10610 *Biochemistry* **1992,** *31,* 10610–10615

Standard Thermodynamic Formation Properties for the Adenosine 5′-Triphosphate Series[†]

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Received February 25, 1992; Revised Manuscript Received June 16, 1992

ABSTRACT: The criterion for chemical equilibrium at specified temperature, pressure, pH, concentration of free magnesium ion, and ionic strength is the transformed Gibbs energy, which can be calculated from the Gibbs energy. The apparent equilibrium constant (written in terms of the total concentrations of reactants like adenosine 5′-triphosphate, rather than in terms of species) yields the standard transformed Gibbs energy of reaction, and the effect of temperature on the apparent equilibrium constant at specified pressure, pH, concentration of free magnesium ion, and ionic strength yields the standard transformed enthalpy of reaction. From the apparent equilibrium constants and standard transformed enthalpies of reaction that have been measured in the adenosine 5′-triphosphate series and the dissociation constants of the weak acids and magnesium complexes involved, it is possible to calculate standard Gibbs energies of formation and standard enthalpies of formation of the species involved at zero ionic strength. This requires the convention that the standard Gibbs energy of formation and standard enthalpy of formation for adenosine in dilute aqueous solutions be set equal to zero. On the basis of this convention, standard transformed Gibbs energies of formation and standard transformed enthalpies of formation of adenosine 5′-triphosphate, adenosine 5′-diphosphate, adenosine 5′-monophosphate, and adenosine at 298.15 K, 1 bar, pH = 7, a concentration of free magnesium ions of 10^{-3} M, and an ionic strength of 0.25 M have been calculated.

The thermodynamic criterion for chemical equilibrium depends on the independent variables that are specified at equilibrium. When temperature and volume are specified, the criterion is the Helmholtz energy A, and $(\mathrm{d}A)_{T,V} \leq 0$, with the equality applying at equilibrium. When the temperature and pressure are specified, the criterion is the Gibbs energy G, and $(\mathrm{d}G)_{T,P} \leq 0$. If, in addition to T and P, the pH and pMg are specified, it is necessary to introduce another thermodynamic property G', the transformed Gibbs energy, as the criterion for chemical equilibrium, and $(\mathrm{d}G')_{T,P,\mathrm{pH},\mathrm{pMg}} \leq 0$ (Alberty, 1992a,b; Alberty & Oppenheim, 1992). The symbol G' is in agreement with the current usage (Wadsö et al., 1976) in biochemistry of K' for the apparent equilibrium constant for a reaction like[1]

$$\mathrm{ATP} + \mathrm{H_2O} = \mathrm{ADP} + \mathrm{P_i} \qquad K' = [\mathrm{ADP}][\mathrm{P_i}]/[\mathrm{ATP}] \quad (1)$$

at specified T, P, pH, pMg, and I (ionic strength), where the concentrations of reactants (sums of species) are in moles per liter. Strictly speaking, there should be a $c^{\circ} = 1$ mol L^{-1} in the denominator of the equilibrium constant expression to make this equilibrium constant dimensionless, but that is omitted here to simplify the equations. The standard transformed Gibbs energy of reaction is calculated using

$$\Delta_r G'^{\circ} = -RT \ln K' \quad (2)$$

In writing this equation, two changes have been made from what is usually used: Since G' is the transformed Gibbs energy, it is the standard value G'° that is involved so that the superscript zero is placed after the prime, the subscript r represents reaction to emphasize the difference from the standard transformed Gibbs energy of formation $\Delta_f G'^{\circ}$ of a reactant (sum of species) at specified T, P, pH, pMg, and I that is calculated in this paper. The transformed Gibbs energy G' is defined by the following Legendre transform of the Gibbs energy G (Alberty, 1992a):

$$G' = G - n'(\mathrm{H^+})\mu(\mathrm{H^+}) - n'(\mathrm{Mg^{2+}})\mu(\mathrm{Mg^{2+}}) \quad (3)$$

where $\mu(\mathrm{H^+})$ and $\mu(\mathrm{Mg^{2+}})$ are the specified chemical potentials of $\mathrm{H^+}$ and $\mathrm{Mg^{2+}}$ at equilibrium and $n'(\mathrm{H^+})$ and $n'(\mathrm{Mg^{2+}})$ are the total amounts of these ions (free and bound) in the system. The use of eq 3 in the fundamental equation of thermodynamics defines the standard transformed Gibbs energy of reaction $\Delta_r G'^{\circ}$, the standard transformed enthalpy of reaction $\Delta_r H'^{\circ}$, and the standard transformed entropy of reaction $\Delta_r S'^{\circ}$ that are related by

$$\Delta_r G'^{\circ} = \Delta_r H'^{\circ} - T\Delta_r S'^{\circ} \quad (4)$$

These three standard transformed reaction properties depend on T, P, pH, pMg, and I, which must therefore be specified. These properties depend on the way the reaction is written. If the standard transformed enthalpy of reaction is independent of temperature, the standard transformed entropy of reaction will also be independent of temperature, and it can be shown (Alberty, 1992b) that

$$\Delta_r H'^{\circ} = [RT_1T_2/(T_2 - T_1)] \ln (K_2'/K_1') \quad (5)$$

so that the standard transformed enthalpy of reaction determines the effect of temperature on K' at specified T, P, pH, pMg, and I. In the calculations presented here, the pH is defined as $-\log\,[\mathrm{H^+}]$ and pMg is defined as $-\log\,[\mathrm{Mg^{2+}}]$ at the ionic strength used.

