

Ab initio study of 2,4-substituted azolidines. III. Theoretical and experimental IR study of pseudothiohydantoin in water solution

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Dedicated to the memory of Prof. Bojidar Jordanov

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The relative stabilities of the tautomers of pseudothiohydantoin were calculated at MP2/6-31+G(d,p) level by considering isolated molecules and their trihydrated complexes. Single-point calculations at MP4/6-31+G(d,p)//MP2/6-31+G(d,p) level of theory were performed to obtain more accurate energies.

The theoretical IR spectra of the tautomers of pseudothiohydantoin were calculated at MP2/6-31+G(d,p) level and compared to experimental data. A good agreement between the *ab initio* predicted and experimentally measured IR spectrum of pseudothiohydantoin was found.

Key words: *ab initio*, tautomerism, pseudothiohydantoin, IR.

INTRODUCTION

Experimental studies on the amino-imino tautomerism of 2-amino-thiazolidine-4-one (2AT, pseudothiohydantoin) have been reported in several papers [1–12]. However, the opinions of the authors are contradictory. Amirthalingam and Muralidharan [6] confirmed by X-ray the existence of the imino form of pseudothiohydantoin. Twenty two years later Steel and Guard [13] redetermined the crystal structure of pseudothiohydantoin at 128 K and showed that the compound exists in the amino form. Using UV-Vis spectral data, Comrie [2] and Akerblom [3] reported that in water solution both tautomeric forms exist with domination of the imino tautomer. By means of IR spectroscopy Khovratovich and Chizhevskaya [4] showed that in chloroform solution the amino form exists. According to Ramsh et al. [10] (IR and NMR data), in DMSO and in water solutions pseudothiohydantoin exists as amino tautomer. A study of 2-amino-thiazolidine-4-one was carried out by IR, ^1H and ^{13}C NMR spectroscopy in DMSO solution and it was shown that 2AT exists in amino form [12].

Recently, we studied the amino-imino tautomerism of 2-amino-thiazolidine-4-one in weakly polar (CHCl_3), polar (DMSO) and protic solvents [14, 15]. In the study of the solvation of 2AT in water the effects of solvent were introduced i) through a continuum description, ii) using solute-

solvent clusters and iii) using the same clusters embedded in an external continuum. Because of the very low concentration of the imino tautomer its signals could not be observed in the ^{13}C NMR spectra. TD DFT B3LYP/aug-cc-pVTZ calculations were performed to predict the absorption maxima of the imino and amino tautomers of 2AT. The absorption maxima of the imino tautomer fall in the same range as those of the amino form. This could explain why the existence of the imino tautomer is not detected by NMR and UV spectroscopy.

In the present work the *ab initio* predicted and experimental IR spectra of pseudothiohydantoin are compared in an attempt to prove the existence of the imino tautomer in water solution.

EXPERIMENTAL

2-Amino-thiazolidine-4-one was synthesized according to Davies et al. [16]. $1 \times 10^{-3} \text{ mol} \cdot \text{dm}^{-1}$ solution of the compound in D_2O was prepared for the IR spectral measurement. The IR spectrum was recorded on a Bruker IFS 113v FTIR spectrometer in the $1800\text{--}1250 \text{ cm}^{-1}$ spectral region at a resolution of 2 cm^{-1} using a CaF_2 liquid cell of 0.12 mm path length.

CALCULATIONS

The *ab initio* calculations were carried out using the PC GAMESS version [17] of the GAMESS (US) quantum chemistry package [18]. The geometries of the tautomeric forms of pseudothiohydantoin (Figure 1) were optimized at MP2/6-31+G(d,p)

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level of theory without symmetry constraints (C_1 symmetry was assumed) by the gradient procedure. Local minima were verified by establishing that the Hessians have zero eigenvalues. The default gradient convergence threshold (1×10^{-5} hartree·Bohr $^{-1}$) was used. Single-point calculations at MP4/6-31+G(d,p)/MP2/6-31+G(d,p) level of theory were performed to obtain more accurate energies. MP2/6-31+G(d,p) zero point energies (ZPE) were added to the total energies. The values of Gibbs free energies (ΔG) and the populations (p_i) were calculated by the formulas $\Delta G = \Delta H - T\Delta S$ and $p_i = e^{-\Delta G_i / RT} / \sum_i e^{-\Delta G_i / RT}$, respectively. To estimate ΔH values, thermal corrections to the enthalpies calculated at MP2/6-31+G(d,p) level were added to the calculated energies. The entropy values were evaluated from the frequency calculations at the same level of optimization. The classical rate constant at 298.15 K was calculated using the Eyring equation, $k = k_B T / h \cdot e^{-\Delta G^\ddagger / RT}$, where k_B and h are the Boltzmann and Planck constants, respectively.

