

Computational investigation of stability and ^{14}N NQR parameters of tautomers of 7-amino-1,3-dioxo-2,5-diphenyl-2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile

Zohreh Khanjari¹, Bita Mohtat^{1,*}, Reza Ghiasi², Hoorieh Djahaniani², Farahnaz Kargar Behbahani¹

¹Department of Chemistry, Karaj Branch, Islamic Azad University, Karaj, Iran

²Department of Chemistry, East Tehran Branch, Islamic Azad University, Tehran, Iran

Received: November 2020; Revised: January 2021; Accepted: January 2021

Abstract: This research examined the tautomerization of a 7-amino-1,3-dioxo-2,5-diphenyl-2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile at CAM-B3LYP/6-311G (d,p) level of theory. The total energy, relative energy and dipole moment values of these molecules was investigated. Moreover, NBO analysis was used to illustrate the hyperconjugative anomeric effect on the conformers. ^{14}N NQR parameters of the tautomers were illustrated. Electric field gradient tensors (q_{xx} , q_{yy} , q_{zz}), nuclear quadrupole coupling constant (χ_{zz} , χ_{yy} , χ_{xx}), asymmetry parameter (η), nuclear quadrupole resonance frequencies (ν_+ , ν_- , ν_0) values were estimated.

Keywords: Tautomerism, Atomic Polar Tensors (APT), Thermodynamics parameters, ^{14}N NQR parameters.

Introduction

Compounds containing pyrazoles [1] are recognized to show various pharmacological activities such as antibacterial, antifungal, anti-inflammatory, analgesic, and antipyretic [2]. Several heterocyclic compounds fused with pyrazole are identified for their diverse biological and industrial uses [3]. The pyrazolotriazole are precursors for photosensitive materials (e.g. inks and toners) [4] and ingredients in cosmetics [5]. 7-amino-1,3-dioxo-1,2,3,5-tetrahydropyrazolo [1,2-*a*][1,2,4]triazole has been synthesized using magnetic Fe_3O_4 nanoparticles coated with (3 aminopropyl)-triethoxysilane as catalyst for the formation of the 7 amino-1,3-dioxo-1,2,3,5-tetrahydropyrazolo[1,2-*a*][1,2,4]triazoles [6]. In a study, we have reported effects of substituent and temperature on the electronic properties and thermodynamics parameters of 1-(Benzothiazolylamino) methyl-2-naphthol at the CAM-B3LYP/6-311G(d,p) level of theory [7].

Nuclear quadrupole resonance (NQR) spectroscopy is useful for characterization of the physical properties of matters [8]. ^{14}N NQR parameters of the many molecules were investigated for illustration of the structural details and the variations in the electronic environment of the nuclei [9-13]. Electric field gradient (EFG) tensors are very sensitive to the electrostatic surroundings at the sites of quadrupole nuclei with spin angular momenta higher than one-half ($I > 1/2$). For example, ^{14}N nucleus has $I=1$. Measurements of quadrupole coupling constants (χ) and asymmetry parameters (η) are possible with experimental NQR investigations. If the experimental NQR studies are not accessible, then high-level quantum chemical calculations can provide the reliable NQR parameters [14-24].

Because of lack of experimental studies on the ^{14}N NQR parameters of the tautomers of 7 amino-1,3-dioxo-2,5-diphenyl-2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile, we encouraged to

*Corresponding author. E-mail: b_mohtat@yahoo.com

computational exploration of these parameters of them. This study is useful for illustration the charge on quadruple nuclei and electron distribution in these molecules. In this paper, we explore the stability and ^{14}NQR parameters of the tautomers are illustrated at the CAM-B3LYP/6-311G(d,p) level of theory.

Computational Methods:

Optimization and vibrational analysis were done using Gaussian 09 software package [25]. The standard 6-311G(d,p) basis set [26-29] was considered for the elements. CAM-B3LYP functional was used for optimizing the geometries of the compound. This functional is Handy et al.'s long range corrected version of B3LYP using the Coulomb-attenuating method [30]. The identities of the optimized structures as an energy minimum were confirmed via vibrational analysis. The identity of the reactants, transition states, and products was confirmed through vibrational analysis. All the transition states (TS) were checked by the intrinsic reaction coordinate (IRC) analysis at the same level of theory [31-34].

