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Theme:

Molecular modeling of a compound of Dithiolethione family 4-p-tolyl-1, 2-dithiol-3-thione is a derivative

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بسم الله الرحمن الرحيم

قال تعالى: (فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ ۗ وَلَا تَعْجَلْ بِالْقُرْآنِ مِن قَبْلِ أَن يُقْضَىٰ إِلَيْكَ وَحْيُهُ ۖ وَقُل رَّبِّ زِدْنِي عِلْمًا)

سورة طه , الآية 114

Dedicate:

I started with more than one hand, and I suffered more than they are, and I suffered from difficulties, and here I am today, thank God, folding the sleepless nights and tired days, and the summary of my journey between the covers of this humble work.

I dedicate this work to the one who pushed me to the turning point of science and knowledge and struggled for my upbringing and education.

To the one who nursed me love and tenderness To the symbol of love and healing balm To the spotless heart My beloved mother is nice, may God prolong her life

And to all my brothers and sisters and all my family with my uncles, aunts and grandfathers, all in his name, and all my loved ones, my friends and girlfriends to whom I dedicate all the love and friendship (Salima, Hanan, Fariha, Ruqayya, Fati, Noor, Fawzia, Shaima and Khadija)

And to all those who helped me without devotion... and to all those whom my memory fits but my memorandum does not fit.

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First and for most, all praise is too "الله" Who gives us the guidance and the power to carry on this study.

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Thank you

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Introduction

Introduction:

Molecular modeling describes the generation, representation and/or manipulation of 3-**D** structure of chemical and biological **molecules**, along with determination of physicochemical properties that **can** help to interpret structural activity relationship (SAR) of the biological **molecules**. is a collection of (computer based) techniques for deriving, representing and manipulating the structures and reactions of **molecules**, and those properties that are dependent on these three dimensional structures.

A **compound** is a material formed by chemically bonding two or more chemical elements. The type of bond keeping elements in a **compound** together may vary: covalent bonds and ionic bonds are two common types. The elements are always present in fixed ratios in any **compound**.

Why is **Molecular** Modeling **Important**? Designing Drugs for the Future: Using **molecular** modeling scientists will be better able to design new and more potent drugs against diseases such as Cancer, AIDS, and Arthritis. Shown to the Left: The 3D structure of a protein drug target.

Molecular formula is based on the actual makeup of the compound. Although the molecular formula can sometimes be the same as the empirical formula, molecular compounds tend to be more helpful. However, they do not describe how the atoms are put together. Molecular compounds are also misleading when dealing with isomers, which have the same number and types of atoms (see above in molecular geometry and structural formula).

In this context, we will try to model the compound 4-p-tolyl-1, 2-dithiol-3-thione and its salt to obtain the molecular structure and determine the links with different programs and various analytical methods between IR and RX.

Chapitre N° 1:

Molecular modeling basics and generalities about Dithiolethione

Introduction:

Theoretical chemistry has become an essential partner of the experimenter thanks to the development of computer resources and the increasing power of computers. In recent years, significant developments in the computer field and the progress made in quantum chemistry computational methods have made it possible to give a good prediction and a good description of the electronic properties of a given entity. These circumstances favor a more common use of these tools in different areas of chemistry for the comparison of experimental and calculated results, as well as a better understanding of reaction mechanics [1].

In this way, we will briefly describe all the basic principles of quantum chemistry and generalities on Dithiolethione compounds.

III. Schrödinger's equation:

In quantum mechanics, the treatment of any poly electronic molecular system, comprising n electrons and M nuclei, involves solving the Schrödinger equation [2] relating to stationary states. This is written:

$$\hat{H}\,\Psi = E\,\Psi \qquad (1)$$

Ĥ is the Hamiltonian operator describing the interactions between the particles constituting the studied system. **E** is the total energy and □ is the wave function describing the state of the system. The Hamiltonian operator for a molecular system comprising electrons of coordinates (r) and nuclei of coordinates (R) is written (in u.a):

$$\hat{H} = \hat{T}_E(r) + \hat{T}_N(R) + \hat{V}_{EE}(r) + \hat{V}_{NN}(R) + \hat{V}_{EN}(r,R) \qquad (2)$$

In this expression the terms $\hat{T}_E$ and $\hat{T}_N$ are the kinetic energy operators of electrons and nuclei, both expressed as the sums of the individual contributions, (in u.a):

$$\hat{T}_E(r) = -\sum_{i=1}^{n} \frac{\Delta_i}{2} \qquad (3)$$

$$\hat{T}_N(R) = -\sum_{K=1}^{M} \frac{\Delta_K}{2M_K} \qquad (4)$$

Δi is the La plician operator relating to the electron i and is written:

$$\Delta_i = \frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2}$$

The terms: $\hat{V}_{EE}$, $\hat{V}_{NN}$ and $\hat{V}_{EN}$, are the electron-electron, nucleus-nucleus and electron-nucleus potential energy operators, respectively, of expressions (in u.a):

$$\hat{V}_{EE}(r) = \sum_{i<j}^{n} \frac{1}{r_{ij}} \quad \textbf{(6)}$$

$$\hat{V}_{NN}(R) = \sum_{K<L}^{M} \frac{Z_K Z_L}{r_{KL}} \quad \textbf{(7)}$$

$$\hat{V}_{EN} = -\sum_{i=1}^{n} \sum_{K=1}^{M} \frac{Z_K}{r_{iK}} \quad \textbf{(8)}$$

Z_K and Z_L denote the charges of the Kth and Lth nucleus. The quantities r_{iK}, r_{ij} and r_{KL} respectively characterize the distance between the electron i and the nucleus K, the distance between the two electrons i and j and finally the distance between the nuclei K and L.

The Hamiltonian will then be written in atomic units:

$$\hat{H} = -\sum_{i=1}^{n} \frac{\Delta_i}{2} - \sum_{K}^{M} \frac{\Delta_K}{2M_K} + \sum_{i<j}^{n} \frac{1}{r_{ij}} + \sum_{K<L}^{M} \frac{Z_K Z_L}{r_{KL}} - \sum_{i=1}^{n} \sum_{K=1}^{M} \frac{Z_K}{r_{iK}} \quad \textbf{(9)}$$

The Hamiltonian operator of the system (9) being a function of the electronic and nuclear coordinates, the total wave function of the system $\Psi_{(r,R)}$ is also a function of the electronic (r) and nuclear (R) coordinates, this makes the mathematical resolution of the equation of Schrödinger (1) for molecular systems, very complex. Therefore, solving equation (1) requires using the following approximations:

- The non-relativistic approximation which consists in neglecting the variation of the mass of a particle as a function of its speed as well as the spin-spin and spin-orbit couplings.
- Born Oppenheimer's approximation [3] (adiabatic approximation) which separates the movement of electrons from that of nuclei. This approximation is

based on the fact that electrons move much faster than nuclei because of the much lower mass of electrons (about 1836 times lower than that of the proton).

The use of the last approximation makes it possible to express $\Psi(r,R)$ in the form of a product of electronic $\Psi_e(r,R)$ and nuclear functions Ψ_N (R). R and r respectively denote the set of nuclear and electronic coordinates.

The resolution of equation (1) then reduces to the resolution of the electronic Schrödinger equation:

$$\hat{H}_e \, \Psi_e(r,R) = E_e \, \Psi_e(r,R) \qquad (10)$$

E_e is electronic energy and $\hat{H}_e$ represents the electronic Hamiltonian whose expression is:

$$\hat{H}_e = \hat{T}_E(r) + \hat{V}_{EN}(r,R) + \hat{V}_{EE}(r) \qquad (11)$$

And in (u.a) we get:

$$\hat{H}_e = -\sum_{i=1}^{n} \frac{\Delta_i}{2} - \sum_{i=1}^{n}\sum_{K=1}^{M} \frac{Z_K}{r_{iK}} + \sum_{i<j}^{n} \frac{1}{r_{ij}} \qquad (12)$$

For a polyelectronic system, the electronic Schrödinger equation cannot be solved exactly because of the term of the electronic repulsion $\hat{V}_{EE}(r)$ which depends on the coordinates of the two electrons i and j and which prevents the separation of the variables, which leads us to perform approximations, these generally relate to the simplification of the Hamiltonian $\hat{H}_e$ or the analytical form of the wave function Ψe .

Two categories of quantum methods are distinguished:

- The first includes non-empirical (ab initio), semi-empirical and empirical methods.
- The second is the density functional theory (DFT).

In the first category, the determination of the electronic properties of any molecular system requires knowledge of the wave function, while in the second; it is rather the knowledge of the electron density that determines these properties.

Molecular modeling:

Molecular modeling is a set of computer techniques based on methods of Theoretical chemistry and experimental data that can be used either to analyze molecules and molecular systems or to predict molecular, chemical and biochemical properties. It serves as bridge between theory and experience for:

1. Extract results for a particular model.
2. Compare the experimental results of the system.
3. Compare the theoretical predictions of the model.
4. Help understand and interpret experimental observations.
5. Correlation between microscopic details at atomic and molecular level and macroscopic properties.
6. Provide information not available from real experiences **[4].**

Molecular modeling consists of the construction of three-dimensional models from the data. It finds its raison d'être on the one hand in the experimental limitations of the methods for determining the structure of proteins and on the other hand in the current inability to predict the 3D structure from sequence information alone. In addition, it makes it possible to investigate the changes of conformations linked to mutations from experimental 3D structures.

Molecular modeling is an application of theoretical methods and computational methods to solve problems involving molecular structure and chemical reactivity. These methods often use very sophisticated info graphic means which greatly facilitate the transformation of impressive quantities of numbers into a few easily interpretable graphic representations.

Molecular modeling involves the use of theoretical calculation methods (molecular mechanics, molecular dynamics, ab-initio or semi-empirical quantum mechanics…) **[5].**

2.1. Quantum Methods (QM)

Quantum mechanical methods are based on the solution of the Schrodinger equation **[6,7]**. This fundamental approach is attractive since 3D structures, molecular energies, and many associated properties can be calculated on the basis of fundamental physical principles, namely electronic and nuclear structures of atoms and molecules. Indeed, the quantum mechanics pioneer Paul Dirac is believed to have expressed the

sentiment that the Schrödinger equation reduces theoretical chemistry to applied mathematics **[8]**.

Although historically quantum calculations were practical only for very small systems, exciting developments in both software and hardware (computer speed as well as memory) have made quantum-mechanical calculations feasible for larger systems, including bimolecular, with various approximations **[9]**.

The Schrödinger equation is perhaps the most important equation in the entire field of quantum mechanics. The time-dependent non-relativistic one-particle variant is:

$$\left[-\frac{1}{2}\nabla^2+\hat{\mathcal{V}}\right]\Psi(\mathbf{x},t)=i\hbar\frac{\partial}{\partial t}\Psi(\mathbf{x},t) \quad (13)$$

Where v^is a possibly time-dependent, possibly position dependent potential. The time independent equation is:

$$\left[-\frac{1}{2}\nabla^2+\hat{\mathcal{V}}\right]\Psi(\mathbf{x})=E\Psi(\mathbf{x}) \quad (14)$$

Where E: is the energy of the system. These equations can be expanded to match a multi-particle system **[10]**.

2.1.1. Ab initio Methods (Hartree-Fock, Roothaan):

'*Ab initio*' quantum chemistry has emerged as a viable and powerful approach to address the issues and problems related to the chemical systems. Quantum chemical calculations offer the real promise of being able to complement experiment as a means to uncover and explore new chemistry. It is used for predicting the properties of new materials even those which are not synthesized in the laboratory, using computer simulation technique **[11]**.

Hartree-Fock-Roothaan method:

The Hartree method is a single electron approximation technique used in multi electron systems. The molecular Hamiltonian is split up into individual single electron Hamiltonians. Consider a molecular system with N-electrons, each with degrees of freedom$r$. The wave function (Hartree function) $\boldsymbol{\psi h}$ ($\boldsymbol{r1}$, $\boldsymbol{r2}$ … $\boldsymbol{rN}i$) is given by the Hartree product as shown in Eq. 3: **[12]**.

$$\psi_h(r_1, r_2, \dots r_N) = \varphi_1(r_1).\varphi_2(r_2).\varphi_N(r_N)$$

(15)

For the n-electron system, the Hamiltonian is given by:

$$\hat{H}_e = \hat{T}_e + \hat{v}_{ne} + \hat{v}_{ee} + \hat{v}_{nn}$$

(16)

The Hartree-Fock (HF) model is a standard tool for computing an approximation of the ground state of a molecular system within the Born-Oppenheimer setting. From a mathematical viewpoint, the HF model gives rise to a non quadratic constrained minimization problem for the numerical solution of which iterative procedures are needed; such procedures are referred to as Self-Consistent Field (SCF) algorithms **[13]**.

It is always possible to decompose ψ (i) on a complete basis of known functions. The problem of determining ψ (i) comes down to that of calculating the numerical coefficients of the development of ψ (i) on the complete basis. It was Roothaan who used the MO-LCAO technique to build the MO, he unblocked the crisis of ab initio methods. This method consists in expressing the molecular orbital ψ (i) by a linear combination of atomic orbital's ϕμ **[14]**.

$$\phi_i = \sum_{\mu=1}^{N} C_{i\mu}\, \varphi_\mu$$

(17)

C iμ: are the coefficients to be varied. (Method of variations), N: is the number of OAs combined.

2.1.2. Density Functional Theory

Density functional theory (DFT) is a quantum-mechanical (QM) method used in chemistry and physics to calculate the electronic structure of atoms, molecules and solids. It has been very popular in computational solid-state physics since the 1970s. However, it was not until the 1990s that improvements to the method made it acceptably accurate for quantum-chemical applications, resulting in a surge of applications. The real forte of DFT is its favorable price/performance ratio compared with electron-correlated wave function-based methods such as Møller–Plesset perturbation theory or coupled cluster. Thus, larger (and often more relevant) molecular systems can be studied with sufficient accuracy, thereby expanding the predictive power inherent in electronic structure theory. As a result, DFT is now by far

the most widely used electronic structure method. The huge importance of DFT in physics and chemistry is evidenced by the 1998 award of the Nobel Prize to Walter Kohn 'for his development of the density-functional theory' **[14]**.

2.2. Semi Empirical methods

Semi empirical calculations are set up with the same general structure as a HF calculation. Within this framework, certain pieces of information, such as two electron integrals, are approximated or completely omitted. In order to correct for the errors introduced by omitting part of the calculation, the method is parameterized, by curve fitting in a few parameters or numbers, in order to give the best possible agreement with experimental data. The merit of semi empirical calculations is that they are much faster than the ab initio calculations. The demerit of semi empirical calculations is that the results can be slightly defective. If the molecule being computed is similar to molecules in the database used to parameterize the method, then the results may be very good. If the molecule being computed is significantly different from anything in the parameterization set, the answers may be very poor. Semi empirical calculations have been very successful in the description of organic chemistry, where there are only a few elements used extensively and the molecules are of moderate size. However, semi empirical methods have been devised specifically for the description of inorganic chemistry as well **[15]**.

In the various semi-empirical methods such as CNDO (Complete Neglect of Differential Overlap), INDO (Intermediate Neglect of Differential Overlap), NDDO (Neglect of Diatomic Differential Overlap), MNDO (Modified Neglected of Differential Overlap), AM1 (Austin Model 1), PM3 (Parametric Method 3), only the valence electrons are taken into account. Through these methods, we have access to different molecular properties such as atomic charges, orbital energies (HOMO, LUMO) among others, the ionization potential, the enthalpy of formation and the electronic distribution **[16]**.

2.3. No Quantum Methods

Empirical methods are methods of molecular mechanics based on concepts of classical mechanics where atoms and their electrons are merged into a collection of material points. The latter act on each other by means of an empirical potential also called field of forces depending only on the relative position of the atoms in space.

