Thermodynamic Properties

The vast majority of chemical research involves macroscopic quantities of matter that are made up of very large numbers of molecules. The behavior of such ensembles of molecules is governed by the empirically determined laws of thermodynamics, and most chemical reactions and many chemical properties are defined in terms of some of the fundamental variables of thermodynamics, such as enthalpy, entropy, free energy, etc. In this chapter, we consider the most common procedures for augmenting electronic structure calculations in order to convert single-molecule potential energies to ensemble thermodynamics properties.

Zero-point vibrational energy

The first step in moving from the microscopic regime to the macroscopic is to recognize that the Born-Oppenheimer PES is fundamentally a classical construct. When the motion of the nuclei on this surface is also accounted for in a quantum mechanical way, energy is tied up in molecular vibrations. Within the harmonic oscillator approximation, the energy of the lowest vibrational level is $h\omega/2$ where h is Planck's constant (6.6261×10^{-34} J s) and ω is the vibrational frequency. The sum of all of these energies over all molecular vibrations – the zero-point vibrational energy (ZPVE or ZPE). The internal energy at 0 K:

$$U_0 = E_{elec} + \sum_i^{\mathrm{mod}es} \frac{1}{2} h\omega_i$$

E_{elec} – the energy for the stationary point on the Born-Oppenheimer PES. As a rule, the harmonic approximations does fairly well in computing ZPE (of course, if the frequencies are computed at a level that ensures their acceptable accuracy).

Thus, if one uses HF theory with some basis set that is known in general to require a scaling factor of 0.9 to bring computed frequencies in line with experiment, the same scaling factor should be used to compute the ZPE (or, equivalently, the ZPE should be computed using the scaled frequencies).

A key feature of ZPE – it is isotope dependent, since the vibrational frequencies themselves are isotope dependent; the reduced mass μ for any mode is a function of the atomic masses for the nuclei involved in the motion. If one is considering a large ensemble of molecules, it must be kept in mind that the computed ZPE refers to an ensemble of isotopically pure molecules, not to an ensemble composed from isotopes at natural abundance. Most electronic structure programs default to using the atomic isotopes of highest natural abundance, and permit use of other isotopes in some keyword-driven way.

GAUSSIAN input for isotope calculations

```
%chk=onco.chk
#N qcisd/6-31g* freq=(readfc,readisotopes) guess=read geom=check

onco

0 2

298.15 1.0 1.0
18
14
12

18
```

Here the ONCO molecule is calculated for the $^{18}\mathrm{O}^{14}\mathrm{N}^{12}\mathrm{C}^{18}\mathrm{O}$ isotope composition.

Ensemble properties and basic statistical mechanics

In order to deal with collections of molecules in statistical mechanics, it is required that certain macroscopic conditions be held constant by external influence. The enumeration of these conditions defines an ‘ensemble’. ‘Canonical ensemble’ – the constants are the total number of particles *N* (identical molecules), the volume *V*, and the temperature *T* – also called as the (*N, V, T*) ensemble. The most important function that characterizes a system in statistical mechanics – the partition function. For the canonical ensemble it is written as

$$Q(N,V,T) = \sum_i e^{-E_i(N,V)/k_B T}$$

i runs over all possible energy states of the system having energy E_i; k_B – Boltzmann’s constant (1.3806×10^{-23} J K^{-1}). Using the partition function, one can compute thermodynamic properties of the system, including internal energy *U*, enthalpy *H*, entropy *S*, and Gibbs free energy *G*:

$$U = k_B T^2 \left(\frac{\partial \ln Q}{\partial T} \right)_{N,V}$$

$$H = U + PV$$

$$S = k_B \ln Q + k_B T \left(\frac{\partial \ln Q}{\partial T} \right)_{N,V}$$

$$G = H - TS$$

Here, *N* and *V* are held constant during differentiation with respect of *T*, and *P* is pressure.

Thus, we need to find a way to calculate the partition function Q. We begin by assuming that our ensemble is an ideal gas, so that the molecules do not interact with each other. Then, the overall partition function of the system can be reduced to the molecular partition function $q(V,T)$:

$$Q(N,V,T) = \frac{1}{N!}\sum_i e^{-\left[\varepsilon_1(V)+\varepsilon_2(V)+\cdots+\varepsilon_N(V)\right]_i/k_BT} =$$

$$\frac{1}{N!}\left[\sum_{j(1)} e^{-\varepsilon_{j(1)}(V)/k_BT}\right]\left[\sum_{j(2)} e^{-\varepsilon_{j(2)}(V)/k_BT}\right]\cdots\left[\sum_{j(N)} e^{-\varepsilon_{j(N)}(V)/k_BT}\right] =$$

$$\frac{1}{N!}\left[\sum_{k}^{levels} g_k e^{-\varepsilon_k(V)/k_BT}\right]^N = \frac{\left[q(V,T)\right]^N}{N!}$$

The factor $1/N!$ derives from the quantum mechanical indistinguishability of the particles, ε - the total energy of an individual molecule. In the second line, we express the exponential of all possible sums of energies as a product of all possible sums of exponentials of individual energies. In the third line, the sum has been changed so that it goes over discrete energy levels, rather than individual states, and g_k is the degeneracy of level k.

