

# Quantum chemical investigation of intramolecular thione-thiol tautomerism of 1,2,4-triazole-3-thione and its disubstituted derivatives

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**Abstract** The one step intramolecular thione-thiol tautomerism of 1,2,4-triazole-3-thione and its disubstituted derivatives has been studied through the use of electronic structure methods. Due to the absence of experimental data for the parent molecule of 1,2,4-triazole-3-thione the structure and energetics of aforementioned tautomers were derived using various basis sets and levels including HF, B3LYP, and MP2 methods. The gas phase results show that in all different levels of theory the most stable tautomer is the thione form. It has also been revealed that B3LYP/6-31G(d,p) level is quite well suited and reliable to investigate these kinds of tautomerism. To account the influence of substituents on the mentioned tautomerization, the tautomerism and conformational properties as well as vibrational analysis of 20 halophenyl and isopyridyl derivatives were investigated using B3LYP/6-31G(d,p) calculations. In all cases the calculations indicate that substituents have no considerable effects on relative stabilities and energy barriers for the thione-thiol proton transfer and the thione forms are the predominant species in the gas phase. In order to figure out the relative stabilities of the species involved in the tautomerism, geometrical and natural bond orbital (NBO) analyses have been employed. It has also been shown that the computed vibrational frequencies of tautomers with different scaling factors could

be used to interpret the vibrational frequencies in IR spectrum of similar species.

**Keywords** *Ab initio* · DFT · NBO analysis · Prototropic tautomerism · Thione–thiol · 1,2,4-triazole-3-thione

## Introduction

1,2,4-triazole derivatives have been shown to possess broad-spectrum biological activities [1–6]. It has been found that the disubstituted 1,2,4-triazole derivatives have much more biological activity than the parent molecule [7, 8]. Furthermore, presence of a sulfur atom at the 3-position of 1,2,4-triazole is essential to enhance various types of biological activities [9]. It has also been reported that combination of two or more heterocyclic and non-heterocyclic systems enhances the biological properties many-fold over the parent molecule [2, 3]. Because of conclusive evidences on significant biological activities of pyridyl group bearing 5-substituted 1,2,4-triazole-3-thiones synthesis of the substituted derivatives of 1,2,4-triazole-3-thione have been of interest [10]. For instance, Iqbal and coworkers have reported the preparation of various substituted 1,2,4-triazole-3-thiones involving benzyl and pyridyl groups [11–18]. A common question has dealt extensively with intramolecular tautomerization encountered in such structures [19–21]. These compounds can exist in two major tautomeric forms that exhibit different reactivities [1–9, 11–18]. For this reason, in the IR spectrum of experimental reports on synthesizing derivatives of the 2,4-dihydro-4-(4-halophenyl)-5-(pyridyl)-3H-1,2,4-triazole-3-thione authors point out the observation of no S-H absorption explicitly [12]. Absence of S-H and presence of N-H and C=S absorption frequencies result in the

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isolation of thione tautomer rather than thiol form. The same result has been observed on the synthesis of 2,4-dihydro-4-(2-phenylethyl)-5-(isomeric-pyridyl)-3H-1,2,4-triazole-3-thione [11]. On the contrary, in another report on the preparation of 4-(2-chlorobenzyl)-5-phenyl-1,2,4-triazole-3-thione and its derivatives products have been reported both as thione and thiol forms [22]. However, the thione-thiol tautomerism of these compounds remains as a matter of controversy, because it is not straightforward to determine which of the two forms is present. The prototropic tautomerism of 1,2,4-triazole-3-thione parent and its disubstituted derivatives containing benzyl and pyridyl groups is of great importance in many areas of chemistry and biochemistry [1–22]. The knowledge of the relative stabilities of tautomeric forms as well as of the conversion from one tautomeric form to another is also important from the point of view of structural chemistry. In addition, knowing how the tautomerization energies change in various derivatives gives an insight into the influence of substituents on molecular stability and reactivity. Therefore, it is worth studying the possibility of tautomerization in the parent molecule of 1,2,4-triazole-3-thione and its disubstituted derivatives [12] using high accuracy methods. To reach this goal, the thione-thiol prototropic tautomerization in 1,2,4-triazole-3-thione has been investigated through an intramolecular one step mechanism using various electronic structure methods including HF, B3LYP, and MP2 methods. Subsequently, to evaluate the effect of substituents, the tautomerization of the halophenyl and isopyridyl derivatives of 1,2,4-triazole-3-thione has been investigated using B3LYP method. The results of quantum chemical calculations of prototropic tautomerization are discussed from energy, geometry, and NBO analysis point of views.

## Computational details

### Methods

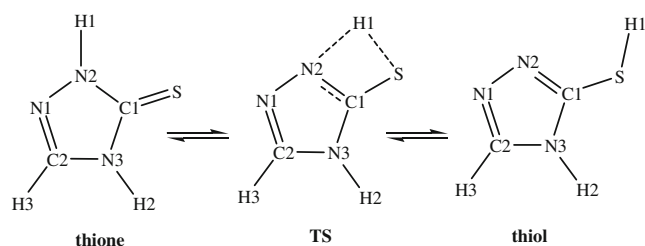
Full geometry optimizations for all tautomers were carried out at the Hartree-Fock (HF), B3LYP density functional [23–25], and second order Møller–Plesset (MP2) [26, 27] levels for parent molecule of 1,2,4-triazole-3-thione and B3LYP for its derivatives. All calculations were performed with a legally licensed version of the GAUSSIAN 98 program [28] using facilities at the institute of postgraduate studies, University of Malaya, Kuala Lumpur, Malaysia. The corresponding harmonic vibrational frequencies were evaluated at the same level of theory to verify that all structures found corresponded to local minima of the potential energy surface (PES). A similar procedure was adopted to locate the transition states (TS) associated with prototropic tautomerization processes. The natural bond

orbital (NBO) analysis has been used to obtain the lone pair hybridization and second order interaction energies ( $\Delta E_i^{(2)}$ ) [29, 30].

### Determining the computational level for parent molecule of 1,2,4-triazole-3-thione

As shown in Fig. 1, for the parent molecule of 1,2,4-triazole-3-thione, two tautomeric forms may exist: the thione (NH) and thiol (SH) forms; The first with a C1=S double bond and latter with the endocyclic double bond C1=N2. There is no crystallographic data on the structure of these species. It is the choice of basis set and method that ultimately determines the accuracy of a calculation. Therefore, the geometry of 1,2,4-triazole-3-thione and its thiol form has been optimized using HF, B3LYP, and MP2 methods and employing various basis sets [31, 32] including Pople's 6-31G, 6-31G(d), 6-31G(d,p), 6-31+G(d,p), 6-31++G(d,p), 6-311G(d,p), 6-311+G(d,p), 6-311++G(d,p) basis sets and Dunning's [33, 34] CC-PVDZ, CC-PVTZ, CC-PVQZ basis sets. Energy calculations were also performed using the same considerable expansion of basis sets to determine the optimum level to be employed and to determine the effect of addition of both polarization and diffuse functions.

The energies of 1,2,4-triazol-3-thione and thiol forms and energy differences calculated at these levels have been compared in Table 1. As expected, by increasing the basis sets size in all methods energy values converge to limit of the method. However, computational consideration direct us to determine a optimum level for describing the system both quantitatively and qualitatively. In the tautomerism process we aim to study the proton transfer from N2 to S atom. So, we expect to see the involvement of valence electrons rather than core electrons in this rearrangement. It also seems necessary to use polarization functions for hydrogen atoms. Comparing the results of 6-31+G(d,p) with 6-31++G(d,p) or 6-311+G(d,p) with 6-311++G(d,p) in Table 1 show the inconsiderable effect of diffuse functions on hydrogen atoms. On the contrary, as we have H, C, N, and S atoms in the system, using polarization functions are suitable to give the wave function flexibility.