[†] Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of research by R.A.A.

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[1] Abbreviations: ATP, adenosine 5′-triphosphate; ADP, adenosine 5′-diphosphate; AMP, adenosine 5′-monophosphate; aden, adenosine; G6P, glucose 6-phosphate; $\mathrm{P_i}$, inorganic phosphate. The designator (aq) is understood as being appended to all species that exist in aqueous solution.

0006-2960/92/0431-10610$03.00/0

MATERIALS AND METHODS

The standard transformed reaction quantities can be written in terms of standard transformed formation properties of the reactants.

$$\Delta_r G'^\circ = \sum \nu_i \Delta_f G'^\circ(i) \qquad (6)$$

$$\Delta_r H'^\circ = \sum \nu_i \Delta_f H'^\circ(i) \qquad (7)$$

$$\Delta_r S'^\circ = \sum \nu_i \Delta_f S'^\circ(i) \qquad (8)$$

The summations are carried out over reactants i, including H_2O if it is a reactant. When a reactant is made up of a number of species, the formation properties apply to the equilibrium mixture of the species at the specified T, P, pH, pMg, and I. The stoichiometric numbers ν_i are taken as positive for products and negative for reactants. Thermodynamic information on biochemical reactions is currently stored as $\Delta_r G'^\circ$ and $\Delta_r H'^\circ$ values at specified T, P, pH, pMg, and I. However, there are advantages in tabulating the formation properties $\Delta_f G'^\circ(i)$ and $\Delta_f H'^\circ(i)$ for individual reactants at specified T, P, pH, pMg, and I so that $\Delta_r G'^\circ$ and $\Delta_r H'^\circ$ for a reaction can be calculated using eqs 6 and 7 by looking up reactants in a table, as in the rest of chemistry. The standard transformed formation properties have already been calculated for inorganic phosphate and glucose 6-phosphate at 298.15 K, 1 bar, pH = 7, pMg = 3, and 0.25 M ionic strength (Alberty, 1992b). These conditions are in line with those suggested by the Interunion Commission (Wadsö et al., 1976) with the exception of the ionic strength and pMg which are consistent with those described as "near-physiological conditions" in equilibrium investigations of metabolic reactions (Guynn & Veech, 1973; Lawson & Veech, 1979).

Sufficient data are available to calculate the standard transformed formation properties of ATP, ADP, AMP, and adenosine relative to each other (Goldberg & Tewari, 1989, 1991; Larson et al., 1992). It has not yet been possible to connect the standard thermodynamic properties ($\Delta_f G^\circ$ and $\Delta_f H^\circ$) of a species of any of these biochemical reactants with the elements in their standard states, but it has been shown that a consistent set of standard formation properties of ionic species can be developed by assigning some zeros, as necessary (Alberty, 1991), just as chemists had to assign $\Delta_f G^\circ = \Delta_f H^\circ = 0$ to the hydrogen ion in aqueous solution. Therefore, in this paper adenosine in dilute aqueous solutions of zero ionic strength is assigned $\Delta_f G^\circ = \Delta_f H^\circ = \Delta_f S^\circ = 0$ in order to make thermodynamic tables. Since this is an arbitrary convention, it is desirable that it be generally accepted until the properties of adenosine relative to the elements can be determined. When $\Delta_f G^\circ$ and $\Delta_f H^\circ$ are determined for adenosine in a dilute aqueous solution of zero ionic strength, the values of $\Delta_f G^\circ$ and $\Delta_f H^\circ$ for the other species in the ATP series can be recalculated. However, this will not alter the equilibrium constants or enthalpies of reaction calculated using the tables in this paper. Better determinations of equilibrium constants and enthalpies of reaction used in calculating the current tables will lead to changes in the tables that will alter equilibrium constants and enthalpies of reaction calculated using tables in this paper.

In order to interpret the effect of T, pH, pMg, and I on the thermodynamics of a biochemical reaction, it is necessary to deal with species rather than reactants. The standard formation properties of species $\Delta_f G^\circ(i)$, $\Delta_f H^\circ(i)$, and $\Delta_f S^\circ(i)$ and the reaction properties $\Delta_r G^\circ$, $\Delta_r H^\circ$, and $\Delta_r S^\circ$ that can be calculated from them are functions of T, P, and I but not of pH and pMg. The standard Gibbs energy of reaction can be used to calculate the equilibrium constant K written in terms of species at specified T, P, and I: $\Delta_r G^\circ = -RT \ln K$. The standard enthalpy of reaction can be calculated from the effect of T on K. These properties obey the familiar eqs 4, 5, 6, 7, and 8 without the primes.