To estimate the effect of the water on the relative stabilities of the tautomers we applied the polarizable continuum model (PCM) as implemented in the GAUSSIAN 98 [19] suite of programs at MP4/6-31+G(d,p) level for the geometries optimized at the same level of theory, i.e. PCM/MP4/6-31+G(d,p)/MP2/6-31+G(d,p).

RESULTS AND DISCUSSION

Pseudothiohydantoin can theoretically exist in five tautomeric forms. These tautomeric forms, shown in Fig. 1, are named: 2-imino-4-oxo-1,3-thiazolidine (**A**), 2-amino-4-oxo-thiazoline (**B**), 4-hydroxy-2-imino-thiazoline (**C**), 4-hydroxy-2-iminothiazoline (**D**) and 2-amino-4-hydroxy-thiazole (**E**).

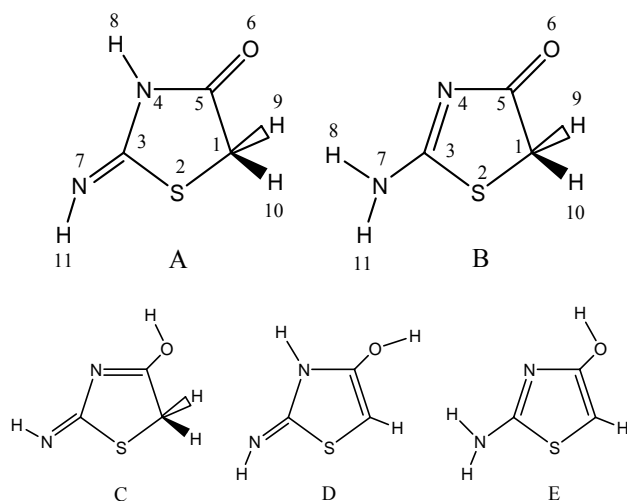


Fig. 1: Tautomeric forms of pseudothiohydantoin.

In our previous papers [14, 15] we studied the relative stabilities of all tautomers of pseudothiohydantoin. We showed that the preferred tautomers **A** and **B** are near in energy in the gas phase and in weakly polar (CHCl_3) and polar (DMSO) solutions (Tables 1 and 2). The amino tautomer **B** is more stable in water solution [15]. The effect of aqueous hydration is simulated using the supermolecule approach in which three water molecules are attached to the imino **A** and amino **B** tautomers. Water molecules are located in the appropriate positions to form intermolecular hydrogen bonds. The differences in the free energies of the trihydrated complexes of tautomers **A** and **B** of pseudothiohydantoin are presented in Fig. 2. The PCM/MP4/6-31+G(d,p)/MP2/6-31+G(d,p) calculated free energy difference (ΔG_{298}) and activation barrier ΔG_{298}^\ddagger are 3.39 and 17.93 kcal·mol $^{-1}$, respectively. On the basis of the energy difference, the percent concentration of tautomer **A** was calculated to be 0.33 %. The rate constant was calculated to be $4.5 \times 10^{-1} \text{ s}^{-1}$.

Table 1. Relative energies (kcal·mol $^{-1}$) calculated at HF/6-31G(d,p), MP2/6-31+G(d,p) and MP2/6-31+G(d,p)+ZPE levels.

	A	B	C	D	E
HF/6-31G(d,p)	0.00	0.85	23.43	27.94	19.54
MP2/6-31+G(d,p)	0.00	0.21			
MP2/6-31+G(d,p)+ZPE	0.00	0.00			
PCM/MP2/6-31+G(d,p)+ZPE ^a	1.55	0.00			
PCM/MP2/6-31+G(d,p)+ZPE ^b	2.24	0.00			

^a solvent CHCl_3 ; ^b solvent DMSO

Table 2. MP2/6-31+G(d,p) calculated total energies (E_T), zero-point energies (ZPE) and total energy in solution (E_{sol}) (a.u.) for tautomers **A** and **B**.

Tautomers	E_T	ZPE	E_{sol}	
	isolated molecule		CHCl_3	DMSO
A	-698.194221	0.077937	-698.275419	-698.277004
B	-698.194216	0.077647	-698.277595	-698.280280

The vibrational spectra of the tautomers **A** and **B** were computed at MP2/6-31+G(d,p) level. Available experimental data for the vibrational frequencies of **A** measured in DMSO are presented for comparison. All results are listed in Table 3. Our assignments for the *ab initio* calculated frequencies are based upon the analysis of the corresponding vibrational eigenvectors. Some modes such as NH, CH, C=O stretching and CH_2 deformation were found to be characteristic. The analysis of the theoretical spectra of the two tautomers shows that the C–S stretching vibrations are also characteristic. They are located in the low frequency region 780–630 cm^{-1} .