**Fig. 1** The mechanism and numbering system proposed for tautomerization of 1,2,4-triazole-3-thione to 1,2,4-triazole-3-thiol and corresponding transition structure (TS)

**Table 1** Energies of 1,2,4-triazol-3-thione and thiol forms in hartree and energy differences in  $\text{kJ mol}^{-1}$  calculated by three methods and various basis sets

	Thione			Thiol			Energy difference		
	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2
6-31G	-638.1807	-640.3422	-638.7373	-638.1275	-640.2972	-638.6986	139.79	117.99	101.67
6-31G(d)	-638.3262	-640.4491	-639.1826	-638.3005	-640.4242	-639.1623	67.40	65.40	53.35
6-31G(d,p)	-638.3364	-640.4577	-639.2088	-638.3105	-640.4325	-639.1901	68.24	66.23	49.16
6-31+G(d,p)	-638.3430	-640.4688	-639.2256	-638.3186	-640.4454	-639.2089	64.18	61.42	43.93
6-31++G(d,p)	-638.3431	-640.4689	-639.2261	-638.3187	-640.4455	-639.2093	64.14	61.46	44.14
6-311G(d,p)	-638.4093	-640.5417	-639.3219	-638.3839	-640.5162	-639.3052	66.73	66.99	43.93
6-311+G(d,p)	-638.4142	-640.5475	-639.3334	-638.3903	-640.5240	-639.3186	62.63	61.63	38.70
6-311++G(d,p)	-638.4142	-640.5475	-639.3338	-638.3904	-640.5241	-639.3190	62.59	61.59	38.99
CC-PVDZ	-638.3684	-640.4876	-639.2412	-638.3455	-640.4652	-639.2247	60.12	58.79	43.43
CC-PVTZ	-638.4490	-640.5742	-639.5295	-638.4264	-640.5523	-639.5122	59.25	57.36	45.44
CC-PVQZ	-638.4702	-640.5982	-639.6269	-638.4479	-640.5768	-639.6100	58.41	56.36	44.35

By comparing the energy values in 6-31G with 6-31G(d) and 6-31G(d,p) this fact could be evidenced. Referring to energy values in 6-31G(d) and 6-31G(d,p) reveal the necessity of polarization function on hydrogen atoms. Thus, data in Table 1 emphasize on the usage of polarization and diffuse functions on hydrogen atom for study of such tautomerization.

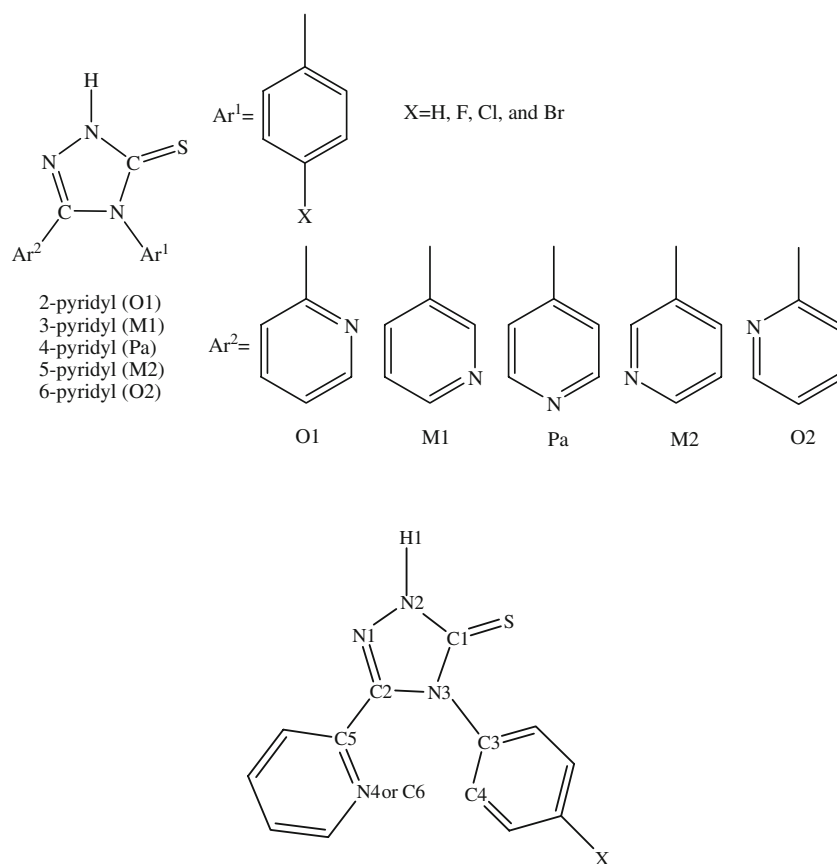
It is known that the better basis set, lower the energy that results in variational HF theory [35]. Considering the HF results in Table 1 reveals that the expansion of basis set relative to 6-31G shows considerable changes in energies. According to this table, the differences between absolute energies in 6-31G(d,p) and CC-PVQZ basis sets in both tautomers are within the range 351–361  $\text{kJ mol}^{-1}$ . Thus, for estimation of absolute energy of each tautomers CC-PVQZ is the most convenient basis set. However, this basis set is extremely computationally demanding. On one hand, the HF method overestimates the electronic repulsion. This fact can be seen clearly in energy estimation of thiol form. On the other hand, due to the presence of lone pairs in nitrogen and sulfur atoms correlated methods show more exact results. So, we should rely on post-Hartree-Fock methods for describing the correlation energy in studying such a system as much as possible. Employing MP2 method in this case, causes a decrease in energy of this species and even in energy differences. B3LYP density functional method offers an electron correlation correction frequently comparable to the MP2 in certain cases, and for certain purposes even superior to MP2, but at considerably lower computational cost [36]. As it is generally found [37] the B3LYP energies are more negative than the ones computed using conventional post-Hartree-Fock methods. By referring to the values of energy differences of two tautomers in Table 1 it is clear that the difference between 6-31G(d,p) and

CC-PVQZ basis sets at B3LYP level is about 10  $\text{kJ mol}^{-1}$ . It has been reported that the error of 10–20  $\text{kJ mol}^{-1}$  in estimation of relative energies in isomerization or tautomerization of a high accuracy method is acceptable. The estimated experimental error in such cases is also about 42  $\text{kJ mol}^{-1}$  [38]. Thus, according to Table 1, B3LYP/6-31G(d,p) level is suggested as a proper level which represent an excellent compromise between accuracy and computational cost to study the relative energy of tautomerization.

Determining the computational level for disubstituted derivatives of 1,2,4-triazole-3-thione

Figure 2 displays different isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione studied in this work. It has been proven that B3LYP is quite reliable to describe geometries, energies, and harmonic vibrational frequencies of medium sized systems [37, 38]. Moreover, it is known that the DFT (B3LYP) method adequately takes into account electron correlation contributions, which are especially important in systems containing extensive electron conjugation and/or electron lone pairs. It has also been reported that B3LYP calculations converge rapidly with increasing the basis set size that cost-to-benefit ratio is optimal at the 6-31G(d) basis set [39]. As mentioned above B3LYP/6-31G(d,p) level is a proper basis set for studying such tautomerism. However, literature survey shows that the X-ray structure of 2,4-dihydro-3H-5-phenyl-4-amino-1,2,4-triazole-3-thione has been collected [40]. In order to choose an appropriate basis set, a series of optimization calculations using various basis sets [31–34] including 6-31G, 6-31G(d), 6-31G(d,p), 6-31+G(d,p), 6-31++G(d,p), 6-311G(d,p), 6-311+G(d,p), 6-311++G(d,p), CC-PVDZ, and CC-PVTZ with B3LYP method were carried

**Fig. 2** Different isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione accompanied by the numbering system used



out on the geometry of aforementioned derivatives. The structural parameters (bond distances and angles) for each level were compared to the corresponding X-ray crystallography data (See T1 in Supplementary Material). At the B3LYP/6-31G(d,p) level, acceptable differences for bond distances of less than 0.01 Å and less than 1° for bond angle values led us to suffice to this level [35, 39]. Thus this level has been used for continuing our calculations on disubstituted derivatives of 1,2,4-triazole-3-thione and their thiol forms.

