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Significant discrepancies between van't Hoff and calorimetric enthalpies. II.

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Abstract

Isothermal calorimetric titration of 18-crown-6 ether with $BaCl_2$ in pure aqueous solution over the temperature range 7-40 °C gives precise binding constants and enthalpy changes. Nonlinear least-squares fitting of the binding constants to the integrated van't Hoff equation, including a temperature-independent change in heat capacity, leads to van't Hoff enthalpies that differ significantly from the observed calorimetric enthalpies. This perplexing discrepancy appears at present to be very widely occurring.

Keywords: calorimetric enthalpies; calorimetry; temperature variation of equilibrium constants; van't Hoff enthalpies

In a recent paper (Naghibi et al., 1995), we pointed out the frequent occurrence of discrepancies between van't Hoff enthalpies derived from the temperature variation of equilibrium constants and enthalpies determined by direct calorimetric measurements. To date we have not found a single case where there is agreement, to within experimental uncertainty, between these two types of enthalpy values. All the systems but two considered in our earlier paper involved proteins, the two exceptions being the binding of cyclohexanol to α- and β-cyclodextrins. Even in these cases involving relatively simple molecules, there were significant differences between van't Hoff and calorimetric enthalpies.

Izatt et al. (1976) and Briggner and Wadsö (1991) published calorimetric data on the binding of barium chloride to 18-crown-6 ether, the latter publication including equilibrium data at three temperatures. This system would appear to be an excellent system for further study of the problem concerning van't Hoff and calorimetric enthalpies because of its simplicity: 18-crown-6 is a solid cyclic polyether of 264 Da molecular mass; both reactants are readily available in very pure form; and they can be weighed and dissolved in pure water for the reaction. Izatt et al. reported data at 25 °C only, and Briggner and Wadsö limited their study to three temperatures. Because our method for analyzing such data requires measurements at four or more temperatures, we have undertaken further study of this system.

Results and discussion

Figure 2 shows a typical titration experiment with $BaCl_2$ (0.09327 M) titrated into 18-crown-6 (0.00945 M) in aqueous solution at 25.0 °C. In Figure 2A, heat evolution in each 9-μL injection with blank corrections is shown; in Figure 2B, observed and calculated titration curves. All the calculations were performed using the ORIGIN software supplied with the calorimeter.

Table 1 lists the results obtained at eight temperatures, with pure water as solvent. Table 2 gives similar data obtained in nine experiments in buffered solution at pH 5.0, the buffer being 0.2 M sodium acetate adjusted with acetic acid to pH 5.0.

Calorimetric enthalpies

The enthalpies listed in the sixth column of Table 1 show a slight curvature as a function of temperature. Least squaring of the data to a quadratic function gives

$$\Delta H_{cal} = -8{,}722.4 + 66.072t - 0.7077t^2, \qquad (1)$$

with a standard deviation (SD) of ±24 cal mol^{-1}. Here t is the temperature in degrees Celsius. ΔC_p (cal) at 25 °C is 30.7 cal K^{-1} mol^{-1}.

Similarly, the enthalpies in 0.20 M sodium acetate buffer at pH 5.0 (Table 2) lead to the equation

$$\Delta H_{cal} = -6{,}888.1 + 24.580t - 0.3030t^2, \qquad (2)$$

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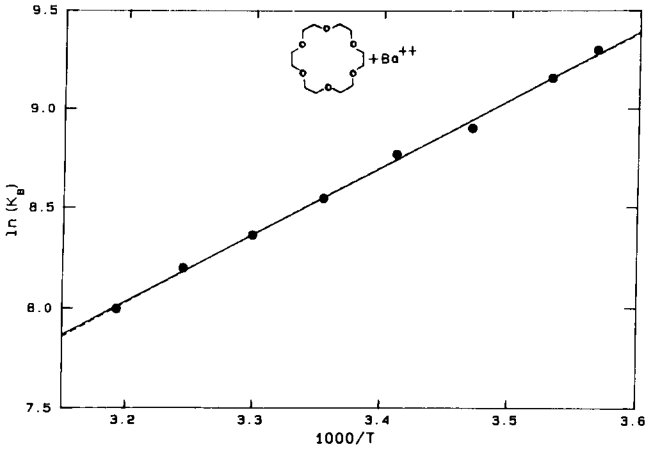

Fig. 1. Plot of ln K_B versus 1,000/T for the titration of 18-crown-6 with $BaCl_2$ in pure H_2O. Experimental points: solid line, data calculated with $\Delta C_p = 8.1$ cal K^{-1} mol^{-1}; dashed line, data calculated with $\Delta C_p = 0$ cal K^{-1} mol^{-1}. The difference between the two calculated lines is barely visible.

with an SD of ±33 cal mol^{-1}, and ΔC_p (cal) = 9.4 cal K^{-1} mol^{-1} at 25 °C.

