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Calculation of Some Bond Parameters and Thermodynamic Properties of Deoxy 5'-Monophosphate Nucleotides

[*1]Gidado A. S., [1]Babaji G., and [2]Shariff M. A.

[1]Department of Physics, Bayero University Kano.
[2]Department of Physics, Federal College of Education Katsina.

Abstract

The bond parameters such as bond lengths, bond angles, total bond length steric energy and total bond angle steric energy as well as thermodynamic properties of the four deoxy 5'-monophosphate nucleotides: Deoxyadenosine '5 -monophosphate, deoxycytidine 5' -monophosphate, deoxyguanosine 5' monophosphate and deoxythymidine 5' -monophosphate are calculated using CONFLEX VER.7.A.0910 software and (Merck Molecular Force Field) MMFF94s. We obtained the average bond length for deoxyadenosine 5'-monophosphate as 1.230Å. ***This compares favorably with experimental and ideal values(using corina program) as*** 1.296Å and 1.294Å ***respectively. A similar comparison is made for average bond length of the other nucleotides. In the same vain, we obtained the average bond angle for deoxyadenosine 5'-monophosphate to be*** $112.883°$. ***This again compares favorably with experimental and ideal values(using corina program) as*** $112.880°$ and $113.015°$ ***respectively. We have also observed that the total angle steric energy contribute more when compared to the total bond steric energy for all the nucleotides. Total internal energy, enthalpy, entropy, free energy and heat capacity for each of the nucleotides have been calculated and reported.***

1.0 Introduction

The molecular building blocks of life are DNA, RNA and proteins. DNA stores the information of the protein structure, RNA participates in the assembly of the proteins, and the proteins are the final devices that perform the tasks[1]. Nucleotides are biological molecules that form the building blocks of nucleic acids (DNA and RNA) and serve to carry packets of energy within the cell[2]. Nucleotides are composed of one to three phosphate groups and a cyclic nitrogenous base, either a purine or a pyrimidine, linked to a pentose sugar. They play important roles as coenzymes and chemical energy sources in most biological processes in cell metabolism. They are also the primary structure units and momomeric precursors in nucleic acids synthesis. They can be synthesized endogenously de novo or salvage pathways, and thus they are not considered as essential dietary nutrients. However, when the endogenous supply is insufficient for normal function under the conditions of certain disease states, limited nutrient intake, or rapid growth, the exogenous nucleotides may become conditionally essential or semi-essential nutrients. Nucleotides are involved in the metabolism of long chain polyunsaturated fatty acids and modify the composition of the intestinal microflora and iron absorption in the gut. Evidence also indicates that nucleotides have other functions such as improvement of gastrointestinal tract repair after damage and participation in the immune response mediated by T cells. Concerning their important biological and trophochemical role of maintaining normal growth and development in infants.There has been an increasing interest in dietary nucleotides in infant nutrition. Human milk is assumed to be the best source of nucleotides for young infants and serves as a gold standard in manufacturing infant formulas. Although most infant formulas are currently made from bovine milk, the compositions of the nucleotides are different from those found in human milk[3,4,5].

One assumes that properties of a particular bond are conserved when this bond is transferred from one molecule to another. In this way, one expects to predict, for example, from the known length values of typical bonds structural features of new molecules or from bond energies the stability of molecules composed of these bonds. The nuclear arrangements of a molecule is defined by a set of coordinates. These coordinates can be the cartesian ones but the internal ones are usually

*Corresponding author: ***Gidado A. S.,*** E-mail: asgidado.phy@buk.edu.ng , Tel.: +2348028276213/08036407447

Figure 2. Bond Length

E_{bend} is the energy required to bend a bond from its equilibrium angle, θ_0. Again this system can be modeled by a spring, and the energy is given by the Hookian potential with respect to angle:

$$E_{bend} = \frac{1}{2} K_{b,ijk}\left(\theta_{ijk} - \theta_0\right)^2 \quad (2)$$

where $K_{b,ijk}$ is the bending force constant and θ_{ijk} is the instantaneous bond angle in Figure 3

