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Estimation of melting points of organics

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ABSTRACT

UPPER (Unified Physical Property Estimation Relationships) is a system of empirical and theoretical relationships that relate twenty physicochemical properties of organic molecules to each other and to chemical structure. Melting point is a key parameter in the UPPER Scheme because it is a determinant of several other properties including vapor pressure, and Solubility. This review describes the first principals calculation of the melting points of organic compounds from structure. The calculation is based on the fact that the melting point, T_m, is equal to the ratio of the heat of melting, ΔH_m, to the entropy of melting, ΔS_m. The heat of melting is shown to be an additive-constitutive property. However, the entropy of melting is not entirely group additive. It is primarily dependent on molecular geometry, including parameters which reflect the degree of restriction of molecular motion in the crystal to that of the liquid. Symmetry, eccentricity, chirality, flexibility, and hydrogen bonding, each decrease molecular freedom in different ways and thus make different contributions to the total entropy of fusion. The relationships of these entropy determining parameters to chemical structure are used to develop a reasonably accurate means of predicting the melting points over 2000 compounds.

BACKGROUND

The melting point is by far the most commonly reported property of organic compounds. It is often among the first properties determined after a new compound is synthesized. There is probably more melting point data available for organic compounds than any other physical, chemical, or biological property. In spite of the tremendous amount of available melting point data, the calculation of the melting point form chemical structure remains an elusive problem. Although melting point is analogous to boiling point, it is far more difficult to predict. The reason for this difficulty is that the melting point of a compound is not solely dependent upon the pairwise interactions of the molecules at the phase transition temperature, as is its boiling point. The melting point is also dependent upon the far less predictable ability of the molecules to be properly arranged for maximum attractive interaction in the crystal lattice. According to Pauling[1,2,] the rate of a crystalline molecule leaving its lattice is dependent only upon its thermal energy, whereas the rate of incorporation into the lattice is dependent upon both thermal energy and alignment.

As a result of the greater complexity of melting compared to boiling, there have been far fewer attempts to estimate melting point form structure than there have been for boiling point. Many of these have been reviewed by Bondi [3,4], Horvath[5], Baum[6], Reinhard and Drefahl[7], Tesconi and Yalkowsky[8] and Katritzky [9,10]. In reviewing the various attempts to estimate melting points. Dearden [11,12] showed that most approaches are restricted to very small series of compounds. Furthermore, Dearden showed that some studies use different prediction schemes