

## A calorimetric study of ligand interactions with protons and metal ions in the 100 to 400 °C range

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*Abstract:* The thermodynamic quantities ( $\log K$ ,  $\Delta H$ ,  $\Delta S$ , and  $\Delta C_p$ ) associated with the interactions of protons and metal ions with ligands in aqueous solutions are strongly influenced by the structure and properties of water. These quantities, especially  $\Delta S$  and  $\Delta H$ , reflect the decrease in hydrogen bonding in water as temperature increases. The magnitude and the sign of  $\Delta S$  and  $\Delta H$  for proton interaction with amino acid and nucleotide anions are indicative of the interaction of charged species with water, the number of water molecules replaced upon complexation, and intra-molecular interactions. The interaction of 18-crown-6 with  $K^+$ ,  $Sr^{2+}$ , and  $Ba^{2+}$  produces  $\Delta S$  and  $\Delta H$  values of opposite sign to those expected from other neutral molecule-cation interactions. This result probably derives from the ability of 18-crown-6 to form a hydrophobic barrier to water molecules attracted by the metal cation. The resulting build-up of water molecules causes a more ordered system and the observed anomalous  $\Delta S$  and  $\Delta H$  values.

### INTRODUCTION

There is much interest in aqueous solutions at elevated temperatures since many important reactions take place in this medium, such as in geothermal wells (1), at or near ocean vents (2), in the generation of steam (3), in supercritical water oxidation processes (4) and other industrial applications (5). It is important to know the extent of the reactions which occur in these systems. This requires a knowledge of  $\log K$  at the conditions (temperature, pressure, ionic strength) of the reaction. The  $\log K$  values as well as the other thermodynamic quantities such as the  $\Delta H$ ,  $\Delta S$  and  $\Delta C_p$  values associated with reactions in aqueous solutions can change in a dramatic fashion with temperature making it difficult to predict them at high temperatures using only low temperature data (6). In order to understand the chemistry occurring in these systems, it is necessary to know what chemical species are present and the concentrations of these species. This requires a knowledge of  $K$  values, activity coefficients, and kinetic rates associated with the important chemical reactions which occur in these solutions. At present, there is no reliable way to extrapolate these data from ambient to high temperatures. Accurate data at elevated temperatures are needed to provide the information required to develop improved theories and to check existing extrapolation methods.

Water is unusual among solvents in undergoing large structural changes between the solid state (273.15 K) and critical point (647 K) (7). These changes have profound effects on the properties of water and on the involvement of water in chemical reactions over this temperature range. The thermodynamic values associated with reactions in aqueous solutions are strongly influenced by the interaction of the reactant and product species with water. Water molecules are highly polar and interact strongly with polar and charged species and with other water molecules. When a chemical reaction takes place, the properties of the water molecules in the neighborhood of the reactants and products change (8). An understanding of the thermodynamic quantities associated with a chemical reaction in aqueous solution must include a consideration of the change in these properties. The water-water interactions consist mainly of the formation of hydrogen bonds and give water a high degree of structure. This structure causes water at or near ambient temperatures to have a high dielectric constant. This high dielectric constant shields the charges on charged and polar species. As the temperature increases along the saturation vapor pressure curve, the kinetic energy of the water molecules breaks the hydrogen bonds to overcome this ordered structure in the water (7) as shown in Figs. 1 and 2.

This decrease in hydrogen bonding results in a decrease in the dielectric constant of water. The changes in density and dielectric constant of water with temperature are shown in Fig. 3 (9). The change of water structure as temperature increases causes the thermodynamic values associated with a chemical reaction in aqueous solution to change dramatically (6).

