Computational studies for effect of electron donor and acceptor groups on 2-amino-1, 3-benzothiazole tautomers by Hartree – Fock (HF) and Density Functional Theory (DFT)

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Abstract

In the present research article, were determined optimized geometries, relative energies, thermodynamic properties, equilibrium constants of 2-amino-1,3benzothiazole tautomers substituted electron donor and electron acceptor at various positions by utilized Hartree – Fock (HF) and density functional theory (DFT)/B3LYP strategies with various 6-311 basis set. The stability order of amine and imine frames with – CN substitution was found to be: ABTC7>ABTC4>ABTC5>ABTC6; IBTC7> IBTC5> IBTC6> IBTC4; ABTC5> ABTC7> ABTC4> ABTC6 and IBTC7> IBTC5> IBTC6> IBTC4 at HF and DFT methods respectively. Global descriptors such as ionization energy (I), electron affinity (EA), molecular hardness (η), chemical potential (μ), electrophilicity (ω), and frontier molecular energy gaps (ΔEg) were determined and used to identify the differences in the reactivity of tautomers. From the estimations of η, μ and ω recommended that amine structure tautomers are all the more vivaciously steady and less receptive. The imine tautomers are having high electrophilicity record (ω) values than amine tautomers, so the imine tautomers are a decent electrophile and amine tautomers are great nucleophile in gas phase.

Keywords: 2-amino-1,3benzothiazole tautomers, HF and DFT methods, Molecular descriptors.

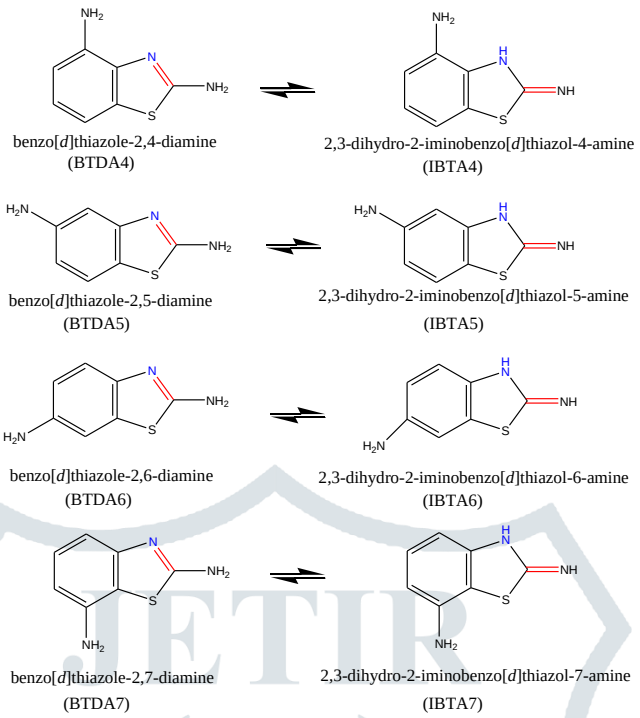
1. Introduction

A compound is one that has a cyclic structure with at least 2 very surprising styles of hetero molecules inside the ring. Nitrogen, oxygen, and sulfur are the chief normal heteroatoms. Benzothiazoles are amalgamated eight membered rings that contain the heterocycles bearing thiazole. Sulfur and nitrogen atoms speak profoundly structure of thiazole and a lot of pharmacologically and naturally dynamic mixes. Benzothiazole might be a compound, powerless base, having fluctuated natural exercises and still of decent logical intrigue right now a days. they're wide found in bioorganic and refreshing science with application in medication disclosure. Benzothiazole derivatives are contemplated and situated to have various concoction reactivity and organic movement. Benzothiazole ring made up of thiazole ring amalgamated with benzol. Thiazole ring might be a five-member ring comprises of one nitrogen and one sulfur atoms inside the ring. Benzothiazole ring observed to have restorative claim to fame exercises like anti- microorganism [1], anti- microorganism [2], and anti- microbic [3] and specialist exercises [4].

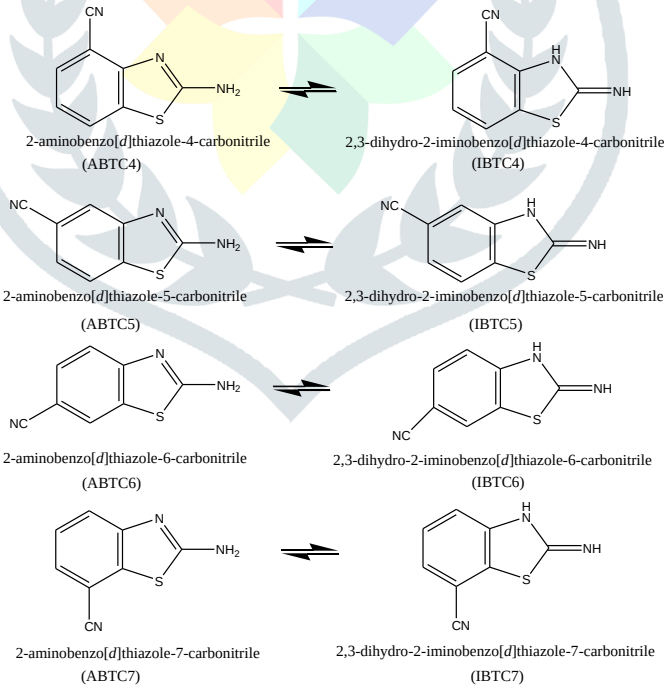
They con jointly useful as anti-allergic [5], anti-diabetic [6], development [7], anti inflammatory [8], anthelmintic, and anti- HIV specialists. Benzothiazoles show growth activity, the phenyl-substituted Benzothiazoles [9, 10] though dense pyrimido benzothiazoles and benzothiazolo quinazolines show anti-viral action. Substituted 6- nitro-and 6-aminobenzothiazoles show antimicrobial movement [11]. Assortment of 2-amino benzo thiazoles are considered as focal muscle relaxants and situated to meddle with salt neurotransmission in natural science, electrophysiological and conduct tests [12].

