Science Journal of Chemistry
2023; 11(1): 10-17
http://www.sciencepublishinggroup.com/j/sjc
doi: 10.11648/j.sjc.20231101.12
ISSN: 2330-0981 (Print); ISSN: 2330-099X (Online)

Study of the Chemical Reactivity of a Series of Dihydrothiophenone Derivatives by the Density Functional Theory (DFT) Method

Fandia Konate[1], Kadjo François Kassi[1], Georges Stephane Dembele[1, 2, *], Chiepi Nadege Dominique Dou[1], Bibata Konaté[1, 2], Doh Soro[1], Guy-Richard Mamadou Kone[1, 2], Nahosse Ziao[1, 2]

[1]Laboratory of Thermodynamics and Physical Chemistry of the Environment, UFR SFA, NANGUI ABROGOUA University, Abidjan, Ivory Coast

[2]Ivorian Research Group in Disease Modelling (GIR2M), UFR SFA, NANGUI ABROGOUA University, Abidjan, Ivory Coast

Email address:

1997sageme@gmail.com (Georges Stephane Dembele)

[*]Corresponding author

To cite this article:

Fandia Konate, Kadjo François Kassi, Georges Stephane Dembele, Chiepi Nadege Dominique Dou, Bibata Konaté, Doh Soro, Guy-Richard Mamadou Kone, Nahosse Ziao. Study of the Chemical Reactivity of a Series of Dihydrothiophenone Derivatives by the Density Functional Theory (DFT) Method. *Science Journal of Chemistry*. Vol. 11, No. 1, 2023, pp. 10-17. doi: 10.11648/j.sjc.20231101.12

Received: December 30, 2022; **Accepted**: January 20, 2023; **Published**: February 14, 2023

Abstract: This chemical reactivity theory study was conducted on ten (10) molecules of a series of dihydrothiophenone (DH) substituted by the quantum chemical method using density functional theory, at the B3LYP/6-31G (d, p) level. A set of global and local descriptors were used to assess the reactivity of the molecular systems. In addition, the most relevant quantum chemical descriptors for the action of the molecule as an inhibitor, such as the highest occupied molecular energy (E_{HOMO}), the lowest vacant molecular orbital energy (E_{LUMO}), the energy gap (ΔE), the dipole moment (μ), electronegativity (χ), overall hardness (η) and overall softness (S) on the heteroatoms were calculated. The analysis of the thermodynamic formation quantities confirmed the formation and existence of the studied series of molecules. The study of the boundary molecular orbitals provided a better overview of the molecular activities. The analysis of the global descriptors revealed that the DH1 molecule has the lowest value of energy gap. This lower gap allows it to be the most reactive (soft) and the least stable molecule. Also we note that it has the lowest hardness, but the highest softness. This indicates that it is the most electrophilic of all the compounds.

Keywords: Chemical Reactivity, Global Descriptors, Local Descriptors

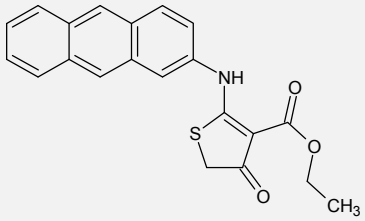
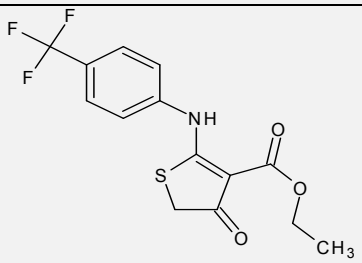
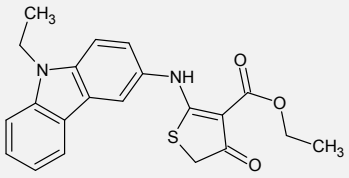
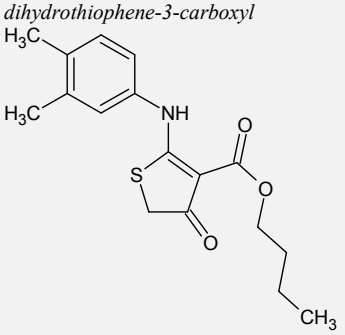
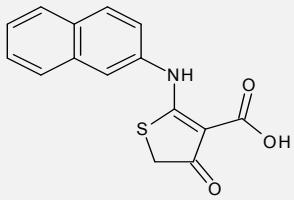
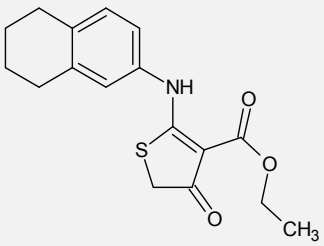
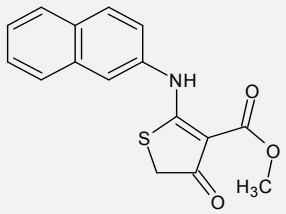
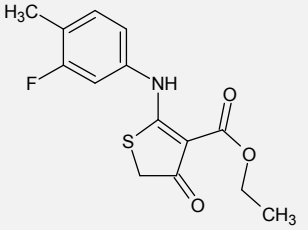
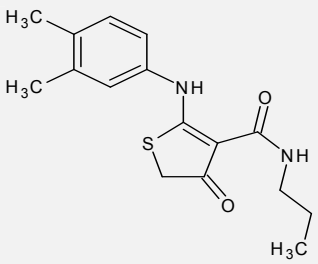
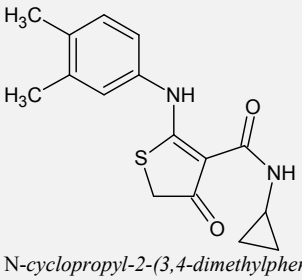
1. Introduction