The electrostatic interaction of a nuclear electric quadrupole moment and the electron charge surrounding the nucleus can increase the existence of pure Nuclear Quadrupole Resonance (NQR) [35]. The Hamiltonian of this interaction for a nucleus of spin I is given [36]:

$$H_Q = \frac{e^2 Q q_{zz}}{4I(2I-1)} [3I_x^2 - I^2 + \frac{\eta}{2} (I_+^2 + I_-^2)];$$

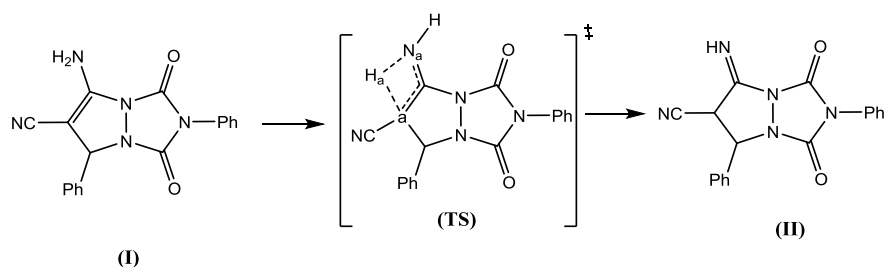


Figure 1: The structures of **(I)** molecule, its tautomer **(II)** and transition state **(TS)** of them.

where, e is elementary charge and all I 's in the denominator include scalar values while all I 's in the square brackets are operators [37]. Quantum chemical calculations result in principal components of the EFG tensor, q_{ii} , in atomic units ($1 \text{ au} = 9.717365 \times 10^{21} \text{ Vm}^{-2}$), with $|q_{zz}| \geq |q_{yy}| \geq |q_{xx}|$. q_{xx} , q_{yy} and q_{zz} are the components of EFG in the directions of x , y and z , respectively. APT charges are also computed by default during vibrational frequency calculations [38].

Results and discussion

Energetic aspects

The structures of 7-amino-1,3-dioxo-2,5-diphenyl-2,3-dihydro-1H,5H-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile **(I)**, 5-imino-1,3-dioxo-2,7-diphenyl tetrahydro-1H,5H-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile **(II)** and transition state **(TS)** of these tautomers are shown in Figure . Table 1 reports the total energy values of these molecules. These values show that **II**-isomer is more stable than **I**-isomer.

Figure 1 presents the transition state geometry of the studied tautomerization reaction. This structure shows a four-membered ring. The frequency analysis calculations illustrate an imaginary frequency for this transition state at -1289.4 cm^{-1} . This imaginary frequency is presented in Figure 2.

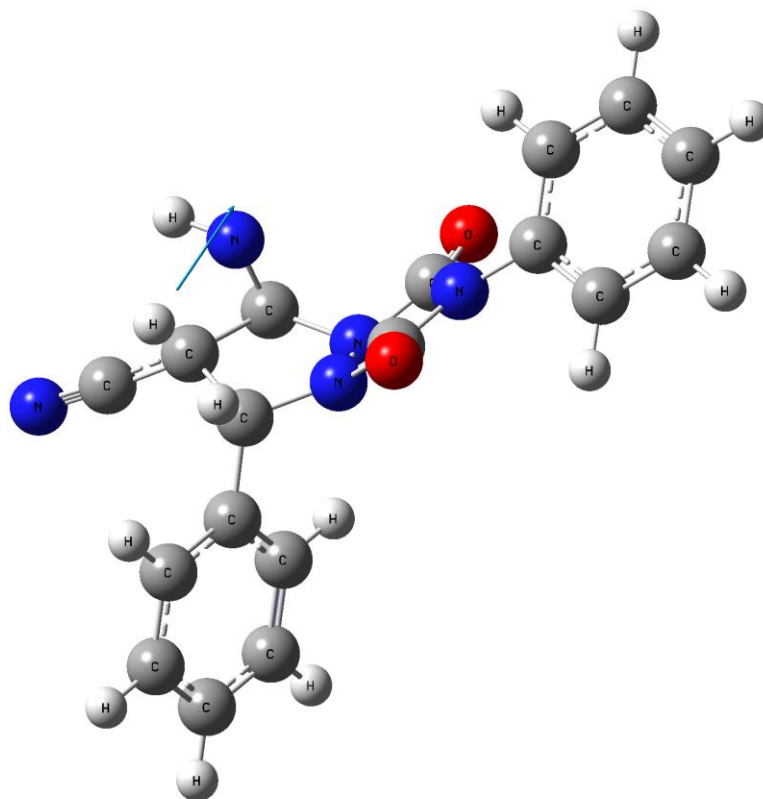


Figure 2: Imaginary frequency mode of transition state in the investigated tautomerization.