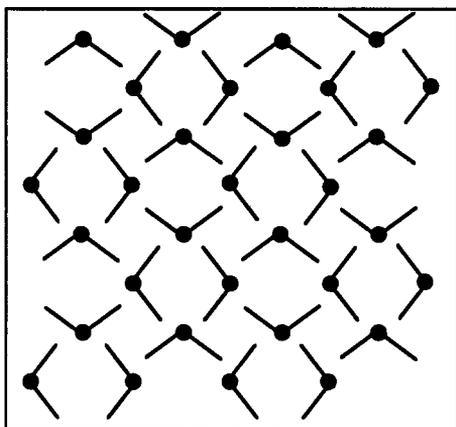


Fig. 1 Schematic representation of structure of ice.

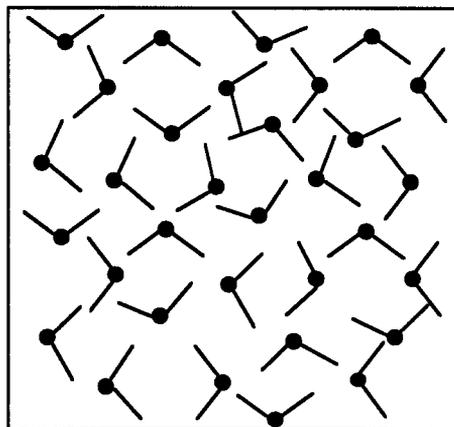


Fig. 2 Schematic representation of liquid water as temperature increases and structure becomes more random.

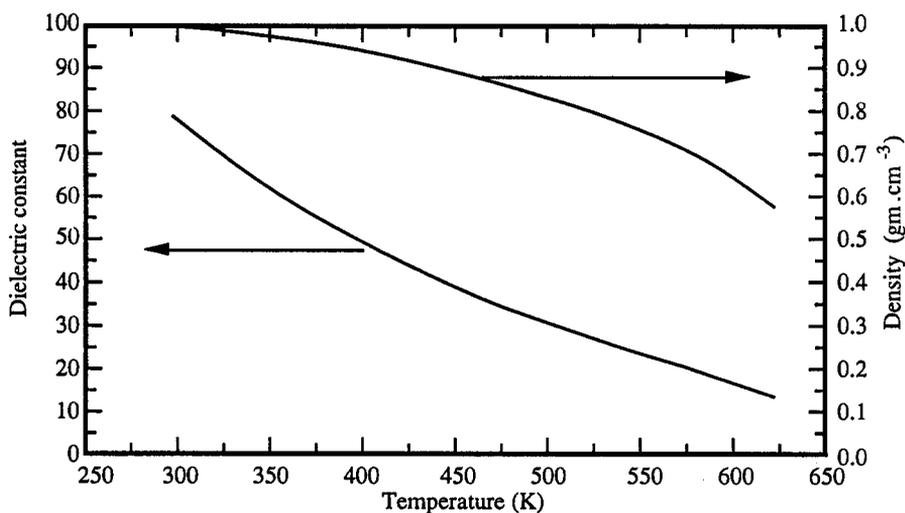
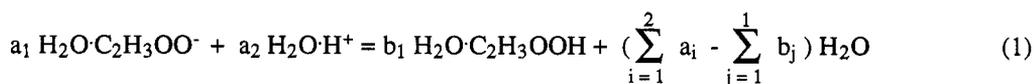


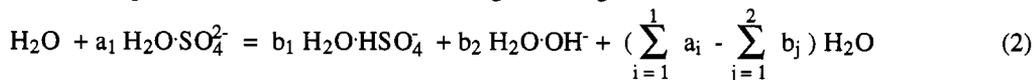
Fig. 3 Plot of dielectric constant and density of liquid water as a function of temperature at the saturated vapor pressure of water.

