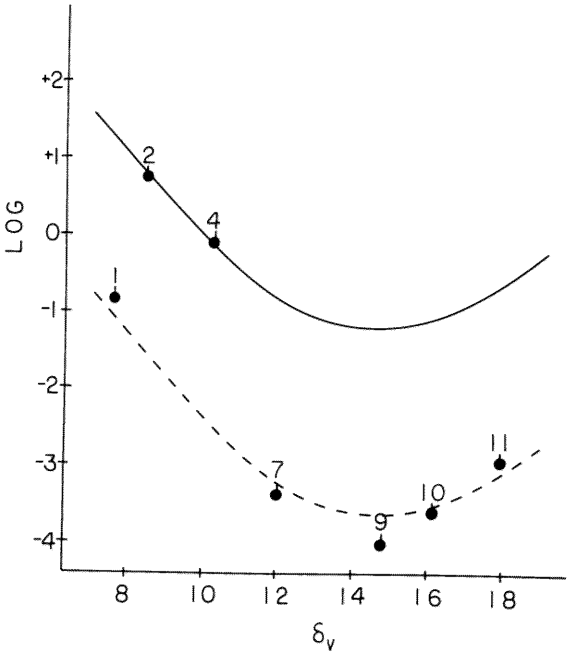

Figure 13.5

experimental $P_i^{s,v}$. This average difference corresponds to the constant in Eq. 13. If the thickness of the stratum corneum is assumed to be about 10 μm, then D_i^s is about 10^{-10} cm^2/s for most of the drugs studied, except for D_i^s for salicylic acid, which is one to two orders of magnitude greater. The calculated D_i^s, then, is of about the right magnitude for such polar molecules.

There are five conclusions that can be reached on the basis of the results given in Table 1 and Figures 2 through 5. First, there is generally a minimum in the log experimental $P_i^{s,v}$ versus δ_v curve that corresponds to those vehicles exhibiting δ_v similar to that of δ_i. The drug also usually exhibits its greatest mole fraction solubility in those same vehicles so that, generally, $P_i^{s,v}$ are inversely related to solubility (30). Second, for single-component vehicles, those vehicles that exhibit δ_v similar to that of δ_s also cause the most damage to the skin as assessed by second application studies. Because those δ_v are similar to δ_s, they may be solubilizing a portion of the membrane that is responsible for providing the diffusional resistance to drug permeation and, especially, to polar molecules exhibiting a δ_i quite different from δ_s. Third, from the knowledge of the solu-