CONFORMATIONAL ANALYSIS OF 2-[(4-SUBSTITUTED-PHENYL)SELENO]-1,3-DITHIANES: A THEORETICAL APPROACH

by

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ABSTRACT

In this study the conformational analysis of 2-(4-substituted-phenyl)seleno-1,3-dithiane with H, Cl, F, CH_3, CF_3, NO_2, OCH_3 and $N(CH_3)_2$ substituents have been studied computationally both in gas phase and in solvent with the semi-emprical PM3 method and ab initio HF/6-31G* basis sets. The optimized geometries have been discussed in terms of endo and exo anomeric effects and their presence in the axial conformers have been confirmed. The conformational free energies have been calculated in gaseous phase in solvent. Comparison between experimental and calculated values has shown that PM3 as well as HF/6-31G* can be used confidentially to treat conformational equilibrium for cyclohexane derivatives with S and Se.

2-[4-SÜBSTİTÜYE-FENİL)SELENO-1,3-DİTİAN MOLEKÜLÜNÜN KONFORMASYONEL ANALİZİ: TEORİK BİR YAKLAŞIM

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Anahtar Kelimeler: 2-(4-sübstitüye-fenil)seleno-1,3-ditian, Konformasyonel Analiz, Konformasyonel Serbest Enerji, Anomerik Etki, PM3.

ÖZET

Bu çalişmada 2-(4-sübstitüye-fenil)seleno-1,3-ditian molekülünün H, F, Cl, CH_3, CF_3, NO_2, OCH_3, $N(CH_3)_2$ gurupları ile gaz fazında ve çesitli çözücüler içinde yarı ampirik PM3 metodu ve ab initio HF/6-31G* bazı ile hesapsal olarak konformasyonel analizi yapıldı. Optimize edilen geometriler endo ve exo anomerik etkisi açısından incelendi ve aksiyal konformerlerde anomerik etkinin varlığı onaylandı. Konformasyonel serbest enerjiler gaz fazında ve çözücü içinde hesaplandı. Hesapsal ve deneysel yöntemlerle bulunan değerler kıyaslandığında PM3 metodunun ve HF/6-31G* bazının sülfür ve selenyum içeren siklohekzan türevlerinin konformasyonel analizinde kullanılabileceği görüldü.

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LIST OF ABBREVIATIONS

ΔA_C	Cavitation energy
ΔA_E	Electrostatic interaction between the solute and the reaction field
ΔA_I	Induced polarization of the solute by the reaction field
ΔA_P	Polarization of the solvent around the cavity
ΔA_S	The energy of solvation
ΔA_T	The translational, rotational and vibrational partition function of the solute
AM1	Austin Model
C	Matrix of LCAO-MO coefficients
C_{ij}	Coefficients of C
CNDO	Complete Neglect of Differential Overlap
e	Electron
g	Proportionality constant
INDO	Intermediate Neglect of Differential Overlap
KE_{el}	Kinetic energy of electrons
LCAO	Linear Combination of Atomic Orbitals
M_A	Mass of atom A
m_e	Mass of electron
NDDO	Neglect of Differential Diatomic Overlap
$PE_{nuclear-el}$	Potential energy of electron-nucleus attraction
PE_{el-el}	Potential energy of electron-electron repulsion
PM3	Parametric Method
r_{Aa}	Distance between nucleus A and electron a
r_{ab}	Distance between electron a and electron b
R_{AB}	Distance between nucleus A and nucleus B
Z_A	Atomic number of A

LIST OF SYMBOLS

Å	Angstrom
ε	Dielectric constant
Φ	Atomic orbital
Ψ	Molecular orbital
σ^*	Antibonding molecular orbital
μ	Dipole moment
$\boldsymbol{\mu}$	Dipole moment operator
∇	Laplacian operator
a_0	Radius of spherical cavity
E	Energy
F	Fock matrix
h	Planck's constant
H	Hamiltonian operator
HF	Hartree Fock
n	Nonbonding atomic orbital
R	Reaction field vector
S	Matrix of overlap integral

1. INTRODUCTION

Heterocyclic compounds are commonly found in nature. Thiosubstituted heterocycles have a medicinally important role and because of their wide usage considerable attention has been centered on their synthesis. There is also an increasing interest in the synthesis and study of selenium analogs of biologically important sulfur compounds[1]. The existence of many naturally occurring heterocyclic compounds has motivated the study of the conformational analysis on them.

Conformational analysis can be defined as the study of the conformations of a molecule and their influence on its properties and behavior. Conformational analysis made its first tentative steps in 1890 when Sachse[2] suggested that cyclohexane could exist in two arrangements, free from angle strain, later termed as "chair" and "boat" conformations. Progress in conformational analysis thereafter slowly gained momentum. In 1943, Hassel[3] set forward the following basic conformational facts about cyclohexane.

1) The chair form is the preferred conformation

2) Substituted cyclohexanes undergo a ring inversion process and the substituent may occupy either axial or equatorial position.

3) In all cases the equatorial form is favored.

These ideas led a new and fundamental understanding of many reactions and have directly and indirectly assisted in many subsequent advances in organic chemistry.

