Possibilities for studying the fusion of metastable forms of compounds using Fast Scanning Calorimetry

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Polymorphism is a condition when molecules or atoms can pack differently, producing different crystal structures. One of the polymorphs will have the lowest free energy at a given temperature. Thus, all other polymorphs are metastable. The fusion properties of polymorphs reflect their relative thermodynamic stabilities and provide a good basis for verifying the crystal energies calculated using quantum mechanics. However, fusion properties of many organic compounds are not accessible using conventional methods such as Differential Scanning Calorimetry when the studied compound decomposes upon heating. Adding inherent instability of the metastable polymorphs on top of that further complicates the study of the fusion of polymorphs.

Due to the high heating rate, Fast Scanning Calorimetry (FSC) offers new possibilities for studying the fusion of organic compounds prone to decomposition. FSC was successfully used to investigate the melting of nucleobases [1, 2], amino acids [3], and fibrillary proteins [4]. Using the appropriate approach, one can determine the melting point and the fusion enthalpy of the compound.

Here we present the FSC studies of the fusion properties of polymorphs of dantrolene [5] and two thiacalix[4]arene derivatives [6]. The application of FSC allowed determining melting points of different polymorphs and gave some hints on the differences in melt/recrystallization tendencies of polymorphs.

The metastability of the polymorphs requires modification of the experimental approaches because some of the typical procedures, e.g., premelting, are not possible. Determination of the fusion enthalpy using FSC relies on accurate data on the specific heat capacity of the compounds, which may not always be available for all polymorphs. We discuss the experimental approach, which does not yield absolute specific fusion enthalpy but provides the relative specific fusion enthalpies of different polymorphs.

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