Ab initio study on tautomerism of 2-thiouracil in the gas phase and in solution

Hülya Yekeler
Faculty of Science and Arts, Chemistry Department, Cumhuriyet University, 58140 Sivas, Turkey

Summary

Ab initio geometry optimizations were carried out at the HF/3-21G and HF/6-31+G** levels for the six tautomeric forms of 2-thiouracil (2TU, 2TU1, 2TU2, 2TU3, 2TU4, 2TU5) in the gas phase and in solution. To obtain a more definitive estimate of the relative stabilities for 2-thiouracil tautomers in the gas phase, single-point MP2/6-31+G** calculations were performed on the HF/6-31+G** optimized geometries. The tautomeric equilibria in 1,4-dioxane ($\varepsilon = 2.21$), acetonitrile ($\varepsilon = 38$), and in water ($\varepsilon = 78.54$) were studied using the self-consistent reaction field (SCRF) theory. The calculated relative free energies indicated that 2TU is the energetically preferred tautomer in the gas phase and in solution. The stability order of 2-thiouracil tautomers depends on the level of theory and the dielectric constant of the solvent. The obtained results are compared with the available experimental data.

Introduction

The sulfur derivatives of pyrimidines and purines are widely used as antitumor agents in clinical treatment [1–3]. In recent years much effort, both experimental and theoretical, has been devoted to the study of their structural properties and stabilities. The tautomerism of purine and pyrimidine bases naturally occurring in nucleic acids, nucleotides, and enzymes may play a role in mutagenesis [4]. The knowledge of physical chemical properties of these compounds is clearly essential in understanding many important biochemical processes. Computational studies permit a direct analysis of such properties. The 2-thiouracil molecule may appear in various tautomeric forms, differing by the positions of the protons, as given in Scheme 1.

All of the experimental [5, 6] and theoretical [7–10] results so far available are consistent with the oxo-thione tautomer being the most stable tautomer. Rostkowska et al. [11, 12] have investigated the tautomerism of thiouracils in an inert matrix environment and in the vapor phase using IR spectroscopy. They concluded that 2-thiouracil exists predominantly in the oxo-thione tautomeric form. The same tautomeric form of 2-thiouracil is also present in solutions [13]

and in the solid phase [14]. These conclusions are consistent with the gas phase proton affinities, which are determined using ion cyclotron resonance mass spectrometry [15]. In the theoretical studies appearing in the literature [7–10], the most likely tautomers of 2-thiouracil were studied by semiempirical approaches as well as ab initio calculations in the gas phase. However, heterocyclic tautomeric equilibria are highly sensitive to environmental effects such as solvent polarity [16–23]. Interactions between solute and solvent molecules are responsible for variations of physical and chemical properties of the solute. Knowing how these tautomerization energies change in different environments can give an insight into the influence of solvent effects on molecular stability. Energy differences between the most stable structure and rare tautomers of nucleic acid bases are also dependent on the level of theory and, especially, on the effects of electron correlation [24–26].

The rare tautomers of thiouracils are simply not observed due to their low concentration in experimental studies. Ab initio calculations can be an invaluable tool to obtain information about the structure and properties of such rare tautomers, which are not easily accessible by experiment. We are not aware of
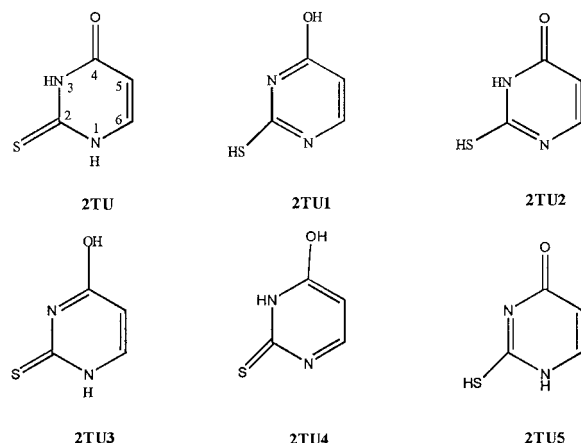
Scheme 1. Tautomers of 2-thiouracil.

any ab initio study dealing with tautomerism of 2-thiouracil in solution. Consequently, in this work, the six tautomer structures of 2-thiouracil were studied using ab initio molecular orbital calculations at the HF (Hartree–Fock) and MP2 (second-order Møller–Plesset perturbation theory) levels with the 3-21G and 6-31+G** basis sets in the gas phase and in solution.

