Thermodynamic Network Calculations Applied to Biochemical Substances and Reactions

Robert N. Goldberg

Biochemical Science Division, National Institute of Standards and Technology,

Gaithersburg, Maryland 20899, U.S.A.

and

Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, Baltimore, MD 21250, U.S.A.

E-mail: robert.goldberg@nist.gov

Abstract

Both organic and inorganic chemistry have benefited greatly from the availability of tables of standard enthalpies of formation $\Delta_f H°$, standard Gibbs energies of formation $\Delta_f G°$, and standard entropies $S°$. These tables of standard thermodynamic properties allow the user to calculate values of enthalpy changes $\Delta_r H°$, Gibbs energy changes $\Delta_r G°$, equilibrium constants K, and entropy changes $\Delta_r S°$ for any reaction in which these standard thermodynamic properties are known for all of the reactants and products. Thus, it is not necessary that actual measurements have been performed on the reaction of interest. While several tables of standard thermodynamic properties have been prepared for biochemical substances, they are not as extensive as the corresponding tables for organic and inorganic substances nor as extensive as they might be if all of the available experimental results in the literature had been utilized. Nevertheless, comprehensive tables could be produced by utilizing all of the data {apparent equilibrium constants K' and calorimetrically determined enthalpies of reaction $\Delta_r H(\text{cal})$} in the *Thermodynamics of Enzyme-catalyzed Reactions Database* [1] together with related property values such as standard enthalpies of combustion, entropies and heat capacities, solubilities, enthalpies of solution, pKs, and enthalpies of binding for the substances of interest. This large set of property values can be used to establish a thermodynamic network, i.e., a system of linear equations, that can be solved for the desired formation properties. Such an undertaking requires extensive literature work, a substantial amount of analysis and computation on the results of the individual studies, and a careful fitting together of the property values by means of a judicious weighting of the property values. It can be viewed as a very large "jig-saw puzzle" of information. But the proper construction of such a network would serve to bring together a large body of related property values and would be of immense practical value to the scientific community. In addition to the aforementioned utility of the standard thermodynamic properties themselves, there are also the following additional benefits: (1) the consistency or lack of consistency of related results are made visible and needed measurements are identified straightforwardly; (2) the calculated formation properties can be easily updated and revised by a relatively quick calculation so as to allow for the inclusion of both new measurements and a revised

weighting of results; and (3) the calculated formation properties can, based on structural similarity, serve as the basis for the estimation of property values that have not yet been measured. The table of formation properties and the estimation procedures can also be embedded in computer codes which a user could use to calculate the position of equilibrium of numerous biochemical reactions.

Introduction

This chapter is an extension of the chapter [2] that I contributed to the *Proceedings of the 3rd International Beilstein Workshop on Experimental Standard Conditions of Enzyme Characterizations (ESCEC)*. An important point made in that chapter was that one can use an equilibrium model together with values of equilibrium constants K and standard enthalpies of reaction $\Delta_r H°$ for *chemical reactions* (i.e., reactions that involve specific species; both atoms and charges must balance in chemical reactions) to calculate the properties of *overall biochemical reactions* that involve sums of species. These calculated properties include the apparent equilibrium constant K', the standard transformed enthalpy of reaction $\Delta_r H'°$, the calorimetrically determined enthalpy of reaction $\Delta_r H(\text{cal})$, the changes in binding $\Delta_r N(\text{X})$ for any ligands ($\text{X} = \text{H}^+$, Mg^{2+}, Ca^{2+}, etc.) associated with the (overall) biochemical reaction, the extent of the biochemical reaction ξ', and the concentrations c of all of the species in solution. Thus, one can obtain a *complete thermodynamic picture* of biochemical reactions if one knows the values of the equilibrium constants K and standard enthalpies of reaction $\Delta_r H°$ for the system of chemical reactions that constitute the overall biochemical reaction. One can obtain values of K and $\Delta_r H°$ directly from the literature, or by means of thermodynamic cycle calculations, or, by using tables of standard thermodynamic properties. Of these three options, tables of standard thermodynamic properties are generally the most useful and convenient. However, these tables do not spontaneously appear in the literature. Indeed, their preparation requires a substantial amount of effort on the part of individuals who have a background both in thermodynamics and in the chemistry of the substances for which the thermodynamic properties are being evaluated and calculated. The aim of this chapter is to briefly describe the use of these tables, how they are prepared, the current status of existing tables that pertain to biochemical reactions, and to provide a vision of what is possible.

