Ab-Initio calculations; structural, physical properties, thermodynamic function and charges for some Bio active compounds

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Abstract:

Ab- Initio calculations have been used to identify the dimensional geometric (lengths and angles bond) when the geometry of a balanced, functions thermodynamic, some physical properties, charge for some thiazolo derivatives compounds .

*Calculation results have shown that the compound **R-PH-Cl** is less activity because it has the high value of ΔE and Electronegativity(χ) and has high value of(Ɠ Electrophilicity) . But the compound **R-PH-OCH₃** has highest value of all thermodynamic functions (E^0 , H^0 , G^0 , A^0 , C_V , C_P ,S^0), This difference in results come according to the difference of substituted groups.*

*The results investigation Heat formation ($\Delta H_f^{\ 0}$ (in kJ/mole) by using (semi-empirical method PM3 model in MOPAC) for these molecules and the results showed that the compound **R-PH-F)** has less value which means high thermal stability than the other's.*

Key words: DFT study, thiazolo compound, Electronegativity, hardness

INTRODUCTION

Cancer is the worldwide health problems and the most frightening disease of human. The development of new

anticancer therapeutic agents is one of the fundamental goals in medicinal chemistry. Cytotoxicity and genotoxicity of anticancer drugs to the normal cells are major problems in cancer therapy and engender the risk of inducing secondary malignancy **[1,2].**
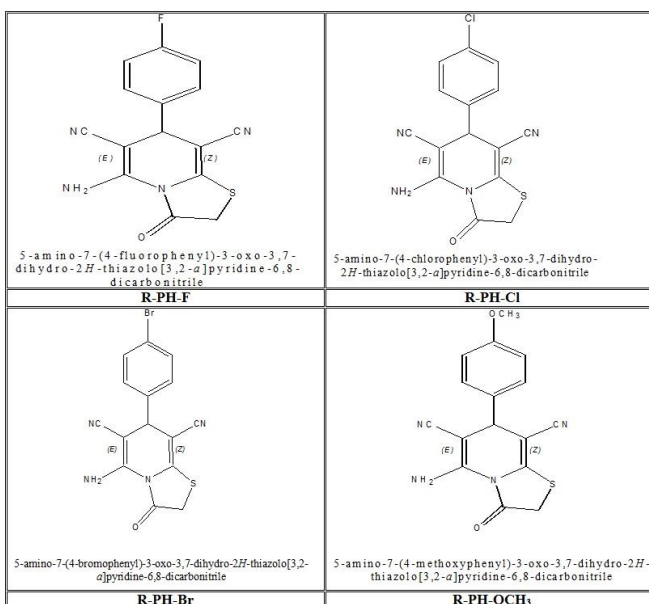
Computational chemistry is the field that uses computer to predict molecular structure and reactivity**[3]** .The latter are now applied routinely to compute molecular properties in a wide variety of chemical applications, including pharmaceuticals and drug design, atmospheric and environmental chemistry , nanotechnology ,and materials science**[4].** density functional theory, DFT" .It allows us to compute all properties of systems by the electron density , *p (r)* which is a function of three variables, , *p (r)*=f(x ,y , z)"[**5,6**].

Kohn and Sham showed that *p* can be expressed as contribution from each electron present in the molecule, and written: $\rho(r) = \sum_{i=1}^{Ne} /\psi i(r)/^2$

ψi is called a Kohn – Sham orbital and is a solution of the Kohn – Sham equation , which closely resembles the form of Schrodinger equation. The Kohn – Sham equation is

$$\left[\frac{h^2}{2m}\nabla^2 + V_{(r)} + V_{H(r)} + V_{XC(r)}\right]\psi i(r) = \varepsilon_i \, \psi_{i(r)}$$

Thus ,the $V_{(r)}, V_{H(r)}, V_{XC(r)}$ are refers to the interaction between an electron and the collation of atomic unclei, the Hartree potential and exchange-correlation contributions to the single-electrons, respectively[**7-10**]. Density functional calculations are reported to provide excellent vibrational wave number of organic compounds if the calculated frequencies are scaled to compensate for the approximate treatment of electron correlation ,for basis set deficiencies and for the an harmonicity**[11-14].**

5-amino-7-(4-fluorophenyl)-3-oxo-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6,8-dicarbonitrile **R-PH-F**	5-amino-7-(4-chlorophenyl)-3-oxo-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6,8-dicarbonitrile **R-PH-Cl**
5-amino-7-(4-bromophenyl)-3-oxo-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6,8-dicarbonitrile **R-PH-Br**	5-amino-7-(4-methoxyphenyl)-3-oxo-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6,8-dicarbonitrile **R-PH-OCH₃**