Method

Ab initio molecular orbital calculations were performed with the Gaussian 94 [27] package. Geometry optimizations for all structures were carried out with the 3-21G and 6-31+G** basis sets at the HF level with $\varepsilon = 1$ (gas phase), $\varepsilon = 2.21$ (1,4-dioxane), $\varepsilon = 38$ (acetonitrile) and $\varepsilon = 78.54$ (water). In addition, vibrational frequency analyses were performed at both levels in the gas phase and in solution. The optimized structures of all tautomers are at stationary points, corresponding to local minima without imaginary frequencies. 2-Thiouracil tautomers are assumed to be planar. To investigate electron correlation on the tautomerization energy of 2-thiouracil in the gas phase, the single-point energy calculations were performed at the MP2 level using the HF/6-31+G** optimized geometries.

The effect of solute–solvent interaction was taken into account via the self-consistent reaction field (SCRF) method implemented in Gaussian 94. This method is based on Onsager's reaction field theory [28] of electrostatic solvation. The solute is modeled as occupying a spherical cavity of radius a_0 in a continuous medium with a dielectric constant ε. The permanent dipole of the solute then induces a dipole

(reaction field) in the surrounding medium, which in turn will interact with the solute's dipole. This solute–solvent interaction is updated until self-consistency is achieved. The solvation energy thus obtained corresponds to the electrostatic contribution to the free energy of solvation. The cavity radius of 4.06 Å for the tautomers was obtained using Wong's approach [29], which involves calculating the volume enclosed by a 0.001 au electron density envelope, scaling by 1.33 to get the liquid molecular volume, and adding 0.5 Å to account for the nearest approach.

Results and discussion

We considered here the six tautomeric forms of 2-thiouracil and used the notation of 2TU, 2TU1, 2TU2... to explain these species. Some tautomers can exist as more than one conformer. In this study, the most stable conformer corresponding to each tautomeric form was chosen as shown in Scheme 1.

The optimized geometries obtained for the six tautomers of 2-thiouracil are given in Figure 1, where bond lengths and angles are given in Å and degrees, respectively. When the HF/6-31+G** geometry of the 2TU tautomer is compared with the crystal structure of 6-methyl-2-thiouracil [30], some interesting differences are found. For example, compared to the HF/6-31+G** geometry, in the crystal, the N1-C2, C2-N3, C5-C6 and C4-O bonds are longer by 0.006, 0.017, 0.029 and 0.042 Å and the N3-C4, C4-C5, C6-N1 and C2-S bonds are shorter by 0.016, 0.043, 0.006 and 0.001 Å. The same differences are observed for the bond angles. The largest change of bond angle occurs in the ∠N3C4O, varying from 120.2° (optimized) to 117.6° (in the crystal). The agreement between theory and experiment is fairly good because of the crystal forces and hydrogen-bonding interactions in the crystalline state. Similar discrepancies were also observed for 2-thiouracil [7, 8, 32], 4-thiouracil [7, 33] and 2,4-dithiouracil [34].

Two sets of calculations were carried out at the HF/3-21G and HF/6-31+G** levels, followed by computations of the harmonic vibrational frequencies, in order to study the basis set dependence of the energies for the six 2-thiouracil tautomers. The single-point energy calculations were done using the 6-31+G** basis set at the MP2 level in the gas phase. Table 1 presents the calculated energies and dipole moments of the six tautomeric forms in the gas phase and in solution, while relative energies are given in Tables 2

Figure 1. The optimized HF/6-31+G** geometries of 2-thiouracil tautomers in the gas phase (Chem Office Pro) [31]. The crystal data of 6-methyl-2-thiouracil [30] are given in parentheses.