Within the computer, the representation of a molecule therefore consists of a set of atomic coordinates, a list of chemical bonds and a set of functions and parameters constituting the interaction potential. The empirical potential which determines the energy conformation it of the molecule is made up of two types of terms representing, respectively, the interactions between the bonded atoms (bond length, valence angle, dihedral angle) and the unbound atoms (Vander Waals, electrostatic) **[17]**.

2.3.1. Molecular Mechanics

The MM appeared in 1930 **[18]**, but developed from the sixties when computers were no longer accessible and more efficient. The MM is based on Born Oppenheimer's approximation that electrons are much faster than nuclei **[19]**.

Molecular mechanics (MM) is the simplest and fastest way to evaluate molecular systems. These methods rely on classical potential functions, and quantum-mechanical properties of systems, such as bond breaking or forming, are entirely neglected.

Molecular mechanics can be used to study small molecules as well as large biological systems or material assemblies with many thousands of atoms, but only in their equilibrium states. In all-atomistic molecular mechanics methods, each atom is represented as a single particle, and each particle is assigned a radius (Typically the Vander Waals radius), polarizability, and a constant net charge, which is derived from quantum-mechanical calculations and/or experiment. Bond interactions are treated as "springs" with an equilibrium distance equal to the experimental or calculated bond length. The collection of potential functions made to describe a molecular system is referred to as a force filed, which can be used to calculate molecular energy based on bond-stretching, valence bond bending, torsions, and non-bonded interactions **[20]**.

Molecular mechanics methods are based on the following principles: Nuclei and electrons are lumped into atom-like particles; Atom-like particles are spherical (radii obtained from measurements or theory) and have a net charge (obtained from theory); Interactions are based on springs and classical potentials; Interactions must be reassigned to specific sets of atoms; Interactions determine the spatial distribution of atom-like particles and their energies; Note how these principles differ from those of quantum mechanics. In short, the goal of molecular mechanics is to predict the detailed structure and physical properties of molecules. Examples of physical properties that can be calculated include enthalpies of formation, entropies, dipole moments, and strain energies.... Molecular mechanics calculate the energy of a molecule and then adjusts the energy through changes in bond lengths and angles to obtain the minimum

energy structure. Steric Energy A molecule can possess different kinds of energy such as bonds and thermal energy. Molecular mechanics calculate the steric energy of a molecule–the energy due to the geometry or conformation of a molecule **[21]**.

Molecular mechanics uses the following approximations:

- Each atom constitutes a particle.
- The atom is considered as a rigid sphere having a radius and a specific charge.
- Energies are calculated by formulas derived from the classical mechanics **[22]**.

a. Term of the force field:

The mathematical model representing the potential energy is called the force field of a molecule

in molecular mechanics.

The "Force Field", which represents as well as possible the variations of the potential energy with the molecular geometry. Its purpose is to calculate the potential energy of a molecule (or of a molecule system) according to the coordinates of the atoms:

$$Ep = f(r1, r2\ldots., Rn)$$

Or: ri: represents the position vector of atom i.

Ep: Potential energy

But a better idea may be obtained by considering the situation physically. Consider a molecule as a collection of atoms held together by elastic forces. (If you want to get even simpler than one could consider a molecule to be a collection of point masses connected by elastic springs). Now the forces can be written in terms of potential energy functions of various structural features such as bond lengths, bond angle, non-bonded interactions etc. The force field is the combination of these potential energy terms. Hence force fields are also sometimes referred to as potentials. Thus, the energy, E, of a molecule in a force field arises from the deviations from the ideal structural features.

The mechanical molecular model considers atoms as spheres and bonds as springs. The mathematics of spring deformation can be used to describe the ability of bonds to stretch, bend, and twist:

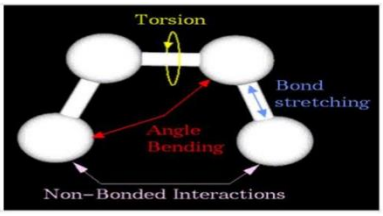


Figure 1: Intermolecular interactions between bound and unbound atom

Non-bonded atoms (greater than two bonds apart) interact through Vander Waals attraction, steric repulsion, and electrostatic attraction/repulsion. These properties are easiest to describe mathematically when atoms are considered as spheres of characteristic radii.

The object of molecular mechanics is to predict the energy associated with a given conformation of a molecule. However, molecular mechanics energies have no meaning as absolute quantities. Only differences in energy between two or more conformations have meaning. A simple molecular mechanics energy equation is given by:

Energy = Stretching Energy + Bending Energy + Torsion Energy + Non-Bonded Interaction Energy

These equations together with the data (parameters) required to describe the behavior of different kinds of atoms and bonds, is called a force-field. Many different kinds of force-fields have been developed over the years. Some include additional energy terms that describe other kinds of deformations. Some force-fields account for coupling between bending and stretching in adjacent bonds in order to improve the accuracy of the mechanical model **[23,24]**.

Steric energy is expressed by the following equation:

$$E = E_{stretching} + E_{bending} + E_{torsion} + E_{vdw} + E_{elec} + E_{Hydrogen}$$

The term **"Stretching"** represents the elongation of bonds.

The term **"Bending"** represents the variation of angles.

The term **"Torsion"** refers to the torsional energy of dihedral angles.

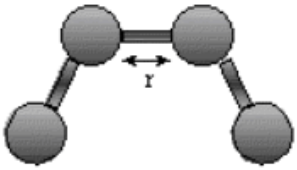
The term **"Vdw"** accounts for the non-covalent interaction energies between atoms unrelated. The term **"Elec"** describes the electrostatic interaction energies between atoms unrelated. The term **"Hydrogen"** describes hydrogen bonds **[25]**.

b. Term of linked atoms

Intermolecular interactions only depend on coordinates internal molecules that is to say, bonds, valence angles, and torsions. In fact, to refine the expression of the

potential term is to make the description of the system; terms of couplings between different atoms have been introduced. The mathematical form of the energy terms varies from force-field to force-field. The more common forms will be described.

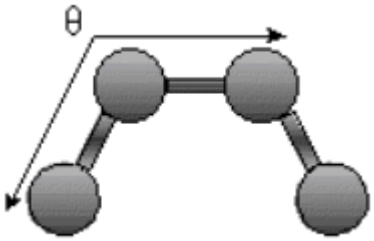
- ***Stretching Energy:***



$$E_{stretch} = \sum_{bonds} k_b (r - r_o)^2$$

The stretching energy equation is based on Hook's law. The kb parameter defines the stiffness of the bond spring. R_0 is the equilibrium distance between the two atoms. It should make sense that deviations from the equilibrium length would be associated with higher energy. Obviously only small changes in r are allowed as to large an r value would lead to bond breaking.

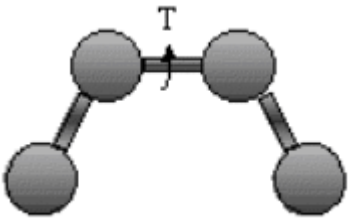
- ***Bending Energy:***



$$E_{bending} = \sum_{angles} k_\theta (\theta - \theta_o)^2$$

The bending energy equation is also based on Hook's law. The kT parameter controls the stiffness of the angle spring, while the T_0 is the equilibrium angle.

- ***Torsion Energy:***



$$E_{torsion} = \sum_{torsions} A[1+\cos(n\ )]$$

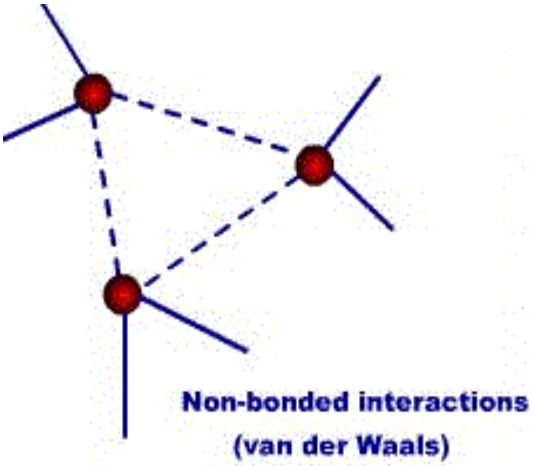
The torsion energy is modeled by a periodic function, much as you have seen with energy plots associated with Newman projections sighting down C-C bonds for example **[26]**.

c. Interaction energy between unbound atoms

Intermolecular interactions take into account interactions that do not interact by terms of bond, angle of curvature and angle of torsion. The non-binding potential is expressed in two terms: a Vander Walls term and an electrostatic energy term.

- ***Vander Waals Interaction*** Vander Waals interactions are non-permanent dipoles with a small range of action. They are numerous and essentially contribute to the search for steric agreement between the ligand and the receptor protein **[27]**.

It is generally expressed in the form of a John Lennard-Jones potential (dispersion and repulsion or a Buckingham potential) **[28]**.



$$E_{\text{van der Waals}} = \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \left[\frac{A_{i,j}}{d_{i,j}^{12}} - \frac{B_{i,j}}{d_{i,j}^{6}} \right]$$

di, j: distance between unbound atoms i and j

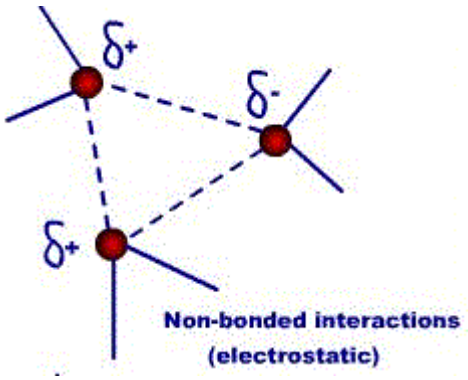
Ai, j: parameters of the force field linked to the repulsion between the atoms i and j

Bi, j: parameters of the force field linked to the attraction between atoms i and j

The radius of Vander Waals corresponds to the minimum distance between the 2 atoms

- ***Interactions electrostatics***

Energy of electrostatic interactions between atoms not covalently linked. It is expressed using a Coulomb potential. This term increases with the polarity of the chemical bonds and can be particularly important, for example in the case of molecules which contain heteroatom **[29]**.



$$E_{\text{électrostatique}} = \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \frac{q_i q_j}{4\pi\epsilon d_{i,j}}$$

$d_{i,j}$: distance between atoms i and j

q_i and q_j: partial charge of unbound atoms i and j. Atomic partial charges can be calculated for small molecules using an ab initio or semi-empirical quantum method (example: MOPAC and AMPAC)

ε: permittivity of the medium = dielectric constant of the environment (the solvent or the molecule itself)

- ***Energy of hydrogen bonds***

Hydrogen bonds are the result of electrostatic (70%) and van der Waals (30%) interactions between an electronegative atom (usually an oxygen or nitrogen atom) carrying a free electron doublet and an atom of hydrogen carried by an electronegative atom **[30]**.

$$E_{\text{Liaison-hydrogene}} = \sum \left[\frac{A'}{r_{AD}^{12}} - \frac{B'}{r_{AD}^{10}} \right] \cos^{m} \theta_{\text{A-H-D}} \cos^{n}\theta_{\text{AA-H-D}}$$

A', B': parameters depending on the nature of the donor and the acceptor of H bonds, distant from r AD.

θA-H-D: angle formed by the acceptor (A), the hydrogen (H) and the donor (D).

θAA-A-H: angle formed by the history of the acceptor (AA), A and H.

m, n: exponents given by the type of D and A, m = 0, 2, 4; n = 0, 2.

d. Different force fields in molecular mechanics:

Different force fields use the same type of energy terms but different Parameters. Force fields in MM can be grouped into three main classes **[31]:**

- Fields of force containing only the harmonic terms.
- Force fields using higher order terms (cubic, quadratic…).
- Fields of force suggested by Allinger et al. **[32]** not only considering the terms of classical molecular mechanics but also chemical effects such as electro negativity.

- **▪ MM2 / MM3 / MM4:**

MM2 is the first force field developed by Allinger et al. **[33,34].** It was initially designed for simple molecules (alkanes, alkenes, unconjugated alkynes, amines, etc.), but its improved versions MM3 (1989) **[35]** and MM4 (1996) **[36]** allow it to process more organic molecules and more complex.

- **▪ OPLS:**

The Optimized Potentials for Liquid Simulations (OPLS) program, as its name suggests, is designed to optimize the potential for describing solvation properties. It is written by W. L Jorgensen and J. Tirado Rives **[37].**

- **▪ GROMOS:**

GROMOS (Groningen Molecular Simulation Program Package), is written by Van Gusteren **[38]** and designed specifically for bio molecules in an aqueous medium for the study of interactions between water molecules and polar groups of proteins.

- **CHARM (Bio +):**

Developed by Karplus et al **[39-40]**, for the calculation of bio molecules. Its concept is similar to that of AMBER. Although initially this force field was designed for amino acids and proteins, now it deals with other bio molecules.

- **SPASIBA:**

(Spectroscopic Potential Algorithm for Simulating bio molecular conformational Adaptability), developed by Gérard Vergoten et al.(1995).

It combines the Urey-Bradly-Shimanouchi modified spectroscopic force field **[41]** and the AMBER force field. It makes it possible to find the structures, the conformational energies and the vibrational frequencies at the minimum energy of a molecule **[42]**.

- **EMO:**

The EMO program (Energy Of Molecule), is developed by B. Blaive**[43-44]**, it is based on the force field MM2

- **AMBER:**

AMBER (Assisted Model Building with Energy Refinement), was written by Kollman **[45]**. The field is configured for proteins and nucleic acids (UCSF, 1994).

e. Minimization of steric energy:

Minimization of a model is done in two steps. First, the energy expression (an equation describing the energy of the system as a function of its coordinates) must be defined and evaluated for a given conformation. Energy expressions may be defined that include external restraining terms to bias the minimization, in addition to the energy terms

Next, the conformation is adjusted to lower the value of the energy expression. A minimum may be found after one adjustment or may require many thousands of

iterations, depending on the nature of the algorithm, the form of the energy expression, and the size of the model.

The efficiency of the minimization is therefore judged by both the time needed to evaluate the energy expression and the number of structural adjustments (iterations) needed to converge to the minimum **[46]**.

2.3.2. Molecular Dynamics:

Molecular dynamics simulations are important tools for understanding the physical basis of the structure and function of biological macromolecules. The early view of proteins as relatively rigid structures has been replaced by a dynamic model in which the internal motions and resulting conformational changes play an essential role in their function **[47]**. Molecular dynamics is the study of how molecules move, deform, and interact over time. Predicting or interpreting these changes is essential in chemistry, physics, biology, engineering, and other fields **[48]**.

a. Molecular Dynamics calculation

Molecular dynamics are generally simulated in these stages:**[49]**

- ***Minimization***

This step involves finding the global minimum energy with respect to the position of side chains atoms that represents the geometry of the particular arrangements of atoms in which the net attractive force on each atom reaches a maximum.

- ***Heating the system***

In heating phase, initial velocities (at 0 K) are assigned to each atom of the system during energy minimization and Newton's equations of motion that represent the time evolution of system are numerically integrated. At short predefined intervals, new velocities are assigned corresponding to a slightly higher temperature and the simulation is allowed to continue until desired temperature is achieved.

- ***Equilibration***

Equilibration stage is used to equilibrate kinetic and potential energies means distribute the kinetic energy "pumped" into the system. In explicit solvent simulation, protein positions are fixed and waters move accordingly. Once the solvent is equilibrated, the constraints on the protein can be removed and the whole system (protein solvent) can evolve in time.

- ***Production phase***

Production phase is the last step of the simulation methodology to remove constraints on protein

- ***Analysis***

In this step, stored coordinates and velocities of the system are used for further analysis.

b. Applications of Dynamic molecular

Molecular dynamics can now be routinely applied in the investigation of a wide range of dynamic properties and processes by researchers in numerous fields, including structural biochemistry, biophysics, enzymologist, molecular biology, pharmaceutical chemistry, and biotechnology. Using MD simulations, one is able to study thermodynamic properties and time-dependent (i.e., kinetic) phenomena. This enables an understanding to be developed of various dynamic aspects of bio molecular structure, recognition, and function. However, when used alone, MD is of limited utility.