Computational details

In this work, there were investigated theoretically using the Density Functional Theory (DFT) calculation [15] at the B3LYP/6-311G(p, d) level of theory to get the optimized geometry . DFT calculations were carried out with Beck's three-parameter hybrid model using the Lee–Yang–Parr correlation functional (B3LYP) method. Molecular geometries were fully optimized by Berny's optimization algorithm using redundant internal coordinates. All optimized structures were confirmed to be minimum energy conformations **[16,17].**

RESULTS AND DISCUSSION

Geometrical parameter.

In this research calculated the geometry (bond lengths and bond angels) of the four molecules of Some thiazolo derivatives compounds.

According to the results calculated and recorded in the (**table 1**and **fig. 1)** . Show that the bond $(C_{19} - X_{22})$ X : -F , -Cl , -Br, -OCH_3 in compound **R-PH-F** has high value compared to other compounds studies it may be due to high electro – negative of **F** atom with substituted group. , Whereas for the same bond length for the compound **R-PH-OCH₃** has less value. And each of bonds $(C_{19} - C_{20})$ and $(C_{19} - C_{18})$ the compound **R-PH-OCH₃** has high value than other compounds.

Also the change of the group substituted had effect on the value of the angles of the compounds studied in this research ,have shown calculation in the (**table 1**and **fig. 1).** That the angles $\angle C_{20}C_{19}C_{18}$ in compound **R-PH-F** has high value may be to the electro – negative of substituted group. Also $\angle C_{17}C_{18}C_{19}$ the results showed that in compound **R-PH-OCH₃** has high value.
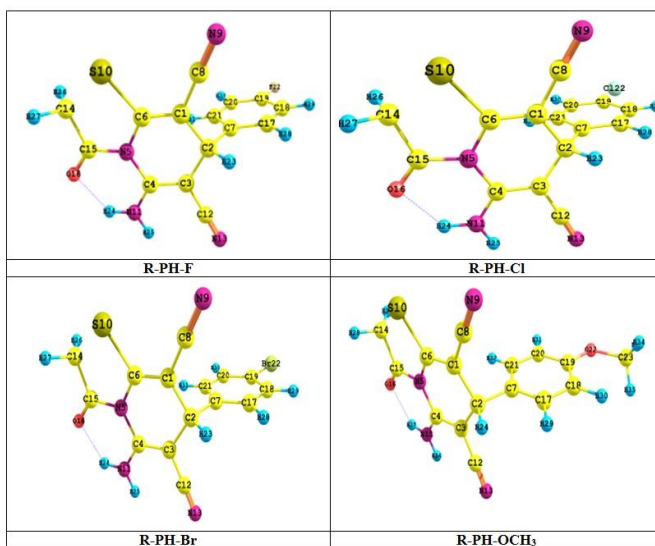

Fig.(1): The geometric equilibrium of some thiazolo derivatives

Table 1: Calculated geometric parameters (bond lengths in Angstrom length angles in degree) of some thiazolo derivatives