Figure 3. Bond Angle

The Gibbs free energy of a system is given by [15,16]

$$\Delta G = \Delta H - T\Delta S \quad (3)$$

where ΔH is enthalpy, ΔS entropy, and T is the temperature
The steric energy calculation in molecular mechanics corresponds to an internal energy

$$\Delta H = \Delta U + \Delta (PV) \quad (4)$$

where ΔU is the internal energy
and

$$PV = nRT \quad (5)$$

The enthalpic contribution to the free energy reflects the specificity and strength of the interactions between both partners. These include ionic, halogen, and hydrogen bonds, electrostatic (Coulomb) and van der Waals interactions, and polarisation of the interacting groups, among others. The simplest description of entropic contribution is that it is a measure of dynamics of the overall system.
The Gibbs' equation can also be written as

$$\Delta G = -RTlnK_d \quad (6)$$

where R is a gas constant, T is the temperature, and K_d is binding constant.

ΔS can be calculated directly from ΔG and ΔH, according to the Gibbs' equation.
The heat capacity is given [17] by the derivative of total energy with respect to tempearture at constant volume as

$$C_V = \left(\frac{\partial U}{\partial T}\right)_V \quad (7)$$

Using Equ (7), we can obtain the heat capacity of the system at a given temperature.

3.0 Methodology

CONFLEX 7 Software

CONFLEX is a program for the conformational search for target molecules and generation of low energy conformations, calculation of standard vibrational analysis, thermodynamic quantities, ultraviolet and visible light absorption spectra, circular dichroism spectra and NMR coupling constants[18]. CONFLEX algorithms take into account conformational searches and conformational distribution for organic molecules using molecular mechanics. CONFLEX algorithms utilize commonly used force fields such as MMFF94s and EMM2 [18].

The CONFLEX Interface is used to submit jobs to the CONFLEX Engine, and to analyze the results.

It comprises the following basic functions:

(i) Opens each type of molecule file and displays the molecular structure

(ii) Opens each type of calculation results file and displays the structure and related data

(iii) Submits jobs to the CONFLEX Engine for calculation locally or on a computational server

(iv) Displays various molecular attributes of structures, e.g. interatomic distance, angle, etc.

(v) Displays molecular surface and tracks using molecular dynamic calculation data

Input Files

CONFLEX provides a file with an .ini extension under the same filename as the molecular structure file. The molecular force field for carrying out CONFLEX calculations is described therein. This file must be present in the same directory (folder) as the molecular structure file. When calculations are carried out using the CONFLEX Interface, it automatically creates an .ini file in real time.

The two input files required by CONFLEX are the molecular structure file (.mol) and the calculation settings file (.ini).

Definition Files for Molecular Structure

In CONFLEX, the file describing the molecular structure must be in one of the formats below:

▪ MDL-Molfile format .

Atom coordinates and information on bonds are contained in a format devised by Molecular Design Limited (currently Accelrys). It is supported by many types of chemical drawing programs such as Chem3D.

•Protein Data Bank (PDB) format

This is file type is primarily used to describe biological molecular structures in a format devised by the Protein Data Bank.

Output Files

During execution, several temporary files are generated and then deleted once calculations have finished. When structural optimization (including crystals) is designated, CONFLEX generates additional files by adding the following to the base file name: -F.mol、-F.pdb、-F.cmf、-F. cif). Other files are generated as well depending on the type of calculation.

OPEN BABEL 2.2.1

Open Babel is a chemical toolbox designed to speak the many languages of chemical data. It's an open, collaborative project allowing anyone to search, convert, analyze, or store data from molecular modeling, Chemistry, Biochemistry, Biophysics or related areas [19]**.**

The molecular geometry of the four deoxy 5'-monophosphate nucleotides: 5'-dAMP, 5'-dGMP, 5'-dCMP and 5'-dTMP were obtained from Ligand-Expo data base [20,21,22,23**].** Ligand Expo (formerly Ligand Depot) is an online database which provides chemical and structural information about small molecules (so-called ligands) within the structure entries of the Protein Data Bank. Tools are provided to search the PDB dictionary for chemical components, to identify structure entries containing particular small molecules, and to download the 3D structures of the small molecule components in the PDB entry.