### REACTION TYPES IN AQUEOUS SOLUTION

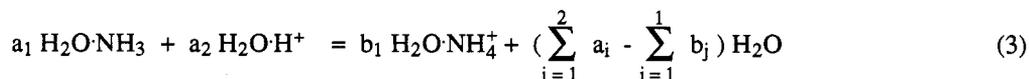
Interactions other than redox reactions involving ions in aqueous solutions can be of three different types. First, a positive charge on one species is neutralized by a negative charge on a second species, such as



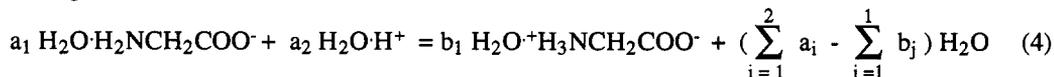
Second, two species associate with no net change in charge, such as



or



Third, a charged species reacts with a charged species of opposite sign but not at a charged site forming a zwitterion, such as



The first type of reaction has a profound effect on the water structure since there is a net reduction of charge resulting in an increase in the number of "bound" water molecules released to the bulk water, as indicated by the last term in Equation (1). Reactions of this type are often endothermic and have positive  $\Delta S$  values because the disorder of the system increases. Since the waters released upon association of the charged species must absorb energy to achieve the vibrational, rotational, and translational motion of the bulk water these reactions characteristically have large, positive  $\Delta C_p$  values which increase with temperature (6, 10, 11). As the temperature increases, the extent of hydrogen bonding in the bulk water decreases resulting in an increasing number of non-hydrogen bonded water molecules in the bulk water, thus increasing the entropy and enthalpy values of the bulk water. Since the enthalpy and entropy values for the solvated species are not expected to change significantly with temperature, the observed increases in  $\Delta H$  and  $\Delta S$  with temperature for reactions of this type are primarily due to the enthalpy and entropy increases of the released water molecules. The increase in  $\Delta H$  and  $\Delta S$  with temperature is amplified due to the increased number of water molecules affected by the charged species as a result of the decrease in the dielectric constant of water.

The second type of interaction is sometimes called an isocoulombic reaction and the net change of the water structure due to the reaction is the smallest of the three types of reactions. Since the net charge on reactants and products is the same, the quantity  $(\sum_i a_i - \sum_j b_j)$  is usually small and can be either positive or negative. Thus,  $\Delta H$ ,  $\Delta S$ , and  $\Delta C_p$  are relatively small and do not change appreciably with temperature (3, 11). A special case of this type of reaction is the association of a cation with a macrocycle to form a complex with the ion enclosed by the macrocycle. The thermodynamic values associated with this type of reaction are influenced by the nature of the macrocyclic ring as will be discussed in the next section.

In the third type of reaction, a zwitterion is formed. In this case, the magnitude of  $(\sum_i a_i - \sum_j b_j)$  depends on the degree of the interaction between the opposite charges on the zwitterion. The degree of interaction shows a strong dependence on the distance between the charges. As this distance decreases, the behavior of the zwitterion toward the solvent molecules approaches that of a neutral molecule, i. e., the effectiveness of the charges in neutralizing each other increases. As the distance increases, the behavior of the zwitterion approaches that of two separate ions. Values of  $\Delta C_p$  for a protonation reaction which forms a zwitterion in which the charges are close together will be large, as in the neutralization type of reaction. On the other hand, if the product charges are far apart,  $\Delta C_p$  values will be small, as in the isocoulombic reaction. This behavior has been seen in the case of amino acids where the  $\Delta C_p$  value for the protonation of the amino group on glycine is  $41 \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$  (12) while that for 6 aminocaproic acid is  $14 \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$  (13).

A listing of several examples of these reaction types is given in TABLE 1.

TABLE 1. Examples of some common reactions of type 1 (charge reduction reactions), type 2 (isocoulombic reactions), and type 3 (formation of a zwitterion).