The second consequence of the ideal gas assumption is that PV may be replaced by Nk_BT. When we are working with one mole of molecules, $N = N_A$ (Avogadro's number), and we may replace PV with RT, where R is the universal gas constant (8.3145 J mol^{-1} K^{-1}).

Separability of energy components

$$q(V,T) = \sum_{k}^{levels} g_k e^{-\varepsilon_k(V)/k_BT} = \sum_{k}^{levels} g_k e^{-\left[\varepsilon_{elec}+\varepsilon_{trans}(V)+\varepsilon_{rot}+\varepsilon_{vib}\right]/k_BT} =$$

$$\left[\sum_{i}^{elec} g_i e^{-\varepsilon_i/k_BT}\right]\left[\sum_{j}^{trans} g_j e^{-\varepsilon_j(V)/k_BT}\right]\left[\sum_{k}^{rot} g_k e^{-\varepsilon_k/k_BT}\right]\left[\sum_{l}^{vib} g_k e^{-\varepsilon_l/k_BT}\right] =$$

$$q_{elec}(T)q_{trans}(V,T)q_{rot}(T)q_{vib}(T)$$

The molecular energy can be expressed as a separable sum of electronic, translational, rotational, and vibrational terms.

In expressions for the thermodynamic functions, Q always appears as the argument of the natural logarithm.

$$\ln\left[Q(N,V,T)\right] = \ln\left\{\frac{\left[q_{elec}(T)q_{trans}(V,T)q_{rot}(T)q_{vib}(T)\right]^N}{N!}\right\} =$$

$$N\left\{\ln\left[q_{elec}(T)\right]+\ln\left[q_{trans}(V,T)\right]+\ln\left[q_{rot}(T)\right]+\ln\left[q_{vib}(T)\right]\right\} - \ln(N!) \approx$$

$$N\left\{\ln\left[q_{elec}(T)\right]+\ln\left[q_{trans}(V,T)\right]+\ln\left[q_{rot}(T)\right]+\ln\left[q_{vib}(T)\right]\right\} - N\ln N + N$$

Here we used Stirling's approximation: $\ln(N!) = N\ln N - N$

The separation of terms by the logarithm function makes evident the separation of components, electronic, translational, rotational, and vibrational, in the thermodynamic functions.

Molecular electronic partition function

The electronic partition function is usually the simplest to compute. For a typical, closed-shell singlet molecule, the degeneracy of the ground state is 1, and the various excited states are so high in energy that, at least at temperatures below thousands of degrees, they make no significant contribution to the partition function, so we might effectively write

$$q_{elec} = e^{-E_{elec}/k_B T}$$

If we evaluate the electronic component of U using

$$U = k_B T^2 \left(\frac{\partial \ln Q}{\partial T} \right)_{N,V}$$

we find that it is independent of temperature, simply E_{elec}. In practice, it is more convenient to use a convention where we define the ground state for each energy component to have an energy of zero.

We view U_{elec} as the internal energy that must be added to U_0, which already includes E_{elec} ($U_0 = E_{elec} + \sum_i^{\mathrm{mod}es} \frac{1}{2} h\omega_i$), as the result of additional available electronic levels. If we use this convention, $q_{\mathrm{elec}} = 1$ and the electronic component of the entropy will be zero.

Now we consider a case when a ground state is of higher spin multiplicity than singlet, but with excited states still sufficiently high in energy that they play no role in the electronic partition function. Then, we still can use $E_{\mathrm{elec}} = 0$, but the degeneracy is now $2S + 1$, where S is the spin multiplicity (1/2 for doublet, 1 for triplet, etc.). Thus, the partition function is also $2S + 1$ This still has no temperature dependence, so it makes no contribution to the internal energy, but it is no longer unity, so it does contribute to the entropy:

$$U_{\mathrm{elec}} = 0 \qquad\qquad S_{\mathrm{elec}} = N k_{\mathrm{B}} \ln(2S + 1)$$

For the molar quantity, we have

$$S_{\text{elec}} = R\ln(2S + 1)$$

This approximation is insufficiently accurate if one or more excited electronic states lie close in energy to the ground state. A typical example: heavy halogen atoms, where spin-orbit coupling creates $^2P_{1/2}$ and $^2P_{3/2}$ states with a narrow energy separation. In such cases, explicit formation of the partition function cannot be avoided, but only a small number of terms typically need to be included.

Molecular translational partition function

To evaluate q_{trans}, we consider the molecule as a particle in a three-dimensional cubic box of dimension a^3 where a is the side length of the cube. The energy levels for this elementary quantum mechanical system (particle in the box) are given by

$$\varepsilon_{trans}\left(n_x, n_y, n_z\right) = \frac{h^2}{8Ma^2}\left(n_x^2 + n_y^2 + n_z^2\right)$$

M – the molecular mass; n_x, n_y, n_z – three unique quantum numbers.

Because the energy levels for the particle in the box are very, very closely spaced (at least for a box of macroscopic dimensions), the partition function sum may be replaced by an indefinite integral, which can be evaluated analytically:

$$q_{trans}\left(V, T\right) = \left(\frac{2\pi M k_B T}{h^2}\right)^{3/2} V$$

Note that it is only the translational partition function that depends on volume, because particle-in-a-box wave functions cannot be normalized without choice of a specific, finite, non-zero volume. This term dictates the necessity of choosing a ‘standard state’ volume to ensure comparison of thermodynamic values in a consistent fashion. We may replace *V* by *RT*/*P* and specify a standard-state pressure instead.