Figure 2. The relative energies (kcal mol^{-1}) of 2-thiouracil tautomers versus theoretical levels in the gas phase.

and 3. The relative stability of the different tautomeric forms has a very fundamental importance for the prediction of the probability of spontaneous mutations [4]. Clearly, in both the gas phase and in solution, the oxo-thione tautomer (2TU) is the most stable species at all theoretical levels. According to the experimental studies [6, 11, 12, 15], the oxo-thione form of 2-thiouracil is the dominant tautomer. Simultaneously, the relative stabilities of the other tautomers depend on the theoretical level applied, as illustrated graphically in Figure 2. Kwiatkowski et al. [25] have proposed that the role of the electron correlation and zero-point vibration effects in estimating relative stabilities of tautomers are not important. In the present work, it was found that these contributions do not change the stability order of 2-thiouracil tautomers.

As seen in Tables 2 and 3, the relative stabilities of 2-thiouracil tautomers are 2TU > 2TU3 > 2TU4 > 2TU2 > 2TU1 > 2TU5 at the HF/3-21G approximation in the gas phase and, the improvement of the theoretical level significantly changes this order at the HF/6-31+G** and MP2/6-31+G** levels. At these levels, the relative energy order was found to be 2TU > 2TU1 > 2TU2 > 2TU3 > 2TU5 > 2TU4. The relative energies of the structures at the HF/6-31+G** level differ considerably from the values obtained from the use of the 3-21G basis set, which includes no polarization functions. For example, while relative energies of 2TU1 and 2TU2 in the gas phase are equal to 34.61 and 31.02 kcal mol^{-1}, respectively, at the HF/3-21G approximation, improvement of the basis set quality to HF/6-31+G** reduces these numbers to 10.35 and 12 kcal mol^{-1}, respectively.
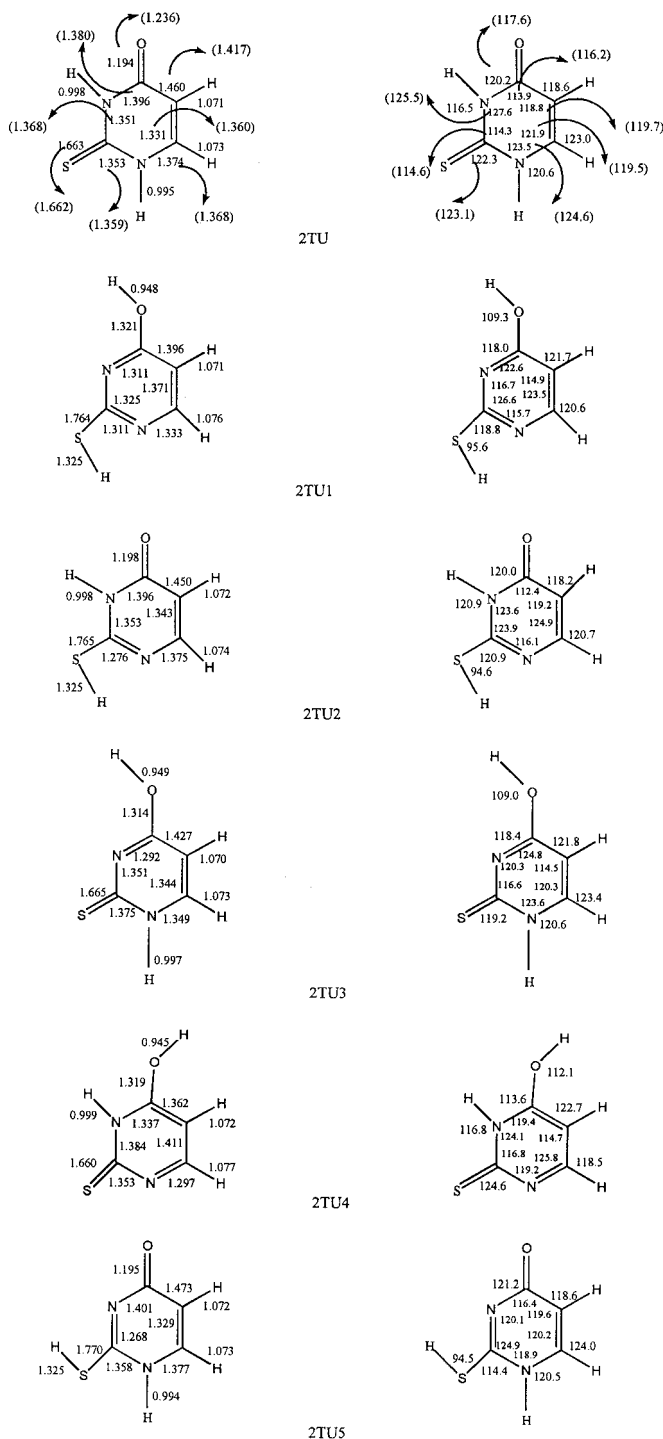
Table 1. Calculated energies[a] and dipole moments[b] in the gas phase ($\varepsilon = 1$) and in solution ($\varepsilon = 2.21$, $\varepsilon = 38$ and $\varepsilon = 78.54$)

