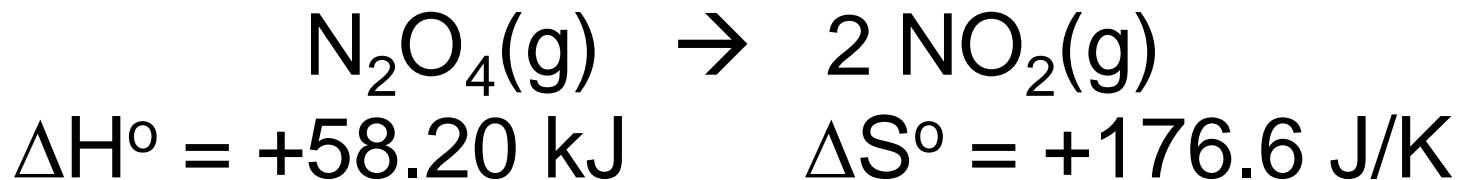


Chemistry 201

Temperature
dependence of K

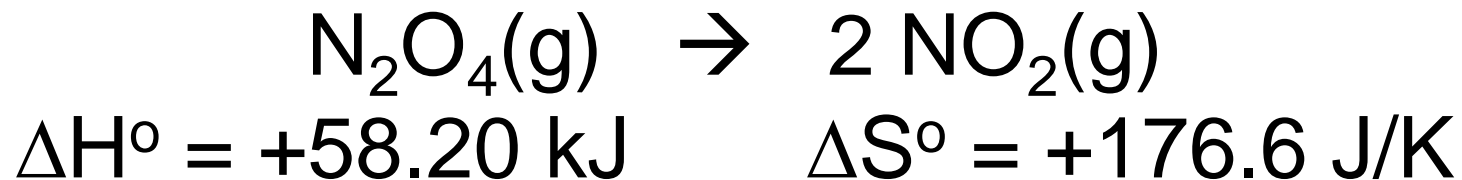
NC State University

Temperature dependence of K



At what temp. does $\Delta G^\circ = 0$?
(K = 1)

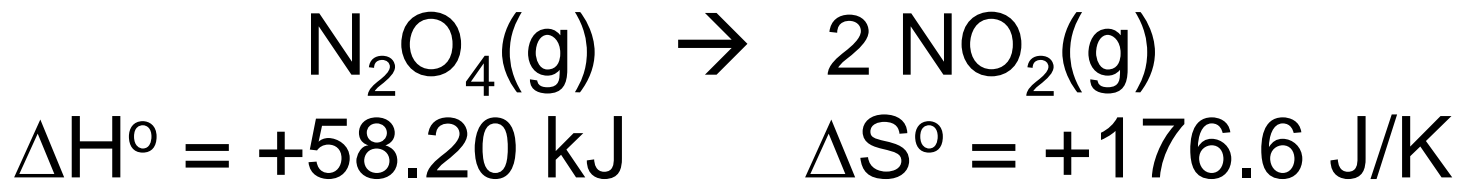
Temperature dependence of K



At what temp. does $\Delta G^\circ = 0$?
($K = 1$)

$$\Delta H^\circ - T\Delta S^\circ = 0$$

Temperature dependence of K

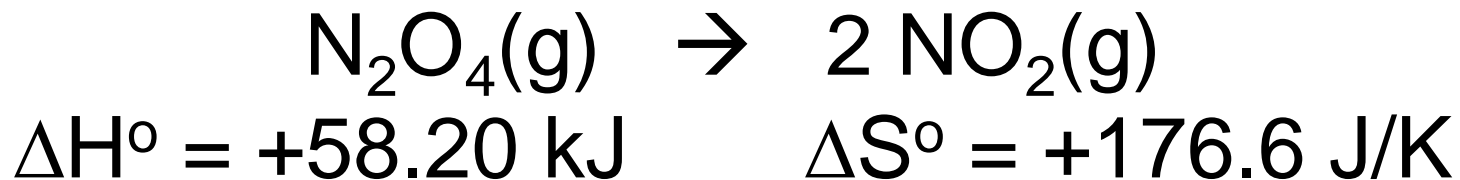


At what temp. does $\Delta G^\circ = 0$?
($K = 1$)

$$\Delta H^\circ - T\Delta S^\circ = 0$$

$$\Delta H^\circ = T\Delta S^\circ$$

Temperature dependence of K



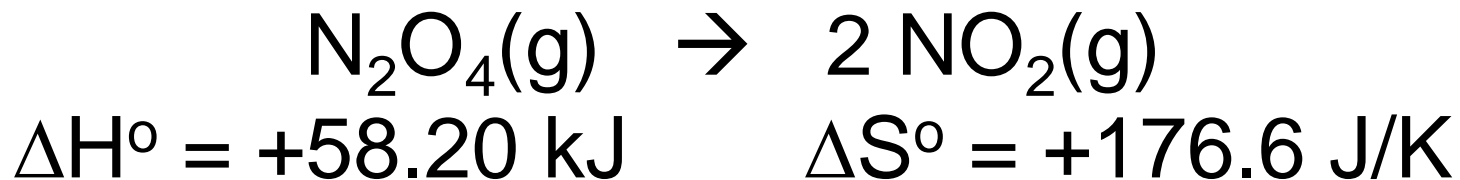
At what temp. does $\Delta G^\circ = 0$?
($K = 1$)

$$\Delta H^\circ - T\Delta S^\circ = 0$$

$$\Delta H^\circ = T\Delta S^\circ$$

$$T = \frac{\Delta H^\circ}{\Delta S^\circ}$$

Temperature dependence of K



At what temp. does $\Delta G^\circ = 0$?
($K = 1$)