An MD trajectory (i.e., the progress of simulated structure with respect to time) generally provides data only at the level of atomic positions, velocities, and single-point energies. To obtain the macroscopic properties in which one is usually interested requires the application of statistical mechanics, which connects microscopic simulations and macroscopic observables **[50]**.

Molecule Dithiolthione:

The remarkable pseudo-aromatic structure of 1,2-dithiole-3-thione (DTT, formerly known as trithione) has attracted much interest due to its properties and applications. Thus, it serves as a precursor to other heterocyclic rings containing sulfur or nitrogen, and several derivatives have been found to exhibit marked pharmaceutical activity. The occurrence of DTT in cruciferous plants has been mentioned several times. In addition, the parent substance was found in sediments from the eastern Gulf of Finland **[51].**

Dithiolethiones are present in significant amounts in cruciferous vegetables, and consumption of these vegetables has been inversely associated with a number of cancers.

Dithiolethiones are naturally present in several edible plant products. Cabbage, Brussels sprouts, and other cruciferous vegetables have been found to contain significant amounts of dithiolethione **[52-53].**

1,2-Dithiol-3-thiones are heterocyclic compounds of general formula shown in Figure 1 **[54]**.

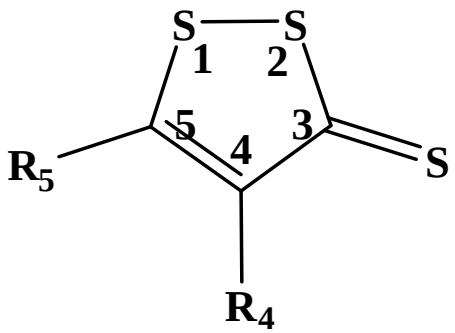


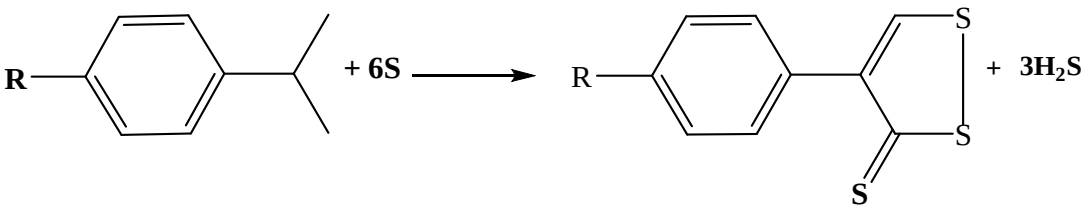
Figure 2: The general structure of 1, 2-dithiole 3-thione

IX. Synthesis of 1, 2-dithiole-3-thione:

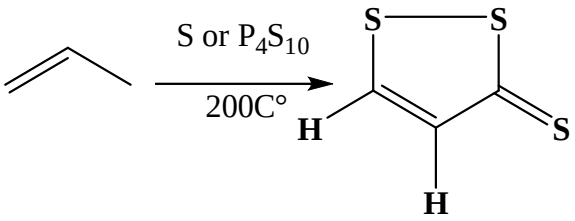
Several organic preparatory methods have been adopted to improve the reaction yield of the preparation of derivatives 1,2-dithiole-3-thiones from organic reactions and different experimental conditions, including from hydrocarbons, ketones, aldehydes and even organic acids. For example, we find the two interactions:

I. From hydrocarbons:

It was in the year 1954 by Filed **[55]** who proposed mechanisms for the reactions of formation of these compounds through sulfation of Cumene or Cymene or sulfation with P4S10 or with sulfur in the presence of a catalyst and in certain conditions. According to the following equations:



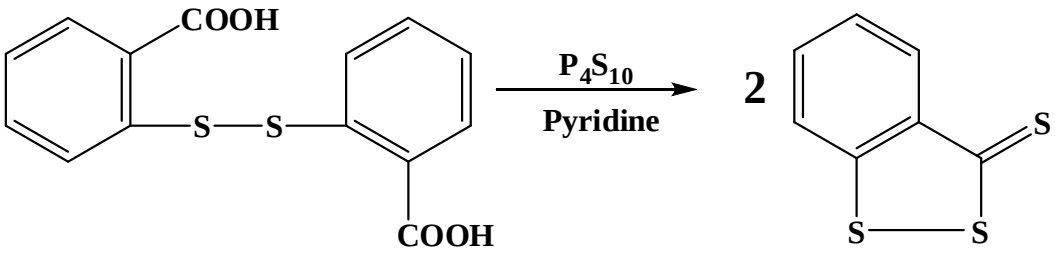
Interaction (I)



Interaction (II)

II. of acids:

With 2, 2'-dibenzoïque acid sulfonation based on the proposed method of Klinsberg et Schreiber **[56]**



Interaction (III)

X. Its general characteristics:

1,2-dithiole-3-thione they are colored crystalline compounds containing aromatic substituent's that have a high melting point, and their color is orange to red and the aliphatic substitutes are yellow. And they are oils if they contain alkyl compounds with a large partial weight.

1,2-dithiole-3-thione is characterized by its thermal stability, which allows it to be distilled without disintegration under normal atmospheric pressure, and it does not oxidize in air. It is soluble in aromatic hydrocarbons and in sulfuric acid, meaning that it is soluble in highly polar organic solvents **[57,58].**

XI. Spectral properties:

D. VIS/UV Spectrum Visible and Ultraviolet:

1,2-dithiole-3-thione compounds are absorbed in the visible and in the ultraviolet, and their strong bands appear at: 225,250,335,417 (nm) **[57], [58].**

E. Infrared (IR) spectrum:

In the infrared spectrum, the absorption range of the basic bonds can be determined **([57], [58].** C=S appears between 1200 -1050 cm^{-1}.

S-S appears in the range 540-500 cm^{-1} and is weak. Also, the electronic displacement in the 1,2-dithiole-3-one compound was studied based on the (IR) spectrum of the carbonyl group absorption and the dipole moment shown in the following diagram: **[59]**

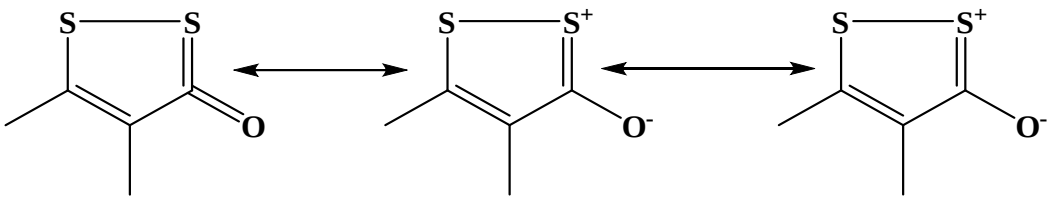
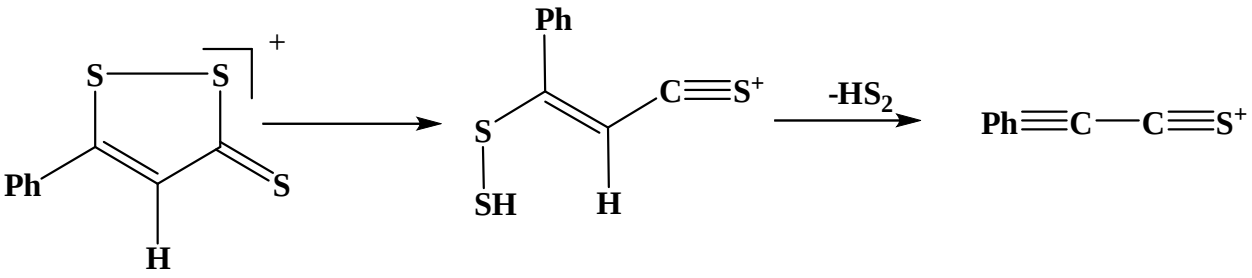


Chart (1)

F. Mass Spectrometry:

The mass spectroscopic information is given as structural guides for the synthesis of 1,2-dithiole-3-thione and 1,2-dithiole-3-one compounds. It turned out that in the mass spectrum of the mono-substituted compounds in the fifth position, strong peaks corresponding to M-HS2 appear which could be the result of the following dissociation **[60]**:



M/Z = 210 **M/Z = 210** **M/Z = 210**

Scheme (2)

But when studying the mass spectra of compounds bearing the following functional groups: -NH2-CONH, -COOC2H5, -CN as substitutions in which peaks corresponding to 2M-HS, but the peaks corresponding to M-S2 and M-HS appeared **[59]**.

G. Nuclear magnetic resonance spectroscopy (RNM-1H):

The proton nuclear magnetic resonance (RNM-1H) spectrum of 1,2-dithiole-3-thione and 1,2-dithiole-3-one does not include any information about the para-aromatic property of the 1,2-dithiole system and that the chemical displacement of the methyl group protons The substituent in the 1,2-dithiole system is identical to the chemical displacement of the substituted methyl group in the aromatic system. Therefore, the non-aromatization of these compounds has not been demonstrated by NMR spectroscopy **[61].** As for the (RNM-1H) spectrum of the two compounds 4-phényl-1,2-dithiole-3-thione and dithiole-3-thione 5-phényl-1,2- the aromaticity of the 1,2-dithiole ring appears. The chemical displacement of the protons connected to the 1,2-dithiole ring appears in the region (ppm) 6.86 to 8.27 so that the chemical displacement of the proton in position 5 is greater than the chemical displacement in position 4 **[62].**

Dorange and F.Tonnard and F.Venien calculated the diamagnetic and paramagnetic values of the various 1,2-dithiole-3-thione and 1,2-dithiole-3-one chains and compared them with the chemical displacements of these compounds. When analyzing the obtained results, they found that the substituted phenyl group at position 5 is at the same level with the dithiole nucleus and that the 1,2-dithiole nucleus is an electrophilic group **[63].**

XII. Analytical study:

The 1,2-dithiole-3-thione compounds were identified and separated by multiple chromatographic methods. Sixteen compounds of the 1,2-dithiole-3-thione chains were discovered by HPLC technique. **[64]**

This last technique was used to verify the compound Oltipraz and determine its concentration in blood serum and urine **[65].**

XIII. Transportability:

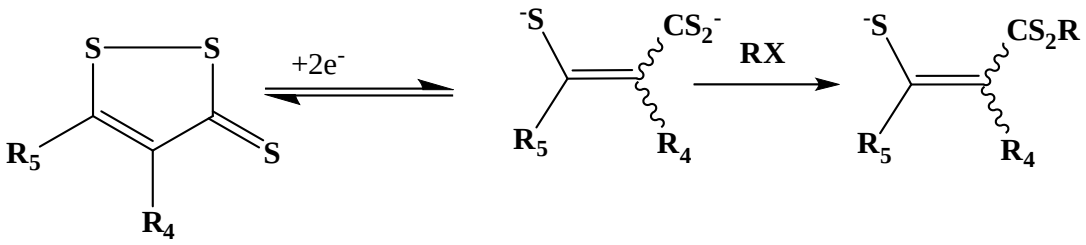
The researcher H.F. Eicke and his colleagues in 1968 measured the conductivity of mixed solutions of thiono compounds and their corresponding oxygen compounds, and found that the conductivity of all solutions was 10^{-14} ohm, depending on the charge transfer of the solute molecule **[67].**

In 1969, the same team measured the conductivity of 1,2-dithiole-3-thione compounds in the liquid and solid state. And they found that the conductivity ranged between 10^{-14}_ 10^{-15} ohm **[68].**

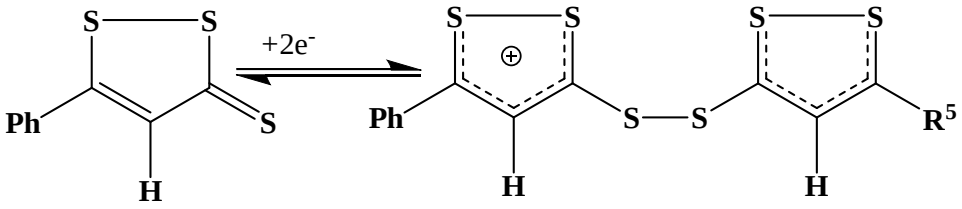
XIV. Electrochemical properties:

Most of the electrochemical studies of 1,2-dithiole-3-thione compounds have been conducted on compounds substituted in position 4 or 5 or both with electronically

inactive groups (aryl...alkyl) and the results showed that these compounds have an oxidation that leads to a reversible chemical reaction. The clarified dication is formed as follows **[69]**:

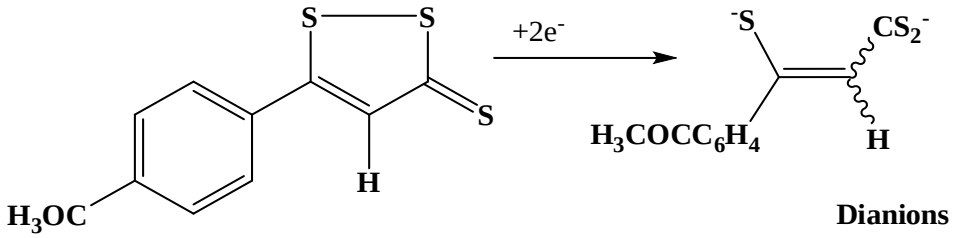


Interaction (IV)



Interaction (V)

Also, returning 1,2-dithiole-3-thione to the two electrons leads to a dianion:



Interaction (VI)

XV. Effectiveness of dithiole-thione:

1,2-dithiole-3-thione is a pentagonal ring (three carbon atoms and two sulfur atoms), the distance between the two atoms S(1) and S(2) forms a bond length of 2.047°A close to the length of 2.08°A suggested by Abrahams **[70]** also notes for the lengths C(3)-S(2) (1.74°A) and C(5)-S(1) (1.73°A) that they are less than the simple bond CS(1.83°A) . This is what distinguishes and confirms that the ring is aromatic and favors resonance of various charges as follows:

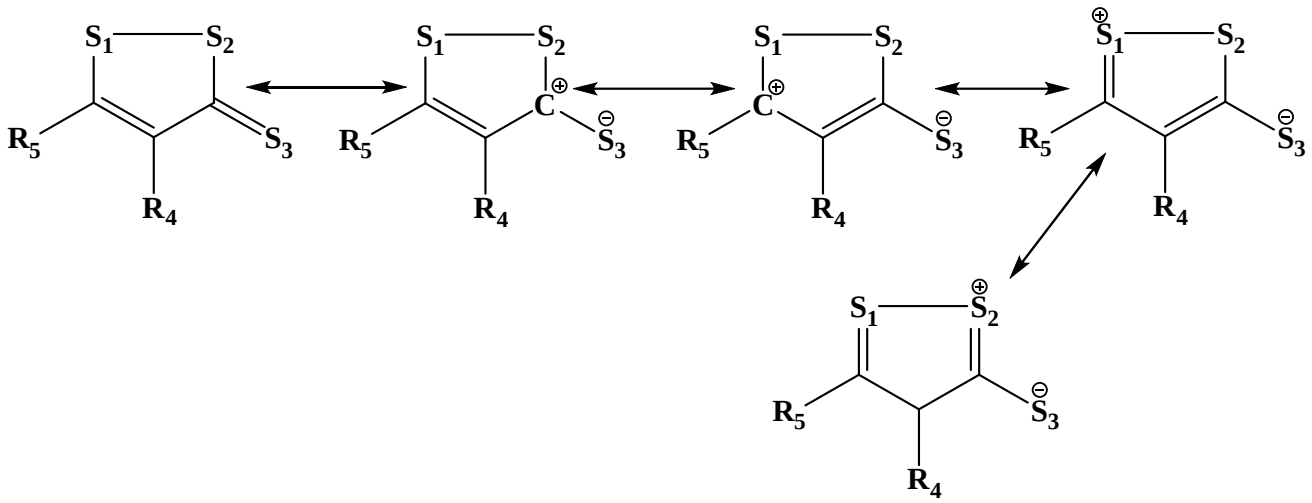
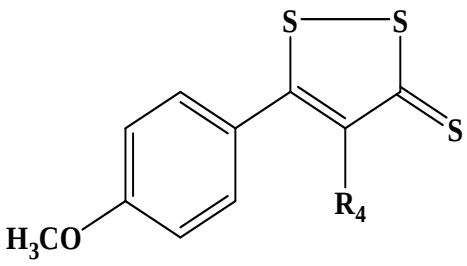


Chart (3)

Based on this resonance, the areas that favor the adhesion to the metal are revealed **[70]**.