R-PH-F		R-PH-Cl		R-PH-Br		R-PH-OCH₃	
Para. Geo.	*Bond length and angle*	*Para. Geo.*	*Bond length and angle*	*Para. Geo.*	*Bond length and angle*	*Para. Geo.*	*Bond length and angle*
R(17-18)	1.398	R(17-18)	1.398	R(17-18)	1.398	R(17-18)	1.400
R(17-28)	1.082	R(17-28)	1.082	R(17-28)	1.082	R(17-29)	1.083
R(18-19)	1.385	R(18-19)	1.388	R(18-19)	1.390	R(18-19)	1.397
R(18-29)	1.079	R(18-29)	1.079	R(18-29)	1.079	R(18-30)	1.079
R(19-20)	1.388	R(19-20)	1.391	R(19-20)	1.394	R(19-20)	1.403
R(19-22)	1.400	R(20-21)	1.395	R(20-21)	1.394	R(19-22)	1.391
R(20-21)	1.394	R(20-30)	1.079	R(20-30)	1.080	R(20-21)	1.388
R(20-30)	1.080	R(21-31)	1.082	R(21-31)	1.082	R(20-31)	1.080
R(21-31)	1.082	R(16-24)	1.883	R(16-24)	1.885	R(21-32)	1.083
R(16-24)	1.883	A(2-1-6)	122.3	A(2-1-6)	122.2	R(22-23)	1.453
R(10-14)	1.886	A(2-1-8)	117.5	A(2-1-8)	117.6	R(23-33)	1.085
A(7-17-18)	120.9	A(7-21-31)	120.0	A(7-21-31)	120.0	A(5-15-16)	125.2
A(7-17-28)	119.8	A(24-11-25)	120.4	A(24-11-25)	120.4	A(17-7-21)	118.5
A(7-21-20)	120.8	A(11-24-16)	130.5	A(11-24-16)	130.4	A(7-17-18)	121.3
A(7-21-31)	119.9	A(15-14-26)	109.8	A(15-14-26)	109.8	A(7-17-29)	119.7
A(24-11-25)	120.4	A(15-14-27)	109.6	A(15-14-27)	109.6	A(7-21-20)	120.9
A(11-24-16)	130.5	A(14-15-16)	121.5	A(14-15-16)	121.6	A(7-21-32)	119.8
A(15-14-26)	109.8	A(26-14-27)	109.8	A(26-14-27)	109.8	A(25-11-26)	120.5
A(15-14-27)	109.5	A(15-16-24)	102.3	A(15-16-24)	102.3	A(11-25-16)	130.5
A(14-15-16)	121.5	A(18-17-28)	119.2	A(18-17-28)	119.2	A(15-14-27)	109.8
A(26-14-27)	109.8	A(17-18-29)	120.8	A(17-18-29)	120.4	A(14-15-16)	121.4
A(26-14-10)	109.8	A(19-18-29)	120.6	A(19-18-29)	120.4	A(27-14-28)	109.8
A(17-18-19)	118.2	A(17-18-19)	118.6	A(17-18-19)	119.1	A(17-18-19)	119.3
A(17-18-29)	121.8	A(20-21-31)	119.1	A(20-21-31)	119.1	A(19-18-30)	121.2
A(18-19-20)	122.8	A(18-19-20)	122.0	A(18-19-20)	121.1	A(18-19-20)	120.1

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Physical properties.

Depending on the Ab initio of method of calculation according to the density function theory (DFT) is calculate some physical properties of the molecules studied in this research; Dipole moments (µ in Debye) , energies (e V) of the high Occupied Molecular Orbital (E_{HOMO}) and the Lower Unoccupied Molecular Orbital (E_{LUMO}) and according Koopmans theorem (the negative E_{HOMO} is equal to the ionization potential) the calculation has been ionization energies (e V) , Also calculated the energy difference (ΔE , e V), And finally calculated (Molecular Hardness) (η) = ½(E_{HOMO} - E_{LUMO}), (Electron Affinity) EA = - E_{LUMO} according Koopmans theorem for N system of electrons[18-21], Electronegativity(χ) according to Mullikan1934 [22] and Electrophilicity (Ꞷ) according to Parr and co-workers 1999[23]. Shown this results **(table :2)** that the compound **R-PH-Cl** is less activity because it has the high value of ΔE and Electronegativity(χ) and has high value of(Ꞷ Electrophilicity) .

Also, the MOPAC computational packages (semi-empirical method , PM3 model) employed to compute physical properties; heats of formation (ΔHf, kJ.mol-1)**[24,25]**. the results showed **(Table 2)** for the compound **R-PH-F** has less value which means high stability than the other's.

Table 2: Energetic properties of some thiazolo derivatives calculated by(DFT) method

Comp.	ΔH$_f$ KJ/Mol	µ Debye	E_{HOMO} eV	E_{LUMO} eV	ΔE eV	IP eV	EA eV	η eV	X eV	Ꞷ eV
R-PH-F	254.4721	6.0988	-6.51854	-2.3276	4.1908	6.51854	2.3276	**2.09543**	**4.4231**	**21.7923**
R-PH-Cl	409.248	6.392	-6.550	-2.357	4.1924	6.550	2.357	**2.096**	**4.453**	**22.369**
R-PH-Br	469.3103	5.9357	-6.5179	-2.3344	4.1835	6.5179	2.3344	**2.0917**	**4.4262**	**21.9308**
R-PH-OCH₃	**276.503**	**3.026**	**-6.225**	-2.1616	**4.064**	**6.225**	2.1616	**2.032**	**4.193**	**18.725**

Thermodynamics functions

Thermodynamic functions calculated by the fundamental vibration frequencies for five compound of *some thiazolo*

molecules along with the rotational constants, obtained in this study, where used to calculate the vibration and rotation contributions to the thermodynamic functions.