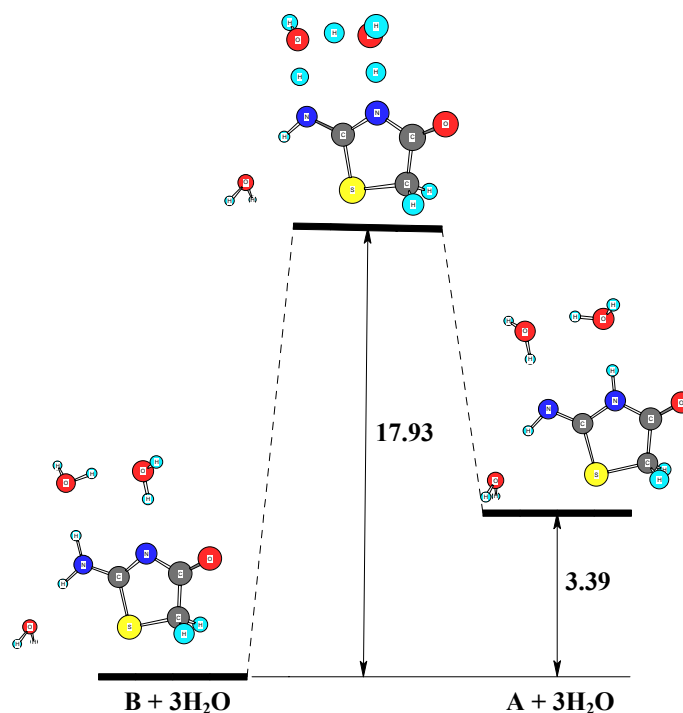


Fig. 2: Energy profile of the tautomerization reactions $\mathbf{B} + 3\mathbf{H}_2\mathbf{O} \rightarrow \mathbf{A} + 3\mathbf{H}_2\mathbf{O}$ of pseudothiohydantoin, calculated at PCM/MP4/6-31+G(d,p)/MP2/6-31+G(d,p) level.

The free energy difference ΔG_{298} and activation barrier ΔG_{298}^\ddagger are given in $\text{kcal}\cdot\text{mol}^{-1}$.

Table 3. MP2/6-31+G(d,p) calculated and experimental IR data for the tautomers **A** and **B** of pseudothiohydantoin. Frequencies, ν , are in cm^{-1} ; intensities, I , are in $\text{km}\cdot\text{mol}^{-1}$.

Tautomer B			Tautomer A		
Calc.	Exptl. ^a	Assignment	Calc.	Assignment	Assignment
ν	I		ν	I	
3568	98	N7–H11 str + N7–H8 str.	3440	90	N4–H8 str.
3429	288	N7–H8 str + N7–H11 str.	3401	20	N7–H11 str.
3068	1108	C–H asym. str.	3046	0	C–H asym. str.
2996	671	C–H sym. str.	2991	5	C–H sym. str.
1687	189	C=O str.	1703	393	C=O str.
1598	721	H8–N7–C3 b. + H11–N7–C3 b. + C3–N7 str.	1609	429	C3–N4 str. + N7C3S2 b.
1532	1342	H11–N7–C3 b. + C3–N4str.	1421	8	CH ₂ def.
1414	1530	CH ₂ def.	1336	90	H8–N4–C3 b + N4–C5 str.
1299	863	C3–N7 str. + H8–N7–C3 b.	1292	155	ring skel.
1193	164	N4–C5 str. + ring def.	1231	59	CH ₂ b + N4–C5 str.
1182	106	H–C–S b. + N4–C5 str.	1187	16	ring skel.
1069	0	H–C–S b. + H–C–S–C tors.	1085	0	CH ₂ def.
1056	160	H11–N7–C3 b. + H8–N7–C3 b.	1034	166	H11–N7–C3 b. + C3–N4 str.
893	117	H–C–S b. + HCSC t	902	6	CH ₂ bend. + ring skel.
814	49	N4–C3–S2 b.	850	1	ring skel.
779	169	C1–S str.	763	8	H11–N7–C3–S2 t.
636	24	C3–S str.	755	38	C1–S str.
593	18	ring def.	647	25	C3–S str.
588	163	ring skel.	576	2	ring def.
528	36	ring def.	546	70	H8–N4–C3–S2 t.
512	15	ring def.	527	42	ring def.
442	183	H8–N7–C3–S2 t + H11–N7–C3–S2 t	496	32	ring def.
439	98	ring skel.	463	38	ring skel.
346	419	ring skel.	346	10	ring skel.
319	30	H11–N7–C3–S2 t + H8–N7–C3–S2 t	151	3	ring skel.
163	471	ring def.	88	0	ring def.
66	187	ring def.	57	4	ring def.