For a molar quantity of particles, we have

$$U_{trans} = \frac{3}{2}RT \qquad S^0_{trans} = R\left\{\ln\left[\left(\frac{2\pi M k_B T}{h^2}\right)^{3/2} V^0\right] + \frac{3}{2}\right\}$$

At this point, we can also consider the last two terms in the equation for the partition function, $N - N\ln N$. As they have no temperature dependence, they do not change U_{trans}, but affect *S*:

$$S^0_{trans} = R\left\{\ln\left[\left(\frac{2\pi M k_B T}{h^2}\right)^{3/2} \frac{V^0}{N_A}\right] + \frac{5}{2}\right\}$$

Since we are working under the assumption of an ideal gas, V^0/N_A can be replaced by $k_\text{B}T/P^0$. All the equations for translational contributions to the partition function are free of the requirement to carry out any electronic structure calculations – an ideal gas is entirely independent of the molecule in question. The translational partition function is a function of both temperature and volume. It is convenient to eliminate the volume dependence of S_{trans} by agreeing to report ‘standard state’ values. The most typical standard state used in theoretical calculations of entropy – the volume occupied by one mole of ideal gas at 298 K and 1 atm pressure: $V^0 = 24.5$ L.

Molecular Rotational Partition Function

Using rotational energy levels obtained by solving the rigid-rotor nuclear Schrödinger equation,

$$E_J = \frac{J(J+1)\hbar^2}{2I}$$

for a linear molecule, the rotational partition function can be expressed as

$$q_{rot}^{linear}(T) = \frac{8\pi^2 I k_B T}{\sigma h^2}$$

σ is 1 for asymmetric linear molecules and 2 for symmetric ones.

$$U_{rot}^{linear} = RT \qquad S_{rot}^{linear} = R\left[\ln\left(\frac{8\pi^2 I k_B T}{\sigma h^2}\right)+1\right]$$

For a non-linear molecule, the rotational partition function is

$$q_{rot}^{linear}(T) = \frac{\sqrt{\pi I_A I_B I_C}}{\sigma}\left(\frac{8\pi^2 k_B T}{h^2}\right)^{3/2}$$

σ - the number of rotations that carry the molecule into itself (rotational symmetry number) – characteristic for symmetry point groups.

$$U_{rot} = \frac{3}{2}RT \qquad S_{rot} = R\left\{\ln\left[\frac{\sqrt{\pi I_A I_B I_C}}{\sigma}\left(\frac{8\pi^2 k_B T}{h^2}\right)^{3/2}\right]+\frac{3}{2}\right\}$$

Evaluating the rotational components of *U* and *S* requires relatively little in the way of molecular information. All that is required is the principal moments of inertia, which derive only from the molecular structure. Thus, any methodology capable of predicting accurate geometries should be useful in the construction of rotational partition functions and their contribution to the thermodynamic variables.

Molecular vibrational partition function

In polyatomic molecule, we assume that the total vibrational energy can be expressed as a sum of individual energies associated with each normal mode:

$$q_{vib}(T) = \sum_i e^{-[\varepsilon_1 + \varepsilon_2 + \cdots + \varepsilon_{3N-6}]/k_B T} = \left[\sum_{j(1)} e^{-\varepsilon_{j(1)}/k_B T}\right]\left[\sum_{j(2)} e^{-\varepsilon_{j(2)}/k_B T}\right]\cdots\left[\sum_{j(3N-6)} e^{-\varepsilon_{j(3N-6)}/k_B T}\right]$$

ε_k – the vibrational energy levels associated with each mode k, and there are $3N - 6$ such modes in a non-linear molecule ($3N - 5$ in a linear molecule) where N is the number of atoms.

We assume that the modes can be approximated as quantum mechanical harmonic oscillators and adopt the convention to include ZPE in the zero energy, so that each zeroth vibrational level has an energy of zero.

$$q_{vib}^{QMHO}(T) = \sum_{k=0}^{\infty} e^{-kh\omega/k_B T}$$

This sum is well-known as a convergent geometric series.

$$q_{vib}^{QMHO}(T) = \frac{1}{1 - e^{-h\omega/k_B T}}$$

$$q_{vib}(T) = \prod_{i=1}^{3N-6}\left(\frac{1}{1 - e^{-h\omega_i/k_B T}}\right)$$

Evaluation of the vibrational components of the internal energy and entropy provides

$$U_{vib} = R\sum_{i=1}^{3N-6} \frac{h\omega_i}{k_B\left(e^{h\omega_i/k_BT}-1\right)} \qquad S_{vib} = R\sum_{i=1}^{3N-6}\left[\frac{h\omega_i}{k_BT\left(e^{h\omega_i/k_BT}-1\right)} - \ln\left(1-e^{-h\omega_i/k_BT}\right)\right]$$

Thus, it is fairly straightforward to convert the potential energy determined from an electronic structure calculation into a wealth of thermodynamic data – all that is required is an optimized structure and its associated vibrational frequencies. Given the many levels of electronic structure theory for which analytic second derivatives are available, it is usually worth effort required to compute the frequencies and then the thermodynamic variables, especially since experimental data are typically measured in this form. For the absolute entropy S^0, theory and experiment are directly comparable: calculated absolute entropies at 300 K for a large number of small molecules at the MP2/6-31G(d) level show agreement with experiment within 0.1 e.u. Absolute heat capacities at constant volume can be also computed