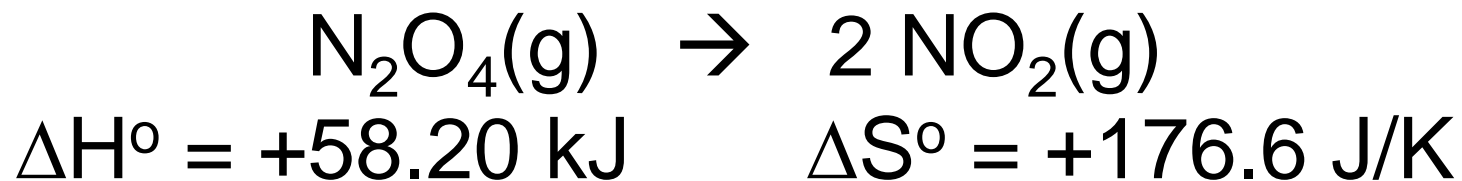
$$\Delta H^\circ - T\Delta S^\circ = 0$$

$$\Delta H^\circ = T\Delta S^\circ$$

$$T = \frac{\Delta H^\circ}{\Delta S^\circ}$$

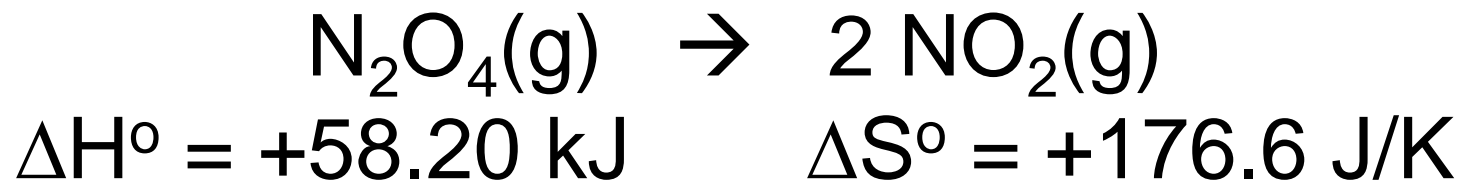
$$T = \frac{58,200 \text{ J}}{176.6 \text{ J/K}} = 329.6 \text{ K}$$

Temperature dependence of K



What is K at 425 K?

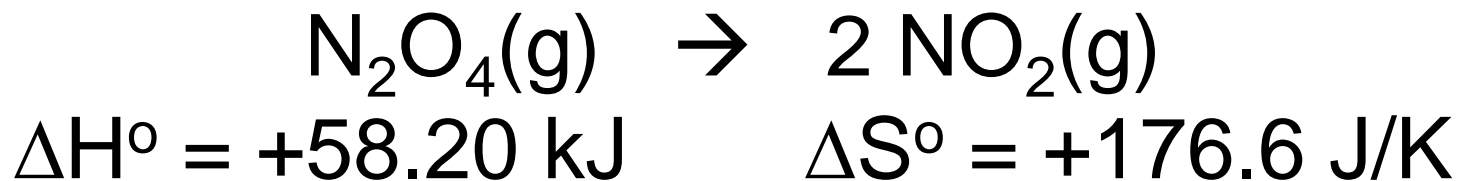
Temperature dependence of K



What is K at 425 K?

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

Temperature dependence of K

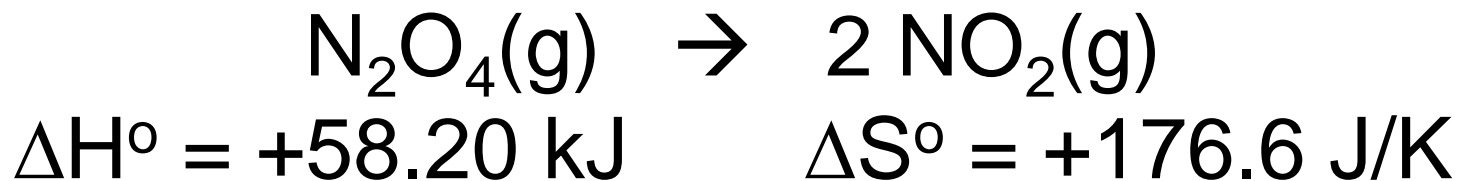


What is K at 425 K?

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

$$K = \exp\left\{-\frac{\Delta G^\circ}{RT}\right\} = \exp\left\{-\frac{\Delta H^\circ - T\Delta S^\circ}{RT}\right\}$$

Temperature dependence of K



What is K at 425 K?

