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## Density functional theory (DFT) calculations of conformational energies and interconversion pathways in 1,2,7-thiadiazepane

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**Abstract:** The molecular structure and conformational analysis of 1,2,7-thiadiazepane conformers were investigated by density functional theory (DFT) calculations at the B3LYP/cc-pVDZ level of theory. Four twist-chair (**TC**), six twist-boat (**TB**), two boat (**B**), two chair (**C**) and four twist (**T**) conformers were identified as minima and transition states for 1,2,7-thiadiazepane. The **TC1** conformer is the most stable conformer and the twist-chair conformers are predicted to be lower in energy than their corresponding boat and chair conformations. DFT predicts a small barrier to pseudo-rotation and a remarkable activation barrier for the conformational interconversion of the twist-chair conformers to their corresponding boat conformers. The simplest conformational process and the one with the lowest barrier is the degenerate interconversion of the twist-chair 3 (**TC3**) conformation with itself *via* the  $C_s$  symmetric chair (**C2**) transition state. The calculated strain energy barrier for this process is 2.41 kJ mol<sup>-1</sup>. The highest conformational interconversion barrier is between **TC2** and twist-boat 3 (**TB3**) forms, which was found to be 75.62 kJ mol<sup>-1</sup>.

**Keywords:** conformational analysis; 1,2,7-thiadiazepane; DFT calculation.

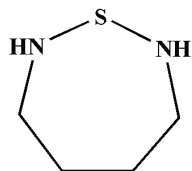
### INTRODUCTION

The chemistry and biological activities of seven-membered heterocyclic compounds has continued to command significant attention in recent years.<sup>1</sup> Cycloheptane and its hetero derivatives (heterocycloheptanes), which are found in Alzheimer drugs, anticancer agents, antimalarials,<sup>2,3</sup> and natural products,<sup>4–8</sup> are important compounds in many areas of science. These compounds can be both fused and non-fused heterocycles, with an emphasis on N, S, and O as the heteroatom in the seven-membered ring components. Many synthetic methods were reported for these compounds in recent decades.<sup>9</sup>

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There are many reports concerning the synthesis and pharmacological activities of cyclic sulfonamide compounds (as heterocycloheptane derivatives).<sup>10–13</sup> These compounds inhibit the HIV protease by affecting its binding to protein.<sup>14–16</sup> Contrary to the abundance of information on the synthesis and pharmacological activities of 7-membered heterocyclic compounds, there is relatively little information available about the conformational properties of these compounds. It is difficult to study experimentally the stereodynamics of compounds containing a seven-membered ring since the conformations are often structurally similar and show complex conformational and pseudo-rotational equilibria with low barriers among the chair (**C**), twist chair (**TC**), boat (**B**), and twist-boat (**TB**) conformations and transition states.

As a continuation of our interest in the conformations of medium ring sized heterocycles,<sup>17–20</sup> this study was undertaken in order to investigate the conformational analysis of 1,2,7-thiadiazepane (Scheme 1) by computational methods to determine their preferred conformers. The effects of changes in bond length, bond angle and torsion angle of these compounds were also of interest. Therefore, the density functional theory (DFT) method was applied in this work to calculate the molecular structures, energy differences and conformational interconversion pathways of 1,2,7-thiadiazepane conformers at the B3LYP/cc-pVDZ//B3LYP/cc-pVDZ level (full optimization).



Scheme 1. Schematic representation of 1,2,7-thiadiazepane.

#### COMPUTATIONAL DETAILS

In the present study, the density functional theory method was used to optimize the conformations of 1,2,7-thiadiazepane. The Becke three-parameter exact exchange functional (B3)<sup>21</sup> combined with the gradient-corrected correlation functional of Lee–Yang–Parr (LYP)<sup>22</sup> of DFT methods, implementing the cc-pVDZ basis set was employed to optimize the molecules.

The nature of the optimized geometries at the B3LYP level was checked with frequency calculations. The vibrational frequencies were calculated at the cc-pVDZ level for all minimum energies and transition states, which were confirmed to have zero and one imaginary frequency, respectively. All calculations were performed using the Gaussian 2003W computational package.<sup>23</sup>

#### RESULTS AND DISCUSSION

The results of the density functional theory (B3LYP/cc-pVDZ//B3LYP/cc-pVDZ) calculations showed that twenty two geometries, of which eleven were energy minima, were important in the description of the conformational pro-

properties of 1,2,7-thiadiazepane (**1**). There are eleven transition states which are required to describe the dynamic conformational properties of compound **1**. Corrected zero point ( $ZPE^\circ$ ) and total electronic ( $E_{el}$ ) energies ( $E^\circ = E_{el} + ZPE^\circ$ ) for conformations of compound **1** are given in Table I. The energy surfaces for the interconversion of the energy-minimum conformers were obtained by changing different torsional angles, as shown in Figs. 1 and 2. The energy minima and transition state geometries are shown in Schemes 2 and 3, respectively.