Goldberg and Tewari (1991) and Larson, Tewari, and Goldberg (1992) have summarized their calorimetric and equilibrium measurements and those of others on the ATP series in terms of the reference reactions

$$ATP^{4-} + H_2O(l) = ADP^{3-} + HPO_4^{2-} + H^+$$
$$K = [ADP^{3-}][HPO_4^{2-}][H^+]/[ATP^{4-}] \qquad (9)$$

$$2ADP^{3-} = ATP^{4-} + AMP^{2-}$$
$$K = [ATP^{4-}][AMP^{2-}]/[ADP^{3-}]^2 \qquad (10)$$

$$AMP^{2-} + H_2O(l) = \text{aden} + HPO_4^{2-}$$
$$K = [\text{aden}][HPO_4^{2-}]/[AMP^{2-}] \qquad (11)$$

and the 13 acid dissociations and magnesium complex dissociations in the ATP series that are important in the range pH 3–10, pMg >2 at 298.15 K. For the purpose of the present calculations, it is convenient to replace reaction 10 with

$$ADP^{3-} + H_2O(l) = AMP^{2-} + HPO_4^{2-} + H^+ \qquad (12)$$

which is the sum of reactions 9 and 10.

Since data on the 16 reactions have been obtained at various ionic strengths and since chemical thermodynamic tables give standard formation properties at $I = 0$, Goldberg and Tewari (1989) and Larson, Tewari, and Goldberg (1992) have used the extended Debye–Hückel theory to adjust $\Delta_f G^\circ$ and $\Delta_f H^\circ$ at 298.15 K from one ionic strength to another (Goldberg & Tewari, 1991; Clarke & Glew, 1980):

$$\Delta_f G_i^\circ(I) = \Delta_f G_i^\circ(I = 0) - \alpha R T z_i^2 I^{1/2}/(1 + B I^{1/2}) \qquad (13)$$

$$\Delta_f H_i^\circ(I) = \Delta_f H_i^\circ(I = 0) + (\partial\alpha/\partial T)_P R T^2 z_i^2 I^{1/2}/(1 + B I^{1/2}) \qquad (14)$$

where α is the Debye–Hückel constant, R is the gas constant, T is the temperature, B is the constant in the extended Debye–Hückel theory that we have taken to be 1.6 $L^{1/2}$ $mol^{-1/2}$, and z_i is the charge on ion i. At $T = 298.15$ K and with the Debye–Hückel constants of Clarke and Glew (1980), αRT is equal to 2.91482 kJ $L^{1/2}$ $mol^{-3/2}$ and $(\partial\alpha/\partial T)_P RT^2$ is equal to 1.4775 kJ $L^{1/2}$ $mol^{-3/2}$. Goldberg and Tewari (1991) have also given equations for the calculation of the activity of the water and for the excess Gibbs energy and enthalpy of the water. These additional corrections are negligible (<0.01 kJ mol^{-1}) at the ionic strengths of concern in this paper.

In the tables presented here, the values of $\Delta_f S^\circ = (\Delta_f H^\circ - \Delta_f G^\circ)/T$ and $\Delta_f S'^\circ = (\Delta_f H'^\circ - \Delta_f G'^\circ)/T$ are not tabulated, but they are readily calculated. Values of $\Delta_f C_p^\circ$ and $\Delta_f C_p'^\circ$ could have been calculated in some cases, but they are not known very accurately.

The input data for the calculation of standard formation properties of species in the ATP series are the values of $\Delta_r H^\circ$ and $\Delta_r G^\circ$ for the three reference reactions (9, 12, and 11), the 13 acid dissociations and magnesium complex dissociations for adenosine, AMP, ADP, and ATP adjusted to 298.15 K and $I = 0$ by Goldberg and Tewari (1991) and Larson, Tewari, and Goldberg (1992), and the acid dissociation and

Table I: Standard Reaction Quantities at T = 298.15 K and I = 0

reaction	$\Delta_rH°$ (kJ mol^{-1})	$\Delta_rG°$ (kJ mol^{-1})	pK	K	$K(I = 0.25\ \text{M})$[a]
$HAMP^- = H^+ + AMP^{2-}$	−5.4	38.42	6.73	1.862×10^{-7}	6.877×10^{-7}
$H_2AMP = H^+ + HAMP^-$	18.1	22.78	3.99	1.023×10^{-4}	1.966×10^{-4}
$MgAMP = Mg^{2+} + AMP^{2-}$	−11.3	15.93	2.79	1.622×10^{-3}	2.212×10^{-2}
$HADP^{2-} = H^+ + ADP^{3-}$	−5.6	40.98	7.18	6.607×10^{-8}	4.689×10^{-7}
$H_2ADP^- = H^+ + HADP^{2-}$	17.6	24.89	4.36	4.365×10^{-5}	1.612×10^{-4}
$MgADP^- = Mg^{2+} + ADP^{3-}$	−19.0	26.54	4.65	2.239×10^{-5}	1.128×10^{-3}
$MgHADP = Mg^{2+} + HADP^{2-}$	−12.5	14.27	2.50	3.162×10^{-3}	4.313×10^{-2}
$HATP^{3-} = H^+ + ATP^{4-}$	−6.3	43.38	7.60	2.512×10^{-8}	3.426×10^{-7}
$H_2ATP^{2-} = H^+ + HATP^{3-}$	15.0	26.71	4.68	2.089×10^{-5}	1.483×10^{-4}
$MgATP^{2-} = Mg^{2+} + ATP^{4-}$	−22.9	35.28	6.18	6.607×10^{-7}	1.229×10^{-4}
$MgHATP^- = Mg^{2+} + HATP^{3-}$	−16.9	20.72	3.63	2.344×10^{-4}	1.181×10^{-2}
$Mg_2ATP = Mg^{2+} + MgATP^{2-}$	−10.8	15.35	2.69	2.042×10^{-3}	2.785×10^{-2}
$H_2PO_4^- = H^+ + HPO_4^{2-}$	3.6	41.20	7.22	6.026×10^{-8}	2.225×10^{-7}
$MgHPO_4 = Mg^{2+} + HPO_4^{2-}$	−12.2	15.47	2.71	1.950×10^{-3}	2.660×10^{-2}
$HG6P^- = H^+ + G6P^{2-}$	−1.8	36.65	6.42	3.802×10^{-7}	1.404×10^{-6}
$MgG6P = Mg^{2+} + G6P^{2-}$	−11.4	14.84	2.60	2.512×10^{-3}	3.462×10^{-2}
$Haden^+ = H^+ + aden$	16.4	19.98	3.50	3.162×10^{-4}	3.162×10^{-4}
$ATP^{4-} + H_2O(l) = ADP^{3-} + HPO_4^{2-} + H^+$	−20.5	3.03	–	2.946×10^{-1}	
$ADP^{3-} + H_2O(l) = AMP^{2-} + HPO_4^{2-} + H^+$	−22.0	6.73	–	6.622×10^{-2}	
$AMP^{2-} + H_2O(l) = aden + HPO_4^{2-}$	0.9	−13.00	–	1.894×10^{2}	
$G6P^{2-} + H_2O(l) = glucose + HPO_4^{2-}$	1.1	−10.87	–	8.023×10^{1}	
$ATP^{4-} + glucose = ADP^{3-} + G6P^{2-} + H^+$	−21.6	13.90	–	3.671×10^{-3}	
$2\ ADP^{3-} = ATP^{4-} + AMP^{2-}$	−1.5	3.70	–	2.248×10^{-1}	