The basis of thermodynamic network calculations

Wagman et al. [3] have given a detailed description of the data evaluation process used in the preparation of the *NBS Tables of Chemical Thermodynamic Properties*. These tables [3] contain values of the standard enthalpy of formation $\Delta_f H^\circ$, the standard Gibbs energy of formation $\Delta_f G^\circ$, the standard entropy S°, and the standard heat capacity at constant pressure C_P° for 92 chemical elements and their compounds. However, the coverage of carbon compounds in these tables stops for substances that contain more than two carbons. Clearly, the scientific principles that underlie the evaluation of the thermodynamic properties of inorganic substances and of small organic molecules are applicable to biochemical substances of any size and complexity. The first and second laws of thermodynamics lead to the definitions of the following state functions: the internal energy U; the enthalpy H; the entropy S; and the Gibbs energy G. A state function has the critically important characteristic that its value depend only on the state of the system (e.g., the temperature T and pressure P) and not upon how the system was brought to that state. The third law of thermodynamics states that the entropy of a pure substance in a perfect crystalline form is zero at $T = 0$. Thus, the laws of thermodynamics provide both the scientific basis for the construction of tables of thermodynamic properties and also give rules for the use of these functions that enables the calculation of the position of equilibrium for chemical reactions. By convention, the values of $\Delta_f H^\circ$ and $\Delta_f G^\circ$ are set equal to zero for the thermodynamically stable phase of each element at $T = 298.15$ K, with the exception of phosphorous, for which the white type is selected as the reference form. Another necessary and important convention used in the construction of thermodynamic tables is that $\Delta_f H^\circ = \Delta_f G^\circ = S^\circ = C_P^\circ = 0$ for H^+(aq). Additionally, one also needs conventions regarding standard states for pure solids, liquids, gases, and solutions. A summary of the standard states commonly used in chemical thermodynamics is given in Wagman et al's [3] table III.

Table 1
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A sample table of thermodynamic properties is shown in table 1. One can use the values in tables of this type to calculate standard Gibbs energy changes $\Delta_r G^\circ$, standard enthalpy changes $\Delta_r H^\circ$, and standard entropy changes $\Delta_r S^\circ$ for chemical reactions, e.g.,

$$\nu_A A + \nu_B B = \nu_C C + \nu_D D. \tag{1}$$

Here ν_A, ν_B, ν_C, and ν_D are the stoichiometric numbers corresponding to the respective substances A, B, C, and D. The equations needed to calculate $\Delta_r G^\circ$, $\Delta_r H^\circ$, and $\Delta_r S^\circ$ from the tabulated values of $\Delta_f G^\circ$, $\Delta_f H^\circ$, and S° are

$$\Delta_r G^\circ = \nu_C \Delta_f G^\circ + \nu_D \Delta_f G^\circ - \nu_A \Delta_f G^\circ - \nu_B \Delta_f G^\circ, \tag{2}$$

$$\Delta_r H^\circ = \nu_C \Delta_f H^\circ + \nu_D \Delta_f H^\circ - \nu_A \Delta_f H^\circ - \nu_B \Delta_f H^\circ, \tag{3}$$

$$\Delta_r S^\circ = \nu_C S^\circ + \nu_D S^\circ - \nu_A S^\circ - \nu_B S^\circ. \tag{4}$$

The equilibrium constant K for a reaction can be calculated from $\Delta_r G^\circ$ by using the well-known relation

$$K = \exp(-\frac{\Delta_r G^\circ}{RT}). \tag{5}$$

Additionally one has the relation

$$\Delta_f G^\circ = \Delta_f H^\circ - T\Delta_f S^\circ. \tag{6}$$

Note that if one knows the value of $\Delta_r H^\circ$ for a given reaction and the values of $\Delta_f H^\circ$ for all of the reactants in that reaction with the exception of one of them, eq. (3) can be used to calculate the value of $\Delta_f H^\circ$ for that one reactant. The same principle applies to the use of eq. (2) for the calculation of $\Delta_f G^\circ$ and to the use of eq. (4) to calculate S° for a given reactant. Thus, eqs. (2) to (6) can be used to calculate values of $\Delta_f G^\circ$, $\Delta_f H^\circ$, and S° from experimentally determined values of K, $\Delta_r H^\circ$, and $\Delta_r S^\circ$. Specific categories of data that comprise the aforementioned three properties are: standard enthalpies of combustion $\Delta_c H^\circ$, standard enthalpies of solution $\Delta_{sol} H^\circ$, saturation molalities m(sat) or solubilities s, activity coefficients γ, all categories of equilibrium constants K and enthalpies of reaction $\Delta_r H^\circ$, standard entropies S°, standard heat capacities C_p°, standard heat capacity changes $\Delta_r C_p^\circ$, and standard electrode potentials E°. One can calculate $\Delta_r G^\circ$ from E° by means of the equation