The number of 2-aminobenzothiazoles was seriously considered, on the grounds that the 2-amino benzothiazole platform is one among favored structure in refreshing science [13, 14] and supposed cytotoxic on malignancy cells. [14] It ought to be focused on that blend of 2-amino benzothiazoles with elective heterocyclic might be a notable way to deal with style new medication like molecules, that grants accomplishing new therapeutic strength profile, activity, danger bringing down. The 2-(4-aminophenyl) benzothiazoles are a novel class of powerful and particular development specialists and show trademark profile of cytotoxic reaction over the cell lines. Furthermore, benzothiazole ring is the blessing in various marine or earthbound regular exacerbates, that have accommodating natural properties. In the past couple of years it had been reputed that benzothiazole, its boosters and subsidiaries had antimicrobial exercises against gram-negative, Gram-positive microscopic organisms (e.g., Enterobacter, Pseudomonas aeruginosa, E. coli, and staphylococci epidermis and so on.) and furthermore the yeast (e.g., organism albicans).

2-amino-1, 3-benzothiazole was leaving two tautomers ;one is amine structure {(benzo[d]thiazol-2-amine (ABTA)}tautomer and other one is imine structure {(benzo[d]thiazol-2(3H)- imine(ABTI) }tautomes. The amine and imine tautomers in whose structures, where in the thiozole ring the amine structure has the NH_2 gathering and one N-H bond while in the imine structure that ring contain two N-H and C=N bonds. In the present examination the impact of electron giving gathering (– NH2) and pulling back gathering (- CN) on 2-amino-1, 3-benzothiazole tautomers at various positions (scheme 1&2) were determined as far as relative energies, thermodynamic and active properties and atomic descriptors by utilizing HF and DFT strategies in gas stage at 298.15k.



Scheme 1: The structures of electron donating group (-NH_2) substituted at different positions on 2-amino-1, 3-benzothiazole tautomers

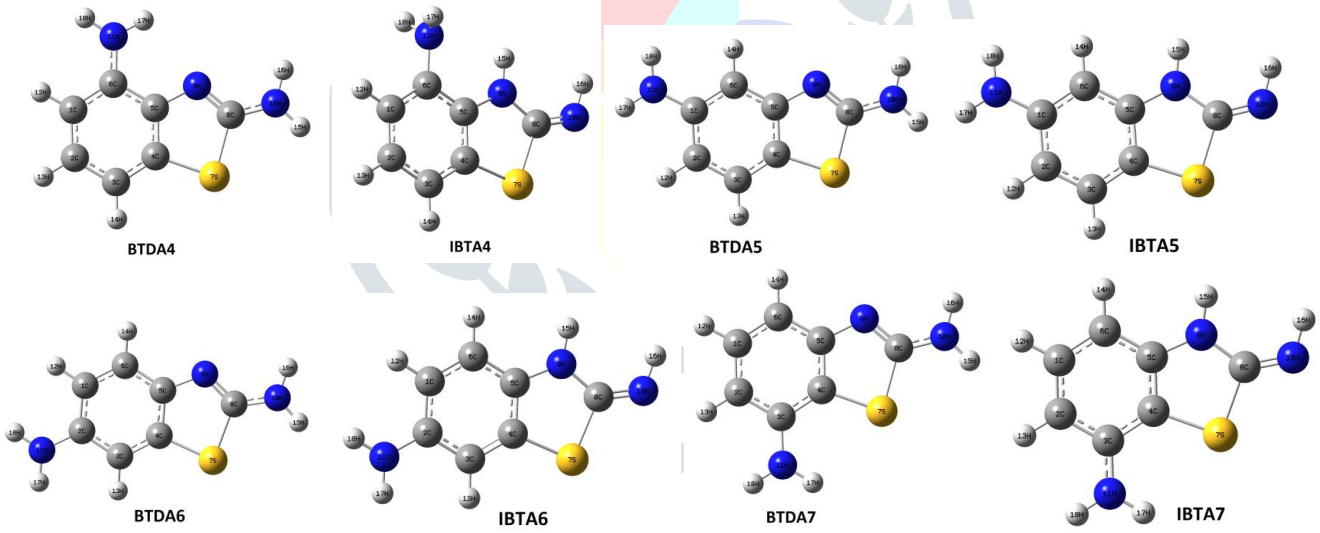


Scheme 2: The structures of electron withdrawing group (-CN) substituted at different positions on 2-amino-1, 3-benzothiazole tautomers

2. Computational details

The initial structures of studied molecules (scheme 1&2) were optimized in a gas phase by HF and Becke's three parameter hybrid density functional theory method (DFT) [15] using the Lee- Yang-Parr correlation functional (B3LYP) [16] with basis set 6-311. The geometries of all tautomers investigated (scheme 1) were completely optimized with the Gaussian 09 [17] program and visualized with the GaussView 5.0 [18] packages. Following the geometry optimizations, analytical frequency calculations were preceded at the HF and DFT methods using standard procedures, to obtain the thermo chemical properties. All geometries were assumed as C1 point group with no special symmetry constrain imposed. The optimized geometrics are shown in Figure 1 in gas phase. Each atom is colored and numbered. Grey is carbon, blue is nitrogen, yellow is oxygen and white is hydrogen.

The underlying structures of examined tautomers (scheme 1&2) were optimized in a gas phase by HF and density functional theory (DFT) [15] method with Becke's three parameter utilizing the Lee-Yang-Parr correlation functional (B3LYP) [16] with 6-311 basis set. The geometries of all tautomers calculated (scheme 1& 2) were totally optimized with the Gaussian 09 [17] program and visualized with the GaussView 5.0 [18] software. Following the geometry improvements, frequency calculations were gone before at the HF and DFT strategies utilizing standard techniques, to acquire the thermodynamic properties. All geometries were accepted as C1 point gather with no uncommon symmetry compel forced. The optimized geometrics are shown in Figure 1 in gas phase.



