JCHR (2021) 11(2), 213-221

Journal of Chemical Health Risks

www.jchr.org

ORIGINAL ARTICLE

Analysis of the Chemical Reactivity of Limonene by the Functional Density Theory Method Using Global Descriptors

Hayat EL Ouafy[1], Tarik EL Ouafy[*2], Mustapha Oubenali[1], Aziz EL Haimouti[2], Ahmed Gamouh[1], Mohamed Mbarki[1]

[1] *Team of Analytical & Computational Chemistry, Nanotechnology and Environment, Department of Chemistry and Environment, Faculty of Science and Technics, Sultan Moulay Slimane University, Beni Mellal, Morocco*

[2] *Team of Analytical & Computational Chemistry, Nanotechnology and Environment, Department of Physics and Chemistry, Polydisciplinary Faculty of Khouribga, Sultan Moulay Slimane University, Beni Mellal, Morocco*

(Received: 22 September 2020 Accepted: 24 February 2021)

KEYWORDS

(R)-Limonene;
(S)-Limonene;
HOMO;
LUMO;
DFT;
Chemical descriptors;
NLO;
Electrostatic molecular potential

ABSTRACT: The optimized molecular geometry is interpreted using structural optimizations based on the Functional Density Theory (DFT) method. Additionally, we used B3LYP / 6-311G (d, p) to determine the chemical descriptor, the ionization potential (I), the electron affinity (A), the chemical potential (μ), the chemical hardness (η), 3D maps of HOMO and LUMO orbits were used to develop the structure, activity, and structure of quantitative relationships. Large basis set-theoretical calculations of the dipole polarizabilities and second hyperpolarizabilities of limonene molecules have been carried out and the results have been used to assess optical properties of atomic contributions to the overall molecular response tensors. Reasonable estimates of the mean second hyperpolarizability response can be obtained from summing atomic parameters obtained here, though the reliability of the estimates is worse than what is found for dipole polarizabilities. The DFT method has been used of which is to compare the angles and lengths of molecular bonds with the experimental results. To understand molecular interactions in a given molecule, electrostatic molecular potential (MEP) is a crucial tool. Also, the sites of relative reactivity for electrophilic and nucleophilic attacks. Theoretical studies of the molecules of (R)-limonene and (S)-limonene made it possible to confirm the results obtained experimentally.

INTRODUCTION

In this context, the enantiomeric forms of limonene (Figure 1) has been widely described as promising antileishmania agents. Further, it should be noted that different limonene-based compounds having antileishmanial activity are shown in the literature. Limonene $C_{10}H_{16}$ is a terpene hydrocarbon present in many essential oils from which it can be obtained by distillation. At room temperature, it is a colorless liquid with a bright, fresh, and clean scent of orange, characteristic of citrus. Limonene is used in particular in perfumery. Limonene is a chiral molecule, and like many chiral molecules, biological sources produce a specific enantiomer. The main industrial source, orange, contains D-limonene ((+) - limonene), which is the dextrorotatory R-enantiomer. Eucalyptus and peppermint, on the other hand, contain L (-) - limonene, which is the levorotatory S enantiomer. Limonene takes its name from the lemon which, like other citrus fruits, contains considerable amounts of this chemical compound, which is largely responsible for their fragrance. Racemic limonene is known as dependence [1]. Molecules that are mirror images of each other, but not superimposable, are called enantiomers and are generally optically active [2]. The chemical reactions of terpene epoxy compounds are of

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*Corresponding author: tarikelouafy@gmail.com (T. EL Ouafy)

DOI: 10.22034/jchr.2021.1910282.1189

considerable interest because various products can be prepared on this basis [3].

Often, at least in the field of science, these theories are quantitative and are expressed by mathematical equations. This quantitative nature allows the theory to be tested by experience. The theories of classical mechanics, for example, could be validated to describe the behaviors of macroscopic systems but proved inapplicable to molecular systems, for which quantum mechanics should instead be used [4,5].

