Sys Rev Pharm 2024; 15(1): 24-28
A multifaceted review journal in the field of pharmacy
E-ISSN 0976-2779 P-ISSN 0975-8453 / DOI: 10.31858/0975-8453.15.1.24-28

Short Communication

Computational Analysis of Density Functional Theory (DFT method), Thermodynamic Investigations and Molecular Docking Studies on 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one

Hacer Gümüş[1*], Cengiz İpek[2]

[1]Department of Marketing, Ali Rıza Veziroğlu Vocational School, Kocaeli University, Kocaeli, Turkey
[2]Department of Civil Engineering, Istanbul Medeniyet University, Istanbul, Turkey

Article History: *Submitted: 11.12.2023* *Accepted: 25.12.2023* *Published: 01.01.2024*

ABSTRACT

In this study, quantum chemical calculations of 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one have been performed using Gaussian 09 program. Theoretical computational analysis data of the molecule in the ground state have been calculated using HSEH1PBE (The exchange part of the screened Coulomb potential of Heyd, Scuseria, and Ernzerhof) and Becke's 3-Parameter (B3LYP) hybrid functional using B exchange and, Lee-Yang-Par (LYP) correlation levels of Density Functional Method (DFT) with the 6-311++G(d,p) basis set. The effect of temperature on the 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one and its thermodynamic parameters entropy, enthalpy, and heat capacity have been analyzed. Mulliken, Natural Bond Orbital (NBO) charges and Atomic Polar Tensor (APT) charges of the investigated molecule have also been calculated. In addition, the molecular frontier orbital energies Highest Occupied Molecular Orbital (HOMO), HOMO-1, Lowest Unoccupied Molecular Orbital (LUMO) and LUMO+1) of the 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one have been calculated. Finally, Molecular Docking (MD) study has been carried out with the help of AutoDock computational program.

Keywords: 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one, DFT, APT charge, Molecular docking

***Correspondence:** Hacer Gümüş, Department of Marketing, Ali Rıza Veziroğlu Vocational School, Kocaeli University, Kocaeli, Turkey, E-mail: cengiz.ipek@medeniyet.edu.tr

INTRODUCTION

Thiophene based materials, due to the richness of thiophene chemistry and the general stability of its compounds, have found applications in fields ranging from antistatic coatings to polymer electronics (Manjunath HR, *et al.*, 2011; Huang W, *et al.*, 1998). In medicinal chemistry, sulfur-containing heterocyclic is well known for its therapeutic applications. Thiophene-containing compounds are also widely used in electroluminescent polymer, electronic and optoelectronic devices, and modern drug design (Blumstengel S, *et al.*, 1999; Batista RM, *et al.*, 2009; Hosmane RS and Liebman JF, 1991). Compounds containing thiophene nucleus possess a broad range of biological activities such as anti-inflammatory, analgesic, antifungal, ocular hypertensive activities, and antimicrobial activities (Lin JW, Dudek LP, 1980; Jen KY, *et al.*, 1986; Hu X and Xu L, 2000).

ABOUT THE STUDY

Computational details

The molecular simulation of 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule was performed with Gaussian 09W program package (Frisch MJ, *et al.*, 2009) and the output files were visualized by means of the GaussianView 5 software (Dennington R, *et al.*, 2009). All theoretical data of 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule were calculated using B3LYP (Becke's three parameter hybrid functional using the LYP correlation functional) (Becke AD, 1992; Lee C, *et al.*, 1988) and HSEH1PBE (Heyd-Scuseria-Ernzerh of functional) (Heyd J and Scuseria GE, 2004; Heyd J, Scuseria GE, 2004; Heyd J, *et al.*, 2005; Heyd J, *et al.*, 2003) levels with 6-311++G(d,p) basis set (Frisch MJ, *et al.*, 1984).

Geometric structure

Optimized geometrical structure of 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule was shown in *Figure 1*.

Thermodynamic properties

The thermodynamic values of the 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule was calculated at DFT/B3LYP and DFT/HSEH1PBE methods. The calculated thermodynamic parameters were presented as shown in *Table 1*.

Mulliken, APT, NBO charge analysis

Mulliken, APT and NBO charges of 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule were calculated and results were given in *Figure 2* and *Table 2*.