Malaria is an acute febrile human disease caused by the Plasmodium parasite that is transmitted by the bites of infected female Anopheles mosquitoes. Two of the five species of malaria parasites that cause human malaria are particularly dangerous: P. falciparum, the parasite that causes the most deaths and is also the most widespread on the African continent, and P. vivax, the dominant species in most countries outside sub-Saharan Africa [1]. Thus, Xu et *al.* [2] have synthesised a series of dihydrothiophenone derivatives against *Plasmodium falciparum dihydroorotate dehydrogenase (PfDHODH)*(Table 1). Nowadays, a number of these heterocyclic derivatives containing atoms such as sulphur are used as intermediates in the design of experimental drugs [3]. Also, computational chemistry provides a lot of information about the electronic structures of molecules and contributes greatly to the development of traditional experimental chemistry [3-5]. In this work, we predicted the reactivity and reactive sites on molecules through a computational study based on density functional theory (DFT/B3LYP) using a 6-31G (d, p) basis set. Descriptors have been tested and studied in the literature by several research groups and are considered very useful for rationalising reactivity models of molecular systems [7, 8].

Geerlings et al. and Roy et al. have examined and tested the theoretical basis of these descriptors and their applications [9, 10]. A set of global and local descriptors for measuring the reactivity of molecular systems has emerged. Fukui indices have also been determined and discussed.

The general objective of this manuscript is to study the reactivity and stability of a series of dihydrothiophenone derivatives. Specifically, the reactivity of dihydrothiophenone will be determined theoretically and the nucleophilic/electrophilic attack sites will be identified by various quantum chemical methods.

Table 1. *Structures and nomenclature of the studied dihydrothiophenones and their codes.*

Structure and nomenclature	Codes	Structure and nomenclature	Codes
 Ethyl 2-(anthracen-2-ylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylate	DH1	 *Ethyl 2-(4-(trifluoromethyl) phenylamino)-4-oxo-4,5-dihydrothiophene-3-carboxyl*	DH6
 Ethyl 2-(9-ethyl-9H-carbazol-3-ylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylate	DH2	 Butyl 2-(3,4-dimethylphenylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylate	DH7
 *2-(naphthalen-2-ylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylic acid*	DH3	 Ethyl 2-(5,6,7,8-tetrahydronaphthalen-2-ylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylate	DH8
 Methyl 2-(naphthalen-2-ylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylate	DH4	 *Ethyl 2-(3-fluorine-4-methylphenylamino)-4-oxo-4,5-dihydrothiophene-3-carboxylate*	DH9
 N-propyl-2-(3,4-dimethylphenylamino)-4-oxo-4,5-dihydrothiophene-3-carboxamide	DH5	 N-*cyclopropyl-2-(3,4-dimethylphenylamino)-4-oxo-4,5-dihydrothiophene-3-carboxamide*	DH10

2. Materials and Methods

2.1. Level of Theory of Calculation

The geometries of the molecules were optimized at the DFT level with the B3LYP [6-8] in the 6-31G(d, p) basis using the Gaussian 09 software. [9] This Hybrid functional gives better energies and is in agreement with high level ab initio methods [10, 11]. As for the split-valence and double-dzeta basis (6-31G (d, p)), it is sufficiently broad and the consideration of polarisation functions are important for the explanation of the free doublets of heteroatoms. The geometries are kept constant for both cationic and anionic systems. The overall reactivity indices were obtained from the conceptual DFT model [12-15]. The local chemical reactivity indices were determined using the electronic populations calculated with the Natural Population Analysis (NPA) [16].

