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Study of [1,3] sigmatropic hydrogen migration in uracil, uridine and uridylic acid by AM1 method

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The geometry and electronic structures of uracil, uridine and uridylic acid involving [1,3] sigmatropic hydrogen migration in the formation of tautomers have been fully optimized and evaluated by semi-empirical molecular orbital AM1 method. In this connection, the heats of formation ($\Delta H_f°$), dipole moments (μ), full atomic charges, and energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) have been calculated and discussed. The mechanistic investigation of [1,3] sigmatropic rearrangement in uracil affected in the conformational changes of uridine and uridylic acid has been studied by the comparison of net charges of atoms in different positions of the molecule. All tautomers exist with in the energy of 20.569 kcal/mol. Furthermore, dipole moment and atomic charges of all tautomers indicated that the dipole-dipole interactions play a vital role during the synthesis of proteins and enzymes.

Keywords: Frontier molecular orbital, AM1, [1,3] sigmatropic rearrangement, tautomers, conformations
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Uridine and uracil derivatives are biologically important[1]. The influence of ultra-violet and visible light on uracil was reported to modify the biological activity[2] and the synthesis of proteins. The [1,3] sigmatropic hydrogen migration in the formation of tautomers of uracil, uridine and uridylic acid may change the hereditary character of an animal or plant to produce new proteins[3]. Proteins play a vital role in all phases of life in the form of enzymes, hormones and haemoglobin and are important constituents of cell membranes, hair, hoof, nail, collagen and muscles. Dimers of uracil-thymine and uracil itself are formed by UV irradiation at RT[4]. Many side effects of chemical therapy prompted medical and biological scientists to lean towards biological therapy. In this connection, the advanced technology of genetic engineering for the synthesis of genes and discovery of miracle enzymes are required to cure many diseases[5].

A gene[6] is a segment of DNA that codes for one polypeptide chain, which is called primary structure of a protein. This protein is stored in a coded form in the specific nucleotide sequence of DNA, and it is transcribed on the messenger RNA's (mRNA). The mRNA acts as a template for the translation of the DNA code into a specific polypeptide. Three bases are required to specify one amino acid from four bases of mRNA (namely, adenine (A), guanine (G), cytosine(C), and uracil (U)), and thus formed triplet of non-overlapping bases is known as codon. About 61 triplets, out of 64 triplets have been found to code for 20 amino acids. The remaining three triplets (UAA, UGA and UAG) are chain-terminating codons and AUG is the chain-initiating codon in the synthesis of polypeptide chain. Transfer RNA's (t-RNA) are adopter molecules[7], which takes part in the recognition both a specific amino acid and a codon during protein synthesis.

In view of these observations in the application of AM1 study for conformational analyses[8], the present investigation on photochemical and thermal [1,3] sigmatropic hydrogen migration in the formation of tautomeric forms of uracil, uridine and uridylic acid have been evaluated by the relative values of the net charges of atoms at different positions of the molecule. The heats of formation ($\Delta H_f°$), dipole moments (μ), and energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) have been determined by full optimization calculations using semi-empirical molecular orbital AM1 method and discussed.

Computational Methodology[9]

Semi-empirical molecular orbital calculations were performed using AM1 (Austin Model 1) method included in the MOPAC93 on Intel Celron-333 MHz PC. Geometries in the ground state were completely optimized (keyword PRECISE, equivalent to GNORM=1.0) until the lowest energy conformations

were found. The keyword MMOK was also used to correct the increase in the barrier to rotation of the amide linkage. The position of the atom in the molecule is mentioned as subscript. The initial molecular geometry was adopted as Pople's standard data[10]. The conformations were designated by Klyne-Prelog terms[11] using *s=syn, a=anti, p=periplanar* (0±30° and 180±30°) and all other angles *c=clinal.*

Results and Discussion

Electronic structures of uracil, uridine and uridylic acid

The electronic structures of uracil, uridine and uridylic acid along with the numbering of the system in this context are shown in **Figure 1**. The calculated heats of formation ($\Delta H_f°$), dipole moments (μ), the energies of frontier orbitals (E_{HOMO} and E_{LUMO}), and the net charges on typical atoms of uracil tautomers (**a** to **f**) (**Table I**), uridine **1-3a** and uridylic acid **1-3b** are presented (**Table II**).

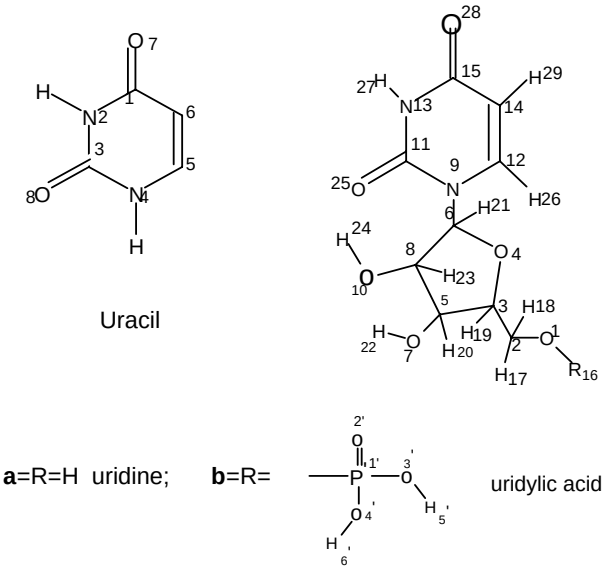


Figure 1

Table I — Heats of formation $\Delta H_f°$ (in kcal/mol), dipole moment (in Debye), energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) (in eV), and the atomic charges on typical-atoms for uracil tautomers **a** to **f** from AM1 calculation