Reaction type	Reaction	$\Delta C_p$ ( $\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$ )	Ref.
1	$\text{H}^+ + \text{C}_2\text{H}_3\text{O}_2^- = \text{HC}_2\text{H}_3\text{O}_2$	860 (at 548 K)	10
1	$\text{H}^+ + \text{SO}_4^{2-} = \text{HSO}_4^-$	264 (at 423 K)	11
1	$\text{H}^+ + \text{OH}^- = \text{H}_2\text{O}$	230 (at 423 K)	6
2	$\text{H}^+ + \text{H}_2\text{N}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{OH} = ^+\text{H}_3\text{N}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{OH}$	-12.2 (298-598 K)	14
2	$\text{H}_2\text{O} + \text{SO}_4^{2-} = \text{HSO}_4^- + \text{OH}^-$	34 (at 423 K)	11
3	$\text{H}^+ + \text{H}_2\text{NCH}_2\text{CO}_2^- = ^+\text{H}_3\text{NCH}_2\text{CO}_2^-$	41 (278-348 K)	12
3	$\text{H}^+ + \text{HAMP}^{2-} = ^+\text{H}_2\text{AMP}^{2-}$	14 (298-398 K)	15

## DISCUSSION

The protonation of the sulfate ion to form a hydrogen sulfate ion (11) is an example of the first type of reaction. In Fig. 4, the  $\Delta G$ ,  $\Delta H$  and  $-\text{T}\Delta S$  values for this reaction are plotted versus temperature. A dramatic increase of  $\Delta H$  and  $\text{T}\Delta S$  with temperature is seen. As temperature increases the  $\text{T}\Delta S$  term increases faster than the  $\Delta H$  term, thus resulting in  $\Delta G$  becoming more negative with increasing temperature. This reaction has a large positive  $\Delta C_p$  value which also increases with temperature(11).

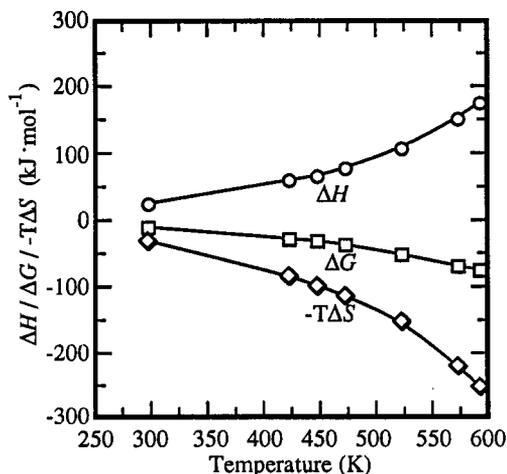


Fig. 4 Plot of  $\Delta G$ ,  $\Delta H$ , and  $-T\Delta S$  as a function of temperature for the reaction:  $\text{H}^+ + \text{SO}_4^{2-} = \text{HSO}_4^-$ .

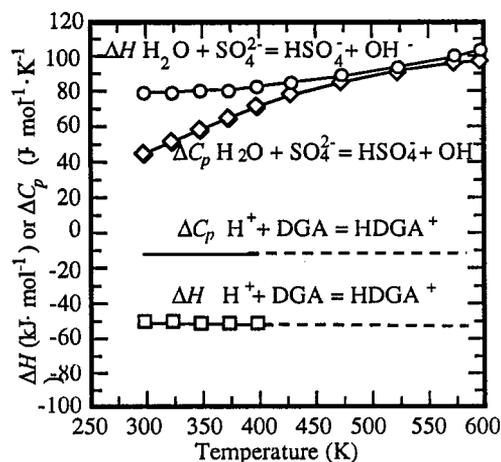


Fig. 5 Plot of  $\Delta H$  and  $\Delta C_p$  as a function of temperature for the isocoulombic reactions:  $\text{H}_2\text{O} + \text{SO}_4^{2-} = \text{HSO}_4^- + \text{OH}^-$  and  $\text{H}^+ + \text{DGA} = \text{HDGA}^+$ .

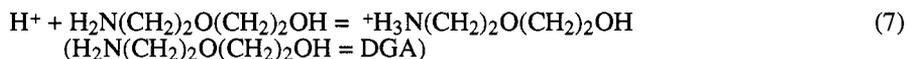
Reactions of the first type can be converted to isocoulombic reactions (second type) by the appropriate addition of the reaction for the ionization of water. For example:



can be written in the equivalent isocoulombic form:



Many isocoulombic reactions are of the type where a charged species reacts with a neutral species such as



The  $\Delta H$  and  $\Delta C_p$  values for reactions (6) and (7) are shown in Fig. 5 (11, 14). The  $\Delta H$  values do not change significantly with temperature and the  $\Delta C_p$  values are small for reactions (6) and (7).