## Results and discussion

Tautomerism of 1,2,4-triazole-3-thione from energy point of view

The proposed mechanism of one step intramolecular tautomerism in 1,2,4-triazole-3-thione has been shown in Fig. 1. As data in Table 1 indicates, the energy differences decreases by using correlated methods and larger basis sets. This is not unexpected as we have lone pairs on the nitrogen and sulfur atoms. Our results also show that with thermodynamics energy differences (*i.e.*, energy differences not involving a TS), consistently obtaining activation energies

to 10–20 kJ mol<sup>-1</sup> with some confidence requires one of the high accuracy methods such as B3LYP method [41].

Activation energies (*E<sub>a</sub>*) for tautomerization of 1,2,4-triazole-3-thione to 1,2,4-triazole-3-thiol calculated by B3LYP method and various basis sets have been compared in Table 2. As can be seen in this table, except for 6-31G and 6-31G(d) basis sets, the activation energies are very close together. This fact shows that activation energy is not very sensitive to the basis set larger than 6-31G(d,p). It also can be seen that adding the diffuse functions do not change the activation energy considerably, while the polarization functions seems necessary. These evidences confirm the selection of B3LYP/6-31G(d,p) level as a proper computational level for investigation of this system.

Considering the ground state energy of 1,2,4-triazole-3-thione and its thiol form as well as tautomerization energies in Table 1 show that thione form is more stable than thiol case (within the range 56–66 kJ mol<sup>-1</sup>) from thermodynamics point of view. High barrier energies in Table 2 (within the range 191–220 kJ mol<sup>-1</sup>) suggest an unfavorable tautomerism from kinetics point of view in the gas phase. It is worth mentioning that probability of such tautomerism is low in the proposed one step intramolecular mechanism. As has been reported elsewhere [42], increasing temperature and considering effect of solvent, other

**Table 2** Activation energies (Ea) for tautomerization of 1,2,4-triazole-3-thione to 1,2,4-triazole-3-thiol calculated by B3LYP method and various basis sets

Basis set	Ea (kJ/mol)
6-31G	220.41
6-31G(d)	212.92
6-31G(d,p)	191.17
6-31+G(d,p)	192.05
6-31++G(d,p)	191.92
6-311G(d,p)	192.67
6-311+G(d,p)	191.63
6-311++G(d,p)	191.50

mechanisms could be alternative choices for observation of tautomerization in such cases.

Tautomerism of 1,2,4-triazole-3-thione from geometry point of view

Optimized structural parameters in 1,2,4-triazol-3-thione and its thiol tautomer calculated at various levels have been summarized in Tables 3 and 4, respectively. These parameters show that both tautomers and the transition state connecting them are completely planar. This fact could be evidenced by referring to Tables 3 and 4 where the selected dihedral angles are approximately 0 or 180° which show completely planar geometries. By taking a closer look at the structure and imaginary frequency of transition state, it reveals that even during the tautomerization process, proton (H1) has been transferred from S to N2 in the molecular plane.

By comparing bond distances of ring atoms, it is determined that single and double bonds of ring are completely localized. As can be seen in Tables 3 and 4, the constant bond distances inside the ring affirm this claim. Besides, the effect of expansion of basis set on geometrical parameters can be seen. In MP2 method inconsiderable changes of bond distances, bond angles, and dihedral angles are observed by increasing basis set size. As discussed before, 6-31G(d,p) basis set present the reliable relative energy results. Therefore, due to lack of experimental data, this method could also yields the most reliable structures. Accordingly, it seems clear that optimization at 6-31G(d) level is necessary to obtain accurate geometries. Due to the presence of proton transfer in our system, however, to improve energy estimations, 6-31G(d,p) basis set should be used [41].

NBO analysis of 1,2,4-triazole-3-thione tautomerism

In order to discuss about relative stabilities of tautomers of 1,2,4-triazole-3-thione and transition structure (TS) connecting them, interactions between atomic orbitals, bond orbitals, and lone pair orbitals have been investigated using

NBO analysis. The contributions involving the lone electron pairs of nitrogens and sulfur were taken into account. Table 5 summarizes hybridization of bonding interactions for the aforementioned reaction. NBO second order interaction energies ( $\Delta E_{ij}^{(2)}$ ) for a few donor-acceptor interactions are mentioned in Table 6.

By taking a closer look at Table 5 it is obvious that lone pairs of N3 and S atoms both weaken the C1-N2 bond in thiol species. Such facts are evidenced from  $\Delta E_{ij}^{(2)}$  values of 308.28 and 124.43 kJ mol<sup>-1</sup> in this table for interaction of LP(1) N3 and LP(2) S lone pairs as donor with  $\sigma$ -antibonding orbital of BD\*(2) C1-N2 as acceptor respectively. Such interactions is not observed in thione form. This fact could be also seen in TS which show that TS is more similar to thiol tautomer rather than thione tautomer. This fact could be approved by having lower energy barrier for backward pathway in thione-thiol tautomerization in Table 2. Further, weakening of S-H1 by LP(1) N2 in TS shows that this TS is consistent with reaction coordinate for annihilation of N2-H1 bond which is also a confirmatory of the obtained transition structure for one step intramolecular tautomerization. It is because a charge transfer from N2 orbital to antibonding interactions between S and H1 atoms has been seen. This fact is obvious from  $\Delta E_{ij}^{(2)}$  value of 612.58 kJ mol<sup>-1</sup> for interaction of LP(1) N2 donor and BD\*(1) S-H1 acceptor. Such interaction shows that the S-H1  $\sigma$  bond in transition structure has been weakened. Further, by referring to data of Table 5 it is determined that the bond between S and H1 is forming in thiol tautomer. These facts could be reasons for increasing activation energy in one step intramolecular conversion.

By taking a look at Table 6, a double bond between C1-N2 and C2-N1 in thiol form, a sp<sup>2</sup> hybridization for N1 and N2 nitrogen atoms of triazole is expected. By considering lone pair of nitrogens in an orbital with p character a strong repulsion between nonbonding electrons of mentioned neighboring nitrogens is expected. However, after formation of thione tautomers, the hybridization of N2 is changed (see Table 6). In the aforementioned table there is no BD(2) C1-N2 for thione form, which shows the disappearance of a  $\pi$  bond between C1 and N2 in thione form. This means that a double bond between C1-N2 is not observed in the latter species. Thus, by being away from lone pair of neighboring nitrogen atoms, the repulsion decreases. It is because the thione form is more stable than thiol. On the other side, as can be seen in Tables 3 and 4, geometries show that N1-N2 bond distance in thione form is smaller than those of thiol. The difference in bond distance could be also related to decrease in repulsion between nonbonding lone pairs. It is also obvious that N2 does not have sp<sup>2</sup> hybridization.

