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Archives of Biochemistry and Biophysics 435 (2005) 363–368
ABB
www.elsevier.com/locate/yabbi

Thermodynamic properties of oxidoreductase, transferase, hydrolase, and ligase reactions☆

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Received 1 December 2004, and in revised form 13 December 2004
Available online 12 January 2005

Abstract

Transferases formally couple together two oxidoreductase reactions or two hydrolase reactions. Therefore the thermodynamic properties of transferase reactions can be calculated from differences between thermodynamic properties of two oxidoreductase or two hydrolase reactions. Ligases couple together two hydrolase reactions, and so their thermodynamic properties can be calculated from differences between two hydrolase reactions. These relationships are demonstrated by calculating standard transformed Gibbs energies of reaction and the changes in binding of hydrogen ions at pHs 5–9 of a number of oxidoreductase, transferase, hydrolase, and ligase reactions by use of the data base BasicBiochemData2 and its recent extensions. Coupling is not restricted to two reactions, and an example is given of the coupling of three reactions.

Keywords: Coupling; Thermodynamic properties; Oxidoreductases; Transferases; Hydrolases; Ligases

The IUBMB classifies enzymes into six classes: oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases [1] and assigns EC numbers. This article is concerned with thermodynamic relations between some of these classes. Transferases couple together two oxidoreductase reactions or two hydrolase reactions. Therefore the thermodynamic properties of transferase reactions can be calculated by taking differences between thermodynamic properties of two oxidoreductase or two hydrolase reactions. Ligases couple together two hydrolase reactions, and so their thermodynamic properties can be calculated by taking differences between two hydrolase reactions. This means that thermodynamic studies of oxidoreductase and hydrolase reactions are especially useful because they can be used to calculate apparent equilibrium constants of transferase reactions and ligase reactions as well.

An example of a transferase reaction is

EC 2.3.1.8 acetyl phosphate + CoA

$$= \text{acetyl-CoA} + \text{P}_\text{i} \quad \Delta_\text{r}G'^0 = -3.28 \text{ kJ mol}^{-1} \qquad (1)$$

where the standard transformed Gibbs energy of reaction is given at 298.15 K, pH 7, and ionic strength 0.25 M. This reaction can be considered to result from the coupling of the following two reactions:

EC 3.6.1.7 acetyl phosphate + H_2O

$$= \text{acetate} + \text{P}_\text{i} \quad \Delta_\text{r}G'^0 = -44.64 \text{ kJ mol}^{-1} \qquad (2)$$

EC 3.1.2.1 acetate + CoA

$$= \text{acetyl-CoA} + \text{H}_2\text{O} \quad \Delta_\text{r}G'^0 = 41.36 \text{ kJ mol}^{-1} \qquad (3)$$

Adding these two reactions yields reaction 1. The standard transformed Gibbs energies of reaction can also be added.

A second example of a transferase reaction is

EC 2.6.1.1 L-aspartate + ketoglutarate

$$= \text{oxaloacetate} + \text{L-glutamate}$$

$$\Delta_\text{r}G'^0 = -1.47 \text{ kJ mol}^{-1} \qquad (4)$$

☆ This research was supported by NIH Grant 5-R01-GM48358-09.
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doi:10.1016/j.abb.2004.12.027

Glossary of terms

This section contains a very short glossary of terms in two sections.

C'	number of components at a specified pH
G	Gibbs energy
G'	transformed Gibbs energy
$\Delta_f G^0$	standard Gibbs energy of formation of a species
$\Delta_f G'^0$	standard transformed Gibbs energy of formation of a reactant (sum of species)
$\Delta_r G'^0$	standard transformed Gibbs energy of a biochemical reaction
$\Delta_f H^0$	standard enthalpy of formation of a species
$\Delta_f H'^0$	standard transformed enthalpy of formation of a reactant (sum of species)
$\Delta_r H'^0$	standard transformed enthalpy of reaction
K	equilibrium of a chemical reaction written in terms of species
K'	apparent equilibrium constant of a biochemical reaction written in terms of reactants
N'	number of reactants in a reaction system
N_H	number of hydrogen atoms in a species
$\Delta_r N_H$	change in the binding of hydrogen ions in a biochemical reaction
R	gas constant
R'	number of independent biochemical reactions in a reaction system
$\Delta_r S'^0$	standard transformed entropy of a biochemical reaction
T	thermodynamic temperature
z	charge number of a species