Property	a	b	c	d	e	f
$\Delta H_f°$ (kcal/, mol)	-53.964	-35.861	-34.800	-44.644	-33.395	-38.331
μ(Debye)	4.284	7.085	3.152	2.838	6.106	4.759
E_{HOMO}(in eV)	-9.970	-9.759	-10.017	-9.551	-9.702	-9.460
E_{LUMO}(in eV)	-0.318	-0.516	-0.333	-0.467	-0.020	-0.512
C_1(atomic charge)	0.3533	0.2134	0.1904	0.3422	0.3035	0.2374
C_3	0.3935	0.3381	0.1813	0.2533	0.2590	0.3391
C_5	0.0480	0.0757	0.0186	0.0171	0.0084	0.0572
C_6	-0.3002	-0.3707	-0.3517	-0.3068	-0.2885	-0.3421
N_2	-0.3648	-0.2155	-0.2493	-0.3147	-0.3137	-0.3578
N_4	-0.3186	-0.3184	-0.1838	-0.2808	-0.2810	-0.2082
O_7	-0.3295	-0.2093	-0.2131	-0.3384	-0.3007	-0.2367
O_8	-0.3609	-0.3180	-0.2040	-0.2485	-0.2592	-0.3187

Table II — Heats of formation $\Delta H_f°$ (in kcal/mol), dipole moment (in Debye), energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) (in eV), and the atomic charges on typical-atoms for uridine **1** to **3a** and uridylic acid **1** to **3b** tautomers from AM1 calculation

Property	1a	2a	3a	1b	2b	3b
$\Delta H_f°$ (kcal/,mol)	-230.064	-208.004	-218.574	-449.294	-423.469	-437.828
μ(Debye)	4.579	6.060	5.016	2.576	7.934	2.397
E_{HOMO}(in eV)	-9.663	-9.453	-9.486	-9.828	-9.511	-9.744
E_{LUMO}(in eV)	-0.092	+0.079	-0.385	-0.269	-0.087	-0.650
C_2 (atomic charge)	-0.0419	-0.0416	-0.0415	-0.0082	-0.0002	-0.0055
C_3	0.0169	0.0196	0.0139	0.0222	-0.0013	0.0170
C_5	0.0263	0.0267	0.0265	0.0276	-0.0156	0.0312
C_8	-0.0230	-0.0325	-0.0171	-0.0225	-0.0507	-0.0125
C_{14}	-0.3171	-0.3041	-0.3195	-0.3169	-0.3091	-0.3173
N_9	-0.2859	-0.2497	-0.2852	-0.2841	-0.2805	-0.2878
N_{13}	-0.3611	-0.3120	-0.3029	-0.3608	-0.2301	-0.3012
P_1,	- - - - -	- - - - -	- - - - -	2.6086	2.6084	2.6150
O_1	-0.3401	-0.3417	-0.3402	-0.7427	-0.7412	-0.7684

—Contd

Table II — Heats of formation $\Delta H_f°$ (in kcal/mol), dipole moment (in Debye), energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) (in eV), and the atomic charges on typical-atoms for uridine **1** to **3a** and uridylic acid **1** to **3b** tautomers from AM1 calculation—*Contd*

Property	**1a**	**2a**	**3a**	**1b**	**2b**	**3b**
O_4	-0.2620	-0.2614	-0.2670	-0.2654	-0.2606	-0.2708
O_7	-0.3239	-0.3207	-0.3265	-0.3222	-0.3116	-0.3225
O_{10}	-0.3334	-0.3251	-0.3367	-0.3340	-0.3358	-0.3343
O_{25}	-0.4003	-0.2783	-0.3705	-0.3968	-0.2401	-0.3699
O_{28}	-0.3328	-0.3038	-0.2324	-0.3290	-0.2944	-0.2307
$O_{2'}$	- - - - -	- - - - -	- - - - -	-1.0755	-1.0739	-1.0502
$O_{3'}$	- - - - -	- - - - -	- - - - -	-0.7790	-0.7769	-0.7876
$O_{4'}$	- - - - -	- - - - -	- - - - -	-0.8177	-0.8164	-0.8129