All in all, the NBO analyses in Tables 5 and 6 reveal similar trends for thiol form and transition structure (TS)

**Table 3** Optimized structural parameters in 1,2,4-triazol-3-thione calculated by HF, B3LYP, and MP2 methods and various basis sets

	6-31G(d)			6-31G(d,p)			6-31++G(d,p)			6-311G(d,p)		
	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2
<b>Dihedral angle (°)</b>												
S-C1-N3-C2	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
H2-N3-C1-N2	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
N3-C1-N2-H1	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
H3-C2-N3-C1	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
<b>Bond angle (°)</b>												
N3-C1-N2	102.26	101.61	101.59	102.39	101.15	100.72	102.39	101.19	100.74	102.39	101.19	100.74
N3-C1-S	128.35	128.64	128.77	128.27	128.93	129.34	128.33	128.99	129.43	128.33	128.99	129.43
C1-N3-C2	109.13	109.55	110.01	108.39	109.13	109.67	108.42	109.12	109.72	108.42	109.12	109.72
N3-C2-N1	111.21	111.29	111.12	111.30	111.53	111.32	111.21	111.45	111.16	111.21	111.45	111.16
C1-N2-H1	125.37	125.75	125.55	125.21	124.72	124.43	125.26	124.85	124.46	125.26	124.85	124.46
C1-N3-H2	123.23	122.71	122.48	123.26	122.57	122.27	123.31	122.67	122.46	123.31	122.67	122.46
N3-C2-H3	123.82	124.48	124.92	123.80	124.06	124.43	123.89	124.15	124.60	123.89	124.15	124.60
<b>Bond distance (Å)</b>												
C1-N3	1.356	1.393	1.399	1.356	1.384	1.382	1.356	1.385	1.383	1.356	1.385	1.383
C1-N2	1.332	1.371	1.378	1.333	1.365	1.366	1.333	1.366	1.368	1.333	1.366	1.368
C1-S	1.673	1.710	1.726	1.673	1.666	1.655	1.674	1.667	1.655	1.674	1.667	1.655
N3-C2	1.367	1.384	1.391	1.366	1.373	1.367	1.367	1.374	1.369	1.367	1.374	1.369
C2-N1	1.269	1.315	1.341	1.270	1.300	1.314	1.270	1.301	1.317	1.270	1.301	1.317
N2-H1	0.994	1.005	1.010	0.993	1.008	1.007	0.993	1.009	1.009	0.993	1.009	1.009
N3-H2	0.995	1.007	1.011	0.994	1.009	1.008	0.994	1.010	1.010	0.994	1.010	1.010
C2-H2	1.068	1.075	1.080	1.069	1.079	1.075	1.069	1.080	1.075	1.069	1.080	1.075
N1-N2	1.383	1.402	1.417	1.361	1.402	1.417	1.360	1.373	1.368	1.360	1.373	1.363

**Table 3** (continued)

MP2	6-311+G(d,p)			6-311++G(d,p)			CC-PVDZ			CC-PVTZ			CC-PVQZ		
	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2
Dihedral angle (°)															
180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
Bond angle (°)															
100.76	102.35	101.20	100.74	102.35	101.20	100.74	102.28	101.13	100.66	102.42	101.24	100.74	102.43	101.33	100.74
129.34	128.29	128.97	129.40	128.29	128.97	129.40	128.28	128.97	129.36	128.16	128.86	129.40	128.13	128.82	129.40
109.52	108.38	109.10	109.55	108.38	109.10	109.55	108.37	109.03	109.50	108.38	109.11	109.55	108.30	109.08	109.55
111.25	111.24	111.43	111.19	111.24	111.43	111.19	111.36	111.58	111.32	111.30	111.50	111.19	111.37	111.38	111.19
124.35	125.27	125.02	124.40	125.27	125.02	124.40	124.93	124.45	123.97	125.25	124.87	124.40	125.21	124.96	124.40
122.37	123.39	122.76	122.46	123.39	122.76	122.46	123.18	122.50	122.28	123.31	122.69	122.46	123.34	122.73	122.46
124.56	123.90	124.15	124.52	123.90	124.15	124.52	123.89	124.08	124.47	123.86	124.13	124.52	123.85	124.14	124.52
Bond distance (Å)															
1.381	1.356	1.384	1.384	1.356	1.386	1.384	1.358	1.386	1.387	1.354	1.380	1.384	1.354	1.380	1.384
1.366	1.333	1.364	1.369	1.333	1.368	1.369	1.336	1.368	1.373	1.330	1.360	1.369	1.329	1.359	1.369
1.655	1.670	1.663	1.651	1.670	1.670	1.651	1.674	1.670	1.663	1.669	1.661	1.651	1.667	1.658	1.651
1.368	1.367	1.373	1.369	1.367	1.374	1.369	1.368	1.374	1.372	1.364	1.368	1.369	1.363	1.369	1.369
1.312	1.267	1.296	1.313	1.267	1.301	1.313	1.270	1.301	1.320	1.266	1.294	1.313	1.264	1.293	1.313
1.009	0.993	1.008	1.009	0.993	1.013	1.009	0.997	1.013	1.016	0.990	1.005	1.009	0.989	1.004	1.009
1.009	0.994	1.007	1.010	0.994	1.013	1.010	0.998	1.013	1.015	0.991	1.005	1.010	0.990	1.004	1.010
1.079	1.069	1.078	1.080	1.069	1.086	1.080	1.076	1.086	1.088	1.068	1.077	1.080	1.067	1.075	1.080
1.362	1.359	1.371	1.363	1.359	1.371	1.363	1.359	1.370	1.365	1.359	1.369	1.365	1.358	1.369	1.365

**Table 4** Optimized structural parameters in 1,2,4-triazol-3-thiol calculated by HF, B3LYP, and MP2 methods and various basis sets

	6-31G			6-31G(d)			6-31G(d,p)			6-31++G(d,p)			6-311G(d,p)		
	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2	HF	B3LYP	MP2
<b>Dihedral angle (°)</b>															
S-C1-N3-C2	180.00	180.00	180.00	180.00	179.96	180.00	180.00	179.96	179.96	180.00	180.04	179.96	180.00	180.00	180.04
C2-N3-C1-N2	180.00	0.04	0.00	0.00	0.04	0.00	0.00	0.04	0.04	0.00	359.96	0.04	0.00	359.91	0.00
C1-N3-C2-N1	180.00	359.97	0.00	0.05	359.97	0.00	0.05	0.00	0.00	0.07	359.97	359.97	0.00	0.05	0.00
N2-C1-S-H1	180.00	0.04	0.00	0.04	0.00	0.00	0.04	0.00	0.00	0.07	359.97	359.97	0.00	0.00	0.00
N2-C1-N3-H2	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	179.93
C1-N3-C2-H3	180.00	180.02	179.94	180.00	180.02	179.94	180.00	180.02	180.02	180.00	180.05	179.95	180.00	180.00	180.03
<b>Bond angle (°)</b>															
N3-C1-N2	110.23	110.83	111.14	110.57	110.62	110.40	110.61	110.62	110.40	110.50	110.41	110.28	110.50	110.41	110.28
N3-C1-S	123.07	122.89	123.09	122.45	122.56	123.00	122.48	122.58	123.05	122.61	122.75	123.15	122.61	122.78	123.17
C1-N3-C2	105.24	105.10	105.53	103.90	104.29	104.87	103.86	104.33	104.91	103.98	104.49	104.97	103.98	104.49	104.97
N3-C2-N1	109.92	110.49	110.98	110.47	110.51	110.48	110.51	110.44	110.38	110.35	110.29	110.33	110.35	110.29	110.33
C1-S-H1	95.20	93.25	92.55	94.57	93.10	92.36	94.62	92.99	92.32	94.42	92.93	92.21	94.42	92.90	92.18
C1-N3-H2	127.34	127.34	127.09	128.01	127.80	127.50	128.00	127.79	127.54	128.01	127.80	127.55	128.01	127.80	127.55
N3-C2-H1	124.12	123.80	123.98	123.41	123.29	123.64	123.47	123.35	123.61	123.65	123.63	123.77	123.65	123.63	123.77
<b>Bond distance (Å)</b>															
C1-N3	1.363	1.379	1.388	1.355	1.370	1.366	1.355	1.369	1.365	1.355	1.370	1.367	1.355	1.370	1.367
C1-N2	1.294	1.325	1.345	1.281	1.312	1.325	1.281	1.312	1.325	1.282	1.313	1.327	1.282	1.313	1.327
C1-S	1.798	1.810	1.826	1.757	1.765	1.755	1.758	1.766	1.755	1.757	1.763	1.752	1.757	1.764	1.753
N3-C2	1.372	1.386	1.393	1.361	1.373	1.368	1.361	1.374	1.368	1.362	1.375	1.371	1.362	1.375	1.371
C2-N1	1.293	1.323	1.346	1.277	1.305	1.320	1.277	1.306	1.321	1.279	1.308	1.322	1.279	1.308	1.322
S-H1	1.349	1.375	1.374	1.324	1.348	1.340	1.325	1.347	1.331	1.325	1.347	1.333	1.325	1.347	1.332
N3-H2	0.990	1.007	1.012	0.994	1.010	1.013	0.992	1.009	1.008	0.994	1.010	1.009	0.994	1.010	1.009
C2-H3	1.062	1.076	1.081	1.069	1.081	1.082	1.070	1.080	1.076	1.069	1.080	1.076	1.069	1.080	1.076
N2-N1	1.396	1.430	1.465	1.368	1.388	1.388	1.368	1.388	1.387	1.368	1.386	1.388	1.368	1.386	1.388