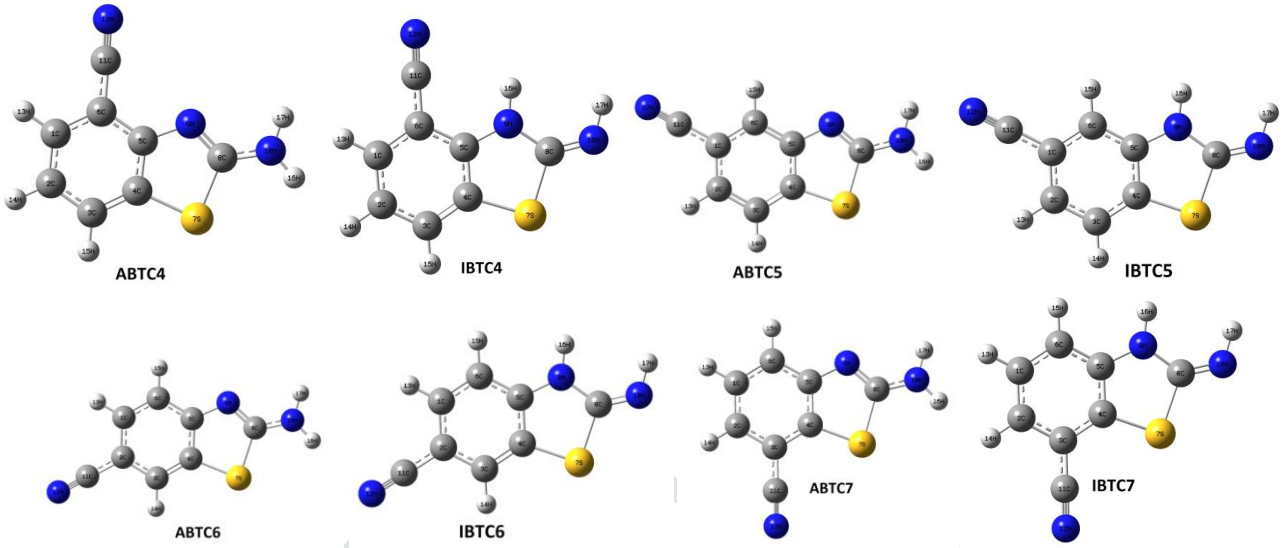


Fig.1 Geometry Optimized structures for all studied molecules at DFT/B3LYP with 6-311G basis set in gas phase.

3. Results and discussion

3.1 Relative stabilities

In Table 1, results are presented for the absolute and relative electronic energy in gas phase, evaluated at the HF and DFT/B3LYP methods with 6-311G basis set. The order of stability of isomers with $–NH_2$ group at different positions for amine form was found to be BTDA6> BTDA5> BTDA7 with respect to stable tautomer BTDA4 in both HF and DFT methods. In case of imine form with $–NH_2$ substitution was found IBTA6> IBTA4>IBTA5 with respect to stable tautomer IBTA7 at HF level and DFT method. The order of stability for amine and imine forms with –CN substitution was found the following order: ABTC7>ABTC4>ABTC5>ABTC6; IBTC7> IBTC5> IBTC6> IBTC4; ABTC5> ABTC7> ABTC4> ABTC6 and IBTC7> IBTC5> IBTC6> IBTC4 at HF and DFT methods respectively.

3.2. Thermodynamics properties

Results gave in Tables 2 are to the change of enthalpy, Gibbs free energy and entropy of the all studied tautomers in gas phase. Gibbs free energy changes were negative shown the reactions is spontaneous process. The ΔH is negative, the reaction is exothermic and the bonds formed in the products are stronger than the bonds broken in the reactants and the products are lower in energy than the reactants.

Table 1. The energies of tautomers (a.u) at HF and DFT/B3LYP methods with 6-311 level in gas phase and the relative energies compared to the most stable isomer. The relative energies are in brackets in kcal mol^{-1} and dipole moments in Debye units.

molecule	Energies at HF method in a.u	Energies at DFT method in a.u	Dipole moments at HF	Dipole moments at DFT
amine form with –NH_2 substitution				
BTDA4	-829.9164219 (0.0000)	-833.3960475(0.0000)	1.6353	2.3949
BTDA5	-829.9135832 (1.7813)	-833.3915761(2.8059)	0.1961	0.6032
BTDA6	-829.9109580 (3.4287)	-833.3904485(3.5134)	1.2979	1.2292
BTDA7	-829.9143979 (1.2701)	-833.3925650(2.1853)	2.4058	2.6533
imine form with –NH_2 substitution				
IBTA4	-829.8938323(3.3635)	-833.3734603(2.6184)	6.2080	5.6799
IBTA5	-829.8969563(1.4031)	-833.3752086(1.5214)	6.6401	6.5020
IBTA6	-829.8930873(3.8309)	-833.3705682(4.4333)	5.7745	5.4614
IBTA7	-829.8991923(0.0000)	-833.3776331(0.0000)	4.1648	3.4408
amine form with –CN substitution				
ABTC4	-866.597720(1.0514)	-870.2715512(0.9504)	5.8199	5.6584
ABTC5	-866.598423(0.6107)	-870.2544915(11.6555)	6.6240	7.0371
ABTC6	-866.599396(0.0000)	-870.2730657(0.0000)	6.3841	7.0067
ABTC7	-866.596869(1.5856)	-870.2711881(1.1782)	4.3922	4.8675
imine form with –CN substitution				
IBTC4	-866.581427(0.0000)	-870.2561918(0.0000)	3.2235	2.4668
IBTC5	-866.579580(1.1587)	-870.2544915(1.0670)	1.4624	2.6706
IBTC6	-866.580761(0.4175)	-870.2550542(0.7139)	5.9679	6.0110
IBTC7	-866.577342(2.5633)	-870.2527043(2.1884)	8.4099	7.9472