The chemical and physical properties of organic molecules depend not only on their gross structure and stereochemistry but also on their conformations. Conformations are stereoisomers that can be interconverted either by rotation about bonds of order approximately one with small distortions of bond lengths and angles or by inversion at a three coordinate center in the molecule.

Substituents on a cyclohexane ring prefer equatorial over axial position[3]. Similar considerations usually apply to substituents of heterocycles. This equatorial preference is rationalized in terms of repulsive interactions present in axial conformation, between substituent and syn-axial hydrogens (Figure 1.1).

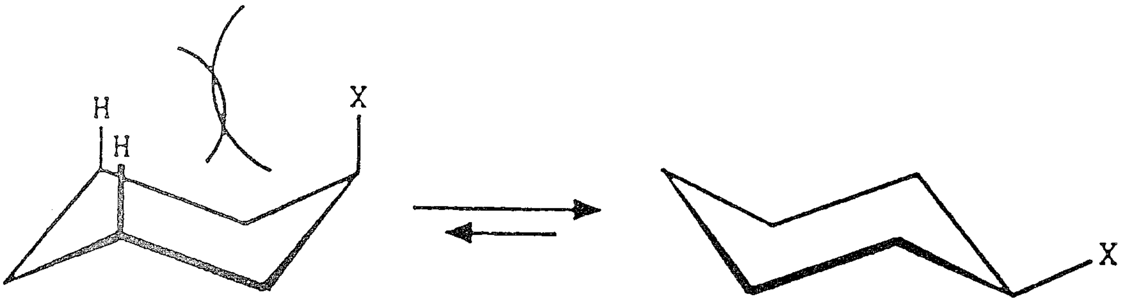


Figure1.1 Unfavorable interactions between substituent and syn-axial hydrogens.

In 1955, J.T. Edward reported[4] that in the pyranose ring (Figure1.2) axial alkoxy groups at C(1) are in general more stable than equatorial ones. His interpretation was based on the orientation of unshared electrons of the ring oxygen. The tendency of the electronegative substituent at C(1)of a pyranoid ring to assume the axial rather than equatorial orientation was later termed as "anomeric effect" and found not to be restricted to carbohydrates or to 6 membered rings.

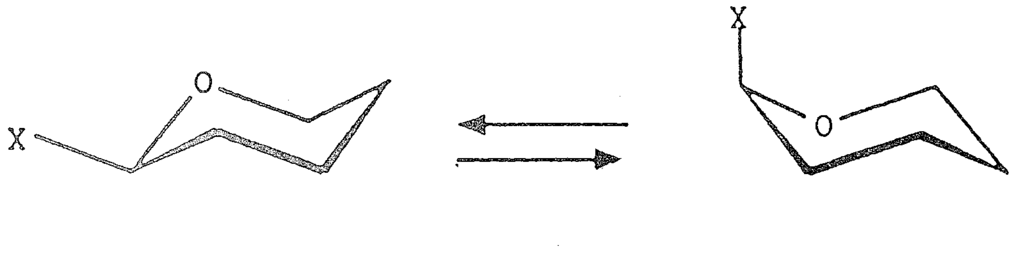


Figure1.2 Conformational equilibrium in substituted pyranose ring

The general anomeric effect is defined[5,6] as the preference of gauche position over the anti in segments R-X-A-Y, as shown in Figure 1.3, where A is an element of intermediate electronegativity (eg. C, P, S), Y is an element more electronegative than A (O, N or halogen), X is an element which possesses lone pairs and R is either H or C.

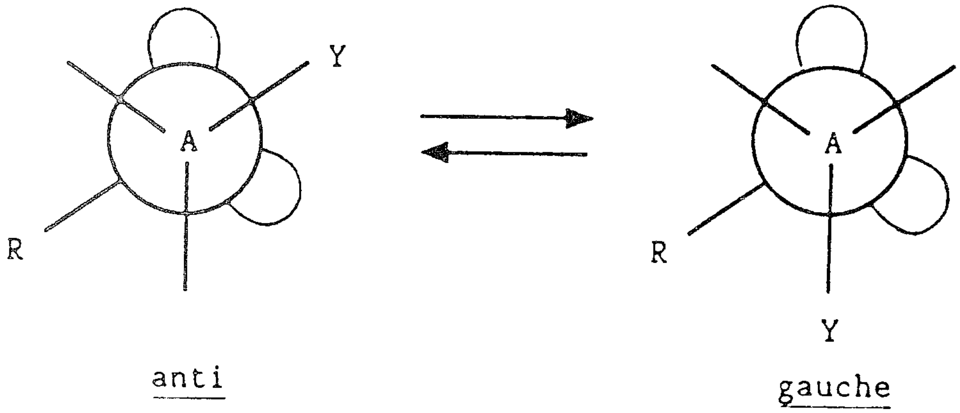


Figure 1.3 Anomeric effect in segments R-X-A-Y

Several explanations for the axial preference over the equatorial have been put forward.

According to electrostatic model[4], the axial preference in terms of unfavorable dipole-dipole interaction between carbon-heteroatom bonds on the ring and the bond from C(1) to the equatorial electronegative substituent. Equatorial conformer has higher dipole moment.