Thermodynamics functions standard and heat capacity for the studied molecules listed **Table: 3** looking   at the calculation results show   that   each of the thermodynamic functions (G^0, A^0, E^0, H^0) and (C_V, C_P)have the same gradient values (different the group substitutes),

$$B > C > D > E > A$$

Table 3: Standard thermodynamics functions at 298.15oK of some thiazolo derivatives calculated by (DFT).

Comp.	E^0 KJ/Mol	H^0 KJ/mol	G^0 KJ/mol	S KJ/mol.deg	A^0 KJ/mol	Cp KJ/mol.deg	Cv KJ/mol.deg
R-PH-F	617.1484	619.6272	437.5619	0.610	255.4966	0.303	0.2949
R-PH-Cl	614.646	617.124	429.885	0.628	242.647	0.306	0.298
R-PH-Br	614.4580	616.9368	428.0289	0.633	239.1211	0.307	0.2994
R-PH-OCH₃	728.443	730.921	537.719	0.648	344.518	0.329	0.321

The Charges

The Calculated for all charges atoms of the molecules studied according to the method (DFT) have shown calculation results of the charges **(Table: 4)** of carbon atom C_{19} in compound **R-PH-Br** has high value of charge (the lowest density electronic), Perhaps the reason for this difference in electrical negative and molecular weight which increase the electronic density.

When the Nitrogen atoms (N_9, N_{11}) have high negative charge value in compound   **R-PH-OCH₃**   can be used as a strong legend when it linked to metal complex formation.

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Table 4. Charge of of some thiazolo derivatives calculated by (DFT).

R-PH-F		R-PH-Cl		R-PH-Br		R-PH-OCH$_3$	
Atom	*Charge*	*Atom*	*Charge*	*Atom*	*Charge*	*Atom*	*Charge*
C$_4$	0.8207	C$_4$	0.8217	C$_4$	0.8213	C$_4$	0.8196
N$_5$	-0.8031	N$_5$	-0.8038	N$_5$	-0.8029	N$_5$	-0.8022
C$_6$	0.0215	C$_6$	0.0216	C$_6$	0.0215	C$_6$	0.0222
C$_7$	0.0734	C$_7$	0.0932	C$_7$	0.0894	C$_7$	0.0883
C$_8$	-0.2353	C$_8$	-0.2351	C$_8$	-0.2348	C$_8$	-0.2336
N$_9$	-0.0831	N$_9$	-0.0817	N$_9$	-0.0823	N$_9$	-0.0866
S$_{10}$	0.4267	S$_{10}$	0.4281	S$_{10}$	0.4271	S$_{10}$	0.4214
N$_{11}$	-0.8775	N$_{11}$	-0.8770	N$_{11}$	-0.8768	N$_{11}$	-0.8784
C$_{12}$	-0.2401	C$_{12}$	-0.2405	C$_{12}$	-0.2402	C$_{12}$	-0.2400
N$_{13}$	-0.1001	N$_{13}$	-0.0992	N$_{13}$	-0.0996	N$_{13}$	-0.1047
C$_{14}$	-0.7242	C$_{14}$	-0.7243	C$_{14}$	-0.7242	C$_{14}$	-0.7240
C$_{15}$	0.6167	C$_{15}$	0.6170	C$_{15}$	0.6165	C$_{15}$	0.6160
O$_{16}$	-0.3997	O$_{16}$	-0.3991	O$_{16}$	-0.3992	O$_{16}$	-0.4025
C$_{17}$	-0.1406	C$_{17}$	-0.1592	C$_{17}$	-0.1484	C$_{17}$	-0.1582
C$_{18}$	-0.1859	C$_{18}$	-0.0431	C$_{18}$	-0.0963	C$_{18}$	-0.1598
C$_{19}$	0.3204	C$_{19}$	-0.2894	C$_{19}$	-0.3641	C$_{19}$	0.2571
C$_{20}$	-0.1993	C$_{20}$	-0.0547	C$_{20}$	-0.1068	C$_{20}$	-0.1758
C$_{21}$	-0.0513	C$_{21}$	-0.0684	C$_{21}$	-0.0616	C$_{21}$	-0.0615
F$_{22}$	-0.3361	Cl$_{22}$	-0.0163	Br$_{22}$	0.1817	O$_{22}$	-0.5206
H$_{23}$	0.2317	H$_{23}$	0.2315	H$_{23}$	0.2313	H$_{23}$	-0.2932
H$_{24}$	0.3830	H$_{24}$	0.3832	H$_{24}$	0.3829	H$_{24}$	0.2267
H$_{25}$	0.3603	H$_{25}$	0.3607	H$_{25}$	0.3604	H$_{25}$	0.3816
H$_{26}$	0.2754	H$_{26}$	0.2758	H$_{26}$	0.2761	H$_{26}$	0.3587
H$_{27}$	0.2747	H$_{27}$	0.2749	H$_{27}$	0.2740	H$_{27}$	0.2741
H$_{28}$	0.1674	H$_{28}$	0.1686	H$_{28}$	0.1668	H$_{28}$	0.2726
H$_{29}$	0.1849	H$_{29}$	0.1915	H$_{29}$	0.1800	H$_{29}$	0.1563
H$_{30}$	0.1808	H$_{30}$	0.1870	H$_{30}$	0.1753	H$_{30}$	0.1745
H$_{31}$	0.1639	H$_{31}$	0.1642	H$_{31}$	0.1621	H$_{31}$	0.1696

