THERMODYNAMIC STUDIES OF SOME NUCLEIC ACID BASES, NUCLEOSIDES AND NUCLEOTIDES IN WATER AND AQUEOUS SOLUTIONS OF SOME SUGARS, SALTS AND UREA

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DEDICATED TO
MY PARENTS

CERTIFICATE

This is to certify that the thesis entitled "THERMODYNAMIC STUDIES OF SOME NUCLEIC ACID BASES, NUCLEOSIDES AND NUCLEOTIDES IN WATER AND AQUEOUS SOLUTIONS OF SOME SUGARS, SALTS, AND UREA" being submitted by Mr. Nand Kishore to the Indian Institute of Technology, Delhi, for the award of the degree of Doctor of Philosophy in Chemistry, is a record of bonafide research work carried out by him. Mr. Nand Kishore has worked under my guidance and supervision, and has fulfilled the requirements for the submission of this thesis which, to my knowledge, has reached requisite standard.

The results contained in this dissertation have not been submitted, in part or in full, to any other university or institute for the award of any degree or diploma.

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January 2, 1989

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(NAND KISHORE)

ABSTRACT

The origin of the forces which stabilize the double helical structure of the nucleic acids is not clearly understood. Water plays an important role in maintaining the native conformation of biological macromolecules like nucleic acids. The interactions of these macromolecules with aqueous solutions are also important in the conformational stability of their helical structure. Owing to the complexity of the interactions involved in a direct study on aqueous solutions of nucleic acids, investigations of the behaviour of the model compounds of nucleic acids viz. nucleic acid bases, nucleosides and nucleotides may lead to better understanding of the factors governing the stability of the nucleic acid helix.

The present work describes the results of thermodynamic investigations carried out on some nucleic acid bases, nucleosides and nucleotides in water and aqueous solutions of glucose, sucrose, sodium chloride, calcium chloride and urea. The thermodynamic parameters comprise of apparent molar heat capacities (ϕ_C) and apparent molar volumes (ϕ_V). A Picker dynamic flow microcalorimeter was employed to measure the apparent molar heat capacities.The apparent molar volumes were determined form density measurements using an Anton Paar DMA 60/602 digital

densitymeter. At infinite dilution, partial molar heat capacities ($\bar{C}^{o}_{p2}$)and partial molar volumes ($\bar{V}^{o}_{2}$) were derived either by linear regression analysis or by taking the average of all the data points depending upon whether concentration dependence was observed or not.

A brief survey of the present status regarding the knowledge of the structure of water in aqueous solutions of solutes is critically reviewed in chapter 1.

Chapter 2 describes the experimental set up of the calorimeter and densitymeter; and the operational procedures used in this study.

In chapter 3, the results on partial molar heat capacities and volumes of some nucleic acid bases, nucleosides and nucleotides in water and aqueous solutions of glucose and sucrose are reported. The $\bar{C}^{o}_{p2}$ and $\bar{V}^{o}_{2}$ values of the nucleic acid bases in water indicates the presence of polar moieties in these bases tends to reduce their hydrophobic effect. The partial molar heat capacities and volumes of the nucleosides in water have been observed to be higher than their corresponding bases which is due to the ribose or deoxyribose group.

The $\bar{C}^{o}_{p2,tr}$ and $\bar{V}^{o}_{2,tr}$ for transfer from water to aqueous solutions of glucose and sucrose have been rationalized in terms of cosphere overlap model. The positive values of the $\bar{C}^{o}_{p2,tr}$ and $\bar{V}^{o}_{2,tr}$ indicate the predominance of hydrophilic -hydrophilic group interactions over the hydrophilic -hydrophobic group interactions between the nucleic acid bases, nucleosides and nucleotides, whereas the negative value of these transfer parameters as in the case of thymine in aqueous glucose solutions indicates larger hydrophobic-hydrophilic group interactions than hydrophilic-hydrophilic group interactions. These transfer parameters are small and similar to those reported for amino acids and peptides. It may be inferred from our studies that the sugar molecules should stabilize the nucleic acid helix.

Chapter 4 consists of the results on $\bar{C}^{o}_{p2}$ and $\bar{V}^{o}_{2}$ measurements on similar set of compounds in aqueous solutions of sodium chloride and calcium chloride. In general, the ion-hydrophilic group interactions have been found to dominate over the ion-hydrophobic group interactions of the salts with various nucleic acid bases, nucleosides and nucleotides. The results have thrown light on the mechanism of stabilization/denaturation of the nucleic acid helix by these salts.

The results of $\bar{C}^{o}_{p2}$ and $\bar{V}^{o}_{2}$ of the nucleic acid bases, nucleosides and nucleotides in various concentrations of aqueous urea solutions are described in chapter 5. The corresponding transfer parameters from water to aqueous urea solutions have been explained in terms of hydrophilic and hydrophobic interactions. These results support that the denaturating ability of urea can be attributed to its ability to disrupt the interchain hydrogen bonds in the nucleic acids and forming hydrogen bonds with the constituents of nucleic acids.

Due acknowledgement has been made where ever the work described is based on the findings of other investigations. The author apologizes for any omission which might have occured due to oversight.

GLOSSARY OF SYMBOLS AND ABBREVIATIONS

ADP	adenosine-5'-diphosphate
AMP	adenosine-5'-monophosphate
ATP	adenosine-5'-triphosphate
C_p	heat capacity of solution
C_p°	heat capacity of solvent
$\bar{C}_{p2}^\circ$	partial molar heat capacity of the solute at infinite dilution
$C_{p,A}$	heat capacity of the liquid A
$C_{p,B}$	heat capacity of the liquid B
ΔC_p	change in the heat capacity
ΔC_p°	heat capacity of dissolution at infinite dilution
d	density of solution
d_0	density of solvent
d_A	density of liquid A
d_B	density of liquid B
DNA	deoxyribo nucleic acid
ΔG_{tr}	free energy of transfer
ΔH	change in enthalpy
ΔH_s°	integral enthalpy of solution at infinite dilution
I_c	calibration current
K	calibration constant
m	molality
M	molecular weight

p	pressure in torr
pK	$-\log_{10}K$
ϕ_c	apparent molar heat capacity
ϕ_v	apparent molar volume
ϕ_c°	apparent molar heat capacity at infinite dilution
ϕ_v°	apparent molar volume at infinte dilution
poly(rA-rU)	polynucleotide with alternating sequences of adenine and uracil
Ribo A_8	ribonucleotide with eight adenine units
Ribo A_{10}	ribonucleotide with ten adenine units
RNA	ribonucleic acid
ΔS	entropy change
ΔS°	standard entropy change
σ	standard deviation
σ_A	heat capacity of liquid A in units of JK^{-1} cm^{-3}
σ_B	heat capacity of liquid B in units of JK^{-1} cm^{-3}
σ_s	shrinkage in volume
$tRNA^{Phe}$	phenylalanine accepting transfer RNA
UMP	uridine-5'-monophosphate
V_s	shrinkage volume
$V_{v.w}$	vander Waals volume
V_Z	zener voltage
$\bar{V}_2^\circ$	partial molar volume at infinite dilution
ΔV	change in volume
$\bar{V}^\circ_{2,tr}$	partial molar volume of transfer of the solute at infinite dilution

W	water
W_o	power input
ΔW	change in power

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