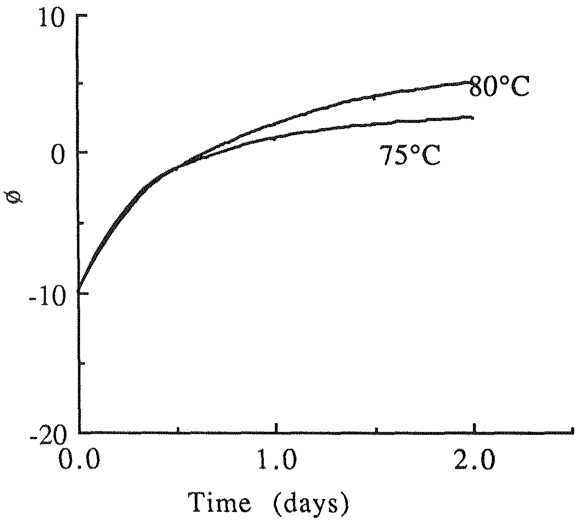

Fig. 11 Figure constructed from data published by Seltzer et al. (1998).

so that the terms k and ΔH may be deduced from nonlinear regression of a plot of heat flow versus time (Fig. 11).

If the reaction is zero order, then ϕ is simply a constant:

$$\phi = k\Delta H \tag{9.30}$$

This allows determination of kinetic profiles and Arrhenius plots of the studied reaction.

The value of Q at time t is obtained through integration (area under) of the curve from zero to t.

It should again be emphasized that at the onset of a new drug program, there are only small amounts of drug substance at hand. One of the first tasks for the preformulation scientist is to establish the framework within which the first clinical batches can be formulated. To this end it is important to know with which common excipients the drug is compatible. In the following, the distinction will be made between solid and liquid dosage forms.

The microcalorimetric methods give no direct information about the chemical nature of the reaction.

9.3. Compatibility Test for Solid Dosage Forms

It is customary to make a small mix of drug substance with an excipient, place it in a vial, place a rubber stopper in the vial, and dip the stopper in molten carnauba wax (to render it hermetically sealed). The wax will harden and form a moisture barrier up to 70°C. A list of common excipients characteristic of this type of test is shown in Table 1. At times it is possible to obtain quantitative relationships of excipient characteristics and interaction rates (Carstensen et al., 1964; Perrier and Kesselring, 1983). In addition to the test as described, a similar set of samples are set up where 5% moisture is added. A storage period of 2 weeks at 55°C is employed [except