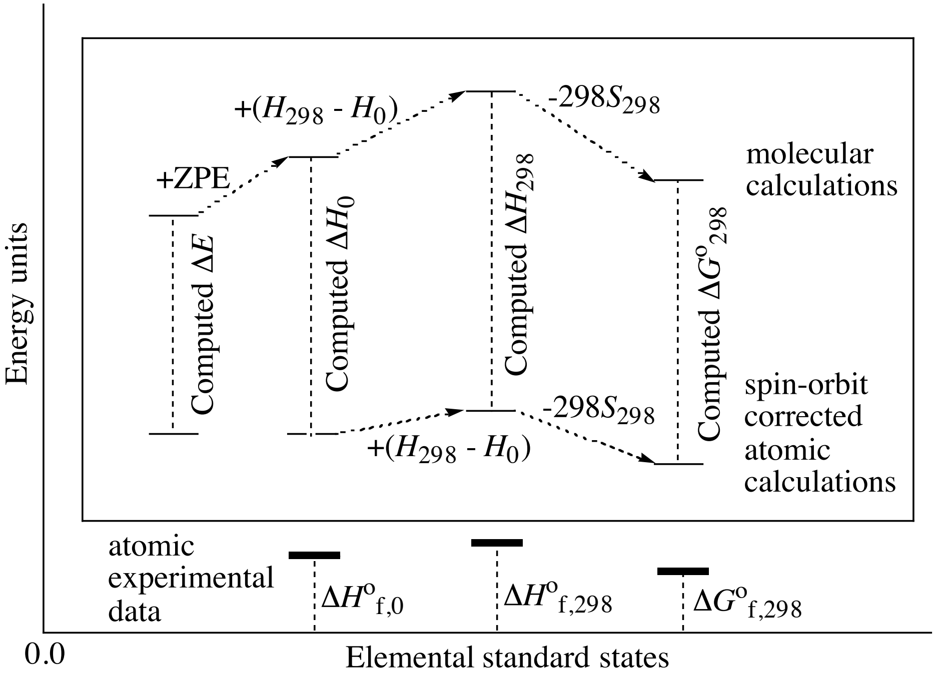
$$C_V = \left(\frac{\partial U}{\partial T}\right)_V$$

However, it is more difficult to compute absolute internal energies, enthalpies, and free energies.

Standard-state heats and free energies of formation and reaction

The experimental convention for assigning a zero to an enthalpy or free-energy scale – the value that corresponds to the heat or free energy of formation associated with every element in its most stable, pure form under standard conditions (273 K, 1 atm). The elemental standard states for the first few elements are hydrogen gas (diatomic), helium gas (monoatomic), solid lithium, solid beryllium, solid carbon (graphite), nitrogen gas (diatomic), oxygen gas (diatomic), fluorine gas (diatomic), and neon gas (monoatomic). Following this convention, the meaning of an experimental heat of formation for a molecule is that it is the molar enthalpy change associated with removing each of the atoms in the molecule from its elemental standard state and assembling them into the molecule.

Two-step procedure: There is first an enthalpy cost to pull each atom out of its elemental standard state (always a non-negative quantity, since the elemental standard states are chosen to be the most stable forms). This is followed by the enthalpy change for combining them into the molecular structure, $-\Delta H_{\text{atom}}$.



$$\Delta H^{o}_{f,298}(\mathrm{M}) = E(\mathrm{M}) + \mathrm{ZPE}(\mathrm{M}) + [H_{298}(\mathrm{M}) - H_0(\mathrm{M})] - \sum_{z}^{atoms}\left\{E(X_z) + \left[H_{298}(X_z) - H_0(X_z)\right]\right\} + \sum_{z}^{atoms} H^{o}_{f,298}(X_z)$$

$H^{o}_{f,298}$ for atoms are taken from experimental data.

Unfortunately, most single levels of theory are disastrously bad for direct calculations of heats of formation, with the problem lying primarily in the computation of ΔE between the molecule and its constituent atoms (atomization energy). As there is vastly more correlation energy in a molecule, with its collection of bonded pairs of electrons, than there is in a collection of atoms, and as practically affordable correlated electronic structure methods capture at best ~70-90% of the correlation energy, the differential error can be very large. Multiple-level methods (‘model chemistries’ in Pople’s language) are developed to address this problem – G2-G4, and CBS methods can provide atomization energies with chemical accuracy of 1-2 kcal/mol and can be applied for direct computation of heats of formation.