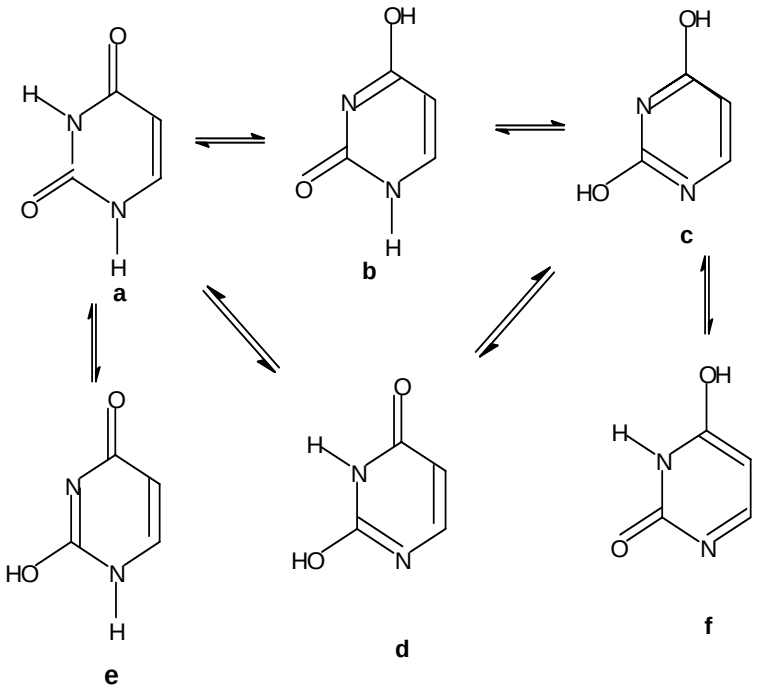
Photochemical or thermal [1,3] sigmatropic rearrangement[12] will take place by shifting of a hydrogen atom with its σ-bond within a π-bond frame-work to a new site in two pathways: *i.e.* the hydrogen moves along the top or bottom face of the π -system or across the π-system from top to bottom or vice versa. The former is called suprafacial and latter antarafacial migration respectively. However, in a photochemical reaction, promotion of an electron from HOMO to LUMO, the suprafacial pathway is allowed in the case of **a** to **f** tautomers (**Figure 1** and **Scheme I**). But [1,3] sigmatropic hydrogen migration of **b**, **d** and **e** tautomers are easily converted to **a** tautomer, which is more stable due to the net charges of O_7 for **b**, O_8 for **d** and **e** are less charges than **a** tautomer. [1,3] Shift of hydrogen in **b**, **d**, and **f** are converted to **c**, which is more susceptible to form an aromatic. According to the heat of formation ($\Delta H_f°$) data, the stability of tautomers follow the order **a** > **d** > **f** > **b** > **c**> **e** (**Table I**). The value of dipole moment (μ) is in the order **b** > **e** > **f** > **a** > **c** > **d**. The dipole-dipole interactions make hydrogen bonding in the formation of the double helix of DNA, and it is also responsible for replication of the molecule, that is the basis of heredity[13]. Polar bonds allow molecules to interact in various ways with other molecules with each other. Such secondary interactions are relatively weak and play a vital role in the chemistry of life, because of contribution to the shape and activity of enzymes and proteins. C_6-atom is more reactive towards electrophilic reagents due to the presence of negative charge in all tautomers (**a** to **f**). N_4-atom has more negative charge in the case of tautomers **a** and **b** and N_2-atom has less negative charge in the case of tautomers **b** and **c**. From this result, it can be predicted that the hydrogen bonding from strong to weak depends upon the solution medium, and it is important in determining the nature of hydrogen bonding in nucleic acids[14].

Uridine tautomers **1-3a** are formed by the attachment of C_6-position of d(-) ribose at N_9-position of uracil tautomers (**a**, **e** and **b** respectively) through a glycosidic bond (**Figure 1** and **Scheme II**). But, a photochemical reaction is allowed the promotion of an electron from HOMO to LUMO in the suprafacial pathway in case of **1a** and **3a** tautomers and uridine tautomer **2a** is allowed antarafacial thermal[1,3]sigmatropic rearrangement (**Figure 1** and **Scheme II**).

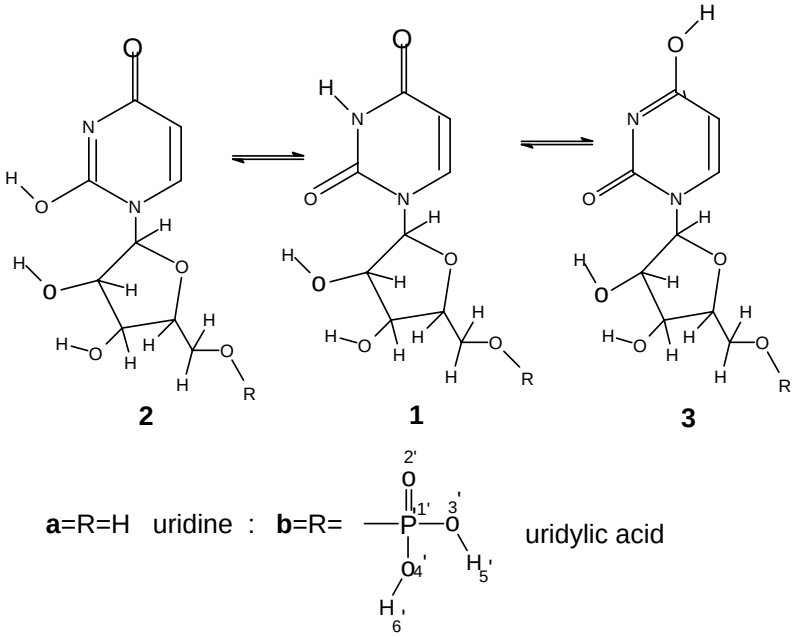
Stereochemically, migration of hydrogen can be suprafacial or antarafacial in the biological systems and natural reactions. In the transition state, a three-center bond is required to involve overlap between the *s* orbital of the hydrogen and lobes of *p* orbitals of the two terminal atoms. But the *s* orbital of the hydrogen and lobes of *p* orbitals in opposite phase, cannot be overlapped or bonded simultaneously to both terminal orbitals then, [1,3] shift of hydrogen is symmetry-forbidden.