$$\Delta_r G° = -|\nu_e| F E°, \qquad (7)$$

where ν_e is the number of electrons in the half reaction for the electrochemical cell and F is the Faraday constant. Apparent equilibrium constants K' and calorimetrically determined enthalpies of reaction $\Delta_r H(\text{cal})$ can also be used in these calculations. However, it is first necessary to calculate values of K and $\Delta_r H°$ for a chemical reference reaction from the measured values of K' and $\Delta_r H(\text{cal})$. It should also be noted that equilibrium constants can be determined by many different methods – chromatography, electrochemistry, chemical analysis, and a wide variety of spectroscopic methods. Equilibrium constants can also be obtained from kinetic experiments by means of Haldane relations. $\Delta_r H°$ can be obtained both by means of calorimetry and by measuring K as a function of temperature:

$$\Delta_r H° = RT^2(\partial \ln K/\partial T)_P. \qquad (8)$$

The most important points follow. Firstly, a wide variety of chemical thermodynamic data must be evaluated in order to construct tables of standard thermodynamic properties. Secondly, this wide variety of data can be reduced to just a few properties (omitting C_P° and $\Delta_r C_P^\circ$), namely $\Delta_r G°$, $\Delta_r H°$, and $S°$.

The collection of such evaluated data is generally referred to as a *reaction catalog*. Thirdly, since $\Delta_r G°$, $\Delta_r H°$, and $S°$ are related via eqs. (2), (3), (4), and (6), values of $\Delta_f H°$, $\Delta_f G°$, and $S°$ can be calculated by solving the system of linear equations that comprise the reaction catalog. These calculations are often referred to as *thermodynamic network calculations*. Lastly, these standard thermodynamic properties can be used to calculate property values (e.g., K, $\Delta_r G°$, $\Delta_r H°$) for many reactions, including those that have not been studied directly.

Thermochemistry of adenosine and the ATP series

A useful and interesting example of the calculation of standard thermodynamic properties is now considered. In 1992, Alberty and Goldberg [6] calculated the standard thermodynamic properties of the ATP series which included the H^+ and Mg^{2+} species that constitute the reactants AMP, ADP, and ATP as well as their hydrolysis reactions. In the absence of formation property data for adenosine(aq), they [6] adopted the convention that $\Delta_r H^\circ = \Delta_r G^\circ = 0$ for adenosine(aq). However, the need for this convention was eliminated when Boerio-Goates et al. [4] reported values for the standard enthalpy of combustion of adenosine(cr), the saturation molality of adenosine(cr), and heat capacities for adenosine(cr) over the temperature range 11 K to 328 K. The heat capacities led, by application of the third law of thermodynamics, to the standard entropy S° for adenosine(cr) at $T = 298.15$ K. The data that enter into these calculations are given as the first three entries in table 2. Entry no. 1 contains the data for the enthalpy of combustion $\Delta_c H^\circ$ of adenosine(cr). Entry No. 2 contains the data for the standard entropy S° of adenosine(cr). And entry No. 3 contains the data for both the enthalpy of solution $\Delta_{sol} H^\circ$ and the standard Gibbs energy of solution $\Delta_{sol} G^\circ$ of adenosine(cr). The latter quantity was calculated by using the formula

Table 2
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$$\Delta_{sol} G^\circ = -RT \ln\{\gamma m(\mathrm{sat}) \cdot a_w^N\}. \tag{8}$$

Here m(sat) is the saturation molality {i.e., the amount of adenosine that is soluble in 1 kg of H_2O(l)} of adenosine(cr) in H_2O(l), γ is the activity coefficient of adenosine(aq), a_w is the activity of water in the saturated solution, and N is the number of waters of hydration associated with adenosine(cr). Since adenosine(cr) is anhydrous, N is equal to zero, and $\mathrm{a}_w^N = 1$. The steps in the calculation of $\Delta_f H^\circ$, $\Delta_f G^\circ$, and S° for adenosine(aq) are now shown schematically:

$\Delta_c H^\circ$ of adenosine(cr) + values of $\Delta_f H^\circ$ for H_2O(l) and CO_2(g) → $\Delta_f H^\circ$ for adenosine(cr),

S° of adenosine(cr) + values of S° for C(cr), H_2(g), N_2(g), and O_2(g) → $\Delta_f S^\circ$ for adenosine(cr),

$\Delta_f H^\circ$ + $\Delta_f S^\circ$ for adenosine(cr) → $\Delta_f G^\circ$ for adenosine(cr),

$\Delta_f H^\circ$ for adenosine(cr) + $\Delta_{sol} H^\circ$ for adenosine(cr) → $\Delta_f H^\circ$ for adenosine(aq),

$\Delta_f G^\circ$ for adenosine(cr) + $\Delta_{sol} G^\circ$ for adenosine(cr) → $\Delta_f G^\circ$ for adenosine(aq),

$\Delta_f H^\circ$ and $\Delta_f G^\circ$ for adenosine(aq) → $\Delta_f S^\circ$ for adenosine(aq),

$\Delta_f S^\circ$ for adenosine(aq) + values of S° for C(cr), H_2(g), N_2(g), and O_2(g) → S° for adenosine(aq).