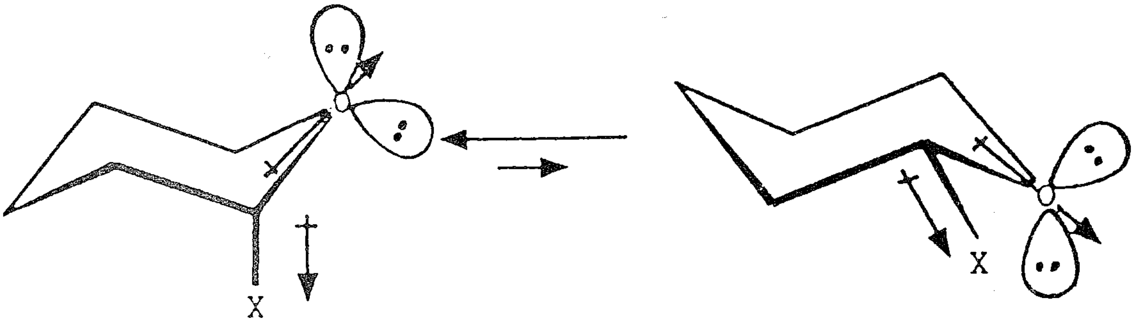


Figure1.4 The dipolar interactions in pyranose ring.

In the gas phase it is generally found that the conformer with the larger dipole moment has larger electrostatic energy and an increased overall energy[7]. In polar solvents, the more polar equatorial conformer is stabilized more so the proportion of the equatorial over the axial will be higher. Both quantum mechanical calculations[8] and experimental findings[9] about greater anomeric effect in less polar media provides support for the electrostatic rationalization of anomeric effect. Electrostatic model by itself cannot explain the variations in bond lengths and bond angles, that are associated with anomeric effect and also there are several reports for axial stabilization in the more polar media[10-12].

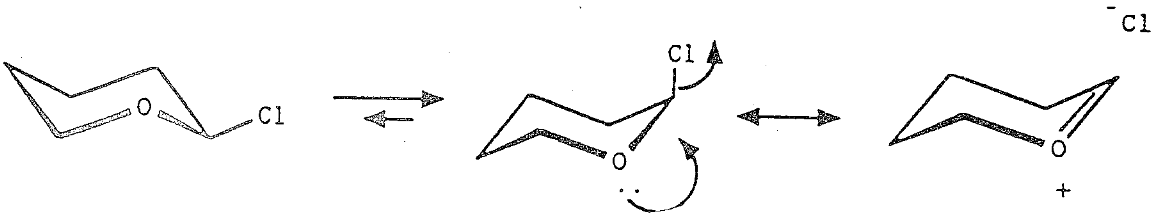


Figure1.5 Representation of double-bond/no-bond model.

Double-bond/No-bond model is another explanation of the anomeric effect[13]. According to this model stabilization of the axial conformer was attributed to delocalization of antiperiplanar lone pair orbital on heteroatom to the antibonding orbital of C-X bond. Bond angle and bond length variations could be explained with this model. It has also been reported that the conformer which has higher dipole moment in its double-bond / no-bond model will be stabilized more in polar solvents.

The explanation for the anomeric effect was suggested by Eliel and is known as Eliel's Rabbit Ear Effect[14]. It is based on dominant n-n interaction with a minor contribution from the n-σ* interaction when two occupied orbitals of similar energy interact through space, they produce two new orbitals. The two orbital-4 electron model has a destabilizing interaction greater than the stabilization gained.

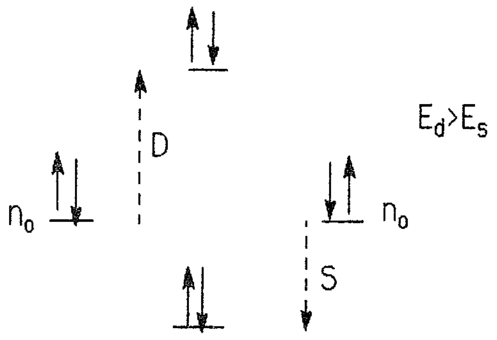


Figure1.6 Two orbital/4-electron interaction in Rabbit Ear Model.

Since the anomeric effect stabilizes the axial orientation at the anomeric center, the same stereoelectronic effect should also influence the orientation of the substituent.

For the stabilization to occur, the best donor atom should be antiperiplanar to the best acceptor bond. If the substituent has the ability to donate electrons from its non-bonding molecular orbital, then it may orient itself for the stabilization to occur. This is shown in methoxy substituted pyranose ring in Figure1.7.