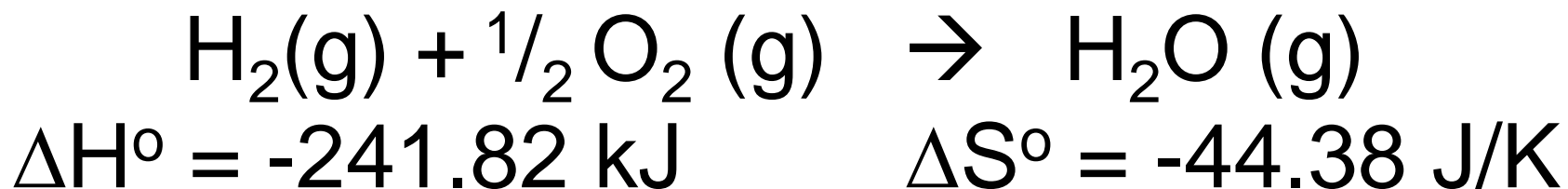
$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

$$K = \exp\left\{-\frac{\Delta G^\circ}{RT}\right\} = \exp\left\{-\frac{\Delta H^\circ - T\Delta S^\circ}{RT}\right\}$$

$$K = \exp\left\{-\frac{58200 - (425)(176.6)}{(8.31)(425)}\right\} = 118$$

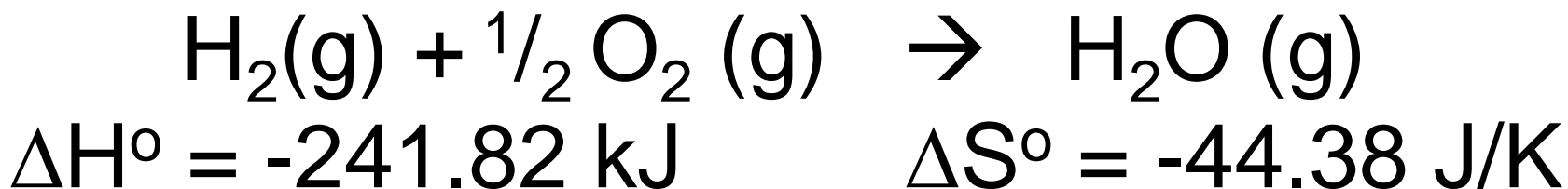
Remember to convert ΔH° to units of J (multiply by 1000)

Temperature dependence of K



At what T, if any, does $K = 1$?

Temperature dependence of K



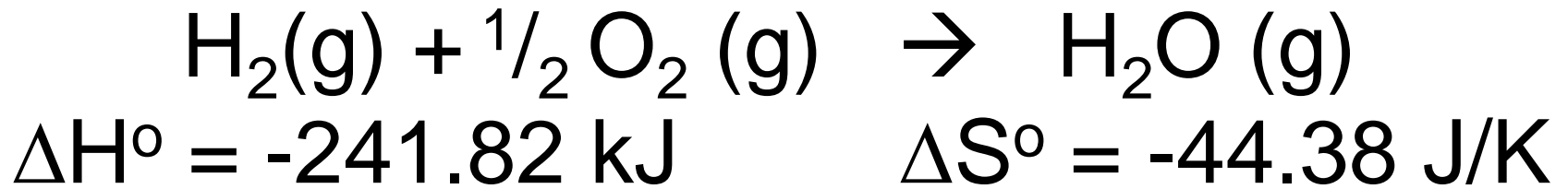
At what T, if any, does K = 1?

The temperature corresponds to $\Delta G^\circ = 0$

$$T = \frac{\Delta H^\circ}{\Delta S^\circ}$$

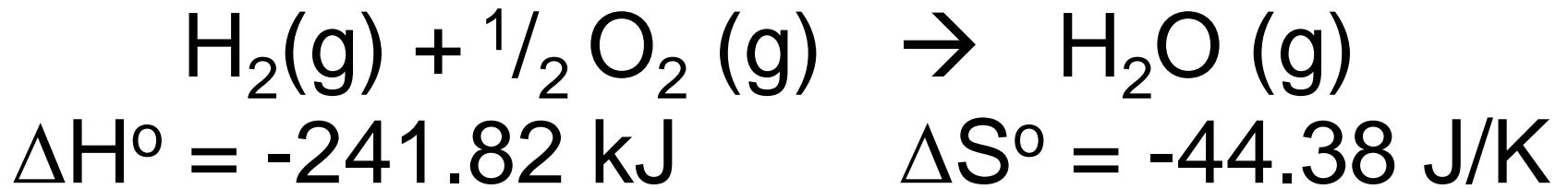
$$T = \frac{-241,820 \text{ J}}{-44.38 \text{ J/K}} = 5450 \text{ K}$$

Temperature dependence of K



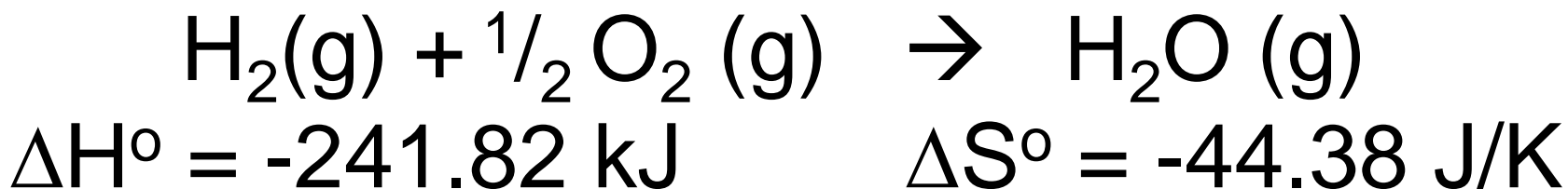
Evaluate K at 1500 K.