Table 2. The enthalpy changes (ΔH), free energy changes (ΔG) in (kcal/mol) and entropy changes (ΔS) in (cal/mol).

equilibrium	**HF**			**DFT**		
	ΔH	**ΔG**	**ΔS**	**ΔH**	**ΔG**	**ΔS**
BTDA4 $\overset{f}{\rightleftharpoons}$ IBTA4	-13.945782	-13.477659	1.57	-13.477659	-15.613076	2.701
BTDA5 $\overset{f}{\rightleftharpoons}$ IBTA5	-10.151229	-10.208332	-0.191	-10.208332	-9.986194	0.517
BTDA6 $\overset{f}{\rightleftharpoons}$ IBTA6	-10.870983	-10.909261	-3.978	-10.909261	-10.411645	0.725
BTDA7 $\overset{f}{\rightleftharpoons}$ IBTA7	-9.297815	-9.443397	-0.49	-9.443397	-9.232554	0.855
ABTC4 $\overset{f}{\rightleftharpoons}$ IBTC4	-9.919678	-9.897087	0.074	-9.233809	-9.303463	0.233
ABTC5 $\overset{f}{\rightleftharpoons}$ IBTC5	-11.480922	-11.453940	0.09	-10.670807	-10.747991	0.259
ABTC6 $\overset{f}{\rightleftharpoons}$ IBTC6	-11.356048	-11.319652	0.123	-10.820782	-10.896083	0.254
ABTC7 $\overset{f}{\rightleftharpoons}$ IBTC7	-11.882529	-11.855546	0.091	-11.079944	-11.140185	0.201

3.3 Equilibrium Constants

The equilibrium constants and pK_T values are determine by the following relation.

$$K = e^{-\Delta G/RT} \text{ and } p^{K_T} = \log K_T \quad (1)$$

Table 3. The equilibrium constants (K) and pKTvalues for the tautomers at DFT/6-311++G(d,p) level in different media

equilibrium	K_T	pK_T	K_T	pK_T
BTDA4 f IBTA4	$1.34706X10^{-10}$	9.8706	$1.34706 X10^{-10}$	9.8706
BTDA5 f IBTA5	$3.33995X10^{-8}$	7.4763	$3.33995 X10^{-8}$	7.4763
BTDA6 f IBTA6	$1.02424X10^{-8}$	7.9896	$1.02424 X10^{-8}$	7.9896
BTDA7 f IBTA7	$1.21326X10^{-7}$	6.9160	$1.21326 X10^{-7}$	6.9160
ABTC4 f IBTC4	$5.64529X10^{-8}$	7.2483	$1.72763 X10^{-7}$	6.7626
ABTC5 f IBTC5	$4.08786X10^{-9}$	8.3885	$1.53122 X10^{-8}$	7.8150
ABTC6 f IBTC6	$5.12677X10^{-9}$	8.2902	$1.18905 X10^{-8}$	7.9248
ABTC7 f IBTC7	$2.07669X10^{-9}$	8.6826	$7.68066 X10^{-9}$	8.1146

The constants were calculated by considering that all the tautomers can be in the equilibrium. Table 3 contained the equilibrium constants (K_T) and the pK_T values at HF and DFT methods. All pK_T values in gas phase and were positive and this confirmed the fact that amine tautomers are most stable. The pK_T were positive; that determine the privileged direction of equilibrium.

3.4 HOMO - LUMO energies

The highest occupied molecular orbital (E_{HOMO}) energy measures the tendency towards the donation of electron by a molecule. The lowest unoccupied molecular orbital (E_{LUMO}) energy indicates the ability of the molecule to accept electrons. Frontier molecular orbital diagrams of all studied tautomers are represented in fig. 2&3. The energy of HOMO provides information about the electron donating ability of the molecule. The molecule with the highest E_{HOMO} value often has the highest tendency to donate electrons to appropriate acceptor molecule of low empty molecular orbital energy .The HOMO and LUMO values are presented in table 4.

3.5 Global and local reactivity descriptors

Theoretical background

As per, the Koopmans' hypothesis [19] for closed shell molecules, ionization potential (I) and electron affinity (A) can be communicated as follows regarding E_{HOMO} and E_{LUMO} the highest occupied molecular orbital energy, and the lowest unoccupied molecular orbital energy, respectively:

$$I = -E_{HOMO} \quad \text{and} \quad A = -E_{LUMO} \qquad (2)$$

the values of I and A are known, one can determine through the following expressions [20] the values of the absolute electron negativity (χ), the absolute hardness (η),the chemical potential (μ) and the softness S[21] (the inverse of the hardness):

$$\chi = \frac{I + A}{2}; \quad \eta = \frac{I - A}{2}; \quad \mu = \frac{(I + A)}{2} \quad \text{and} \quad S = \frac{1}{\eta} \qquad (3)$$

The electrophilicity is a descriptor of reactivity that allows a quantitative classification of the global electrophilic nature of a molecule within a relative scale. Parr have proposed electrophilicity index as a measure of energy lowering due to maximal electron flow between donor and acceptor and defined electrophilicity index (ω) as follows[22].