In this work, we were interested in the study of the structural properties of R-limonene and S-limonene. We used the DFT method to calculate the thermochemical descriptors (the optimization of the geometries, the lengths and the bond angles of the molecules, the energies and the densities of the frontier molecular orbitals HOMO and LUMO, the electronic chemical potential, electronegativity, chemical hardness, overall softness, overall electrophilic index, overall nucleophilic index, nonlinear magnetic optical properties) to compare the stability and reactivity of these molecules and to study their biological activities by electrostatic potential molecular.

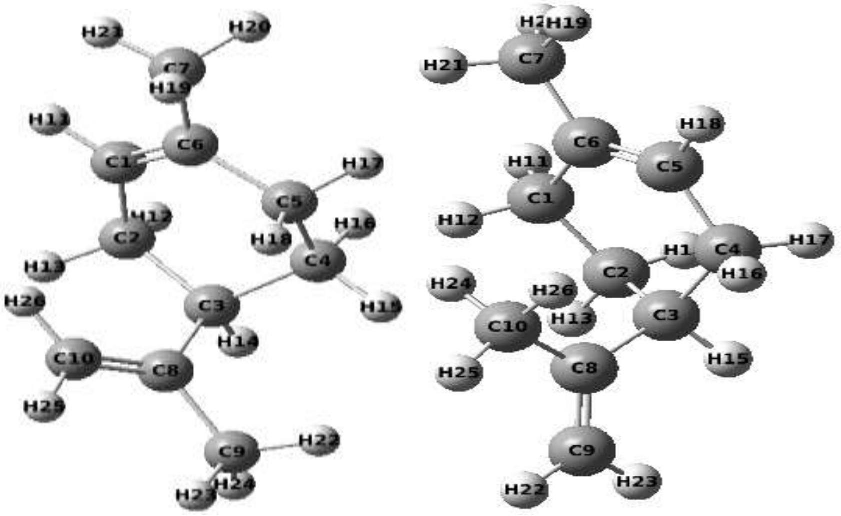

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Figure 1. Optimized molecular structure of (A) (R)-limonene, (B) (S)-limonene**.**

COMPUTATIONAL METHOD

The optimized geometry of the enantiomers of limonene was studied by the B3LYP / 6-311G (d, p) method [6]. All the calculations of this study were carried out with the Gaussian 09 Program. The length and the angle of connection have been fully optimized by the method DFT. The DFT method we used to include popular local methods, gradient correction [7]. The following quantum the chemical indices have been taken into account: the energy of the highest occupied molecular orbit (E_{HOMO}), the energy of the lowest unoccupied molecular orbit (E_{LUMO}), the energy band gap $\Delta E = E_{HOMO}-E_{LUMO}$, the quantum descriptors, the electronic affinity (A), the ionization potential (I) and the atomic partial charges were calculated for the two structures from the potential electrostatic surface (ESP) according to the same theory of levels [8].

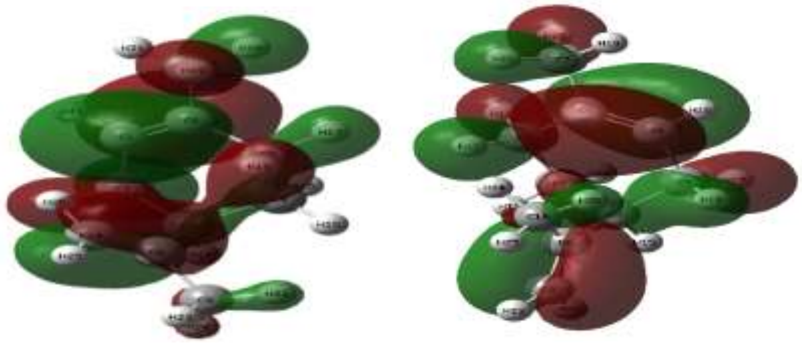
RESULTS AND DISCUSSION

Quantum chemical calculation

The main orbitals involved in chemical stability are the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The HOMO represents the capacity to yield an electron while the LUMO represents the capacity to gain an electron. The HOMO and LUMO energies are calculated by the B3LYP / 6-311G (d, p) method. Electronic absorption corresponds to the transition from the ground to the first excited state described by an electronic excitation from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) [9] with the optimized structures of the enantiomers of limonene are illustrated in Figure 2.