	$\varepsilon = 1$	$\varepsilon = 2.21$	$\varepsilon = 38$	$\varepsilon = 78.54$
2TU				
E(HF/3-21G)	−731.274433	−731.277140	−731.280924	−731.281088
E(HF/6-31+G**)	−735.121694	−735.124140	−735.127660	−735.127816
E(MP2/6-31+G**)	−736.266553	–	–	–
ZPE[c]	0.091641	0.091635	0.091606	0.091604
μ	5.39	5.93	6.73	6.77
2TU1				
E(HF/3-21G)	−731.219279	−731.219597	−731.220054	−731.220074
E(HF/6-31+G**)	−735.105205	−735.105433	−735.105774	−735.105789
E(MP2/6-31+G**)	−736.254452	–	–	–
ZPE[c]	0.087666	0.087610	0.087531	0.087527
μ	1.63	1.83	2.12	2.13
2TU2				
E(HF/3-21G)	−731.225000	−731.225634	−731.226555	−731.226595
E(HF/6-31+G**)	−735.102575	−735.103458	−735.104794	−735.104855
E(MP2/6-31+G**)	−736.250910	–	–	–
ZPE[c]	0.087583	0.087535	0.087453	0.087449
μ	3.20	3.60	4.21	4.24
2TU3				
E(HF/3-21G)	−731.242262	−731.246838	−731.253766	−731.254081
E(HF/6-31+G**)	−735.100634	−735.104752	−735.111356	−735.111669
E(MP2/6-31+G**)	−736.247852	–	–	–
ZPE[c]	0.091473	0.091461	0.091475	0.091473
μ	6.85	7.87	9.52	9.60
2TU4				
E(HF/3-21G)	−731.226466	−731.235350	−731.249853	−731.250543
E(HF/6-31+G**)	−735.084200	−735.091967	−735.105344	−735.106006
E(MP2/6-31+G**)	−736.231816	–	–	–
ZPE[c]	0.090574	0.090713	0.090728	0.090862
μ	9.27	10.96	13.84	13.98
2TU5				
E(HF/3-21G)	−731.210571	−731.213989	−731.218834	−731.219046
E(HF/6-31+G**)	−735.087410	−735.091661	−735.097972	−735.098257
E(MP2/6-31+G**)	−736.236084	–	–	–
ZPE[c]	0.087119	0.087119	0.087253	0.087253
μ	7.06	7.87	9.09	9.15

[a] All energies in hartrees.
[b] HF/6-31+G** values in debye.
[c] HF/6-31+G** values.

Table 2. Relative energies[a] for the six tautomeric forms of 2-thiouracil in the gas phase

Tautomer	HF/3-21G	HF/6-31+G**	MP2/6-31+G**	MP2 + ZPE[b]
2TU	0	0	0	0
2TU1	34.61	10.35	7.59	5.10
2TU2	31.02	12.0	9.82	7.27
2TU3	20.19	13.22	11.74	11.63
2TU4	30.10	23.53	21.80	21.13
2TU5	40.07	21.51	19.12	16.28

[a]Relative to 2TU, and all the relative energies in kcal mol^{-1}.
[b]Including ZPE (HF/6-31+G**) corrections.