$$\omega = \frac{\mu^2}{2\eta} \tag{4}$$

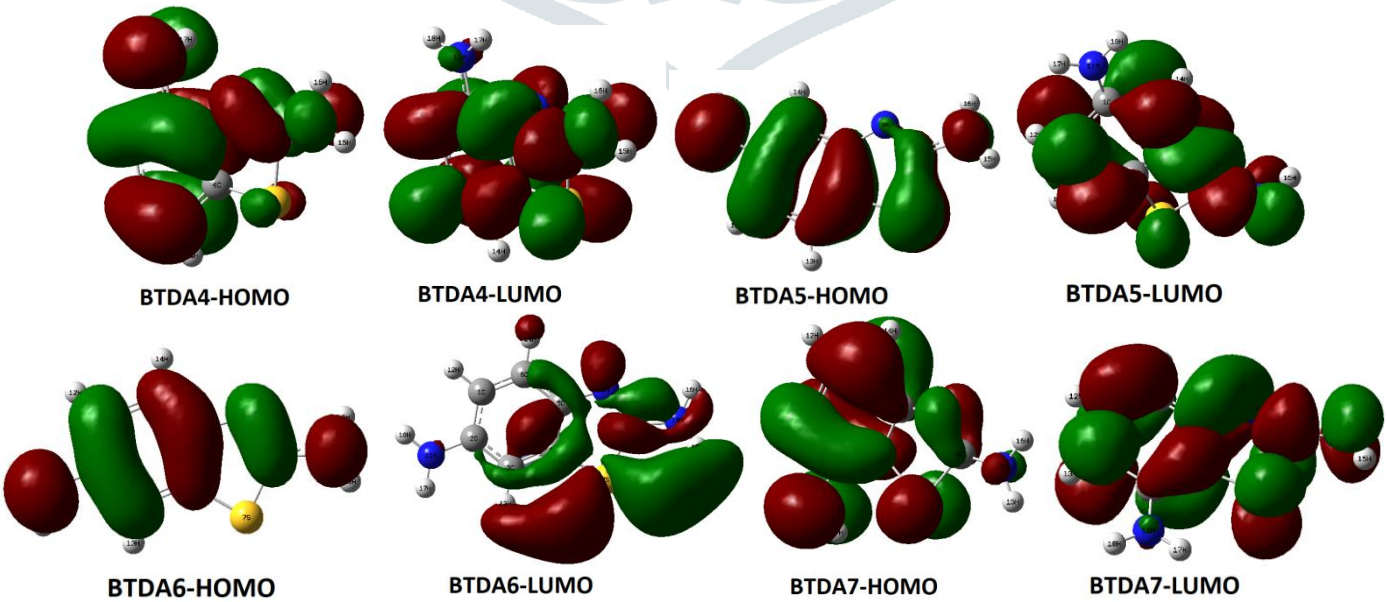
According to the definition, this index measures the propensity of chemical species to accept electrons. A good, more reactive, nucleophile is characterized by lower value of μ, ω, and conversely a good electrophile is characterized by a high value of μ, ω. This new reactivity index measures the stabilization in energy when the system acquires an additional electronic charge ΔNmax from the environment [23].

$$\Delta N_{\max} = -\frac{\mu}{\eta} \tag{5}$$

The maximum charge transfer ΔNmax towards the electrophile was evaluated using Eq. (5). Thus, while the quantity defined by Eq. (3) describes the propensity of the system to acquire additional electronic charge from the environment; the quantity defined in Eq. (5) describes the charge capacity of the molecule. Very recently, Ayers and co-workers [24, 25] have proposed two new reactivity indices to quantify nucleophilic and electrophilic capabilities of a leaving group, nucleofugality (ΔEn) and electrofugality (ΔEe), defined as follows,

$$\Delta E_n = -A + \omega = \frac{(\mu+\eta)^2}{2\eta} \quad \text{and} \quad \Delta E_e = I + \omega = \frac{(\mu-\eta)^2}{2\eta} \tag{6}$$

Table 4 summarized the important global chemical parameters. Ionization energy is a fundamental descriptor of the chemical reactivity of atoms and molecules. High ionization energy indicates high stability and chemical inertness and small ionization energy indicates high reactivity of the atoms and molecules [26].



