



## Ab Initio and DFT Study of Uracil-Water Complexes

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### ABSTRACT

Uracil is a naturally occurring pyrimidine derivative and is one of the four nitrogenous bases found in RNA. Hydrogen bond plays a significant role in the structure determination of nucleic acids. Various types of hydrogen bond formed by purine and pyrimidine bases have been investigated and are of great significance. The effect of hydrogen bond on various Uracil-Water complexes has been investigated. In this paper four cyclic isomers of uracil forming hydrogen bonds with the water molecule have been discussed. Optimized geometries of all the isomers of uracil-water complex have been obtained at MP2/6-311++G (d,p), B3LYP/6-311++G (d,p), B3LYP/Aug-CC-pVDZ levels for the first time upto this level. Structural parameters of the optimized geometries, total energies and the APT charges of uracil-water complex have been computed. We show that addition of water molecules in uracil, the strength of the binding energy decreases i.e. stability increases. The optimized bond length and bond angles are in agreement with the corresponding experimental results.

**Keywords:** Uracil-water complex; Ab-initio and DFT calculations; Molecular structure; Optimized geometry

### INTRODUCTION

The overall structure of RNA (ribonucleic acid) consists of four nitrogenous bases adenine (A), cytosine (C), guanine (G), and uracil (U). These bases compose the backbone of their strands. In RNA, uracil binds to adenine via two hydrogen bonds. Uracil is a common and naturally occurring pyrimidine.

The hydration of biomolecules is useful in molecular biology, since numerous biological processes involve a ligand binding to a nucleic acid or protein and thereby displacing the water of hydration. Thus, accurate force fields for the interactions of nucleic acid or protein fragments with water are required for realistic simulations of biochemical processes. However, ab initio studies on the key geometries on the potential energy surface can provide accurate energies at these points, as well as providing valuable insight into the details of the interaction. The uracil molecule contains a row of alternating C=O and N-H groups. Therefore hydrogen-bonded arrangements are possible for uracil-water complexes. The Crystal Structure of Uracil was first studied by G. S. Parry [1] and bond lengths and bond angles between various atom of uracil and that the C-N bond lengths in uracil contains two different values. The potential energy surface for the interaction of uracil with one water molecule is investigated using second-order Møller-Plesset perturbation theory (MP2) and DZPi basis set by Mourik et al [2]. Rydbak [3] for the first time studied uracil-water system using correlated calculations. Smets et al [4] studied uracil-water complexes using MP2/6-31++G\*\* which were first optimized at the SCF/6-31+G\* level of theory. 5-halogenated Uracil was studied theoretically and experimentally by Singh [5]. DFT study of Interaction of silver ion with uracil tautomer has been done by Tavakol [6]. Uracil- water binary complex have been studied experimentally for all four theoretically predicted isomers by growth in helium nanodroplets [7]. Excited singlet state of Uracil-water complex has been studied theoretically using Ab-initio method by Yoshikawa et al [8]. The thymine-water complex are studied using density functional theory (B3LYP) combined with the 6-31++G (d, p) basis set by Chandra et al [9].

Four stable structure for uracil-water complex has been found in this work. The four isomers of uracil-water reported here have been reported earlier [2,8,10]. Optimized geometries of all the four isomers of uracil-water complex have been obtained at MP2/6-311++(d,p), B3LYP/6-311++ G (d,p), B3LYP/Aug-CC-pVDZ levels. Structural parameters of the optimized geometries, total energies and the APT charges of uracil-water complex have been computed. We show that addition of water molecules in uracil, the strength of the binding energy decreases i.e. stability increases. The optimized bond length and bond angles are in agreement with the corresponding experimental results.

### COMPUTATIONAL METHODOLOGY

The ground state geometries and vibrational spectra for free Uracil and its hydrogen-bonded complexes with molecules of water have been optimized. The total energies, structural parameters of the optimized geometries and the APT charges of have been computed using ab initio method:-(i) MP2 [11]and hybrid density functional theory (DFT) methods- (ii) B3LYP which uses Becke's three-parameter functional [12-14] with nonlocal correlation provided by Lee-Young-Parr expression [15] with 6-311++ G (d,p) and Aug-CC-pVDZ basic sets. For theoretical study, we have used GAUSSIAN 09 [16] package of programs without any constraint on the geometry.