Eqs. (2), (3), (4), and (6) were the only equations used in the above schematic calculation. However, in addition to the property values shown in entries no. 1 to 3, accurate property values for key substances such as H_2O(l), CO_2(g), C(cr), N_2(g), and O_2(g) were also required. These values were taken from the CODATA Tables [5]. By using this pathway, the calculated formation properties of adenosine(aq) are: $\Delta_f H° =$ $-(621.3 \pm 3.6)$ kJ·mol^{-1}, $\Delta_f G° = -(194.5 \pm 3.6)$ kJ·mol^{-1}, and $S° = (364.6 \pm 0.7)$ J·K^{-1}·mol^{-1}.

A second thermodynamic pathway that leads to $\Delta_f G°$ for adenosine(aq) uses entries no. 4 to 10 in table 2. The basis for these entries is given in the footnotes in that table. The steps in the calculation of $\Delta_f G°$ for adenosine(aq) are similar to those shown above except that they are based on the formation properties of adenine and of ribose. A link from these two substances to adenosine is obtained by means of the value of *K′* measured by Camici et al. [15] for the reaction:

$$\text{adenosine(aq)} + H_2O(\text{l}) = \text{adenine(aq)} + \textbf{D}\text{-ribose(aq)}. \qquad (9)$$

The value $\Delta_f G° = -(192.4 \pm 6.3)$ kJ·mol^{-1} for adenosine(aq) obtained by this second pathway, is in excellent agreement with the result obtained by use of the first pathway described above. However, since the situation is not always this favorable, one must, in general, either select one set of data over another over another or one must weight the data in some reasonable way in order to obtain a set of "best" property values.

Table 3
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By having reliable values of $\Delta_f H°$, $\Delta_f G°$, and $S°$ for adenosine(aq), it is then possible to use the property values selected by Alberty and Goldberg [6] (see table 3) for aqueous AMP, ADP, and ATP reactions in order to calculate the property values for the AMP, ADP, and ATP species shown in table 1. Again, in performing these calculations, it was necessary to use auxiliary property data for Mg^{2+}(aq) and for HPO_4^{2-} (aq). Values for these properties were also taken from the CODATA Tables [5]. Note that the calculation of the standard thermodynamic properties of adenosine(aq) required the use of several different properties for adenosine(cr): $\Delta_c H°$, $S°$, $\Delta_{sol} H°$, and $\Delta_{sol} G°$. The value of $\Delta_{sol} G°$ required the use of eq. (8) and a knowledge of several additional properties, namely, *m*(sat), γ, and *N*, the number of waters of hydration associated with adenosine(cr). However, once the standard thermodynamic properties of adenosine(aq) were established, the calculation of the standard formation properties for the AMP, ADP, and ATP species required only the values of $\Delta_r H°$ and $\Delta_r G°$ for reactions occurring in aqueous solution. Thus, by having obtained a thermodynamic connection of one substance, namely adenosine(aq), to the elements, one was then able to establish the formation properties of many other biochemical substances. Similar tactics are applicable to many other biochemical substances for which values of $\Delta_c H°$, $S°$, $\Delta_{sol} H°$, and $\Delta_{sol} G°$ either have been or can be measured.

Discussion

Clearly, these calculations are very detailed and great care is required to make certain that property values have been properly extracted from the literature and treated properly. However, with modern computers, the solution of thermodynamic networks is made substantially easier and is accomplished much more rapidly than the old, sequential method which was used above for illustrative purposes. The essential point is that once the thermodynamic catalog has been established (tables 2 and 3, together with the necessary auxiliary property values, constitute a catalog), the calculation of values of $\Delta_f H°$, $\Delta_f G°$, and $S°$ can be done almost instantaneously. Thus, when new and better experimental results appear, they can be easily incorporated into the catalog and new values of $\Delta_f H°$, $\Delta_f G°$, and $S°$ can be obtained with little effort. *Thus, the central problem becomes the construction of the master thermodynamic catalog for biochemical substances and reactions.*