**Table 4** (continued)

	6-311G(d,p)			6-311++G(d,p)			CC-PVDZ			CC-PVTZ			CC-PVQZ		
	MP2	B3LYP	HF	MP2	B3LYP	HF	MP2	B3LYP	HF	MP2	B3LYP	HF	MP2	B3LYP	HF
Dihedral angle (°)															
179.92	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
0.09	0.04	0.00	0.04	0.00	0.00	0.00	359.96	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00
359.95	359.93	0.00	359.93	0.00	0.00	0.00	0.12	0.00	0.00	359.88	0.00	0.00	0.00	0.00	0.00
359.91	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	359.96	0.00	0.00	0.00	0.00	0.00
180.07	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00	180.00
179.97	180.02	180.00	180.02	180.00	180.00	180.06	179.98	180.00	180.00	180.02	180.00	180.00	180.00	180.00	180.00
Bond angle (°)															
110.35	110.55	110.39	110.55	110.39	110.28	110.68	110.57	110.51	110.58	110.47	110.28	110.55	110.47	110.28	110.28
123.17	122.53	122.77	122.53	122.77	123.11	122.45	122.66	122.90	122.40	122.58	123.11	122.43	122.58	122.58	123.11
104.69	103.84	104.37	103.84	104.37	104.80	103.79	104.32	104.60	103.96	104.46	104.80	103.97	104.46	104.46	104.80
110.39	110.41	110.37	110.41	110.37	110.33	110.43	110.41	110.51	110.41	110.39	110.33	110.39	110.39	110.39	110.33
91.92	94.48	92.88	94.48	92.88	92.11	94.18	92.35	91.73	94.60	93.04	92.11	94.68	93.04	92.11	92.11
127.68	128.05	127.83	128.05	127.83	127.64	127.95	127.74	127.56	127.98	127.72	127.64	127.94	127.72	127.64	127.64
123.66	123.56	123.48	123.56	123.48	123.77	123.51	123.44	123.59	123.57	123.50	123.77	123.58	123.50	123.77	123.77
Bond distance (Å)															
1.365	1.355	1.369	1.355	1.369	1.366	1.356	1.370	1.370	1.352	1.365	1.366	1.352	1.365	1.365	1.366
1.323	1.279	1.309	1.279	1.309	1.324	1.283	1.315	1.330	1.278	1.307	1.324	1.276	1.305	1.324	1.324
1.753	1.755	1.763	1.755	1.763	1.750	1.761	1.770	1.764	1.754	1.759	1.750	1.751	1.756	1.750	1.750
1.369	1.363	1.374	1.363	1.374	1.370	1.363	1.375	1.372	1.359	1.369	1.370	1.358	1.369	1.370	1.370
1.317	1.274	1.302	1.274	1.302	1.319	1.278	1.309	1.326	1.273	1.300	1.319	1.272	1.299	1.319	1.319
1.336	1.329	1.348	1.329	1.348	1.336	1.336	1.358	1.349	1.327	1.345	1.336	1.325	1.342	1.336	1.336
1.010	0.993	1.008	0.993	1.008	1.010	0.997	1.013	1.015	0.990	1.005	1.010	0.989	1.005	1.010	1.010
1.080	1.070	1.078	1.070	1.078	1.080	1.076	1.087	1.088	1.067	1.076	1.080	1.067	1.076	1.080	1.080
1.381	1.367	1.385	1.367	1.385	1.382	1.367	1.385	1.385	1.368	1.384	1.384	1.368	1.382	1.381	1.381

**Table 5** NBO second order interaction energies ( $\Delta E_{ij}^{(2)}$ ) for some donor-acceptor interactions for tautomerization of 1,2,4-triazole-3-thione calculated at B3LYP/6-31G(d,p) level

NBO		$\Delta E_{ij}^{(2)}$ (kJ/mol)		
donor	acceptor	thione	TS	thiol
LP(1)N3	BD*(2) C1-N2	...	397.61	308.28
LP(1) N2	BD*(1) S-H1	...	612.58	...
LP(2) S	BD*(2) C1-N2	...	195.85	124.43

which show that TS is more similar to thiol species from electronic configuration view.

Tautomerism of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione from energy point of view

To investigate the substituent effects on the tautomerization of 1,2,4-triazole-3-thione the derivatives involving phenyl, halophenyl, and pyridyl groups of parent molecule has been considered. As can be seen in Fig. 2, one substituent is a phenyl groups ( $Ar^1$ ) in which a *para* hydrogen is replaced by halogen atom ( $X=Br, Cl, \text{ and } F$ ). Another substituent is a pyridyl groups ( $Ar^2$ ) which nitrogen heteroatom can lie on 2-, 3-, 4-, 5-, or 6-pyridyl atoms and is designated by the *ortho* (O1 and O2), *meta* (M1 and M2), or *para* (Pa). In total 20 derivatives and their thiol forms have been studied at B3LYP/6-31G(d,p) level. Total energies and differences for all the stable tautomers under study are summarized in Table 7. Also, activation energy ( $E_a$ ) for the tautomerization of various isomers of bromo-phenyl thione derivatives to their thiol form is offered in Table 8. The same route is seen for other derivatives (not shown). The first conspicuous fact in Table 7 is that the thione tautomer is the most

stable one for all the disubstituted derivatives, in accordance with the parent molecule (The tautomeric energy differences,  $\Delta E^{(a)}$ , are within the range 55–68 kJ mol<sup>-1</sup>). Thus, these reactions are thermodynamically disfavored. By paying attention to the high activation energies (within the range 180–186 kJ mol<sup>-1</sup>) it is also suggested that reactions do not occur from kinetics point of view. For this reason as has been reported before [11, 12], it is predicted that the concentration of thiol form to be much less than thione form in equilibrium mixture. In the case of observation of thiol form in the equilibrium mixture it is suggested that tautomerization is not occurred through a one step intermolecular mechanism [42]. Comparing the results of Tables 1 and 2 with 7 and 8 reveals that substituents show inconsiderable effects in the energy differences between two tautomeric forms ( $\Delta E^{(a)}$ ) as well as in the activation energy of tautomerization in 1,2,4-triazole-3-thione parent.

Energy values in Table 7 for different isomers of bromo derivative shows that energy differences ( $\Delta E^{(b)}$ ) between two *meta* position of pyridine (M1 and M2) in thione form are not so much. The energy of these positions are not also very different from *para* (Pa) isomer. On the contrary, two *ortho* positions (O1 and O2) in thione form are not the same and their energy difference is about 13 kJ mol<sup>-1</sup>. Among various thione isomers, O1 isomer has the most while O2 isomer has the least stability. By considering this table the same pattern is seen for all other derivatives.