Initially Ab initio calculations were done using MP<sub>2</sub>/6-311++G (d,p) level. The optimized geometry at the MP<sub>2</sub>/6-311++ G (d,p) level was taken as the input structure for the DFT calculation using B3LYP/6-311++ G (d,p) level. Similarly, the optimized geometry at the B3LYP/6-311++ G (d, p) level was used as the input structure for the calculation at the B3LYP/ Aug-CC-pVDZ level. The geometries were optimized by minimizing the energies without imposing any constraint on the geometry. It has well known that this level of theory is sufficient to reliably predict molecular geometries hydrogen bonded systems.

The geometry of the free uracil and uracil-water complex have been fully optimized by ab-initio using MP<sub>2</sub>/6-311++G (d,p) and the density functional theory using B3LYP/6-311++ G (d,p), B3LYP/Aug- CC-pVDZ levels for the first time. The optimized structure of free uracil and four isomers at B3LYP/6-311++ G (d,p) along with atomic numbering have been shown in Figures 1 and 2 (a-d) respectively.

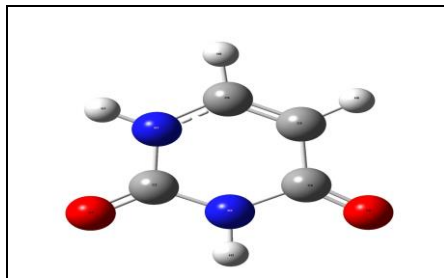


Figure 1: Optimized structure of free Uracil at B3LYP/6-311++G (d,p)

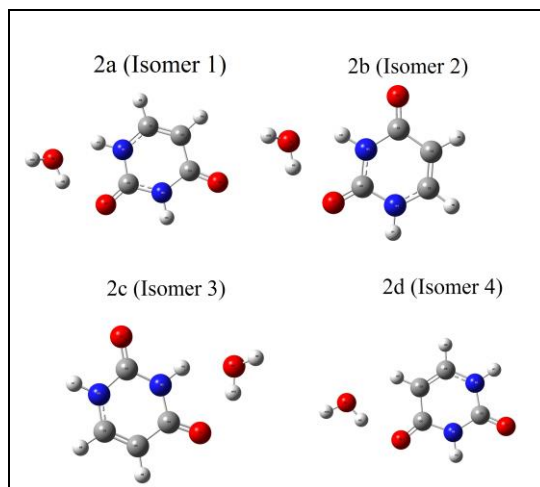


Figure 2: (a-d): Optimized structure of four stable isomers of Uracil-Water complexes obtained at B3LYP/6-311++G (d,p) level. (Red: Oxygen; Blue: Nitrogen; Grey: Carbon; White: Hydrogen)

## RESULT AND DISCUSSIONS

### Total energies (Hartree) for free Uracil and Uracil-Water complexes

Table 1 shows energies of free uracil and uracil-water complexes. From Table 1 we see that stability of uracil molecule increases when we use DFT method B3LYP than the ab-initio method MP2. Also in four isomers of Uracil-Water complexes, the isomer 1 is most stable having least optimized energy while isomers 2 and 3 are always higher in energies and very similar energies. Isomer 4 has higher energy to all isomers as weak hydrogen bond is involved in this isomer. We also see that as uracil-water complex is more stable than the free uracil molecule.

**Table 1: Total energies for free Uracil and Uracil-Water complexes**

Complex	MP2/6-311++G (d,p)	B3LYP/6-311++G (d,p)	B3LYP/Aug-CC-pVDZ
Uracil	-413.849589	-414.9461817	-414.8842574
Isomer 1	-490.1425106	-491.4215643	-491.3447523
Isomer 2	-490.1393317	-491.4180688	-491.3413123
Isomer 3	-490.1399392	-491.4191045	-491.3424643
Isomer 4	-490.1369726	-491.4160114	-491.3398372

### Structural parameters

The optimized geometrical parameters namely bond lengths (in Å) and bond angles (in Degree) of the uracil and uracil-water complexes computed at the B3LYP/ 6-311++G (d,p) and B3LYP/Aug-CC-pVDZ levels are collected in Tables 2 and 3.