TABLE I. Calculated total, zero-point vibrational energies and relative energies between the most stable minimum stereoisomers and transition states

B3LYP/cc-pVDZ///	B3LYP/cc-pVDZ, Hartree	$ZPE^\circ$ , Hartree	$E_{rel}$ / kJ mol <sup>-1</sup>
<b>TC1</b>	-666.133904	0.147023	0
<b>TC3</b>	-666.1325829	0.147161	3.83
<b>C2</b>	-666.1316392	0.147009	5.91
<b>C4</b>	-666.1313194	0.146932	6.53
<b>TC2</b>	-666.130937	0.146846	7.33
<b>TC4</b>	-666.1306823	0.146799	7.88
<b>TC5</b>	-666.1315934	0.147977	8.54
<b>C1</b>	-666.1285964	0.146740	13.2
<b>C3</b>	-666.1264443	0.146967	19.44
<b>TB1</b>	-666.1268317	0.147617	20.11
<b>TB3</b>	-666.1244648	0.147199	25.24
<b>B3</b>	-666.1248174	0.147561	25.25
<b>TB4</b>	-666.1241074	0.147335	26.53
<b>TB5</b>	-666.1239418	0.147215	26.65
<b>TB2</b>	-666.122806	0.147186	29.56
<b>B2</b>	-666.1222725	0.147020	30.53
<b>TB6</b>	-666.1205977	0.147129	35.21
<b>B1</b>	-666.118878	0.147375	40.36
<b>T4</b>	-666.1167305	0.146650	44.12
<b>T2</b>	-666.1165628	0.147106	45.75
<b>T3</b>	-666.1075709	0.147107	69.36
<b>T1</b>	-666.1027653	0.144662	75.624

#### *Molecular structures of 1,2,7-thiadiazepane conformers*

Conformational studies of 1,2,7-thiadiazepane revealed some minima and transition states with similar energies and geometries among the twist-chair, chair, boat, twist-boat and twist conformations and transition states. The S and N atoms occupy positions which avoid transannular hydrogen–hydrogen steric and the lone pair–lone pair interactions. The geometrical parameters of 1,2,7-thiadiazepane conformers were calculated and are presented in Tables II and III. Five twist-chair (**TC**), six twist-boat (**TB**), three boat (**B**), four chair (**C**) and four twist (**T**) conformers were identified as minima and transition states for compound **1** (Schemes 2 and 3). The possible minima forms are: **TC1–TC5** for the twist-chair

structure, **C1–C4** for the chair structure, **B1–B3** for the boat structure, **TB1–TB6** for the twist-boat structure and **T1–T4** for twist structure. The **TC1** conformer is the most stable, with the highest dihedral angles of  $\varphi_4$  and  $\varphi_7$  (Table II) of the minimum conformers. In the **TC5** conformer, the dihedral angles of  $\varphi_2$  and  $\varphi_6$  (which geometrically correspond to  $\varphi_4$  and  $\varphi_7$  of **TC1**) were increased in comparison with the others. The lowest value of the dihedral angle of  $\varphi_7$  was observed in the **TB2** conformer and  $\varphi_1$  was decreased in the **TB6** structure. While the dihedral angle of  $\varphi_5$  in the **TB1** conformer and  $\varphi_4$  in the **B3** conformer were decreased, these dihedral angles have the highest values in the **TC3** and **TC1** conformers, respectively. The **TC2** conformer has the highest value of dihedral angle of  $\varphi_3$  which is decreased in the **TB1** conformer.

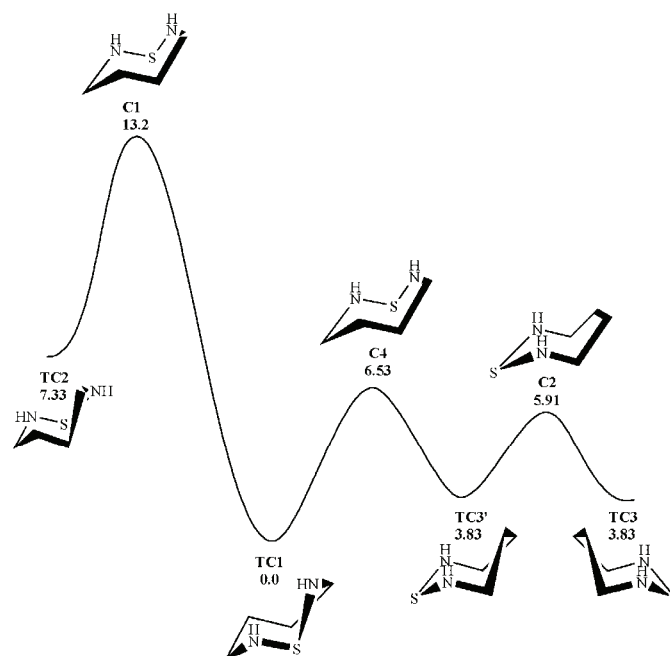


Fig. 1. Calculated B3LYP/cc-pVDZ// B3LYP/cc-pVDZ strain energy ( $\text{kJ mol}^{-1}$ ) profiles for the conformational interconversion of the twist-chair family of 1,2,7-thiadiazepane.