Isodesmic equations

An alternative method for computing heats (or free energies) of formation – consideration of a balanced chemical equation: $m\mathrm{A} + n\mathrm{B} \rightarrow r\mathrm{C} + s\mathrm{D}$

Then, $\Delta H^{\mathrm{o}}_{\mathrm{rxn},298} = [r\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{C}) + s\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{D})] - [m\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{A}) + n\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{B})]$

This can be rewritten as $\Delta H^{\mathrm{o}}_{\mathrm{rxn},298} = [rH_{298}(\mathrm{C}) + sH_{298}(\mathrm{D})] - [mH_{298}(\mathrm{A}) + nH_{298}(\mathrm{B})]$

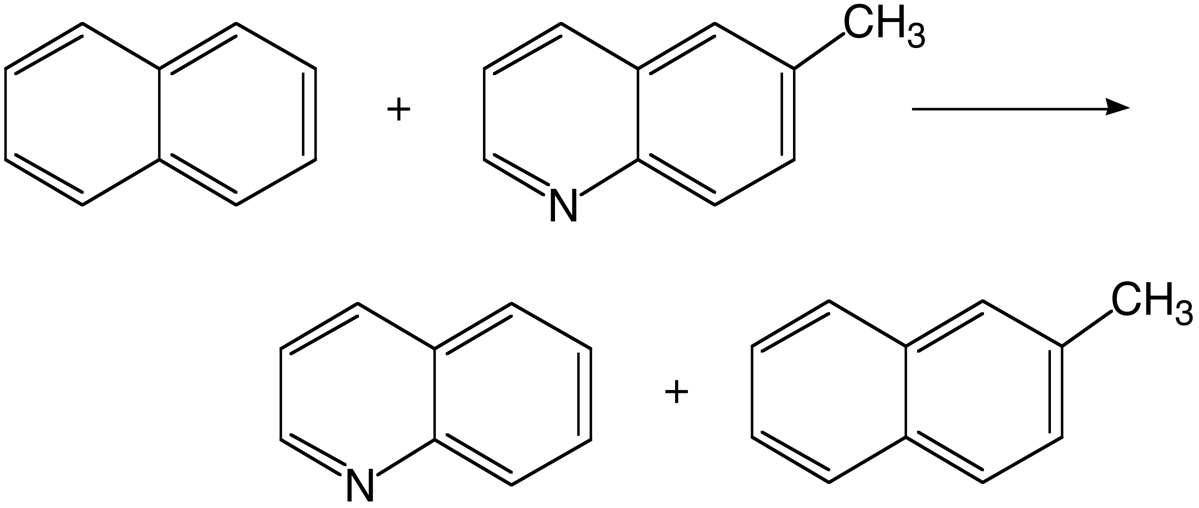
H_{298} is the quantity addressed theoretically, i.e., the enthalpy relative to all nuclei and electrons infinitely separated and at rest. If experimental heats of formation are known for all but one species, the above equations can be used to compute the unknown.

$$\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{B}) = (-1/n)\{[rH_{298}(\mathrm{C}) + sH_{298}(\mathrm{D})] - [mH_{298}(\mathrm{A}) + nH_{298}(\mathrm{B})]\}$$
$$- [r\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{C}) + s\Delta H^{\mathrm{o}}_{\mathrm{f},298}(\mathrm{D})] + mH_{298}(\mathrm{A})$$

We must compute H_{298} for four different species in this example, but the great advantage is that the difficulty in computing heats of atomization can be avoided. Computed heats of atomization tend to be highly inaccurate unless heroic levels of theory are employed.

However, assuming experimental data are available, we may select our balanced chemical equation in such a way that the various bonds on the left- and right-hand sides are essentially identical. That being the case, we would expect bond-by-bond errors in correlation energy to largely cancel in the computed heat of reaction. Such a reaction is called ‘isodesmic’.

Example:



Heat of formation of 6-methylquinoline: so long as heats of formation for the common molecules naphthalene, quinoline, and 2-methylnaphthalene are known, we may then compute enthalpies for all four species and predict the heat of formation of 6-methylquinoline. By construction, all the bonds on the l.h.s. are essentially identical to those on the r.h.s. As such, we might expect a much more affordable level of theory, say DFT, to be accurate enough to evaluate the heat of formation.

Equilibrium populations over multiple minima

It is not uncommon for a single molecule to have multiple populations. At non-zero temperatures, the population of different conformations will be dictated by Boltzmann statistics: the equilibrium fraction *F* of any given conformer *A* at temperature *T* may be computed as

$$F(A) = \frac{e^{-G_A^o/RT}}{\sum_i e^{-G_i^o/RT}}$$

i runs over all possible conformers, each characterized by its own free energy G^o. In measurements on systems at equilibrium, it is rarely possible to determine the free energies of individual components of the equilibrium. Rather, one refers to the free energy of the whole equilibrium population:

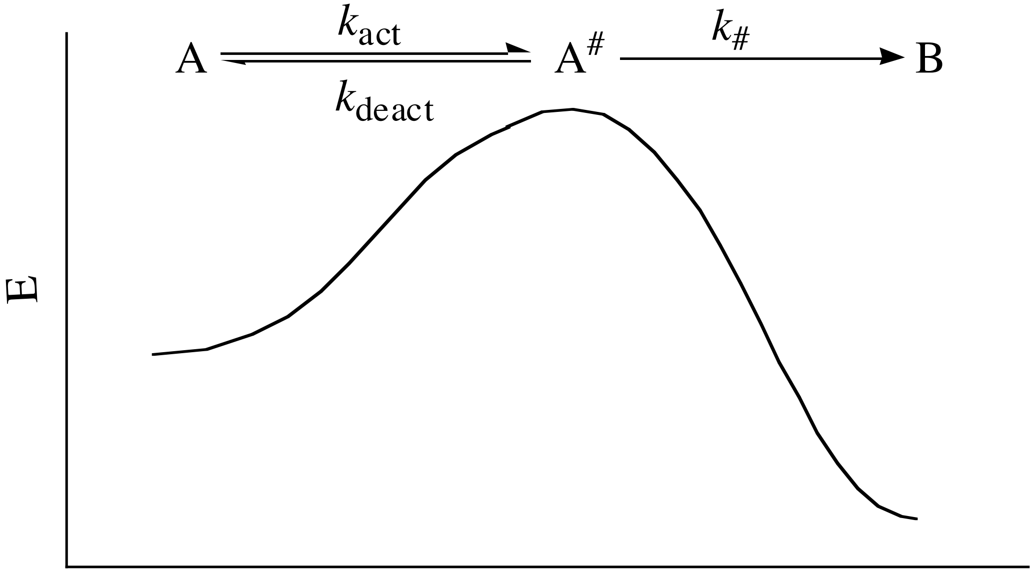
$$G_{\{A\}}^o = -RT \ln \sum_{i \in \{A\}} e^{-G_i^o/RT}$$