2.2. Thermodynamic Formation Quantities

The thermodynamic quantities of the molecules were carried out from optimisation and calculation of frequencies at the level B3LYP/6-31G (d, p). The quantities such as entropy, enthalpy and free enthalpy of formation of DHs were determined via the following formulae proposed by Otchersky et al [9].

$$\Delta H_f^0(M,0K) = \sum_{atoms} x\Delta H_f^0(X,0K) - \sum D_0 \quad (1)$$

$$\Delta H_f^0(M,298K) = \Delta H_f^0(M,0K) + \left(H_M^0(298K) - H_M^0(0K)\right) - \sum_{atoms} x\left(H_X^0(298K) - H_X^0(0K)\right) \quad (2)$$

With:

$$\sum D_0 = \sum x\varepsilon_0 - \varepsilon_0(M) - \varepsilon_{ZPE} \quad (3)$$

$\sum D_0$: Atomisation energy;
$\varepsilon_0(M)$: Total energy of the molecule;
ε_{ZPE}: Zero-point energy of the molecule;
$H_X^0(298K) - H_X^0(0K)$: Enthalpy corrections for atomic elements. These values are included in the Janaf table [17];
$H_M^0(298K) - H_M^0(0K) = H_{corr} - \varepsilon_{ZPE}(M)$: Enthalpy correction of the molecule;
H_{corr}: Thermal correction enthalpy.

$$\Delta S_f^0(M,298K) = S_M - \sum_{atoms} x\Delta S(298K) \quad (4)$$

x: Number of atoms of X in the molecule.

$$\Delta G_f^0(M,298K) = \Delta H_f^0(M,298K) - T\Delta S_f^0(M,298K) \quad (5)$$

2.3. Reactivity Descriptors

2.3.1. Global Reactivity Descriptors

We determined several descriptors of overall reactivity using the conceptual density functional theory method. These descriptors have proven to be very effective in predicting reactivity patterns. Based on the study by Koopmans [18]. These are: global hardness (η), global softness (S) energy gap ΔEgap. The global reactivity descriptors are calculated using the boundary energies, E_{HOMO}, E_{LUMO} molecular orbitals. These descriptors have been tested and studied in the literature by several research groups and are considered very useful for rationalising reactivity models of molecular systems [8, 19].

Table 2. *Global reactivity values according to Koopmans.*

Energy gap	Global hardness	Global softness
$\Delta E_{gap}=E_{Lumo}- E_{Homo}$	$\eta= \Delta E_{gap}/2$	$S=1/\eta$
Overall electrophilicity index	*Chemical potential*	*Electronegativity*
$\varpi=(\mu^2)/2*\eta$	$\mu=-(E_{Lumo}+E_{Homo})/2$	$\chi=+(E_{Lumo}+ E_{Homo})/2$

2.3.2. Local Reactivity Descriptors

The local reactivity descriptor as the Fukui function indicates the preferred regions where a chemical (molecule) will change its density when the number of electrons is changed. It indicates the tendency of the electron density to deform at a given position when accepting or donating electrons [20, 21]. They are used to decide the relative reactivity of the different atoms in the molecule. The Fukui function [19, 22] is one of the most widely used local density functional descriptors for modelling chemical reactivity and site selectivity. It is defined as the derivative of the electron density ρ(r) with respect to the total number of electrons N. In the system, these functions are calculated according to the procedure proposed by Yang and Mortier [22]. This function describes the sensitivity of the chemical potential of a system to a local external potential. Using the left and right derivatives with respect to the number of electrons, one can define the electrophilic, nucleophilic and local softness Fukui function. To describe the site selectivity or reactivity of an atom in a molecule, it is necessary to condense the values of (r) and (r) around each atomic site into a single value that characterises the atom in a molecule. This can be achieved by an electronic population analysis. Thus, for an atom k in a molecule, depending on the type of electron transfer, we have three different types of condensed Fukui function of atom k.

$$f_k^+ = q_k(N+1) - q_k(N) \quad (6)$$

$$f_k^- = q_k(N) - q_k(N-1) \quad (7)$$

f_k^+ for nucleophilic attack.
f_k^- for electrophilic attack.
$q_k(N)$: Electron population of atom k in the neutral molecule.
$q_k(N+1)$: Electron population of atom k in the anionic molecule.
$q_k(N-1)$: Electron population of atom k in the cationic molecule.

3. Results and Discussion

3.1. Thermodynamic Formation Quantities

The thermodynamic quantities of formation of Dihydrothiophenone derivatives, namely enthalpy, entropy and

free enthalpy of formation were calculated at B3LYP/ 6-31 G(d, p). The values of these quantities are given in Table 3.

Table 3. *Thermodynamic values for the formation of DHs optimised at B3LYP/ 6-31G (d, p).*

Code	$\Delta_f S^0$ (Kcal/mol.K)	$\Delta_f G^0$ (Kcal/mol)	$\Delta_f H^0$ (Kcal/mol)
DH1	-1289.847	-654.364	-1038.931
DH2	-1397.001	-654.364	-920.022
DH3	-926.910	-514.566	-790.924
DH4	-987.983	-485.689	-780.256
DH5	-1268.410	-311.561	-689.737
DH6	-1007.072	-636.855	-937.114
DH7	-1245.601	-558.346	-929.722
DH8	-1202.059	-557.350	-915.744
DH9	-1031.965	-521.843	-829.523
DH10	-1131.519	-261.103	-598.466

The values of the different thermodynamic quantities are all negative. This result indicates that dihydrothiophenone derivatives can be formed spontaneously, exothermically with a decrease in disorder at the level of theory used.