Based on the above discussion, it highly desirable that the master catalog contain values of $\Delta_f H°$, $\Delta_f G°$, and $S°$ for as many biochemical substances as possible. A good start for a list of biochemical substances to be included in the master catalog is the ~1200 biochemical reactants found in the *Thermodynamics of Enzyme-catalyzed Reactions Database* [1]. As seen above, the thermodynamic properties that are of interest are: standard enthalpies of combustion $\Delta_c H°$, standard enthalpies of solution $\Delta_{sol} H°$, saturation molalities m(sat) or solubilities s, activity coefficients γ, all types of equilibrium constants K and enthalpies of reaction $\Delta_r H°$, and standard entropies $S°$. In some cases, standard electrode potentials $E°$ may prove valuable in the calculation of values of $\Delta_r G°$. While of interest, but of secondary importance to values of $\Delta_r G°$, $\Delta_r H°$, and $S°$, are standard heat capacities C_p° and standard heat capacity changes $\Delta_r C_p^\circ$ for reactions. An examination of the *Thermodynamics of Enzyme-catalyzed Reactions Database* [1] shows that many of the most useful pathways will involve the use of apparent equilibrium constants K' and calorimetrically determined enthalpy changes $\Delta_r H(\text{cal})$ for enzyme-catalyzed reactions. As stated earlier, values of K and $\Delta_r H°$ can be calculated from the experimentally reported values of K' and $\Delta_r H(\text{cal})$. This can be done by means of chemical equilibrium modeling calculations [20]. However, in performing such calculations, in general, one requires a knowledge of the pKs and corresponding $\Delta_r H°$ values for the H^+ and Mg^{2+} and, possibly, Ca^{2+} binding constants for the reactions under consideration. Clearly, the amount of literature work required both to extract and to *evaluate* all of this data is very considerable and will require several years of effort by skilled workers. But, assuming that it has been done, one is still left with the task of performing the network calculations, including the assignment of weights, in order to obtain a set of "best" standard thermodynamic properties. In two previous evaluation efforts [19, 21] involving biochemical reactions, the computer codes described by Pedley et al. [22, 23] and by Garvin et al. [24] were used to solve the thermodynamic networks and to obtain the desired formation properties.

The above discussion has outlined both the importance of creating the master thermodynamic catalog for biochemical substances and reactions as well as the very formidable logistical matter of collecting and evaluating the necessary data and of performing the essential calculations. However, once the master catalog has been established and a reasonable set of weights assigned to the entries, the calculation of the desired standard thermodynamic properties can be accomplished almost instantaneously. Thus, as new data is published in the literature or if existing entries in the master catalog need to be corrected or weighted differently, the calculation of the revised standard thermodynamic properties is easily done.

Finally, once one has tables of standard thermodynamic properties in hand, one clearly wants to have them in a database that can be accessed by application programs. One application that many users should find particularly useful is to be able to simply write an overall biochemical reaction and specify the conditions of the reaction, namely, T, I, pH, and pMg. The program then obtains the required data from a table of standard thermodynamic properties and returns all of the desired information that the user might wish to know, namely, K', $\Delta_r H'^\circ$, $\Delta_r H(\text{cal})$, and $\Delta_r N(\text{X})$ for any ligand (X = H^+, Mg^{2+}, Ca^{2+}, etc.) associated with the biochemical reaction under a specified set of conditions. Values of the standard electrode potential E and the apparent standard electrode potential E'° can also be calculated. A *Mathematica* package that does much of this is *Basic Data for Biochemistry* [25, 26]. This package is available for download from: http://library.wolfram.com/infocenter/MathSource/797. Additionally, the *Mathematica* package *BioEqCalc* [20] is useful in calculating the concentrations of species and reactants once one has entered the reactions and the values of the equilibrium constants for the reactions. *BioEqCalc* can also be used to calculate values of K', $\Delta_r H'^\circ$, $\Delta_r H(\text{cal})$, $\Delta_r N(\text{X})$ as well as calculate the values of K and $\Delta_r H^\circ$ for chemical reference reactions from values of K', $\Delta_r H'^\circ$, and $\Delta_r H(\text{cal})$.

Table 4
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Table 4 summarizes the various publications that contain substantial numbers of entries for the standard thermodynamic properties of biochemical substances. The most extensive of the thermodynamic tables (Wilhoit [28]) contains data for 246 species. However, given the fact that there are ~1200 biochemical reactants in the *Thermodynamics of Enzyme-catalyzed Reactions Database* [1], it is clear that a considerable amount of effort is still needed in order to extract what is a very substantial amount of useful data from the existing literature. But, if this task were to be completed, one would have available not only a very useful table of standard thermodynamic properties, but also, as pointed out above, a reaction catalog that could be updated relatively easily as new and improved data became available. The reaction catalog would also serve as a guide as to which measurements were most valuable both in terms of resolving discrepancies in already published results and in where the measurement needs were most urgent for new reactions and substances.