Temperature dependence of K



Evaluate K at 1500 K.

Temperature dependence of K



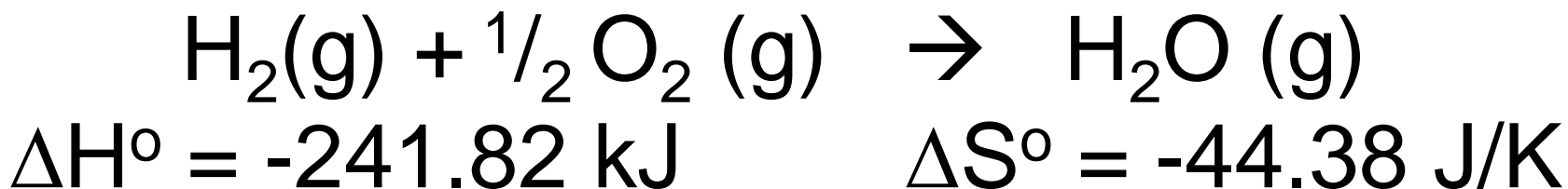
Evaluate K at 1500 K.

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

$$\Delta G^\circ = -241,820 \text{ J} - (1500 \text{ K})(-44.38 \text{ J/K})$$

$$\Delta G^\circ = -176,000 \text{ J}$$

Temperature dependence of K



Evaluate K at 1500 K.

$$\Delta G^\circ = -176,000 \text{ J}$$

$$K = \exp \left\{ -\frac{\Delta G^\circ}{RT} \right\} = \exp \left\{ -\frac{-176,000 \text{ J}}{(8.31 \text{ J/K})(1500 \text{ K})} \right\}$$

$$K = 1.35 \times 10^6$$

The temperature dependence of ΔG°

As we have shown previously, ΔG , will decrease until it reaches 0. Then we have reached equilibrium. The equilibrium condition is

$$\Delta G^\circ = -RT \ln K$$

Next we consider the fact that we can use the temperature dependence of the free energy to obtain information about the enthalpy.

$$\Delta H^\circ - T\Delta S^\circ = -RT \ln K$$

If we assume that ΔH° and ΔS° are independent of temperature, then we can obtain the values of K at two temperatures as follows,

$$\begin{aligned}\Delta H^\circ - T_1\Delta S^\circ &= -RT_1 \ln K_1 \\ \Delta H^\circ - T_2\Delta S^\circ &= -RT_2 \ln K_2\end{aligned}$$

The temperature dependence of ΔG°

Then we can divide each equation by its respective temperature to obtain,

$$-RT_2 \ln K_2 = \Delta H^\circ - T_2 \Delta S^\circ$$

$$-RT_1 \ln K_1 = \Delta H^\circ - T_1 \Delta S^\circ$$

We divide each equation by its respective temperature to obtain

$$\ln K_2 = -\frac{\Delta H^\circ}{RT_2} + \frac{\Delta S^\circ}{R}$$

$$\ln K_1 = -\frac{\Delta H^\circ}{RT_1} + \frac{\Delta S^\circ}{R}$$

Then we subtract the equation at temperature T_1 from the equation at T_2 .

The temperature dependence of ΔG°

The subtracted equation is:

$$\ln K_2 - \ln K_1 = - \left(\frac{\Delta H^\circ}{RT_2} - \frac{\Delta H^\circ}{RT_1} \right)$$

Finally we factor the equation to obtain

$$\ln \frac{K_2}{K_1} = - \frac{\Delta H^\circ}{R} \left(\frac{1}{T_2} - \frac{1}{T_1} \right)$$

This is known as the van't Hoff equation. This equation says that if we plot $\ln(K)$ vs $1/T$, we obtain a line, and the slope of that line is $-\Delta H^\circ / R$.