This reaction can be considered to result from the coupling of the following two oxidoreductase reactions.

$$\text{EC 1.4.1.5} \quad \text{L-aspartate} + \text{NAD}_{ox} + \text{H}_2\text{O} = \text{oxaloacetate} + \text{NAD}_{red} + \text{ammonia}$$

$$\Delta_r G'^0 = 36.68 \text{ kJ mol}^{-1} \tag{5}$$

$$\text{EC 1.4.1.2} \quad \text{ketoglutarate} + \text{ammonia} + \text{NAD}_{red} = \text{L-glutamate} + \text{NAD}_{ox} + \text{H}_2\text{O}$$

$$\Delta_r G'^0 = -38.14 \text{ kJ mol}^{-1} \tag{6}$$

Reaction 2.6.1.1 can be obtained by adding reaction 1.4.1.2 to reaction 1.4.1.5. This additivity applies to other thermodynamic properties as well.

When pH is used as an independent variable, the transformed Gibbs energy G' provides the criterion for spontaneous reaction and equilibrium [2,3]. The calculation of the standard transformed Gibbs energy of formation $\Delta_f G'^0$ of a biochemical reactant at 298.15 K as a function of pH and ionic strength is rather complicated and really requires a computer with a mathematical application. Mathematica [4] is very suitable for these calculations because of its facilities for symbolic calculations, taking partial derivatives, and making tables and plots. The advantage of calculating $\Delta_f G'^0$ as a function of pH and ionic strength at 298.15 K or as a function of temperature, pH, and ionic strength is that all the other standard thermodynamic properties can be obtained by taking partial derivatives [5]. The most efficient way to store thermodynamics data on biochemical reactions is to store small matrices that give $\Delta_f G^0$, $\Delta_f H^0$, z, and N_H for each species in a separate row, with the species with the fewest hydrogen atoms listed first. The charge number is represented by z, and the number of hydrogen atoms is represented by N_H. The four properties are the standard Gibbs energy of formation, the standard enthalpy of formation, the charge number, and the number of hydrogen atoms, respectively. The energies are in kJ mol^{-1} at 298.15 K and zero ionic strength. These small matrices of species properties are available on the web [6] for 131 reactants and can be downloaded into a personal computer with Mathematica installed. The calculations of these species properties have been greatly facilitated by the compilations and evaluations of experimental thermodynamic data on enzyme-catalyzed reactions by Goldberg and Tewari [7–12].

The web site BasicBiochemData2 [6] also makes available programs for using these small matrices to derive functions of pH and ionic strength that give the standard transformed Gibbs energies of formation $\Delta_f G'^0$ and other properties of reactants in the data base. More of these species matrices have been made available subsequently [13–16]. These functions are given simple names starting with lower case letters, like atp and sucrose, because initial capital letters indicate operations in Mathematica. Changes in the standard transformed thermodynamic properties in an enzyme-catalyzed reaction can be calculated by simply typing in the biochemical reaction. The program for calculating $\Delta_r G'^0$ at specified pHs and ionic strengths is called calctrGerx and the program for calculating the change in binding of hydrogen ions $\Delta_r N_H$ in a biochemical reaction is called calcNHrx [6]. When $\Delta_f H^0$ values are known for all species in a biochemical reaction, the standard transformed enthalpy of reaction $\Delta_r H'^0$ and the standard transformed entropy of reaction $\Delta_r S'^0$ can also be calculated over a range of temperatures where $\Delta_f H^0$ is essentially constant [3,5].