Tautomerism of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione from geometry point of view

To consider the effect of substituents on the tautomeric equilibrium following geometrical parameters have been selected: C4-C3-N3-C2 (D), N3-C2-C5-N4 (D'),

**Table 6** Hybridization of bonding interactions for tautomerization of 1,2,4-triazole-3-thione calculated at B3LYP/6-31G(d,p) level

Interaction	Thione	TS	Thiol
BD(1) C1-N2	0.6164*(sp <sup>2.42</sup> ) <sub>C1</sub> +0.7874*(sp <sup>1.57</sup> ) <sub>N2</sub>	0.6330*(sp <sup>2.22</sup> ) <sub>C1</sub> +0.7742*(sp <sup>1.93</sup> ) <sub>N2</sub>	0.6529*(sp <sup>1.75</sup> ) <sub>C1</sub> +0.7575*(sp <sup>1.74</sup> ) <sub>N2</sub>
BD(2) C1-N2	...	0.5782*p <sub>C1</sub> +0.8159*p <sub>N2</sub>	0.6553*(p) <sub>C1</sub> +0.7554*(p) <sub>N2</sub>
BD(1) C1-S	0.5353*p <sub>C1</sub> +0.8447*p <sub>S</sub>	0.7682*(sp <sup>1.67</sup> ) <sub>C1</sub> +0.6402*(sp <sup>6</sup> ) <sub>S</sub>	0.7398*(sp <sup>2.05</sup> ) <sub>C1</sub> +0.6728*(sp <sup>4.95</sup> ) <sub>S</sub>
BD(2) C1-S	0.7771*(sp <sup>1.36</sup> ) <sub>C1</sub> +0.6293*(sp <sup>4.38</sup> ) <sub>S</sub>	...	...
BD(1) N3-C2	0.7920*(sp <sup>1.91</sup> ) <sub>N3</sub> +0.6106*(sp <sup>2.31</sup> ) <sub>C2</sub>	0.7978*(sp <sup>1.98</sup> ) <sub>N3</sub> +0.6029*(sp <sup>2.4</sup> ) <sub>C2</sub>	0.7982*(sp <sup>1.92</sup> ) <sub>N3</sub> +0.6024*(sp <sup>2.41</sup> ) <sub>C2</sub>
BD(1) N3-H2	0.8493*(sp <sup>2.3</sup> ) <sub>N3</sub> +0.5280*p <sub>H2</sub>	0.8486*(sp <sup>2.28</sup> ) <sub>N3</sub> +0.5291*p <sub>H2</sub>	0.8465*(sp <sup>2.27</sup> ) <sub>N3</sub> +0.5324*p <sub>H2</sub>
BD(1) N2-N1	0.7369*(sp <sup>2.36</sup> ) <sub>N2</sub> +0.6760*(sp <sup>3.58</sup> ) <sub>N1</sub>	0.7300*(sp <sup>2.74</sup> ) <sub>N2</sub> +0.6834*(sp <sup>3.2</sup> ) <sub>N1</sub>	0.7102*(sp <sup>3.07</sup> ) <sub>N2</sub> +0.7040*(sp <sup>3.16</sup> ) <sub>N1</sub>
BD(1) N2-H1	0.8472*(sp <sup>2.21</sup> ) <sub>N2</sub> +0.5313*s <sub>H1</sub>	...	...
BD(1) S-H1	...	0.8780*(sp <sup>9.59</sup> ) <sub>S</sub> +0.4787*s <sub>H1</sub>	0.7644*(sp <sup>5.98</sup> ) <sub>S</sub> +0.6448*s <sub>H1</sub>
BD(1) C2-N1	0.6440*(sp <sup>1.94</sup> ) <sub>C2</sub> +0.7650*(sp <sup>1.67</sup> ) <sub>N1</sub>	0.6462*(sp <sup>1.86</sup> ) <sub>C2</sub> +0.7631*(sp <sup>1.73</sup> ) <sub>N1</sub>	0.6514*(sp <sup>1.86</sup> ) <sub>C2</sub> +0.7588*(sp <sup>1.75</sup> ) <sub>N1</sub>
BD(2) C2-N1	0.6477*p <sub>C2</sub> +0.7619*s <sub>N1</sub>	0.6647*p <sub>C2</sub> +0.7471*p <sub>N1</sub>	0.6606*p <sub>C2</sub> +0.7507*p <sub>N1</sub>
BD(1) C2-H3	0.7808*(sp <sup>1.79</sup> ) <sub>C2</sub> +0.6248*s <sub>H3</sub>	0.7797*(sp <sup>1.79</sup> ) <sub>C2</sub> +0.6261*s <sub>H3</sub>	0.7784*(sp <sup>1.78</sup> ) <sub>C2</sub> +0.6278*p <sub>H3</sub>

**Table 7** Energy differences calculated at B3LYP/6-31G(d,p) level for the tautomerization of different derivatives and isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione to their thiol forms

Derivative	Thione	Thiol	$\Delta E^{(*)}$ (kJ/mol)	$\Delta E^{(S)}$ (kJ/mol)
BrO1	-3689.7146	-3689.6919	59.66	0.00
BrPa	-3689.7114	-3689.6898	56.82	8.41
BrM1	-3689.7117	-3689.6868	65.31	7.61
BrM2	-3689.7117	-3689.6860	67.61	7.61
BrO2	-3689.7096	-3689.6854	63.43	13.14
ClO1	-1578.2058	-1578.1831	59.62	0.00
ClPa	-1578.2026	-1578.1809	56.78	8.41
ClM1	-1578.2029	-1578.1780	65.27	7.61
ClM2	-1578.2029	-1578.1771	67.61	7.61
ClO2	-1578.2007	-1578.1766	63.43	13.39
FO1	-1217.8455	-1217.8238	56.86	0.00
FM1	-1217.8409	-1217.8193	56.82	12.09
FPa	-1217.8406	-1217.8190	56.53	12.84
FM2	-1217.8408	-1217.8184	58.99	12.34
FO2	-1217.8385	-1217.8144	63.30	18.37
HO1	-1118.6120	-1118.5927	50.75	0.00
HM1	-1118.6100	-1118.5888	55.81	5.27
HPa	-1118.6098	-1118.5886	55.52	5.77
HM2	-1118.6100	-1118.5848	66.15	5.27
HO2	-1118.6076	-1118.5839	62.22	11.55

$\Delta E^*$  shows energy difference between thione and thiol tautomers of a derivative

$\Delta E^S$  shows the energy differences between different thione isomers and the most stable thione isomer (O1) in each series of derivatives

N2-C1-S-H1 ( $D''$ ) dihedral angles and S-H1 ( $R'$ ), N2-H1 ( $R''$ ), N1-N2 ( $R'''$ ) bond distances. These parameters also could describe the structure variation caused by changing nitrogen atom position in pyridyl group (*i.e.*, O1, O2, Pa, M1, or M2), or X atom (X=H, Br, Cl, and F) in phenyl ring during the tautomerization. It is notable that by elimination of bond between atom 2 and 1 (N-H1), the H1 atom bond with atom S (S-H1) and C1-S converted to C1=S. Therefore the  $R'$  and  $R''$  are virtual parameters in thione and thiol respectively.  $D$  and  $D'$  dihedral angles show the situation of phenyl and pyridyl groups with respect to triazole ring, respectively.  $D''$  dihedral angle shows the position of sulfur (S) and H1 relative to triazole ring. Tables 9 and 10 shows these geometrical parameters in optimized structures of some isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-1,2,4-triazole-3-thione, thiol and their TS.

