



Theoretical Study of Uric Acid and its Ions in Aqueous Solution

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Abstract

Uric acid vapor is studied with density functional theory. Using the best method from past experience for each property, we predict the equilibrium geometry, vibrational spectrum, dipole moment, static dipole polarizability, UV absorption spectrum, and vertical ionization energies of both valence and core electrons. In addition, we find that time-dependent DFT with the PBE0 functional can predict the UV absorption spectra of uric acid and its anions in aqueous solution, even with the continuum dielectric model.

Keywords: UV absorption; Uric acid; TDDFT; Vertical ionization energies; ESCA; Gout

Introduction

Uric acid is one of the most interesting molecules in the human body susceptible to theoretical studies. Large amount of information can be obtained online nowadays, although some websites may contain serious errors. While there is no disagreement in uric acid being a diprotic acid, there is no uniformity in the name given to its -1 anion. Let us call the -1 anion by the name **biurate** (analogous to bicarbonate and bisulfate) and the -2 anion by the name of **urate** (in contrast to the name given to the -1 anion in many websites). Uric acid is a product of purine in food intake and is excreted in urine. A proper balance is maintained in the human body. Out of balance, hypouricemia is believed to be associated with multiple sclerosis, while hyperuricemia is linked to gout and some form of kidney stones. Gout is caused by precipitation of uric acid in blood, usually in the joints and some kidney stones are caused by precipitation of sodium biurate, according to several websites.

There is also some confusion to the values of the acid dissociation constants. Early studies have been summarized by Wilcox et al. [1], whose determination gave $pK_{a1}=5.62$ at 26°C and 5.57 at 37°C , as well as $pK_{a2}=9.05$ at 20°C . Also, in the 1970s, Finlayson and Smith [2] obtained a pK_{a1} of 5.61 at 25°C and 5.47 at 38°C . In the 1980s, Simic and Jovanovic [3] reported the acid dissociation constants of 5.40 and 9.80 at 20°C , while Wang and Königsberger [4] found $pK_{a1}=5.26$ at 25°C and 5.19 at 37°C . Surprisingly, one finds 3.89 for pK_{a1} in the online Handbook of Chemistry and Physics. To get a semi-quantitative picture, we take 5.4 and 9.8 as the two pK_a values and construct the distribution diagram [5], shown in Figure 1, assuming unity activity coefficients. Although there may be a slight decrease in pK_a at 37°C , one expects over 98% of total uric acid in humans exists in the form of biurate and less than 1% as undissociated uric acid at the normal blood pH of 7.4 . However, at a urine pH of 6.5 , for example, the distribution is approximately 12% uric acid and 88% of biurate. Since uric acid is about 20 times less soluble than sodium biurate, the likely effect of hyperuricemia is that uric acid would precipitate in the blood vessels in one's foot and that sodium biurate would precipitate as kidney stones (barring supersaturation). More recently, Ngo and Assimos [6] gave a thorough review of the epidemiology and pathophysiology of uric acid stones.

In the present work, we make a theoretical study of uric acid and its ions because of their interesting properties, mainly using density functional theory (DFT). Throughout this paper, we use the Pople shorthand notation of method1/basis1//method2/basis2 to denote

that method 1, with basis set 1 is used to compute the property of interest at the geometry optimized by method 2 with basis set 2. All of our predictions of properties were only calculated at the equilibrium geometry optimized by B3LYP/6-311+(d,p). A convenient shorthand notation for uric acid is H_2U and that the biurate anion, HU^- . The salt NaHU is sometime known as monosodium monohydrogen urate (MSMU).

Computational Method

During the past few decades, many chemical and physical properties have been studied with density functional theory (DFT). Some workers try to design better and better functionals for all properties, while we among others look for best procedures for each property of interest. In both cases, experimental results are needed to validate the methods used. In this work, we wish to calculate several properties of uric acid and its ions using the best DFT method for each property, gained from experience with other molecules.