A sigmatropic rearrangement depends on the symmetry of terminal orbitals and on the geometry of the system. Thus, the transition state would be extremely strained[15], when thermal [1,3] sigmatropic migration is allowed to take place antarafacial [1,3] shift. Since they would require the π- framework to be twisted far from the planarity that it requires for delocalization of electrons. It can be shown that the net charges of O_{25} and O_{28} are decreased in the order of **1a** > **3a** > **2a** and **1a** > **2a** > **3a**, respectively. The [1,3] sigmatropic hydrogen migration is more susceptible to form tautomers **2a** and **3a**. Usually, the oxygen atom with larger value of net charge accepts proton shifts more easily, when the proton is shifting from N_{13}- to O_{25} in the case of **1a** to **2a**. The atomic charges are decreased at N_{13}- and O_{25}- to –0.3120 and –0.2783 respectively in the case of **2a**. If the proton is shifting from N_{13}- to O_{28} in the case of tautomers **1a** to **3a** with decreasing net charges at O_{25}, O_{28}, N_{13}, C_8 and C_3 atoms (**Table II**).

According to the heats of formation ($\Delta H_f°$) data, the stability of uridine tautomers is in the order of **1a** > **3a** > **2a**. It can be predicted that the conversion of **1a** to **3a** is a lower energy process than the conversion



Scheme I— [1,3]sigmatropic hydrogen migration in uracil (**a-f**)



Scheme II— [1,3]sigmatropic hydrogen migration in uridine (**1a-3a**) and uridylic acid (**1b-3b**)

of **1a** to **2a**. So that former (**1a** to **3a**) and latter (**1a** to **2a**) are allowed respectively suprafacial and antarafacial thermal [1,3] sigmatropic rearrangement. These tautomers are formed with the difference in the heats of formation of 22.06 k.cal/mol and 11.49 k.cal/mol respectively in the case of **1a** to **2a** and **1a** to **3a**. The value of dipole moment (μ) is in the order of **2a** > **3a** > **1a**. The hydrogen bonding is a strong kind of dipole-dipole attraction, in which a hydrogen atom stands as a bridge between the electronegative atoms by holding one with a covalent bond and the other by purely electrostatic forces. The position of equilibrium depends upon the polarity of the solution and tautomers (**2a** and **3a**).Tautomers of

uridylic acid **1-3b** are formed by attachment of phosphate at O_1-atom position of uridine (**Figure 1** and **Scheme II**). However, in a photochemical reaction, the suprafacial pathway allows the promotion of an electron from HOMO to LUMO. It can be shown that the net charge of O_1-atom is 0.40 to 0.428. This is more in the case of **1-3b** tautomers, when it is compared with uridine tautomers **1-3a**.

The proton shifting from N_{13}- to O_{25} in the case of **1b** to **2b** is considered by increasing the atomic charges at C_3-, C_5- and C_8-and decreasing at O_{25}-, O_{28}- and N_{13}-atoms (**Table II**).

The proton shifting from N_{13}- to O_{28} in the case of tautomers **1b** to **3b** is considered by decreasing net charges at O_{25}, O_{28}, N_{13}, C_8 and C_3 atoms and increasing at O_1-, O_4- and C_5-atoms. The net charges are highest at oxygen atoms (*i.e.*, O_1, O_2', O_3' and O_4'), when they are attached to phosphorus atom.

According to the heats of formation ($\Delta H_f°$) data, the stability of uridylic acid tautomers is in the order of **1b** > **3b** > **2b**. These tautomers are formed with the difference in the heats of formation of 25.825 k.cal/mol and 11.466 k.cal/mol respectively in the case of **1b** to **2b** and **1b** to **3b**. From this data, it can be predicted that the conversion of **1b** to **3b** is a lower energy process than the conversion of **1b** to **2b**. The value of dipole moment (μ) is more in the case of tautomer **2b**, and it may exist in more polar medium.

The molecular geometry of uridine 1-3a

From the results of AM1 calculation, the [1,3] sigmatropic hydrogen migration in uracil of uridine can be shown in the **Scheme II**. The change in the parameters of bond lengths, bond angles, dihedral angles and the change in energy content of the molecule may undergo the molecular deformations. The spatial arrangement of atoms in a molecule is considered for the [1,3] sigmatropic hydrogen migration in uracil of uridine and its conformations are shown in **Scheme II**. The main data of bond lengths (**Table III**), bond angles (**Table IV**), and dihedral angles (**Table V**) of uridine tautomers **1-3a** are only listed for the sake of simplicity from full optimized AM1 calculations.