Considering  $D$  values in this table, it is obvious that in all the derivatives both thione and thiol are not planer.  $D''$  values could show that S and H1 atoms are in the same

**Table 8** Activation energies ( $E_a$ ) calculated at B3LYP/6-31G(d,p) level for the tautomerization of different derivatives and isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione to their thiol forms

Isomer	$E_a$ (kJ/mol)
BrO1	180.83
BrPa	184.05
BrM1	184.01
BrM2	185.31
BrO2	186.65

plane in thiol and TS species.  $R'$ ,  $R''$ , and  $R'''$  bond distances are suggestive of increasing C1-S, N2-H1, and decreasing S-H1 during the conversion of thione to thiol and transition from TS. This finally leads to formation of S-H1 and change in C1=S double bond to a C1-S single bond which are followed by increasing the bond distance and annihilation of N2-H1 bond. Data in these tables offer that transition state are more similar to thiol form except for the distance between S and H1. The most considerable variation in thiol species for reaching to transition state could be the bond angle between S, N2, and H1 as well as previous bond distances.

By taking a look at the mentioned tables it could be understood that the dihedral angle between rings of the phenyl and pyridyl in O1 is larger than other conformers. In fact in these conformers substituents rings are orthogonal to each other. According to this table this trend can be seen in all O1 conformers. It seems that strain between nitrogen atom of pyridyl and phenyl group in O1 conformers causes the rotation of phenyl group with respect to pyridine rings. This fact could also be related to the repulsion between lone pair of nitrogen atom of pyridyl group and electron cloud of phenyl group, which decreases by mentioned rotation. When nitrogen of pyridyl ring is in the side of phenyl ring (conformer O1) the phenyl ring rotates to be farther from the pyridyl ring. It is obvious that by rotation of phenyl ring relative to pyridyl ring, and the distance created, the repulsion between two rings decreases and as a result the energy of the system decreases. Whereas, in the conformer

**Table 9** Dihedral angles calculated at B3LYP/6-31G(d,p) level for some isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-1,2,4-triazole-3-thione, thiol and their TS's

Dihedral angles (°)	C4-C3-N3-C2 (D)			N3-C2-C5-N4 (D') <sup>a</sup>			N2-C1-S-H1 (D'') <sup>b</sup>		
	thione	TS	thiol	thione	TS	thiol	thione	TS	thiol
BrM1	58.95	52.73	66.56	33.41	33.40	28.57	0.80	-0.19	-133.35
BrM2	58.90	52.37	65.34	34.04	34.95	31.87	0.71	-0.19	-131.68
BrO1	74.30	-74.31	90.64	15.62	-8.22	0.47	0.53	0.07	160.11
BrO2	54.66	48.15	58.19	-143.47	-141.04	-141.36	0.46	-0.31	-2.50
BrPa	-59.71	-53.59	-65.36	-30.05	-29.75	-24.77	-0.75	0.18	1.41
ClO1	76.76	82.03	90.21	14.62	4.61	0.66	0.48	-0.04	161.66
ClO2	54.36	48.63	58.38	-143.92	-141.07	-141.55	0.42	-0.31	-2.53
ClPa	58.89	54.10	66.35	30.44	29.67	24.38	0.78	-0.19	-1.63
FO2	57.02	51.27	66.43	-144.55	-142.14	-146.68	0.43	-0.33	-1.63
HM2	59.64	54.72	68.19	33.50	33.66	30.33	0.71	-0.18	-139.93
HO1	74.06	91.63	91.42	18.00	-0.01	0.02	0.60	0.00	0.00
HO2	56.18	50.39	58.38	-145.04	-142.65	-142.42	0.43	-0.30	-2.87

<sup>a</sup> C6 is used instead of N4 in M1, M2, Pa isomers. <sup>b</sup> is imaginary dihedral angle for thione forms

O2 the lone pair of pyridyl ring are far from the phenyl ring. These results are evident from the smaller angle of phenyl and pyridyl rings with respect to other conformers which resonates the repulsion between electrons of rings. Therefore, as has been reported by Iqbal and coworkers [12] it is plausible to separate two *ortho* derivatives. It is because the O1 is more stable than O2. On the other hand, the barrier energy for rotation is not so much and the rotation over single C2-C5 bond is not hindered. Thus two *meta* positions are assumed the same which is in accord with the energy values in Table 7 and experimental reports [11, 12].

NBO analysis of tautomerism of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione

The results of NBO analysis of tautomerization in some of the different isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-1,2,4-triazole-3-thione are presented in Tables 11 and 12. By taking a look at Table 11, a charge transfer from N2 orbital to antibonding interaction between S and H1 of TS is seen. Such interactions is related to charge transfer from LP(1) N2 to BD\*(1) S-H1 with  $\Delta E_{ij}^{(2)}$  value of 453.96 kJ mol<sup>-1</sup> for TS in Table 12. This interaction belongs to strong weakening of S-H1 bond

**Table 10** Bond distances calculated at B3LYP/6-31G(d,p) level for some isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-1,2,4-triazole-3-thione, thiol and their TS's

Bond distance (Å)	C1-S (R)			S-H1 (R') <sup>a</sup>			N2-H1 (R'') <sup>b</sup>			N1-N2 (R''')		
	thione	TS	thiol	thione	TS	thiol	thione	TS	thiol	thione	TS	thiol
BrM1	1.665	1.726	1.766	2.994	1.728	1.350	1.008	1.368	3.467	1.364	1.367	1.372
BrM2	1.665	1.726	1.767	2.995	1.727	1.350	1.008	1.369	3.459	1.364	1.367	1.372
BrO1	1.665	1.725	1.765	2.994	1.732	1.349	1.008	1.363	3.553	1.360	1.362	1.371
BrO2	1.667	1.727	1.767	2.993	1.722	1.347	1.008	1.373	2.602	1.363	1.367	1.378
BrPa	1.664	1.724	1.766	2.995	1.729	1.347	1.008	1.367	2.604	1.362	1.364	1.374
ClO1	1.665	1.724	1.765	2.995	1.733	1.348	1.008	1.363	3.556	1.360	1.362	1.371
ClO2	1.668	1.727	1.767	2.993	1.722	1.347	1.008	1.373	2.602	1.363	1.367	1.378
ClPa	1.665	1.724	1.765	2.994	1.729	1.347	1.009	1.367	2.606	1.362	1.364	1.374
FO2	1.667	1.727	1.767	2.994	1.723	1.347	1.008	1.373	2.607	1.364	1.367	1.374
HM2	1.666	1.726	1.766	2.992	1.727	1.350	1.008	1.368	3.494	1.364	1.367	1.373
HO1	1.665	1.725	1.765	2.991	1.733	1.347	1.008	1.362	2.607	1.360	1.361	1.372
HO2	1.667	1.727	1.768	2.991	1.722	1.347	1.008	1.372	2.600	1.363	1.366	1.377

<sup>a</sup> and <sup>b</sup> are imaginary bond distances for thione and thiol forms respectively

**Table 11** NBO second order interaction energies ( $\Delta E_{ij}^{(2)}$ ) for some donor-acceptor interaction in tautomerization of different isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-1,2,4-triazole-3-thione calculated at B3LYP/6-31G(d,p) level

NBO		$\Delta E_{ij}^{(2)}$ (kJ/mol)		
donor	acceptor	thione	TS	thiol
LP(1) N3	BD*(2) C1-N2	...	524.42	190.29
LP(1) N2	BD*(2) C1-N2	...	528.02	...
LP(2) S	BD*(2) C1-N2	...	...	79.08
LP(1) N2	BD*(1) S-H1	...	453.96	...

which is in complete accord with reaction coordinate for conversion of thione form to thiol. Also, it could be suggestive of the correct transition state for connecting two tautomers. In addition, the weakening of  $\pi$  bond between C1 and N2 in thiol is seen which is the result of charge transfer from atom lone pair of N2 to C1-N2 BD\*(2) C1-N2. This could be evidenced by energy values of 524.42 kJ mol<sup>-1</sup> for interaction of LP(1)N2 donor with C1-N2 BD\*(2) C1-N2 acceptor. The same interaction is seen in TS with energy value of 190.29 kJ mol<sup>-1</sup> which shows resemblance to thiol. Such a fact can be accounted for the instability of thiol form relative to thione.

