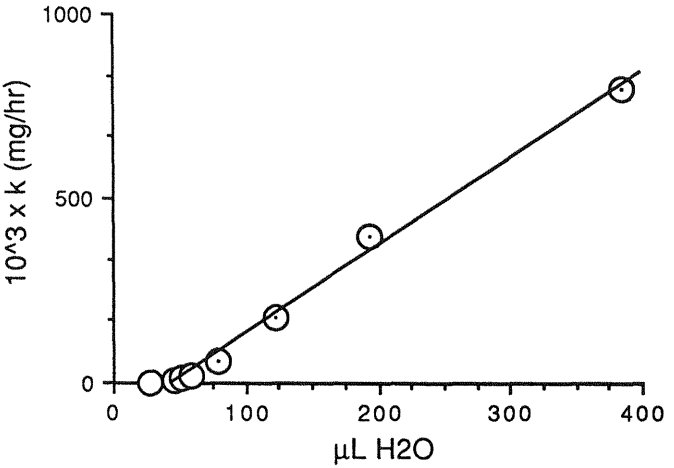

Fig. 8 Rate constants (pseudo zero order) from plots such as shown in Fig. 7 of Chapter 10, graphed versus added moisture. (Figure constructed from data published by Gerhardt, 1990, and Gerhardt and Carstensen, 1989.)

conversely, if it is acid-sensitive, one may employ bases (e.g., sodium carbonates) in an attempt to make an adjustment of "the microenvironmental pH." In the area shown as Fig. 1C, D, and E, if one may "buffer" a solid dosage form, Nikfar 1990, Nikfar et al. 1990a,b, Gerhardt 1990, Gerhardt and Carstensen 1989 have demonstrated the existence of a "solid pH-profile" that parallels (but is not identical with) the traditional pH profiles of the drug in solution. This is another piece of evidence of the sorbed moisture layer having solvent properties.

But how to define the microenvironmental pH? This a question that is not fully resolved yet. The shift in position of the kinetic pH profile in solution from the values obtained from solid state decomposition may be attributed to the fact that one assumes that the pH value of a saturated buffer solution is the same pH used for graphing of data from the moist solid. But the sorbed solution could be of a pH value displaced from that observed in solution.

There is also the possibility of a kinetic salt effect. It is seen from Fig. 9 (Nikfar, 1990; Nikfar et al. 1990a,b) that a displacement of 1.4 pH units applies to the rate constants in the solid state. The displaced values are symbolized by squares in Fig. 9, and if such a shift is made, then the data in solution would coincide with those in the solid state. In the work published by Gerhardt (1990) it would be necessary to force a 6 pH unit shift to obtain coincidence, so that are still unexplained factors at work.

7. VERY LOW MOISTURE CONTENTS

Such a case is shown in Figs. 1B and 1C. Nikfar (1990) and Nikfar et al. (1990a,b) suggested the term *immobile water* for cases such as the ones depicted in Fig. 1c. They have demonstrated that the decomposition in such a case translates into a pseudo-first-order profile (Fig. 10). At these levels of moisture the active sites in a Prout–Tompkins sense disappear by dissolution somewhat like what happens