3.2. Overall Reactivity Indices

The study of the global reactivity of molecules is based on the calculation of global indices deduced from the electronic properties. Global hardness (η), global softness (S) and global reactivity descriptors are very effective in predicting reactivity trends based on the Koopman study [18]. The overall indices of the reactivity of the investigated HDs are shown in Table 4.

Table 4. *Overall reactivity indices.*

Code	ΔEgap (eV)	μ(eV)	χ(eV)	η(eV)	S(eV^{-1})
DH1	3.4051	5.7834	-5.7834	1.7026	0.2937
DH2	4.2164	7.7076	-7.7076	2.1082	0.2372
DH3	4.2888	5.9335	-5.9335	2.1444	0.2332
DH4	4.2937	5.9410	-5.9410	2.1469	0.2329
DH5	4.3525	2.8289	-2.8289	2.1762	0.2298
DH6	4.5177	5.5103	-5.5103	2.2588	0.2214
DH7	4.5182	6.3369	-6.3369	2.2591	0.2213
DH8	4.5540	6.6810	-6.6810	2.2770	0.2196
DH9	4.5634	4.8711	-4.8711	2.2817	0.2191
DH10	4.6168	6.3652	-6.3652	2.3084	0.2166

According to the theoretical calculations made, it was found that the DH1 molecule has the lowest value of energy gap (3.4051ev). This lower gap allows it to be the most reactive (soft) and least stable molecule. Also we find that it has the lowest hardness (η = 1.7026 eV), but the highest softness (0.2937 ev). This indicates that this molecule is the most reactive of all the compounds.

Thus, the following sequence can be established in order of increasing reactivity:

ΔE: DH 1>DH > 2> DH 3> DH4 > DH5> DH 6>DH7> DH8 >DH 9> DH10.

This DH1 compound is therefore more polarisable and is associated with high chemical reactivity, low kinetic stability and is also called a "soft molecule". This indicates that it is the most electrophilic of all the compounds.

On the other hand, the same calculations reveal that the DH10 molecule with the highest energy gap (4.6168 eV) the highest hardness (2.3084 eV) and the lowest softness (0.2166 eV) is the least reactive compound. Therefore, the most nucleophilic compound.

3.3. Local Reactivity

In the context of the isodensity map study, a site is likely to be nucleophilic or electrophilic if it belongs to a larger lobe. The isodensity maps showing the likely nucleophilic and electrophilic attack sites using the bulky lobes of the ten (10) compounds studied are shown in Figures.

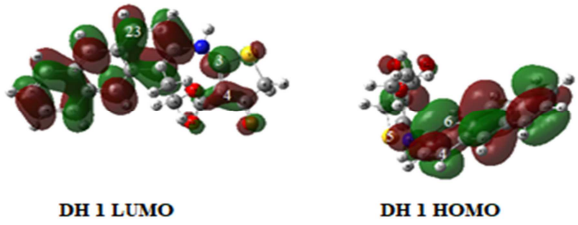


Figure 1. *LUMO and HOMO isodensity map of compound DH 1.*

Analysis of the maps through HOMO indicates that the largest lobe containing the entire S5 atoms would be the likely nucleophilic sites of the DH1 series. With regard to the electrophilic attack sites obtained from the LUMO; the C23 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