Table 3. Relative energies[a] for the six tautomeric forms of 2-thiouracil in solution

Tautomer	$\varepsilon = 2.21$		$\varepsilon = 38$		$\varepsilon = 78.54$	
	HF/3-21G	HF/6-31+G**	HF/3-21G	HF/6-31+G**	HF/3-21G	HF/6-31+G**
2TU	0	0	0	0	0	0
2TU1	36.11	11.74	38.20	13.73	38.29	13.82
2TU2	32.32	12.98	34.12	14.35	34.20	14.41
2TU3	19.02	12.17	17.04	10.23	16.95	10.13
2TU4	26.22	20.19	19.50	14.00	19.17	13.69
2TU5	39.63	20.38	38.96	18.63	38.93	18.55

[a]Relative to 2TU, and all the relative energies in kcal mol^{-1}.

It was also found that zero-point energies contribute to the relative energies of the 2-thiouracil tautomers. Taking the energy of 2TU1 relative to 2TU as an example, it is 10.35 kcal mol^{-1} at the HF/6-31+G** level, 7.59 kcal mol^{-1} at the MP2/6-31+G** level and inclusion of the ZPE corrections to the calculated energies at the MP2 level changes this energy to 5.10 kcal mol^{-1} in the gas phase (see Figure 2, Table 2). Because the tautomers of 2-thiouracil are not present in detectable amounts, no experimental data are available to test our results. Additionally, no absorption which could be assigned to the SH and OH stretching vibrations was found for 2-thiouracil in the vapor phase and in low temperature matrices by Rostkowska et al. [11, 12]. In this work, the predicted stability order of 2-thiouracil tautomers using the relative energies in the gas phase is in agreement with the ab initio MO results obtained by Leś et al. [7], but in disagreement with the semiempirical MO results obtained by Katritzky et al. [8] and Leś et al. [9].

Probably one of the most crucial factors determining the tautomer distribution in the biological material is the environment. The study of the interactions between solute and solvent is complicated. This study employed the SCRF theory [29] to examine the solvent effect on this tautomerism. A continuum model like the SCRF theory allows one to take into account long-range interactions. Because of the lack of solvent structure, the model is not appropriate for solvents that have important specific interactions (like hydrogen bonds) with the solute. Nevertheless, it has the advantage of allowing the geometry and dipole moment of the solute to be adjusted to reflect the interaction with the medium. Also, it is particularly simple to implement and it is a computationally efficient method for the prediction of general structural and stability trends in polar media. Consideration of the solvent causes some reordering of the stability of 2-thiouracil tautomers, which is predicted to be 2TU > 2TU1 > 2TU3 > 2TU2 > 2TU4 > 2TU5 in 1,4-dioxane ($\varepsilon = 2.21$), 2TU > 2TU3 > 2TU1 > 2TU4 > 2TU2 > 2TU5 in acetonitrile ($\varepsilon = 38$) and 2TU > 2TU3 > 2TU4 > 2TU1 > 2TU2 > 2TU5 in water ($\varepsilon = 78.54$) at the HF/6-31+G** level. It should be noted that for 2-thiouracil the polar solvent effects favor the 2TU3 tautomer instead of 2TU1. Using the HF/6-31+G** energies, relative energy values for the investigated 2-thiouracil tautomers increase in going from the gas phase to solution, whereas the same values decrease as the solvent polarity increases, except for 2TU1 and

Table 4. Zero-point energies (ZPE), entropies (S), thermal corrections (H − H$_o$) and relative free energies (ΔG)[a] for the six tautomeric forms of 2-thiouracil in the gas phase at 25 °C[b]

	2TU	2TU1	2TU2	2TU3	2TU4	2TU5
ZPE	57.51	55.01	54.96	57.40	56.84	54.67
S	80.16	80.28	81.27	79.71	80.24	82.44
H − H$_o$	4.43	4.53	4.65	4.38	4.47	4.79
ΔE[c]	0	10.35	12.0	13.22	23.53	21.51
ΔE[d]	0	7.59	9.82	11.74	21.80	19.12
ΔG[c]	0	7.91	9.34	13.19	22.88	18.35
ΔG[d]	0	5.15	7.49	11.71	21.15	15.96