REFERENCES

[1] Panda, S. S. *"Aqua Mediated Synthesis of Bio-active Compounds"*; J. of *Mini-Reviews in Medicinal Chemistry, 13,* 784-801; 2013.

[2] Aydemir, N.; Bilaloglu, R., "Genotoxicity of two anticancer drugs, gemcitabine and topotecan, in mouse bone marrow *in vivo. Mutat. Res.*, *537*, 43-51; 2003.

[3] Atkins, P.,Depaula , J .and Fridman,R.," Quanta, Matter and Charge: A Molecullar Approach to Physical Chemists" , 1st ed. ,W.H. Freeman and company , New York, USA, 2009.

[4] Young C.,; J.of Comput. Chem.;"A practical guide for applying techniques to red-world problems", st ed. , John Wiley and Sons, USA,2001.

[5] Jerzy, L. and Manoj, K.S., Practical Aspects of Computational Chemistry: Methods, Concepts and Applications , USA, 2009.

[6] David, S.S. and Janice ,A.S., Density Functional Theory :A practical Introduction , John Wiley and Sons, USA, 2009.

[7] Nalewajski, R.F. Density Functional theory; Fundamentals and Effective Potential , Springer , Germany, 1996.

[8] Wolfram, K. and Max. C.H., A Chemist's Guide to Chemistry Functional Theory , 2nd edition, Wiley-VCH , Germany, 2001.

[9] Hohenberg, P. and Kohn, W., J. Phys. Res. 136(3B),PP864-871; 1964.

[10] Kohn, W. Sham, L., J.Phys.Rev.,140(4A), 1133-1138; 1965.

[11] Young D C Computational chemistry: A practical guide for applying techniques to real world problems, John Wiley & Sons Inc, p. 42; 2001.

[12] Chis V, Filip S, Miclaus V, Pirnau A, Tanaselia C, Almasan V and Vasilescu M J. Mol. Struct.744–747 363; 2005.

[13] Becke D 1993 J. Chem. Phys. 98 5648

[14] Lee C, Yang W and Parr R G 1988 Phys. Rev. B37 785.

[15] Ahmed A., Yasser R., Elmurssi, M.;J.of theort.and Comput.Chem.,13(08), 2014.

[16] Toy M., Tank H.; J.of Theor.comput.Chem.,11(4), 2012.

[17] Landers J., Gor G. Yu., V. Neimark;J.of Physicochem. Eng. Aspects, 437 , ,pp:3– 32, 2013.

[18] Moore C. E. ,*"Ionization Potentials and Ionization Limits Derived from The Analyses of Optical Spectra"*, NSRDS-NBS, USA, 1970 .

[19] Vanfleteren D., Neck D. V., Ayers P. W., Morrison R. C. and Bultinck P.,*The J. of Chemical Physics,*130,194104(1)-194104(10) , 2009.

[20] Hotop H. and Lineberger W. C., *J. of Physical Chemistry,* 4,539-576, (1975).

[21] Zhan C. G., J. A. Nicholsand ,D. A. Dixon, *J. of Physical Chemistry A*, 107,. 4184-4195, (2003).

 [22] Mulliken R. S. , *J.of Chemical Physics,* 2, 782-793; 1934 .

 [23] Parr R. G., L. V. Szentpály and S. Liu, *J. of the American Chemical Society*, 121, 1922-1924; 1999 .

[24] Pearson R.G., *"Chemical Hardness"*, Wiley-VCH, Germany; 1997.

[25] Pearson R.G., *Proceedings of the National Academy of Sciences of the United States of America*, 83, 8440-8441; 1986.