The geometry optimization was carried out using *CONFLEX VER.7.A.0910 software. OPEN BABEL VER 2.2.1* software was used to convert the molecules obtained from Ligand-expo to a CONFLEX readable format **(**MDL-Molfile format**).** Five optimization methods: Newton-Raphson, steepest descent, conjugate gradient, variable metric and precise were used to optimize the molecules using the MMFF94s force field. The MMFF94s force field is parameterized toward performing calculations on small organic compounds, especially nucleic acids and proteins, and as such, is well suited for the present study. The results produced by Newton-Raphson were the best and the data obtained from such results were used to plot the graphs. All graphs were plotted using the plotting software Origin 5.0.

4.0 Results and Discussion

BOND LENGTHS

We calculated the average bond length for deoxyadenosine 5'-monophosphate as 1.230Å. This is compared favorably with experimental and ideal values as 1.296Å and 1.294Å [24] respectively. A similar comparison shows the respective values for this work, experimental and ideal as 1.297Å, 1.296Å and 1.291Å, 1.291Å, 1.289Å and 1.287Å, and 1.293Å, 1.289Å and 1.295Å respectively in the order of the nucleotides named above. Figures 4-7 show the graphs of bond lengths against bonded atoms for the first fifteen values. The graphs compared the results obtained for this work with those obtained from experimental and ideal models [24 – 27]. Of the five optimization methods used, Newton-Raphson method was found to be the best.

Bonded atoms

Figure 4. A graph of Bond length(Å) against bonded atoms for 5'-dAMP

Bonded atoms

Figure 5. A graph of Bond length(Å) against bonded atoms for 5'-dGMP

Bonded atoms

Figure 6. A graph of Bond length(Å) against bonded atoms for 5'-dCMP

Bonded atoms

Figure 7. A graph of Bond length(Å) against bonded atoms for 5'-dTMP

BOND ANGLES

We calculated the average bond angle for deoxyadenosine 5'-monophosphate as112.883°. This compares favorably with experimental and ideal values as 112.880° *and* 113.015° [24] respectively. A similar comparison shows the respective values for this work, experimental and ideal as 113.117°, 113.103° and 113.206°, 112.668°, 112.607° and 112.585°, 112.306°, 112.548° and 112.394° respectively in the order of the nucleotides named above. Figures 8-11 show the graphs of bond lengths against bonded atoms for the first fifteen vlues. The graphs compared the results obtained for this work with those obtained from experimental and ideal models [24 - 27].

Bonded atoms

Figure 8. A graph of Bond Angle(°) againts bonded atoms for 5'-dAMP

Bonded atoms

Figure 9. A graph of Bond Angle(°) againts bonded atoms for 5'-dGMP

Bonded atoms

Figure 10. A graph of Bond Angle(°) againts bonded atoms for 5'-dCMP

Bonded atoms

Figure 10. A graph of Bond Angle(°) againts bonded atoms for 5'-dTMP

Table 1. Total Bond and Angle Steric Energy

NUCLEOTIDE	TOTAL BOND STERIC ENERGY(Kcal/mol)	TOTAL ANGLE STERIC ENERGY(Kcal/mol)
5'-dGMP	4.21376	18.9903
5'-dGMP	3.93137	23.8595
5'-dCMP	3.58167	25.2312
5'-dTMP	3.55032	18.1884

Table 2. Thermodynamic Properties of the Nucleotides at Temperature = 298.15K

NUCLEOTIDE	TTOTAL INTERNAL ENERGY (KCAL/MOL)	TOTAL ENTHALPY (KCAL/MOL)	TOTAL ENTROPY (EU)	TOTAL FREE ENERGY (KCAL/MOL)	TOTAL HEAT CAPACITY (CAL/MOL/K)
5'-dGMP	84.9629	85.5554	144.5683	42.4524	77.3810
5'-dGMP	28.5005	29.0930	152.1713	-16.2769	81.1395
5'-dCMP	-41.4440	-40.8515	145.5967	-84.2611	74.0262
5'-dTMP	-11.3817	-10.7892	151.6479	-56.0030	78.0572

Conclusion

We have calculated bond lengths and bond angles of the four deoxy 5'-monophosphate nucleotides and established a good agreement with data from experimental and other models (using corina program). The results further show that *CONFLEX VER.7.A.0910* software is a powerful tool for molecular modeling using the concepts of classical mechanics. We have also observed that the total angle steric energy contribute more when compared to the total bond steric energy for all the nucleotides. Total internal energy, enthalpy, entropy, free energy and heat capacity for each of the nucleotides have been calculated and reported.

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