[a] $\Delta G = \Delta H - T\Delta S$, $\Delta H^{298} = \Delta E^{298} + \Delta(PV)$, $\Delta E^{298} = \Delta E_e^0 + \Delta(ZPE) + \Delta(\Delta E_V)^{298} + \Delta E_R^{298} + \Delta E_T^{298}$.
[b] All energy terms except S in kcal mol^{-1}, S in cal mol^{-1}K^{-1}. ZPE, H − H$_0$ and S based on the HF/6-31+G** optimized geometries.
[c] HF/6-31+G** energies.
[d] MP2/6-31+G** energies.

Table 5. Zero-point energies (ZPE), entropies (S), thermal corrections (H − H$_o$) and relative free energies (ΔG)[a] for the six tautomeric forms of 2-thiouracil in solution at 25 °C[b]

		2TU	2TU1	2TU2	2TU3	2TU4	2TU5
	ZPE	57.50	54.98	54.93	57.39	56.92	54.72
	S	80.10	80.31	81.21	79.71	79.93	82.21
$\varepsilon = 2.21$	H − H$_o$	4.42	4.53	4.64	4.38	4.43	4.81
	ΔE	0	11.74	12.98	12.17	20.19	20.38
	ΔG	0	9.27	10.30	12.14	19.67	17.36
	ZPE	57.48	54.93	54.88	57.40	56.93	54.75
	S	80.03	80.35	81.14	79.57	79.88	81.94
$\varepsilon = 38$	H − H$_o$	4.42	4.54	4.63	4.37	4.43	4.73
	ΔE	0	13.73	14.35	10.23	14.00	18.63
	ΔG	0	11.21	11.63	10.24	13.51	15.64
	ZPE	57.48	54.92	54.88	57.40	57.02	54.75
	S	80.03	80.35	81.14	79.57	79.54	81.93
$\varepsilon = 78.54$	H − H$_o$	4.42	4.54	4.63	4.37	4.38	4.72
	ΔE	0	13.82	14.41	10.13	13.69	18.55
	ΔG	0	11.29	11.69	10.14	13.34	15.55

[a] $\Delta G = \Delta H - T\Delta S$, $\Delta H^{298} = \Delta E^{298} + \Delta(PV)$, $\Delta E^{298} = \Delta E_e^0 + \Delta(ZPE) + \Delta(\Delta E_V)^{298} + \Delta E_R^{298} + \Delta E_T^{298}$.
[b] All energy terms based on the HF/6-31+G** optimized geometries. ZPE, H − H$_0$, ΔE and ΔG in kcal mol^{-1}, S in cal mol^{-1}K^{-1}.

2TU2, whose dipole moments are 1.63 D and 3.20 D (in the gas phase), respectively. Of course, the influence of a polar environment can be estimated by comparing the solute dipole moments. The tautomer which has the largest dipole moments will be more stable in polar environment. By comparing the data obtained in 1,4-dioxane and in water, relative energies of 2TU1 and 2TU2 tautomers extend to 2.08 and

1.43 kcal mol^{-1}, respectively. The calculated value of 5.39 D for 2TU in the gas phase is significantly larger than the experimental dipole moment of 4.20 D [7]. Note that there is a substantial enhancement of the dipole moment values of the tautomers in going from the gas phase to polar medium.

In many cases the estimation of the relative stability of tautomers is done only by consideration of

the difference between the electronic energies of both tautomers, assuming that the contribution of the zero-point vibrational energies and entropies for both tautomers is the same. In the present study, we took into account the contribution of the zero-point vibrational energies and entropies to the electronic energies for each tautomer in the gas phase and in solution. The relative free energies for 2-thiouracil tautomers were calculated in the gas phase and in solution. The obtained relative free energies are listed in Tables 4 and 5. The energy differences, ΔE, were calculated using the MP2/6-31+G** energies in the gas phase, and HF/6-31+G** energies in solution. The free energy difference between the two tautomers, ΔG, was obtained by correcting ΔE with the zero-point vibrational energy difference (ΔZPE), the thermal correction difference ($\Delta(H - H_o)$) and the entropic difference (ΔS). All of these correction terms were calculated at the HF/6-31+G** level.