The tables of standard formation properties would also allow one to apply the Benson group-contribution method [32-36] in order to obtain characteristic values for distinct chemical groups. These group values can then be used to estimate the properties of substances that have not been the subject of a direct study. The Benson method is particularly useful for the estimation of values of $\Delta_r S°$. These estimated values of $\Delta_r S°$, can then be used with measured values of $\Delta_r H°$ to calculate values of $\Delta_r G°$ and K for reactions where the measurement of the equilibrium constant is either difficult or essentially impossible due to the fact that the reaction of interest goes largely to completion. An obvious, but important point, is that the usefulness of tables of standard thermodynamic properties substantially increases with the number of substances in the tables. Given the increased interest in quantitative biochemistry (e.g., metabolic engineering, metabolic control analysis, and systems biology) and the direct tie to kinetic data via the Haldane relations, the important task of creating such a reaction catalog and the accompanying tables of standard formation properties is obviously one that needs to be undertaken and accomplished. Clearly, this task will require a concerted effort by several individuals over an extended period of time. Alternatively, given the size and never-ending nature of the task, it would be desirable to have a central depository where contributions to the master thermodynamic catalog can be deposited. An important part of such a central depository would be to insure a very high, but still reasonable degree of quality control over any input contributed to it.

Glossary of Symbols and Terminology[a]

Symbol	Name	Units
c	concentration	mol·dm^{-3}
C°_{P}	standard heat capacity at constant pressure	J·K^{-1}·mol^{-1}
$\Delta_r C^{\circ}_{P}$	standard heat capacity change for a reaction at constant pressure	J·K^{-1}·mol^{-1}
E°	standard electrode potential of a cell	V
E'°	standard apparent electrode potential of a cell	V
F	Faraday constant (96 485.339 9 C mol^{-1})	C·mol^{-1}
G	Gibbs energy	J
$\Delta_r G^{\circ}$	standard Gibbs energy change for a reaction	J·mol^{-1}
$\Delta_r G'^{\circ}$	standard transformed Gibbs energy change for a biochemical reaction	J·mol^{-1}
H	enthalpy	J
$\Delta_r H^{\circ}$	standard enthalpy change for a reaction	J·mol^{-1}
$\Delta_r H'^{\circ}$	standard transformed enthalpy change for a biochemical reaction	J·mol^{-1}
$\Delta_r H$(cal)	calorimetrically determined enthalpy change for a biochemical reaction	J·mol^{-1}
I	ionic strength	mol·dm^{-3}
K	equilibrium constant	dimensionless
K'	apparent equilibrium constant	dimensionless
m(sat)	saturation molality	mol·kg^{-1}
N	number of waters of hydration associated with a crystalline substance	dimensionless
$\Delta_r N$(X)	change in binding of species X for a biochemical reaction	dimensionless
P	pressure	bar
pH	$-\log_{10}[H^+]$	dimensionless
pK	$-\log_{10}K$	dimensionless

pMg	$-\log_{10}[Mg^{2+}]$	dimensionless
R	gas constant ($8.314\ 472\ J \cdot K^{-1} \cdot mol^{-1}$)	$J \cdot K^{-1} \cdot mol^{-1}$
s	solubility	$mol \cdot dm^{-3}$
S	entropy	$J \cdot K^{-1}$
$S°$	standard entropy	$J \cdot K^{-1} \cdot mol^{-1}$
$\Delta_r S°$	standard entropy change for a reaction	$J \cdot K^{-1} \cdot mol^{-1}$
T	temperature	K
U	internal energy	J
γ	activity coefficient	dimensionless
ν	stoichiometric number	dimensionless
$\lvert \nu_e \rvert$	number of electrons in a half reaction	dimensionless
ξ'	extent of a biochemical reaction	mol

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[a] The subscript "r" following a "Δ" denotes a reaction. Subscripts "c", "f", and "sol" are used, respectively, to denote combustion, formation, and solution reactions. A subscript "m" is often used to denote molar quantities, but this is not necessary if the units or context are clearly specified. The symbols (aq), (cr), and (l) denote, respectively, an aqueous species, a crystalline substance, and a liquid substance. An "M" is often used as an abbreviation for $mol \cdot dm^{-3}$ or $mol \cdot L^{-1}$.