**Table 2: Optimized Bond lengths (Å) and Bond angles (Degree) of free Uracil and Uracil-Water complexes at B3LYP/ 6-311++ G (d,p) level**

Parameters	Experimental Ref. [1]	Free uracil	Isomer 1	Isomer 2	Isomer 3	Isomer 4
<b>Bond length</b>						
C2N3	1.384	1.38339	1.37772	1.37437	1.38308	1.38624
C2N1	1.344	1.39339	1.38337	1.38772	1.39668	1.39135
C6N1	1.341	1.37493	1.37236	1.37646	1.37135	1.37491
C5C6	1.408	1.34722	1.34886	1.34586	1.34835	1.34793
C4N3	1.374	1.41255	1.41472	1.41232	1.4009	1.40289
C4C5	1.411	1.45789	1.45552	1.4601	1.45367	1.45351
C4O8	1.241	1.21498	1.21521	1.21439	1.22663	1.22418
C2O7	1.23	1.2122	1.22404	1.22357	1.21134	1.21146
N3H3		1.01273	1.0127	1.02386	1.02451	1.01284
N1H1		1.00895	1.02124	1.00888	1.00908	1.00922
C5H5		1.07917	1.07923	1.07932	1.079	1.08044
C6H6		1.08273	1.08273	1.08263	1.0828	1.08261
<b>Bond angles</b>						
C4-N3-C2	124.7	128.12607	127.74067	127.24236	127.26523	127.83081
N3-C2-N1	115.6	112.90466	113.90883	114.05	113.22123	112.80472
C2-N1-C6	123.6	123.60374	122.89299	123.30203	123.63668	123.63392
N1-C6-C5	121.5	121.9612	122.32781	121.62174	121.67947	122.08342
C6-C5-C4	116.4	119.88331	119.80474	119.96155	119.54833	119.29929
C5-C4-N3	118.1	113.52102	113.32405	113.82122	114.64848	114.34784
O8-C4-N3	118.3	120.28353	120.117	120.51049	120.64984	119.60417
C4-N3-H3	-	116.26129	116.36453	117.54972	116.15971	116.52173
C2-N3-H3	-	115.61264	115.89391	115.20785	116.57506	115.64746
N3-C2-O7	119.9	124.29132	123.13393	124.39713	124.4642	124.05135
N1-C2-O7	124.5	122.80401	122.95723	121.55283	122.31453	123.14394
C2-N1-H1	-	115.18978	115.05502	115.33292	115.06602	115.18923
C6-N1-H1	-	121.20648	122.05183	121.3644	121.29728	121.17685
N1-C6-H6	-	115.34806	115.08547	115.4048	115.57602	115.36752
C5-C6-H6	-	122.69074	122.58672	122.97344	122.74451	122.54905
C6-C5-H5	-	121.91086	121.98232	121.91339	122.10197	122.36799
C4-C5-H5	-	118.20583	118.2129	118.12505	118.34957	118.33272
C5-C4-O8	123.6	126.19545	126.55895	125.66826	124.70167	126.048

Also the Optimized bond lengths (in Å) and bond angles (in Degree) of free uracil and Isomer 1 (most stable isomer) of uracil-water complexes at MP2/6-311++ G (d,p) level are collected in Table 4. For atomic numbering scheme, see Figures 1 and 2(a-d). The magnitudes of the bond lengths between the pairs (C<sub>2</sub>=O<sub>7</sub>) and (C<sub>4</sub>=O<sub>8</sub>) in uracil are found to be nearly equal and the slightly difference is due to the higher electro-negativity of the O<sub>7</sub> atom which attracts more the C atom than the O<sub>8</sub> atom in their respective bonds with the resulting a little smaller bond length than other bond in the all molecules. Here, it is noticeable that the N<sub>1</sub>-C<sub>6</sub> bond is found to be the smallest bond due the formation of the lone pair bond between N<sub>1</sub> and C<sub>6</sub> atoms as shown in Figure 2a uracil as accordance to the uracil molecule due to one with single bonding and another localized double bond respectively. The bond lengths and bond angles obtained theoretically are in better agreement to their corresponding experimental values [1].