Our results indicate that the 2TU (oxo-thione) form is present in both polar and nonpolar solutions. The results obtained at the HF/6-31+G** level show that, in going from the gas phase to polar medium, the relative free energies of 2TU3, 2TU4 and 2TU5 reduce to 3.05, 9.54 and 2.80 kcal mol^{-1} respectively, in contrast to 2TU1 and 2TU2 whose relative free energies increase by 3.38 and 2.35 kcal mol^{-1}, respectively. This trend is very likely due to the fact that 2TU3, 2TU4 and 2TU5 have a much larger dipole moment, and thus stronger solvent stabilization, than 2TU1 and 2TU2. It is clear that the tautomers having the largest dipole moment are highly stabilized by polar media. There is, however, no direct correlation between dipole moment and relative stability under SCRF conditions. For example, the 2TU4 tautomer has the highest dipole moment (9.27 D in the gas phase) but it is the third most stable structure in water at the HF/6-31+G** level. This is because the continuum model is incapable of treating first-hydration-shell effects, which should stabilize 2TU4 more than the other tautomers. These results are consistent with the relative energy findings mentioned above.

Using the relative free energy changes at the HF/6-31+G** level, the stability orders in acetonitrile ($\varepsilon = 38$) and water ($\varepsilon = 78.54$) were found to be 2TU> 2TU3> 2TU1> 2TU2> 2TU4> 2TU5, which is different from the relative energy orders in the same solvents.

However, the relative free energy orders in the gas phase ($\varepsilon = 1$) and 1,4-dioxane ($\varepsilon = 2.21$) are the same compared to the relative energy order. Both the relative free energy order and the relative energy order do not change in the gas phase and in nonpolar solvent, whereas they are different from each other in the polar solvents. It is concluded that the relative stability order of 2-thiouracil tautomers can be predicted using the relative energies in the gas phase and in nonpolar solvents, while the same energies do not allow us to predict the same order relative stability in aqueous or other polar solutions. Consequently, the relative free energy changes should be considered in predicting the relative stability.

Conclusions

The main conclusions from the present study can be outlined as follows:

1. According to calculations done in this study, the 2TU tautomer of 2-thiouracil is found to be the most stable form in the gas phase and in solution, in agreement with the experimental data.
2. The stability order is very sensitive to the level of theory and environment. The results clearly show that rare tautomeric forms can be stabilized by the polar solvents.
3. The relative energy values and the relative free energy changes, except for 2TU1 and 2TU2, decrease with the solvent polarity.
4. The relative free energy changes should be taken into account in the prediction of the stability order of these compounds in the polar solvents.
5. Finally, the 2-thiouracil molecule can form hydrogen bonds with some solvents (e.g., water). The SCRF theory is not sufficient to describe short-range interactions such as hydrogen bonding. For this reason, consideration of the microscopic interactions with the solvent molecules can alter our results obtained in solution.

Acknowledgements

References

1. Thewald, U. and Bugg, C.E., J. Am. Chem. Soc., 94 (1972) 8892.
2. Saenger, W. and Suck, D., Eur. J. Biochem., 82 (1973) 473.

