

Solubility Determination from Clear Points upon Solvent Addition

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ABSTRACT: A method is described for determining the solubility of multicomponent crystalline compounds from clear points upon sample dilution at a constant temperature. Clear points are established by continuously adding a solvent mixture to a suspension of known composition until a clear solution appears. For validation, this solvent addition method is compared to the traditional equilibrium concentration method at constant temperature and the more recent temperature variation method with which clear point temperatures are determined upon increasing the sample temperature. Solubility data of binary systems (1 solute, 1 solvent) measured using the solvent addition method are obtained relatively quickly compared to the equilibrium concentration method. These solubility data are consistent with those of the temperature variation and the equilibrium concentration method. For the temperature variation method, the results are dependent on the heating rate. Likewise, for the solvent addition method, they are dependent on the addition rate. Additionally, for ternary systems involving anti-solvent or co-crystals, solubilities are determined at a constant temperature using the solvent addition method. The use of the solvent addition method is especially valuable in the case of solvent mixtures and other complex multicomponent systems, in which the temperature variation method cannot be applied easily.