{A} emphasizes computation over the population of all conformers of A. Free-energy changes, then, between two species each of which exists as populations over multiple conformers, must be computed as the differences between their averages. This formalism may also be applied to determine averaged transition state free energies if multiple transition state structures exists all of which lead to the same product; the difference between an averaged reactant free energy and an averaged transition state free energy defines free energy of activation.

Sometimes, one conformer in a population has a free energy that is much lower than that of any of the other possibilities. It is clear that in that case, only the low-energy term contributes significantly to the sum – its free energy may be taken as the population free energy.

Transition state theory

Consider the simple unimolecular reaction, where the objective is to compute the forward rate constant k_1.



Transition state theory supposes that the nature of the activated complex, $A^{\#}$, is such that it represents a population of molecules in equilibrium with one another, and also in equilibrium with the reactant A. That population partitions between an irreversible forward reaction to produce B, with an associated rate constant $k_{\#}$, and deactivation back to A, with a reverse rate constant of k_{deact}. The rate at which molecules of A are activated to $A^{\#}$ is k_{act}. The first-order kinetic equations for the rate at which B is produced:

$$k_1[A] = k_{\#}[A^{\#}] \qquad\qquad k_1 = k_{\#}[A^{\#}]/[A] = k_{\#}K^{\#}$$

$K^{\#}$ - the equilibrium constant between the activated complex and the reactants.

$$K^{\#} = e^{-(G_{\#}-G_A)/k_B T}$$

The difference in free energy between the activated complex and the reactants is referred to as the activation free energy, $\Delta G^{\#}$.

Using the thermodynamical concepts,

$$U = k_B T^2 \left(\frac{\partial \ln Q}{\partial T} \right)_{N,V} \qquad H = U + PV$$

$$S = k_B \ln Q + k_B T \left(\frac{\partial \ln Q}{\partial T} \right)_{N,V} \qquad G = H - TS$$

we can write $G = U_0 + PV + k_{\mathrm{B}} T \ln Q$

Q is the partition function. Combining the equations, we write

$$K^{\#} = e^{-\left[\left(U_{\#,0} + PV_{\#} + k_B T \ln Q_{\#} \right) - \left(U_{A,0} + PV_A + k_B T \ln Q_A \right) \right] / k_B T} = \frac{Q_{\#}}{Q_A} e^{-\left(U_{\#,0} - U_{A,0} \right)/k_B T} e^{-\left(PV_{\#} - PV_A \right)/k_B T} \approx \frac{Q_{\#}}{Q_A} e^{-\left(U_{\#,0} - U_{A,0} \right)/k_B T}$$

We assumed that PV changes are negligible for this case (unimolecular reaction). We can write then

$$k_1 = k^{\#} \frac{Q_{\#}}{Q_A} e^{-\left(U_{\#,0} - U_{A,0} \right)/k_B T}$$

The zero-point-energy-including difference in internal energies between A and $A^{\#}$ in the exponential term is easily computable from an electronic structure calculation (for the electronic energy) and a frequency calculation (to determine ZPE) for the minimum energy and TS structures corresponding to A and $A^{\#}$, respectively. In addition, the availability of frequencies for A permits easy computation of Q_{A}. Some attention has to be paid to the nature of the partition function for the activated complex $Q_{\#}$.

The TS structure is a species that is a minimum in $3N - 7$ degrees of freedom – the missing degree of freedom is the reaction coordinate. Thus, we may readily define the electronic, translational, and rotational components of the partition function.

For the vibrational component, we separate out the partition function for the reaction coordinate degree of freedom:

$$k_1 = \frac{k^\#}{1-e^{-h\omega_\#/k_BT}}\frac{Q^\#}{Q_A}e^{-\left(U_{\#,0}-U_{A,0}\right)/k_BT}$$

$Q^\#$ - the reduced partition function over the $3N - 7$ bound degrees of freedom and $\omega_\#$ - the 'vibrational frequency' associated with the reaction coordinate. If we use a power series expansion for the exponential function of $\omega_\#$, truncating after the first two terms,

$$k_1 = \frac{k^\#}{1-\left(1-\dfrac{h\omega_\#}{k_BT}\right)}\frac{Q^\#}{Q_A}e^{-\left(U_{\#,0}-U_{A,0}\right)/k_BT} = \frac{k^\# k_BT}{h\omega_\#}\frac{Q^\#}{Q_A}e^{-\left(U_{\#,0}-U_{A,0}\right)/k_BT}$$

