If the study is carried out at temperatures below the eutectic temperature, T^*, then the reaction will be solid to solid + gas. If above the eutectic temperature, then the reaction will be solid to solid + liquid + gas. The compounds reported in literature to be of the solid to solid + gas type are most often inorganic salts, e.g., potassium permanganate (Prout and Tompkins, 1944), silver permanganate (Goldstein and Flanagan, 1964), and some organic compounds, such as oxalic acid and *p*-aminosalicylic acid (Kornblum and Sciarrone, 1964; Pothisiri and Carstensen, 1975; Carstensen and Pothisiri, 1975).

Olsen et al. (1997) showed cefaclor monohydrate to decompose (as judged by related substances) by first-order kinetics. The rate constants could be plotted by Arrhenius plotting and were consistent with ambient rate constants. The reaction scheme, when amorphous material was present, was such that the rates were faster at early time points and then became equal to those of the crystalline modification. The conclusion was that the initial phase was decomposition of amorphous content parallel to conversion of amorphous to crystalline drug.

At times the solid state reaction cannot be completely specified yet can be descried in analytical terms. Tzannis and Prestrelski (1999) described the effect of sucrose on the stability of trypsinogen during spray-drying by plotting denaturation temperatures as a function of melting temperature and found a linear increase between residual activity after spray-drying and melting temperature. Adler and Lee (1999) have reported on the stability of lactate dehydrogenase in spray-dried trehalose.

4. THE SOLID TO LIQUID + GAS REACTION

Many more compounds seem to decompose by this reaction scheme than by the solid to solid + gas. The reaction kinetics are usually referred to as Bawn kinetics (Bawn, 1955). This situation at time t is as shown in Fig. 6, and as seen there will be a certain amount of liquid decomposition product. This amount corresponds to the amount of drug decomposed. However, the liquid decomposition product will dissolve parent compound to the extent, S (mole drug/mole decomposition product), to which it is soluble, so that the amount present in the solid state at time t is the original number of moles, A_0, minus the amount decomposed, A_0x, minus the amount dissolved, A_0Sx.

The rate of decomposition would be the sum of the rates of decomposition in the solid state (assumed first order with rate constant k_s, time^{-1} and in the dissolved state (assumed first order with rate constant k_1 time^{-1}. The rate equation, hence, is

$$\frac{dA}{dt} = -k_s[A_0(1-x) - A_0xS] - k_1[A_0xS] \tag{6.16}$$

Noting that

$$\frac{A}{A_0} = (1-x) \tag{6.17}$$

it follows, by division through by A_0, that

$$\frac{d(1-x)}{dt} = -k_s[1-x-xS] - k_1xS \tag{6.18}$$