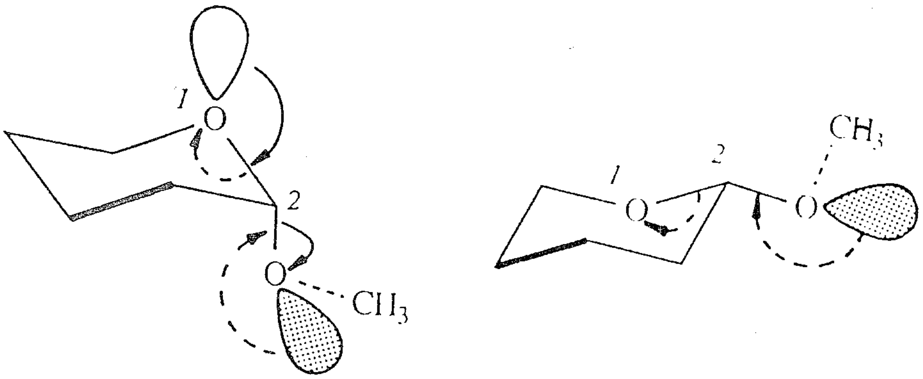


Figure1.7 Representation of endo and exo anomeric effects.

This stabilization, shown in dashed arrows in Figure1.7 is described as "exo anomeric effect". In endo case, the donor atom is endocyclic oxygen atom which may be denoted by dotted arrows in Figure1.7. Both exo and endo anomeric effect may be present in axial conformer but only exo in equatorial case.

There are numerous reports on the first and second row atoms of the periodic table having anomeric effect but theoretical or experimental work on selenium as well as other third row atoms are relatively scarce[15-25].

In his work, B.M. Pinto [16-18, 21] has discussed the anomeric effect of selenium by concentrating on 2-[(4-substituted-phenyl)seleno]-1,3-dithiane with NMe_2, OMe, NO_2, CF_3, CH_3, F, Cl, H substituents. He determined the structure and conformational preference at different temperatures and in different solvents by NMR analysis.

It was reported that the 1,3-dithiane ring exists in chair form with the arylseleno moiety in the axial orientation. K_{eq}, ΔG_{eqrxn} and the relative preference of substituents for axial orientation have also been determined.

The aim of this study is to computationally analyze the conformational equilibrium of 2-[(4-substituted-phenyl)seleno]-1,3-dithiane with H, Cl, F, NO_2, NMe_2, CH_3, CF_3 substituents.

To discuss the existence of anomeric behavior of 3rd row elements is one of the purposes of the study. Another objective is to check if PM3 parameters for selenium are well established by making calculations for a series of compounds and to compare them with the experimental results. To find out which thermodynamic property (ΔH or ΔS) is more operative in forcing the conformational equilibrium is another point of interest.

Additionally, a correlation between the substituent and the conformation will be established. The final goal is to test how well exact calculations (ab-initio) for several substituents reproduce the experimental trend quantitatively so that it can be used for further studies on the behavior of substituents not studied experimentally yet.

2 THEORY

2.1 Introduction

Computational chemistry is a new multidisciplinary area of research that transcends boundaries between biology, chemistry and physics.

A definition of computational chemistry given by E.Clementi[26] in his paper is as follows: "Use of quantum and statistical mechanics and other aspects of molecular physics, chemical physics and physical chemistry to determine molecular properties." An explicit definition was published in 1985 by A.J. Hopfinger[27] in which he defined computational chemistry as quantitative modeling of chemical behavior on a computer by the formalisms of theoretical chemistry.

Computational methods are much like experiments in that both may be employed in data collection and in looking for the unusual. Calculations are easy to perform. They may be performed on highly reactive molecules and reaction transition states as easily and as reliably as on stable molecules. Experiments become increasingly more difficult with decreasing stability and cannot be performed on transition states. Calculations are becoming less and less costly to perform and are safe. The cost of calculations increases rapidly with molecular size whereas the cost of experiments is generally independent of size. On the other hand, there is only one experimental result but calculations yield different results depending on the specific model employed.

Two methods are involved in computational chemistry. One of them is the electronic structure method which makes no reference to chemical bonds and attempts to solve the Schrödinger equation for interactions of the electrons and nuclei which make up the molecular system. The other method is the molecular mechanics method which makes use of empirical force fields to describe the energy. In this study, quantum chemical calculations are performed.

By calculations, structures, relative stabilities and properties of isolated molecules, including molecules in solution, can be determined. Chemical reactivity and product selectivity can be modeled and additionally energetics of intra and intermolecular interactions, leading to parameterization of empirical force fields for use in molecular mechanics and molecular dynamics calculations can be evaluated. Fundamentally quantum mechanical calculations involves computing the electron distribution in the molecule.

2.2 Quantum Mechanics

In quantum mechanical theory, solutions to the Shrödinger equation,

$$H\Psi = E\Psi \tag{2. 1}$$

are sought. Here the wavefunction Ψ describes the x, y, z spatial coordinates of the particles in the system in some state. The wavefunction itself is not a physical observable, but the square of the wavefunction, $\Psi^2(x,y,z)$ is proportional to the probability of finding the electron density in a given region of space. The eigenvalue E is the energy of the system in that state. H is the Hamiltonian, an operator to derive the kinetic energy and potential energy of a system of electrons and nuclei. It contains no explicit term for chemical concepts, such as resonance, induction, hyperconjugation, steric effects and hydrogen bonding. Hamiltonian operator contains the following terms :