The Mulliken charges of the two molecules are given in Figure 3.

HOMO



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LUMO

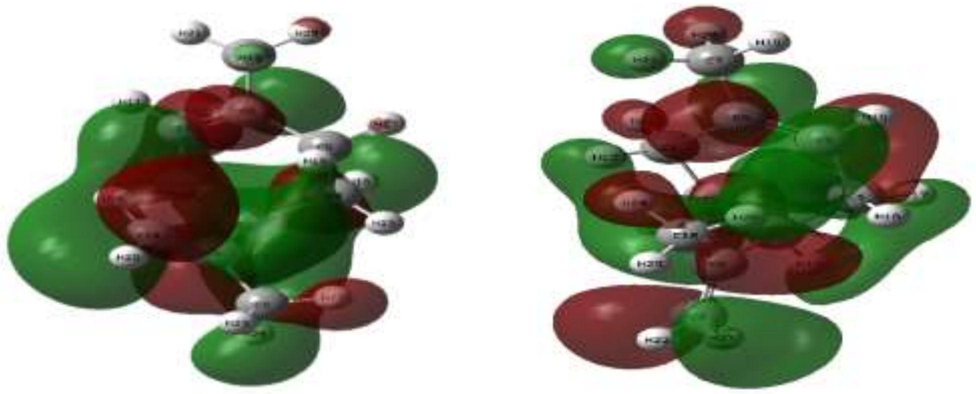

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Figure 2. HOMO and LUMO of (A) (R)-limonene, (B) (S)-limonene.

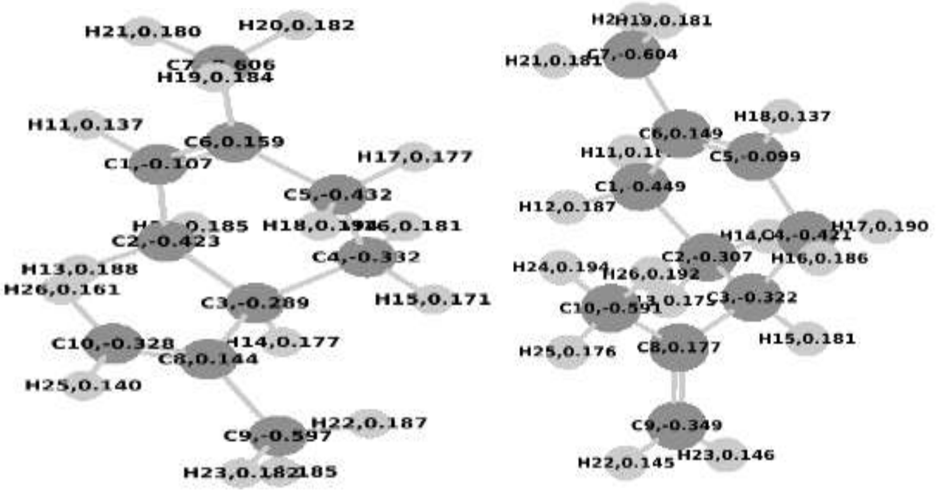

Figure 3. Mulliken charges of (A) (R)-limonene, (B) (S)-limonene by the B3LYP method.

Many applications are available on the utilization of the HOMO and LUMO gap as a quantum descriptor in correlates in different biochemical and chemical systems [10].

The following quantum descriptors have been calculated from the optimized structure obtained: Ionization potential:

$I = -E_{HOMO}$

Electronic affinity: $A = -E_{LUMO}$

Absolute electronegativity: $\chi = \frac{I+A}{2}$

Overall hardness: $\eta = I - A$

Overall softness: $\sigma = \frac{1}{\eta} = \frac{1}{E_{LUMO}-E_{HOMO}}$

Electronic chemical potential: $\mu = -\frac{(I+A)}{2}$

Maximum charge transfer: $\Delta N\max = -\frac{\mu}{\eta}$

Overall electrophilicity: $\omega = \frac{\mu^2}{2\eta}$

Overall nucleophilia N: $N = E_{HOMO} - E_{HOMO(TCE)}$ with $E_{HOMO(TCE)}$ = -9.3686 eV calculated by DFT/B3LYP 6-311G (d, p).