The  $\Delta C_p$ ,  $\Delta H$ , and  $\Delta S$  values for the association of  $\text{K}^+$ ,  $\text{Ba}^{2+}$ , and  $\text{Sr}^{2+}$  with 18-crown-6 (18C6) are large and negative (16), as shown in Figs. 6 and 7. The  $\Delta S$  values for these reactions are negative, except for the value at 298 K for the association of  $\text{Sr}^{2+}$  with 18C6 and become more negative with increasing temperature. Most isocoulombic reactions where an ion reacts with a neutral species have smaller absolute values of  $\Delta C_p$  and positive  $\Delta S$  values (11,14). These negative values indicate that the water structure becomes more organized with the formation of the complex. One possible explanation for this anomalous behavior is shown schematically in Fig. 8. When the metal ion associates with the crown ether, all of the oxygen atoms in the macrocycle are directed inward leaving the hydrophobic methylene groups exposed on the exterior of the ring. Thus, the hydrophobic exterior of the 18C6 consisting primarily of a linkage of methylene groups lies between the cation and the dipolar water molecules which feel the long-range effect of the cation charge. The hydrophobic forces which repel water molecules are strong but short-ranged. The force associated with the charge of the complex is long-ranged and attracts the negative dipoles of the water molecules well beyond the range of the hydrophobic forces. However, the waters close to the complex are repelled by the strong, hydrophobic forces and thus form a highly organized shell of water molecules around the complex similar in structure to hydrates that form around small hydrocarbons (17). In other words, the waters are trapped in a potential well around the complex forming a highly organized cage of water molecules around its surface. As temperature increases and the dielectric constant of the water and the amount of hydrogen bonding decrease, the number of molecules influenced by the charge increases and the differences between the bound and bulk water molecules also increase resulting in increasingly negative  $\Delta H$  and  $\Delta S$  values with temperature.

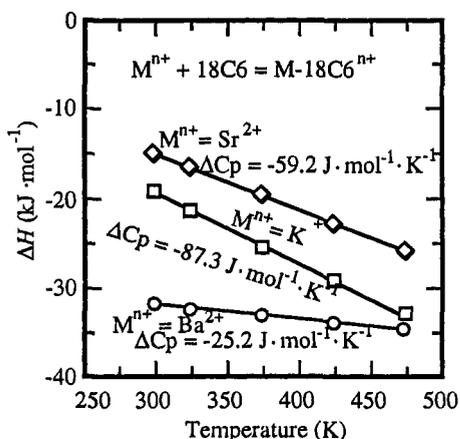


Fig. 6 Plot of  $\Delta H$  for the association of metal ion with 18C6 as a function of temperature.

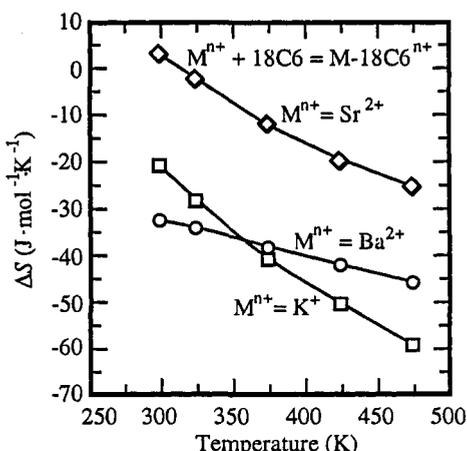


Fig. 7 Plot of  $\Delta S$  for the association of metal ion with 18C6 as a function of temperature.

