

The Standard Molar Enthalpy of the 4'-Hydroxyacetophenone. Polymorphic Phase Transition as Benchmark for Solution Calorimetry Measurements

I.O. Feliciano, C.E.S. Bernardes, M.E. Minas da Piedade

Centro de Química Estrutural, Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016, Portugal

E-mail: idfeliciano@fc.ul.pt

The ability to control the organization of the molecules of organic substances in solid-state – Polymorphism – has become a critical issue to the fine chemical industry (particularly the pharmaceutical industry), as different crystal phases can exhibit significant changes in the physical properties of the materials (e.g., solubility, dissolution rate, fusion temperature, etc.) [1]. An important aspect within this scope is the assessment of the relative stability of polymorphs. A good indicator of that stability is the standard molar enthalpy of transition between forms, $\Delta_{\text{trs}}H_m^{\circ}$, since close to ambient temperature polymorph stability is often enthalpically controlled. This value, which reflects the difference in lattice energy between phases, can be experimentally determined from measurements of solution enthalpy, $\Delta_{\text{sln}}H_m^{\circ}$, using the scheme in Fig. 1. By this method, each polymorph (I and II) is dissolved in the same solvent to give a solution with the same concentration, so that,

$$\begin{aligned} \Delta_{\text{trs}}H_m^{\circ}(\text{cr II} \rightarrow \text{cr I}) \\ = \Delta_{\text{sln}}H_m^{\circ}(\text{II}) - \Delta_{\text{sln}}H_m^{\circ}(\text{I}). \end{aligned}$$

Typically, $\Delta_{\text{trs}}H_m^{\circ}$ is small ($\sim 1 \text{ kJ}\cdot\text{mol}^{-1}$), so that, reference values of the same magnitude are desirable for the assessment/validation of new calorimetric systems or procedures to investigate the lattice energy difference between polymorphs. Thus, in this work, we propose the use of the 4'-hydroxyacetophenone (HAP) solid phases as a benchmark system for the assessment of solution calorimetry methodologies since (i) both polymorphs (I and II) can be easily prepared with high phase and chemical purity, and (ii) measurements performed using two different apparatus and solvents led to similar results (Isoperibol solution calorimetry, ethanol, $\Delta_{\text{trs}}H_m^{\circ}(\text{cr II} \rightarrow \text{cr I}) = 0.49 \pm 0.13 \text{ kJ}\cdot\text{mol}^{-1}$ [2]; LKB 2277 Thermal Activity Monitor, DMSO, $\Delta_{\text{trs}}H_m^{\circ}(\text{cr II} \rightarrow \text{cr I}) = 0.48 \pm 0.10 \text{ kJ}\cdot\text{mol}^{-1}$ [3]), leading to the weighted mean value recommended in this work: $\Delta_{\text{trs}}H_m^{\circ}(\text{cr II} \rightarrow \text{cr I}) = 0.48 \pm 0.08 \text{ kJ}\cdot\text{mol}^{-1}$.