Comparison between the calculated bond angles indicated that  $\theta_1$  ( $110.90^\circ$ ) in the **TC4**,  $\theta_6$  ( $117.54^\circ$ ) in the **TC2**,  $\theta_7$  ( $122.71^\circ$ ) in the **TC1**,  $\theta_5$  ( $117.89^\circ$ ) and  $\theta_3$  ( $117.93^\circ$ ) in the **TC3** and  $\theta_2$  ( $119.64^\circ$ ) in the **TB3** conformers were wider than the corresponding bond angles of the other conformers (stereo-electronic effects). B3LYP/cc-pVDZ calculations predicted that the bond length of  $\text{N}_1\text{--S}$  was the shortest and the bond length of  $\text{N}_2\text{--S}$  was the longest in the **TB5** conformer, while in the **TB2** conformer, the bond distance of  $\text{N}_1\text{--S}$  was the longest and  $\text{N}_2\text{--S}$  was the shortest.

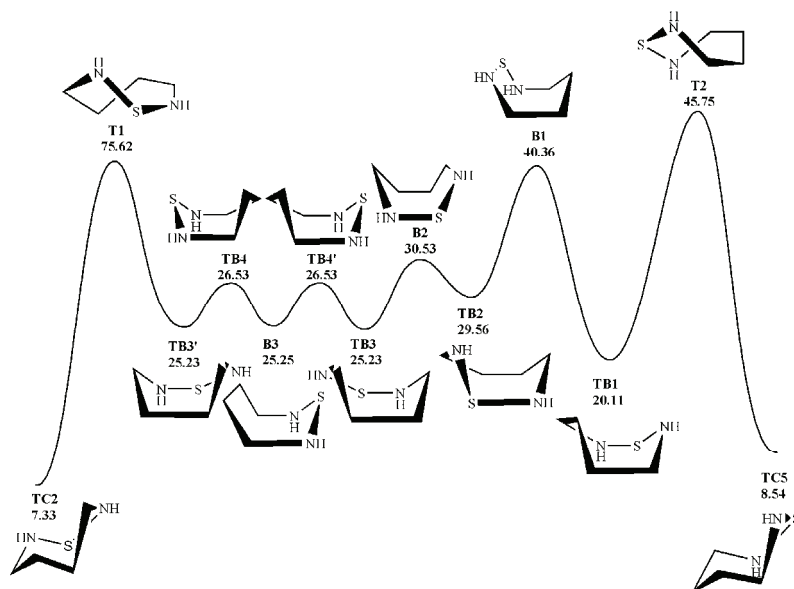
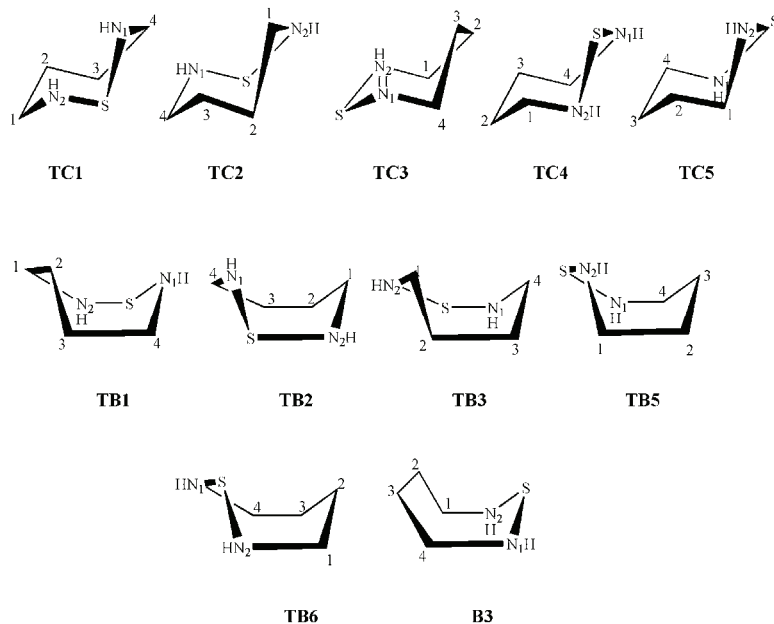
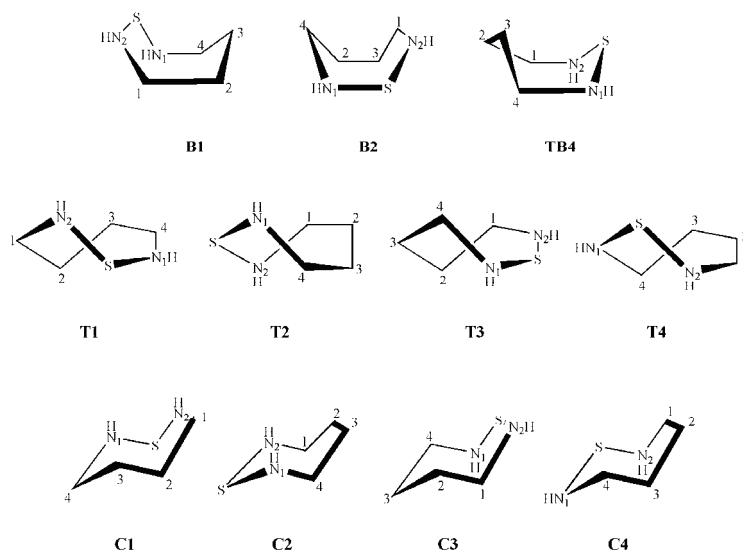