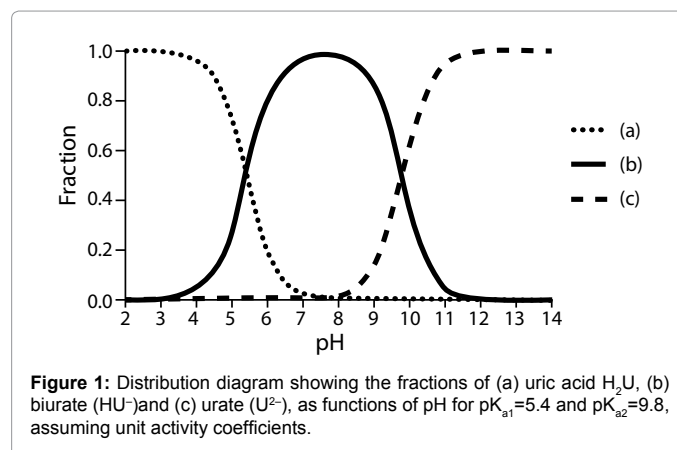


Figure 1: Distribution diagram showing the fractions of (a) uric acid H_2U , (b) biurate (HU^-) and (c) urate (U^{2-}), as functions of pH for $pK_{a1}=5.4$ and $pK_{a2}=9.8$, assuming unit activity coefficients.

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In this study, we used two programs: Gaussian09 [7] and ADF2012 [8]. Within the Gaussian09 package, many basis sets of contracted Gaussian functions are available. Workers tend to use Dunning's correlation-consistent basis sets for small molecules and Pople's split-valence sets, such as 6-31G for very large systems. For uric acid and its ions studied in this work, as well as other medium-size organic molecules, we opt for the polarized split-valence triple-zeta set 6-311+G(d,p). On the other hand, the ADF Program [8] provides a wide selection of basis sets of Slater-type orbitals. As in our recent studies, we favor the two sets of our own design [9,10]. For general properties of small to medium-size molecules, our favourite choice is the even-tempered polarized quadruple-zeta set (et-pVQZ) [9]. However, for polarizability and excitation calculations, a better basis set is the augmented polarized triple-zeta (aug-TZP) set [10]. From past experience, the smaller set of polarized triple-zeta (TZP) functions seems to be quite adequate for vertical ionization energies (VIEs) of both valence and core orbitals [11,12]. Hence, for larger molecules, one can save computing times by using the smaller TZP set. However, uric acid and its ions are small enough so that we can perform the calculations with the larger et-pVQZ basis set.

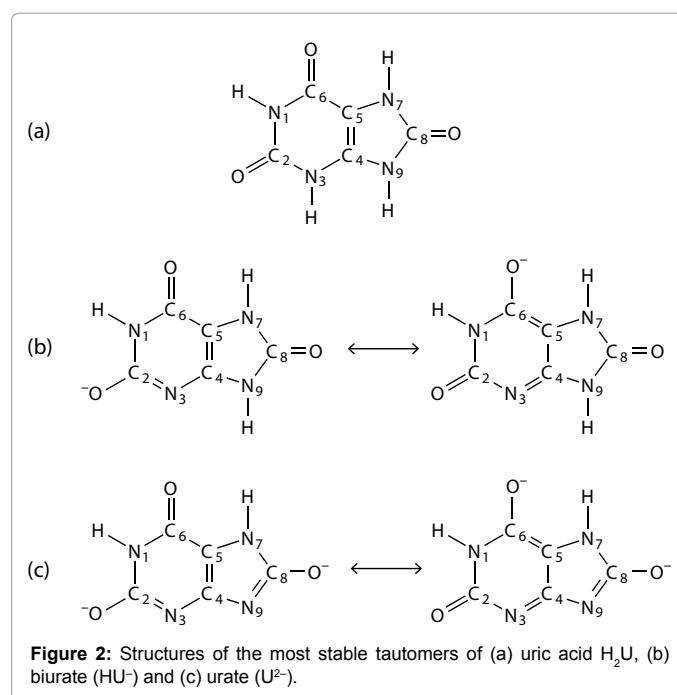
As stated above, all of our predictions of properties (with the exception of the UV absorption spectra in aqueous solutions) were calculated at the equilibrium geometry optimized by B3LYP/6-311+(d,p). The B3LYP method has been thoroughly tested by Riley et al. [13] and Tirado-Rives and Jorgensen [14], on closed-shell organic molecules. For the geometry of uric acid and its ions in aqueous solution, we used the Polarizable Continuum Model (PCM) in the Gaussian09 program [7], by including

SCRF=(Solvent=Water) to the input

For the time-dependent DFT calculation of the excitations, we used the Conductor-like Screening Model (COSMO) in the ADF2012 program [8], by adding the following input lines

```
Solvation
SOLV Name=Water
End
```