Table 1: total energy (E, a.u) and dipol moment values (μ , Debye) of studied tautomers and transition state between them (a.u). ΔE^\ddagger and ΔE_r are energy barrier and reaction energy of the tautomerisation (kcal/mol). ω_{lowest} is imaginary wave-number of transition state (in cm^{-1}).

Phase	E(I)	E(TS)	E(II)	μ (I)	μ (II)	ΔE^\ddagger	ΔE_r	ω_{lowest}
gas	-1117.6485	-1117.4482	-1117.6695	4.24	3.41	125.68	-13.19	-1289.4

The thermodynamic parameters of the studied tautomerization reaction are outlined in Table 2. The negative values of the reaction free energy (ΔG_r) reveal that the studied reaction is spontaneous.

The enthalpy values of the reaction (ΔH_r) are listed in Table 2. The negative values of the studied reaction show that this reaction is exothermic.

Table 2: Thermodynamic parameters of tautomerism of 7-amino-1,3-dioxo-2,5-diphenyl-2,3-dihydro-1H,5H-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile in gas phase and various solvents.

Phase	ΔG^\ddagger	ΔG_r	ΔH^\ddagger	ΔH_r
gas	122.19	-13.20	121.46	-12.87

Dipole moment

As a larger dipole moment can increase the overall energy corresponding to a conformation, the population corresponding to the conformation with a larger dipole moment can be reduced compared with the conformation with a less dipole moment [39]. A greater dipole moment is associated with greater charge distribution (polarization). Thus, the conformations with greater dipole moments can be softer than those with smaller dipole moments.

The results show that the dipole moments of the **II**-isomer compounds are smaller compared with their **I**-isomer (Table 1).

^{14}NQR parameters

Electric field gradient tensor:

Table 3 denotes the Electric field gradient (EFG) tensors of $^{14}\text{N}_a$ in studied tautomers. The EFG tensors in the nitrogen molecule include are: $Q(\text{xx}) = Q(\text{yy}) = -$

$Q(zz)/2$. To compute the nuclear quadrupole coupling constants, χ_{ii} , the calculated q_{ii} values were used:

$$\chi_{ii}(\text{MHz}) = \frac{e^2 Q q_{ii}}{h} \quad i = x, y, z;$$

where Q is the nuclear quadrupole moment of the ^{14}N nucleus, e is the elementary charge and h is Planck's constant. The standard values of quadrupole moment,

Table 3. ^{14}N NQR parameters: Electric field gradient tensors (q_{xx} , q_{yy} , q_{zz} in a.u), nuclear quadrupole coupling constant (χ_{zz} , χ_{yy} , χ_{xx} , in MHz), asymmetry parameter (η), nuclear quadrupole resonance frequencies (ν_+ , ν_- , ν_0 in MHz) of studied tautomers.

X	Q(zz)	Q(yy)	Q(xx)	χ_{zz}	χ_{yy}	χ_{xx}	η	ν_+	ν_-	ν_0
I	0.582670	-0.423803	-0.158867	2.799	2.036	0.763	0.455	2.417	1.781	0.636
II	0.659790	-0.626773	-0.033017	3.169	3.010	0.159	0.900	3.090	1.664	1.426

Nuclear quadrupole coupling constant

Usually, the NQR parameters are reported experimentally as the nuclear quadrupole coupling constant in the units of frequency:

$$QCC = \chi(\text{MHz}) = \frac{e^2 Q q_{zz}}{h};$$

Since it calculates the deviation of the field gradient tensor from axial symmetry.

Nuclear quadrupole coupling constants of ^{14}N in studied molecules are collected in Table 3. The calculated χ_{zz} for nitrogen atoms in N_2 free molecule is 5.824 (MHz) at the CAM-B3LYP/6-311G(d,p) level of theory.

It can be realized, χ_{zz} values are larger for the N_a atom in **II**-isomer as compared to N_a atom in **I**-isomer.

Asymmetry parameter:

Asymmetry parameter (η) is defined as:

$$\eta = \left| \frac{(q_{yy} - q_{xx})}{q_{zz}} \right|; 0 \leq \eta \leq 1;$$

Table 3 represents the asymmetry parameters of ^{14}N in examined molecules. These value display the distribution of electric charge around the nitrogen nucleus is noticeably dissimilar from cylindrical symmetry in comparison with that in nitrogen molecules.

It can be understood, η values are larger for the N_a atom in **II**-isomer as compared to N_a atom in **I**-isomer.