[a] Equilibrium constants at I = 0.25 M.

magnesium complex dissociation constants already known for inorganic phosphate. These values are given in Table I. The standard reaction quantities for the hydrogen and magnesium dissociation reactions given by Goldberg and Tewari (1991) were based on a value of B = 1.5 L$^{1/2}$ mol$^{-1/2}$. We have recalculated these quantities with a value of B = 1.6 L$^{-1/2}$ mol$^{-1/2}$ for consistency with the formation properties given by Goldberg and Tewari (1989). There is no fundamental reason for preferring either of these values of B. The number of known equilibrium relationships is 3 + 13 + 2 = 18. These 18 equilibria involve 23 species, but the standard thermodynamic properties are known for four species (H^+, Mg^{2+}, HPO_4^{2-}, and $H_2O(l)$) (Cox et al., 1989), and so there are 19 species for which we do not know the standard formation properties. Since it has not yet been possible to connect the standard thermodynamic properties of any species involving adenosine with the elements in their standard states, it is necessary to assign $\Delta_fH° = \Delta_fG° = 0$ to one of these species, and adenosine has been chosen. The standard formation properties of the remaining species can then be calculated. This can be done by hand; for example, knowledge of the acid dissociation constant of $Haden^+$ makes it possible to calculate $\Delta_fG°(I = 0)$ of $Haden^+$. However, it is easier to make these calculations using a computer, as has been described earlier (Alberty, 1991). The standard formation properties of H^+, Mg^{2+}, HPO_4^{2-}, and $H_2O(l)$ that have been used in these calculations are given in Table II (Alberty, 1992b; Cox et al., 1989; Clarke et al., 1954). The properties of $H_2PO_4^-$ and $MgHPO_4$ are not used in these calculations, but they are included for completeness. On a similar basis, the properties of glucose, $G6P^{2-}$, and $HG6P^-$ are also included (Goldberg & Tewari, 1989; Alberty, 1992b). The transformed thermodynamic properties of these substances will also be included in the subsequent tables.

Table II: Standard Formation Properties[a] at T = 298.15 K and I = 0

substance	$\Delta_fH°$ (kJ mol^{-1})	$\Delta_fG°$ (kJ mol^{-1})
ATP^{4-}	−2997.91	−2573.49
$HATP^{3-}$	−2991.61	−2616.87
H_2ATP^{2-}	−3006.61	−2643.58
$MgATP^{2-}$	−3442.01	−3064.07
$MgHATP^-$	−3441.71	−3092.89
Mg_2ATP	−3898.21	−3534.72
ADP^{3-}	−2005.24	−1711.55
$HADP^{2-}$	−1999.64	−1752.53
H_2ADP^-	−2017.24	−1777.42
$MgADP^-$	−2453.24	−2193.39
$MgHADP$	−2454.14	−2222.10
AMP^{2-}	−1014.07	−845.91
$HAMP^-$	−1008.67	−884.33
H_2AMP	−1026.77	−907.11
$MgAMP$	−1469.77	−1317.14
$Haden^+$	−16.40	−19.98
aden	0.00	0.00
$H_2O(l)$	−285.83	−237.19
H^+	0.00	0.00
Mg^{2+}	−467.00	−455.30
HPO_4^{2-}	−1299.00	−1096.10
$H_2PO_4^-$	−1302.60	−1137.30
$MgHPO_4$	−1753.80	−1566.87
glucose	−1262.19	−915.90
$G6P^{2-}$	−2276.44	−1763.94
$HG6P^-$	−2274.64	−1800.59
$MgG6P$	−2732.04	−2234.08

[a] The formation properties of adenosine and H^+ have been set equal to zero.