XVI. Dithiole-thione compounds and their derivatives present in the study:



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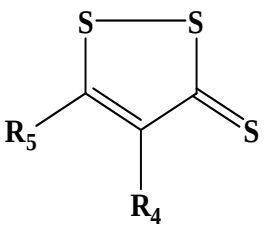

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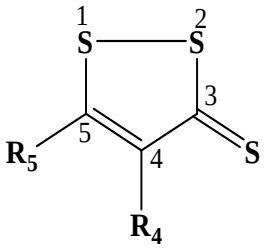

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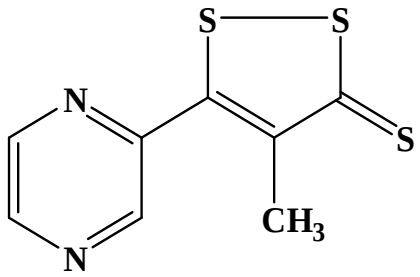

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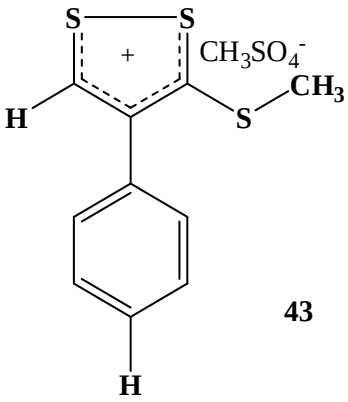

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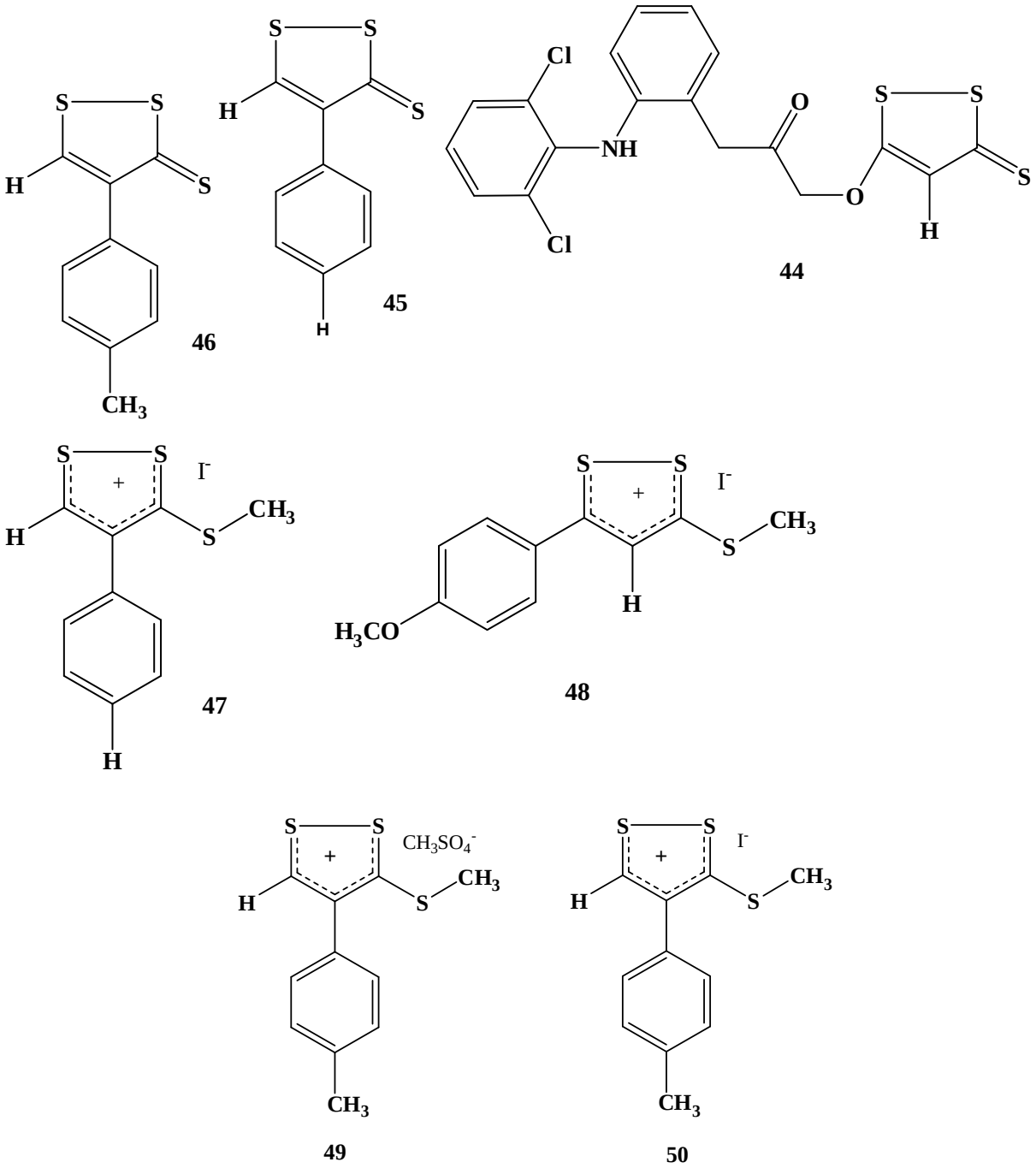


Chart (4)

XVII. Its uses:

C. Scientifically:

These compounds have been used in several electrochemical studies, the aim of which is:

- Determination of the electronic action of some 1,2-dithiole-3-thione substitutions by metric cyclic voltaic **[71]**.
- In the electrodé position of aniline in an acidic medium (H2O/CH3CN) **[72].**

- Determining the correlation relationship (QSAR) between one of the properties of the compound, which is LogP, and the structure of the compound to determine its effectiveness, and it was found that 1,2-dithiole-3-thione is very effective **[73].**

D. industrially:

Because of its stability against oxidation in air, it is used:

- As antioxidants, they are added to fuels and engine lubricants and to prevent the influence of ultraviolet rays on rubber and plastic [74], [75].
- Inhibitors of polymerization in the reactions of free radicals [76].
- As inhibitors of carbon dioxide corrosion in petroleum installations [77], [78].
- It was tested as a material for making an electrode in batteries [79].
- It is also a protective agent for the iron surface from corrosion by hydrochloric acid.
- Plant insecticides and fungicides [80].

E. medically:

These compounds have several medicinal benefits that have been known since their appearance, and we have limited some of them in this following table:

Table 1: Medicinal benefits of some 1,2-dithiole-3-thione derivatives

compound	Medicinal properties	Ref
Oltipraz **42**	* Activity against the tropical worm disease, Bilharziosis, which is called Al-Baqiri disease, a disease caused by the Schistosoma masoni worm when it enters the human body, causing bloody urine. * Passivation (inactivation) of toxic compounds, especially cancerous ones, such as skin and lung cancer. * Contributes to an increase in hepatic glutathione, and to a reduction in hepatic RNA damage. * Slowing down the processes of free radicals. * The effectiveness of this compound in increasing and strengthening the body's immunity and inhibiting the activity of the virus that causes HIV, by inhibiting reverse transcription.	**[82][81]** **[84] [83]** **[85]** **[86]** **[87]** **[82]** **[88]**
Sulfarlem **Anétholetrithione** **41**	* As a stimulant for the secretion of bile. * Activates the salivary glands, which helped treat dry mouth disease. * It is used against diseases of the thyroid gland. * slow down the processes of free radicals.	**[81] [89]** **[91] [90]** **[92]** **[94] [93]** **[95]**
Dithiolethione **39**	* Protection of nerve cells. * Protection from microbes * Loading (inactivation) toxic compounds, especially cancerous ones.	**[96]** **[97]** **[98]**
S-Diclofenac **44**	* Anti-inflammatory and aches.	**[99]**

- **Contributing to the study and preparation of 1,2-dithiole-3-thione and its derivatives from salts:**

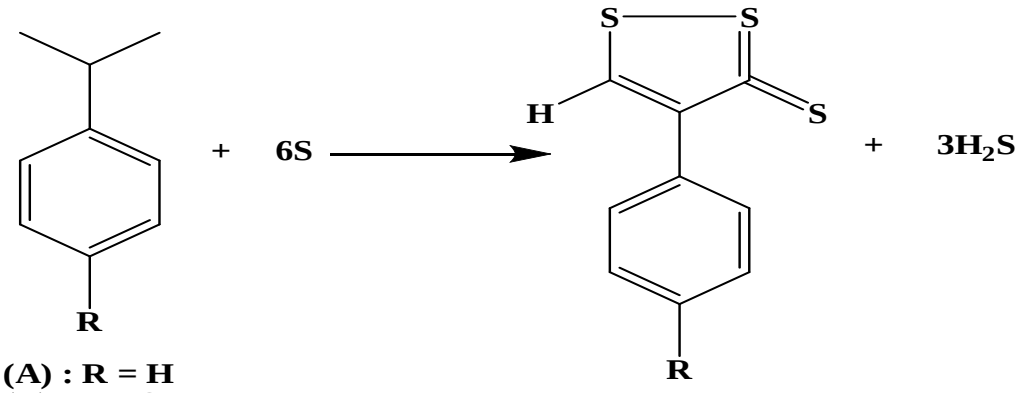
The prepared compounds are listed in the following table:

Table 2: Name and symbol of the prepared compounds

Number	The name of the compounds is in Latin	code
45	4-phényl-1,2- dithiole-3-thione	**(A)**
46	4-p-tolyl-1,2-dithiole-3-thione	**(B)**
41	5- p- méthoxyphényl -1,2dithiole -3-thione	**(C)**
43	3-méthylthio4-phényl-1,2dithiolylium Centre ion ($CH_3SO_4^-$)	**(1A)**
47	3-méthylthio4-phényl-1,2dithiolylium Centre ion(I^-)	**(2A**
49	3-méthylthio4-p .tolyl-1,2dithiolylium Centre ion ($CH_3SO_4^-$)	**(1B)**
50	3-méthylthio4-p .tolyl-1,2dithiolylium Centre ion(I^-)	**(2B)**
48	3-méthylthio -5p méthoxyphényl-1,2dithiolylium Centre ion(I^-)	**(1C)**

C. Contribution to the preparation of 1,2-dithiole-3-thione compounds:

A. Working principle: These compounds were prepared based on the Filed method [55] according to the following equation:



(A) : R = H
(B): R = CH_3

Interaction (VII)

D. working method:

Compounds (A) and (B) were prepared from sulfur of cumène or cymène by applying (140 ml) of the first or (160 ml) of the second, respectively. Add to it (50g) of sulfur and an amount of catalyst di-ortho-tolylguanidine (0.4g) in a three-necked 500 ml spherical flask equipped with a reversible condenser and thermostat placed on a heating device. The temperature was fixed at 156°C for a full week for compound (A) and 186°C for 21 h for compound (B). They are accredited in tracking the progress of the interaction with the following detection methods:

- Thin layer chromatography (CCM) with Toluène moving medium
- Note the continuity of the launch of H2S

After the experiment ends with the release of H2S, it is placed in a becher to cool for an hour and a half, and then we filter it under vacuum and leave it to dry in the air. And wash it with: (50 ml) (hexane + Toluene) in proportions 3: 1

D. Diagnostics of the prepared compounds:

a. Compound (A):

- Red crystals (Toluene)
- Melting point 120°C
- Yield %75.31
- RMN-IH Spectrum: ppm/TMS) CD Cl3, [62].
- (S,1H) 8.46 ; (m,5H) 7.56

b. Compound (B):

- Sparkling brown crystals (Toluène)
- Melting point 130°C
- Yield 51.80%
- Infrared spectrum **[61, 99]** See Table 3.

c. Compound (C):

This compound has a common name, and it is sulferlam because it can be recovered from the drug sulferlam, which is a type of polymer-coated tablets (chemical compound) with a yellow-orange color (a box of 60 tablets) each tablet contains 25 mg **[100]**.

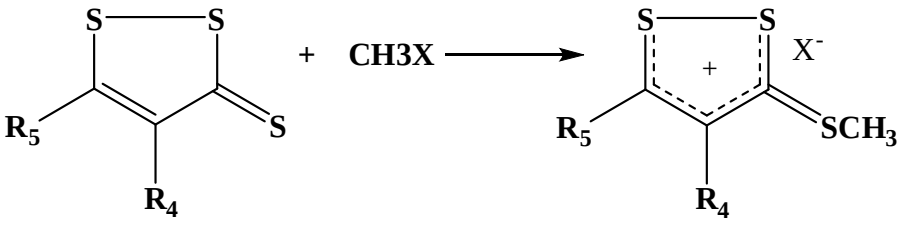
We dissolve 30 tablets in 50 ml of Toluene after total dissolution of the compound. Filter the solution, then wash 50 ml of distilled water 3 times. After evaporation of Toluene and recrystallization in hexane, we get red-orange needle crystals.

- red-orange needle crystals (hexane)
- return 66%
- Melting point 109 °C **[84] [101]**
- Retention coefficient Rf = 0.64
- Infrared (IR): [85] [102] See Table 3.
- UV-Visible Spectrum:
- The aromatic ring of benzene appeared between 280-200 nm, λ max = 276.9 nm
- The thionyl group C=S appeared between 250-350 nm, which indicates the n → π transition.

E. Contributing to the preparation of the 3-methylthio-1,2dithiol iumcation:

c) Working principle:

This work was done based on the Botcher method **[99]** according to the following reaction:



(1A):R_4 = C_6H_4, R_5 = H, X = $CH_3SO_4^-$
(1B):R_4 = $CH_3C_6H_4$, R_5 = H, X = I^-
(1C): R_4 = H, R_5 = $CH_3OC_6H_5$, X = I^-

(2A):R_4 = $C6H_5$, R_5 = H, X = I^-
(2B): R_4 = $CH_3C_6H_4$, R_5 = H, X = $CH_3SO_4^-$

Interaction (VIII)

d) The method of work:

Compounds (1A), (2A), (1B), (2B) and (1C) were prepared by alkylation of compounds (A), (B) and (C) respectively by dissolving them in (50ml) of Toluene in 250 ml. ml is equipped with a reversible cooler and has a magnetic rod placed on a device for shaking and heating by means of a water bath. After dissolving the entire compound, we add an amount of iodure de methyl or (10ml) sulfate de methyl at a temperature of 40 ° C and the experiment remains for a whole day. We tracked it by changing the color of the medium to red and the appearance of precipitated salt. Then we filter it and let it air dry.

e) Prepared cations:

i) Compound (1A) conjugate ion - CH3SO4:

- yellow crystals (Toluene)
- Melting Point 178°C
- The yield is good 75%

ii) Compound (2A) conjugate ion I-:

- yellow crystals (Toluene)
- Melting Point 160°C
- Good yield %92

iii) Compound (1B) conjugate ion - CH3SO4:

- yellow crystals (Toluene)
- Melting Point 180°C
- The return is good 80%.

iv) Compound (2B) conjugate ion I-:

- yellow crystals (Toluene)
- Melting Point 180°C
- The yield is good, 87%

v) Compound (1C) the conjugate ion I-:

- Yellow radioactive crystals (Toluene)
- Melting point 155°C [102]
- return 51%
- RMN-1H : 3.72 (S, 3H, OMe); 6.70(d, 2H, J=10Hz) [101] 7.4 (d, 2H, J=10Hz) ; 7.76 (S, 1H)

Conclusion:

In this chapter, we got acquainted with the approximations of the solutions of the Schrödinger equation and the various methods of molecular modeling. We also touched on dithiolethione compounds and their derivatives from the substituted salts in position 4 and 5 prepared by the professor [103].