From **Table III**, it is found that the bond length of N_{13}-H_{27} in **1a** (0.9975 Å) is larger than O_{25}-H bond in **2a** (0.9744 Å) and O_{28}-H bond in **3a** (0.9741Å). When [1,3] sigmatropic hydrogen migration from N_{13}- to O_{25}- and N_{13}- to O_{28}- are involved with the formation of respective tautomers **2a** and **3a**. The proton shifting from N_{13}- to O_{25}- is in the formation of **2a** from **1a**, the bond lengths are decreased in the case of C_6-N_9**,** N_9-C_{11}**,** C_{11}-N_{13} and O_{10}-H_{24} by 0.0054 Å, 0.0134 Å, 0.077 Å, and 0.003 Å and increased in the case of O_4-C_6**,** C_8-O_{10}**,** N_9-C_{12}, N_{13}-C_{15} and C_{11}-O_{25} by 0.0021 Å, 0.0017 Å, 0.009 Å, 0.0106 Å and 0.1311 Å. According to the **Table IV**, bond angles of $C_6N_9C_{11}$, $N_9C_{11}N_{13}$ and $N_{13}C_{15}O_{28,}$ are increased from 116.63° to 120.47°, 118.52° to 126.93° and 118.44° to 120.06° and decreased from 122.71° to 117.85° and 120.2° to 112.53° in case of bond angle of $C_{11}N_{13}C_{15}$ and $N_9C_{11}O_{25}$ from **1a** to **2a** tautomer. As per **Table V**, dihedral angle is changed from *-ap* to *–ac*, *+sp* to *–sp*, and *+ac* to *+ap* in the conformation of tautomers **1a** to **2a** in the case of $O_4C_6N_9C_{11}$, $N_9C_{11}N_{13}C_{15}$, and $C_3C_5O_7H_{22}$. It is revealed that the dihedral angle is changed from *-ap* in the conformation of $N_9C_{11}N_{13}H_{27}$, of **1a** to *+ap* in the conformation of $N_9C_{11}O_{25}H$, of tautomer **2a**.

[1,3] Sigmatropic hydrogen migration from N_{13}- to O_{28}- is in the formation of **3a** from **1a**. The bond lengths of N_9-C_{11}, C_{11}-N_{13}**,** C_{12}-C_{14} and C_{15}-O_{28} are increased by 0.026 Å, 0.0053 Å, 0.0171 Å, and 0.1251 Å and decreased in the case of N_9-C_{12} and N_{13}-C_{15} by 0.0143 Å and 0.0779 Å (**Table III**). **Table IV** shows that the bond angles of $C_{11}N_{13}C_{15}$ and $N_9C_{11}O_{25}$ are decreased from 122.71° to 117.62° and 120.20° to 117.01° and increased from 118.44° to 120.21° in case of bond angle of $N_{13}C_{15}O_{28.}$ The bond angle of $C_{11}N_{13}H_{27}$ in **1a** (117.24°) is changed to $C_{15}O_{28}H$ in tautomer **3a** (110.09°). **Table V** presents that the change of dihedral angle is *-ap* to *+ap* in the conformation of tautomer **1a** to **3a** in the case of $N_9C_{12}C_{14}H_{29}$. The dihedral angle is *–ap* conformation in the case of $N_9C_{11}N_{13}H_{27}$ tautomer **1a** and *+sp* conformation in the case of $N_{13}C_{15}O_{28}H$ of tautomer **3a**. It can be predicted that the sequence of [1,3] sigmatropic hydrogen migration in uracil of uridine from **1a** to **2a** or **3a**, changes the conformation and dipole moment. The polar bonds may interact in various ways with other molecules. Further, it is relatively weak in the secondary interactions and play vital role in the synthesis of proteins depending upon the polarity of medium.

The molecular geometry of uridylic acid 1-3 b

Table III represents that the bond length of N_{13}-H_{27} in **1b** (0.9979 Å) is decreased to O_{25}-H bond in **2b** (0.9751 Å) and O_{28}-H bond in **3b** (0.9744Å), if the

Table III — Bond lengths (Å) of uridine **1-3a** and uridylic acid **1-3b** from AM1 calculation

Bond lengths (Å)	**1a**	**2a**	**3a**	**1b**	**2b**	**3b**
O_4-C_6	1.4285	1.4306	1.4296	1.4314	1.4348	1.4294
C_5-O_7	1.4126	1.4129	1.4123	1.4122	1.4089	1.4121
C_5-C_8	1.5410	1.5415	1.5407	1.5412	1.5401	1.5417
C_6-N_9	1.4618	1.4564	1.4602	1.4608	1.4492	1.4624
C_8-O_{10}	1.4092	1.4109	1.4089	1.4082	1.4139	1.4081
N_9-C_{11}	1.4202	1.4068	1.4462	1.4215	1.4212	1.4462
N_9-C_{12}	1.3845	1.3934	1.3702	1.3847	1.3899	1.3707
C_{11}-N_{13}	1.3977	1.3208	1.4030	1.3960	1.3137	1.4032
N_{13}-C_{15}	1.4121	1.4227	1.3342	1.4122	1.4279	1.3335
O_1-H_{16}	0.9646	0.9646	0.9645	-----	-----	-----
O_7-H_{22}	0.9668	0.9668	0.9665	0.9673	0.9679	0.9669
O_{10}-H_{24}	0.9709	0.9679	0.9713	0.9708	0.9684	0.9709
C_{11}-O_{25}	1.2545	1.3856	1.2502	1.2541	1.3876	1.2499
N_{13}-H_{27}	0.9975	-----	-----	0.9979	-----	-----
C_{15}-O_{28}	1.2412	1.2412	1.3663	1.2409	1.2407	1.3656
O_{25}-H	-----	0.9744	----	----	0.9751	----
O_{28}-H	----	----	0.9741	----	----	0.9744
$O_{2'}$-$P_{1'}$	----	----	----	1.4502	1.4507	1.4479
$O_{3'}$-$P_{1'}$	----	----	----	1.5848	1.5832	1.5865
$O_{4'}$-$P_{1'}$	----	----	----	1.5905	1.5901	1.5919
$O_{4'}$-$H_{6'}$	----	----	----	0.9537	0.9539	0.9533
$O_{3'}$-$H_{5'}$	----	----	----	0.9568	0.9539	0.9560