The Table II data of standard formation properties at 298.15 K and I = 0 have been calculated using a computer with RowReduce in Mathematica (Wolfram Research, Inc., Champaign, IL 61820-7237).[2] The values in this table can be verified by using them to calculate the input data. $H_2O(l)$ is included in Table II because its standard Gibbs energy of formation must be used in calculating an apparent equilibrium constant $K'$and the standard enthalpy of reaction of a reaction

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[2] Certain commercial materials and products are identified in this paper to specify adequately the experimental procedure. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology.

Table III: Standard Formation Properties at T = 298.15 K and I = 0.25 M

substance	$\Delta_f H^\circ$ (kJ mol^{-1})	$\Delta_f G^\circ$ (kJ mol^{-1})	n(H)[a]	n(Mg)[a]
ATP^{4-}	−2991.34	−2586.44	12	0
$HATP^{3-}$	−2987.92	−2624.16	13	0
H_2ATP^{2-}	−3004.97	−2646.82	14	0
$MgATP^{2-}$	−3440.37	−3067.31	12	1
$MgHATP^-$	−3441.30	−3093.70	13	1
Mg_2ATP	−3898.21	−3534.72	12	2
ADP^{3-}	−2001.55	−1718.84	12	0
$HADP^{2-}$	−1998.00	−1755.77	13	0
H_2ADP^-	−2016.83	−1778.23	14	0
$MgADP^-$	−2452.83	−2194.20	12	1
MgHADP	−2454.14	−2222.10	13	1
AMP^{2-}	−1012.43	−849.15	12	0
$HAMP^-$	−1008.26	−885.14	13	0
H_2AMP	−1026.77	−907.11	14	0
MgAMP	−1469.77	−1317.14	12	1
$Haden^+$	−15.99	−20.79	14	0
aden	0.00	0.00	13	0
$H_2O(l)$	−285.83	−237.19	2	0
H^+	0.41	−0.81	1	0
Mg^{2+}	−465.36	−458.54	0	1
HPO_4^{2-}	−1297.36	−1099.34	1	0
$H_2PO_4^-$	−1302.19	−1138.11	2	0
$MgHPO_4$	−1753.80	−1566.87	1	1
glucose	−1262.19	−915.90	12	0
$G6P^{2-}$	−2274.80	−1767.18	11	0
$HG6P^-$	−2274.23	−1801.40	12	0
MgG6P	−2732.04	−2234.08	11	1

[a] The total numbers of hydrogens and magnesiums in each species are given in columns 4 and 5, respectively.

Table IV: Standard Transformed Formation Properties at T = 298.15 K, pH = 7, pMg = 3, and I = 0.25 M

substance	$\Delta_f H'^\circ$ (kJ mol^{-1})	$\Delta_f G'^\circ$ (kJ mol^{-1})	r_i[a]
ATP^{4-}	−2996.26	−2097.24	0.102610
$HATP^{3-}$	−2993.25	−2094.20	2.99503×10^{-2}
H_2ATP^{2-}	−3010.71	−2076.09	2.01958×10^{-5}
$MgATP^{2-}$	−2979.93	−2102.45	0.834905
$MgHATP^-$	−2981.27	−2088.07	2.53601×10^{-3}
Mg_2ATP	−2972.41	−2094.20	2.99786×10^{-2}
ADP^{3-}	−2006.47	−1229.64	0.475089
$HADP^{2-}$	−2003.33	−1225.81	0.101320
H_2ADP^-	−2022.57	−1207.50	6.28536×10^{-5}
$MgADP^-$	−1992.39	−1229.34	0.421179
MgHADP	−1994.11	−1216.47	2.34918×10^{-3}
AMP^{2-}	−1017.35	−359.95	0.839846
$HAMP^-$	−1013.59	−355.18	0.122124
H_2AMP	−1032.51	−336.38	6.21180×10^{-5}
MgAMP	−1009.33	−352.28	3.79677×10^{-2}
$Haden^+$	−21.73	549.94	3.16155×10^{-4}
aden	−5.33	529.96	0.999684
$H_2O(l)$	−286.65	−155.66	
H^+	0.41	−0.81	
Mg^{2+}	−465.36	−458.54	
HPO_4^{2-}	−1297.77	−1058.57	0.672508
$H_2PO_4^-$	−1303.01	−1056.58	0.302110
$MgHPO_4$	−1288.85	−1050.44	2.52822×10^{-2}
glucose	−1267.11	−426.70	
$G6P^{2-}$	−2279.31	−1318.75	0.909002
$HG6P^-$	−2279.15	−1312.20	6.47437×10^{-2}
MgG6P	−2271.19	−1309.99	2.62543×10^{-2}

[a] Fractions of the substances under the conditions stated are given in column 4.

involving $H_2O(l)$. However, the concentration of $H_2O(l)$ is not included in the equilibrium constant expression because it is the solvent.

The standard formation properties of the species in the ATP series at $I = 0.25$ M were calculated using eqs 13 and 14, and the results are given in Table III. A Mathematica program was written to make these adjustments. There is a theoretical basis for ionic strength corrections (Kirkwood, 1934) for the uncharged species, but these corrections are so small that they are ignored. The values in this table can be used to calculate K, $\Delta_r G^\circ$, and $\Delta_r H^\circ$ for various reactions in terms of species at 298.15 K and $I = 0.25$ M.