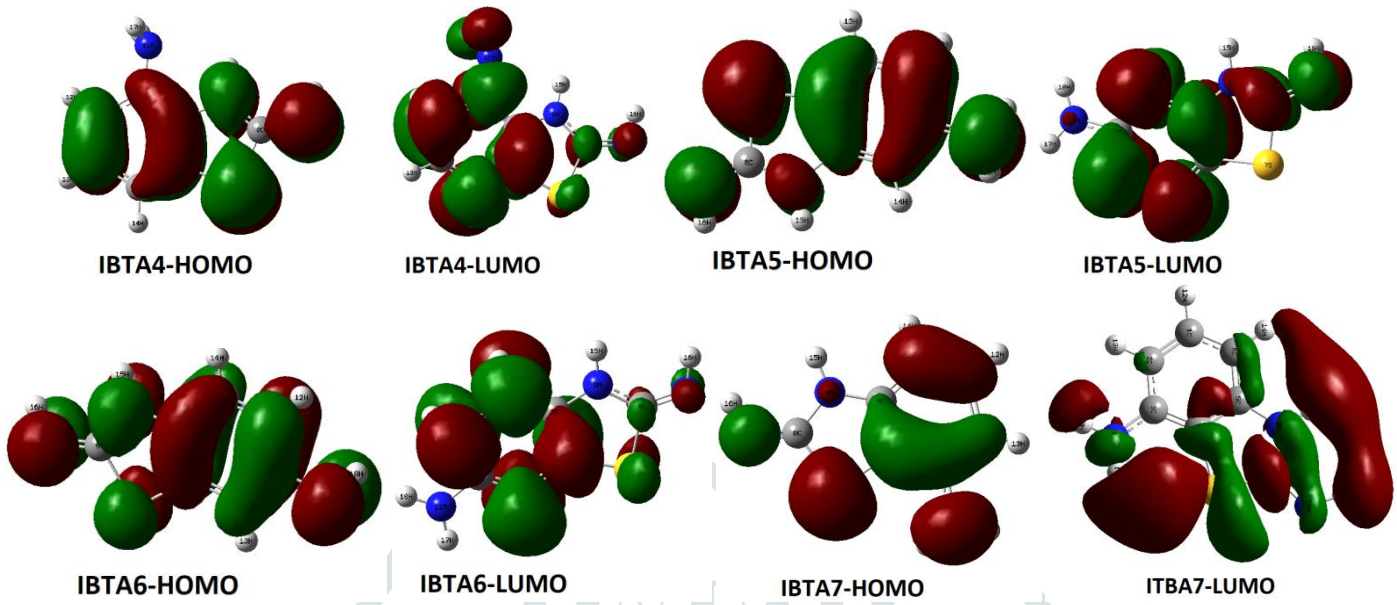
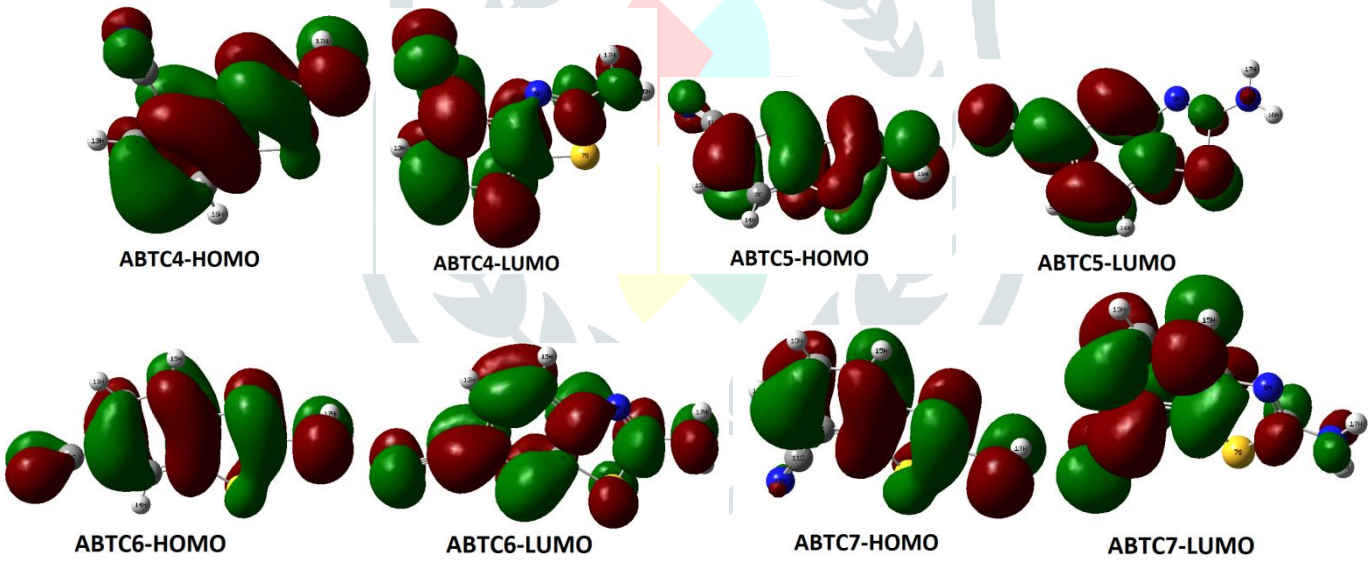


Fig:2. The HOMO and LUMO frontier molecular orbitals of amine form with $–NH_2$ substitution in different positions at DFT/6-311 level in gas phase. In surface box, grey= available; Red= displayed



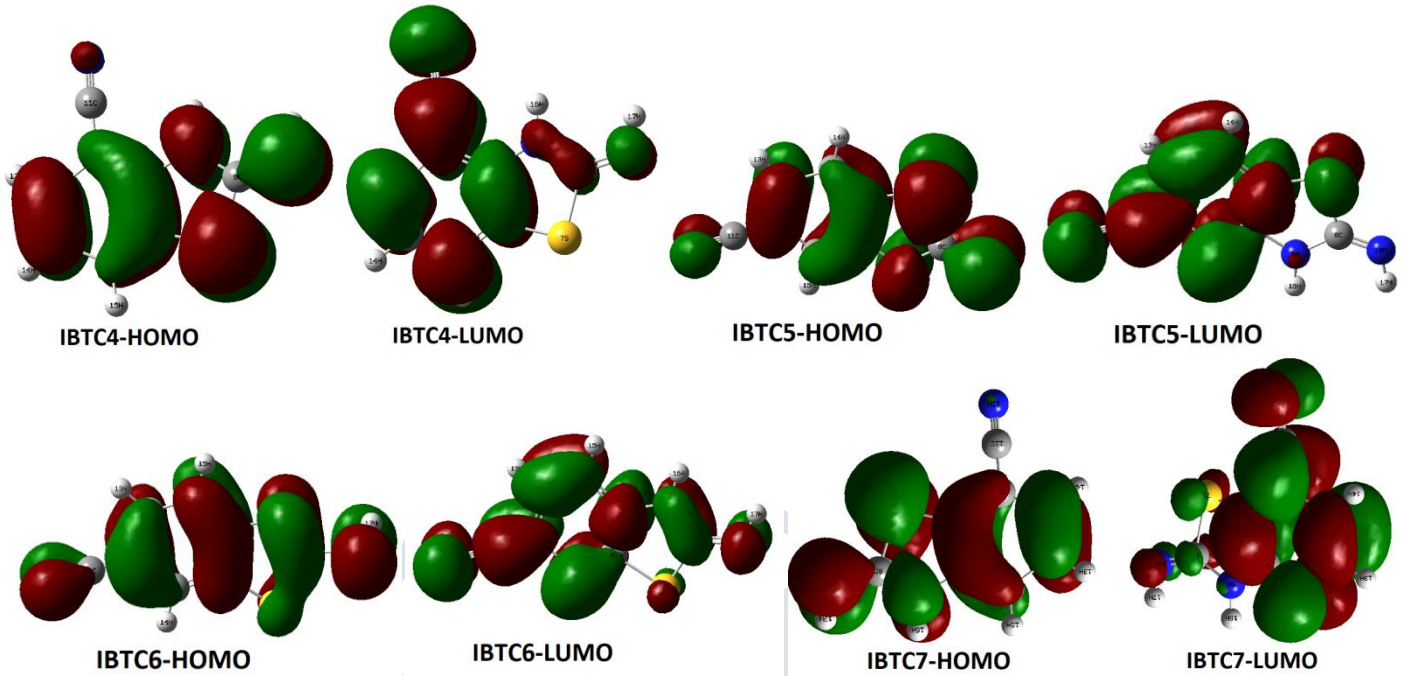


Fig :3. The HOMO and LUMO frontier molecular orbitals of imine form with $–NH_2$ substitution in different positions at DFT/6-311 level in gas phase. In surface box, grey= available; Red= displayed