$$\hat{H}\Psi = E\Psi$$

$$\hat{H} = \underbrace{\frac{-h^2}{8\pi^2}\sum_{A}^{\text{nuclei}}\frac{1}{M_A}\nabla_A^2}_{\text{nuclear kinetic}} \underbrace{\frac{-h^2}{8\pi^2 m_e}\sum_{a}^{\text{electrons}}\nabla_a^2}_{\text{electron kinetic}} \underbrace{- e^2\sum_{A}^{\text{nuclei}}\sum_{a}^{\text{electrons}}\frac{Z_A}{r_{Aa}}}_{\text{nuclear/electron potential}}$$

$$\underbrace{+ e^2\sum_{A}^{\text{nuclei}}\sum_{> B}\frac{Z_A Z_B}{R_{AB}}}_{\text{nuclear/nuclear potential}} \qquad \underbrace{+ e^2\sum_{a}^{\text{electrons}}\sum_{> b}\frac{1}{r_{ab}}}_{\text{electron/electron potential}} \tag{2.2}$$

Quantum mechanics deals with the basic physics of the particles, namely, their kinetic energy of motion and potential energy of interaction. Any chemistry that comes out of the theory is because of the fundamental physics of the system being obeyed.

To solve the Schrödinger equation for most molecules many approximations must be made. The most common implementation is molecular orbital theory. Hamiltonian operator does not explicitly depend on time, so the wavefunction corresponds to a stationary state and therefore is a function of only spatial coordinates. This is the "time independence" assumption.

"Neglect of relativistic effects" is an assumption that electrons have the same mass regardless of how fast they travel. The electronic wavefunction is obtained in the field of fixed nuclei. The Hamiltonian operator then becomes :

$$H_{el} = KE_{el} + PE_{\text{nuclear-el attraction}} + PE_{\text{el-el repulsion.}} \tag{2.3}$$

Solution of the electronic equations provides the potential that governs nuclear motion. This is "the Born-Oppenheimer approximation."

In the "orbital approximation" the true wavefunction is represented as a combination of mathematical functions (orbitals), each dependent on the coordinates only of one electron. The electrons are assembled in what is called a "slater determinant", which mathematically preserves the physics of the system. A slater determinant corresponds to one electron configuration, i.e., one possible occupancy of the orbitals. Normally, the orbitals are filled by the Aufbau principle, i.e., they are filled starting from the lowest energy orbital until all the electrons are accounted for. The unoccupied orbitals are called "virtual orbitals". The mathematical form of the slater determinant is as follows, where $\Psi_i(j)$ the i^{th} one electron orbital, is a function of coordinates of the j^{th} electron, and there are n electrons.

$$\Psi = (n!)^{1/2} \begin{vmatrix} \Psi_1(1)\alpha(1) & \Psi_1(1)\beta(1) & \Psi_2(1)\alpha(1) & \Psi_{n/2}(1)\beta(1) \\ & & & \\ \Psi_1(n)\alpha(n) & & & \ldots\ldots\Psi_{n/2}(n)\beta(n) \end{vmatrix} \qquad (2.4)$$

"Linear combination of atomic orbitals" (LCAO) is the last approximation made. The molecular orbitals denoted by, Ψ_i are described by

$$\Psi_i = \sum_{j=1,n} C_{ij}\Phi_j \qquad (2.5)$$

where Φ_j are "atomic orbitals" (atomic orbitals, also called basis functions) centered on each of the constituents atoms in a molecule, and C_{ij} is the coefficient of the j^{th} basis function in the i^{th} molecular orbital. A further approximation is made that the basis set is finite.

With these approximations, determination of the energy and wavefunction of a molecular system reduces to solving the Hartree-Fock self-consistent field (SCF) equation,

$$FC=SCE \tag{2.6}$$

In the SCF equation, F is the Fock matrix with elements consisting of the kinetic energy, electron-nuclear attraction, and electron-electron (two-electron) repulsion integrals C is the matrix of the LCAO-MO coefficients, S is the matrix of overlap integrals between the basis functions, and E is the eigenvalue matrix.

2.2.1 Semi-empirical Methods

In semi-empirical models, rather than solving all the integrals of the Schrödinger equation, parameters originating from experimental data are used. Semi-empirical models can be used to yield continuous energy surfaces. They are neither variational nor size consistent. More importantly, semi-empirical methods are inherently dependent on the choice of parameters. The parameterization is then tested against a limited set of molecules to ensure its accuracy. This dependence on parameters can be minimized by using a large and varied training set of molecules to establish parameters. Like numerical iteration, this process is a continuing one. Parameters are introduced in order to reproduce experimental equilibrium geometries, heats of formation, electric dipole moments and ionization potentials.

In solving the Schrödinger equation , the number of off-diagonal one electron integrals H_{ij} and S_{ij} rapidly becomes very large and computationally burdensome. To handle this task, the approximation was made to set the overlap integrals between different atomic orbitals to zero. With this assumption the secular determinant for the Hartree-Fock method reduces to

$$|F-E| = 0 \tag{2.7}$$

Fock matrix here is the sum of the usual one-electron and two-electron positions. The latter present a particularly difficult hurdle since the number of integrals of the form are encountered.

$$\iint \Psi_i(1)\, \Psi_j(2)\, (1/r_{12}) \Psi_k(1)\, \Psi_l(2)\, \delta\tau\,(1) \delta\tau(2) \tag{2.8}$$

The overlap assumption sets these integrals to zero except in the case where i=j and k=l. This assumption led to the designation of CNDO, complete neglect of differential overlap. An additional assumption was that the off-diagonal resonance integral H_{ij} could be made proportional to the overlap integral i.e., although the overlap matrix disappears, values are still assigned to certain S_{ij} to allow evaluation of the H_{ij} and for later computation of charge distribution. A somewhat later upgrade in the parameterization was forthcoming under the title CNDO/2. Although the CNDO methods did not introduce electron-electron repulsions, they do not handle the question of the interactions between electrons with parallel or antiparallel spins, especially when the electrons are on the same atom.