Using equilibrium data to obtain ΔH° and ΔS°



$$T_1 \text{ at } 190 \text{ K} \qquad K_1 = 18.4$$

$$T_2 \text{ at } 200 \text{ K} \qquad K_2 = 681$$

find ΔH° and ΔS°

Using equilibrium data to obtain ΔH°

Solution: starting with the equation

$$\ln\left(\frac{K_2}{K_1}\right) = -\frac{\Delta H^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

Solve for ΔH°

$$\Delta H^\circ = \frac{-R \ln\left(\frac{K_2}{K_1}\right)}{\left(\frac{1}{T_2} - \frac{1}{T_1}\right)}$$

Substitute in the given values

$$\Delta H^\circ = \frac{-(8.31 \frac{J}{molK}) \ln\left(\frac{681}{18.4}\right)}{\left(\frac{1}{200K} - \frac{1}{190K}\right)} = 114.0 \text{ kJ/mol}$$

Using equilibrium data to obtain ΔS°

If we know both ΔG° and ΔH° , then we can calculate ΔS°

$$\Delta S^\circ = \frac{\Delta H^\circ - \Delta G^\circ}{T}$$

The value of ΔG° can be obtained from the equilibrium constant.

$$\Delta G^\circ = -RT_2 \ln K_2$$

Note that we could have chosen to use either of the equilibrium constants. We simply must be consistent and use the proper temperature in the entropy expression.

Using equilibrium data to obtain ΔS°

For the smog reaction (using the 200 K data) we have:

$$\Delta G^\circ = - \left(8.31 \frac{J}{mol} \right) (200 K) \ln 681$$

So that

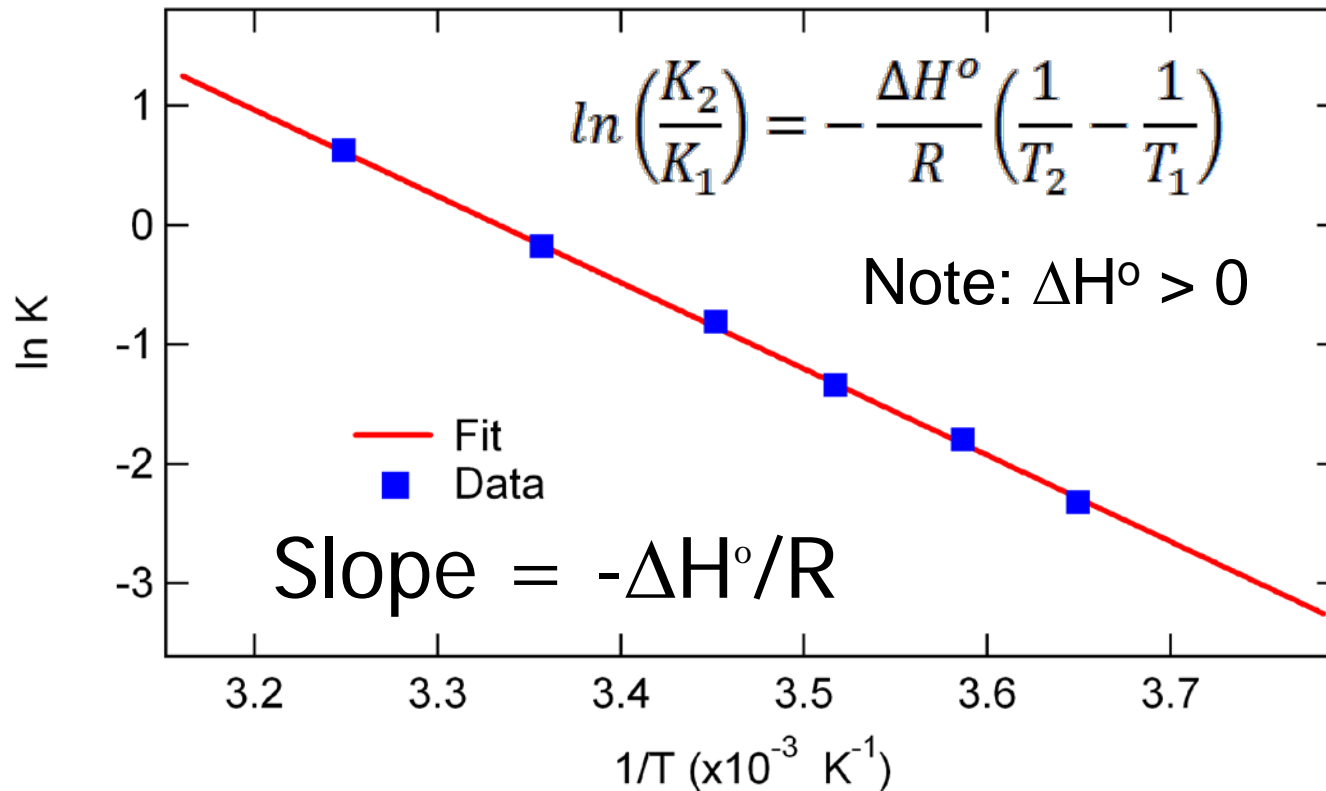
$$\Delta G^\circ = -10,840 J/mol$$

Therefore,

$$\Delta S^\circ = \frac{(114,000 - (-10,840)) J/mol}{200 K}$$

$$\Delta S^\circ = 642 J/molK$$

Van't Hoff plots



The standard method for obtaining the reaction enthalpy is a plot of $\ln K$ vs. $1/T$