Table IV — Bond angles (°) of uridine **1-3a** and uridylic acid **1-3b** from AM1 calculation

Bond angle (°)	**1a**	**2a**	**3a**	**1b**	**2b**	**3b**
$O_1C_2C_3$	108.84	108.89	108.86	110.76	110.41	110.07
$C_2C_3O_4$	110.02	109.98	109.83	110.17	109.54	110.02
$C_3C_5O_7$	107.15	106.95	107.41	107.01	112.68	107.19
$C_3C_5C_8$	105.21	105.17	105.34	104.98	105.36	105.29
$O_4C_6N_9$	110.97	110.49	111.27	110.57	110.94	111.01
$C_5C_8O_{10}$	109.39	108.94	109.59	108.97	112.63	109.19
$C_6N_9C_{11}$	116.63	120.47	117.14	116.92	119.92	117.44
$C_6N_9C_{12}$	123.25	123.31	123.04	122.98	123.07	122.72
$N_9C_{11}N_{13}$	118.52	126.93	119.76	118.60	125.81	119.72
$C_{11}N_{13}C_{15}$	122.71	117.85	117.62	122.89	118.19	117.77
$C_5O_7H_{22}$	108.42	108.03	108.86	108.18	107.99	108.65
$C_8O_{10}H_{24}$	106.79	106.87	106.74	107.21	107.33	106.88
$N_9C_{11}O_{25}$	120.22	112.53	117.01	120.21	116.02	117.22
$N_{13}C_{15}O_{28}$	118.44	120.06	120.21	118.58	119.83	120.29
$C_{11}N_{13}H$	117.24	----	----	117.16	----	----
$C_{11}O_{25}H$	----	108.35	----	----	108.00	----
$C_{15}O_{28}H$	----	----	110.09	----	----	110.16
$O_{2'}P_{1'}O_{4'}$	----	----	----	114.38	114.43	121.01
$O_{2'}P_{1'}O_{3'}$	----	----	----	122.04	121.99	119.29
$P_{1'}O_{4'}H_{6'}$	----	----	----	118.27	118.25	118.77
$P_{1'}O_{3'}H_{5'}$	----	----	----	116.76	116.94	117.05
$P_{1'}O_{2'}O_{3'}$	----	----	----	34.80	34.62	34.83

Table V — Dihedral angles (°) of uridine tautomers **1** to **3 a** from AM1 calculation

Dihedral angles (°)	**1a**		**2a**		**3a**	
	Angle	*	Angle	*	Angle	*
$O_1C_2C_3O_4$	-66.35	-*sc*	-74.12	-*sc*	-66.32	-*sc*
$C_2C_3C_5O_7$	125.02	+*ac*	126.01	+*ac*	122.79	+*ac*
$C_3O_4C_6N_9$	-122.57	-*ac*	-125.15	-*ac*	-121.72	-*ac*
$C_3C_5C_8O_{10}$	-127.19	-*ac*	-128.95	-*ac*	-125.15	-*ac*
$O_4C_6N_9C_{11}$	-163.27	-*ap*	-149.62	-*ac*	-165.75	-*ap*
$C_6N_9C_{11}N_{13}$	175.01	+*ap*	175.62	+*ap*	175.61	+*ap*
$N_9C_{11}N_{13}C_{15}$	1.08	+*sp*	-0.11	-*sp*	1.98	+*sp*
$C_3C_2O_1H_{16}$	-172.62	-*ap*	-175.86	-*ap*	-170.85	-*ap*
$C_3C_5O_7H_{22}$	148.24	+*ac*	155.55	+*ap*	140.78	+*ac*
$C_5C_8O_{10}H_{24}$	177.49	+*ap*	174.40	+*ap*	179.61	+*ap*
$C_6N_9C_{11}O_{25}$	-5.59	-*sp*	-5.71	-*sp*	-4.86	-*sp*
$C_{11}N_{13}C_{15}O_{28}$	-179.44	-*ap*	-178.98	-*ap*	-179.89	-*ap*
$N_9C_{12}C_{14}H_{29}$	-179.96	-*ap*	-179.73	-*ap*	179.84	+*ap*
$N_9C_{11}N_{13}H_{27}$	-179.08	-*ap*	--	--	--	--
$N_9C_{11}O_{25}H$	--	--	176.83	+*ap*	--	--
$N_{13}C_{15}O_{28}H$	--	--	--	--	0.18	+*sp*

* Conformational analyses[11] using prefixes *a = anti, s = syn, p = peri-planar, c = clinal, and* + & - signs.