Chapter N° 2:

Materials and methods

Introduction:

In this chapter, we will list materials and tools used and then describe the techniques (RX, IR) that will bring us to the overall formula and crystal structure.

VI. Molecule Utilize:

The molecules we used in this research are:

* 4-p-tolyl-1, 2-dithiol-3-thione is a derivative of the Dithiolethione family (N°46 cod B).
* The second molecule is a salt of the added Dithiolethione derivative.

VII. Spectroscopic IR analysis:

Infrared spectroscopy (IR) is one of the simplest and least expensive spectroscopy methods for studying materials. This technique allows the determination of the chemical bonds involved in the molecular structures of organic-non-crystalline and non-crystalline materials [1], without affecting their properties.

IR spectra were record between 4000 and 400 cm^{-1} on an **Agilent technology Cary 630 FTIR IR** spectrometer of El-Oued University. Samples were putted on without any protocol of preparation.

VIII. X-ray diffraction analysis:

Since ROTTINGEN discovered X-rays in 1895, this region of the electromagnetic spectrum has become a source of enrichment and contribution to the knowledge of atomic structure. Work in this field has developed in a large and large way until the use of X-rays has increased in more than one field. X-rays are electromagnetic waves with a wavelength equal to the distance between atoms in crystals. Atoms play the role of a scattering center for X-rays [2].

c. X-ray diffraction condition:

The purpose of using the X-ray diffraction technique is to study the exact structure of the material and know its crystal structure, where X-ray diffraction is the most effective way to determine the structure of crystallized bodies. The material is a polycrystalline particle consisting of a large number of grains, each of which is called a single crystal. It is a regular stacking of atoms. This stacking can be described by a set of crystal levels defined by lattice spaces ($d_{hkl)}$ [3].

d. Device used:

X-ray powder diffractiometre using CuKa radiation. The theoretical X-ray diffraction patterns were calculated using the Mercury program.

Figure 3: X-ray machine at Hama Lakhdar El-Oued University

3. Identification of the phases by logical High score:

For phase identification we use the Crystallographic data, file of a similar compound we found in research of BY Yu WANG and H. C. LIN in 1985, with a geranial formula **$C_{10}H_9S_3O$** AND Cif N° 1135779. We downloaded the Cif file (1135779) and open it in MERCERY. We click in buttom pattern to calculate the theoretical diffractograme. This one will be compared with the experimental one to confirm the structure identification.

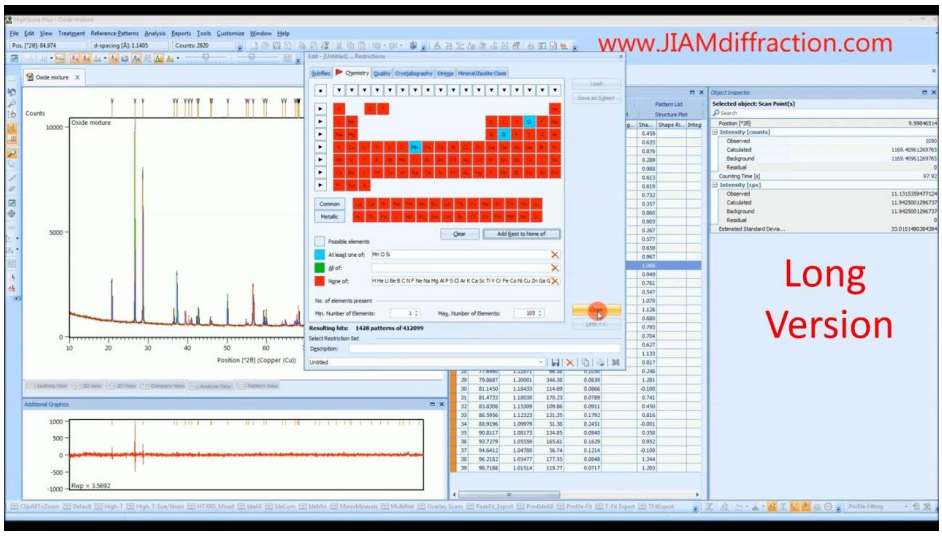


Figure 4: High score plus environnent

4. Indexation du diagram:

The diagram indexation when done With fullprof softword to calculate the: a, b, c, α, β, y parameters for the phase identification.

Figure 5: Full prof environment

IX. Ordinate:

We used computer for this job:

The twelfth laptop by the **HP** brand, **Windows 7** edition integral copyright **2009 Microsoft corporation** all rights reserved, and the system type is **64 bit** operating system and the processor **Intel ® core ™ i5 CPU M520 2.40GHz .**

I have used software with large memory in this computer such as **GAUSSIAN** and **HIGH SCORE** software.

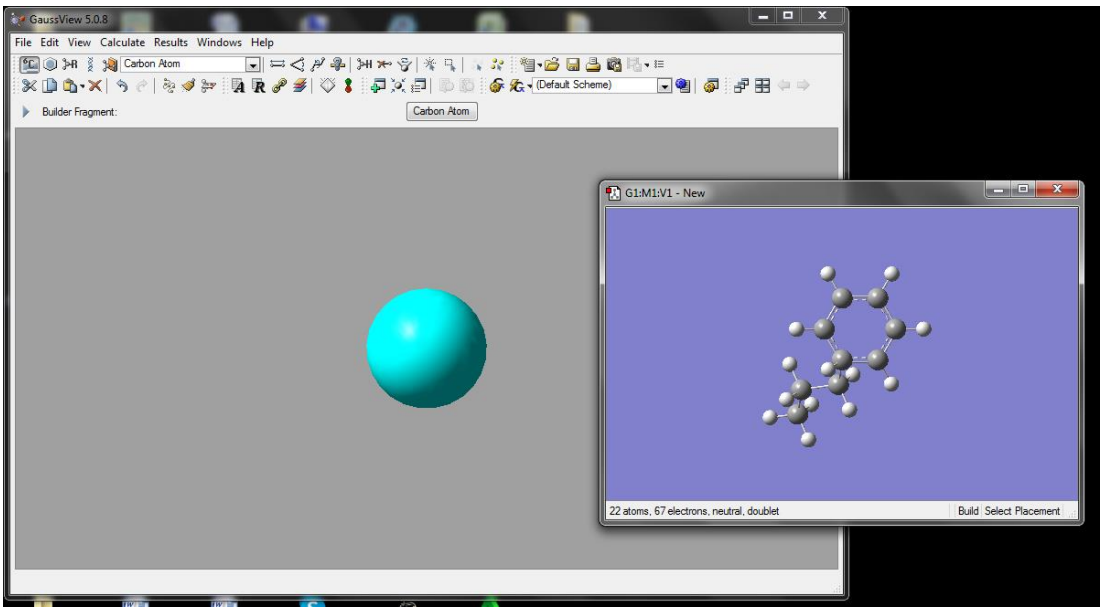


Figure 6: Gaussian (Gauss View) environment

III – 2- GAUSSIAN software:

Gauss View is a graphical user interface designed to help you prepare input for submission to Gaussian and to examine graphically the output that Gaussian produces.

Gauss View is not integrated with the computational module of Gaussian, but rather is a front-end/back-end processor to aid in the use of Gaussian. GaussView provides three main benefits to Gaussian users.

First, through its advanced visualization facility, GaussView allows you to rapidly sketch in even very large molecules, then rotate, translate and zoom in on these molecules through simple mouse operations. It can also import standard molecule file formats such as PDB files.

Secondly, Gauss View makes it easy to set up many types of Gaussian calculations. It makes preparing complex input easy for both routine job types and advanced methods like ONIOM, STQN transition structure optimizations (i.e., **Opt=QST2/QST3**), CASSCF calculations, periodic boundary conditions (PBC) calculations, and many more. You can also use GaussView to launch jobs as well if Gaussian is installed on the same computer. Lastly, you can define default and named calculation templates—known as schemes—to speed up the job setup process.

Finally, Gauss View lets you examine the results of Gaussian calculations using a variety of graphical techniques. Gaussian results that can be viewed graphically include the following:

- Optimized molecular structures.
- Molecular orbitals.
- Electron density surfaces from any computed density.
- Electrostatic potential surfaces.
- Surfaces for magnetic properties.
- Surfaces may also be viewed as contours.
- Atomic charges and dipole moments.
- Animation of the normal modes corresponding to vibrational frequencies.
- IR, Raman, NMR, VCD and other spectra.
- Molecular stereochemistry information.

- Animation of geometry optimizations, IRC reaction path following, potential energy surface scans, and ADMP and BOMD trajectories. Two variable scans can also be displayed as 3D plots.
- Plots of the total energy and other data from the same job types as in the previous item.

This help system provides a reference to all of Gauss View's features. Each of the program's features is documented in detail. Items are arranged into several groups based on their general purpose. Within a group, items are arranged in a logical progression, beginning with the simplest, most widely used ones and then progressing to more complex and unusual capabilities.

Chapter N° 3:

RESULT AND DISCUS

In this chapter will be described modeling, IR spectra and X-Rays diffraction identification of molecules studied, were we began by superposition of the molecule and its salt in the goal to detect what pics modified between the two molecules. In a second time will be dechifred the spetra of 4-p-tolyl-1, 2-dithiol-3-thione molecule to propose a formula. After will be calculated the tow IR spectrum of the molecule and its salt to unsure from functional groupements detected in the experimental investigation.

I. Molecular Structure Optimization of the Dithiolethione molecule In GAUSSIAUN software:

The molecule before optimization:

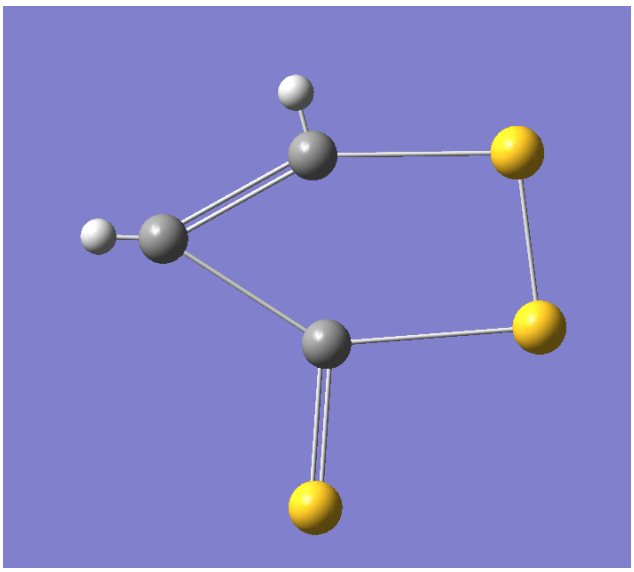


Figure7: The Dithiolethione molecule before optimization

The molecule after optimization:

After drawing the particle we go to the taskbar and we click on the broom icon shown in the figure below to organize the shape of the molecule and then choose Calculate

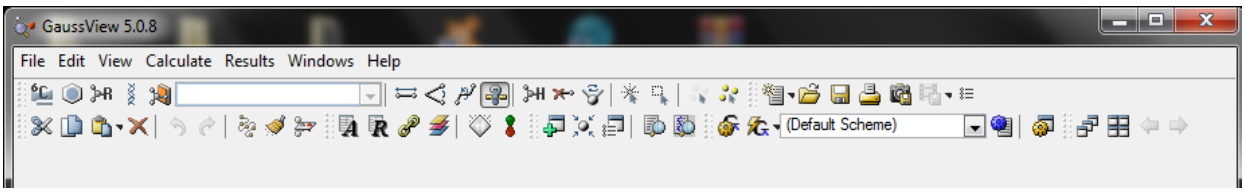


Figure 8: logistical GAUSSIAN commands

After clicking on **Calculate**, a list of different calculation methods appears, so we choose the first option Gaussian Calculation setup a new dialog box appears, as shown in the picture below:

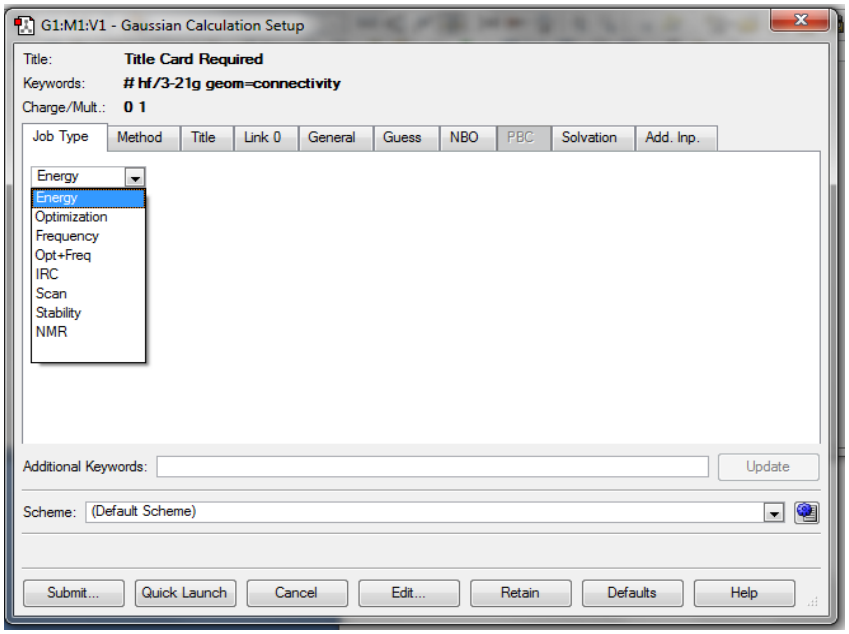


Figure 9: Optimization methods in logical GAUSSIAN

We go to the icon **Energy** and choose **Optimization** to improve the structure of the molecule or choose **Frequency** to improve and calculate properties such as bonds and angles...

Then we go to the method icon and choose the method we want, we chose the DFT method, then we click on Submit..