The methods used in this work have been published many times in the literature. Because different methods were used for different



properties, we need to give a brief description of each method used. For the geometry optimization of the structures of uric acid and its ions, we used the DFT method of B3LYP with an adequate basis set known as 6-311+G(d,p), available in the Gaussian09 [7] program. The results of the most stable tautomers shown in Figure 2 and Table 1, agree with previous studies. The vibrational frequencies and IR intensities of H_2U vapor were calculated at the same B3LYP/6-311+(d,p) level of theory. However, as an approximate correction to the harmonic approximation used, the predicted wave numbers have been scaled by a factor of 0.958, following the work of Asami et al. [15]. For the dipole moment and polarizability, as well as UV excitation spectrum, we preferred the exchange-correlation potential V_{xc} known as statistical averaging of orbital potentials (SAOP) [16-18]. For VIEs of valence electrons, the method abbreviated as Δ BPBE0 (SAOP) was used [19]. It

	Previous work on uric acid			Present work ^d			
	Crystal ^a	B3LYP ^b	B3LYP ^c	H_2U (vac)	H_2U (aq)	HU^- (aq)	U^{2-} (aq)
N1-C2	1.369	1.388	1.386	1.386	1.383	1.410	1.408
C2-N3	1.383	1.403	1.401	1.401	1.389	1.359	1.347
N3-C4	1.360	1.370	1.368	1.368	1.363	1.334	1.358
C4-C5	1.364	1.367	1.364	1.363	1.369	1.387	1.406
C5-C6	1.410	1.433	1.430	1.430	1.423	1.409	1.397
C6-N1	1.401	1.423	1.422	1.422	1.416	1.404	1.408
C5-N7	1.388	1.399 ^e	1.399	1.399	1.398	1.405	1.400
N7-C8	1.361	1.381	1.379	1.379	1.373	1.371	1.396
C8-N9	1.378	1.426	1.424	1.424	1.411	1.395	1.369
N9-C4	1.361	1.370	1.368	1.368	1.363	1.386	1.366
C2-O	1.237		1.212	1.212	1.220	1.245	1.259
C6-O	1.246		1.217	1.217	1.227	1.245	1.258
C8-O	1.252		1.209	1.209	1.221	1.231	1.255

^aRingertz [29]

^bB3LYP/6-31G(d), Chen et al. [30]

^cB3LYP/6-311++G(d,p), Allen et al. [31]

^dB3LYP/6-311++G(d,p)

^emislabeled as C6-N7

Table 1: Optimized bond lengths (in Angstroms) of uric acid and its anions.

Present work ^a			2011 ^b	1981 ^c	1990 ^d	2007 ^e	2007 ^f	2010 ^g	2011 ^h
ν	I	Assignment	Vapor	KBr pellet					
80	2.5	A ^{''}							
122	0.2	A ^{''}							
141	1.8	A ^{''}							
204	6.5	A ^{''}							
224	7.9	A [']							
264	27.4	A ^{''}							
345	8.5	A [']							
365	15.0	A ^{''}							
396	3.3	A ^{''}			385				
436	20.2	A [']							
457	3.6	A [']							
463	237	A ^{''}			472				476
526	13.5	A [']			503				515
575	14.3	A [']			562				569
586	14.1	A ^{''}							
636	82.8	A ^{''}			627			619	613
657	23.7	A [']			659			655	
696	61.5	A ^{''}							
709	6.0	A ^{''}		705	707	710		705	706
717	4.9	A ^{''}		745		750		744	744
740	8.2	A [']		780	784	780		784	787
840	0.8	A [']		880	885			877	881
913	83.8	A [']							
945	7.4	A [']		995	999			992	990
1038	68.7	A [']		1035	1039		1021	1026	1022
1121	21.0	A [']		1125	1122				1116
1190	5.3	A [']							
1213	5.7	A [']			1234			1222	
1254	129	A [']			1288			1309	
1301	77.9	A [']		1300					1307
1330	76.9	A [']							1345
1354	1.3	A [']		1400	1356			1400	1400
1416	1.1	A [']			1406			1436	1437
1530	233	A [']		1480	1499				
1607	96.2	C4-C5		1580	1595	1590		1592	1585
1691	929	C6-O			1652	1675	1638	1637	1667
1718	1342	C2-O			1684				
1757	496	C8-O						2025	
3449	90.8	N1-H	3450					2817	2803
3483	104	N3-H	3493					3018	3016
3506	116	N9-H	3519						3109
3516	116	N7-H	3526					3483	3420