3. Gottschalk, E., Kopp, E. and Lezius, A.G., Eur. J. Biochem., 24 (1971) 168.
4. Löwdin, P.O., Adv. Quantum Chem., 2 (1965) 213.
5. Winckelmann, I. and Larsen, E.H., Synthesis, (1986) 1041.
6. Ghomi, M., Letellier, R., Taillandier, E., Chinsky, L., Laigle, A. and Turpin, P.Y., J. Raman Spectrosc., 17 (1986) 249.
7. Leś, A. and Adamowicz, L., J. Am. Chem. Soc., 112 (1990) 1504.
8. Katritzky, A.R., Szafran, M. and Stevens, J., J. Chem. Soc. Perkin Trans. II, (1989) 1507.
9. Leś, A. and Ortega-Blake, I., Int. J. Quantum Chem., 30 (1986) 225.
10. Aruna, S. and Shanmugan, G., Indian J. Chem., 25A (1986) 256.
11. Rostkowska, H., Barski, A., Szczepaniak, K., Szczesniak, M. and Person, W.B., J. Mol. Struct., 176 (1988) 137.
12. Rostkowska, H., Szczepaniak, K., Nowak, M.J., Leszczynski, J., KuBulat, K. and Person, W.B., J. Am. Chem. Soc., 112 (1990) 2147.
13. Psoda, A. and Shugar, D., Acta Biochim. Pol., 26 (1979) 55.
14. Okabe, N., Fujiwara, T., Yamagata, Y. and Tomita, T., Bull. Chem. Soc. Jpn., 56 (1983) 1543.
15. Katritzky, A.R., Baykut, G., Rachwal, S., Szafran, M., Caster, K.C. and Eyler, J., J. Chem. Soc. Perkin Trans. II, (1989) 1499.
16. Karelson, M.M., Katritzky, A.R., Szafran, M. and Zerner, M.C., J. Org. Chem., 54 (1989) 6030.
17. Wong, M.W., Leung-Toung, R. and Wentrup, C., J. Am. Chem. Soc., 115 (1993) 2465.
18. Parchment, O.G., Green, D.V.S., Taylor, P.J. and Hillier, I.H., J. Am. Chem. Soc., 115 (1993) 2352.
19. Cieplak, P., Bash, P., Singh, U.C. and Kollman, P.A., J. Am. Chem. Soc., 109 (1987) 6283.
20. Cao, M., Teppen, B.J., Miller, D.M., Pranata, J. and Schäfer, L., J. Phys. Chem., 98 (1994) 11353.
21. Cramer, C.J. and Truhlar, D.G., J. Am. Chem. Soc., 115 (1993) 8810.
22. Orozco, M. and Luque, F.J., Biopolymers, 33 (1993) 1851.
23. Kwiatkowski, J.S., Zielinski, T.J. and Rein, R., Adv. Quantum Chem., 18 (1986) 85.
24. Gould, I.R. and Hillier, I.H., Chem. Phys. Lett., 161 (1989) 185.
25. Kwiatkowski, J.S., Bartlett, R.J. and Person, W.B., J. Am. Chem. Soc., 110 (1988) 2353.
26. Leś, A. and Adamowicz, L., J. Phys. Chem., 93 (1989) 7078.
27. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Robb, M.A., Cheeseman, J.R., Keith, T.A., Petersson, G.A., Montgomery, J.A., Raghavachari, K., Al-Laham, M.A., Zakrzewski, V.G., Ortiz, J.V., Foresman, J.B., Cioslowski, J., Stefanov, B.B., Nanayakkara, A., Challacombe, M., Peng, C.Y., Ayala, P.Y. and Chen, W., GAUSSIAN 94, Revision B.3., Gaussian Inc., Pittsburgh, PA, 1995.
28. Onsager, L., J. Am. Chem. Soc., 58 (1936) 1486.
29. Wong, M.W., Frisch, M.J. and Wiberg, K.B., J. Am. Chem. Soc., 113 (1991) 4776.
30. Delage, C., H'Naifi, A., Goursolle, M. and Carpy, A., C. R. Seances Acad. Sci. Paris, Serie II, 302 (1986) 219.
31. ChemOffice Pro for Windows, Cambridge Scientific Computing Inc., Cambridge, MA.
32. Hawkinson, S.W., Acta Crystallogr., B33 (1977) 80.
33. Lesyng, B. and Saenger, W.Z., Naturforsch., C: Biosci., 36 (1981) 956.
34. Leszczyński, J. and Lammertsma, K., J. Phys. Chem., 95 (1991) 3128.
35. Psoda, A., Kazimierczuk, Z. and Shugar, D., J. Am. Chem. Soc., 96 (1974) 6832.