It is interesting that these enthalpies are of smaller magnitude than those in Table 1. Izatt et al. (1976) report the binding constant of sodium ions to 18-crown-6 to be 6.3 M^{-1} with an enthalpy change of −2,250 cal mol^{-1} at 25 °C, to form a 1:1 complex. With sodium ions at a concentration of 0.20 M, in large excess, the degree of saturation of the ether would thus be $0.20\,K_B/(1 + 0.20\,K_B) = 0.56$. Replacement of Na^+ by Ba^{++} would therefore lead to a decrease of 1,260 cal mol^{-1} in the magnitude of the enthalpy of binding of Ba^{++}, giving −6,250 cal mol^{-1}. This figure is 3.5% less than the average value at 25 °C in Table 2.

Table 1. *Thermodynamic data for the binding of $BaCl_2$ to 18-crown-6 in pure water*[a]

		$K_B \times 10^{-3}$ (M^{-1})		$-\Delta H_{vH}$	$-\Delta H_{cal}$
t (°C)	n	Obs.	Calc.	(kcal mol^{-1})	
7.0	1.01	10.92 ± 0.40	10.77	6.86	8.32
10.0	1.02	9.46 ± 0.29	9.46	6.83	8.13
15.0	1.00	7.34 ± 0.21	7.66	6.79	7.85
20.0	1.02	6.44 ± 0.08	6.26	6.75	7.70
25.0	1.03	5.14 ± 0.04	5.16	6.71	7.51
30.0	1.02	4.28 ± 0.05	4.28	6.67	7.41
35.0	1.01	3.64 ± 0.04	3.58	6.63	7.27
40.0	1.00	2.97 ± 0.03	3.01	6.59	7.20

[a] SD in $K_B \times 10^{-3}$ = ±0.15; ΔC_p (vH) = 8.1 cal K^{-1} mol^{-1}; ΔC_p (cal) = 33.3 cal K^{-1} mol^{-1}.

Table 2. *Thermodynamic data for the binding of $BaCl_2$ to 18-crown-6 in 0.20 M sodium acetate buffer, pH 5.0*[a]

		$K_B \times 10^{-3}$ (M^{-1})		$-\Delta H_{vH}$	$-\Delta H_{cal}$
t (°C)	n	Obs.	Calc.	(kcal mol^{-1})	
7.0	1.00	5.01 ± 0.03	5.10	7.12	6.72
10.0	.98	4.58 ± 0.04	4.46	6.93	6.66
15.0	1.00	3.61 ± 0.02	3.62	6.62	6.61
15.0	1.00	3.62 ± 0.03	3.62	6.62	6.60
25.0	1.00	2.49 ± 0.02	2.50	5.98	6.44
25.0	1.00	2.48 ± 0.02	2.50	5.98	6.51
35.0	1.00	1.85 ± 0.04	1.83	5.35	6.34
45.0	1.00	1.41 ± 0.04	1.42	4.72	6.39
45.0	1.00	1.42 ± 0.01	1.42	4.72	6.43

[a] SD in $K_B \times 10^{-3}$ = ±0.051; ΔC_p (vH) = 63 cal K^{-1} mol^{-1}; ΔC_p (cal) at 25 °C = 9.4 cal K^{-1} mol^{-1}.

van't Hoff enthalpies

The van't Hoff equation in integrated form can be written as

$$\ln\frac{K}{K_0} = \frac{\Delta H_0 - T_0\Delta C_p}{R}\left(\frac{1}{T_0} - \frac{1}{T}\right) + \frac{\Delta C_p}{R}\ln\frac{T}{T_0} \qquad (3)$$

where T_0 is an arbitrarily chosen reference temperature (in K) and K_0 and ΔH_0 are temporarily assigned values of the equilibrium constant and van't Hoff enthalpy at that temperature. The heat capacity change, ΔC_p, is assumed to be independent of temperature. Values for K_0, ΔH_0, and ΔC_p that minimize the SD between calculated and observed values of ln K are then selected by a procedure of successive approximations designed to avoid local minima.

Fitting the equilibrium constants in the third column of Table 1 leads to the results given in the fourth and fifth columns of the table, with the SD between calculated and observed values of ln K_B equal to ±0.0204. The calculated values of K_B thus are in good agreement with the observed values in Table 1, with an SD of ±150 M^{-1}. It is important to note that the calculated values of ΔH_{vH} differ significantly from the observed values for ΔH_{cal} in Table 1 by amounts well beyond experimental uncertainty, with the ratio $\Delta H_{cal}/\Delta H_{vH}$ varying from 1.21 at 7 °C to 1.09 at 40 °C, and that ΔH_{vH} varies with temperature with ΔC_p (vH) = 8.1 cal K^{-1} mol^{-1}. As noted in our earlier paper (Naghibi et al., 1995), we have yet to find a set of data for which ΔC_p (vH) as evaluated from the equilibrium data is zero within experimental uncertainty. In other words, we have not yet found a system for which the usual procedure of linear least squaring of ln K versus 1/T is appropriate. Linear least squaring in this case gives an apparent ΔH_{vH} of −6.73 kcal mol^{-1}, with a coefficient of determination $r = 0.998$ and an SD of ±0.0219 kcal mol^{-1}. Despite this high value for r, which would ordinarily be taken as proof of strict linearity, the data are sufficiently precise to show a small curvature in the ln K_B versus 1/T plot shown in Figure 1.