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Table 1. Standard thermodynamic properties for several substances at $T = 298.15$ K and $P = 0.1$MPa[a]

Substance and state	$\Delta_f H^\circ$ / kJ·mol^{-1}	$\Delta_f G^\circ$ / kJ·mol^{-1}	S° / J·K^{-1}·mol^{-1}
O_2(g)	0	0	205.152
H^+(aq)	0	0	0
H_2(g)	0	0	130.680
OH^-(aq)	-230.015	-157.220	-10.90
N_2(g)	0	0	191.609
H_2O(l)	-285.830	-237.14	69.95
P(cr, white)	0	0	41.09
C(cr)	0	0	5.74
CO_2(g)	-393.51	-394.37	213.785
AMP^{2-}(aq), $C_{10}H_{12}N_5O_7P^{2-}$	-1635.37	-1040.45	214.5
$HAMP^-$(aq), $C_{10}H_{13}N_5O_7P^-$	-1629.97	-1078.86	361.4
H_2AMP(aq), $C_{10}H_{14}N_5O_7P$	-1648.07	-1101.63	377.1
MgAMP(aq), $C_{10}H_{12}N_5O_7PMg$	-2091.07	-1511.77	168.8
ADP^{3-}(aq), $C_{10}H_{12}N_5O_{10}P^-$	-2626.54	-1906.13	207.4
$HADP^{2-}$(aq), $C_{10}H_{13}N_5O_{10}P^-$	-2620.94	-1947.10	363.6
H_2ADP^-(aq), $C_{10}H_{14}N_5O_{10}P$	-2638.54	-1971.98	388.0
$MgADP^-$(aq), $C_{10}H_{12}N_5O_{10}P_2Mg^-$	-3074.54	-2388.06	223.1
MgHADP(aq), $C_{10}H_{13}N_5O_{10}P_2Mg$	-3075.44	-2416.77	316.3
ATP^{4-}(aq), $C_{10}H_{12}N_5O_{13}P^-$	-3619.21	-2768.10	182.8
$HATP^{3-}$(aq), $C_{10}H_{13}N_5O_{13}P^-$	-3612.91	-2811.48	349.4
H_2ATP^{2-}(aq), $C_{10}H_{14}N_5O_{13}P^-$	-3627.91	-2838.18	388.7
$MgATP^{2-}$(aq), $C_{10}H_{12}N_5O_{13}P_3Mg^{2-}$	-4063.31	-3258.77	240.9
$MgHATP^-$(aq), $C_{10}H_{13}N_5O_{13}P$	-4063.01	-3287.59	338.5
Mg_2ATP(aq), $C_{10}H_{12}N_5O_{13}P_3Mg_2$	-4519.51	-3729.52	191.6

Table 1 (continued)

[a] The property values for the AMP, ADP, and ATP species are from Boerio-Goates et al. [4]. The remaining property values are from the CODATA Tables [5]. The standard state for aqueous solutes is the hypothetical ideal solution of unit molality.

Table 2. Thermodynamic quantities at $T = 298.15$ K and pressure $P = 0.1$ MPa for reactions and for substances used in thermodynamic network calculations. The empirical formulas of the various substances are: adenine, $C_5H_5N_5$; adenosine, $C_{10}H_{13}N_5O_4$; and **D**-ribose, $C_5H_{10}O_5$. The standard state for aqueous solutes is the hypothetical ideal solution of unit molality

Entry No.	Substance or Reaction	$\Delta_r H^\circ$ / $kJ\cdot mol^{-1}$	$\Delta_r G^\circ$ / $kJ\cdot mol^{-1}$	S° / $J\cdot K^{-1}\cdot mol^{-1}$
1	$C_{10}H_{13}N_5O_4(cr) + 11.25\ O_2(g) = 10\ CO_2(g) + 6.5\ H_2O(l) + 2.5\ N_2(g)$	-5139.4±3.3[a]		
2	$C_{10}H_{13}N_5O_4(cr)$			289.57±0.6[b]
3	$C_{10}H_{13}N_5O_4(cr) = C_{10}H_{13}N_5O_4(aq)$	32.26±0.17[c]	9.89±0.02[d]	
4	$C_5H_5N_5(cr) + 6.25\ O_2(g) = 5\ CO_2(g) + 2.5\ H_2O(l) + 2.5\ N_2(g)$	-2779.0±1.3[e]		
5	$C_5H_5N_5(cr)$			151.0±3[f]
6	$C_5H_5N_5(cr) = C_5H_5N_5(aq)$	33.47±1.0[g]	11.98±0.3[h]	
7	$C_{10}H_{13}N_5O_4(aq) + H_2O(l) = C_5H_5N_5(aq) + C_5H_{10}O_5(aq)$		-9.84±0.4[i]	
8	$C_5H_{10}O_5(cr) + O_2(g) = 5\ CO_2(g) + 5\ H_2O(aq)$		-2349.5 ± 1.0[j]	
9	$C_5H_{10}O_5(cr) = C_5H_{10}O_5(aq)$	13.2 ± 0.3[k]	-8.7 ± 0.5[l]	
10	$C_5H_{10}O_5(cr)$			175.7 ± 0.6[m]

Table 2 (continued)

[a] Based on the standard enthalpy of combustion $\Delta_c H°$ of adenosine(cr) reported by Boerio-Goates et al. [4].

[b] Based on the standard entropy $S°$ of adenosine(cr) reported by Boerio-Goates et al. [4].