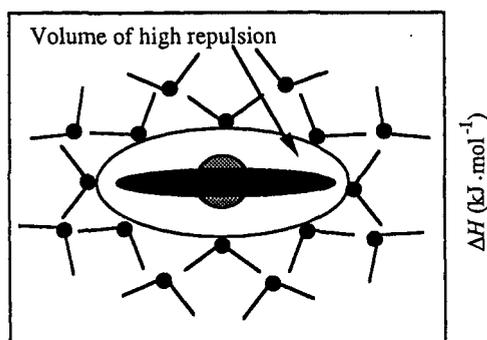


Fig. 8 Schematic representation of water molecules around metal ion crown ether complex. Dark solid oval represents the crown ether.

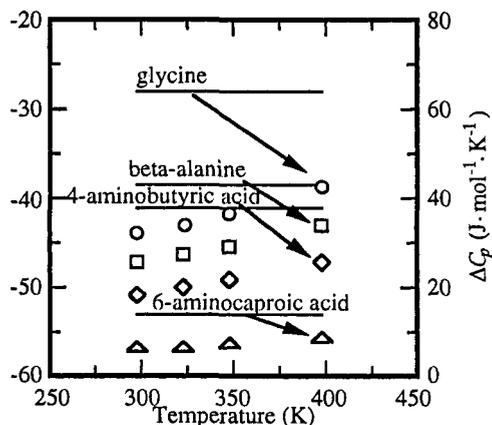


Fig. 9 Plot of  $\Delta H$  and  $\Delta C_p$  for the protonation of the amino group on several amino acids as a function of temperature. Lines are  $\Delta C_p$  and symbols are  $\Delta H$ .

The protonation of the amino group on an amino acid (12, 13) is a typical type 3 reaction. The  $\Delta H$  and  $\Delta C_p$  values for several of these reactions are shown in Fig. 9. Reactions involving protonation of alpha-amino groups (represented by glycine) have  $\Delta C_p$  values approaching those associated with charge reduction reactions. As the number of methylene groups between the charges increases, the  $\Delta C_p$  values approach those of typical isocoulombic reactions. When the amino and carboxylate groups are close together, the zwitterion behaves towards water like a neutral species. As the distance between the two functional groups increases, the interaction of the zwitterion with the water molecules approaches that of two independent, charged species. Hence, when the charges are close together the reactions are similar to charge reduction reactions. When the charges are more distant, the reactions become similar to those for isocoulombic reactions.

In Fig. 10 are given  $\Delta H$  and  $\Delta C_p$  values for the protonation of the  $N_1$  group on  $\text{AMP}^-$ ,  $\text{ADP}^{2-}$ , and  $\text{ATP}^{3-}$  (15) (Figure 11). The  $\Delta C_p$  values for these reactions increase in the order  $\text{AMP} < \text{ADP} < \text{ATP}$ . Furthermore, the  $\Delta C_p$  value in the case of AMP is typical of those found for isocoulombic reactions whereas the value in the case of ATP is typical of those found for charge reduction reactions. The value in the case of ADP lies between. A possible explanation for this behavior is that the  $\text{HN}_1^+$  group forms a hydrogen bond with a negative charge on the phosphate chain in the case of ATP, but not in the case of AMP.

Hence, the protonation of the  $N_1$  group on ATP is similar to a charge reduction reaction while the protonation of the  $N_1$  group on AMP is similar to an isocoulombic reaction. Thus, the change of  $\Delta H$  with temperature in these systems provides evidence for the presence or absence of intramolecular interactions.

The systems discussed here demonstrate that the structures formed by molecules, ions, and metal complexes in aqueous solution influence the changes with temperature of the  $\log K$ ,  $\Delta H$ , and  $\Delta S$  values for proton ionization and metal complexation. Conversely, the changes of these thermodynamic values with temperature (particularly the  $\Delta C_p$  values) provide insight into the structure of species in solution. Specifically, information can be gained concerning the presence or absence of intramolecular interactions and the effect of neighboring groups on the chemical reactivity of each other. The determination of  $\log K$ ,  $\Delta H$ ,  $\Delta S$ , and  $\Delta C_p$  values as a function of temperature for selected aqueous chemical reactions should provide greater insight into the chemical reactivity of ligands and the structure of their cation complexes at elevated temperatures.