^a DMSO, Ref. [10]

A low intense carbonyl stretching band was calculated at 1687 cm^{-1} for tautomer **B** and was observed at 1660 cm^{-1} in DMSO solution of pseudothiohydantoin (Table 3). This band is calculated to shift up to 1703 cm^{-1} for tautomer **A**. It is a consequence of the lack of conjugation between the imino and carbonyl groups.

The stretching modes of the C=N bond of tautomers **A** and **B** are more complex since there are additional contributions to the skeleton vibration of the ring system. The C=N normal vibrations are calculated at 1598 cm^{-1} and 1609 cm^{-1} for tautomers **B** and **A**, respectively, (Table 3).

The difference between the two frequencies of the C=N bond can be explained by the fact that the bond is exocyclic for tautomer **A** while for tautomer

B it is endocyclic. The same tendency is observed (Table 4) in the trihydrated complexes of **B** + $3\text{H}_2\text{O}$ and **A** + $3\text{H}_2\text{O}$ shown in Fig. 2. However, upon going from gas phase to water complex the frequency of the C=N bond decreases by 36 cm^{-1} for **B** and increases by 17 cm^{-1} for **A**. Most probably this is due to the formation of intermolecular hydrogen bonds. Two new bands at 1687 and 1578 cm^{-1} are observed in D_2O . The first can be assigned to C=O stretching while the second one – to C=N stretching of tautomer **A** that is in accordance with calculated frequencies. There is a good agreement between calculated and experimental data (Table 4). The low intensity of these bands can be explained by the small amount ($>3\%$) of the imino tautomer.

Table 4. MP2/6-31+G(d,p) calculated IR data for tautomers **A** and **B** of pseudothiohydantoin in D_2O and H_2O . Frequencies, ν , are in cm^{-1} and intensities, I , (in brackets) are in $\text{km}\cdot\text{mol}^{-1}$. Potential energy distributions (PED) are in %. Experimental data in D_2O are also given.

Calculated		Experimental		PED, Assignment
ν (I)	ν (I)	ν^a	ν^b	
B + $3\text{H}_2\text{O}$	B + $3\text{D}_2\text{O}$			
3436 (7862)	2542 (4567)			80 (N7–H11) + 19 (N7–H8)
3197 (86)	2325 (8)			16 (N7–H8) + 76 (N7–H11)
1685 (128)	1674 (267)	1667 w	1653	78 (C=O)
1542 (11640)	1566 (1080)	1546 s	1545	44 (C3–N7) + 33 (C3=N4)
A + $3\text{H}_2\text{O}$	A + $3\text{D}_2\text{O}$			
3091 (780)	2458 (271)			91 (N4–H8)
3357 (213)	2279 (399)			89 (N7–H11)
1699 (432)	1692 (362)	1687 vw		81 (C=O)
1626 (412)	1598 (667)	1578 vw		76 (C3–N7) + 11 (C3=N4)

^a our data; ^b Ref. [10]

CONCLUSION

The IR spectrum of pseudothiohydantoin in D_2O indicates the presence of two tautomeric forms. 2-Amino-4-oxo-thiazoline (**B**) dominates while 2-imino-4-oxo-1,3-thiazolidine (**A**) is detected in small amounts near the detection threshold of the method.

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AB INITIO ИЗСЛЕДВАНЕ НА 2,4-ЗАМЕСТЕНИ АЗОЛИДИНИ.
III. ТЕОРЕТИЧНО И ЕКСПЕРИМЕНТАЛНО ИЧ ИЗСЛЕДВАНЕ
НА ПСЕВДОТИОХИДАНТОИН ВЪВ ВОДЕН РАЗТВОР

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(Резюме)

Относителните стабилности на тавтомерите на псевдотиохидантоина са изчислени на ниво MP2/6-31+G(d,p) за изолирани молекули и техните трихидратирани комплекси. Еднократни изчисления на ниво MP4/6-31+G(d,p)//MP2/6-31+G(d,p) са направени за да се получат по-точни енергии.

Теоретично изчисленията на ниво MP2/6-31+G(d,p) ИЧ спектри на тавтомерите на псевдотиохидантоина са сравнени с експериментални данни. Намерено е добро съответствие между *ab initio* предсказанията и експерименталният ИЧ спектър на псевдотиохидантоина.