In a similar way to parent molecule, the interactions of BD(2) C1-N2 and BD(2) C2-N1 of thiol and TS in disubstituted compounds show the repulsion of N1 and N2 lone pairs. This fact can be evidenced by referring to BD(2) C2-N1 and BD(2) C1-N2 in Table 12. This fact is not seen in thione form. Table 12 for thione shows that the bond between N2 and H1 has been annihilated which is in accordance with reaction coordinate and is confirmatory of NBO results. Thus according to this table, as has been discussed previously, the vicinity of lone pairs of N1 and

N2 atoms in the same plane causes instability in thiol form relative to thione form.

Vibrational analysis of tautomerism of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thione

Density functional theory calculations are reported to provide excellent vibrational frequencies of organic compounds if the calculated frequencies are scaled to compensate for approximate treatment of electron correlation, for basis set deficiencies and for anharmonicity [37, 38]. Unlike ab initio and semiempirical frequencies, DFT frequencies are not always significantly lower than observed ones, indeed, calculated values slightly higher than experimental frequencies have been reported. It has been also reported that B3LYP is an excellent and cost effective way to calculate the IR spectra [43, 44]. Therefore, IR vibrational calculations has been carried out on the equilibrium geometries at B3LYP/6-31G(d,p) level for all derivatives. However, these results do not adequately reproduce the experimental pattern of vibrational frequencies with the accuracy desired, and thus to reduce the error it is necessary to scale the vibrational frequencies. Thus, to fit the theoretical frequencies results with experimental ones for B3LYP methods, we have scaled the data with different factors (see Tables T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12, T13, T14, T15, T16, T17, T18 in Supplementary Material) [45]. Scaled results seemed to be in good agreement with experimental ones. For instance, in bromo BO1 derivative for frequencies which are less than 1000 cm<sup>-1</sup> a 0.826 scaling factor and for the range 1000-2000 cm<sup>-1</sup> scale factor 0.897 is used. Accordingly, for assigning S-H bond absorption frequency in BO1 thiol form which is higher than 1000 cm<sup>-1</sup> the value of 0.897 should be used. As a result, these scales could be used as a reference in interpreting vibrational data of this compounds

**Table 12** Hybridization of some bonding interactions in tautomerization of different isomers of 2,4-dihydro-4-(4-halophenyl)-5-(isomeric pyridyl)-1,2,4-triazole-3-thione calculated at B3LYP/6-31G(d,p) level

Interaction	Thione	TS	Thiol
BD(1) N3-C1	0.7945*(sp <sup>2.16</sup> ) <sub>N3</sub> +0.6073*(sp <sup>2.48</sup> ) <sub>C1</sub>	0.7909*(sp <sup>2.10</sup> ) <sub>N3</sub> +0.6119*(sp <sup>2.11</sup> ) <sub>C1</sub>	0.7973*(sp <sup>2.19</sup> ) <sub>N3</sub> +0.6035*(sp <sup>2.12</sup> ) <sub>C1</sub>
BD(1) N3-C2	0.7935*(sp <sup>2.04</sup> ) <sub>N3</sub> +0.6073*(sp <sup>2.36</sup> ) <sub>C2</sub>	0.7991*(sp <sup>2.10</sup> ) <sub>N3</sub> +0.7983*(sp <sup>2.48</sup> ) <sub>C2</sub>	0.7994*(sp <sup>2.01</sup> ) <sub>N3</sub> +0.6007*(sp <sup>2.47</sup> ) <sub>C2</sub>
BD(1) C1-N2	0.6350*(sp <sup>2.24</sup> ) <sub>C1</sub> +0.7725*(sp <sup>1.93</sup> ) <sub>N2</sub>	0.6350*(sp <sup>2.24</sup> ) <sub>C1</sub> +0.7725*(sp <sup>1.93</sup> ) <sub>N2</sub>	0.6531*(sp <sup>1.82</sup> ) <sub>C1</sub> +0.7573*(sp <sup>1.71</sup> ) <sub>N2</sub>
BD(2) C1-N2	...	...	0.6631*p <sub>C1</sub> +0.7485*p <sub>N2</sub>
BD(1) C1-S	0.7805*(sp <sup>1.37</sup> ) <sub>C1</sub> +0.6252*(sp <sup>4.32</sup> ) <sub>S</sub>	0.7692*(sp <sup>1.71</sup> ) <sub>C1</sub> +0.6390*(sp <sup>5.75</sup> ) <sub>S</sub>	0.7429*(sp <sup>2.08</sup> ) <sub>C1</sub> +0.6694*(sp <sup>4.73</sup> ) <sub>S</sub>
BD(1) C2-N1	0.6448*(sp <sup>2.14</sup> ) <sub>C2</sub> +0.7644*(sp <sup>1.62</sup> ) <sub>N1</sub>	0.6474*(sp <sup>2.07</sup> ) <sub>C2</sub> +0.7621*(sp <sup>1.67</sup> ) <sub>N1</sub>	0.6534*(sp <sup>2.07</sup> ) <sub>C2</sub> +0.7570*(sp <sup>1.71</sup> ) <sub>N1</sub>
BD(2) C2-N1	0.6458*p <sub>C2</sub> +0.7635*p <sub>N1</sub>	0.6634*p <sub>C2</sub> +0.7482*p <sub>N1</sub>	0.6591*p <sub>C2</sub> +0.7520*p <sub>N1</sub>
BD(1) N1-N2	0.6801*(sp <sup>3.44</sup> ) <sub>N1</sub> +0.7331*(sp <sup>2.36</sup> ) <sub>N2</sub>	0.6864*(sp <sup>3.11</sup> ) <sub>N1</sub> +0.7272*(sp <sup>2.68</sup> ) <sub>N2</sub>	0.7083*(sp <sup>3.03</sup> ) <sub>N1</sub> +0.7059*(sp <sup>3.05</sup> ) <sub>N2</sub>
BD(1) S-H1	...	0.8737*(sp <sup>9.91</sup> ) <sub>S</sub> +0.4865*s <sub>H1</sub>	0.7583*(sp <sup>5.74</sup> ) <sub>S</sub> +0.6520*s <sub>H1</sub>
BD(1) N2-H1	0.8576*(sp <sup>2.16</sup> ) <sub>N2</sub> +0.5144*s <sub>H1</sub>	...	...

and their similar derivatives in high resolution IR spectroscopy in future researches. These calculations are also valuable for providing insight into the vibrational spectra and molecular parameters of such species.

## Conclusions

One step intramolecular prototropic tautomerization of 1,2,4-triazole-3-thione and its 20 disubstituted involving halophenyl and pyridyl groups have been investigated using quantum chemical methods. First of all, the parent molecule of 1,2,4-triazole-3-thione and its thiol form has been studied employing HF, B3LYP, and MP2 methods and various basis sets. It is determined that in all level of theories and basis sets the thione form is the predominant tautomer. The predicted energy differences between thione and thiol tautomers was within the range 56–66 kJ mol<sup>-1</sup> while the activation energy of thione-thiol tautomerization process was within the range 191–220 kJ mol<sup>-1</sup>. Thus, tautomerization in parent molecule is not occurred from both thermodynamics and kinetics point of views. For the disubstituted derivatives the thione forms are within the range 55–68 kJ mol<sup>-1</sup> more stable than thiol forms. On the other hand, the activation energies for the tautomerization were estimated to be within the range 180–186 kJ mol<sup>-1</sup>. These high barrier energies as well as thermodynamics make the tautomerism processes energetically unfavored. Based on the NBO and geometrical analyses results, transition structure is more similar to thiol form rather than thione one. Furthermore, computed and experimental vibrational frequencies of the disubstituted derivatives have been compared. Vibrational frequencies of thione forms at B3LYP/6-31G(d,p) level are correlated with experimental data by employing different scaling factors in various frequency regions. These scaling factors can be used in predicting vibrational frequencies of similar compounds with respect to the frequency regions.

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