where C_0 is the initial concentration. This will be true if only the surface of the solid interactant is affected. The extent of decomposition will be slight, because (unless the drug is extremely finely subdivided) only a small fraction of the molecules are on the surface. If, however, the ibuprofen penetrates the crystal, then Jander kinetics should prevail. A similar situation may be at work in the aspirin incompatibilities mentioned earlier.

14. AMORPHATES

As mentioned earlier, solids can occur either in crystalline form or as particulate amorphates. The chemical stability of the solid in crystalline form will differ from the same entity in amorphous form. In most cases the crystalline form, under the same conditions, will be more stable than the comparable amorphate.

The most interest and the largest body of work of amorphates is in the field of macromolecules. These usually possess a glass transition temperature*, T_g, and the states are referred to as "glassy" below† and "rubbery" above T_g.

Only a few articles have appeared on the subject of chemical stability of amorphates. In general, a compound is more stable in the crystalline state than in an amorphous state, but exceptions exist (Sukenik et al., 1975; O'Donnel and Whittaker, 1992; Stacey et al., 1959). There *are* cases that have been reported (Lemmon et al., 1958) where the crystalline state is less soluble than the molecule in solution, but they are rare.

In general, in a crystalline state, molecules are to a great extent fixed in position. In cases where the situation exists where a group from one molecule reacts with another group in a neighbor, the situation as shown in Fig. 24 arises.

Pothisiri and Carstensen (1975) have shown that in a situation such as the case of substituted benzoic acids the decomposition is between two groups in the same molecule.

Suppose parts A and B of the molecule depicted in Fig. 24 react. In such a case arrangement C would give better stability than arrangement D, because A would be further away from B in the former arrangement. Arrangement D can be more adverse than a random orientation as well, and if that is the case, then the amorphous form would be more stable than the crystalline (arrangement D). This is the exception rather than the rule.

In the presence of moisture, conversions from amorphous to crystalline modifications are promoted (Carstensen and Van Scoik, 1990; Van Scoik and Carstensen, 1990), and the material developed in the following all refers to anhydrous conditions.

In the work by Carstensen and Morris (1993), amorphous indomethacin was produced by melting a crystalline form of it to above melting (162°C) and recooling it to below 162°C. Amorphates made in this manner are morphologically stable down to 120°C‡ so that their chemical stability can be monitored. At a range of temperatures below this temperature, crystallization occurs too rapidly to allow for assessment of chemical stability. Amorphous samples were placed at several con-

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* More than one glass transition temperature may exist.

† The highest T_g in the case of multiple glass transition temperatures.

‡ If the temperatures are lowered rapidly, then stable amorphates can be formed at room temperature, but kinetics cannot be followed easily because of the slow reaction rate at room temperature.