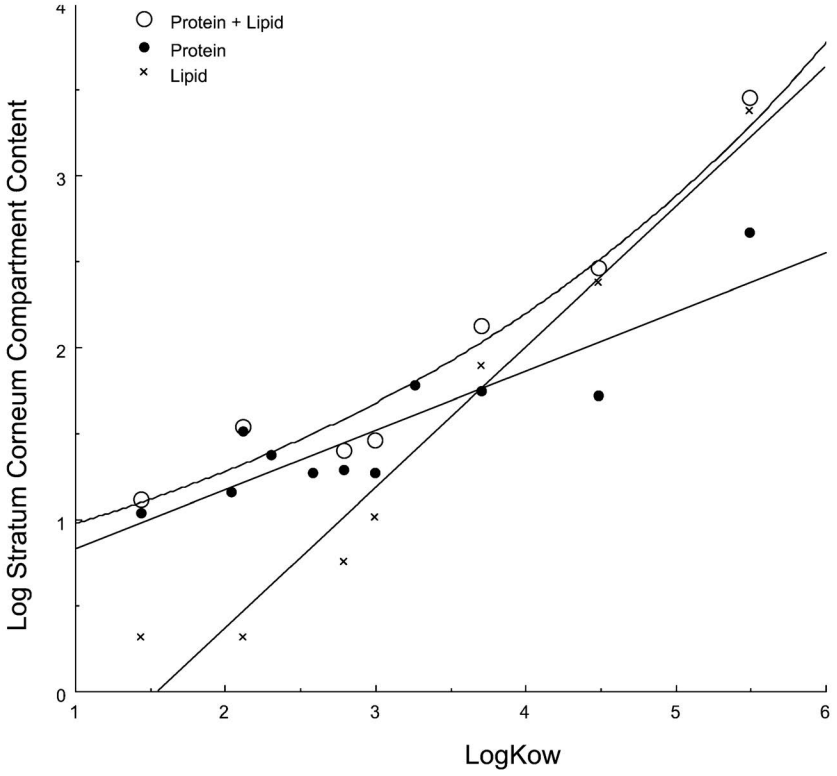

FIGURE 4.3 Plot of log apparent stratum corneum (protein and lipid)–water partition coefficient versus log octanol–water partition coefficient (ratio of 0.85 protein:0.15 lipid). Also shown is the contribution of the stratum corneum protein domain (0.85 protein) and stratum corneum lipid domain (0.15 lipid) to the partition coefficient. (Data abstracted from Reference 12.)

4.4.2 Stratum Corneum Partitioning or Capacity

The second determinant of the reservoir effect, the amount of drug in the stratum corneum, is defined by the affinity of the drug for the stratum corneum. In general, "like dissolves like" so that a lipophilic drug dissolved in a polar vehicle such as water will have a high affinity for the stratum corneum, whereas a lipophilic drug dissolved in a nonpolar vehicle such as oil will have a lower affinity. Figure 4.2b shows that increasing the affinity of drug for the stratum corneum results in a greater amount taken up into the stratum corneum but does not affect the time to be taken up or the fractional rate of reservoir depletion. Vickers (1) further suggested that the vehicle in which the steroid was applied was important. He suggested that the average duration of reservoir for 95% alcohol > hydrophilic cream > greasy ointment. If the 95% alcohol effectively left a solvent-deposited solid, the results may arise in part from the partitioning being in the same rank order. However, these vehicles are also likely to affect skin hydration, and stratum corneum diffusivity may be expected to be in the reverse order. Either or a combination of the two effects may explain the reservoir duration results obtained.

The nature of the drug may also affect the amount present in the reservoir. In general, following the principle of "like dissolves like," solutes having the greatest affinity for stratum corneum components would be expected to show the greatest stratum corneum reservoir effect. Figure 4.3 shows that the partitioning of various hydrocortisone-21-esters from water into the stratum corneum increases with lipophilicity, as defined by the octanol–water partition coefficient. These data suggest that partitioning occurs into both the lipid and protein domains of the stratum corneum, showing a