In order to highlight the electrophilic/nucleophilic character of the molecules, we calculated: the ionization potential I, the electronic affinity A, the electronic chemical potential μ, the absolute electronegativity χ, the overall hardness η, the overall softness σ, the overall electrophilicity index ω, the index of overall nucleophilic N and the maximum charge transfer ΔN_{max} (Table 1).

The energy gaps are 6.6796 eV and 6.7052 eV for the (R)-limonene and the (S)-limonene, respectively. As a result, the reactivity and stability of the two molecules are almost equal.

The overall electrophilicity index values are 0.6386 eV and 0.6736 for (R)-limonene and (S)-limonene, respectively, indicating that the two molecules have the same reactivity towards attack nucleophile.

The overall nucleophilicity index values are 3.1078 eV and 3.0104 for (R)-limonene and (S)-limonene, respectively, indicating that the two molecules have the same reactivity to electrophilic attack.

The maximum charge transfer ΔN_{max} of the two molecules is almost equal to 0.43 eV.

Table 1. Quantum theoretical parameters of (A) (R)-limonene, (B) (S)-limonene, calculated by B3LYP / 6-311G (d, p).

Parameters (eV)	E_{LUMO}	E_{HOMO}	ΔE	I	A	μ	χ	η	σ	ω	N	ΔN_{max}
(R)-Limonene	0.418	-6.260	6.679	6.260	-0.418	-2.921	2.921	6.679	0.149	0.638	3.107	0.437
(S)-Limonene	0.347	-6.358	6.705	6.358	-0.347	-3.005	3.005	6.705	0.149	0.673	3.010	0.448

Non-linear optical properties

Intermolecular interactions are widely understood by dipole moment and the energetic terms of hyperpolarization of the first and second-order. The dipole moment (μ), the polarizability (α), the first hyperpolarizability (β) and the second hyperpolarizability (γ) are calculated using a basic set of DFT on the basis of the B3LYP 6-311G approach (d, p). The complete equations to calculate the amplitude of the total static dipole moment (μ), the polarizability (α), the first hyperpolarizability (β) and the second hyperpolarizability (γ), using the components x, y, z of 09W The Gaussian output is as follows [11]:

$$\mu = (\mu_x^2 + \mu_y^2 + \mu_z^2)^{1/2}$$

$$\alpha = \frac{(\alpha_{xx} + \alpha_{yy} + \alpha_{zz})}{3}$$

$$\beta = (\beta_x^2 + \beta_y^2 + \beta_z^2)^{1/2}$$

$$\beta_x = \beta_{xxx} + \beta_{xyy} + \beta_{xzz}$$

$$\beta_y = \beta_{yyy} + \beta_{xxy} + \beta_{yzz}$$

$$\beta_z = \beta_{zzz} + \beta_{xxz} + \beta_{yyz}$$

$$< \gamma > = \frac{1}{5}\,(\gamma_{xxxx} + \gamma_{yyyy} + \gamma_{zzzz} + 2\,[\gamma_{xxyy} + \gamma_{yyzz} + \gamma_{xxzz}])$$

The results for the dipole moment, linear polarizability, first hyperpolarizability, and second hyperpolarizability of molecules are tabulated in Table 2.

The dipole moment of the molecules is again calculated using DFT and method B3LYP with basic set 6-311G (d, p). The dipole moment reflects the distribution of molecular charges and is given as a three-dimensional vector. Consequently, it can be utilized as a descriptor to represent the charge movement through the molecule as a function of the negative and positive charge centers. Dipole moments are necessarily determined for neutral molecules. For charged molecules, its values depend on the orientation and the choice of the origin of the molecular.