The only unknowns remaining here are $k_\#$ and $\omega_\#$. In this case, the vibrational frequency $\omega_\#$ should not be thought as the imaginary frequency that derives from the standard harmonic oscillator analysis, but rather the real inverse time constant associated with the motion along the reaction coordinate – it is exactly motion along the reaction coordinate that converts the activated complex into product B. That is, $k_\# = \omega_\#$. This results in the canonical TST expression:

$$k_1 = \frac{k_BT}{h}\frac{Q^\#}{Q_A}e^{-\left(U_{\#,0}-U_{A,0}\right)/k_BT}$$

For the bimolecular reaction involving reactants A and B,

$$k_1 = \frac{k_B T}{h} \frac{Q^{\#}}{Q_A Q_B} e^{-(U_{\#,0}-U_{A,0}-U_{B,0})/k_B T}$$

Let us consider the units for this particular case. All portions in the equations are unitless except for $k_B T/h$, which has units of s^{-1}, consistent with the units expected for a unimolecular rate constant. However, a bimolecular rate constant has units of concentration^{-1} s^{-1}.

At this point, one must pay close attention to standard-state conventions. The magnitude of the translational partition function depends on specification of a standard-state volume (or pressure, under ideal gas conditions). Thus, a more complete way to write the bimolecular rate equation is

$$k_1 = \frac{k_B T}{h} \frac{Q^{\#}}{Q_A Q_B} \frac{Q_A^o Q_B^o}{Q^{\#,o}} e^{-(U_{\#,0}-U_{A,0}-U_{B,0})/k_B T}$$

The various Q^o terms have values of 1 and carry the standard-state volume units used for the translational partition function. Care must be taken that if the molecular translational partition function is computed for a volume of 24.5 L (the volume occupied by one mole of an ideal gas at 298 K and 1 atm pressure), and the rate constant is in molecules cm^{-3} s^{-1}, the appropriate conversion in standard states is made.

In a general form, then, we have the canonical expression

$$k_1 = \frac{k_B T}{h} \frac{Q^{\#}}{Q_R} \frac{Q_R^o}{Q^{\#,o}} e^{-\Delta U/k_B T}$$

R refers generically to either unimolecular or bimolecular reactants, and $\Delta U^{\#}$ is the difference in zero-point-including potential energies of the reactants and TS structure. When working in molar quantities, the equation becomes

$$k_1 = \frac{k_B T}{h} \frac{Q^{\#}}{Q_R} \frac{Q_R^o}{Q^{\#,o}} e^{-\Delta U / RT}$$

We can absorb the standard-state partition functions back into the exponential and write

$$k_1 = \frac{k_B T}{h} e^{-\Delta G^{o,\#} / RT}, \qquad \Delta G^{\mathrm{o},\#} \text{ - the free energy of activation.}$$

We may also write
$$k_1 = \frac{k_B T}{h} e^{-\Delta H^{o,\#} / RT} e^{\Delta S^{o,\#} / R}$$

If we include units in the equation, we get the most general form:

$$k_1 = \left(V^o\right)^{\Delta n^{\#}} \frac{k_B T}{h} e^{-\Delta G^{o,\#} / RT}$$

Here, V^{o} is the standard volume and $\Delta n^{\#}$ is the change of the number of moles from reactants to the transition state.

Relation between theory and experiment

In the theoretical computation of a rate constant using TST, one locates all necessary stationary points – one TS structure and one or two minima – and evaluates their energies and their partition functions under the rigid-rotor-harmonic-oscillator approximation. On the other hand, experiment measures rate constants typically with the goal of deriving such quantities as the free energy of activation.

One analysis of experimental data involves carrying out rate constant measurements at a series of temperatures, and then plotting ln(*k/T*) against 1/*T*. We may rearrange the rate equation as

$$\ln\left(\frac{k}{T}\right) = -\frac{\Delta H^{o,\#}}{RT} + \frac{\Delta S^{o,\#}}{R} + \ln\left(\frac{k_B}{h}\right)$$

Therefore, the slope of such a plot should be $-\Delta H^{o,\#}/R$ and the intercept is a function of $\Delta S^{o,\#}/R$. From these quantities, the activation free energy may be easily computed for any temperature within the range of the data points and compared directly to a theoretical value.

An alternative analysis has a long history – it is simply to plot ln *k* vs. 1/*T*, this procedure is motivated by the empirically derived Arrhenius expression

$$k = Ae^{-E_a/RT}$$

A – the pre-exponential factor, E_a – the Arrhenius activation energy.

A plot of ln *k* vs. 1/*T* will have slope - E_a/R and intercept ln *A*. We can express the relationship between the Arrhenius quantities and the thermodynamic quantities as

$$E_a = \Delta H^{o,\#} + RT \qquad A = \frac{k_B T}{h} e^{\left(1+\Delta S^{0,\#}/R\right)}$$

One point of interest deriving from the equations of TST (and Arrhenius theory) is that the upper limit for the 298 K rate constant of a unimolecular reaction that takes place with zero activation energy is roughly 10^{13} s^{-1}. In some sense, this is conceptually obvious because that is on the order of a molecular vibrational frequency, which is thought of as the mechanism by which a transition state goes to its products.