As a correction, differential overlap between electrons on the same atom as covered by one-electron integrals was reintroduced, the method was called the "intermediate neglect of differential overlap" (INDO).

NDDO (Neglect of differential diatomic overlap) model is another.semi-emprical model. It includes orbital anisotropies and the requirements for spherically averaging two-center, two-electron integrals is removed.

The first practical NDDO method was introduced by Dewar and Thiel[28] in 1977, called "modified neglect of diatomic overlap" (MNDO). This model was parameterized on experimental molecular geometries, heats of formation, dipole moments and ionization potentials. The MNDO model is a very successful model, but it has also some limitations in reproducing hydrogen bondings successfully.

In this study the semi-empirical PM3 model which is the third parameterization of the original MNDO model is used. This is a NDDO method which utilizes more adjustable parameters for the core-core repulsion term. In PM3 all quantities that enter the Fock matrix and the total energy expressions have been treated as pure parameters. To accomplish this task of optimizing parameters an automatic procedure was introduced, allowing a parameter search over many elements simultaneously. These now include H, C, N, O, F, Br, Cl, I, Si, P, S, Al, Be, Mg, Zn, Cd, Hg, Ga, In, Tl, Ge, Sn, Pb, As, Sb, Bi, Se, Te, Br and I [29]. This model employs minimal valence basis of slater type orbitals. For hydrogen 1s, for first row elements 2s, 2p,and for second row elements 3s, 3p, 3p, 3p orbitals are used.

Each atom is characterizied through the 13-16 parameters that is present in AM1 and additionally five parameters that define the one-center, two-election integrals. In PM3, the parameters were optimized using an automatic optimization routine that used a large set of reference molecular data. This allowed 12 elements to be optimized simultaneously. It is the most precisely parametrized semi-emprical model but again it has some limitations. Lone-pair lone-pair repulsions are not always well represented in these methods and care must be taken.

2.2.2 Ab-initio Methods

The term "ab-initio" ("from the beginning") is used to describe calculations in which all the integrals of the theory, be it variational or perturbative, are exactly evaluated. Firstly the Hamiltonian operator H is written down, then a mathematical form Ψ is selected as trial wavefunction and finally energy is minimized with respect to variations in parameters in equation 2.9.

$$E=\int \Psi * H \Psi \, \delta\tau \, / \int \Psi * \Psi \, \delta\tau \qquad (2.9)$$

The level of theory refers to the type of theory employed. Common levels of theory would include Hartree Fock, or molecular orbital theory, configuration interaction, perturbation theory, etc.

Ab initio theory requires a rigorous nonparameterized molecular orbital treatment by which it is possible to obtain chemical accuracy but the cost of computer time is enormous. It is not completely true that ab initio calculations are performed from first principles. There are a number of simplifying assumptions made. Hartree Fock approximation and Linear Combination of Atomic Orbitals approximation together with Born-Oppenheimer lead to a set of models termed ab initio molecular orbital models.

The solution involves an iterative procedure; in which the following steps take place:

1-) Guessing the molecular orbital coefficients, C

2-) Forming the density matrix

3-) Forming the Fock matrix, F

4-) Solving FC=ESC for C

5-) Comparing new molecular orbital coefficients with those from previous iterations.

If the new coefficients differ from the old coefficients the process continues with step 2. If the new coefficients are the same as the old coefficients, then the process is finished. Such an iterative procedure is commonly referred to as a "self consistent field method".

The trial function Ψ is made up of slater determinants containing spin orbitals Φ, used in LCAO approximation. If it is an atom that is considered, the Φ's are atomic spin orbitals and if it is a molecule, they are molecular spin orbitals. Two electrons, one of each spin are assigned to each atomic orbital, starting with lowest atomic orbital and working up all the electrons are assigned. If the last electron completes the filling of all the atomic orbitals at a given energy level, then it is called a "closed subshell". A similar situation holds for molecules, such that electrons of paired spins occupy identical molecular orbitals.

Essentially all basis sets used in ab initio calculations employ Gaussian type basis function, written in terms of polynomials in x, y, z times an expression in r^2

$$x^l y^m z^n \exp(\alpha r^2) \qquad (2.10)$$

where α is constant

The functions are referred to as s, p, d, etc., depending on the order of the polynomial. The sum of integers l, m, n is zero for an s function, one for a p function, two for a d function, etc.

The simplest representation, termed a minimal basis set, comprises the smallest numbers of functions needed to hold all the electrons in an atom and still maintain the spherical symmetry of the atom. For example for Na the minimal basis sets are 1s, 2s, $2p_x$, $2p_y$, $2p_z$, 3s.