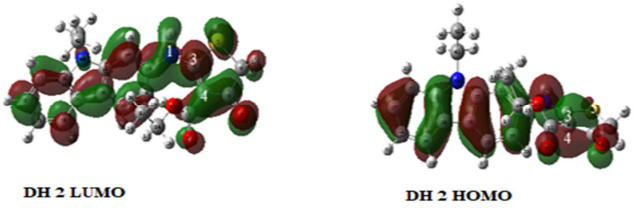


Figure 2. *LUMO and HOMO isodensity map of compound DH 2.*

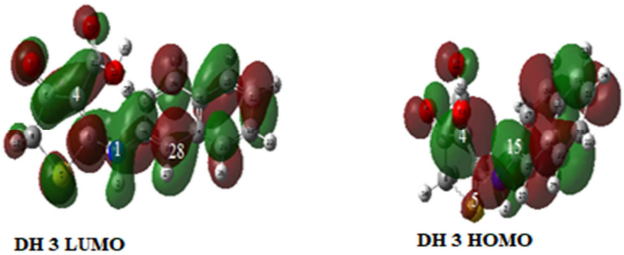


Figure 3. *LUMO and HOMO isodensity map of compound DH 3.*

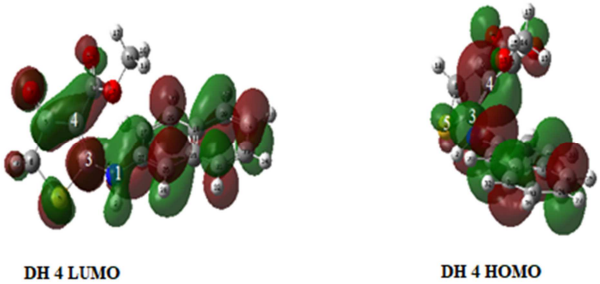


Figure 4. *LUMO and HOMO isodensity map of compound DH 4.*

The analysis of the maps through HOMO indicates that the largest lobe entirely containing atoms S7, C4 would be the likely nucleophilic sites of the DH2; DH3; DH4 series of compounds. With regard to the electrophilic attack sites obtained from LUMO; the 1N, C4 atoms present the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

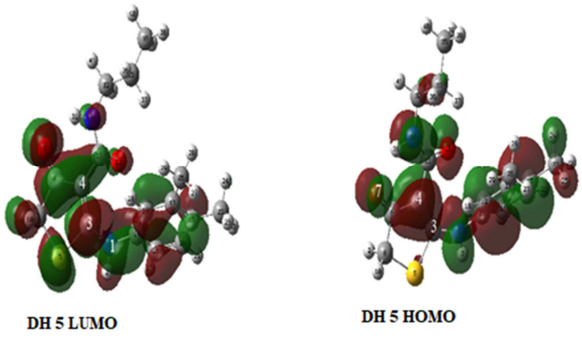


Figure 5. *LUMO and HOMO isodensity map of compound DH 5.*

The analysis of the maps through HOMO indicates that the largest lobe containing the entire O7, C3 atoms would be the likely nucleophilic sites of the DH5 series. With regard to the electrophilic attack sites obtained from LUMO; the 1N, C3 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

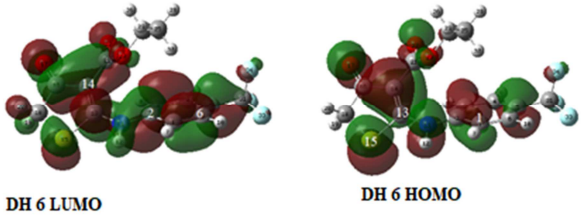


Figure 6. *LUMO and HOMO isodensity map of compound DH 6.*

Analysis of the maps through HOMO indicates that the largest lobe containing all C1 atoms would be the likely nucleophilic sites of the DH6 series. With regard to the electrophilic attack sites obtained from LUMO, the C6 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

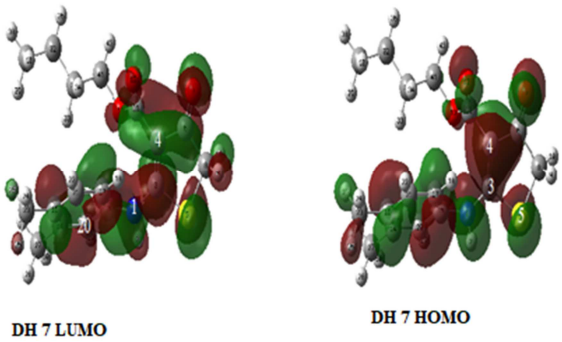


Figure 7. *LUMO and HOMO isodensity map of DH 7.*

Analysis of the maps through HOMO indicates that the larger lobe containing the entire S7, C4 atoms would be the likely nucleophilic sites of the compound series. DH7. With regard to the electrophilic attack sites obtained from LUMO; the 1N, C4 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

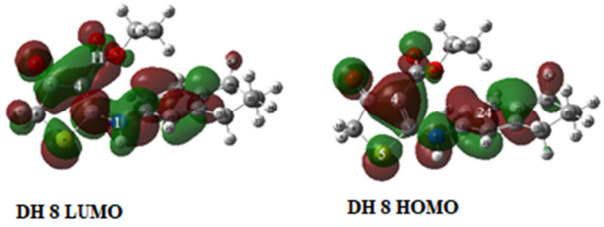


Figure 8. *LUMO and HOMO isodensity map of compound DH 8.*

Analysis of the maps through HOMO indicates that the largest lobe containing the entire C24 atoms would be the likely nucleophilic sites of the DH8 series. With regard to the electrophilic attack sites obtained from LUMO; the C11 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

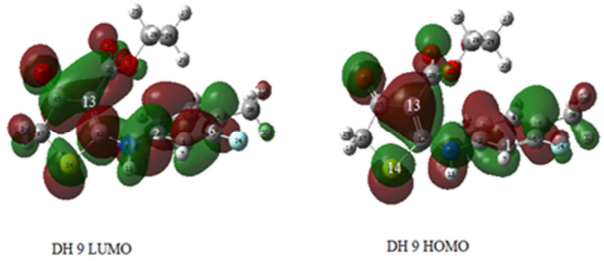


Figure 9. *LUMO and HOMO isodensity map of DH 9.*

Analysis of the maps through HOMO indicates that the largest lobe containing all C1 atoms would be the likely nucleophilic sites of the DH9 series. With regard to the electrophilic attack sites obtained from LUMO, the C6 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