Table 4: Calculated Global Quantities ionization potential (I), electron affinity (A) ,Chemical potential (μ), Electronegativity (χ), Hardness (η), Softness (s), and Electrophilicity (ω) of studied tautomers in eV at DFT/6-311 level in gas phase.

Tautomers	HF											
	HOMO	LUMO	**I**	**A**	**χ**	**η**	**S**	**μ**	**ω**	**ΔN_{max}**	**ΔE_n**	**ΔE_e**
BTDA4	-7.4143	3.4120	7.4143	-3.4120	2.0011	5.4132	-2.0011	0.1847	0.3699	0.3697	3.7819	7.7842
BTDA5	-7.6029	3.4240	7.6029	-3.4240	2.0894	5.5134	-2.0894	0.1814	0.3959	0.3790	3.8199	7.9988
BTDA6	-7.2888	3.4333	7.2888	-3.4333	1.9278	5.3611	-1.9278	0.1865	0.3466	0.3596	3.7799	7.6355
BTDA7	-7.6910	3.3952	7.6910	-3.3952	2.1479	5.5431	-2.1479	0.1804	0.4162	0.3875	3.8113	8.1072
IBTA4	-8.0826	3.1595	8.0826	-3.1595	2.4615	5.6211	-2.4615	0.1779	0.5390	0.4379	3.6985	8.6216
IBTA5	-7.5737	3.4284	7.5737	-3.4284	2.0727	5.5011	-2.0727	0.1818	0.3905	0.3768	3.8188	7.9642
IBTA6	-7.4546	3.2142	7.4546	-3.2142	2.1202	5.3344	-2.1202	0.1875	0.4213	0.3975	3.6355	7.8759
IBTA7	-8.0875	3.4406	8.0875	-3.4406	2.3234	5.7641	-2.3234	0.1735	0.4683	0.4031	3.9089	8.5558
ABTC4	-8.8026	2.0898	8.8026	-2.0898	3.3564	5.4462	-3.3564	0.1836	1.0342	0.6163	3.1241	9.8369
ABTC5	-8.8530	2.1309	8.8530	-2.1309	3.3610	5.4919	-3.3610	0.1821	1.0285	0.6120	3.1594	9.8814
ABTC6	-8.7953	2.0305	8.7953	-2.0305	3.3824	5.4129	-3.3824	0.1847	1.0568	0.6249	3.0873	9.8520
ABTC7	-8.8105	2.0376	8.8105	-2.0376	3.3865	5.4240	-3.3865	0.1844	1.0572	0.6243	3.0947	9.8677
IBTC4	-8.7509	1.7538	8.7509	-1.7538	3.4986	5.2523	-3.4986	0.1904	1.1652	0.6661	2.9190	9.9161
IBTC5	-8.7577	1.8120	8.7577	-1.8120	3.4729	5.2849	-3.4729	0.1892	1.1411	0.6571	2.9531	9.8988
IBTC6	-8.7498	2.0670	8.7498	-2.0670	3.3414	5.4084	-3.3414	0.1849	1.0322	0.6178	3.0992	9.7820
IBTC7	-8.7180	1.7799	8.7180	-1.7799	3.4690	5.2489	-3.4690	0.1905	1.1464	0.6609	2.9262	9.8643
	DFT/B3LYP											
BTDA4	-5.1030	-0.2708	5.1030	0.2708	2.6869	2.4161	-2.6869	0.4139	1.4940	1.1121	1.2232	6.5969
BTDA5	-5.1906	-0.3306	5.1906	0.3306	2.7606	2.4300	-2.7606	0.4115	1.5681	1.1361	1.2375	6.7587
BTDA6	-5.0129	-0.1687	5.0129	0.1687	2.5908	2.4221	-2.5908	0.4129	1.3856	1.0697	1.2169	6.3985
BTDA7	-5.3579	-0.3380	5.3579	0.3380	2.8479	2.5100	-2.8479	0.3984	1.6157	1.1346	1.2777	6.9736
IBTA4	-5.7563	-0.5880	5.7563	0.5880	3.1722	2.5841	-3.1722	0.3870	1.9470	1.2276	1.3590	7.7033
IBTA5	-5.2461	-0.3374	5.2461	0.3374	2.7918	2.4543	-2.7918	0.4074	1.5878	1.1375	1.2504	6.8339
IBTA6	-5.1536	-0.4014	5.1536	0.4014	2.7775	2.3761	-2.7775	0.4209	1.6233	1.1689	1.2219	6.7769
IBTA7	-5.5974	-0.1804	5.5974	0.1804	2.8889	2.7085	-2.8889	0.3692	1.5407	1.0666	1.3603	7.1380
ABTC4	-6.4899	-1.6057	6.4899	1.6057	4.0478	2.4421	-4.0478	0.4095	3.3547	1.6575	1.7490	9.8446
ABTC5	-6.5345	-1.5208	6.5345	1.5208	4.0277	2.5069	-4.0277	0.3989	3.2356	1.6067	1.7148	9.7701
ABTC6	-6.5033	-1.6591	6.5033	1.6591	4.0812	2.4221	-4.0812	0.4129	3.4383	1.6850	1.7793	9.9416
ABTC7	-6.4943	-1.6354	6.4943	1.6354	4.0648	2.4294	-4.0648	0.4116	3.4006	1.6732	1.7652	9.8948
IBTC4	-6.4156	-1.9377	6.4156	1.9377	4.1767	2.2390	-4.1767	0.4466	3.8957	1.8655	1.9580	10.3113
IBTC5	-6.4295	-1.8229	6.4295	1.8229	4.1262	2.3033	-4.1262	0.4342	3.6959	1.7914	1.8730	10.1254
IBTC6	-6.4320	-1.6991	6.4320	1.6991	4.0655	2.3664	-4.0655	0.4226	3.4923	1.7180	1.7932	9.9242
IBTC7	-6.3816	-1.8664	6.3816	1.8664	4.1240	2.2576	-4.1240	0.4429	3.7667	1.8267	1.9003	10.1484