^aB3LYP/6-311G(d,p)//B3LYP/6-311G(d,p), scaled by a factor of 0.958

^bAsami et al. [15]

^cModlin and Davies [32]

^dKodati et al. [33]

^eKhalil and Azooz [34]

^fChanna et al. [35]

^gWilson et al. [36]

^hSekkoum et al. [37]

Table 2: Vibrational wave numbers (in cm⁻¹) and IR intensities (in km mol⁻¹) of uric acid.

means the energy difference between parent and cation calculated with the parameter-free exchange-correlation functional E_{xc} known as PBE0 [20-22], for the electron density computed with V_{xc} =SAOP [16-18]. Finally, for core-electron binding energies (CEBEs), we use the method developed in 1999 [11,23,24], namely $\Delta PW86-PW91+C_{rel}$, which stands for the energy difference between parent and cation calculated with the exchange functional PW86 [25] and the correlation functional PW91 [26]. A small relativistic correction C_{rel} , derived empirically in

1995 [27], was added. These methods have been tested on many organic molecules. See our recent paper [28] and references therein.

Results and Discussion

The optimized bond lengths of uric acid H₂U we obtained from B3LYP/6-311+G(d,p) are compared with previous studies [29-31] in Table 1, together with those of H₂U, HU⁻, and U²⁻ in aqueous solution. Many of the changes in bond lengths of the anions can be rationalized

in terms of resonance, such as the lengthening of C4-C5 and the three C-O bonds, as well as the shortening of C2-N3, N3-C4, C5-C6, and C8-N9 in urate(aq). However, simple valence-bond bond order cannot explain the changes in the other bonds.

In Table 2, we present the vibrational wave numbers of uric acid vapor after scaling with a constant factor of 0.958, following Asami et al. [15] and the IR intensities in km mol^{-1} , together with the experimental values in gas phase [15], and in KBr pellets [32-37]. The agreement seems quite reasonable, especially when we notice the discrepancies between the results from different workers.

We believe that use of V_{xc} =SAOP leads to reliable electron densities. The dipole moments from SAOP are 3.349, 3.444, and 3.384 D from et-pVQZ, aug-TZP, and aug-et-pVQZ basis sets, respectively, to be compared with 3.92 D from the B3LYP/6-31G** calculation of Altarsha et al. [38]. On the other hand, the average static dipole polarizabilities we obtained are 99.40, 100.55, and 100.28 au from et-pVQZ, aug-TZP, and aug-et-pVQZ basis sets, respectively; while the polarizability anisotropies are 132.29, 133.26, and 130.97 au from et-pVQZ, aug-TZP, and aug-et-pVQZ, respectively. We believe that the results from aug-et-pVQZ basis to be more reliable.

The study of UV absorption of uric acid and its anions is more difficult. Each of the three species, H_2U , HU^- and U^{2-} absorbs UV light to be excited to two or more excited states. First, we summarize the wavelengths (in nm) of the experimental absorption maxima in Appendix A and include the most likely (in our opinion) vertical excitation energies (in eV) for the observed transitions. We do not have any experience in modeling UV-visible absorptions of organic molecules in aqueous solutions by continuum dielectric approximations and decide to test over 30 functionals in this study. In Table 3, we report the results of time-dependent DFT calculations of the three species in aqueous solutions. Only transitions with oscillator strengths greater than 0.1 are included. Calculated vertical excitation energies within 0.1 eV of the best estimates of the excitation energies are considered excellent and are indicated in red, while those within 0.2 eV of the best estimates fairly good and are shown in green. We see that many of the functionals tested do not give reliable estimates of the excitation energies. The best functionals appear to be PBE0 and mPW1PW, while the functional, X3LYP and B1LYP can also provide reasonable predictions. In Table 4, we present some of our results, now with *f*-values, to compare with the recent calculation of Altarsha et al. [39]. Note that our dielectric continuum models for the effect of solvation are undoubtedly a crude approximation for aqueous solutions, in which hydrogen bonds with the solutes are present. To include the effects of hydrogen bonds, would require inclusion of discreet water molecules with procedures, such as the ONIOM method [G09], which is beyond the scope of the present study. Of all the solvents for UV-visible excitation calculations, water is probably the most difficult to model. It would be interesting to see whether or not such a method applies to UV-visible absorption of other organic molecules in aqueous solution.