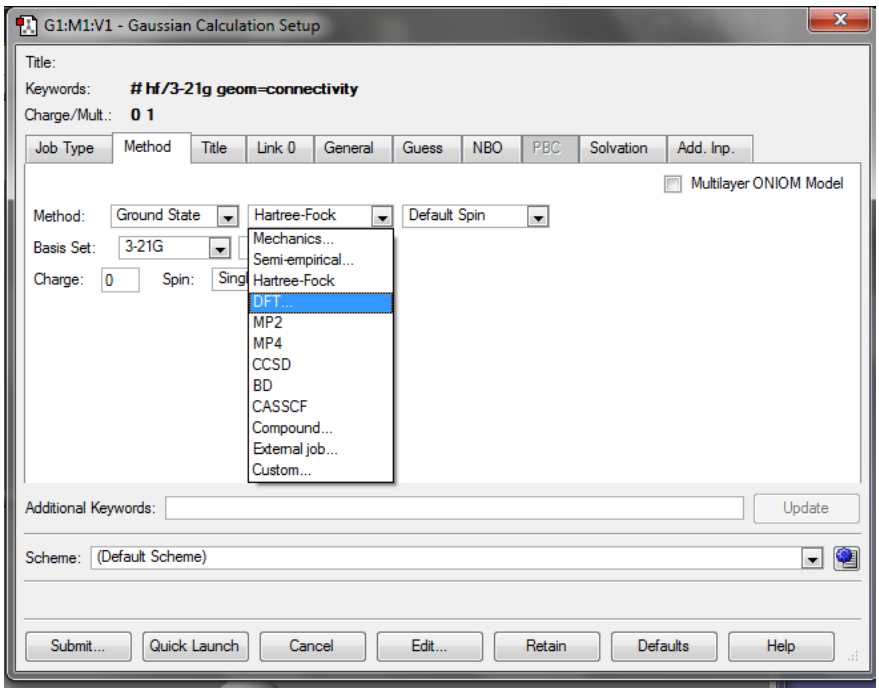


Figure 10: Various molecular modeling methods in Gaussian

After following the previous steps, we save the work on the computer after giving it any suggested name

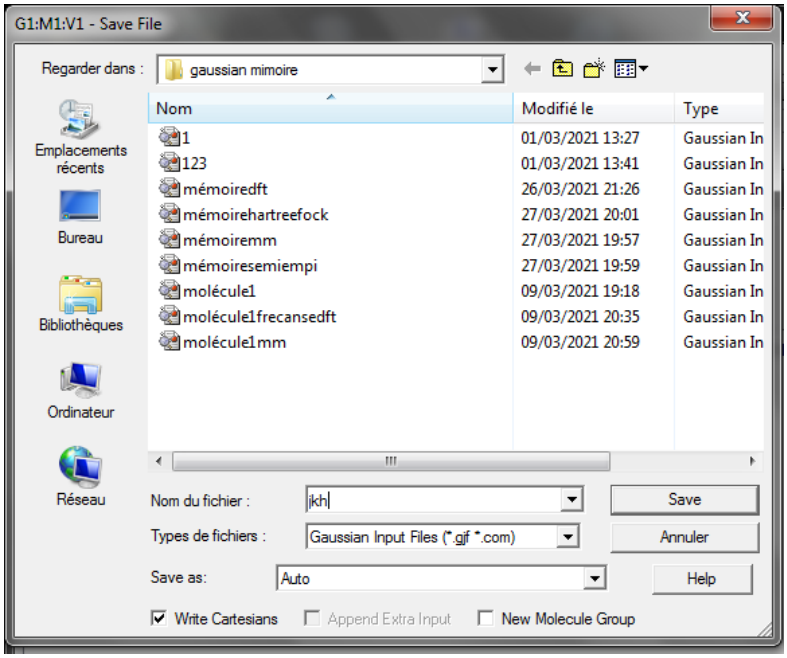


Figure 11: Save work on the computer

After saving, click on the **Save** icon, a dialog box will appear, and we will press **OK** The Logical will start calculating and optimizing

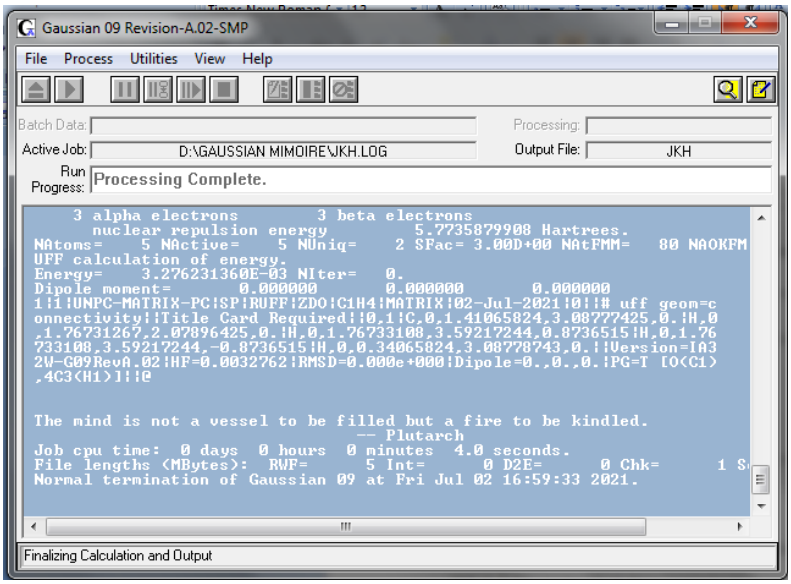


Figure 12: Beginning of improvement

After the calculation is completed, we will click on OK, and we will get the result shown in the figure:

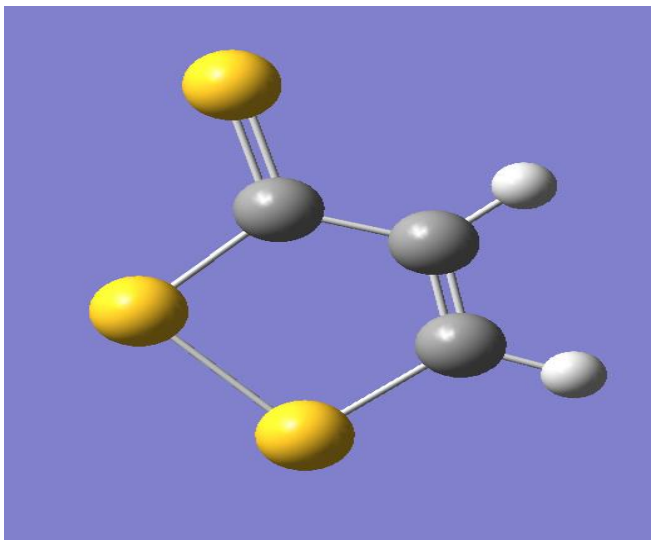


Figure 13: The Dithiolethione molecule after optimization

After following all the previous steps, we get the following results:

Title Card Required		
File Name	molécule1frecansedft	
File Type	.chk	
Calculation Type	FREQ	
Calculation Method	UB3LYP	
Basis Set	3-21G	
Charge	0	
Spin	Doublet	
Total Energy	-1303.72784453	a.u.
RMS Gradient Norm	0.18176759	a.u.
Imaginary Freq		
Dipole Moment	2.6963	Debye
Point Group		

Figure14: Card required

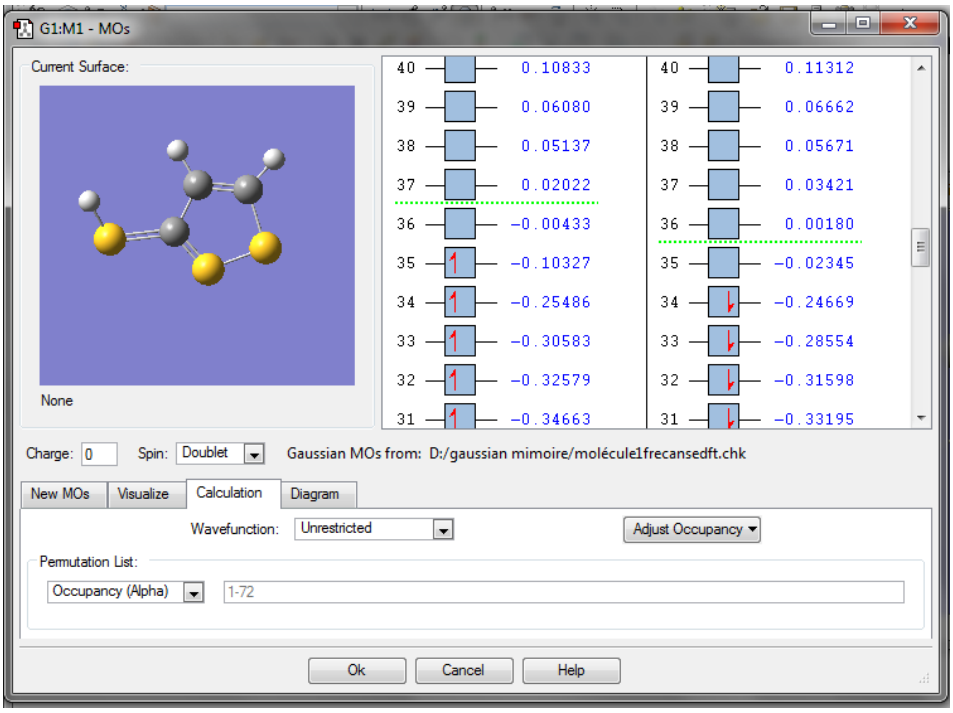


Figure15: HOMO and LUMO orbital

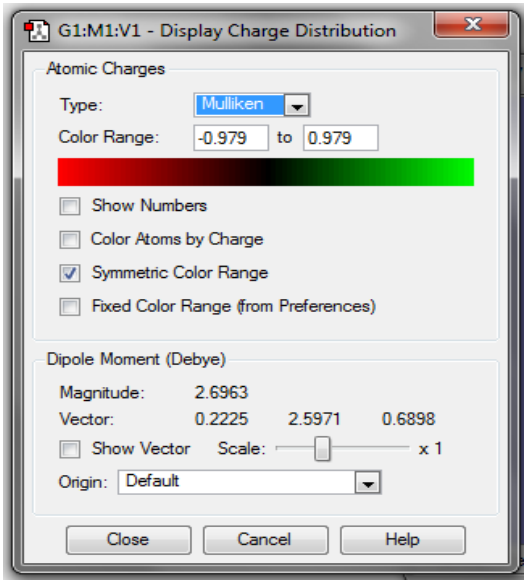


Figure 16: Display charge the Dithiolethione

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.394369	1.262383	-0.009580
2	6	0	0.022521	1.383117	-0.023940
3	6	0	-0.617739	0.102117	-0.015646
4	16	0	1.869957	-0.340558	0.013706
5	1	0	2.104157	2.087233	-0.012611
6	1	0	-0.528531	2.325147	-0.039982
7	16	0	0.302273	-0.922479	0.005376
8	16	0	-2.385991	-0.101471	-0.031061
9	1	0	-2.950379	0.934043	0.539268

II. Molecular Structure Optimization of the 4-p-tolyl-1,2-dithiol-3-thione molecule:

By following all the steps involved in optimizing the structure

The molecule before optimization:

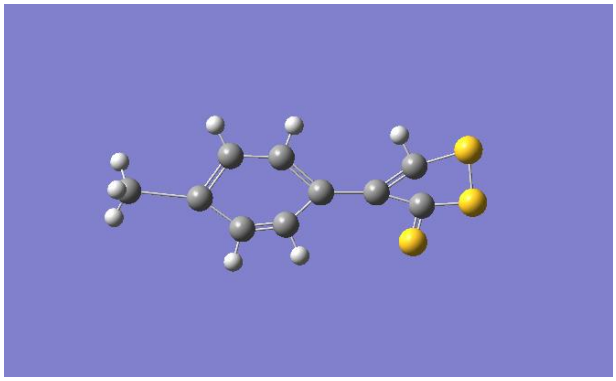


Figure 17: the 4-p-tolyl-1,2-dithiol-3-thione molecule before optimization

The molecule after optimization:

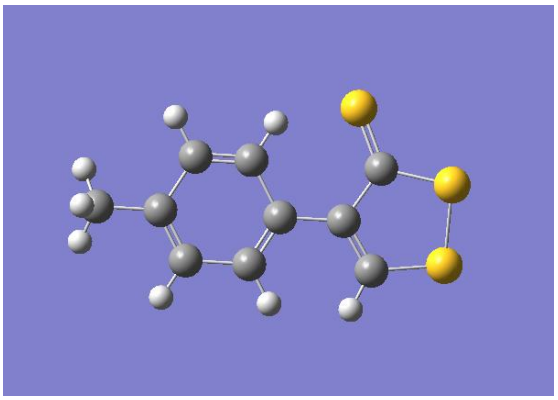


Figure 18: the 4-p-tolyl-1,2-dithiol-3-thione molecule after optimization

After following all the previous steps, we get the following results:

Title Card Required		
File Name	mémoiredft	
File Type	.chk	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	3-21G	
Charge	0	
Spin	Singlet	
Total Energy	-1572.33294639	a.u.
RMS Gradient Norm	0.03397699	a.u.
Imaginary Freq		
Dipole Moment	3.2863	Debye
Point Group		

