

MICROCALORIMETRIC DETERMINATION OF THE ENTHALPIES OF DISTRIBUTION OF ORGANIC SOLUTES BETWEEN WATER AND OILS

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There is much pharmaceutical interest in the partitioning of solutes between water and oils since it is believed that this provides information on their hydrophobicity - information that can be used in drug design, dosage form design and in analysis. Although the partition coefficient (K_d) is commonly sought, this free-energy based parameter only indicates the extent of distribution and does not reveal how or why it occurs. Problems associated with the change in standard state with temperature in determining the enthalpies of distribution (ΔH) of solutes (Kinkel et al 1981) has led us to determine directly these ΔH values. Accordingly we are determining the ΔH of neutral solute transfer between water (buffered) and various oils including 2,2,4-trimethylpentane, octan-1-ol, cyclohexane and chloroform/carbon tetrachloride mixtures. These measurements are being performed using a LKB flow microcalorimeter with water-to-oil and oil-to-water values being determined. Transfer occurs in a flow mix cell, and to determine the extent of distribution we have incorporated into the system a phase-splitting device (Kinkel and Tomlinson 1980) at the flow mix cell outlet. Table 1 gives some of our initial findings with the water/2,2,4-trimethylpentane system, together with literature values.

Table 1. Microcalorimetrically determined enthalpies of distribution in the water/2,2,4-trimethylpentane system, at 25°C.

Solute	log K_d (o/w) mole fraction	ΔH (oil to water) kJ.mol ⁻¹	literature ΔH values	
			van't Hoff operator water to oil (Kinkel et al 1981)	microcalorimetry oil to water (Breslauer, 1978)
phenol	-1.92	-16.38	16.4	-16.3
p-chlorophenol	-1.45	-14.52	10.6	
p-chloroaniline	-0.48	-9.10	5.8	

(All ΔH values are in kJ.mol⁻¹)

It is shown from Table 1 that there is very close agreement between the present results and those measured elsewhere using microcalorimetry, and that using van 't Hoff operators the agreement is reasonable. Results here indicate that microcalorimetry can be used successfully to determine the enthalpy of distribution of organic solutes, and our studies are continuing into this. Of particular concern to us is the determination of ΔH in solvent pairs of high mutual solubility (e.g. water/octan-1-ol) since we have argued recently (Kinkel et al 1981) that reported enthalpy-entropy compensation (Rogers and Wong 1980) in such systems are experimental artefacts, and that, following the suggestion of Beezer et al (1980), only directly determined values are valid.

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