The calculation of the standard transformed formation properties of HPO_4^{2-}, $H_2PO_4^-$, and $MgHPO_4$ has been discussed earlier (Alberty, 1992a,b). It is done by writing formation reactions with H^+ at a specified concentration and Mg^{2+} at a specified concentration on the left side of the formation reaction. Various conventions could be adopted for deciding how many hydrogen adjustments should be made for a given species. For example, the hydrogen atom in HPO_4^{2-} is only dissociated in the neighborhood of pH 12 and could be ignored. However, all of the hydrogen atoms in an organic ion can be removed in metabolism. Therefore, the convention of correcting for all hydrogen atoms in organic and inorganic species is adopted. This device also serves to avoid computational problems that can arise when all the hydrogens and magnesiums are not removed. This includes the two hydrogens of H_2O. This should be an international convention if it is to be possible to take standard formation properties from tables prepared by different investigators. Adjustments for hydrogen atoms that are not affected in a particular reaction cancel.

The numbers of hydrogens in various species are given in Table III. The standard transformed formation properties of species at 298.15 K, pH = 7, pMg = 3, and $I = 0.25$ M are given in Table IV. The last column gives the equilibrium mole fractions r_i of species or a reactant like ATP.

The Legendre transform (eq 2) shows that $\Delta_f G'^\circ(i)$ for ion i is calculated from $\Delta_f G^\circ(i)$ by subtracting $n(H)\Delta_f G^\circ(H^+) + n(Mg^{2+})\Delta_f G^\circ(Mg^{2+})$ where n(H) and n(Mg) are the numbers of H and Mg in the species.

The standard transformed formation properties of species containing H^+ and Mg^{2+} were calculated using a computer program written in Mathematica. The input to the program is a matrix giving $\Delta_f H^\circ(I = 0)$, $\Delta_f G^\circ(I = 0)$, electric charge, number of hydrogens, and number of magnesium ions for the species. This program handles any number of species.

The calculation of standard transformed formation properties has been discussed in connection with the calculation of these properties for glucose 6-phosphate (Alberty, 1992b). The principles in this calculation are the same for any substance, including a complex one such as ATP. Thus, when pH and pMg are specified, the various species of a reactant like ATP become pseudoisomers. Therefore, the thermodynamic equations for isomer groups have to be used to calculate the $\Delta_f G'^\circ$ and $\Delta_f H'^\circ$ for the pseudoisomer group at the specified pH and pMg (Smith & Missen, 1982; Alberty, 1983). The following example utilizes inorganic phosphate.

$$\Delta_f G'^\circ(P_i) = \Delta_f G^\circ(HPO_4^{2-}) - RT \ln\{1 + 10^{-pH}/K(H_2PO_4^-) + 10^{-pMg}/K(MgHPO_4)\} \quad (15)$$

where

$$K(H_2PO_4^-) = [H^+][HPO_4^{2-}]/[H_2PO_4^-] = \exp\{-[\Delta_f G^\circ(H^+) + \Delta_f G^\circ(HPO_4^{2-}) - \Delta_f G^\circ(H_2PO_4^-)]/RT\} \quad (16)$$

Table V: Standard Transformed Formation Properties at T = 298.15 K, pH = 7, pMg = 3, and I = 0.25 M

substance	$\Delta_f H'^\circ$ (kJ mol^{-1})	$\Delta_f G'^\circ$ (kJ mol^{-1})
adenosine	−5.34	529.96
AMP	−1016.59	−360.38
ADP	−2000.19	−1231.48
ATP	−2981.79	−2102.88
glucose	−1267.11	−426.70
G6P	−2279.09	−1318.99
P_i	−1299.13	−1059.55
$H_2O(l)$	−286.65	−155.66

Table VI: Results Calculated with Standard Transformed Formation Properties Given in Table V (T = 298.15 K, pH = 7, pMg = 3, and I = 0.25 M)[a]

reaction		$\Delta_r H'^\circ$ (kJ mol^{-1})	$\Delta_r G'^\circ$ (kJ mol^{-1})	K'
ATP + $H_2O(l)$ = ADP + P_i	(A)	−30.88	−32.49	4.920×10^5
ADP + $H_2O(l)$ = AMP + P_i	(B)	−28.88	−32.79	5.553×10^5
AMP + $H_2O(l)$ = adenosine + P_i	(C)	−1.23	−13.55	236.5
G6P + $H_2O(l)$ = glucose + P_i	(D)	−0.50	−11.60	107.7
glucose + ATP = ADP + G6P	(E)	−30.38	−20.89	4568
2 ADP = AMP + ATP	(F)	2.00	−0.30	1.129

[a] Thermodynamics imposes the following constraints: $\Delta_r H'^\circ(B) = \Delta_r H'^\circ(A) + \Delta_r H'^\circ(F)$ and $\Delta_r H'^\circ(E) = \Delta_r H'^\circ(A) - \Delta_r H'^\circ(D)$ as well as two similar ones for $\Delta_r G'^\circ$. These cycles close exactly.

$$K(\mathrm{MgHPO_4}) = [\mathrm{Mg^{2+}}][\mathrm{HPO_4^{2-}}]/[\mathrm{MgHPO_4}] = \exp\{-[\Delta_f G^\circ(\mathrm{Mg^{2+}}) + \Delta_f G^\circ(\mathrm{HPO_4^{2-}}) - \Delta_f G^\circ(\mathrm{MgHPO_4})]/RT\} \quad (17)$$

The standard formation properties and equilibrium constants are for the desired ionic strength.