Fig. 2. Calculated B3LYP/cc-pVDZ// B3LYP/cc-pVDZ strain energy ( $\text{kJ mol}^{-1}$ ) profiles for the conformational interconversion of the twist-boat geometries of 1,2,7-thiadiazepane.



Scheme 2. The various minimum conformations of 1,2,7-thiadiazepane.

The bond lengths tend to depend more on the type of bond and the dihedral angles depend more on the conformation of the molecule.



Scheme 3. The transition state conformations of 1,2,7-thiadiazepane.

### Conformational analysis

The results of the DFT calculations showed that there are eleven minima (twist-chair, **TC1**, **TC2**, **TC3**, **TC4** and **TC5**; twist-boat, **TB1**, **TB2**, **TB3**, **TB4** and **TB5**; boat, **B1**) and eleven transition states (chair, **C1**, **C2**, **C3** and **C4**; twist, **T1**, **T2**, **T3** and **T4**; twist-boat, **TB6**; boat, **B2** and **B3**) in the 1,2,7-thiadiazepane conformations (Schemes 2 and 3). The conformational interconversion pathways and structure optimization of **1** are shown in Figs. 1 and 2 and Tables II and III. The most stable conformation of **1** is the unsymmetrical **TC1** form, which by changing the twist of S–N<sub>1</sub>C<sub>4</sub>C<sub>3</sub> the **TC2** conformer was formed (7.33 kJ mol<sup>-1</sup>) (Fig. 1). The structure of the transition state was obtained from the QST3 sub-routine using the optimized geometries of the **TC1** and **TC2** conformations. The calculated energy barrier for interconversion of these two conformers occurs *via* the unsymmetrical chair (**C1**) as the transition state. The second energy minimum conformation of **1** is twist-chair 3 (**TC3**), which is higher in energy than **TC1** by 3.83 kJ mol<sup>-1</sup>. The degenerate interconversion of **TC3** with its mirror image occurs *via* the C<sub>s</sub> symmetric chair 2 (**C2**), as the transition state. Moreover, the **TC3** conformation could transform *via* chair 4 (**C4**) to **TC1**. The strain energy barrier for this process is 6.53 kJ mol<sup>-1</sup>.

The twist-chair 4 (**TC4**) is another energy-minimum structure, which was found to be less stable than the **TC1** conformer by 7.88 kJ mol<sup>-1</sup> and more stable than twist-chair 5 (**TC5**), which has the opposite twist in the C–N–S–N angle in the ring (see Scheme 2). The transition state linking **TC5** and **TC4** is the unsymmetrical chair 3 (**C3**) with the calculated strain energy barrier for this process being 19.44 kJ mol<sup>-1</sup> (Fig. 3).

TABLE II. Calculated geometrical parameters for the minimum conformers of 1,2,7-thiadiazepane (1)