[c] Based on the standard enthalpy of solution $\Delta_{sol} H$ of adenosine(cr) reported by Stern and Oliver [7].

[d] Based on the saturation molality m_{sat} of adenosine(cr) reported by Boerio-Goates et al. [4].

[e] Based on the standard enthalpy of combustion $\Delta_c H°$ of adenine(cr) reported by Kirklin and Domalski [8].

[f] Based on the standard entropy $S°$ of adenine(cr) reported by Stiehler and Huffman [9].

[g] Based on the standard enthalpy of solution $\Delta_{sol} H°$ of adenine(cr) reported by Kilday [10].

[h] Based on the mean of the values of m(sat) for adenine(cr) in water obtained from four investigations [11-14].

[i] Based on the value of K' measured by Camici et al. [15] for the reaction: {adenosine(aq) + H_2O(l) = adenine(aq) + **D**-ribose(aq)}.

[j] Based on the standard enthalpy of combustion $\Delta_c H°$ of ribose(cr) reported by Colbert et al. [16].

[k] Based on the standard enthalpy of solution $\Delta_{sol} H°$ of ribose(cr) reported by Jasra and Ahluwalia [17] and by Stern and Hubler [18].

[l] Based on the saturation molality m_{sat} of ribose(cr) reported by Goldberg and Tewari [19].

[m] Based on the third law entropy $S°$ of ribose(cr) reported by Boerio-Goates et al. [4].

Table 3. Thermodynamic quantities selected by Alberty and Goldberg [6] for aqueous AMP, ADP, ATP, and phosphate reactions at $T = 298.15$ K. $P = 0.1$ MPa, and ionic strength $I = 0$

Reaction	$\Delta_r H^\circ$ / kJ·mol^{-1}	$\Delta_r G^\circ$ / kJ·mol^{-1}
$HAMP^- = H^+ + AMP^{2-}$	-5.4	38.42
$H_2AMP = H^+ + HAMP^-$	18.1	22.78
$MgAMP = Mg^{2+} + AMP^{2-}$	-11.3	15.93
$HADP^{2-} = H^+ + ADP^{3-}$	-5.6	40.98
$H_2ADP^- = H^+ + HADP^{2-}$	17.6	24.89
$MgADP^- = Mg^{2+} + ADP^{3-}$	-19.0	26.54
$MgHADP = Mg^{2+} + HADP^{2-}$	-12.5	14.27
$HATP^{3-} = H^+ + ATP^{4-}$	-6.3	43.38
$H_2ATP^{2-} = H^+ + HATP^{3-}$	15.0	26.71
$MgATP^{2-} = Mg^{2+} + ATP^{4-}$	-22.9	35.28
$MgHATP^- = Mg^{2+} + HATP^{3-}$	-16.9	20.72
$Mg_2ATP = Mg^{2+} + MgATP^{2-}$	-10.8	15.35
$ATP^{4-} + H_2O(l) = ADP^{3-} + HPO_4^{2-} + H^+$	-20.5	3.03
$ADP^{3-} + H_2O(l) = AMP^{2-} + HPO_4^{2-} + H^+$	-22.0	6.73
$AMP^{2-} + H_2O(l) = \text{adenosine} + HPO_4^{2-}$	0.9	-13.00

Table 4. Published tables of standard thermodynamic properties for biochemical substances[a]

Publication	No. of substances/species	Content	Properties in table
Krebs et al. [27]	130	General biochemistry	$\Delta_f G°$
Wilhoit [28]	246	General biochemistry	$\Delta_f G°$, $\Delta H_f°$, $S°$, C_P°
Thauer et al. [29][b]	165	General biochemistry	$\Delta_f G°$
Goldberg and Tewari [19]	74	Carbohydrates (pentoses and hexoses) and their monophosphates	$\Delta_f G°$, $\Delta H_f°$, $S°$, C_P°
Miller and Smith-Magowan [21]	26	Krebs cycle compounds	$\Delta_f G°$
Ould-Moulaye et al. [30, 31]	109	Purines, pyrimidines, nucleosides, nucleotides, and nucleotide phosphates	$\Delta_f G°$, $\Delta H_f°$, $S°$, C_P°
Alberty [25, 26]	199	General biochemistry – aqueous species	$\Delta_f G°$, $\Delta H_f°$

[a] The user of any of these tables is cautioned about the risks in combining data from two or more different tables to calculate property values for a given reaction. Specifically, while each of the aforementioned thermochemical tables is presumably internally consistent, the values may not be consistent with the values given in another table. Thus, serious errors can result if values from two or more tables are combined to calculate property values for a given reaction.

[b] Many of the values of $\Delta_f G°$ were taken from other tables.