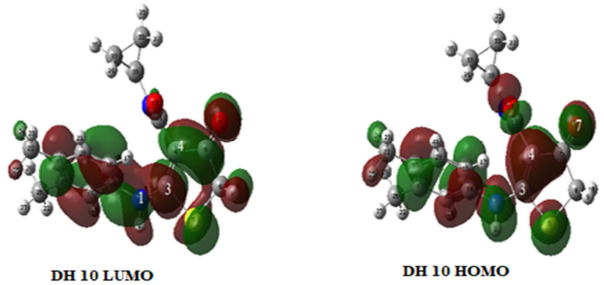


Figure 10. *LUMO and HOMO isodensity map of compound DH 10.*

The analysis of the maps through HOMO indicates that the largest lobe containing the entire O7, C3 atoms would be the likely nucleophilic sites of the DH10 series. With regard to the electrophilic attack sites obtained from LUMO; the 1N, C3 atoms show the largest lobes. These would appear to be the likely electrophilic sites for the DH series studied.

Table 5. *Fukui descriptors of compound DH 1.*

Compound DH 1			
ATOM	f^+	**ATOM**	f^-
4C	0.07999	1N	0.07594
5S	0.10665	3C	0.01071
6C	0.02771	4C	0.01267
7O	0.09664	5S	0.01428
12O	0.03825	7O	0.01138
14C	0.01419	12O	0.01236
15C	0.01111	22C	0.03982
22C	0.0484	23C	0.11423
23C	0.07226	25C	0.00852
28C	0.07131	28C	0.09709
29C	0.06827	29C	0.05139
31C	0.03766	31C	0.05832
35C	0.03733	35C	0.03148
37C	0.03852	37C	0.04775
38C	0.04451	38C	0.0516
42C	0.04735	42C	0.09463

Table 6. *Fukui descriptors of compound DH 2.*

Compound DH 2			
ATOM	f^+	**ATOM**	f^-
3C	0.03109	1N	0.10894
4C	0.05589	3C	0.01651
5S	0.14243	4C	0.09794
6C	0.04836	5S	0.02206
7O	0.11282	7O	0.0423
12O	0.09276	11C	0.00757
14C	0.00763	13O	0.03081
15C	0.02185	21C	0.06058
23C	0.06026	22C	0.04656
24C	0.01209	26C	0.06738
25C	0.1015	27C	0.08492
26C	0.04995	29C	0.04944
27C	0.05138	30C	0.03342
29C	0.04304	36C	0.0365
30C	0.05153	40N	0.08664

Table 7. *Fukui descriptors of compound DH 3.*

Compound DH 3			
ATOM	f^+	**ATOM**	f^-
3C	0.04263	1N	0.1089
4C	0.10189	3C	0.006
5S	0.13449	4C	0.06798
7O	0.11775	5S	0.04959
12O	0.06232	7O	0.04931
15C	0.0413	12O	0.04574
19C	0.05126	15C	0.02725
21C	0.05481	19C	0.03502
25C	0.04743	21C	0.08058
28C	0.05254	25C	0.07794
29C	0.05084	28C	0.12234

Table 8. *Fukui descriptors of compound DH 4.*

Compound DH 4			
ATOM	f^+	**ATOM**	f^-
3C	0.04658	1N	0.13845
4C	0.10383	4C	0.07588
5S	0.11992	5S	0.06366
6C	0.04991	7O	0.0536
7O	0.11631	12O	0.04698
12O	0.0518	13O	0.01532
19C	0.01833	20C	0.04511
20C	0.03933	222C	0.04861

Compound DH 4			
ATOM	f^+	**ATOM**	f^-
26C	0.08716	24C	0.06941
29C	0.05192	26C	0.08704
31C	0.05755	31C	0.06542

Table 9. *Fukui descriptors of compound DH 5.*

Compound DH 5			
ATOM	f^+	**ATOM**	f^-
3C	0.06324	1N	0.16346
4C	0.10321	3C	0.04303
5S	0.1591	4C	0.03081
6C	0.10348	5S	0.05048
7O	0.20601	8C	0.00633
12O	0.1009	13C	0.01955
13C	0.01469	14C	0.05451
15C	0.05943	15C	0.11931
16C	0.03361	16C	0.045
20C	0.02544	19C	0.00635
26C	0.00315	20C	0.00488
30N	0.01181	30N	0.11605

Table 10. *Fukui descriptors of compound DH 6.*

Compound DH 6			
ATOM	f^+	**ATOM**	f^-
1C	0.25668	2C	0.14066
3C	0.07566	4C	0.14825
5C	0.16704	5C	0.00345
13C	0.08926	6C	0.33343
14C	0.06182	11N	0.14445
15S	0.16979	14C	0.18658
16C	0.05782	15S	0.0873
17O	0.12065	17O	0.09325
22O	0.11059	21C	0.05989
23O	0.14941	22O	0.01997