The standard transformed enthalpy of formation $\Delta_f H'^\circ(i)$ of a reactant at a specified pH and pMg can be calculated as a mole fraction weighted average of the standard transformed enthalpies of formation of the species in a reaction. For P_i

$$\Delta_f H'^\circ(\mathrm{P_i}) = r(\mathrm{HPO_4^{2-}})[\Delta_f H^\circ(\mathrm{HPO_4^{2-}}) - \Delta_f H^\circ(\mathrm{H^+})] + r(\mathrm{H_2PO_4^-})\{\Delta_f H^\circ(\mathrm{H_2PO_4^-}) - 2\Delta_f H^\circ(\mathrm{H^+})\} + r(\mathrm{MgHPO_4})\{\Delta_f H^\circ(\mathrm{MgHPO_4^{2-}}) - \Delta_f H^\circ(\mathrm{H^+}) - \Delta_f H^\circ \times (\mathrm{Mg^{2+}})\} \quad (18)$$

where

$$r(\mathrm{HPO_4^{2-}}) = \exp\{[\Delta_f G'^\circ(\mathrm{P_i}) - \{\Delta_f G^\circ(\mathrm{HPO_4^{2-}}) - (\Delta_f G^\circ(\mathrm{H^+}) + RT \ln [\mathrm{H^+}])\}]/RT\} \quad (19)$$

The standard transformed properties at 298.15 K, pH = 7 pMg = 3, and I = 0.25 M for the ATP series are given in Table V. Table VI gives the values of $\Delta_r H'^\circ$, $\Delta_r G'^\circ$, and K' for the six reactions calculated from Table V.

A useful check on the validity of this calculation is to calculate $\Delta_r H'^\circ$, $\Delta_r H'^\circ$, and K' for the six reactions in Table VI with a chemical equilibrium model (Goldberg & Tewari, 1989). This was done with the same set of input data (Table I) as that used in the calculation involving transformed thermodynamic properties and described in this paper. The results obtained with the equilibrium model are given in Table VII. The greatest difference between the results in Table VI and Table VII is 0.02 kJ mol^{-1}. This difference is judged to be within rounding errors made at several points in each of these calculations. Thus, these two independent sets of calculations are in agreement.

Table VII: Results Calculated Directly from Table I for T = 298.15 K, pH = 7, pMg = 3, and I = 0.25 M[a]

reaction		$\Delta_r H'^\circ$ (kJ mol^{-1})	$\Delta_r G'^\circ$ (kJ mol^{-1})	K'
ATP + $H_2O(l)$ = ADP + P_i	(A)	−30.88	−32.49	4.927×10^5
ADP + $H_2O(l)$ = AMP + P_i	(B)	−28.87	−32.80	5.574×10^5
AMP + $H_2O(l)$ = adenosine + P_i	(C)	−1.22	−13.55	236.7
G6P + $H_2O(l)$ = glucose + P_i	(D)	−0.48	−11.62	108.5
glucose + ATP = ADP + G6P	(E)	−30.40	−20.88	4541
2 ADP = AMP + ATP	(F)	2.01	−0.31	1.131

[a] Thermodynamics imposes the following constraints: $\Delta_r H'^\circ(B) = \Delta_r H'^\circ(A) + \Delta_r H'^\circ(F)$ and $\Delta_r H'^\circ(E) = \Delta_r H'^\circ(A) - \Delta_r H'^\circ(D)$ as well as two similar ones for $\Delta_r G'^\circ$. The results below are consistent to within 0.01 kJ mol^{-1} with these constraints. The greatest difference between the results in Table VI and this table is 0.02 kJ mol^{-1}.

DISCUSSION

Although the equations and nomenclature used here are rather different from those used over the past 25 years, the two approaches are actually equivalent. The advantage of the approach described here is that it deals with the thermodynamic properties of reactants, and the thermodynamic properties of reactions are calculated using tables of standard transformed formation properties. This has the advantage that calculations of Gibbs energies and enthalpies of reaction are linear. This makes it much simpler to treat new systems and larger systems.

The standard transformed formation properties of reactants at pH = 7 and pMg = 3 can be added to Table VI in the three following ways.

(1) If data are available on all species of a reactant (for example, P_i) or the properties of all species can be calculated since the reactant is formed from reactants with known properties (for example, glucose 6-phosphate and a number of other organic phosphate compounds where thermodynamic studies have been made on the organic precursor), $\Delta_f H'^\circ$ and $\Delta_f G'^\circ$ can be calculated directly. Further examples of the first type are pyrophosphate, carbon dioxide, and ammonia.

(2) If a reactant is a derivative of a substance like adenosine for which $\Delta_f H^\circ$ and $\Delta_f S^\circ$ are not known in dilute aqueous solution, the device of assigning zero to one species as described here can be used.