**Table 3: Optimized Bond lengths (Å) and Bond angles (Degree) of free Uracil and Uracil-Water complexes at B3LYP/ Aug-CC-pVDZ level**

Parameters	Experimental Ref. [1]	Free uracil	Isomer 1	Isomer 2	Isomer 3	Isomer 4
<b>Bond length</b>						
C2N3	1.384	1.38379	1.37786	1.37514	1.3835	1.38654
C2N1	1.344	1.39332	1.38357	1.38755	1.39646	1.39145
C6N1	1.341	1.37622	1.37355	1.37797	1.37255	1.37617
C5C6	1.408	1.35292	1.35439	1.35146	1.35409	1.3535
C4N3	1.374	1.41198	1.41459	1.41186	1.40084	1.40299
C4C5	1.411	1.45946	1.45706	1.46136	1.45484	1.45513
C4O8	1.241	1.22142	1.22142	1.22066	1.233	1.23018
C2O7	1.23	1.21924	1.2313	1.23056	1.21826	1.21842
N3H3		1.01455	1.01456	1.02533	1.02615	1.01469
N1H1		1.01078	1.02291	1.01071	1.01092	1.01102
C5H5		1.08566	1.08568	1.08571	1.08536	1.08629
C6H6		1.0889	1.08893	1.08872	1.08894	1.08873
<b>Bond angles</b>						
C4-N3-C2	124.7	127.91886	127.56052	127.02846	127.05782	127.64314
N3-C2-N1	115.6	113.20029	114.19961	114.33195	113.49625	113.09175
C2-N1-C6	123.6	123.54823	122.80735	123.25737	123.59786	123.58258
N1-C6-C5	121.5	121.83719	122.24781	121.49153	121.56538	121.953
C6-C5-C4	116.4	119.77634	119.68783	119.86325	119.43234	119.23066
C5-C4-N3	118.1	113.71905	113.49646	114.02611	114.84951	114.49886
O8-C4-N3	118.3	120.1309	119.93547	120.35202	120.47552	119.46035
C4-N3-H3	-	116.36731	116.40148	117.79625	116.09093	116.6656
C2-N3-H3	-	115.71383	116.03754	115.17519	116.85096	115.69126
N3-C2-O7	119.9	124.15848	122.99076	124.23177	124.33458	123.91724
N1-C2-O7	124.5	122.64111	122.80962	121.43624	122.16914	122.99101
C2-N1-H1	-	115.1463	114.94037	115.33972	115.03313	115.15279
C6-N1-H1	-	121.30547	122.25225	121.40265	121.36896	121.26464
N1-C6-H6	-	115.47778	115.21662	115.5177	115.69808	115.47378
C5-C6-H6	-	122.68503	122.53556	122.99076	122.73654	122.57321
C6-C5-H5	-	121.88643	121.93955	121.88474	122.03224	122.29462
C4-C5-H5	-	118.33722	118.37261	118.252	118.53531	118.47471
C5-C4-O8	123.6	126.15004	126.56807	125.62184	124.67497	126.04079

### Atomic Polar Tensor (APT) charges

The atomic polar tensor (APT) charges for the uracil and uracil-water complexes computed at the B3LYP/ 6-311++ G (d,p) and B3LYP/Aug-CC-pVDZ levels are collected in Tables 5 and 6. Also the APT charges for free uracil and Isomer 1 (most stable isomer) of uracil-water complexes at MP2/6-311++ G (d,p) level are collected in Table 7. For atomic numbering scheme, see Figures 1 and 2(a-d) respectively. In term of the electron charge  $1e = 1.602188 \times 10^{-19}$  C. From Tables 5-7, we see that due to high negativity of the respective atoms compared to the other atoms results enhancement of the bond length. In free uracil we see that the bond length of the magnitudes of the bond lengths between the pairs (C<sub>2</sub>=O<sub>7</sub>) and (C<sub>4</sub>=O<sub>8</sub>) are found to be differed due as O<sub>7</sub> is more negative than the O<sub>8</sub>. Thus O<sub>7</sub> attracts more to C atom than O<sub>8</sub> which gives difference in their bond lengths. Hence the bond length of (C<sub>2</sub>=O<sub>7</sub>) is shorter than the bond length of (C<sub>4</sub>=O<sub>8</sub>). Similarly, with the help of APT charges we can explain the difference in the bond length of others pairs e.g. C2N1 & C6N1; C4C5 & C5C6.

