or employing X, the mole fraction decomposed:

$$\ln\left[X + \frac{z}{M_0}\right] = k^* t + \ln\left[\frac{z}{M_0'}\right] \tag{6.65}$$

Recalling that z is a small number, the term z/M_0 is small, and the Eq. (6.65) then simplifies to

$$\ln[X] = k^* t + \ln\left(\frac{z}{M_0'}\right) \tag{6.66}$$

Data are plotted in this fashion in Fig. 21. It is seen that the linearity is quite good. The value of z may be estimated from the intercept and comes to about 0.1 mg per tablet, which is a reasonable figure. This, in essence, shows that the theories suggested by Wright (1983) are correct.

It is obviously of pharmaceutical importance in most situations to slow down the reaction in the solid state and yet maintain the reactivity in the solid state. (An exception to this is when a reaction is purposely carried out during a granulation, for instance.) One way of retarding the reaction rate is to preheat the bicarbonate to 95°C for a certain length of time (White, 1963, Mohrle, 1980). This will react by the scheme

$$2NaHCO_3 \rightarrow Na_2CO_3 + H_2O \tag{6.67}$$

The water formed granulates the mixture and makes it easier to compress. But more importantly, the sodium carbonate formed can form double salts with the bicarbonate. These are dodecahydrates and act as moisture scavengers. They hence stabilize the acid/base mixture in the solid state (if reasonable moisture barriers are provided): any *small* amount of moisture created by a beginning reaction of the type of Eqs. (6.48) or (6.49) will react with a mixture of the carbonate and bicarbonate to form a double salt hydrate.

9. INCOMPATIBILITY PREVENTION TECHNIQUES

Frequently, interactions are particle size dependent. This stands to reason, because the finer a powder is, the more contact points there will be in the tablet mass, hence the larger the potential for interaction. Means of overcoming this are as follows.

In double granulation or pocketing techniques, one component is placed in one granulation, the other in another; keeping the granulations coarse will give fewer contact points, hence less interaction. This is a technique often used in vitamin granulations. Here the more famous incompatibilities are usually those involving (a) cyanacobalamine, iron, and ascorbic acid (b) vitamin A, (c) calcium pantothenate, and (d) tocopherol. The first of these cases is one where *pocketing* is used. This can be accomplished by actually coating (rather than just granulating) the iron salt (often ferrous fumarate) in order to separate it from the remaining ingredients. The other cases will be dealt with separately below.

Other means of separating incompatible ingredients is to make a compression-coated tablet. This consists of an inner tablet compressed in a coating granulation. This principle can be extended to a tablet within a tablet within a tablet