Table 11. *Fukui descriptors of compound DH 7.*

Compound DH 7			
ATOM	f^+	**ATOM**	f^-
3C	0.09459	1N	0.13658
4C	0.10035	4C	0.11868
5S	0.16528	5S	0.06799
6C	0.06628	7O	0.06624
7O	0.1391	12O	0.06308
11C	0.00463	13O	0.00089
12O	0.0553	14C	0.0277
13O	0.01582	15C	0.02001
14C	0.02904	16C	0.11248
15C	0.02582	17C	0.04621
16C	0.06766	20C	0.04645
17C	0.03229	31C	0.00772

Table 12. *Fukui descriptors of compound DH 8.*

Compound DH 8			
ATOM	f^+	**ATOM**	f^-
3C	0.03801	1N	0.13481
4C	0.13401	3C	0.0451
5S	0.1401	4C	0.08261
6C	0.05485	5S	0.08621
7O	0.12037	7O	0.0838
13O	0.1413	11C	0.15748
23C	0.09721	12O	0.14538
24C	0.57208	21C	0.07837
28C	0.0577	22C	0.12488

Table 13. *Fukui descriptors of compound DH 9.*

Compound DH 9			
ATOM	f^+	**ATOM**	f^-
1C	0.32518	2C	0.14182
3C	0.08637	4C	0.15582
5C	0.18964	6C	0.48824
12C	0.08388	10N	0.12803
13C	0.06448	13C	0.16543
14S	0.17514	14S	0.06934
15C	0.06638	16O	0.08383
16O	0.12826	20C	0.06478
21O	0.10565	21O	0.0185
22O	0.15114	23C	0.11646
34F	0.09268	24C	0.14051

Table 14. *Fukui descriptors of compound DH 10.*

Compound DH 10			
ATOM	f^+	**ATOM**	f^-
3C	0.06938	1N	0.16709
4C	0.11809	3C	0.00854
5S	0.16678	4C	0.09518
6C	0.10041	5S	0.06276
7O	0.17342	7O	0.048
12O	0.06524	12O	0.03518
13C	0.02065	13C	0.02854
14C	0.04489	14C	0.00517
15C	0.07542	15C	0.10226
16C	0.02354	16C	0.04423
20C	0.02666	19C	0.03698

The analysis of the local descriptors in Table DH6 and DH9 shows that the 1C carbon atom is the most reactive site for nucleophilic attack and the 6C carbon atom is the most reactive site for electrophilic attack.

Also, that of table DH8 illustrates that the 24C atom is the most reactive site for nucleophilic attacks and the 11C is the most reactive site for electrophilic attacks. On the other hand, those of tables DH5 and DH10 show that the oxygen atom 7O is the most reactive site for nucleophilic attacks and the nitrogen atom 1N is the most reactive site for electrophilic attacks. The values of the local descriptors in Table DH2, DH7 and DH4 show that the 5S sulphur atom is the nucleophilic attack site and the 1N nitrogen atom is the electrophilic attack site. Also, Table DH1 shows that the 5S sulphur atom is the nucleophilic attack site and the 23C carbon atom is the electrophilic attack site. Table DH3 shows that the 5S sulphur atom is the nucleophilic attack site and the 28C carbon atom is the electrophilic attack site.

4. Conclusion

The methods of Quantum Chemistry and Molecular Modelling were employed on ten (10) molecules of the dihydrothiophenone family to study their chemical stability and reactivity. This theoretical study was carried out by exploiting the density functional method (DFT) with the B3LYP/6-31G (d, p) level.

The analysis of the global descriptors revealed that the DH1 molecule has the lowest energy gap value (3.4051ev). This lower gap allows it to be the most reactive (soft) and least stable molecule. This indicates that it is the most electrophilic of all the compounds. In the future, we intend to carry out molecular docking in order to evaluate the interaction sites between these molecules and the *plasmodim*.

References

[1] Organisation Mondiale de la Santé, «OMS,» 06 Décembre 2021. [En ligne]. Available: https://www.who.int/fr/news-room/fact-sheets/detail/malaria#:~:text=Le%20paludisme%20est%20une%20maladie,de%20paludisme%20dans%20le%20monde.. [Accès le 2022 Décembre 28].

[2] M. Xu, J. Zhu, Y. Diao, H. Zhou, X. Ren, D. Sun, J. Huang, D. Han, Z. Zhao, L. Zhu, Y. Xu et H. Li, «Novel Selective and Potent Inhibitors of Malaria Parasite Dihydroorotate Dehydrogenase: Discovery and Optimization of Dihydrothiophenone Derivatives,» Journal of Medicinal Chemistry, vol. 56, n° %120, pp. 7911-7924, 2013.