A representation is termed a "split-valence basis set" where the core region is described by a minimal basis and valence region is split into inner and outer parts. A common split-valence set is 3-21G where the numbers refer to the number of Gaussian functions which make up core orbitals. The (*) nomenclature is used to indicate that d type functions are available on 2nd row and heavier main group elements in describing the structures and energies of molecules. Another kind of basis set is polarization basis sets where d-type functions are added to heavy atoms and p-type functions are added to hydrogens. One of the most common basis sets is 6-31G* which is also used in this study in ab initio calculations.

2.3 Self Consistent Reaction Field

The effect of solvent interacting with a molecule can be taken into account in quantum chemical computations by means of the self-consistent reaction field approach. There are two different approaches to treat molecules in solution. One of them is the explicit model and the other is the implicit approach.

In the explicit model the solute is considered as immersed in a box containing a large but finite number of solvent molecules. In this model specific solute-solvent, solvent-solvent interactions and the effect of bulk solvent could also be calculated, but it is computationally very expensive.

In the implicit approach, the solvent is represented by a continuum with macroscopic dielectric properties. It is computationally simple and straightforward to parameterize the experimental solvation energies but it does not allow specific solute-solvent or solvent-solvent interactions. In this study implicit approach is employed. The molecule undergoes an electric potential arising from the polarization by the molecular charge distribution of the solvent. In this approach, the charge distribution and the electric potential as well as its derivatives of increasing order at this point are related to the moments through reaction field factors whose values depend on the geometry of the boundary of the continuum and on its dielectric properties only.

A solute molecule is assumed to be surrounded by an arbitrary large number of solvent molecules in a liquid phase. The solute is considered as a quantum system perturbed by its surrounding. To analyze this perturbation, the system is considered in an averaged configuration and solute is removed without any modification either in the solvent or in the solute structure. The volume previously occupied by the solute is called the "solute's cavity". In this cavity, the averaged electric potential is non-zero. It usually varies from one point to another giving rise to a non-uniform electric field which is called the "reaction field". This field has two effects. Firstly, it disturbs the charge distribution of each solvent molecule creating an induced electric moment and secondly it generates an angular correlation between the solvent and solute molecules especially in the case of dipolar species.

The solvation process decomposed in a series of steps by Rivail[30] is as follows:

1-) Creation of the cavity in the solvent.(Free energy variation ΔA_C is sometimes called "cavitation energy".)

2-) Polarization of the solvent around the cavity ΔA_P

3-) Induced polarization of the solute by the reaction field. ΔA_I

4-) Electrostatic interaction between the polarized solute and the reaction field ΔA_E

5-) Contribution of the dispersion and repulsion forces between the solute and the neighboring solvent molecules ΔA_D

6-) Finally, the translational, rotational and vibrational partition function of the solute ΔA_T

The free energy of solvation ΔA_S is the sum of all the contributions.

$$\Delta A_S=\Delta A_C+\Delta A_P+\Delta A_I+\Delta A_E+\Delta A_D+\Delta A_T \qquad (2.11)$$

A dipole in the molecule will induce a dipole in the medium, and the electric field applied to the solute by the solvent will in turn interact with the molecular dipole to lead to net stabilization. In molecular orbital theory, the electrostatic solvent effect may be taken as an additional term, H_i in the Hamiltonian of the isolated molecule, **Ho**.[31]

$$H_{rf}=H_0+H_i \qquad (2.12)$$

The perturbation term (H_i) describes the coupling between the molecular dipole operator (μ) and the reaction field, R

$$H_i = -\mu R \qquad (2.13)$$

The reaction (electric) field, R, is proportional to the molecular dipole moment, μ:

$$R = g\mu \qquad (2.14)$$

g which is the proportionality constant, gives the strength of the reaction field, depends on the dielectric constant of the medium ε and on the radius of the spherical cavity, a_0:

$$g = 2(\varepsilon - 1)/(2\varepsilon + 1)a_0^3 \qquad (2.15)$$

A general expression of g has been proposed by Tapia and Goscinski [32] to estimate the degree of solute-solvent coupling. The effects of the reaction field can be expressed as an additional term in the Fock matrix.

$$F_{\lambda\sigma} = F^0_{\lambda\sigma} - g\mu \langle \Phi_\lambda | \mu | \Phi_\sigma \rangle \qquad (2.16)$$

where Φ_λ and Φ_σ are basis functions. When the solvent polarity is included, the energy of the system is as follows:

$$E = \langle \Psi | \mathbf{Ho} | \Psi \rangle - 1/2\, \mu R \qquad (2.17)$$

where Ψ is the full wavefunction of the molecule.

The self consistent reaction field may be applied to any method of computing electronic energies i.e., ones that include electron correlation. The only adjustable parameter in a solvent effect calculation is the cavity radius. Main criticism one can make against this approach is the shape of the cavity.

