which integrates to

$$C = C_{\infty}[1 - e^{-k_1 t}] \tag{2.41}$$

i.e., the reaction occurs as if B were not in the picture at all.

In general, if there is such a fast step in the first step of a complex reaction, it is not incorrect to consider it an A–B–C reaction.

The same arguments can be made in the case of A → B → C → D reaction where the B → C was much more rapid than the others, and in such a case it would be justified to think of this as an A → C → D reaction. To be more exacting, a steady-state approach would probably be better. It should be pointed out however, that the steady-state approach is a fundamental approximation, and if it is used, then the reasonableness of the approximation should always be checked.

The steady-state approach is often used, particularly in Michaelis–Menten type kinetics. Here, as an example, let us consider the situation, often occurring, that *many* low level decomposition products are encountered. There are different regulatory views on this, one being that no more than 1% of a product may be formed for it to be considered a minor decomposition product. The situation is hazy, at best, at all times, because often the compounds are unknown. In such cases the "amount" of the decomposition product in the small peak is estimated by the ratio of its area to that of the main peak. But if the decomposition product has a different $\lambda_{\max}$ then this estimate is incorrect, and this is likely to occur if, for instance, in an HPLC setup a single-wavelength UV detector is used.

A well documented and elucidated example is the case reported by Vilanova et al. (1994), who showed in alkaline hydrolysis of cefotaxime the presence of deacetylcefotaxime, the 7-epimer of cefotaxime, the 7-epimer of deacetylcefotaxime, the exocyclic methylene compound, and examine compounds. With such an array of decomposition products, it is important to establish the major products, and treat, in approximation, the decomposition in this light. In the simplest case, cefotaxime shows an A–B–C and A–D–E reaction, with two B curves and three C curves.

Another case that serves as such an example is the case of relaxin oxidation by hydrogen peroxide reported by Nguyen et al. (1993) shown in Fig. 9 where there are two intermediates (B and C) showing maxima and a final product, D, showing the monotonically increasing pattern.

6. PSEUDO-ZERO-ORDER REACTIONS

When only small amounts of decomposition occur, it is difficult to distinguish between zero- and first-order reactions. This is because for small values of x (< 0.15)

$$\ln[1 - x] \approx -x \tag{2.42}$$

where x is the fraction decomposed. If the initial amount of drug substance is A_0, then the fraction decomposed is

$$\frac{A_0 - A}{A_0} = 1 - \frac{A}{A_0} = x \tag{2.43}$$