Figure 19: Card required the molecule1

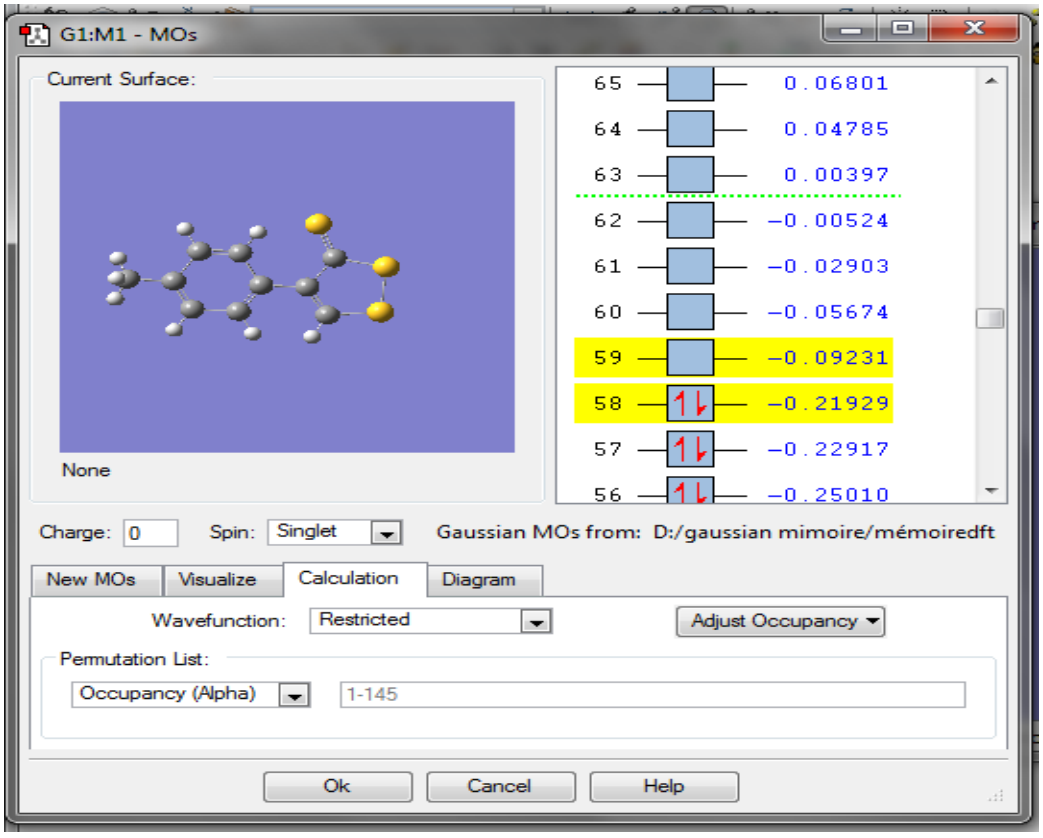


Figure 20: HOMO and LUMO the molecule1

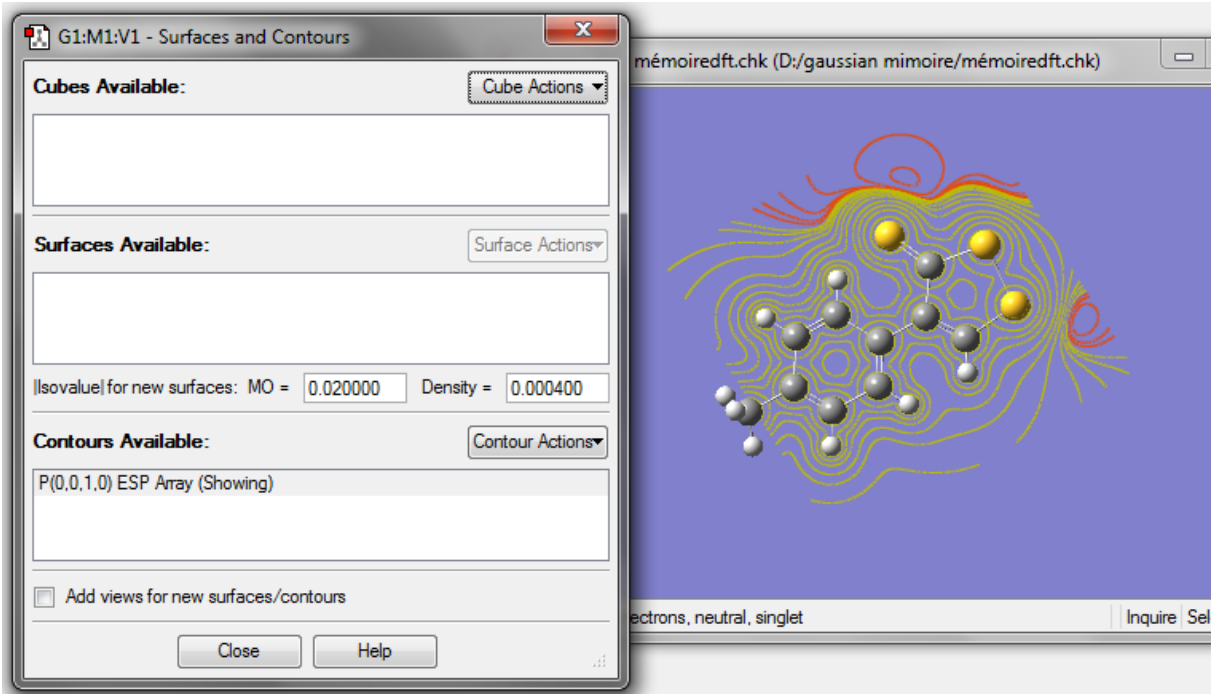


Figure 21: Surfaces and Contours the molecule1

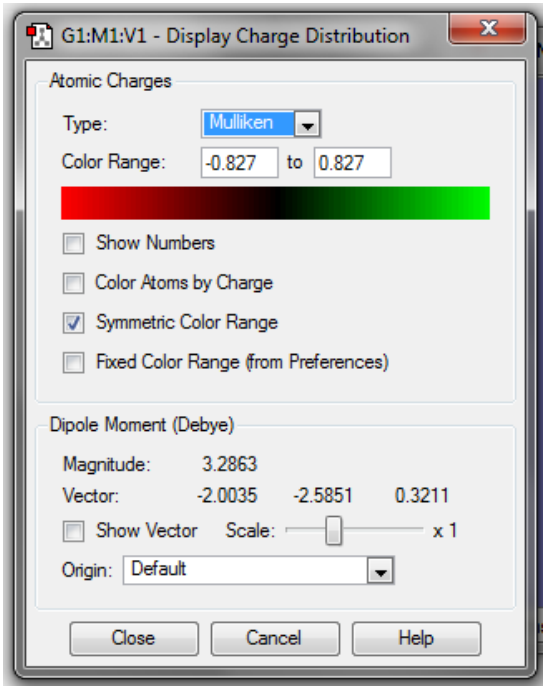


Figure 22: Display Charge Distribution the molecule1

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-5.295637	-0.087350	0.009867
2	6	0	-3.758308	-0.177891	0.014554
3	6	0	-2.911223	1.108207	0.013851
4	6	0	-3.150893	-1.389333	0.019299
5	6	0	-1.613564	-1.479874	0.023981
6	6	0	-1.558374	1.028531	0.017974
7	6	0	-0.868129	-0.348108	0.023361
8	6	0	0.669200	-0.438648	0.028044
9	6	0	1.576043	0.817883	0.027998
10	6	0	1.335676	-1.637164	0.033289
11	16	0	3.100087	-1.509360	-0.205213
12	16	0	3.288416	0.428403	0.268394
13	16	0	1.036696	2.276508	-0.159425
14	1	0	-5.598849	0.804516	-0.497615
15	1	0	-5.701590	-0.939759	-0.493622
16	1	0	-5.654615	-0.063899	1.017579
17	1	0	-3.390809	2.064702	0.010106
18	1	0	-0.969815	1.922118	0.017485
19	1	0	-3.739452	-2.282920	0.019791
20	1	0	-1.133978	-2.436369	0.027724
21	1	0	0.837178	-2.574721	0.165146

III. Molecular Structure Optimization of the 3-(iodothio)-4-phenyl-3H-1,2-dithiol-3-ylium molecule (sel):

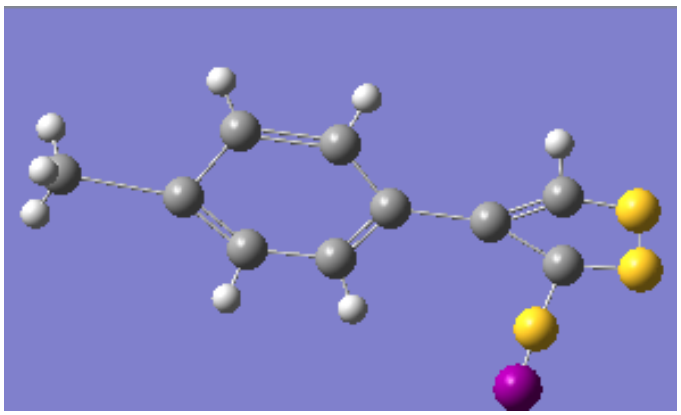


Figure 23: the 3-(iodothio)-4-phenyl-3H-1,2-dithiol-3-ylium molecule (sel) before optimization

The molecule after optimization:

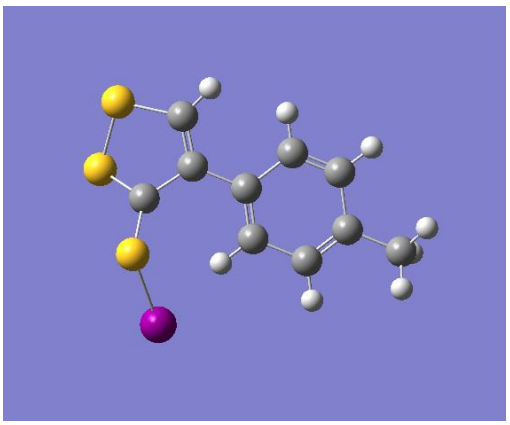


Figure 24: the 3-(iodothio)-4-phenyl-3H-1,2-dithiol-3-ylium molecule (sel) after optimization

After following all the previous steps, we get the following results:

Title Card Required		
File Name	seldithiolthionedft	
File Type	.chk	
Calculation Type	FREQ	
Calculation Method	RB3LYP	
Basis Set	3-21G	
Charge	1	
Spin	Singlet	
Total Energy	-8462.58458129	a.u.
RMS Gradient Norm	0.03247734	a.u.
Imaginary Freq		
Dipole Moment	5.5396	Debye
Point Group		

Figure 25: Card required the molecule2

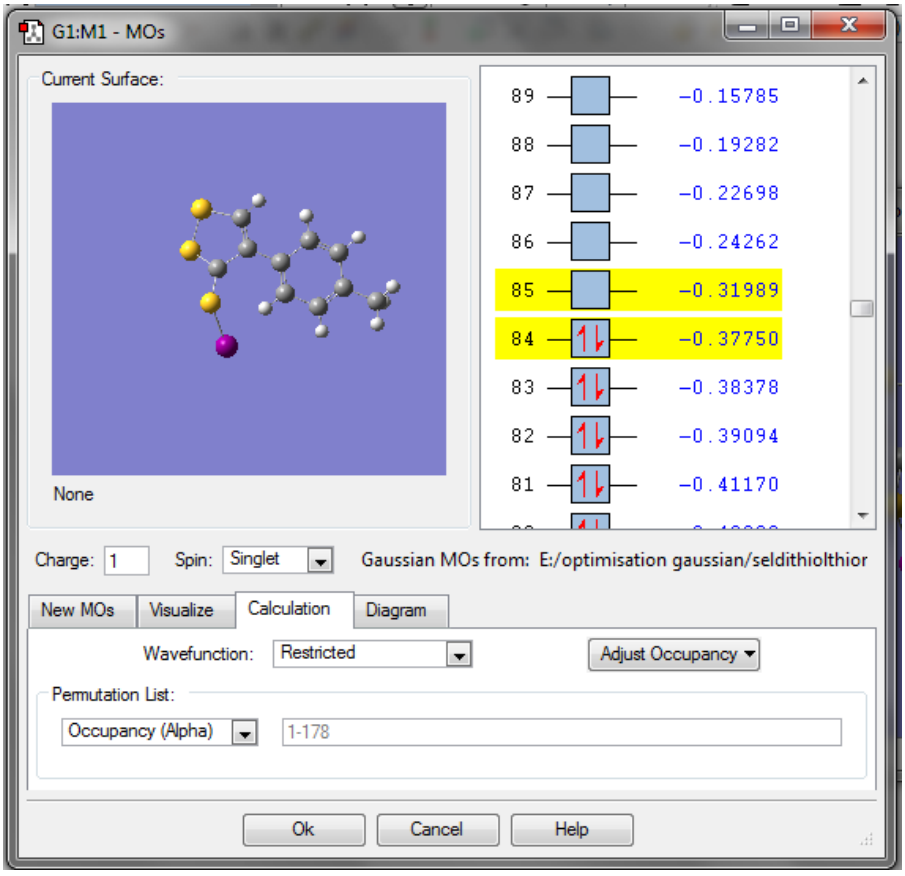


Figure 26: HOMO and LUMO the molecule2

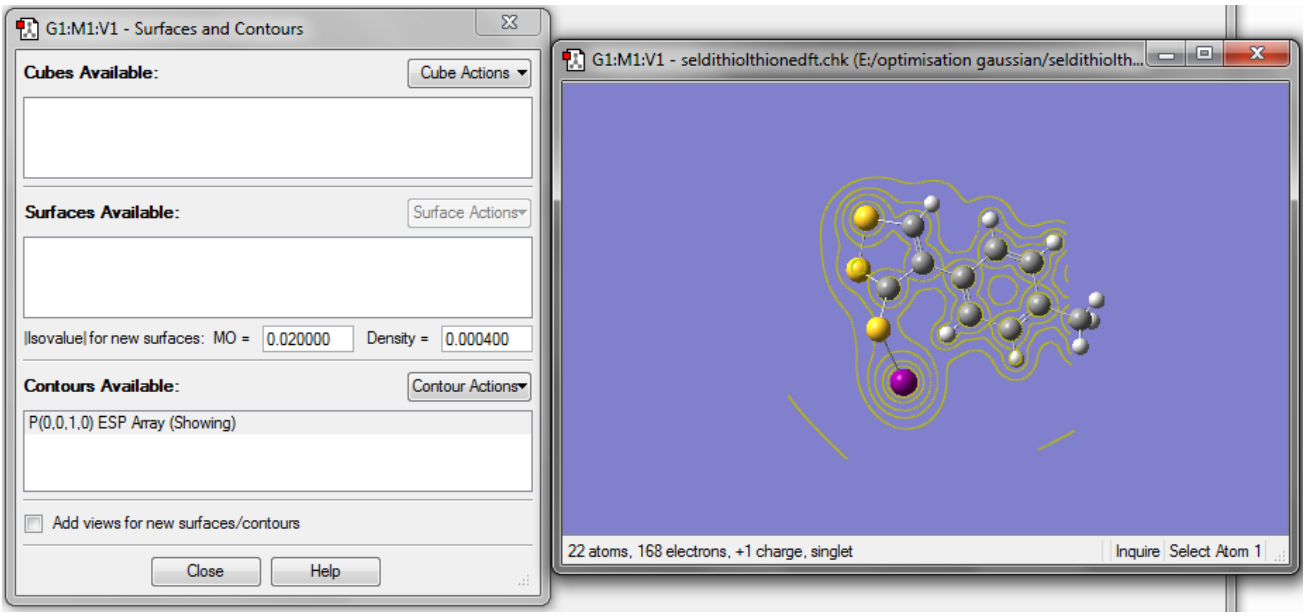


Figure 27: Surfaces and Contours the molecule2

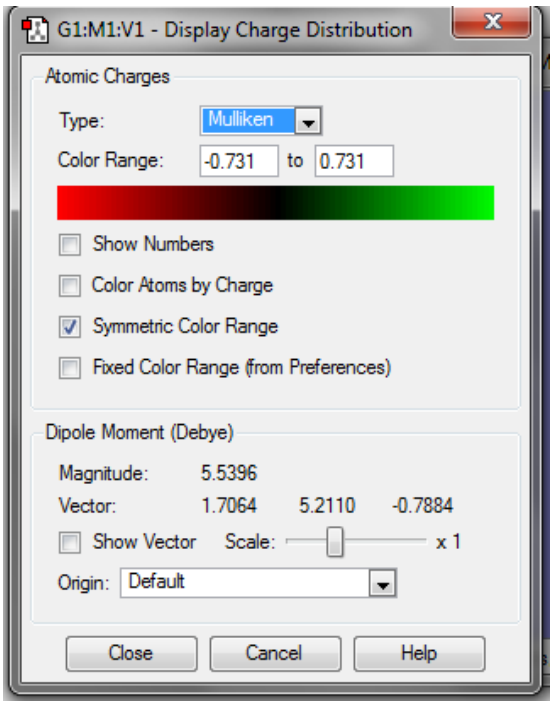


Figure 28: Display Charge Distribution the molecule2

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	16	0	-2.023970	3.431683	-0.036908
2	16	0	-2.497715	1.651060	-0.885152
3	6	0	-0.315720	3.056213	0.362522
4	6	0	-1.333793	0.882220	0.179358
5	6	0	-0.051588	1.727474	0.242522
6	6	0	1.369724	1.147102	0.121520
7	6	0	2.590610	2.084718	0.165270
8	6	0	3.841364	1.573991	0.058788
9	6	0	4.041790	0.056004	-0.105965
10	6	0	2.967411	-0.769098	-0.144466
11	6	0	1.546099	-0.188727	-0.023462
12	6	0	5.463102	-0.524368	-0.226968
13	16	0	-1.635901	-0.600191	1.117222
14	53	0	-0.960944	-2.462474	-0.128543
15	1	0	6.148143	0.093959	0.314595
16	1	0	5.479672	-1.514629	0.178010
17	1	0	5.749026	-0.555679	-1.257583
18	1	0	2.451353	3.139424	0.279739
19	1	0	4.689642	2.225451	0.089187
20	1	0	3.106668	-1.823804	-0.258936
21	1	0	0.697821	-0.840187	-0.053860
22	1	0	0.415088	3.792614	0.624310

IV. IR Identification Par Infra:

Both experimental spectra exhibit the characteristic bands of **4-p-tolyl-1, 2-dithiol-3-thione** (1) and its salt (2), which are strictly at the same wave number for (1) and (2) : The red experimental infrared spectra of (1) is presented in figure 13 .The comparison between the spectrum recorded in red for the sample and a literature spectrum in black shows the majority of the peaks, taking into account the difference in the device used and also the difference in the scale of the drawing

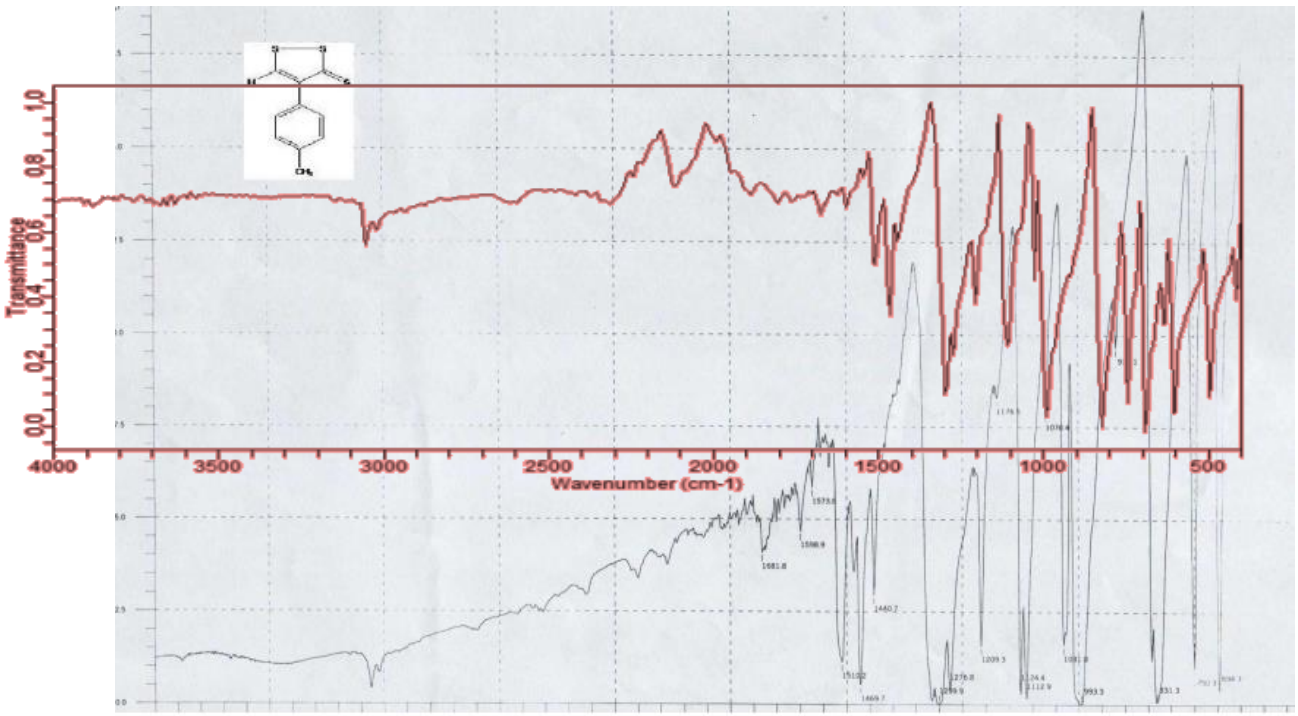


Figure 29: IR experimental spectra of 1 and 2

Figure 29 show the IR theoretical spectra of molecule 1. This spectrum was calculated to proving the proposed interpretation of the experiment one.

