For a reactant isomerization (such as reaction (1)), the sign of $\Delta C_p^{0\prime}$ is negative. For a reaction sequence involving a product isomerization step, however, the sign of $\Delta C_p^{0\prime}$ is positive.

In Fig. 2 we have plotted $\Delta C_p^{0\prime}$ as a function of temperature according to equation (4) using the best-fit parameters and algebraic sense of Fig. 1.

Because the sign of the $\Delta C_p^{0\prime}$ is negative, if there is a single (implicit) isomerization in the overall reaction, it must involve one of the reactants rather than one of the products. An attempt to fit the data to an equation similar to that for reaction (2) expanded to include an isomerization of the E–NADPH complex as well as one of E, indicated no contribution from that added feature. Thus, although there may be an isomerization of the enzyme–ligand complex, evidently such an equilibrium either is not poised in or near the experimental temperature range or must not involve a substantial $\Delta H^{0\prime}$. As reaction (2) is symmetrical in E and NADPH, an isomerization of the ligand could account for the data as well as an isomerization of E. While NADPH is known to exist as an equilibrium mixture of folded and unfolded forms, the T_2 for this process is below 20 °C and its $\Delta H^{0\prime}$ is too small to make an appreciable contribution to the observed process[9]. The attempted inclusion of finite intrinsic $\Delta C_p^{0\prime}$ terms for steps 1 and 2 of reaction (2) also failed to improve the fit of the equation to the data.

We conclude, therefore, that the observed $\Delta C_p^{0\prime}$ of the formation of the glutamate dehydrogenase–NADPH complex is fully accounted for by a poised isomerization of the free enzyme involving a very large enthalpy change that is largely compensated by an opposing large entropy change, the step in itself involving no detectable $\Delta C_p^{0\prime}$ and H^+ transfer to or from the buffer not contributing significantly to the measured enthalpy change.

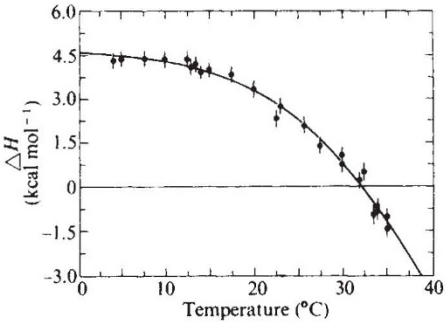

Fig. 1 The temperature dependence of $\Delta H^{0\prime}$ of the glutamate dehydrogenase–NADPH complex in 0.1 M phosphate buffer, *p*H 7.6. The reaction heats, *q*, were determined in a flow microcalorimeter using apparatus, reagents and procedures as previously described[3]. The enzyme concentration was usually ~90μM (active sites). At each temperature, calorimetric measurements were made at saturating concentrations of NADPH starting at $20 \times K_D$ and extending to $200 \times K_D$. A plot of *q* versus [NADPH] was linear with a slope of $0 \pm 6 \times 10^{-4}$ kcal per mol NADPH in each case. As noted in the text, while the free enzyme is stable at 50 °C, its reduced coenzyme complex denatures rapidly above 37 °C. The following controls and precautions assure us that the data presented are unaffected by errors due to denaturation. (1) The solution emerging from the calorimeter was assayed for enzymatic activity. The activities so measured agreed with those of the initial solution to within 5% and showed no trend indicating denaturation. As the solution remains at an elevated temperature for some time after leaving the sensing chamber of the instrument, any time-dependent denaturation would be magnified several-fold by the time the solution actually emerged from the instrument. (2) The value of *q* was unchanged on raising the flow rate from 10 μl s^{-1} to 13 μl s^{-1}. Had there been any significant time-dependent denaturation, the value of *q* would have differed because the two flow rates correspond to different residence times. The solid line is calculated from a nonlinear least-squares fit to reaction (3). The $\Delta H^{0\prime}$ value at 15 °C differs from that reported prevously using a batch calorimeter. The batch value (and the very small $\Delta C_p^{0\prime}$ calculated from it) must now be presumed to be erroneous.

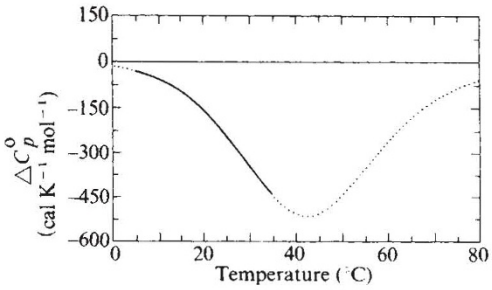

Fig. 2 The temperature dependence of $\Delta C_p^{0\prime}$ of the glutamate dehydrogenase–NADPH complex. The line is calculated from equation (4) using parameters from Fig. 1. The solid line portion of the curve indicates the region covered by experimental data.

A similar mechanism, involving a temperature-induced shift between multiple forms of the free enzyme, is consistent with the recently reported large $\Delta C_p^{\ddagger}$ in the glutamate dehydrogenase-catalysed reaction[8]. We cannot say how general the phenomenon reported here may be, but we note that $\Delta C_p^{0\prime}$s reported for complexes of other dehydrogenases at 20 °C are of a similar magnitude to that of glutamate dehydrogenase at its maximum near 40 °C. Thus, the differences between the $\Delta C_p^{0\prime}$s of the various enzymes may simply reflect differences in the T_2s of otherwise similar mechanisms.

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Corrigendum

In the letter 'Competition relatedness and efficiency' by J. R. W. Harris, *Nature* **292,** 54–55, the parameter *x* in equation (2) should be replaced by *z*.

Errata

In the article 'Seismotectonics of the El Asnam earthquake' by M. Ouyed *et al.*, *Nature* **292,** 26–31, the legend to Fig. 6 was reproduced incorrectly in some copies of *Nature*. It should read: *a*, The 1.30-m left lateral slip measured on a ploughed field at Zebadja near the centre of the fault. *b*, Southern segment of the fault. Typical pressure ridges showing the uplift of the northwestern block (to the left), and collapse due to gravity. Extension cracks follow the compression axis.

In the news item 'Yugoslavian nuclear power: Locals late reacting', *Nature* **291,** 446, the name of the head of the Croatian Commission for the Human Environment was given incorrectly. It should read Marko Branica.