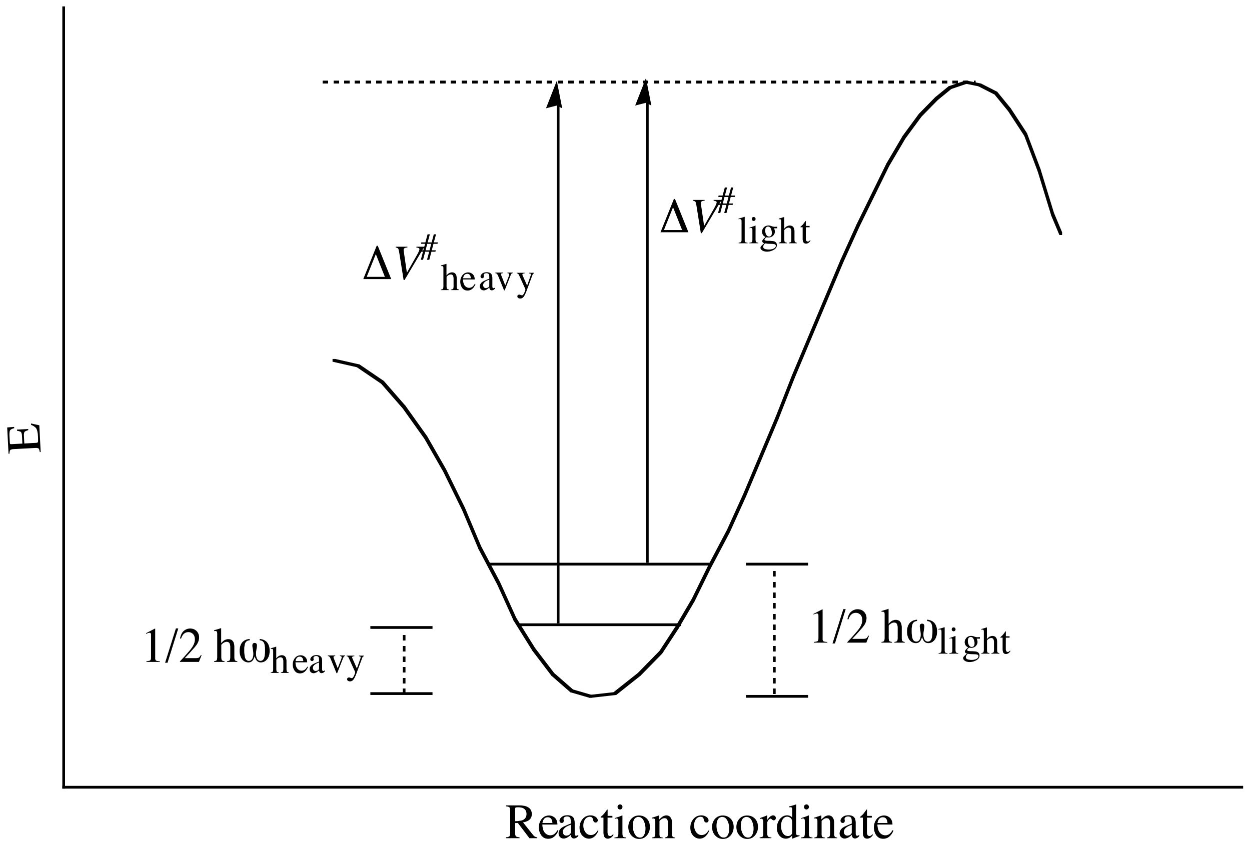
Kinetic isotope effects

The zero-point energy, and the translational, rotational, and vibrational partition functions all depend on the isotopic masses of the atoms – so too does the rate constant for a given reaction. A difference in rates for two different isotopically substituted reactants is referred to as a kinetic isotope effect (KIE), usually expressed as a ratio of rates. Isotope effects are divided into two classes: primary isotope effects refer to situations where the isotopic substitution involves one of the two atoms involved in a breaking (or making) bond, while secondary isotope effects cover all other possibilities. In general, a KIE may be computed as

$$\frac{k_{light}}{k_{heavy}} = \frac{\dfrac{Q^{\#}_{light}}{Q_{R,light}} e^{-\Delta U^{\#}_{light}/k_B T}}{\dfrac{Q^{\#}_{heavy}}{Q_{R,heavy}} e^{-\Delta U^{\#}_{heavy}/k_B T}} = \frac{Q^{\#}_{light}}{Q^{\#}_{heavy}} \frac{Q_{R,heavy}}{Q_{R,light}} e^{-\left(\Delta ZPE^{\#}_{light} - \Delta ZPE^{\#}_{heavy}\right)/k_B T}$$

From a theoretical point of view, isotope effects are fairly trivially computed. The stationary points on the PES and their electronic energies are independent of atomic mass, as are molecular force constants. Thus, one simply needs to compute the isotopically dependent zero-point energies and translational, rotational, and vibrational partition functions.

Primary isotope effects are dominated by the difference in zero-point energies.



Because the reaction coordinate is the breaking bond, and because there is little or no ZPE associated with this mode in the TS structure, the full difference in reactant ZPEs enters the difference in zero-point-including potential energy barriers. Then KIE can be computed as

$$\frac{k_{light}}{k_{heavy}} \approx e^{-\frac{1}{2}h\left(\omega_{heavy}^{R.\#}-\omega_{light}^{R.\#}\right)/k_B T}$$