Bond	TC1	TC2	TC3	TC4	TC5	TB1	TB2	TB3	TB5	TB6	B3
$r / \text{\AA}$											
N <sub>1</sub> -S ( $r_1$ )	1.709	1.717	1.728	1.737	1.736	1.734	1.780	1.754	1.703	1.700	1.722
S-N <sub>2</sub> ( $r_2$ )	1.730	1.733	1.719	1.715	1.736	1.734	1.708	1.704	1.798	1.752	1.722
N <sub>2</sub> -C <sub>1</sub> ( $r_3$ )	1.464	1.478	1.464	1.465	1.466	1.463	1.489	1.481	1.467	1.472	1.477
C <sub>1</sub> -C <sub>2</sub> ( $r_4$ )	1.541	1.532	1.547	1.537	1.541	1.564	1.535	1.531	2.628	1.538	1.533
C <sub>2</sub> -C <sub>3</sub> ( $r_5$ )	1.541	1.544	1.546	1.543	1.538	1.539	1.546	1.557	1.537	1.539	1.564
C <sub>3</sub> -C <sub>4</sub> ( $r_6$ )	1.536	1.537	1.544	1.532	1.541	1.564	1.533	1.534	1.536	1.532	1.533
C <sub>4</sub> -N <sub>1</sub> ( $r_7$ )	1.473	1.465	1.468	1.478	1.466	1.463	1.470	1.471	1.471	1.487	1.477
$\theta / ^\circ$											
N <sub>1</sub> -S-N <sub>2</sub> ( $\theta_1$ )	108.89	110.86	109.54	110.90	108.58	107.77	107.05	108.02	107.63	107.79	108.57
S-N <sub>2</sub> -C <sub>1</sub> ( $\theta_2$ )	117.95	121.84	116.92	116.40	118.76	118.13	118.86	120.45	113.92	115.67	117.58
N <sub>2</sub> -C <sub>1</sub> -C <sub>2</sub> ( $\theta_3$ )	117.56	116.06	117.93	117.53	114.05	116.65	115.00	113.75	117.19	116.89	113.91
C <sub>1</sub> -C <sub>2</sub> -C <sub>3</sub> ( $\theta_4$ )	114.82	115.01	118.33	116.64	117.85	114.55	116.99	116.61	116.29	116.49	117.89
C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub> ( $\theta_5$ )	116.49	116.62	118.61	114.89	117.85	114.55	117.08	117.75	116.36	114.67	117.89
C <sub>3</sub> -C <sub>4</sub> -N <sub>1</sub> ( $\theta_6$ )	116.89	117.54	115.01	116.00	114.05	116.65	115.79	114.79	115.45	113.11	113.91
C <sub>4</sub> -N <sub>1</sub> -S ( $\theta_7$ )	112.71	116.38	117.58	121.47	118.76	118.13	114.55	114.47	120.52	119.28	117.58
$\phi / ^\circ$											
N <sub>1</sub> -S-N <sub>2</sub> -C <sub>1</sub> ( $\phi_1$ )	66.69	43.16	66.51	-76.06	38.85	-45.06	-71.74	65.45	-15.00	-15.00	-53.52
S-N <sub>2</sub> -C <sub>1</sub> -C <sub>2</sub> ( $\phi_2$ )	-56.91	22.68	-82.92	66.19	-84.86	61.88	11.16	7.13	75.43	-62.31	-29.03
N <sub>2</sub> -C <sub>1</sub> -C <sub>2</sub> -C <sub>3</sub> ( $\phi_3$ )	68.95	-81.10	36.51	-58.15	71.78	20.68	65.88	-69.85	-29.43	46.58	71.40
C <sub>1</sub> -C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub> ( $\phi_4$ )	-88.94	80.84	39.44	79.99	-54.32	-80.25	-35.00	20.35	-61.64	50.30	-0.01
C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub> -N <sub>1</sub> ( $\phi_5$ )	52.66	-58.71	-85.53	-82.62	71.78	20.69	-59.51	68.93	50.30	-69.04	-71.40
C <sub>3</sub> -C <sub>4</sub> -N <sub>1</sub> -S ( $\phi_6$ )	22.68	65.55	71.50	25.52	-84.86	61.87	60.21	-50.37	40.88	-16.42	29.05
C <sub>4</sub> -N <sub>1</sub> -S-N <sub>2</sub> ( $\phi_7$ )	-70.66	-75.84	-50.95	41.10	38.84	-45.07	23.35	-35.00	-64.19	71.14	53.50

TABLE III. Calculated geometrical parameters for the transition states conformers of 1,2,7-thiadiazepane (I)