Ionization vitality is a key descriptor of the compound reactivity of atoms and molecule. High ionization energy shows high solidness, less reactivity and little ionization energy demonstrates high reactivity of the atoms and molecules. From table 2 the high ionization energies for amine and imine structure with – NH2 substitution tautomers contrast and – CN substitution tautomers. On account of the – CN group is electron pulling back nature. Absolute hardness and softness quality are imperative properties to gauge the molecular dependability and reactivity. It is clear that the synthetic hardness on a very basic level means the obstruction towards the disfigurement or polarization of the electron haze of the atoms, molecules or molecules under little bother of compound response. A similar pattern for the situation hardness esteems like Ionization vitality.

The electrophilicity list (ω) has been utilized as basic descriptor for the examination of the chemical reactivity of molecules. It measures the tendency of a species them to accept electrons. A good, more reactive, nucleophile is characterize by a lower value of (ω), in opposite a good electrophile is characterized by a high value of (ω). The electrophilicity list esteems are displayed in table 4. The imine tautomers are having high electrophilicity index (ω) values than amine tautomers, so the imine tautomers are a decent electrophile and amine tautomers are great nucleophile in gas stage. Physically, compound potential (μ) portrays the getting away propensity of electrons from a harmony framework. The more noteworthy the electronic concoction potential, the less steady or increasingly responsive is the compound.

4. Conclusion

A computational study of the relative energies and molecular descriptors was calculated at the HF and density functional theory (DFT) methods with 6-311G basis set in the gas phase at 298.15k. The relative stabilities determined for isomers in gas phase with respect to stable isomer respectively. The ionization energies for amine and imine form with $–NH_2$ substitution tautomers higher than compare with –CN substitution tautomers. Because of the –CN group is electron withdrawing nature. The imine tautomers are having high electrophilicity index (ω) values than amine tautomers, so the imine tautomers are a good electrophile and amine tautomers are good nucleophile in gas phase.

References

1. Akihama S, Okhude M, Mizno A, Yakka M and Kenkyu Kiyo D.1968. Chem Abstr.6810369.
2. Russo F and Santagati M.1976. Farmaco Ed Sci. 41, 31.
3. Ghoneim KM, Basil SEI, Osman AN, Said MM and Megahed SA. 1999.RevRoumChim. 36,1355.
4. Singh SP and Seghal S.1988. Indian J Chem. 27B, 941.
5. Musser JH, Brown RE, Love B, Baily K, Jones H, Kahen R, et al.1984. J Med Chem. 27,121.
6. Pattan SR, Suresh C, Pujar VD, Reddy VVK, Rasal VP and Kotti BC.2005. Indian J Chem.4B,2404.

7. Yoshida M, Hayakawa I, Hyashi N, Agatsuma T, Oda Y and Tanzawa F,et.al.2005. Bioorg Med Chem Letter. 15, 3328.
8. Sawhney SN and Bansal OP.1977. Indian J Chem.15B,121.
9. Bradshaw TD, Bibby MC, Double JA, Fichtner I, Cooper PA, Alley MC, Donohue S, Stinson SF, Tomaszewjski JE, Sausville EA and Stevens MFG.2002. Mol. Cancer. Therapeutics. 1, 239.
10. Hutchinson I, Jennings SA, Vishnuvajjala BR, Westwell AD and Stevens MFG.2002 J. Med. Chem. 45, 744.
11. El-Sherbeny MA. 2000.Arzeneim-Forsch. 50, 843.
12. Bryson M, Fulton B and Benfield P.1996. Drugs, 52, 549.
13. Reddy P, Lin Y and Chang H. 2007.Arcivoc. xvi, 113.
14. Piscitelli F, Ballatore C and Smith A.2010. Bioorg Med Chem Lett. 20,644.
15. Becke AD. 1993.J. Chem. Phys. 98,5648.
16. Lee C,Yang W and Parr RG.1988. Phys. Rev. B 37, 785.
17. Frisch M, Trucks GW and Schlegel HB, et al. 2009. Gaussian 09, Rev. A.1 Gaussian, Inc.,Walling ford CT.
18. Gaussview Rev. 5.0,2009. Windows version. Gaussian Inc., Pittsburgh.
19. Koopmans T. 1993.Physica. 1, 104.
20. Becke AD.1993. J. Chem. Phys. 98, 5648.
21. Pearson RG .1963. J.Am.Chem.Soc. 85(22), 3533.
22. Lesar A and Milosev I. 2009.Chem. Phys. Lett.483(4-6), 198.
23. Parr RG, Szentpaly L and Liu S.1999. J. Am. Chem. Soc.121.
24. Ayers PW, Anderson JSM and Bartolotti LJ.2005. Int. J. Quantum Chem. 101, 520.
25. Roos G, Loverix S, Brosens E, Van Belle K, Wyns L, Geerlings P and Messens J.2006. ChemBioChem. 7, 981.
26. Chakraborty T and Ghosh DC.2010. Mol. Phys. 108 (16), 2081.