Table VI — Dihedral angles (°) of uridylic acid tautomers (**1** to **3)b** from AM1 calculation

Dihedral angles (°)	**1b**		**2b**		
	Angle	*	Angle	*	Ang
$O_1C_2C_3O_4$	-65.23	-*sc*	-67.57	-*sc*	-76.
$C_2C_3C_5O_7$	131.00	+*ac*	121.79	+*ac*	123.
$C_3O_4C_6N_9$	-127.74	-*ac*	-131.60	-*ac*	-121.
$C_3C_5C_8O_{10}$	-135.48	-*ac*	-124.34	-*ac*	-125.
$O_4C_6N_9C_{11}$	-159.57	-*ap*	-154.55	-*ap*	-175.
$C_6N_9C_{11}N_{13}$	174.21	+*ap*	-179.85	-*ap*	176.
$N_9C_{11}N_{13}C_{15}$	0.20	+*sp*	-2.71	-*sp*	0.6
$C_3C_5O_7H_{22}$	153.87	+*ap*	59.47	+*sc*	145.
$C_5C_8O_{10}H_{24}$	170.14	+*ap*	-49.50	-*sc*	-175.
$C_6N_9C_{11}O_{25}$	-7.02	-*sp*	3.22	+*sp*	-4.1
$N_9C_{11}N_{13}H_{27}$	-179.79	-*ap*	- - -	- - -	- -
$C_{11}N_{13}C_{15}O_{28}$	-179.91	-*ap*	-179.82	-*ap*	179.
$N_9C_{11}O_{25}H$	- - -	- - -	-63.42	-*sc*	- -
$N_{13}C_{15}O_{28}H$	- - -	- - -	- - -	- - -	0.9
$P_1{\cdot}O_2{\cdot}O_1C_2$	-162.65	-*ap*	-162.75	-*ap*	-154.
$O_1O_2{\cdot}P_1{\cdot}O_4{\cdot}$	-119.06	-*ac*	-118.29	-*ac*	-115
$O_1O_2{\cdot}P_1{\cdot}O_3{\cdot}$	122.96	+*ac*	122.95	+*ac*	123.
$O_2{\cdot}P_1{\cdot}O_4{\cdot}H_6{\cdot}$	10.69	+*sp*	6.93	+*sp*	101.
$O_2{\cdot}P_1{\cdot}O_3{\cdot}H_5{\cdot}$	141.22	+*ac*	147.33	+*ac*	137.

* Conformational analyses[11] using prefixes a = *anti, s = syn, p = peri-planar, c = clinal,* and + & - signs.

[1,3] sigmatropic hydrogen migration is involved from N_{13}- to O_{25}- and N_{13}- to O_{28}- in the formation of respective tautomers **2b** and **3b**. When the [1,3] migration of proton from N_{13}- to O_{25}- in uracil of uridylic acid with the formation of **2b** from **1b**, the bond lengths of C_5-O_7**,** C_6-N_9**,** C_{11}-N_{13} and O_{10}-H_{24} are decreased by 0.0033 Å, 0.0116 Å, 0.0823 Å, and 0.0024 Å and increased in the case of C_8-O_{11}**,** N_{13}-C_{15}**,** and C_{11}-O_{25} by 0.0057 Å, 0.0157 Å and 0.1335 Å. At the time of [1,3] migration of proton, N_{13}-H_{27} (0.9979 Å) in **1b** is changed to O_{25}-H bond (0.9751 Å) in **2b**.

Table IV shows that the bond angles of $C_3C_5O_7$, $C_5C_8O_{10}$, $C_6N_9C_{11}$, and $N_9C_{11}N_{13,}$ are increased from 107.01° to 112.68°, 108.97° to 112.63°, 116.92° to 119.92° and 118.60° to 125.81° and decreased from 122.89° to 118.19° and 120.21° to 116.02° in case of bond angle of $C_{11}N_{13}C_{15}$ and $N_9C_{11}O_{25}$ from **1b** to **2b** tautomer. The bond angle of $C_{11}N_{13}H_{27}$ in **1b** (117.16°) is changed to $C_{11}O_{25}H$ with the bond angle of 108.0° in **2b**. As per **Table VI**, dihedral angle is changed from +*ap* to –*ap*, +*sp* to –*sp*, +*ap* to +*sc*, +*ap* to –*sc* and -*sp* to +*sp* in the conformation of tautomers

from **1b** to **2b** in the case of $C_6N_9C_{11}N_{13}$, $N_9C_{11}N_{13}C_{15}$, $C_3C_5O_7H_{22}$, $C_5C_8O_{10}H_{24}$ and $C_6N_9C_{11}O_{25}$. Dihedral angle is changed from *-ap* in the conformation of $N_9C_{11}N_{13}H_{27}$, of **1b** to *-sc* in the case of $N_9C_{11}O_{25}H$, of tautomer **2b**.When the [1,3] migration of proton from N_{13}- to O_{28}- in the formation of uridylic acid tautomer **3b** from **1b**, the bond lengths of N_9-C_{11}, C_{11}-N_{13} and C_{15}-O_{28} are increased by 0.0247 Å, 0.0072 Å and 0.1247 Å and decreased in the case of N_{13}-C_{15} and C_{11}-O_{25} by 0.0787 Å and 0.0042 Å (**Table III**). From **Table IV**, it is revealed that the bond angles of $N_9C_{11}N_{13}$, $N_{13}C_{15}O_{28}$ and O2′P1′O4′ are increased from 118.60° to 119.72°, 118.58° to 120.29° and 114.38° to 121.01° and decreased from 122.89° to 117.77°, 120.21° to 117.22° and 122.04° to 119.29° in the case of bond angle of $C_{11}N_{13}C_{15}$, $N_9C_{11}O_{25}$ and $O_{2'}P_{1'}O_{3'}$. The bond angle of $C_{11}N_{13}H_{27}$ in **1b** (117.16°) is changed to $C_{15}O_{28}H$ in **3b** (110.16°) tautomer. **Table VI** presents that dihedral angle is changed the conformation from *+ap* to *+ac*, *+ap* to *–ap*, *-ap* to *+ap* and *+sp* to *+ac* in the case of $C_3C_5O_7H_{22}$, $C_5C_8O_{10}H_{24}$, $C_{11}N_{13}C_{15}O_{28}$ and $O_{2'}P_{1'}O_{4'}H_{6'}$ in the formation of tautomer **3b** from **1b** respectively. The dihedral angle is *-ap* conformation in the case of $N_9C_{11}N_{13}H_{27}$, of tautomer **1b** and *+sp* conformation in the case of $N_{13}C_{15}O_{28}H$ of tautomer **3b** and rests of positions are moderately changed.