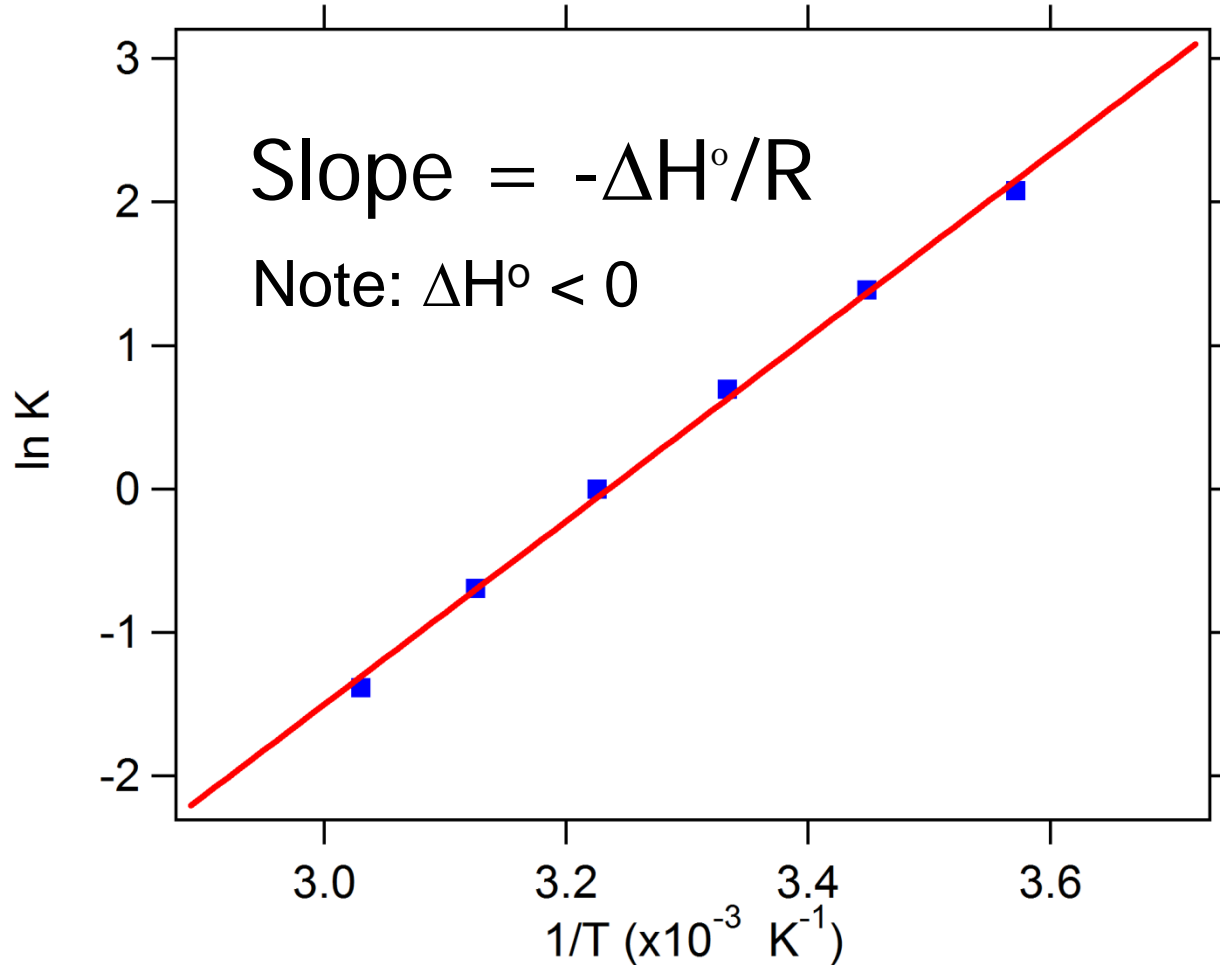
Van't Hoff plot for drug binding

A practical example of the application of the van't Hoff equation can be found in drug binding.

The equilibrium constant for drug binding to an active site can be measured by fluorescence, NMR, etc. at various temperatures. Then one may plot $\ln K$ vs. $1/T$ and fit the result to a line.