Bond	C1	C2	C3	C4	T1	T2	T3	T4	B1	B2	TB4
	<i>r</i> / Å										
N <sub>1</sub> -S ( <i>r</i> <sub>1</sub> )	1.755	1.721	1.695	1.727	1.678	1.733	1.705	1.697	1.727	1.746	1.720
S-N <sub>2</sub> ( <i>r</i> <sub>2</sub> )	1.696	1.721	1.810	1.717	1.728	1.733	1.751	1.742	1.718	1.708	1.739
N <sub>2</sub> -C <sub>1</sub> ( <i>r</i> <sub>3</sub> )	1.485	1.466	1.467	1.462	1.482	1.461	1.489	1.474	1.470	1.489	1.475
C <sub>1</sub> -C <sub>2</sub> ( <i>r</i> <sub>4</sub> )	1.536	1.540	1.545	1.563	1.572	1.559	1.535	1.530	1.550	1.532	1.534
C <sub>2</sub> -C <sub>3</sub> ( <i>r</i> <sub>5</sub> )	1.544	1.561	1.536	1.539	1.536	1.566	1.537	1.551	1.537	1.549	1.566
C <sub>3</sub> -C <sub>4</sub> ( <i>r</i> <sub>6</sub> )	1.534	1.540	1.533	1.544	1.540	1.559	1.558	1.566	1.533	1.539	1.532
C <sub>4</sub> -N <sub>1</sub> ( <i>r</i> <sub>7</sub> )	1.467	1.466	1.465	1.464	1.459	1.461	1.460	1.474	1.475	1.472	1.480
	$\theta$ / °										
N <sub>1</sub> -S-N <sub>2</sub> ( $\theta$ <sub>1</sub> )	102.64	109.01	109.67	109.12	103.75	106.32	112.33	107.25	107.96	107.92	109.85
S-N <sub>2</sub> -C <sub>1</sub> ( $\theta$ <sub>2</sub> )	120.09	117.31	116.84	119.14	126.07	115.02	125.60	115.67	116.52	119.04	115.70
N <sub>2</sub> -C <sub>1</sub> -C <sub>2</sub> ( $\theta$ <sub>3</sub> )	117.35	116.48	118.26	119.41	120.48	118.01	120.30	111.90	117.24	112.19	113.69
C <sub>1</sub> -C <sub>2</sub> -C <sub>3</sub> ( $\theta$ <sub>4</sub> )	117.01	119.90	116.94	118.68	122.56	122.68	117.65	117.43	116.36	115.37	116.72
C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub> ( $\theta$ <sub>5</sub> )	116.91	119.90	115.99	116.34	115.99	122.68	115.42	122.61	116.36	118.34	116.23
C <sub>3</sub> -C <sub>4</sub> -N <sub>1</sub> ( $\theta$ <sub>6</sub> )	111.24	116.48	114.67	116.50	112.12	118.00	115.24	120.79	115.37	118.64	113.36
C <sub>4</sub> -N <sub>1</sub> -S ( $\theta$ <sub>7</sub> )	113.89	117.31	120.97	117.97	117.06	115.02	119.35	122.36	120.23	116.31	118.52
	$\varphi$ / °										
N <sub>1</sub> -S-N <sub>2</sub> -C <sub>1</sub> ( $\varphi$ <sub>1</sub> )	-62.27	-58.00	-2.22	75.27	-29.33	-46.22	0.81	-43.10	5.00	-68.29	-42.52
S-N <sub>2</sub> -C <sub>1</sub> -C <sub>2</sub> ( $\varphi$ <sub>2</sub> )	-2.22	82.09	64.45	-63.90	-19.99	83.38	8.23	-40.44	72.11	-3.93	-42.30
N <sub>2</sub> -C <sub>1</sub> -C <sub>2</sub> -C <sub>3</sub> ( $\varphi$ <sub>3</sub> )	70.52	-65.46	-86.83	-2.22	-4.54	-24.70	-69.12	90.91	-36.21	76.52	74.24
C <sub>1</sub> -C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub> ( $\varphi$ <sub>4</sub> )	-81.45	0.00	63.55	68.15	71.07	-19.17	72.50	-36.34	-53.19	-37.00	13.16
C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub> -N <sub>1</sub> ( $\varphi$ <sub>5</sub> )	61.77	65.46	-61.78	-84.26	-49.01	-24.70	9.11	-12.39	55.71	-52.54	-74.79
C <sub>3</sub> -C <sub>4</sub> -N <sub>1</sub> -S ( $\varphi$ <sub>6</sub> )	-73.71	-82.09	83.95	62.50	-45.00	83.38	-78.69	-22.08	32.54	43.73	25.88
C <sub>4</sub> -N <sub>1</sub> -S-N <sub>2</sub> ( $\varphi$ <sub>7</sub> )	91.41	58.00	-64.50	-55.34	88.74	-46.22	56.66	75.75	-66.74	37.17	54.06



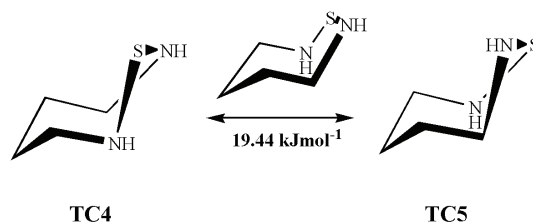


Fig. 3. The strain energy barrier for the conformational interconversion of **TC4** and **TC5**.

The results of calculations showed that there are a number of twist-boat conformations, which are energy minima in the pseudorotation pathways and are also higher in energy than the twist-chair conformers. The most stable conformer in the twist-boat family is twist boat 1 (**TB1**), which is 20.11 kJ mol<sup>-1</sup> higher in energy than **TC1** (the most stable conformer of the twist-chair family) (Table I).

The **TB1** conformer can be related to the twist-boat 2 (**TB2**) geometry *via* the unsymmetrical boat conformer (**B1**), requiring an energy of 40.36 kJ mol<sup>-1</sup> (Fig. 2) Moreover, by changing the C–C–N–S twist in the **TB2** conformer, it could be converted to twist-boat 3 (**TB3**) *via* the unsymmetrical boat form (**B2**). The calculated strain energy barrier for this process is 30.53 kJ mol<sup>-1</sup>. The degenerate interconversion of **TB3** with its mirror image could occur *via* the unsymmetrical twist-boat 4 (**TB4**) as the transition state, as well as the *C<sub>s</sub>* symmetric boat 3 (**B3**) geometry as a local minimum. Moreover, the twist-boat 5 (**TB5**), as another minimum conformation, could be converted to twist-boat 6 (**TB6**) *via* **B1** as the transition state.