[3] N. B. Patel et F. M. Shaikh, «New 4-Thiazolidinones of Nicotinic Acid with 2-Amino-6-methylbenzothiazole and their Biological Activity,» Sci. Pharm, vol. 78, p. 753, 2010.

[4] M. Kurt, T. R. Sertbakan et M. Ozduran, «Spectrochim, An experimental and theoretical study of molecular structure and vibrational spectra of 3-and 4-pyridineboronic acid molecules by density functional theory calculations,» Acta Part A: Mol. Biomol. Spectrosc., vol. 70, n° %13, pp. 664-673, 2008.

[5] K. V. Bohoussou, A. Benié, M. G. Koné, A. Kakou, K. Bamba et N. Ziao, «Theoretical Study of the Reaction of (2, 2)-Dichloro (Ethyl) Arylphosphine with Bis (2, 2)-Dichloro (Ethyl) Arylphosphine by Hydrophosphination Regioselective by the DFT Method,» Computational Chemistry, vol. 5, pp. 113-128, 2017.

[6] D. Soro, L. Ekou, M.-R. Koné, T. Ekou et N. Ziao, «DFT Study of Molecular Stability and Reactivity on Some Hydroxamic Acids: An Approach by Hirshfeld Population Analysis,» EJERS, European Journal of Engineering Research and Science, vol. 4, n° %12, pp. 45-49, 2019.

[7] N. T. Tuo, G. S. Dembele, D. Soro, F. Konate, B. Konate, C. Kodjo et N. Ziao, «Theoretical Study of the Chemical Reactivity of a Series of 2, 3-Dihydro-1H-Perimidine,» International Research Journal of Pure & Applied Chemistry, vol. 23, n° %11, pp. 13-25, 2022.

[8] T. Mineva et T. Heine, «Efficient computation of orbitally resolved hardness and softness within density functional theory,» J. Phys. Chem. A., vol. 108, pp. 11086-11091, 2004.

[9] R. K. Roy et S. Saha, «Studies of regioselectivity of large molecular systems using DFT based reactivity descriptors,» Annual Reports Section "C" (Physical Chemistry), vol. 106, pp. 118-162, 2010.

[10] S. Saha et R. K. Roy, «One-into-many" model: an approach on DFT based reactivity descriptor to predict the regioselectivity of large systems,» The Journal of Physical Chemistry B, vol. 111, n° %132, pp. 9664-9674, 2007.

[11] C. Lee, W. Yang et R. Parr, «Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density,» Physical Review Journals, vol. B37, p. 785, 1988.

[12] B. D. Axel, «Density-functional thermochemistry III. The role of exact exchange,» Journal of Chemical Physics, vol. 98, p. 5648, 1993.

[13] A. L. Bédé, A. B. Assoma, K. D. Yapo, M. G.-R. Koné, S. Koné, M. Koné, B. N'Guessan et E.-H. S. Bamba, «Theoretical Study by Density Functional Theory Method (DFT) of Stability, Tautomerism, Reactivity and Prediction of Acidity of Quinolein-4-One Derivatives,» Computational Chemistry, vol. 6, pp. 57-70, 2018.

[14] Gaussian 09, Revision A. 02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

[15] N. T. Tuo, B. Ouattara, M. G. R. Kone, G. S. Dembele, D. Soro, F. Konate et N. Ziao, «Theoretical Study of Reactivity and Stability of a Thiazoline Derivative Series by the Density Functional.

[16] R. G. Parr et W. Yang, «Density-functional theory of the electronic structure of molecules,» Annual Review Physical Chemistry, vol. 46, pp. 701-728, 1995.

[17] M. W. Chase, C. A. Davies, J. R. Downey, D. J. Frurip, R. A. McDonald et A. N. Syverud, «JANAF Thermochemical Tables,» J. Phys. Ref., vol. 14, n°11, 1985.

[18] T. Koopmans, «Über die zuordnung von wellenfunktionen und eigenwerten zu den einzelnen elektronen eines atoms,» Physica, vol. 1, n° %11-6, pp. 104-113, 1993.

[19] P. K. Chattaraj et B. Maiti, «Reactivity dynamics in atom−field interactions: a quantum fluid density functional study,» The Journal of Physical Chemistry A, vol. 105, n° %11, pp. 169-183, 2001.

[20] R. G. Parr, L. V. Szentpály et S. Liu, «Electrophilicity index,» Journal of the American Chemical Society, vol. 121, n° %19, pp. 1922-1924, 1999.

[21] P. W. Ayers et M. Levy, «Perspective on "Density functional approach to the frontier-electron theory of chemical reactivity,» Theoretical Chemistry Accounts, vol. 103, n° %13, pp. 353-360, 2000.

[22] W. Yang et W. J. Mortier, «The use of global and local molecular parameters for the analysis of the gas-phase basicity of amines,» Journal of the American Chemical Society, vol. 108, n° %119, pp. 5708-5711, 1986.