The results indicate that the calculated value of the dipole moment of (S)-limonene (0.7092 D) is greater than that of (R)-limonene (0.2923D) which reflects the stability of (S)-limonene with respect to (R)-limonene.

The results show that the value of the dipolar polarizability tensors of (R)-limonene is slightly elevated in all three directions compared to the values of the polarizability tensors of (S)-limonene. The calculated high dipolar polarization value is -64.4361 D in (R)-limonene while the low dipolar polarization value (-65.0400 D) is observed in (S)-limonene. So (R)-limonene is slightly polarizable and which is slightly chemically active.

The transitions of (S)-limonene -3.6928 D and -2.1551 D are observed along the x and z axes with a negative direction and 0.7683 D along the y-axis with a positive direction, while the transitions of (R)-limonene -2.8653 D, -1.1543 D and -1.8125 D are found along the x, y and z axes with a negative direction.

The high and low β is calculated to be 7.1162 D and 4.5563 in (R)-limonene and (S)-limonene, respectively. Therefore, electron delocalization and charge transfer increase in (R)-limonene, resulting in a greater β response of paracetamol compared to (S)-limonene.

The values of the second-order hyperpolarizability γ, as well as their contributing tensors, are also observed to be large in (R)-limonene compared to (S)-limonene.

Table 2. Electric dipole moments (Debye) by the DFT method of (A) (R)-limonene, (B) (S)-limonene calculated using B3LYP / 6-311G (d, p).

	Parameters	**(R)-Limonene**	**(S)-Limonene**
Dipole moment (Debye)	μ_x	-0.2503	-0.6661
	μ_y	0.1496	-0.1981
	μ_z	0.0191	0.1411
	μ	0.2923	0.7092
Polarizability (Debye)	α_{xx}	-63.6086	-65.0200
	α_{yy}	-64.6398	-64.8270
	α_{zz}	-65.0601	-65.2734
	α	-64.4361	-65.0400
First Hyperpolarizability (Debye)	β_{xxx}	-2.8653	-3.6928
	β_{xyy}	2.3845	1.1801
	β_{xzz}	-5.5234	-1.5236
	β_{yyy}	-1.1543	0.7683
	β_{xxy}	-1.0881	-0.2404
	β_{yzz}	-1.5694	0.5279
	β_{zzz}	-1.8125	-2.1551
	β_{xxz}	0.1488	-1.0548
	β_{yyz}	1.4176	0.5563
	β	7.1162	4.5563
Second Hyperpolarizability (Debye)	γ_{xxxx}	-1145.6601	-1051.9166
	γ_{yyyy}	-490.2167	-509.2520
	γ_{zzzz}	-363.3176	-362.7382
	γ_{xxyy}	-274.4458	-264.7394
	γ_{yyzz}	-144.5548	-148.8647
	γ_{xxzz}	-245.6170	-240.1383
	γ	-532.7624	-515.5298

Thermodynamic parameters

We determined for each molecule the enthalpy H, the entropy S, and the free enthalpy G (Table 3). The enthalpy H is the sum of the internal energy of a system and the product of its pressure by its volume. Entropy S, it characterizes by the degree of disorder or unpredictability of the information contained in a system. We found that the two enantiomers have very close G values, which confirms the similarity of the stability and the reactivity of the two molecules.

Table 3. Thermodynamic parameters of (R)-limonene, (S)-limonene.

Molecules	ΔH (Kcal/mol)	ΔS (Kcal/mol/K)	ΔG (Kcal/mol)
(R)-Limonene	-244986.91	0.0992	-245282.53
(S)-Limonene	-244982.27	0.0991	-245277.59

Bond length and angle properties

In this article, we will deepen our studies on selective bond lengths (Å) and angles (degrees). The DFT level has been used with the B3LYP/6-311G (d, p) method, the utility of which is to describe the molecular physical and chemical properties [7].

Tables 4 and 5 show the comparison of the optimized bond length and the angle between experimental and calculated atomic numbered positions as (Figure 1) the optimized structures using a periodic DFT calculation corresponds exactly to an experimental result. The study of the geometric product, therefore, showed an excellent agreement between theoretical and experimental results.