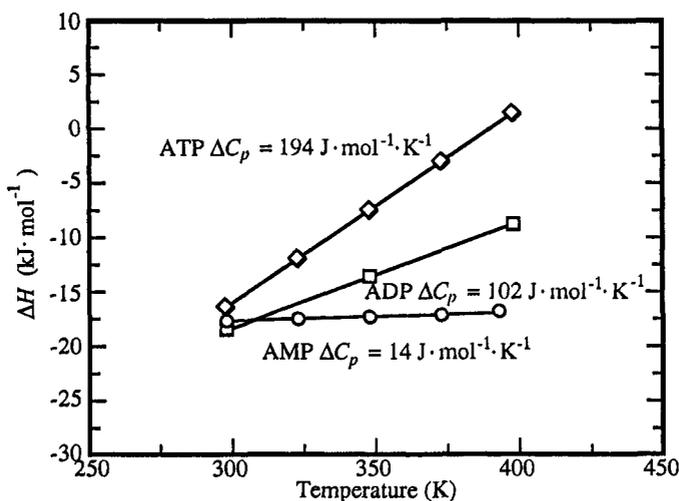


Fig 10. Plot of  $\Delta H$  as a function of temperature for the protonation of the  $N_1$  site of AMP, ADP, and ATP.

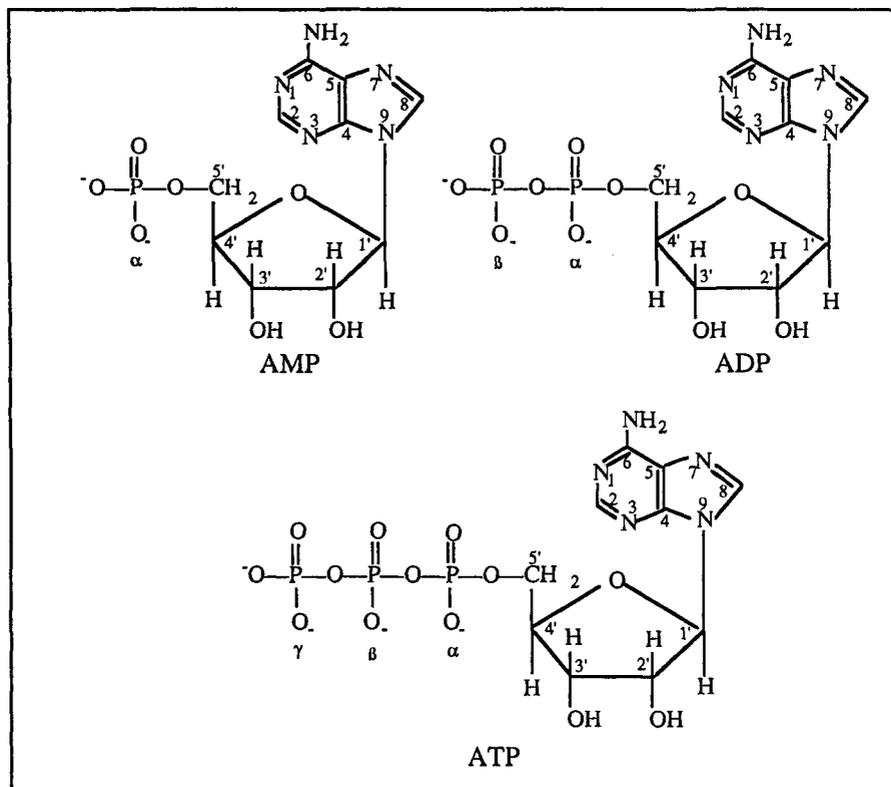


Fig. 11 Structures of AMP, ADP, and ATP.

## ACKNOWLEDGMENT

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