Electronic properties

The HOMO and LUMO are very important parameters in the electronic studies by quantum chemical calculations. The total energy, HOMO and LUMO energies, the energy gap (ΔE), the ionization potential (I), the electron affinity (A), the absolute electronegativity (c), the absolute hardness (h) and softness (S) for 1-(2′-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one were calculated at B3LYP and HSEH1PBE levels in the 6-311++G(d,p) basis set, and the results were presented in *Table 3*. The frontier orbital picture was depicted in *Figure 3* with the 3D plots for the gas phase, and the positive and negative phases are represented in red and green color, respectively.

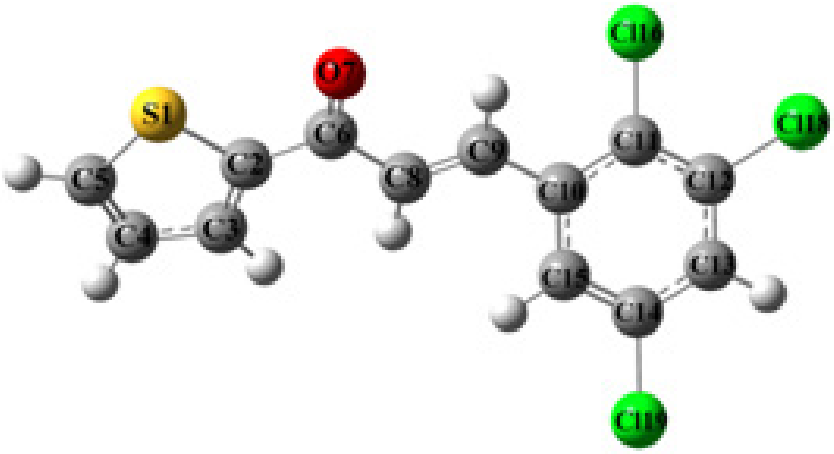

Figure 1: The optimized structure of 1-(2'-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one calculated at B3LYP/6-311++G(d,p)

Table 1: Thermodynamic parameters of 1-(2'-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one

Thermal energy, E (Kcal/mol)	B3LYP/6-311++G (d,p)	HSEH1PBE/6-311++G (d,p)
Rotational	0.889	0.889
Translational	0.889	0.889
Vibrational	109.807	110.72
Total	111.584	112.498
Heat capacity, Cv (cal/mol K)		
Rotational	2.981	2.981
Translational	2.981	2.981
Vibrational	54.395	53.917
Total	60.356	59.879
Entropy, S (cal/mol K)		
Rotational	35.331	35.299
Translational	43.147	43.147
Vibrational	59.322	58.899
Total	137.8	137.345
Rotational constants (GHz)		
A	0.48472	0.49041
B	0.11713	0.11839
C	0.09612	0.0971
Rotational temperature (Kelvin)		
A	0.02326	0.02354
B	0.00562	0.00568
C	0.00461	0.00466
Thermal properties (Hartree/particle)		
Zero-point correction	0.161242	0.162813
Thermal correction to energy	0.177821	0.179276
Thermal correction to enthalpy	0.178765	0.18022
Thermal correction to Gibbs free energy	0.113292	0.114963
Sum of electronic and zero-point Energies	-2353.67	-2352.47
Sum of electronic and thermal energies	-2353.65	-2352.45
Sum of electronic and thermal free energies	-2353.72	-2352.52
Zero point vibrational energy (kcal/mol)	101.1809	102.1668

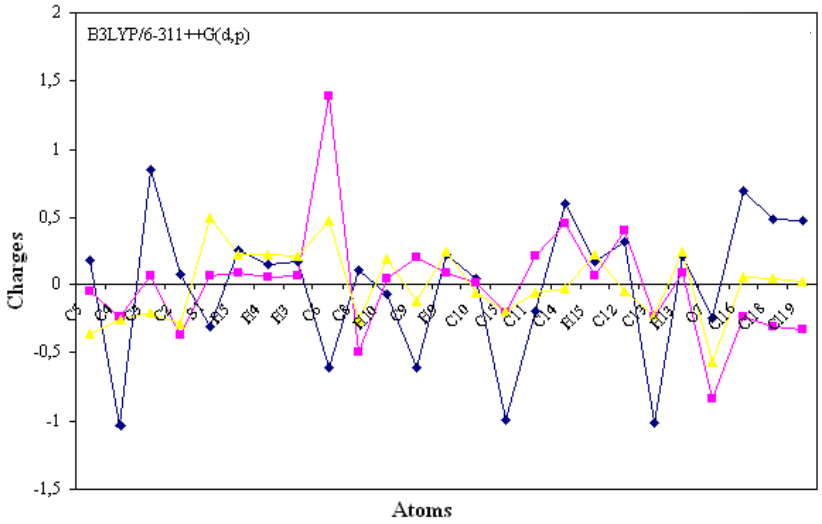

Figure 2: Mulliken, APT and NBO charges plots of 1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one
Note: (—◆—): Mulliken; (—■—): APT; (—▲—): NBO