Treatment of the equilibrium constants in the third column of Table 2 by the procedure outlined above gives the results listed in columns four and five of the table. Here the observed and calculated values of ln K_B differ with an SD of ±0.0124, and the values for K_B with an SD of $\pm 54\ M^{-1}$.

It is surprising to find significant discrepancies between ΔH_{vH} and ΔH_{cal}, and between ΔC_p (vH) and ΔC_p (cal), in a system as simple as the one treated here, especially when run in pure water as solvent. At the end of a titration, the concentration of uncomplexed $BaCl_2$ is roughly 10 mM. According to Ardizzone et al. (1976), the activity coefficient of $BaCl_2$ at this concentration is 0.728 at 10 °C and 0.718 at 40 °C, a change of only 1.4%. Although no such information is available for 18-crown-6 either complexed or uncomplexed, it can be assumed that deviations from ideal behavior can have only a very small effect on this system. Although we are unable to make a definite suggestion as to the cause of the observed discrepancies, the removal of water originally associated with the crown ether and/or with $BaCl_2$ on formation of the complex could conceivably play a significant role. Such effects would obviously be very difficult to evaluate.

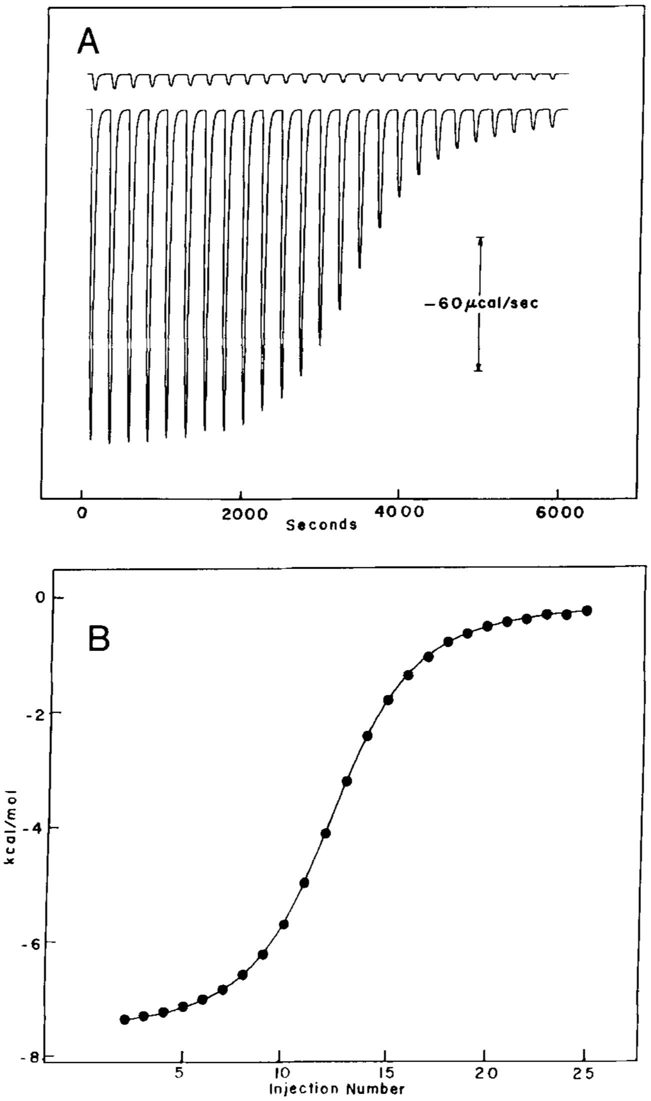

Fig. 2. The results obtained in a typical titration experiment. 18-crown-6 ether (9.5 mM in the titration cell) titrated with $BaCl_2$ (93.3 mM in 9-μL injections) at 25 °C in H_2O as solvent. **A:** Injection records with corresponding baseline injections. **B:** Enthalpy data with calculated titration curve. Number of binding sites per molecule, 1.03; binding constant, 5,140 ± 40 M^{-1}; enthalpy of binding, −7,510 ± 7 kcal mol^{-1}. The record for the first injection has been deleted because of diffusion of titrant into the cell during the initial thermal equilibration.

Materials and methods

18-Crown-6 of 99.5+% purity was purchased from Sigma. $BaCl_2 \cdot 2H_2O$ of 99.4+% purity was purchased from Baker.

Calorimetric titrations were run in an OMEGA instrument (Wiseman et al., 1988) manufactured by Microcal, Inc. (Northampton, Massachusetts).

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