1. STATES OF MATTER: CRYSTALLINITY AND AMORPHICITY

Prior to discussing the stability of drugs in the solid state, it is necessary to outline some characteristics of solids. A detailed discussion of the state of matter in regards to solids is outside the scope of this book. Suffice it here to say that solids may be characterized by being (a) crystalline or (b) amorphous. Crystalline solids are associated with a lattice, and amorphous solids are solids that are not crystalline. Some of the characteristics (those that apply to stability) of these two categories will be discussed in the immediate following.

There are seven crystal systems and two types of amorphates.

2. POLYMORPHISM

Inorganic (particularly ionic) solids usually are associated with one and only one crystal system. Well-known to all is that sodium chloride is cubic.

Organic solids, however, depending on how they are recrystallized, may occur in several different crystal modifications (polymorphs). There are two types of polymorphism, enantiotropes and monotropes. They are distinguished by their vapor pressure diagrams as shown in Figs. 1 and 2.

The situation referred to in Fig. 1 is one where there is a transition temperature, and DSC traces in such cases often have the appearance of either Fig. 2 or 3.

It is seen in Fig. 2 that two common situations may occur: first, the transformation may take place, so that there is an endotherm for the transformation followed by an endotherm for the melting. The melting point of form II (the room-temperature labile form) is recorded in this case as is the transition temperature.

The other possibility is that the transition is passed by, giving the melting point of the (now unstable) form I (lower trace). This forms an unstable melt, and often form II precipitates out, giving the exotherm shown in the lower graph followed by endotherm for the melting point of form II.

In some cases the exotherm is missing, and in such cases the melting endotherm of form II is also missing, i.e., the trace simply looks like the trace of melting of form

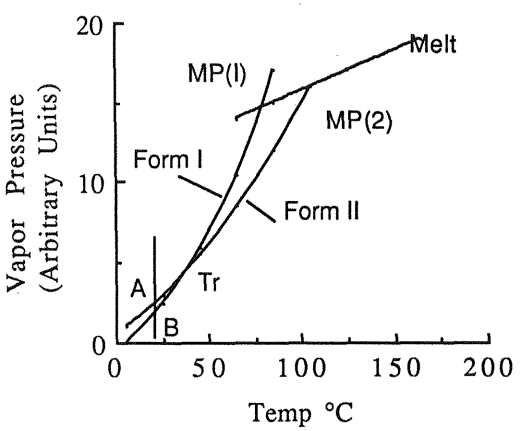

Fig. 1 Vapor pressure diagram of an enantiotropic pair.