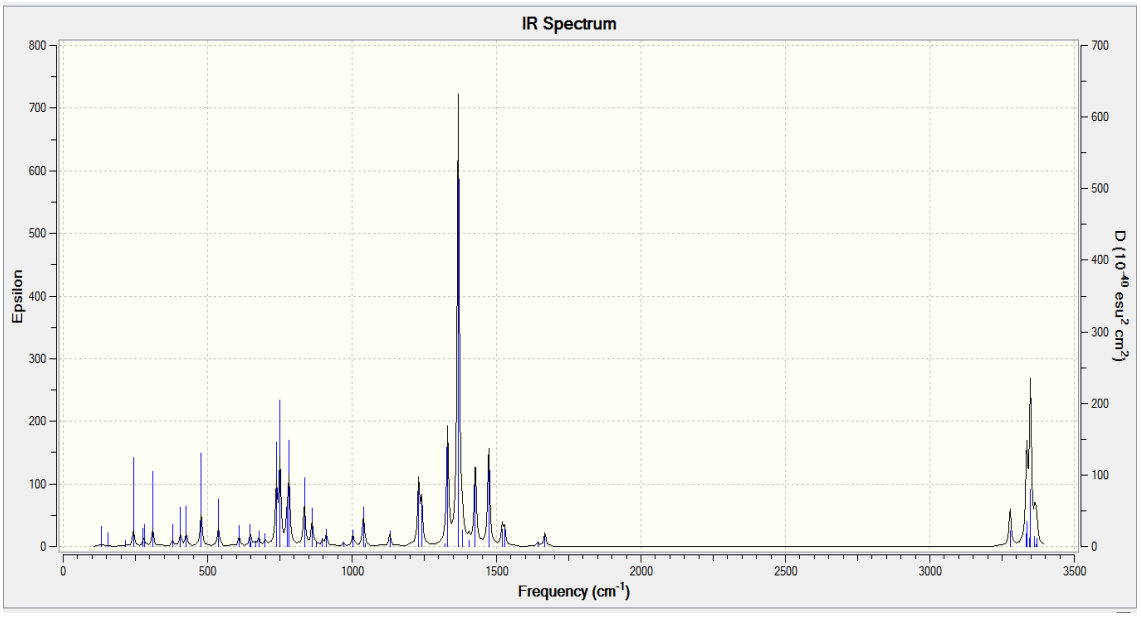


Figure 30: IR calculate spectra of 1 and 2

around 3323,51cm^{-1} υ(C–H) indication of CH_3 elongation, 3423,61 cm^{-1} υ (C-H) indication of CH elongation, 1572,93cm^{-1} υ (C-H) indication of CH elongation symmetric, 1558,49 cm^{-1} υ(C-C) indication of C=C elongation, 1407,98- 1415,51 cm^{-1} two picks indication of $(C=C)_{Ar}$ elongation , 1354,67- 1346,27 cm^{-1} two picks indication of $(C-H)_{elg}$ symmetric and asymmetric

836,97cm^{-1} indication of $(C-S)_{elg}$ symmetric and 782,61cm-1 indication of $(C-S)_{elg}$ asymmetric and 436,07cm^{-1} indication of (C-S) deformation and 377,17 cm^{-1} indication of (C-C) deformation , 703,38cm^{-1} indication of υ(S–S)elongation of the carbon ring.

V. Spectroscopie IR du produit et de sont sel

The comparison between the infrared spectrum of the molecule and its salt shows the difference in the position of the peaks characterizing the molecules. The difference is obvious which confirms the production of salt from the molecule

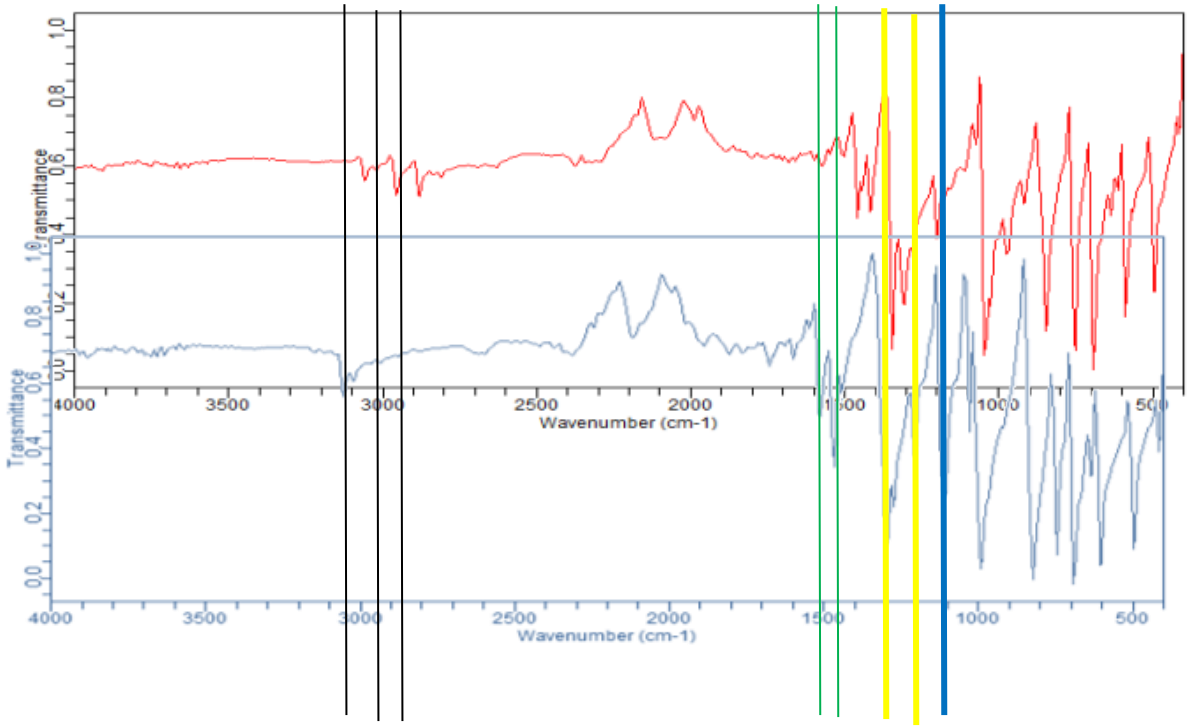


Figure 31: Spectroscopie IR du produit et de sont sel

VI. XDR analysis:

1) Diffract meter of (1) Indexation:

As indicated before, the studied molecule does not include crystallographic data, this is why in this part of our work, and we recorded a diffractogramme with powder diffractometer of X-ray the in order to seek the crystallographic data for this molecule.

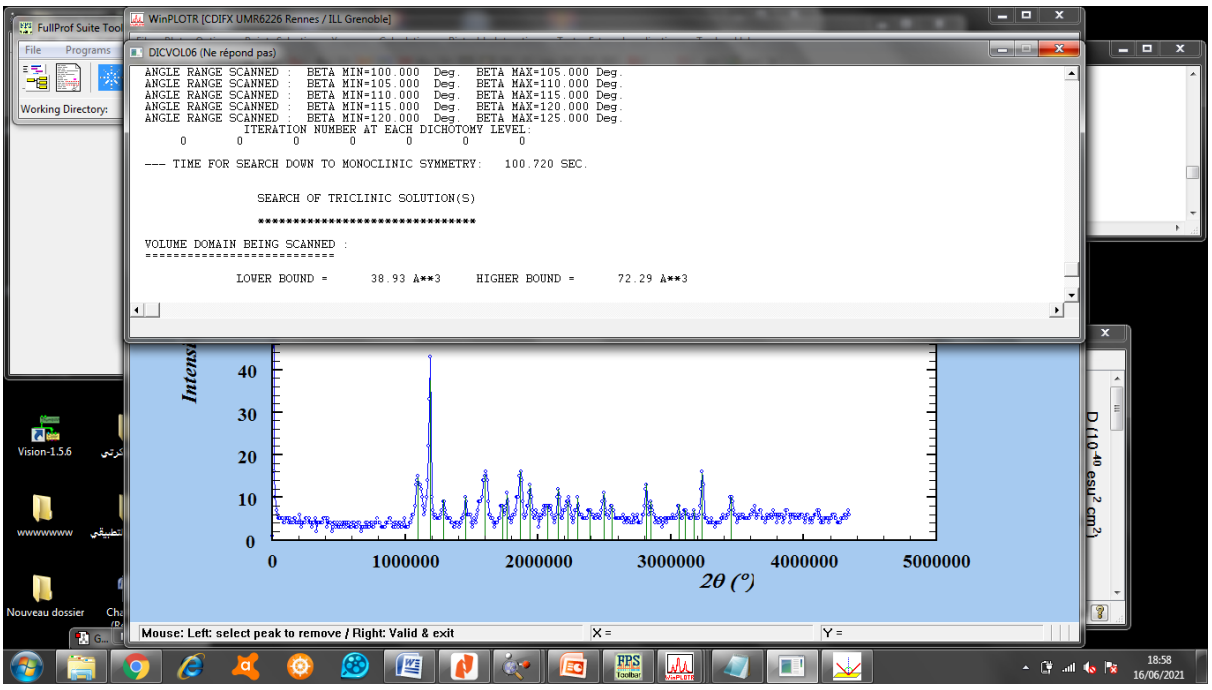


Figure 32: Diffractogram indexation with fullprof

Figure 32 shows the operation of the indexing of the obtained diffractometer and indicates that the operation finished without any solution. This means that the compound is heterogeneous.

The search for a similar crystalline phase is carried out by identification and consultation of databases. This operation is carried out with the HighScore Plus software as shown in the figure below.

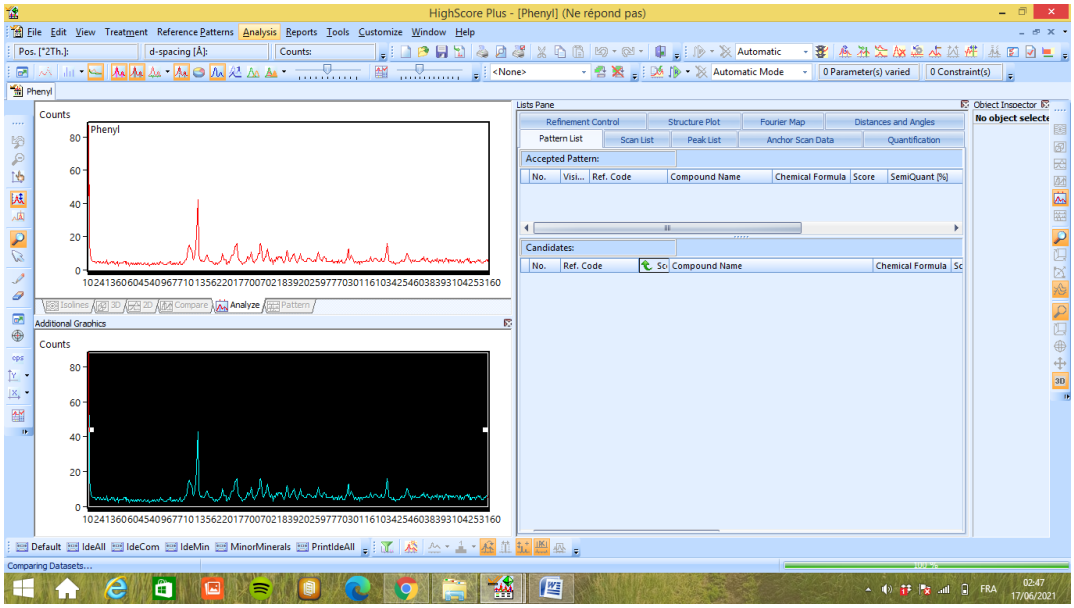


Figure 33: Diffractogram identification with Fullprof

The identification and consultation of databases with the High Score software does not provide a solution, which means that this phase has not been processed. This is why we will present the data of the length of chemical bonds, the values of the angles and the coordinates of the atoms in this compound. This information was calculated using the Gaussian software. These information ar reported in the annexes.

Conclusion

On behalf this results of IR interpretation of the old and new spectra we conclude that the reactivity of the compound against time is stable, that's mean that this compound do not change structure in time.

Conclusion

Conclusion:

Through this study in our research of conducting an empirical study and trying to model the experimental results in a theoretical way and then inferring the validity of the experimental results through the theoretically calculated results, we were able to:

Giving a molecular model in 3D space of a compound whose molecular structure was determined in only 2D in previous studies.

Interpreting the results of the IR spectrum through an experimentally calculated spectrum using the Gaussian program, especially watching the movements of functional groups,

We completed an X-ray spectrum, but we were not able to index it, but we were able to inspect the databases for this spectrum, and we concluded that there is no compound to describe it.

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[103]mémoire de Mrs Daghmouch messaouda

Abstract:

In this work we carried out a theoretical and experimental study for the molecule **4-p-tolyl-1,2-dithiol-3-thione** and its salt by molecular modeling tools theoretically and by infrared spectroscopy and X-ray diffraction experimentally on samples synthesized for these two phases deduct more than 10 years. This means that this compound does not change structure over time.

X-ray diffractogram indexing did not give a lattice parameter, so the construct is heterogeneous.

Key word; molecular modeling, X-ray, dithiol-thione

ملخص:

في هذا العمل قمنا بدراسة نظرية وتجريبية للجزيء المشتق من مركب

4-p-tolyl-1,2-dithiol-3-thione وملحه المرافق بواسطة أدوات النمدجة الجزيئية نظريًا ومن خلال التحليل الطيفي بالأشعة تحت الحمراء وانحراف الأشعة السينية تجريبيًا على العينات تم تصنيعها لهذين الطورين لمزيد من المعلومات. من 10 سنوات, فهذا يعني ان المركب لا يغير الهيكل بمرور الوقت. لا تعطي فهرسة حيود الأشعة السينية متغيرًا شبكيًا ، وبالتالي فإن البنية غير متجانسة.

الكلمات المفتاحية : النمدجة الجزيئية ,الأشعة السينية , dithiol-thione

Résumé :

Dans ce travail nous avons réalisé une étude théorique et expérimentale pour la molécule **4-p-tolyl-1,2-dithiol-3-thione** et son sel par les outils de modélisation moléculaire théoriquement et par spectroscopie infrarouge et diffraction des rayon X expérimentalement sur des échantillons synthétisé pour ces deux phases déduis plus de 10 ans. Cela signifie que ce composé ne change pas de structure au cours du temps.

L'indexation des diffractogrammes des rayons X n'ont pas données de paramètre de maille, donc le produit de synthèse est h des rayon X étérogène.

Mots clée : modélisation moléculaire, des rayon X , dithiol-thione