Nuclear quadrupole resonance frequencies

A nucleus of unit spin (such as ^{14}N) has three energy levels, consequently, there are three nuclear quadrupole resonance frequencies [36]:

$$\nu_+ = \frac{3}{4} \chi_{zz} \left(1 + \frac{\eta}{3}\right)$$

$$\nu_- = \frac{3}{4} \chi_{zz} \left(1 - \frac{\eta}{3}\right)$$

Q , provided by Pyykkö [40] were utilized in equation (1), $Q(^{14}\text{N}) = 20.44$ mb.

It can be deduced, $Q(zz)$ value is larger for the N_a atom in **II**-isomer as compared to N_a atom in **I**-isomer.

$$\nu_0 = \frac{3}{4} \chi_{zz} \eta$$

The nuclear quadrupole resonance frequencies $^{14}\text{N}_a$ in these tautomers are listed in Table 3. In these molecules, the nitrogen atoms are located in the electric field of the other nuclei, hence, the symmetry of the EFG nearby them varies. This variation results in the splitting of the energy levels of ^{14}N nuclei, thus three NQR frequencies for $^{14}\text{N}_a$ will be observed. The variations between the frequencies of N_a atom can be related to the straight contribution of the electron pairs of N_a atom through chemical bond formation or diatropic current in the ring. It can be found the larger ν_+ and ν_0 values for the N_a atom in **II**-isomer as compared to N_a atom in **I**-isomer.

The Atomic Polar Tensors (APT) charges:

The partial atomic charges calculated by the APT method for N_a atom in two tautomers are -0.2152 and -0.4860 e for **I** and **II** isomers, respectively. The results indicate that the more negative partial atomic charge on the N_a nucleus of **II**-isomer.

Conclusion

Computational investigation of the tautomerization of 7-amino-1,3-dioxo-2,5-diphenyl-2,3-dihydro-1H,5H-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile were studied at CAM-B3LYP/6-311G (d,p) level of theory reveal that **II**-isomer was more stable than **I**-isomer. The negative values of ΔG_r and ΔH_r showed that the studied reaction was exothermic, respectively. Calculated ^{14}N NQR parameters revealed the χ_{zz} , η , ν_+ and ν_0 values for the N_a atom in **II**-isomer as compared to N_a atom in **I**-isomer. APT results indicated that the more negative partial atomic charge on the N_a nucleus of **II**-isomer than **I**-isomer.