The results of the B3LYP/cc-pVDZ calculations for the conformational interconversion pathways showed that the twist-chair families can be related to the boat families *via* twist conformers as the transition states. The **TC1** geometry could be converted to **B3** *via* twist 1 (**T1**) as the transition state, for which the strain energy barrier is 75.62 kJ mol<sup>-1</sup>. The **TB2** conformer, from the twist boat family, could be converted to twist chair conformations *via* two conformational processes. The simplest conformational process is the interconversion of the **TB1** and **TC5**, *via* the *C<sub>2v</sub>* symmetric twist 2 (**T2**) as the transition state, which requires 45.75 kJ mol<sup>-1</sup> (Fig. 2). The second (high-energy) process involves the conformational interconversion of the **TB1** and **TC3** forms that occurs *via* the unsymmetrical twist 3 (**T3**) as the transition state (Fig. 4). The strain energy barrier for this process is 69.36 kJ mol<sup>-1</sup>. On the other hand, the **TC2** conformation could transform *via* twist geometry 4 (**T4**) to the **B3** geometry with an energy barrier to interconversion of 44.12 kJ mol<sup>-1</sup> (Fig. 5).

As can be seen from the results of DFT in Table I and Figs. 1 and 2, the twist-chair conformer (**TC1**) is lower in energy than the boat and twist-boat conformers, and the chair transition states (**C1**, **C2**, **C3** and **C4**) are lower in energy than the boat and twist-boat conformers. Based on the energetic results, it could

be concluded that, among the various conformations of compound **1**, the twist-chair and chair conformers are the most important forms, as they could be significantly populated at room temperature.

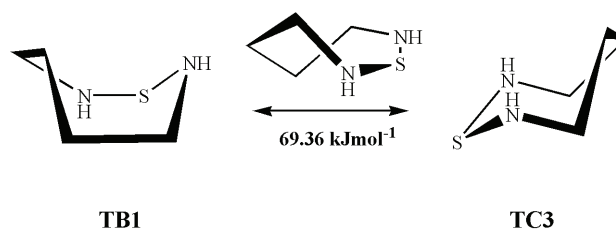


Fig. 4. The strain energy barrier for the conformational interconversion of **TB1** and **TC3**.

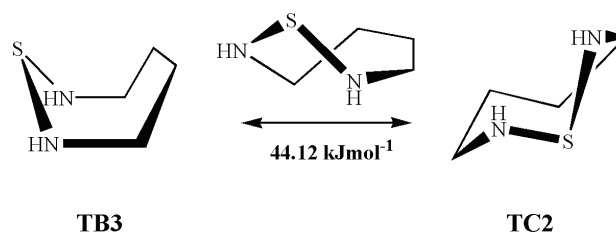


Fig. 5. The strain energy barrier for the conformational interconversion of **B3** and **TC2**.

#### CONCLUSIONS

The stability of 1,2,7-thiadiazepane conformers were studied by DFT calculations. Four chair, five twist-chair, three boat, six twist-boat and four twist conformers were identified as minima and transition states for 1,2,7-thiadiazepane. Among the various conformations of compound **1**, the unsymmetrical **TC1** form was found to be the most stable geometry, the **TC3** form, as the second lowest energy minimum, has the simplest conformational process, with the lowest energy barrier, namely the degenerate interconversion of **TC3** with itself *via* the  $C_s$  symmetric chair (**C2**) transition state. The results of the calculations showed that the twist-chair and chair conformers are more stable than the twist-boat conformers, as the minimum energy conformation of twist-boat family is  $20.11 \text{ kJ mol}^{-1}$  less stable than the lowest energy form (**TC1**) of **1**. Therefore the twist-chair conformations are the most important because they are expected to be significantly populated at room temperature.

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## ИЗВОД

## РАЧУНАЊЕ ЕНЕРГИЈЕ КОНФОРМЕРА 1,2,7-ТИАДИАЗЕПАНА И ПУТЕВА ЗА ЊИХОВУ ИНТЕРКОНВЕРЗИЈУ DFT МЕТОДОМ

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Помоћу DFT израчунавања истраживана је молекулска структура и конформације 1,2,7-тијадиазепана, на нивоу теорије B3LYP/cc-pVDZ. Идентификоване су четири конформације облика увијене столице (*twist chair*, **ТС**), шест облика увијене лађе (*twist boat*, **ТВ**), две облика лађе (*boat*, **В**), две облика столице (*chair*, **С**) и четири увијене (*twist*, **Т**) као енергетски минимуми или прелазна стања 1,2,7-тијадиазепана. Конформер **ТС1** је најстабилнији, док је за конформере **ТВ** предвиђено да имају нижу енергију од **В** и **С** конформација. DFT предвиђа малу баријеру за псеудоротацију али знатну активациону баријеру за интерконверзију **ТС** конформера у **В** конформере. Најједноставнији процес, онај с најнижом баријером, јесте дегенерисана интерконверзија конформера **ТС3** у самог себе преко  $C_2$ -симетричног прелазног стања облика **С2**. Израчуната енергетска баријера за овај процес је  $2,41 \text{ kJ mol}^{-1}$ . Највиша баријера је за интерконверзију **ТС2** у **ТВ3** форму, и нађена је да износи  $75,62 \text{ kJ mol}^{-1}$ .