In Table 5, we compare the vertical ionization energies of valence electrons computed by various methods, all calculated at the geometry optimized by B3LYP/6-311+(d,p). From our experience with other molecules, the reliability of the prediction is ranked as follows: Koopmans' theorem (KT)<meta-Koopmans' theorem (mKT)<outer-valence Green's function (OVGF)< Δ PBE0(SAOP)/TZP. In principle, the method of SAC-CI should be most accurate. However, because of the computational demands of SAC-CI, many actual calculations

have been performed with limited basis sets. Such seems to be the case with the present case of uric acid vapor (unless Farrokhpour and Ghandehari [41] somehow missed one of the low-lying cations). On the other hand, our DFT approach of Δ PBE0(SAOP) has been tested with many organic molecules and the basis set of et-pVQZ is large enough for almost all applications. Therefore, it is our belief that the column labeled DFT in Table 5 to be most reliable. Although the DFT calculations of some of the cations have not converged, we based the assignment of the observed values mainly on the DFT values. It would be interesting to have a new measurement of the photoelectron spectrum of uric acid, hopefully with better resolution extending to higher VIEs.

Finally, the core-electron binding energies from our DFT calculations are presented in Table 6, in which calculated charges and the electrostatic potentials from the SAOP/et-pVQZ method are also listed for comparison. None of the calculated quantities offers a good correlation with the CEBEs. Since it is possible to measure the valence VIEs of uric acid vapor even back in 1978, we hope that an ESCA experiment with X-ray or synchrotron radiation can be performed on the core-electron binding energies also.

Summary

In this study, we have relied on our experience with DFT to predict the various properties of uric acid with what we believe to be the best method for each property. The properties include (a) the equilibrium geometry, (b) the vibrational spectrum, (c) the dipole moment, (d) the static dipole polarizability, (e) the UV absorption spectrum, (f) the vertical ionization energies of the valence electrons, and (g) the core-electron binding energies. In addition, we determined the best method (namely time-dependent DFT with the PBE0 functional) for the calculation of vertical excitation energies of uric acid and its anions in aqueous solution, even using the continuum dielectric models. It would be interesting to see whether such a method applies to UV-visible absorption other organic molecules in aqueous solution. Moreover, we encourage experimentalists to make new measurements of the ionization energies of both valence and core electrons.

Appendices

Appendix A- Experimental UV spectra

There have been many measurements of the UV absorption spectra of uric acid and its anions in aqueous solution, some with specific pH controlled by buffers and some without specified pH values [37,42-52]. In Supplementary table, we summarize the measurements in order to assess the reliability of calculated vertical excitation energies and present the midrange value for each transition, after rejecting some likely outliers, indicated in italics. Those without specific pH values are included in the likely range based on the observed wavelengths of maximum absorption. It should be noted that absorption maxima do not necessarily correspond to vertical excitations because of vibrational effects.

Appendix B-Personal example

It may be of interest to some readers to see an actual example of the effect of pH on the possibility of gout and kidney stone. The following reasoning is based on several approximations, including unit activity coefficients. The acid dissociation constants of uric acid determined by Wilcox et al. [1] correspond to $\text{p}K_{a1}=5.57$ and $\text{p}K_{a2}>10.70$ at 37°C. Using these values, the fractions of H_2U , HU^- and U^{2-} are 0.0145, 0.982 and