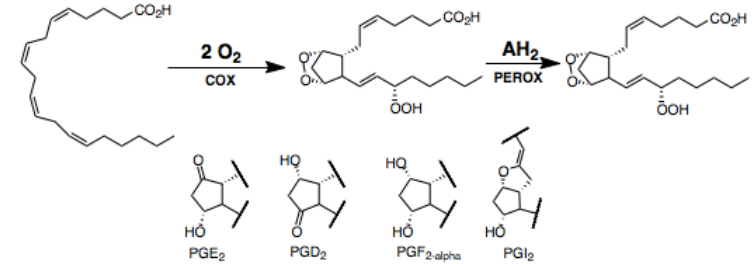
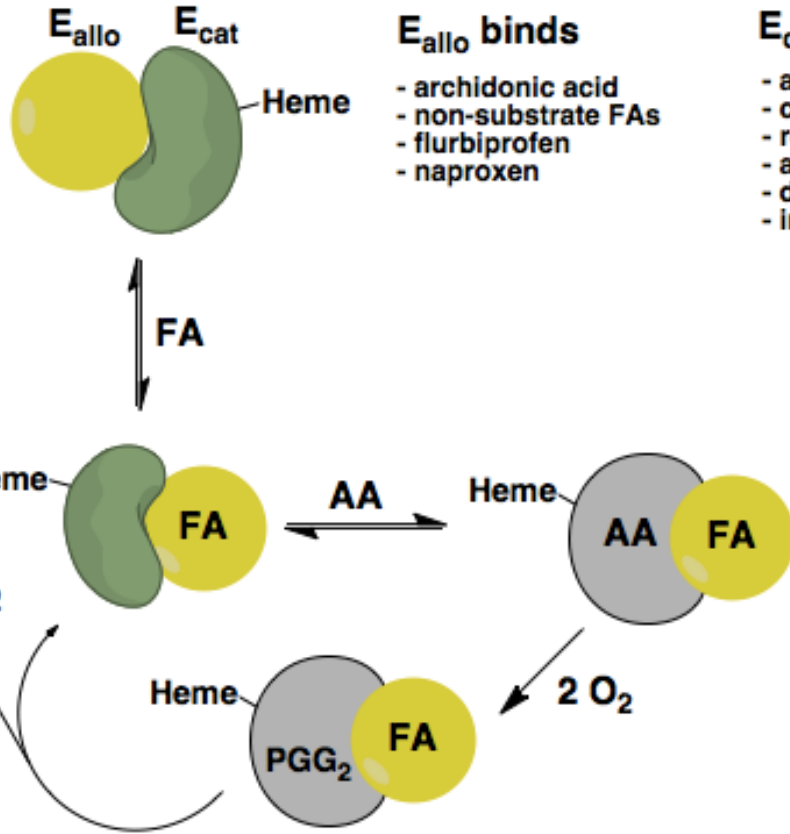
In most cases the binding will be exothermic to that $\Delta H^\circ < 0$ and then slope of the line will be positive rather than negative as shown in the previous slide.

Van't Hoff plot for drug binding

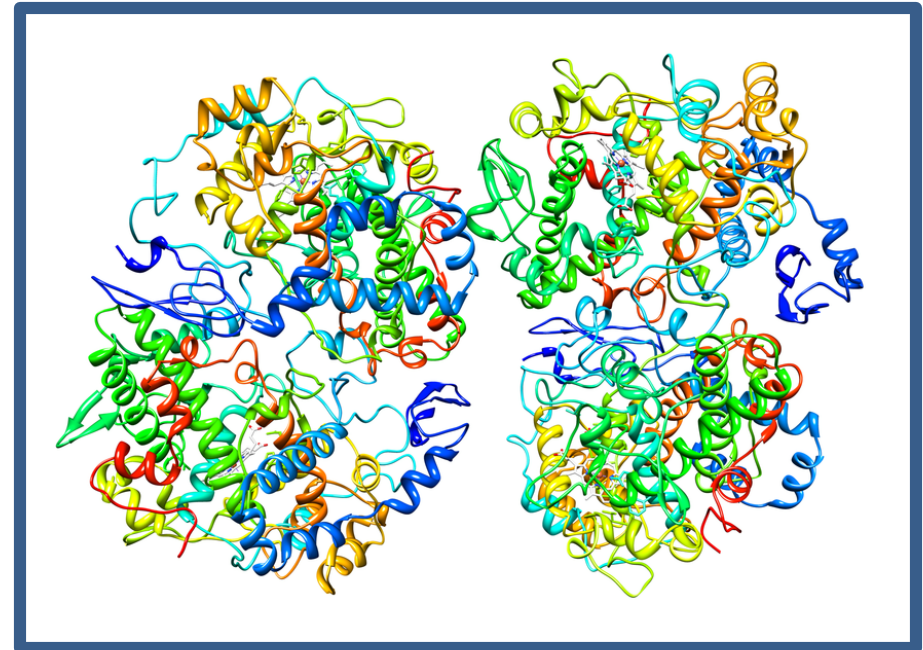


In this example, the slope is positive because the enthalpy of binding is negative (i.e. binding is exothermic).