**Table 4: Optimized Bond lengths(Å) and Bond angles (Degree) of free Uracil and Isomer 1 (most stable isomer) of Uracil-Water complexes at MP2/6-311++ G (d,p) level**

Parameters	Experimental Ref. [1]	Free uracil	Isomer 1
<b>Bond length</b>			
C2N3	1.384	1.38596	1.38107
C2N1	1.344	1.39037	1.382
C6N1	1.341	1.37657	1.3748
C5C6	1.408	1.35421	1.35569
C4N3	1.374	1.40878	1.41191
C4C5	1.411	1.46014	1.45757
C4O8	1.241	1.22016	1.22027
C2O7	1.23	1.21643	1.22658
N3H3		1.01447	1.01461
N1H1		1.0102	1.02044
C5H5		1.08144	1.08152
C6H6		1.08483	1.08492
<b>Bond angles</b>			
C4-N3-C2	124.7	128.66806	128.04385
N3-C2-N1	115.6	112.64157	113.54913
C2-N1-C6	123.6	123.77855	122.84186
N1-C6-C5	121.5	121.82799	122.23064
C6-C5-C4	116.4	119.79445	119.70211
C5-C4-N3	118.1	113.28939	113.03578
O8-C4-N3	118.3	120.61166	120.41584
C4-N3-H3	-	116.13808	115.97318
C2-N3-H3	-	115.19386	115.20727
N3-C2-O7	119.9	124.16814	123.07981
N1-C2-O7	124.5	123.19028	123.3458
C2-N1-H1	-	115.15105	114.93917
C6-N1-H1	-	121.0704	121.57557
N1-C6-H6	-	115.44958	115.17097
C5-C6-H6	-	122.72243	122.57592
C6-C5-H5	-	121.63621	121.62585
C4-C5-H5	-	118.56934	118.60949
C5-C4-O8	123.6	126.09895	126.54145

**Table 5: APT Charges at various atomic sites of free Uracil molecule and Uracil-Water Complexes at B3LYP /6-311++G (d,p) Level**

Atom	Free uracil	Isomer 1	Isomer 2	Isomer 3	Isomer 4
N1	-0.481	-0.39	-0.367	-0.356	-0.35
N3	-0.591	-0.417	-0.413	-0.445	-0.424
O7	-0.392	-0.376	-0.38	-0.33	-0.332
O8	-0.357	-0.318	-0.31	-0.352	-0.321
C2	0.501	0.331	0.32	0.344	0.332
C4	0.133	0.015	0.071	-0.01	0.022
C5	0.038	-0.088	-0.098	0.035	-0.01
C6	-0.231	0.068	0.002	-0.067	-0.077
H1	0.442	0.431	0.343	0.353	0.346
H3	0.444	0.358	0.443	0.441	0.36
H5	0.252	0.215	0.211	0.213	0.273
H6	0.242	0.171	0.181	0.173	0.186

**Table 6: APT Charges at various atomic sites of free Uracil molecule and Uracil-Water Complexes at B3LYP / Aug-CC-pVDZ Level**

Atom	Free uracil	Isomer 1	Isomer 2	Isomer 3	Isomer 4
N1	-0.092	0.107	-0.043	-0.103	-0.074
N3	-0.03	-0.001	0.105	0.096	-0.086
O7	-0.513	-0.571	-0.575	-0.517	-0.519
O8	-0.56	-0.574	-0.561	-0.645	-0.621
C2	0.562	0.5	0.512	0.535	0.543
C4	0.296	0.295	0.229	0.203	0.352
C5	1.376	1.37	1.4	1.55	1.637
C6	0.56	0.572	0.591	0.536	0.447
H1	-0.148	-0.086	-0.151	-0.146	-0.142
H3	-0.146	-0.15	-0.123	-0.127	-0.144
H5	-0.681	-0.69	-0.687	-0.727	-0.767
H6	-0.623	-0.712	-0.654	-0.621	-0.627