Table 2: The Mulliken, APT and NBO charges of 1-(2'-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one

Atom	Mulliken		APT		NBO	
	B3LYP	HSEH1PBE	B3LYP	HSEH1PBE	B3LYP	HSEH1PBE
C_5	0.182877	0.242625	-0.0512	-0.06046	-0.35915	-0.37059
C_4	-1.02756	-1.2941	-0.23192	-0.23498	-0.26104	-0.26769
C_3	0.853826	1.084759	0.067185	0.060301	-0.19995	-0.2062
C_2	0.078725	0.04221	-0.37674	-0.38242	-0.28708	-0.29755
S_1	-0.30987	-0.44474	0.069065	0.074749	0.49527	0.50474
H_5	0.253474	0.302216	0.088389	0.094965	0.22764	0.23554
H_4	0.155224	0.195729	0.057511	0.063034	0.22129	0.22823
H_3	0.168715	0.222099	0.071079	0.076065	0.21709	0.22409
C_6	-0.61573	-0.69056	1.382795	1.390493	0.4781	0.47821
C_8	0.113801	0.137899	-0.49717	-0.50789	-0.25304	-0.26317
H_{10}	-0.07143	-0.07955	0.045291	0.050518	0.19546	0.20248
C_9	-0.60694	-0.66571	0.206979	0.205659	-0.11967	-0.1259
H_9	0.22852	0.271274	0.087625	0.09289	0.24091	0.24828
C_{10}	0.049648	0.08434	0.013585	0.011463	-0.06042	-0.06498
C_{15}	-0.98813	-1.104	-0.20286	-0.20434	-0.19811	-0.20342
C_{11}	-0.18953	-0.31847	0.211441	0.205244	-0.05607	-0.0634
C_{14}	0.598797	0.530977	0.455038	0.44591	-0.02654	-0.03697
H_{15}	0.175482	0.214328	0.066657	0.069803	0.22553	0.2322
C_{12}	0.321991	0.361641	0.402394	0.403663	-0.0519	-0.06075
C_{13}	-1.00449	-1.04518	-0.24013	-0.23866	-0.225	-0.23029
H_{13}	0.217082	0.259692	0.088641	0.092138	0.23997	0.24648
O_7	-0.24489	-0.22566	-0.83519	-0.83888	-0.56578	-0.5613
Cl_{16}	0.690923	0.785682	-0.23989	-0.23626	0.05408	0.06401
Cl_{18}	0.490234	0.561975	-0.30383	-0.30188	0.04816	0.05759
Cl_{19}	0.479251	0.570533	-0.33476	-0.33111	0.02024	0.03037

Table 3: Fragment Molecular Orbital (FMOs), energies and calculated physico-chemical properties

Electronic properties	B3LYP /6-311++G(d,p)	HSEH1PBE/6-311++G(d,p)
E_{HOMO} (eV)	-7.10196	-6.91447
E_{LUMO} (eV)	-2.95382	-3.14593
$\Delta E=E_{LUMO}-E_{HOMO}$ (eV)	4.148136	3.768535
I (eV)	7.101955	6.914468
A (eV)	2.953819	3.145933
χ (ες)	5.027887	-5.0302
η (ες)	2.074068	-1.88427
S (eV^{-1})	0.070403	-0.07231
E_{Total} (a.u)	-2353.83	-2352.63