(3) If the apparent equilibrium constant of a biochemical reaction can be determined at pH = 7, pMg = 3, and I = 0.25 M, the transformed formation properties of a reactant can be entered directly into Table V without information on its species. The problem here is in calculating pMg at chemical equilibrium. However, if the concentration of free magnesium ions is highly buffered, pMg can be closely estimated without knowing the magnesium dissociation constants for all of the biochemical reactants, provided the thermodynamic properties of the buffer are well-known.

The principle advantage of this approach is that it is easier to look up properties of reactants than to look up reactions. These properties can then be added and subtracted to calculate $\Delta_r H'^\circ$ and $\Delta_r G'^\circ$ for an unknown reaction like the net reaction for glycolysis.

NOMENCLATURE

A	extensive Helmholtz energy of a system (kJ)
B	constant in the extended Debye–Hückel theory (L$^{1/2}$ mol$^{-1/2}$)
c°	standard state concentration (1 M = 1 mol L^{-1})
$\Delta_f C_p{}^\circ$	standard heat capacity of formation at constant pressure (J K^{-1} mol^{-1})
$\Delta_f C_p{}'^\circ$	standard transformed heat capacity of formation at constant pressure (J K^{-1} mol^{-1})
G	extensive Gibbs energy of a system (kJ)
$\Delta_r G^\circ$	standard Gibbs energy of a specified reaction in terms of species at specified T, P, and I (kJ mol^{-1})

$\Delta_f G^\circ(i)$	standard Gibbs energy of formation of species i at specified T, P, and I (kJ mol^{-1})
G'	extensive transformed Gibbs energy of a system (kJ)
$\Delta_r G'^\circ$	standard transformed Gibbs energy of a specified reaction in terms of reactants (sums of species) at specified T, P, pH, pMg, and I (kJ mol^{-1})
$\Delta_f G'^\circ(i)$	standard transformed Gibbs energy of formation of species i or reactant i (sum of species) at specified T, P, pH, pMg, and I (kJ mol^{-1})
$\Delta_r H^\circ$	standard enthalpy of reaction of a specified reaction in terms of species at specified T, P, and I (kJ mol^{-1})
$\Delta_f H^\circ(i)$	standard enthalpy of formation of species i at specified T, P, and I (kJ mol^{-1})
$\Delta_r H'^\circ$	standard transformed enthalpy of a specified reaction in terms of reactants (sums of species) at specified T, P, pH, pMg, and I (kJ mol^{-1})
$\Delta_f H'^\circ(i)$	standard transformed enthalpy of formation of species i or reactant i (sum of species) at specified T, P, pH, pMg, and I (kJ mol^{-1})
I	ionic strength calculated with ionic concentrations in moles per liter (M)
K	equilibrium constant for a specified reaction written in terms of concentrations of species, omitting H_2O (dimensionless)
K'	apparent equilibrium constant for a specified reaction written in terms of concentrations of reactants (sums of species), omitting H_2O (dimensionless)
$n'(i)$	amount of reactant i (that is, sum of species) (mol)
r_i or $r(i)$	equilibrium mole fraction of i within a specified class of molecules (dimensionless)
pH	$-\log([H^+]/c^\circ)$ (dimensionless)
pMg	$-\log([Mg^{2+}]/c^\circ)$ (dimensionless)
P	pressure (bar)
R	gas constant (8.31451 J K^{-1} mol^{-1})
$\Delta_r S^\circ$	standard entropy of reaction of a specified reaction in terms of species at specified T, P, and I (J K^{-1} mol^{-1})
$\Delta_f S^\circ(i)$	standard entropy of formation of species i at specified T, P, and I (J K^{-1} mol^{-1})
$\Delta_r S'^\circ$	standard transformed entropy of a specified reaction in terms of reactants (sums of species) at specified T, P, pH, pMg, and I (J K^{-1} mol^{-1})
$\Delta_f S'^\circ(\text{i})$	standard transformed entropy of formation of species i or reactant i (sum of species) at specified T, P, pH, pMg, and I (J K^{-1} mol^{-1})
T	temperature (K)
z_i	charge of ion i (dimensionless)
α	Debye–Hückel constant (L$^{1/2}$ mol$^{-1/2}$)
ν_i	stoichiometric number of reactant i in a specified chemical reaction (dimensionless)
$\mu^\circ(i)$	standard chemical potential of species i at specified T, P, and I (kJ mol^{-1})

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Registry No. ATP^{4-}, 13265-06-0; $HATP^{3-}$, 64344-01-0; H_2ATP^{2-}, 64363-04-8; MgATP, 1476-84-2; Mg_2ATP, 74804-12-9; ADP^{3-}, 52322-03-9; $HADP^{2-}$, 73679-94-4; H_2ADP^-, 89595-39-1; MgADP, 7384-99-8; AMP^{2-}, 6042-43-9; $HAMP^-$, 47287-36-5; H_2AMP, 61-19-8; MgAMP, 73077-74-4; $Haden^+$, 18475-49-5; aden, 58-61-7; $G6P^{2-}$, 76939-52-1; $HG6P^-$, 79101-58-9; MgG6P, 6810-04-4; H_2O, 7732-18-5; H^+, 12408-02-5; Mg, 7439-95-4; HPO_4^{2-}, 14066-19-4; $H_2PO_4^-$, 14066-20-7; $MgHPO_4$, 7757-86-0; glucose, 50-99-7.