Conclusion

The present work offers a convenient and potentially useful approach to predict weak interactions, which play a vital role in the chemistry of life and contribute to the shape and activity of different enzymes and proteins. Photochemical or thermal [1,3] sigmatropic hydrogen migration in uracil has effects in the conformations of uridine and uridylic acid. Thus, the tautomers studied exist within the energy range of 20.569 kcal/mol. Dipole moment and total charge in tautomers portray dipole-dipole interactions for hydrogen bonding, which is responsible for the existence of stable conformations during the synthesis of proteins. Further, the utility of theoretical prediction is important for evaluating the nature of hydrogen bonding in nucleic acids, enzymes, protein synthesis and storage/retrieval/transfer of genetic information. This study reveals that the stability of conformations is highly dependent upon the polarity of the medium.

References

1 (a) Zorbach W W & Tipson R S, *Synthetic Procedure in Nucleic Acid Chemistry*, Vol I, (Interscience, New York) **1968**, 412p; (b) Brokes J, Hrebabecky H & Baranok J, *Coll Czech Chem Commun*, 44, **1979**, 439; (c) Marumoto R & Honjo M, *Chem Pharm Bull*, 22, **1974**, 128.

2 (a) Chanon M T, Pugmire R J, Grent D M, Panzica & Townsend L B, *J Amer Chem Soc*, 97, **1975**, 4636; (b) Ignacimuthu S, *Plant Biotechnology*, (Oxford & IBH Publishing Co Ltd, New Delhi) **1997**; (c) Hathway D E & Kolar G F, *Chem Soc Revs*, 9, **1980**, 241; (d) Maclaren A D & Shuger D, *Photochemistry of Proteins and Nucleic Acids*, (Pergamon Press Ltd, Oxford) **1964**; (e) Sivarama Sastry K, *J Sci Ind Res*, 27, **1968**, 275.

3 Kwiatkowski J S & Pullman B, *Adv Heterocycl Chem*, 18, **1975**, 199.

4 Smith K C, *Photophysiology*, Vol II, edited by Giese A L, (Academic Press Inc, New York) **1964**.

5 (a) Jacob F & Monod J, *J Mol Biol*, 3, **1961**, 318; (b) Davis B D, *Science*, 170, **1970**, 1279.

6 (a) Watson J D, *Molecular Biology of the Gene*, 3rd edition, (W A Benjamin, New York) **1976**; (b) Swanson C P & Webster P L, *The Cell*, 5th edition, (Prentice Hall of India Pvt Ltd, New Delhi) **1990**, p93; (c) Sinnott E W, Dunn L C & Dobzhansky T, *Principles of Genetics*, (Tata-McGraw-Hill Book Company Ltd, New Delhi) **1992**, p377.

7 (a) Grobstein C, *Sci Amer*, 237, **1977**, 22; (b)Marx J L, *Science*, 197, **1977**, 146.

8 (a) Rajeshwar Rao B, *Indian J Chem*, 41B, **2002**, 1697; (b) Rajeshwar Rao B, *Indian J Chem*, 41B, **2002**, 1702; (c) Rajeshwar Rao B, *Indian J Chem*, 42B, **2003**, 3081.

9 (a) Dewar M J S, Zeobisch E G, Healy E F & Stewart J J P, *J Am Chem Soc*, 107, **1985,** 3902; (b) Stewart J J P, MOPAC, *A General Molecular Orbital Package, QCPE455*, 5th edition, **1988**.

10 Pople J A & Beveridge D L, *Approximate Molecular Orbital Theory* (McGraw-Hill, New York) **1970**.

11 Klyne W & Prelog V, *Experintia*, 16, **1960**, 521.

12 (a) Woodward R B & Hoffmann R, *The Conservation of Orbital Symmetry*, (Academic Press Inc, New York) **1970**, 131p; (b) March J, *Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, 2nd edition, (McGraw-Hill, Kogakusha Ltd, Tokyo) **1977**, 103p.

13 (a) Bishop J M, *Scientific Amer*, 246, **1982**, 80; (b) Cooper G M, *Science*, 218, **1982**, 801; (c) Rechavi G, Govol D & Canaai E, *Nature*, 300, **1982**, 607.

14 Lewin B L, *Genes*, (John Wiley and Sons Inc, New York) **1983**.

15 (a) Berson J A & Nelson G L, *J Amer Chem Soc*, 89, **1967**, 5305; (b) Baldwin J E & Fleming R H, *J Amer Chem Soc* 94, **1972**, 2140.