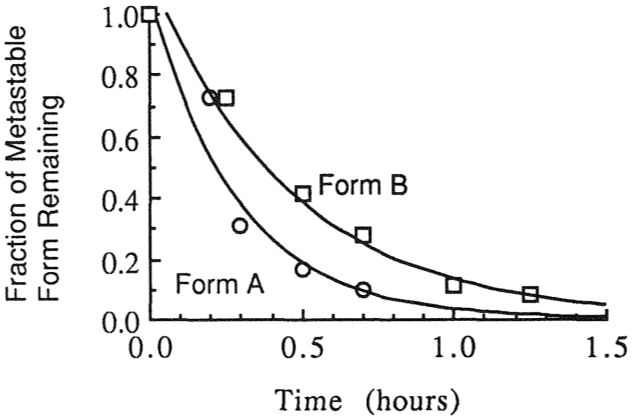

Fig. 16 Literature data dealing with two polymorphic transformations allegedly diffusional because it adheres (somewhat) to a Jander model.

(I, II, and amorphate) and found all to have fairly much the same solubility. Neither form I nor form II changed after storage at 40°C/75% and 0% RH for 2 months. DSC for form I showed no peak other than a sharp melting endotherm at 167.4°; form II showed a slight endotherm at 116.8°C and a sharp endotherm at 166.6°C. The amorphate showed a (slight) exotherm peaking at 81.5°C, presumably due to crystallization, and a sharp endotherm at 167.3°C. From this it would be reasonable to conclude that form II is stable at room temperature and transform to I at 116.8°C, this latter form being stable at the higher temperatures.

The authors estimated the polymorphic stability of form II by way of the Kissinger equation (Kissinger, 1956):

$$\partial\left\{\frac{\ln(\phi/T_{\max}^2)}{\partial(1/T_{\max})}\right\} = \frac{-E}{R} \tag{6.48}$$

where ϕ is the rate of heating, $T_{\max}$ is the temperature at the peak maximum in the DSC, E is the activation energy, and R is the gas constant. If the experiment is conducted at different heating rates, different $T_{\max}$ values result, and in the case of glybuzole there were four such values.

It can be seen from the graph that the activation energy is $24.723 \times 1.99 = 49.2$ kCal/mol. Otsuka et al. (1991, 1993, 1999) employed the Jander equation to explain crystallization rates of compounds, e.g., amorphous glybuzole. As mentioned above, however, the Jander equation is based on an assumption of a layer of "reaction product," and such a layer (i.e., such a model) cannot be conceived of in a polymorphic transformation. What would be the "reaction product"?

8. GENERAL INTERACTIONS IN DOSAGE FORMS

It is tempting to think of a tablet as an agglomeration of individual particles, independent of one another, but this cannot be the case. By their mere nature, particles