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## REFERENCES

1. J. A. Smith, P. P. Molesworth, J. H. Ryan, *Prog. Heterocycl. Chem.* **21** (2009) 491
2. H.-X. Jin, Q. Zhang, H.-S. Kim, Y. Wataya, H.-H. Liu, Y. Wu, *Tetrahedron* **62** (2006) 7699
3. K. J. McCullough, M. Nojima, *Curr. Org. Chem.* **5** (2001) 601
4. J. G. Rodriguez, A. Perales, *J. Nat. Prod.* **58** (1995) 564
5. A. F. Barrero, M. M. Herrador, J. M. Molina, J. F. Quilez, M. Quiros, *J. Nat. Prod.* **57** (1994) 873
6. J. J. Piwinski, J. K. Wong, T. M. Chan, M. J. Green, A. K. Ganguly, *J. Org. Chem.* **55** (1990) 3341
7. A. Romo de Vivar, G. Delgado, M. Soriano-Garcia, R. A. Toscano, E. Huerta, R. G. Reza-Garduno, *J. Nat. Prod.* **50** (1987) 284
8. K. C. Nicolaou, F. P. J. T. Rutjes, E. A. Theodorakis, J. Tiebes, M. Sato, E. Untersteller, *J. Am. Chem. Soc.* **117** (1995) 1173
9. a) O. V. Denisko, *Comprehensive Heterocyclic Chemistry III*, Elsevier, Oxford, 2008, p. 489; b) G. I. Yranzo, E. L. Moyano *Comprehensive Heterocyclic Chemistry III*, Elsevier, Oxford, 2008, p. 399; c) A. Kiselyov, A. Khvat *Comprehensive Heterocyclic Chemistry III*, Elsevier, Oxford, 2008, p. 387; d) R. Kumar, S. Perumal, M. Balasubramanian *Comprehensive Heterocyclic Chemistry III*, Elsevier, Oxford, 2008, p. 433; e) T. Tsuchiya, *Comprehensive Heterocyclic Chemistry II*, Elsevier, Oxford, 1996, p. 299; f) J. T. Sharp, *Comprehensive Heterocyclic Chemistry*, Elsevier, Oxford, 1984, p. 593
10. J. Hultn, H. O. Andersson, W. Schaal, H. U. Danielson, B. Classon, I. Kvarnstrm, A. Karln, T. Unge, B. Samuelsson, A. Hallberg, *J. Med. Chem.* **42** (1999) 4054
11. D. Giannotti, J. G. Viti, P. Sbraci, V. Pestellini, G. Volterra, F. Borsini, A. Lecci, A. Meli, P. Dapporto, P. Paolio, *J. Med. Chem.* **34** (1991) 1356
12. N. Lebegue, S. Gallet, N. Flouquet, P. Carato, B. Pfeiffer, P. Renard, S. Léonce, A. Pierre, P. Chavatte, P. Berthelot, *J. Med. Chem.* **48** (2005) 7363

13. W. Schaal, A. Karlsson, G. Ahlsèn, J. Lindberg, H. O. Andersson, U. H. Danielson, B. Classon, T. Unge, B. Samuelsson, J. Hultèn, A. Hallberg, A. Karlèn, *J. Med. Chem.* **44** (2001) 155
14. R. F. Kaltenbach, D. A. Nugiel, P. Y. S. Lam, R. M. Klabe, S. P. Seitz, *J. Med. Chem.* **41** (1998) 5113
15. K. Bäckbro, S. Löwgren, K. Österlund, J. Atepo, T. Unge, *J. Med. Chem.* **40** (1997) 898
16. J. Hultn, N. M. Bonham, U. Nillroth, T. Hansson, G. Zuccarello, A. Bouzide, J. Qvist, B. Classon, U. H. Danielson, A. Karln, I. Kvarnstrm, B. Samuelsson, A. Hallberg, *J. Med. Chem.* **40** (1997) 885
17. M. Haghdadi, M. Hamzehlouiyian, *Chin. J. Chem.* **26** (2008) 1
18. M. Haghdadi, *Asian J. Chem.* **20** (2008) 3331
19. I. Yavari, M. Haghdadi, R. Amiry, *Phosphorus, Sulfur Silicon Relat. Elem.* **181** (2006) 1693
20. I. Yavari, M. Haghdadi, R. Amiry, *Phosphorus, Sulfur Silicon Relat. Elem.* **181** (2006) 2163
21. A. D. Beke, *Phys. Rev. A* **38** (1998) 3098
22. C. Lee, Y. Wang, R. G. Parr, *Phys. Rev. B* **37** (1988) 785
23. *Gaussian 98, Revision A. 6*, Gaussian. Inc., Pittsburgh, PA, 2003.