**Table 7: APT Charges at various atomic sites of free Uracil and Isomer 1 (most stable isomer) of Uracil-Water complexes at Mp2/6-311++G (d, p) level**

Atom	Free uracil	Isomer 1
N1	-0.546	-0.562
N3	-0.591	-0.59
O7	-0.438	-0.474
O8	-0.405	-0.405
C2	0.568	0.527
C4	0.211	0.134
C5	-0.155	-0.21
C6	0.086	0.204
H1	0.387	0.488
H3	0.406	0.401
H5	0.251	0.256
H6	0.228	0.225

## CONCLUSIONS

The optimized geometries of uracil and four isomers of uracil-water complexes have been calculated employing ab-initio with MP2/6-311++G (d,p) level and DFT with the hybrid functional B3LYP/6-311++G (d,p) and B3LYP /Aug-CC-pVDZ levels. The most of the geometrical parameters for uracil-water complexes remains the same as uracil excepted the geometry of the site of the water bonded atom. Structural parameters of the optimized geometries, total energies and the APT charges of uracil-water complex have been discussed in detail. We show that addition of water molecules in uracil, the strength of the binding energy decreases i.e. stability increases. The optimized bond length and bond angles are in agreement with the corresponding experimental results.

## ACKNOWLEDGEMENT

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## REFERENCES

- [1] GS Parry. *Acta Cryst.* **1954**, 7, 313.
- [2] T van Mourik; SL Price; DC Clary. *J Phys Chem A.* **1999**, 103, 1611-1618.
- [3] S Rybak; K Szalewicz; B Jeziorski; G Corongiu. *Chem Phys Lett.* **1992**, 199, 567.
- [4] J Smets; WJ McCarthy; LJ Adamowicz. *Phys Chem.* **1996**, 100, 14655.
- [5] JS Singh. *Spectrochimica Acta Part A.* **2003**, 117, 502-518.
- [6] H Tavakol. *A J Chem.* **2017**, 10, S786-S799.

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- [7] MY Choi; RE Miller. *Phys Chem Chem Phys.* **2005**, 7, 3565-3573.
- [8] A Yoshikawa; S Matsika. *Chem Phys.* **2008**, 347, 383-404.
- [9] AK Chandra; MT Nguyen; T Zeegers-Huyskens. *J Phys Chem A.* **1998**, 102, 6010-6016.
- [10] RB Zhang; T Zeegers-Huyskens; A Ceulemans; MT Nguyen. *Chem Phys.* **2005**, 316, 35-44.
- [11] C Møller; MS Plesset. *Phys Rev.* **1934**, 46, 618-622.
- [12] AD Becke. *J Chem Phys.* **1992**, 97, 9173.
- [13] AD Becke. *J Chem Phys.* **1993**, 98, 5648.
- [14] AD Becke. *J Chem Phys.* **1996**, 104, 1040.
- [15] C Lee; W Yang; RG Parr. *Phys Rev B.* **1988**, 37, 785.
- [16] MJ Frisch; GW Trucks; HB Schlegel; GE Scuseria; MA Robb; JR Cheeseman; VG Zakrzewski; JA Montgomery; RE Stratmann; JC Burant; S Dapprich; JM Millam; AD Daniels; KN Kudin; MC Strain; O Farkas; J Tomasi; V Barone; M Cossi; R Cammi; B Mennucci; C Pomelli; C Adamo; S Clifford; J Ochterski; GA Petersson; PY Ayala; Q Cui; K Morokuma; DK Malick; AD Rabuck; K Raghavachari; JB Foresman; J Cioslowski; JV Ortiz; BB Stefanov; G Liu; A Liashenko; P Piskorz; I Komaromi; R Gomperts; RL Martin; DJ Fox; T Keith; MA Al-Laham; CY Peng; A Nanayakkara; C Gonzalez; M Challacombe; PMW Gill; BG Johnson; W Chen; MW Wong; JL Andres; M Head-Gordon; ES Replogle; JA Pople. Gaussian 03, Revision D.01, Gaussian Inc., Pittsburgh, PA, **2009**.