDS

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Calorimetry has long been established as an essential tool to investigate the energetics of molecules, and complex molecular systems, such as crystals and living cells. It is also normally accepted that, in general, great benefits can be expected if the calorimetric measurements are complemented by information from e.g. structural analysis and theoretical calculations. This type of approach will be illustrated here using two recent examples from our laboratory: (i) the study of polymorphism in molecular organic solids and (ii) the influence of crystal size on the lattice energy of NaCl.

Since the middle of the last century, it has been widely recognized that many organic compounds exhibit polymorphism i.e. the ability to exist in more than one crystal structure. The various polymorphs differ by their packing arrangements and also, occasionally, by the conformations of the molecules in the crystal lattice. These structural variations are normally reflected by differences in physical properties (e.g. color, fusion temperature, solubility, dissolution rate), so that, each polymorph should, in fact, be regarded as a different material. The detection and control of polymorphism is, therefore, of considerable technological interest, because the irreproducible formation of different polymorphs may wreak havoc with the production, processing and end use specifications of a product (e.g. the color of dyes, the conductivity organic conductors, or the bioavailability of drugs). This problem is currently having a particularly strong impact in the pharmaceutical industry. Calorimetric methods have been very helpful in the identification of polymorphism and in the definition of the stability hierarchy of different forms. This last aspect which is quite relevant for the selection of the appropriate polymorph for development and reproducible manufacture of a product will be highlighted by using hydroxyacetophenone as a model system.[1]

Another currently important topic related to solid state materials and, in particular, nanomaterials, is the change in properties that normally accompanies a decrease in particle size. Enthalpy of solution measurements in water, carried out with sodium chloride samples spanning a 500 fold particle size range, combined with molecular dynamic simulation results, evidenced the change in cohesive energy of NaCl with particle size.[2] The largest variations are expected to occur for particle sizes below ~100 nm, where a steep decrease in lattice energy (spanning a ~230 $kJ \cdot mol^{-1}$ range) down to the limit of monomeric NaCl is predicted.

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References

1. (a) Bernardes, C. E. S.; Piedade, M. F. M.; Minas da Piedade, M. E., Polymorphism in 4'-Hydroxyacetophenone: Structure and Energetics. *Cryst. Growth Des.* **2008**, *8*, 2419-2430; (b) Bernardes, C. E. S.; Piedade, M. F. M.; Minas da Piedade, M. E., Structure and Energetics of a New Hydrate of 4'-Hydroxyacetophenone. *Cryst. Growth Des.* **2010**, *10*, 3070-3076; (c) Bernardes, C. E. S.; Minas da Piedade, M. E., Crystallization of 4'-Hydroxyacetophenone from Water: Control of Polymorphism via Phase Diagram Studies. *Cryst. Growth Des.* **2012**, *12*, 2932-2941; (d) Bernardes, C. E. S.; Minas da Piedade, M. E.; Canongia Lopes, J. N., Polymorphism in 4'-Hydroxyacetophenone: A Molecular Dynamics Simulation Study. *J. Phys. Chem. B* **2012**, *116*, 5179-5184; (e) Bernardes, C. E. S.; Ilharco, L. M.; Minas da Piedade, M. E., Polymorphism in 4'-Hydroxyacetophenone: A Vibrational Analysis. *J. Mol. Struct.* **2014**, *1078*, 181-187.

2. Range, S.; Bernardes, C. E. S.; Simões, R. G.; Epple, M.; Minas da Piedade, M. E., Size Matters: An Experimental and Computational Study of the Influence of Particle Size on the Lattice Energy of NaCl. *J. Phys. Chem. C* **2015**, Article ASAP (DOI: 10.1021/jp5124772).