measure the principal refractive indices; simply measuring two that are unique and reproducible is sufficient. These are termed the key refractive indices that, according to these researches, are all that are needed to identify any particular compound.

6.3 Polymorphism

Both organic and inorganic pharmaceutical compounds can crystallize into two or more solid forms that have the same chemical composition; this is called polymorphism. Polymorphs have different relative intermolecular and/or interatomic distances and unit cells, resulting in different physical and chemical properties, such as density, solubility, dissolution rate, bioavailability, and so on. Crystal structures containing solvents (or water) are often called psudopolymorphs, with distinct physical and chemical properties. It is possible for each pseudopolymorph to have many polymorphs. In polymorphism, the crystal lattice formation can take place through two mechanisms: packing polymorphism and conformational polymorphism. Packing polymorphism represents the formation of different crystal lattices of conformationally rigid molecules that can be rearranged stably into different 3D structures through different intermolecular mechanisms. When a nonconformationally rigid molecule can be folded into alternative crystal structures, the polymorphism is categorized as conformational polymorphism.

Polymorphs and pseudopolymorphs can also be classified as monotropes or enantiotropes, depending upon whether or not one form can transform reversibly into another. In a monotropic system, Form I does transform to Form II, because the transition temperature cannot appear before the melting temperature (Figure 6.5, monotropy). In Figure 6.6 (enantiotropy), Form II is stable over a temperature range below the transition temperature, at which two solubility curves meet, and Form I is stable above the transition temperature. At the transition temperature, reversible transformation between the two forms occurs. Figure 6.7 (enantiotropy with metastable phases) shows the kinetic effects on the thermodynamic property of solubility, which shows Ostwald ripening effect.

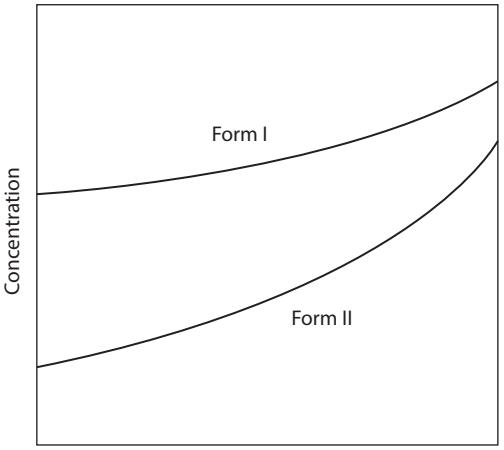

FIGURE 6.5 Monotropic system as a function of temperature (*x*-axis).