Example: preventing inflammation by binding to prostaglandin synthase 2



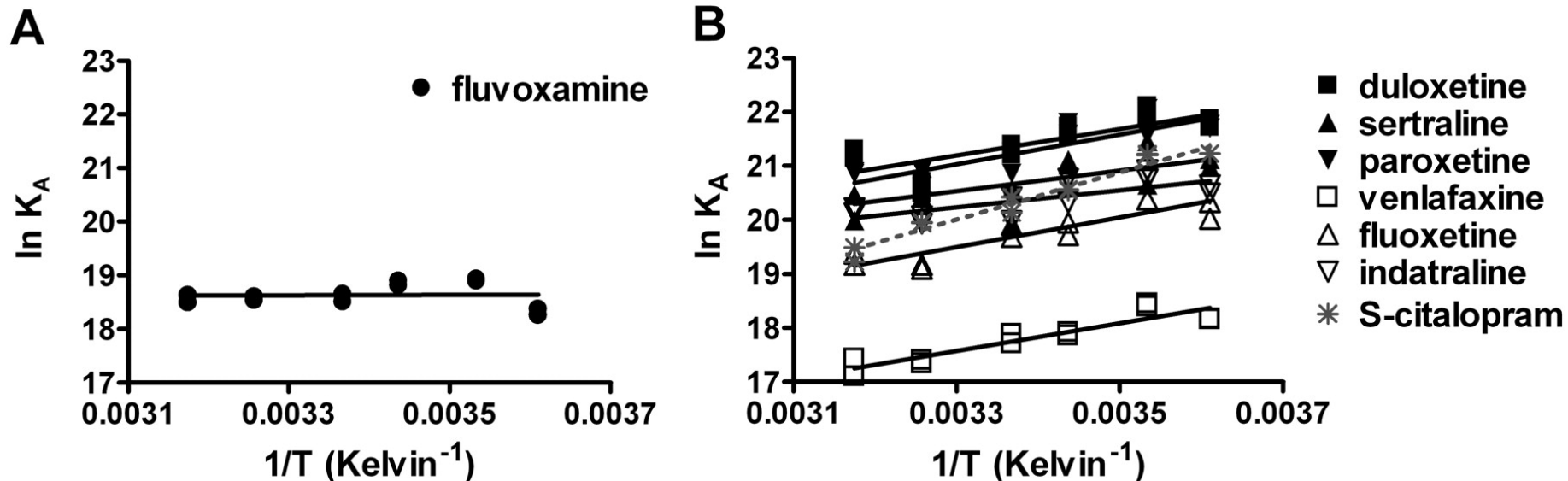
COX-2 crystal structure



ΔH° and ΔS° can be measured using $\ln(K)$ as a function $1/T$.

Example: preventing depression serotonin transport inhibitors

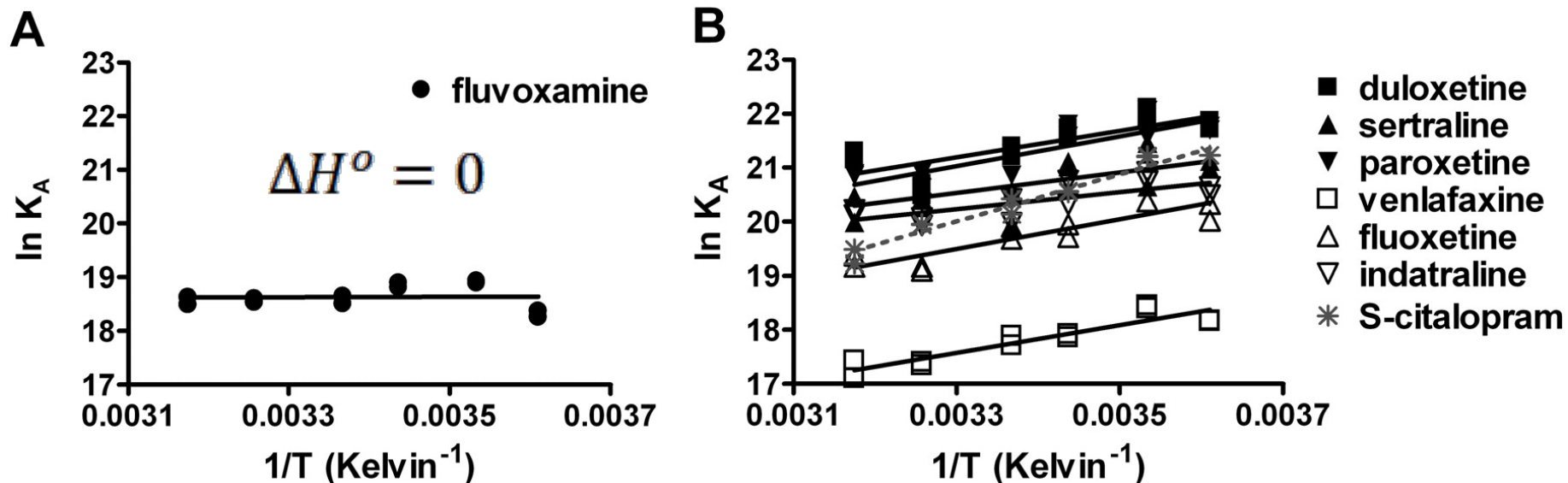
ΔH° and ΔS° can be measured using $\ln(K)$ as a function $1/T$.



This article shows specific differences in the enthalpy of binding of drugs based on analysis of so-called van't Hoff plots (i.e. plots of $\ln(K)$ vs. $1/T$).

Kinetic and Thermodynamic Assessment of Binding of Serotonin Transporter Inhibitors. J Pharm Exp Tech (2008) vol. 327, pp. 991-1000

Basic conclusion: fluvoxamine binds exclusively based on entropic driving force



Entropically driven binding is relatively rare. Usually the entropy of binding is unfavorable since a flexible drug molecule (large W) will be forced to adopt a fixed conformation (small W or $W = 1$) upon binding to a protein.

Kinetic and Thermodynamic Assessment of Binding of Serotonin Transporter Inhibitors. J Pharm Exp Tech (2008) vol. 327, pp. 991-1000