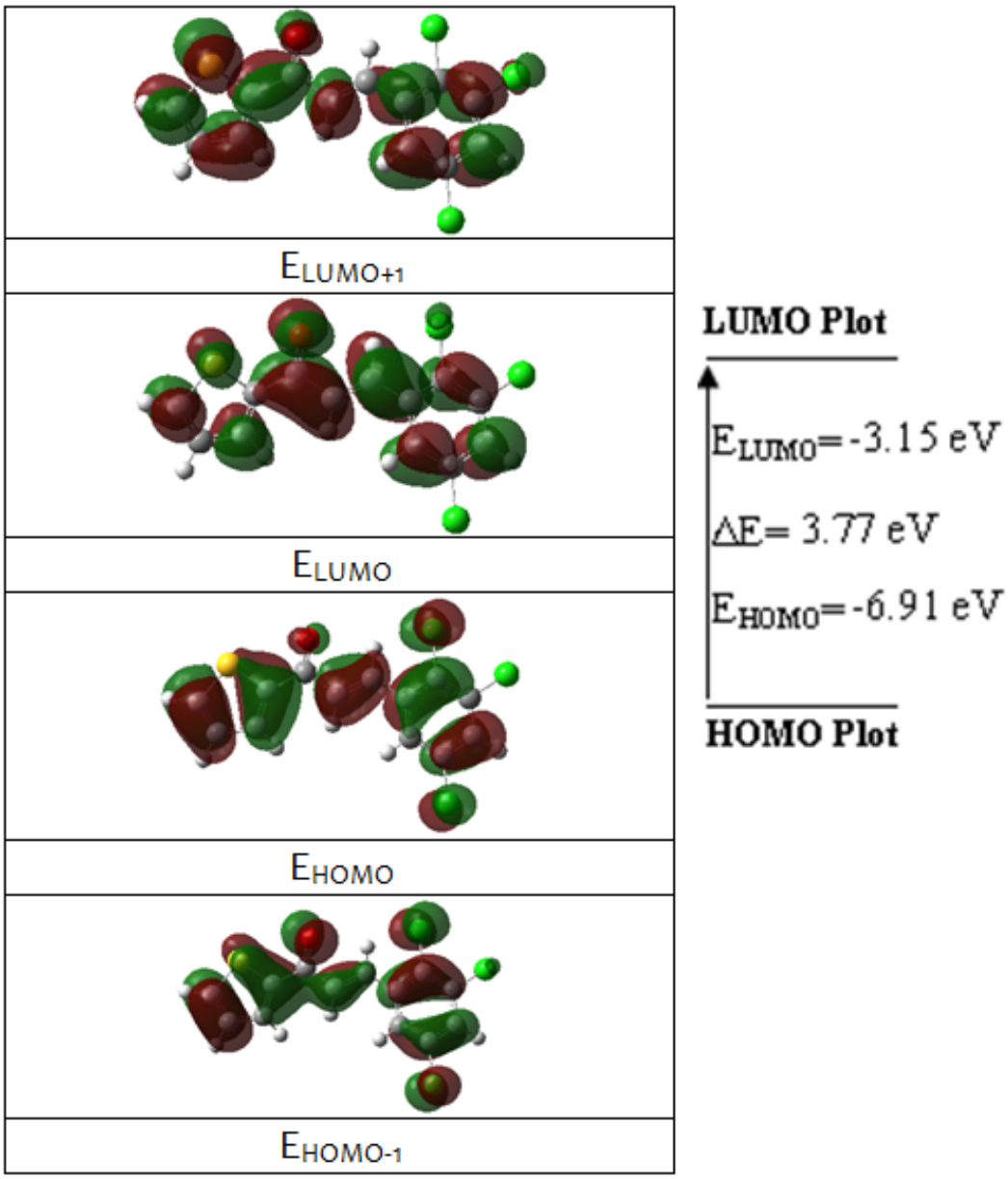

Figure 3: Molecular orbital pictures for 1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one at HSEH1PBE/6-311++G(d,p)

Molecular docking

1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule docking has been examined in active sites of the selected protein. The 1Z8V protein exhibits the min binding energy of -4.95 kcal/mol, intermolecular energy of -5.4 kcal/mol, and inhibition constant of 234.9 micromolar (uM). The deviation between the ligand-protein has been analyzed, where the Root Mean Square Deviation (RMSD) value has been calculated as 2.63 for 1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one. The molecular interaction diagrams of target protease Protein Data Bank (PDB) 1Z8V and ligand (1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one) were shown in *Figure 4*.