Table 4. Bond lengths (Å) of (R)-limonene, (S)-limonene. (The experimental values [8, 12]).

Bond length (Å)	(R)-Limonene	(S)-Limonene	Exp
C1-C2	1.496	1.523	1.521
C2-C3	1.523	1.4516	1.487
C3-C4	1.451	1.523	1.523
C4-C5	1.523	1.4971	1.384
C5-C6	1.497	1.3369	1.401
C6-C1	1.337	1.4971	1.402
C6-C7	1.497	1.497	1.370
C3-C8	1.497	1.4969	1.482
C8-C10	1.337	1.497	1.356
C8-C9	1.497	1.337	1.407

Table 5. Angles (θ°) of (R)-limonene, (S)-limonene. (The experimental values [8, 13]).

Angles (θ°)	(R)-Limonene	(S)-Limonene	Exp
C1-C2-C3	109.4704	104.4713	108.2
C3-C4-C5	104.4726	109.4639	120.0
C5-C6-C7	119.2993	119.3031	120.3
C3-C8-C10	120.0005	120.0017	120.1
C3-C8-C9	119.9959	120.0033	119.3
C10-C8-C9	120.0035	119.995	119.2

Molecular electrostatic potential

Molecular electrostatic potential (MEP) gives detailed information for studies on chemical reactivity or the biological activity of a compound. The spatial distribution and the values of the electrostatic potential determine the attack of an electrophilic or of a nucleophilic agent as the primary event of a chemical reaction. Furthermore, the three-dimensional distribution of the electrostatic potential is largely responsible for the binding of a substrate at the active site of a receptor [13].

The molecular electrostatic potential (MEP) is mainly used in the form of the reactivity map showing the most likely regions for the electrophile attack of point reagents loaded on organic molecules. It is very important in molecular modeling studies. Contour MEP, the map offers a simple tool to predict how different geometries can interact.

The total electronic density and the MEP surface of the molecules studied are constructed by B3LYP / 6-311 Method G (d, p). Electrostatic potential maps and contour electrostatic potential of (R)-limonene and (S)-limonene are shown in figures 4 and 5.

The color scheme for the MESP surface is red, rich in electrons, partially negative charge; blue, electron-deficient, partially positive charge; light blue, slightly electron-deficient Region; yellow region, slightly rich in electrons; green, neutral, respectively. Blue represents electropositive and red the electronegative regions, respectively [14].

The electrophilic attack sites are (C7, C10) and (C5, C9) for (R)-limonene and (S)-limonene, respectively. Nucleophilic attacks can occur at (C9, C3) and (C3) sites for (R)-limonene and (S)-limonene, respectively.