Wanted ^a		%HF Exchange	H ₂ U(aq) 4.38&5.28	HU ⁻ (aq) 4.25&5.26&6.21	U ²⁻ (aq) 4.20&5.44
LDA	VWN	0	3.97&4.58&5.73	3.92&4.72&5.50	3.82&4.61&4.88
GGA	PBE	0	4.01&4.64&5.76	3.97&4.77&5.47	3.86&4.64&4.88
GGA	RPBE	0	4.04&4.66&5.77	3.98&4.78&5.57	3.87&4.94&4.95
GGA	revPBE	0	4.03&4.66&5.77	3.99&4.79&5.58	3.88&4.64&4.95
GGA	KT1	0	4.06&4.71&5.85	4.01&4.84&5.65	3.90&4.68&5.02
GGA	KT2	0	4.09&4.73&5.87	4.04&4.86&5.68	3.93&4.73&5.04
GGA	PW91	0	4.01&4.63&5.76	3.96&4.76&5.47	3.86&4.63&4.87
GGA	mPBE	0	4.02&4.84&5.76	3.97&4.77&5.46	3.86&4.64&4.94
GGA	OPBE	0	4.10&4.75&5.84	4.05&4.87&5.66	3.94&4.73&5.04
GGA	SSB-D	0	4.09&4.73&6.03	4.04&4.86&5.57	3.92&4.72&4.96
GGA	BP86	0	4.02&4.65&5.78	3.98&4.78&5.54	3.87&4.67&4.91
GGA	BLYP	0	4.00&4.60&5.91	3.95&4.72&5.52	3.84&4.89&5.61
metaGGA	TPSS	0	4.15&4.79&5.95	4.10&4.91&5.69	3.99&4.80&5.06
metaGGA	M06-L	0	4.41&5.07&6.32	4.36&5.17&6.07	4.23&5.04&5.37
model	SAOP	0	4.21&4.83&6.09	4.17&4.97&5.81	4.07&4.88&5.15
model	LB94	0	3.92&4.43&5.74	3.88&4.60&5.45	3.80&4.78&5.40
metaHybrid	TPSSH	10	4.30&5.08&6.27	4.24&5.15&6.01	4.12&5.07&5.32
Hybrid	O3LYP	12	4.15&4.91&5.77	4.10&5.00&5.85	3.98&4.92&5.17
Hybrid	B3LYP&	15	4.23&5.03&6.25	4.16&5.09&5.98	4.05&5.00&5.26
Hybrid	B3LYP	20	4.31&5.17&6.40	4.24&5.20&6.13	4.11&5.12&5.38
Hybrid	X3LYP	21.8	4.33&5.21&6.44	4.25&5.23&6.17	4.13&5.13&5.23
Hybrid	mPW1K	25	4.63&5.81&7.03	4.54&5.73&6.76	4.40&5.69&5.79
Hybrid	B1LYP	25	4.38&5.30&6.53	4.30&5.30&6.26	4.17&5.19&5.29
Hybrid	PBE0	25	4.40&5.35&6.08	4.32&5.36&6.29	4.20&5.30&5.54
Hybrid	OPBE0	25	4.46&5.43&6.63	4.39&5.44&6.37	4.26&5.36&5.61
Hybrid	B1PW91	25	4.41&5.27&6.13	4.34&5.38&6.31	4.21&5.33&5.55
metaHybrid	M06	27	4.37&5.27&6.06	4.27&5.06&5.36	4.01&4.18&5.47
Hybrid	mPW1PW	42.8	4.41&5.35&6.09	4.33&5.36&6.30	4.20&5.30&5.54
Hybrid	BHandH	50	4.63&5.86&7.11	4.53&5.74&6.84	4.40&5.73&6.01
Hybrid	BHandHLYP	50	4.68&5.93&7.18	4.58&5.80&6.89	4.45&5.78&6.06
metaHybrid	M06&2X	54	4.38&5.58&6.74	4.28&5.37&5.45	4.14&5.42&5.69
Hybrid	KMLYP	55.7	4.72&6.04&7.30	4.62&5.90&7.02	4.49&5.88&5.94

^aSee Supplementary table

Table 3: Calculated observable (f >0.1) excitations of uric acid and its ions in aqueous solution.

	Abs max	PBE0/aug-TZP	B3LYP/aug-TZP	B3LYP/6-311G++ ^b
H ₂ U	4.38	4.40 (0.)	4.31 (0.)	4.52 (0.237)
	5.28	5.35 (0.)	5.17 (0.)	5.32 (0.255)
HU ⁻	4.25	4.32 (0.)	4.24 (0.)	4.46 (0.360)
	5.26	5.36 (0.)	5.20 (0.)	5.39 (0.335)
	6.21	6.29 (0.)	6.13 (0.)	
U ²⁻	4.20	4.20 (0.)	4.11 (0.)	4.29 (0.242)
	5.44	5.30 (0.)	5.12 (0.)	5.58 (0.126)

^aSee Appendix A

^bAltarsha et al. [38]

Table 4: Excitation energies in eV with f-values in parentheses calculated with continuum dielectric models compared to observed absorption maxima^a of uric acid and its ions in aqueous solution.

