## 7. PARTITION COEFFICIENT

Partition coefficients between water and an alkanol (e.g., octanol) should be determined in preformulation programs (Yalkowsky et al., 1983). The partition coefficient of a compound that exists as a monomer in two solvents is given by

$$K = \frac{C_1}{C_2} \tag{9.19}$$

If its exists as an $n$-mer in one of the phases, the equation becomes

$$K - \frac{(C_1)^n}{C_2} \tag{9.20}$$

or

$$\log k = n \log C_1 - \log C_2 \tag{9.21}$$

The easiest way to determine the partition coefficient is to extract $V_1$ cm$^3$ of saturated aqueous solution with $V_2$ cm$^3$ of solvent and determine the concentration $C_2$ in the latter. The amount left in the aqueous phase is $C_1V_1 - C_2V_2 = \mathrm{M}$, so that the partition coefficient is given by

$$K = \frac{M}{V_1 C_1} \tag{9.22}$$

If it is assumed that the species is monomeric in both phases, the partition coefficient becomes the ratio of the solubilities, and it is simply sufficient to determine the solubility of the drug substance in the solvent (since it is assumed that the solubility is already known in water):

$$K = \frac{S_1}{S_2} \tag{9.23}$$

## 8. HYGROSCOPICITY

Hygroscopicity is, of course, an important characteristic of a powder. It can be shown for a fairly soluble compound that the hygroscopicity is related to its solubility (Carstensen, 1977, VanCampen et al., 1980), although it has been shown that the heat of solution plays an important part in what is conceived as "hygroscopicity" (VanCampen et al., 1983a,b,c). As mentioned in Chapter 8, a hygroscopicity experiment is carried out most easily by exposing the drug substance to an atmosphere of a known relative humidity (e.g., storing it over saturated salt solutions in desiccators). Each solution will give a certain relative humidity (RH), and the test simply consists of weighing the powder from time to time and determining the amount of moisture adsorbed (weight gained). This does not work with drug substances that decompose as, for instance, effervescent mixtures, which start losing weight due to carbon dioxide evolution (Carstensen and Usui, 1984).