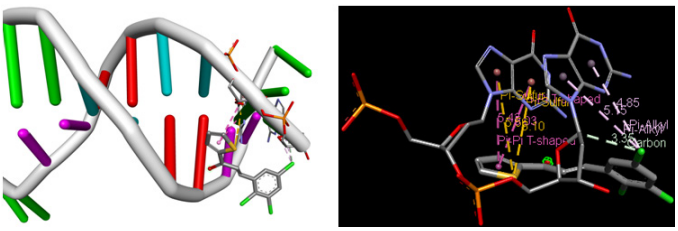

Figure 4: Detailed view of the interaction between protein and ligand

CONCLUSION

The geometry of 1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one molecule was optimized in different levels with DFT/B3LYP and DFT/HSEH1PBE method using 6-311++G(d,p) basis set. The correlations between the statistical thermo-dynamics and temperature are also obtained. It is seen that the heat capacities, entropies and enthalpies increase with the increasing temperature owing to the intensities of the molecular vibrations increase with increasing temperature. Frontier molecular orbitals, energies and energy gap between HOMO and LUMO were calculated. Additionally, interaction between 1-(2´-Thiophen)-3-(2,3,5-trichlorophenyl)-2-propen-1-one and PDB 1Z8V protein has been docked.

REFERENCES

1. Manjunath HR, Kumar PR, Naveen S, Ravindrachary V, Sridhar MA, Prasad JS, *et al.* Growth, characterization, crystal and molecular structure studies of 1-(2′-thiophen)-3-(2, 3, 5-trichlorophenyl)-2-propen-1-one. J Cryst Growth. 2011; 327(1): 161-166.
2. Huang W, Yu WL, Meng H, Pei J, Li SF. New series of blue-light-emitting polymers constituted of 3-alkylthiophenes and 1, 4-di (1, 3, 4-oxadiazolyl) phenylene. Chem Mater. 1998; 10(11): 3340-3345.
3. Blumstengel S, Sokolik I, Dorsinville R, Voloschenko D, He M, Lavrentovich O, *et al.* Photo-, and electroluminescence studies of 2, 5-bis [2′-(4 ″-(6-hexoxy benzyl))-1′-ethenyl]-3, 4-dibutyl thiophenes. Synth Met. 1999; 99(1): 85-90.
4. Batista RM, Costa SP, Belsley M, Raposo MM. Synthesis and optical properties of novel, thermally stable phenanthrolines bearing an arylthienyl-imidazo conjugation pathway. Dyes Pigm. 2009; 80(3): 329-336.
5. Hosmane RS, Liebman JF. Aromaticity of heterocycles: Experimental realization of dewar-breslow definition of aromaticity. Tetrahedron Lett. 1991; 32(32): 3949-3952.
6. Lin JW, Dudek LP. Synthesis and properties of poly (2, 5-thienylene). J Polym Sci Polym Chem Ed. 1980; 18(9): 2869-2873.
7. Jen KY, Miller GG, Elsenbaumer RL. Highly conducting, soluble, and environmentally-stable poly (3-alkylthiophenes). J Chem Soc Chem Commun. 1986; 17: 1346-1347.
8. Hu X, Xu L. Structure and properties of 3-alkoxy substituted polythiophene synthesized at low temperature. Polymer. 2000; 41(26): 9147-9154.
9. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, *et al.* Gaussian 09, Revision A.1. Gaussian, Inc., Wallingford CT. 2009
10. Dennington R, Keith T, Millam J. GaussView, version 5. 2009.
11. Becke AD. Density-functional thermochemistry. I. The effect of the exchange-only gradient correction. J Chem Phys. 1992; 96(3): 2155-2160.
12. Lee C, Yang W, Parr RG. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. Phys Rev B Condens Matter. 1988; 37(2): 785.
13. Heyd J, Scuseria GE. Efficient hybrid density functional calculations in solids: Assessment of the Heyd-Scuseria-Ernzerhof screened Coulomb hybrid functional. The J Chem Phys. 2004; 121(3): 1187-1192.
14. Heyd J, Scuseria GE. Assessment and validation of a screened Coulomb hybrid density functional. J Chem Phys. 2004; 120(16): 7274-7280.
15. Heyd J, Peralta JE, Scuseriaa GE, Martin RL. Proof copy 301539JCP. J Chem Phys. 2005; 123: 1.
16. Heyd J, Scuseria GE, Ernzerhof M. Hybrid functionals based on a screened Coulomb potential. J Chem Phys. 2003; 118(18): 8207-8215.
17. Frisch MJ, Pople JA, Binkley JS. Self-consistent molecular orbital methods 25. Supplementary functions for Gaussian basis sets. J Chem Phys. 1984; 80(7): 3265-3569.