0.004, respectively, at pH=7.4 and 0.105, 0.8945, and 0.000 at pH=6.5. Wilcox et al. [1] also determined that the solubility of H₂U is 0.35 mM and the K_{sp} of NaHU to be 4.15x10⁻⁵ M² or 7.92x10⁻⁵ M², depending on which method one uses. Now, my recent urine analysis gave pH=6.5. If we assume that the total uric acid concentration=0.458 mM, and [Na⁺]=0.139 M are the same in my blood as in my urine, we can reach the following conclusions: The total uric acid concentration times the fractions give [H₂U]=0.0075 mM in my blood and [HU⁻]=0.410 mM in my urine. In my urine, the concentration product [Na⁺][HU⁻] can

be estimated to be 5.7x10⁻⁵ M², and therefore, there is a possibility of NaHU precipitating in my kidney in principle, although it is known that supersaturation is common with NaHU. On the other hand, the estimated concentration of H₂U in my blood is well below the solubility of 0.35 mM, thanks to the drug allopurinol. (The interested reader can see Ref. [53] for a DFT study of allopurinol). Since both gout and sodium biurate stones are caused by precipitations, drinking more water is certainly advisable. On the other hand, some internet websites advise drinking aqueous solution of baking soda, increasing

MO	KT ^a	mKT ^b	OVGF ^c	DFT ^d	Expt ^e [40]	SAC-CI/6-31+G(d) ^f
8a ^g	8.96	10.01	8.00	8.32	8.55	8.09
7a ^g	12.30	11.86	10.73	nc ^g		10.26
35a ^g	12.67	11.16	10.80	nc ^g		10.75
34a ^g	12.95	11.55	11.20	10.13	10.5	10.78
6a ^g	12.94	12.35	11.14	10.69	10.7	11.32
33a ^g	13.79	12.01	11.89	11.29	11.2	
5a ^g	13.53	12.92	11.80	11.78	11.8	
4a ^g	15.16	14.09	13.51	13.07		
32a ^g	17.24	14.93	15.13	nc ^g		
3a ^g	16.17	14.89	14.36	14.04		
31a ^g	17.67	15.23	15.55	14.47		
2a ^g	17.87	16.09	15.77	15.29		
30a ^g	18.05	15.51	15.90	15.34		
29a ^g	18.89	16.53	16.68	nc ^g		
27a ^g	19.53	17.49	17.56	15.65		
28a ^g	19.14	16.89	16.97	16.34		
1a ^g	19.30	17.23	16.90	16.44		
26a ^g	20.79	18.25	18.42	17.81		
25a ^g				18.66		
24a ^g				19.82		
23a ^g				20.82		
22a ^g				21.46		

^aKoopmans' theorem /6-311+G(d,p) [41]

^bmeta-Koopmans' theorem(SAOP)/et-pVQZ

^cOuter-valence Green's function/6-311+(d,p)

^dΔPBE0(SAOP)/et-pVQZ

^eDougherty et al. [40]

^fFarrokhpour and Ghandehari [41]

^gNo convergence

Table 5: Vertical ionization energies (in eV) of uric acid vapor.

Input	Ms	CEBE (in eV)	NBO ^a	Mulliken ^b	Hirshfeld ^b	Voronoi ^b	Electrostatic Potential ^b
O14	O2	537.46	-0.613	-0.713	-0.358	-0.392	22.476
O11	O8	537.28	-0.618	-0.732	-0.369	-0.399	22.484
O16	O6	537.03	-0.601	-0.719	-0.354	-0.382	22.485
N5	N3	407.47	-0.612	0.239	-0.098	-0.148	18.352
N7	N9	407.31	-0.613	0.220	-0.100	-0.146	18.359
N9	N7	406.93	-0.595	0.181	-0.100	-0.142	18.379
N3	N1	406.63	-0.648	0.402	-0.109	-0.153	18.386
C1	C5	294.80	-0.036	0.058	-0.001	-0.034	14.743
C4	C2	294.80	0.809	0.335	0.258	0.295	14.627
C6	C4	294.49	0.391	0.049	0.125	0.132	14.672
C8	C8	294.49	0.788	0.488	0.244	0.284	14.642
C2	C6	293.75	0.632	0.320	0.189	0.217	14.668

^aCharges from NBO calculation with Gaussian09 using 6-311+(d,p) basis set

^bFrom ADF program using SAOP/et=pVQZ

Table 6: Calculated core electron binding energies of uric acid vapor.

the blood pH, to reduce the risk of uric acid precipitation. However, from the estimates given above, we see that such a procedure would not be advisable in my case.

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