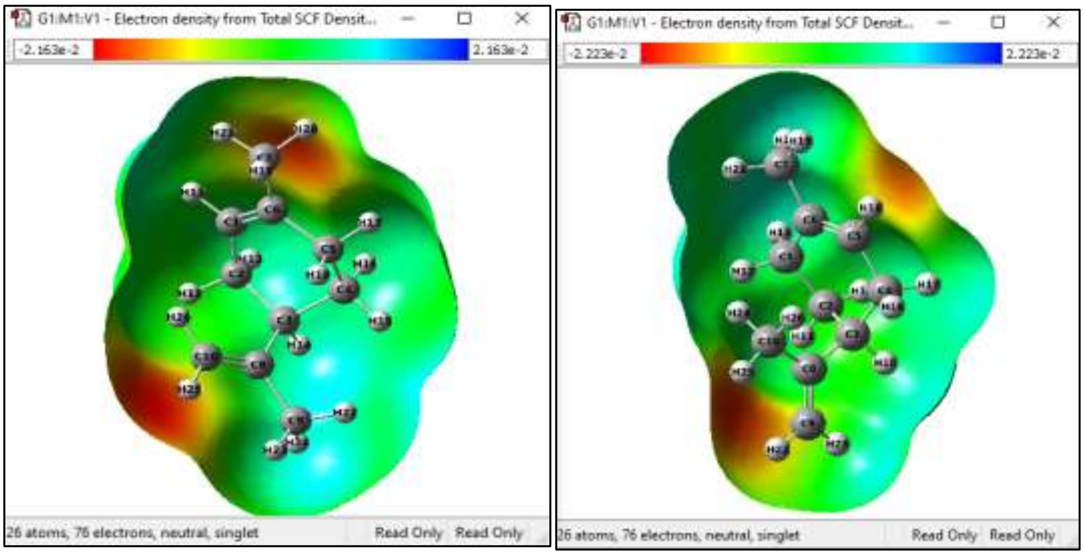

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Figure 4. Electrostatic potential maps around the (A) (R)-limonene, (B) (S)-limonene.

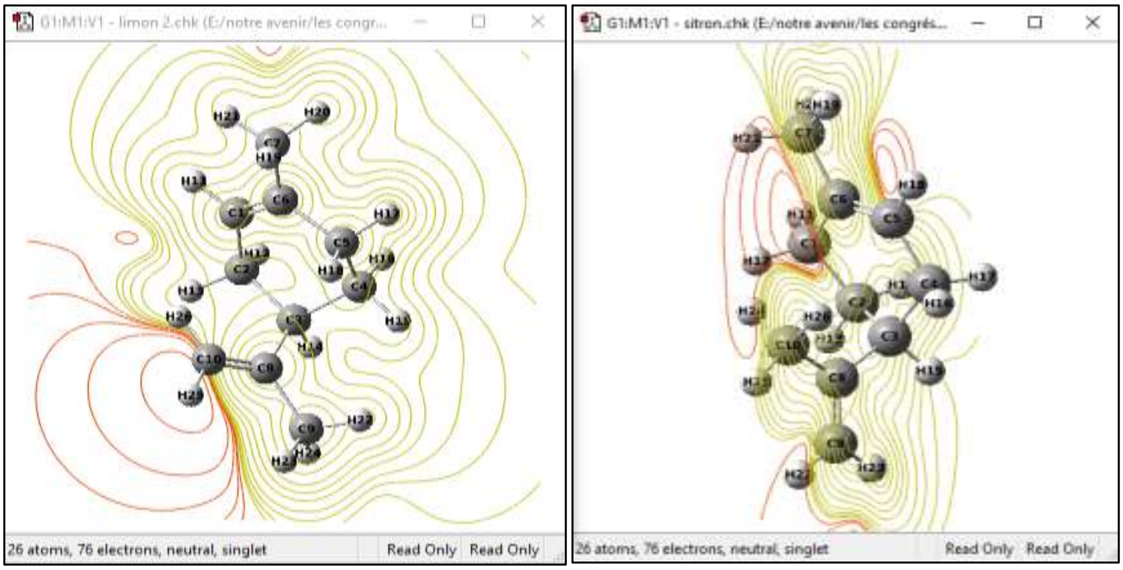

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Figure 5. Contour electrostatic potential around the (A) (R)-limonene, (B) (S)-limonene.

CONCLUSIONS

In the present work, the determination of interatomic distances, the prediction of the local reactivity of molecules, the analysis of the potential energy surface, the values of enthalpy, entropy, and free enthalpy of molecules of (R)-limonene and (S)-limonene, and the transition states were performed using the gradient corrected function of Becke, Lee, Yang, and Parr (B3LYP) exchange and correlation with the standard base 6-311G (d, p) with DFT methods, and curves of electrostatic potential and electrostatic potential around the molecule of (R)-limonene and the molecule of (S)-limonene. We have presented an efficient approach for the computation of local electric dipole moments with an emphasis on periodic systems. Also, the length results and their angular connections were optimized at B3LYP by the DFT method based on 6-311G (d, p) levels, the aim of which is to describe the molecular physical and chemical properties.

ACKNOWLEDGEMENTS

The authors would like to thank the Analytical Chemistry & Computer Science, Nanotechnology and Environment Team (CAINE) for their contributions to production.

Conflict of interests

The authors declare no conflict of interest.

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