References

- [1] Haddad, N.; Salvango, A.; Busacca, C., *Tetrahedron Lett.* **2004**, *45*, 5935.
- [2] Tanitame, A.; Oyamada, Y.; Ofugi, K.; Fujimoto, M.; Iwai, N.; Hiyama, Y.; Suzuki, K.; Ito, H.; Terauchi, H.; Kawasaki, M.; Nagai, K.; Wachi, M.; Yamagishi, M.J.I., *J. Med. Chem.* **2004**, *47*, 3693.
- [3] Varano, F.; Catarzi, D.; Colotta, V.; Lenzi, O.; Filacchioni, G.; Galli, A.; Costagli, C., *Bioorg. Med. Chem.* **2008**, *16*, 2617.
- [4] Bailey, J., *J. Chem. Soc. Perkin Trans.* **1977**, *118*, 2047.
- [5] Plos, G.; Lagrange, A., *Eur. Pat. Appl. Patent EP.* **2000**, 1062937.
- [6] Shaterian, H.R.; Moradi, F., *Research on Chemical Intermediates* **2015**, *41*, 223.
- [7] Khanjari, Z.; Mohtat, B.; Ghiasi, R.; Djahanian, H.; Behbahani, F.K., *Org. Chem. Res.* **2021**, *7*, 12.
- [8] Das, T.P.; Han, E.L., *Nuclear Quadrupole Resonance Spectroscopy*. Academic Press: New York, 1958.
- [9] Seliger, J.; Žagara, V.; Latosińskac, J.N., *Phys. Chem. Chem. Phys.* **2010**, *12*, 13007.
- [10] Seliger, J.; Žagar, V., *J Phys Chem A.* **2013**, *117*, 1651.
- [11] Lavrič, Z.; Pirnat, J.; Lužnik, J.; Puc, U.; Trontelj, Z.; Srčič, S., *J. Pharm. Sci.* **2015**, *104*, 1909.
- [12] Gregorovič, A., *J. Chem. Phys.* **2017**, *146*, 194306.
- [13] A, A.G.; Apih, T.; Žagar, V.; Seliger, J., *Phys. Chem. Chem. Phys.* **2018**, *21*, 306.
- [14] Rezaeyani, F.; Ghiasi, R.; Fazaeli, R.; Yousefi, M., *J. Chin. Chem. Soc.* **2018**, *65*, 416.
- [15] Sarraf, S.; R.Ghiasi, *Structural Chemistry.* **2018**, *29*, 435.
- [16] Ghiasi, R.; Amini, E., *Journal of Structural Chemistry.* **2015**, *56*, 1458.
- [17] Fashami, M.Z.; Ghiasi, R., *Journal of Structural Chemistry.* **2015**, *56*, 1474.
- [18] Ghiasi, R.; Peikari, A., *Journal of Applied Spectroscopy* **2017**, *84*, 148.
- [19] Partovi, T.; Mirzaei, M.; Hadipour, N.L., *Z. Naturforsch.* **2006**, *61a*, 383.
- [20] Mirzaei, M.; Hadipour, N.L., *J. Phys. Chem. A.* **2006**, *110*, 4833
- [21] Ghiasi, R.; Sadeghi, N., *Journal of Applied spectroscopy.* **2020**, *87*, 538.
- [22] Ghiasi, R.; Fashami, M.Z., *Journal of Theoretical and Computational Chemistry.* **2014**, *13*, 1450041.
- [23] Rezaeyani, F.; Ghiasi, R.; Fazaeli, R.; Yousefi, M., *J. Chin. Chem. Soc.* **2018**, *65*, 416.
- [24] Nasrolahi, M.; Ghiasi, R.; Shafiee, F., *J. Chin. Chem. Soc.* **2019**, *66*, 1577.
- [25] Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Scalman, G.; Barone, V.; Mennucci, B.; Petersson, G.A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H.P.; Izmaylov, A.F.; Bloino, J.; Zheng, G.; Sonnenberg, J.L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; T. Nakajima; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J.A.; Jr.; Peralta, J.E.; Ogliaro, F.; Bearpark, M.; Heyd, J.J.; Brothers, E.; Kudin, K.N.; Staroverov, V.N.; Kobayashi, R.; J. Normand; Raghavachari, K.; Rendell, A.; Burant, J.C.; Iyengar, S.S.; J. Tomasi; Cossi, M.; Rega, N.; Millam, J.M.; Klene, M.; Knox, J.E.; Cross, J.B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R.E.; Yazyev, O.; Austin, A.J.; Cammi, R.; Pomelli, C.; Ochterski, J.W.; Martin, R.L.; Morokuma, K.; Zakrzewski, V.G.; Voth, G.A.; Salvador, P.; Dannenberg, J.J.; Dapprich, S.; Daniels, A.D.; Farkas, O.; Foresman, J.B.; Ortiz, J.V.; Cioslowski, J.; Fox, D.J. *Gaussian 09*, Revision A.02; Gaussian, Inc.: Wallingford CT, 2009.
- [26] Hay, P.J., *J. Chem. Phys.* **1977**, *66*, 4377.
- [27] Krishnan, R.; Binkley, J.S.; Seeger, R.; Pople, J.A., *J. Chem. Phys.* **1980**, *72*, 650.
- [28] McLean, A.D.; Chandler, G.S., *J. Chem. Phys.* **1980**, *72*, 5639.
- [29] Wachters, A.J.H., *J. Chem. Phys.* **1970**, *52*, 1033.
- [30] Yanai, T.; Tew, D.; Handy, N., *Chem. Phys. Lett.* **2004**, *393*, 51.
- [31] Fukui, K., *Acc. Chem. Res.* **1981**, *14*, 363.
- [32] Fukui, K., *J. Phys. Chem.* **1970**, *74*, 4161.
- [33] Gonzalez, C.; Schlegel, H.B., *J. Phys. Chem.* **1990**, *94*, 5523.
- [34] Gonzalez, C.; Schlegel, H.B., *J. Chem. Phys.* **1989**, *90*, 2154.
- [35] Graybeal, J.D., *Molecular Spectroscopy*. McGraw-Hill, 1988.
- [36] Seliger, J., *Nuclear Quadrupole Resonance, Theory – Encyclopedia of Spectroscopy and Spectrometry*. Academic Press 2000.
- [37] Slichter, C.P., *Principles of Magnetic Resonance*. Third ed.; Springer-Verlag: Heidelberg, 1990.
- [38] Cioslowski, J., *J. Am. Chem. Soc.* **1989**, *111*, 8333.

[39] Perrin, C.L.; Armstrong, K.B.; Fabian, M.A.,
J. Am. Chem. Soc. **1994**, *116*, 715.

[40] Tokman, M.; Sundholm, D.; Pyykkö, P.;
Olsen, J., *Chem. Phys. Lett.* . **1997**, *265*, 60.