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Buffer Ionisation Heats and other "Hidden Variable" Effects

Calorimetry measures the totality of heat effects in any process, and this has long been used to advantage for example to detect otherwise unsuspected protonation changes involved in ligand binding and other processes (see [1,2] for recent examples, though the effects has been in use for over 20 years [3-5]). It is sometimes claimed that calorimetry is unique in this respect, and that more indirect, spectroscopic/van't Hoff methods do not show this. But this is incorrect, as can be shown simply as follows.

Imagine a simple equilibrium process involving the release of n hydrogen ions:

$$X \rightarrow Y + nH^+$$

In a well-buffered system each released H^+ ion would be taken up by the buffer conjugate base (A^-), with heat effect $-\Delta H_I$ (where ΔH_I is the heat of protonation of the buffer):

$$A^- + H^+ \rightarrow AH \qquad ; \quad \Delta H_I$$

so the overall heat effect measured (isothermally) in the calorimeter would be the sum of two effects:

$$\Delta H_{cal} = \Delta H_{X\rightarrow Y} + n.\Delta H_I$$

Now imagine the same process followed by some spectroscopic or other indirect technique, where one might measure the apparent equilibrium constant:

$$K_{app} = [Y]/[X]$$

unaware that the true equilibrium constant, taking account of protonation changes, should be:

$$K = [Y][H^+]^n/[X] = K_{app}[H^+]^n$$

The apparent van't Hoff enthalpy (ΔH_{VH}), determined from measurements of K_{app} at different temperatures, would consequently reflect both the intrinsic temperature dependence of the process ($\Delta H_{X\rightarrow Y}$) and, unwittingly, the way in which the change in buffer pH with temperature affects the equilibrium. Algebraically this is as follows:

$$\Delta H_{VH} = RT^2.d(\ln K_{app})/dT = RT^2.d(\ln K)/dT - nRT^2.d(\ln [H^+])/dT$$

$$= \Delta H_{X\rightarrow Y} + n.\Delta H_I \qquad (\equiv \Delta H_{cal})$$

where the final step follows because, in any buffered system:

$$dpH/dT = dpK_A/dT = \Delta H_I/2.303RT^2$$

In other words, regardless of whether one measures the enthalpy directly by calorimetry or indirectly using the van't Hoff equation, the answer is the same and - importantly - includes any additional heats due to buffer protonation whether one is aware of them or not. The same will be true for any other "hidden variables" (i.e. additional process that are not included explicitly in the equilibrium constant expression used in the van't Hoff analysis) as a consequence of the fundamental theories of thermodynamic linkage [4,5].

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