The idea of using a cavity in the mean field theories of molecular liquids is quite old. A major contribution to this treatment is found in Onsager's paper[33] in which a detailed analysis of the electric field acting on a polarizable molecule, represented by a point dipole at the center of a spherical cavity, led to a simple and quite satisfactory description of the dielectric constant of non associated polar liquids in terms of molecular quantities. The only parameter of this theory , the volume of the cavity, is shown to be well defined and equal to molecular volume in the case of pure liquids.

The success of the model of Onsager indicates that it is suitable to evaluate the orientational dependence of the interaction energy of a dipolar, polarizable molecule with a uniformly polarized medium. It is obvious that the representation of a molecule by a point dipole is an over-simplified view. A multipolar expansion of the molecular charge distribution at the center of the cavity becomes therefore necessary and some successfull representations of the displacement of conformational equilibrium with the dielectric properties at the solvent provides one with some other facts in favor of this approach. The 6-31G* results presented in this study have all been obtained with the help of a spherical cavity.

3. RESULTS AND DISCUSSION

3.1 Historical Background

Although there have been many experimental and theoretical investigations of anomeric effect, these studies have generally dealt with interactions involving first and second row elements. Studies on related systems containing lower row elements are scarce.

In 1985, Pinto et.al. reported [16] the axial conformational preference of the arylseleno moiety in 2-(arylseleno)-1,3-dithianes.

Later, they extended their study on the solution conformational behavior of 2-[(4-substituted-phenyl)seleno]-1,3-dithianes with NO_2, CF_3, Cl, F, H, CH_3, OMe, NMe_2 substituents and reported that the magnitude of anomeric effect decreases as electron-withdrawing ability of substituents decreases. This behavior was rationalized in terms of dominant $n_S \rightarrow \sigma^*_{Se}$ orbital interaction[18]. The study on solvent dependence of the conformational equilibria for selected compounds did not show significant correlation with dielectric constant although anomeric effects and substituent effects were still observed in polar medium. The results are interpreted in terms of the dominance of the orbital interaction component over the electrostatic component.

In 1988, the same group studied the conformational equilibrium of 2-[(4-methoxyphenyl)seleno]-1,3-dithiane in four different solvents at low temperature by ^{77}Se NMR spectroscopy[21]. The preferential stabilization in enthalpy terms of the axial isomer in acetone versus metylene chloride and its destabilization in entropy terms is interpreted in terms of the dominance of n_S-σ^*_{C-Se} orbital interactions over dipolar interactions which leads to double-bond/no-bond structure.

Additional evidence for anomeric effect of Se was brought up by the same Canadian group[19] by examining 2-phenylthio and 2-phenylseleno-1,3-diselenanes by means of NMR spectroscopy. It has been also reported that there exists a significant endo Se-C-S and Se-C-Se anomeric effect.

Pinto[20,22] has also reported evidence for the existence of a Se endo anomeric effect causing an unusual solid-state conformation in selenium coronand.

In 1991, Mikolajczyk[34] has published data on the cis-trans equilibration of 2-(dimethoxyphosphoryl)-5-t-butyl-1,3-diselenanes. Preference for axial isomer was observed as evidence of anomeric effect of 2.4 kcal/mol.

The first theoretical work on Se is reported by Salzner and Scheyer[23] in 1990 in which different conformations of $CH(SH)_2(SeH)$, $CH_2(SeH)$ are studied computationally to mimic Pinto's 2-[(4-substituted)phenylseleno]-1,3-dithiane. They predict hyperconjugation to be unimportant in Se systems since S, C, and Se have similar electronegativities. They based their prediction on the theoretical investigations that showed negative hyperconjugation to diminish when 2nd row elements are involved owing to their decreasing electronegativity and their lower π-donor ability. Contrary to Pinto's result, Se's charge is calculated to be positive and it is stated that Se acts as π donor and S as σ acceptor rather than S acting as π donor and Se as σ acceptor.

A later study was reported by Schleyer and Salzner[24]. They examined the origin of generalized anomeric effect in methanediol and its S, Se and Te derivatives by ab initio calculations through the MP2 level and by NBO analyses of the Hartree-Fock wavefunctions. According to their calculations, gauche preferences of SH, SeH and TeH substituents decrease but do not vanish and orbital interactions are less effective with lower row elements.

In 1994, Pinto et.al[25] published an ab initio study of the torsional g-g, g-a, a-a, a-g behavior of $HSCH_2SH$, $HSCH_2SeH$, $HSeCH_2SeH$, $HTeCH_2TeH$, $HSCH_2TeH$ and $HSeCH_2TeH$ with different levels of basis sets. They examined bond lengths, bond angles, dihedrals and energies of model molecules. They found out that at all levels of computation the total energies of dithiomethane, dieselenomethane and selenothiomethane increase in the order g-g, g-a and a-a. They reported the existence of anomeric effect by methyl stabilization energies obtained from isodesmic reactions and they concluded that the anomeric interactions do exist for third row elements.

3.2 Methodology

Most molecules of interest can adopt more than one conformation. The conformations of a molecule are typically present in different amounts. Stable conformations of a molecule correspond to local minima in the potential energy surface.

To perform a conformational search it is necessary to determine those minimum energy conformations that are believed to contribute to the overall conformational partition function.

In this study the conformational equilibrium of 2-[(4-substituted-phenyl)seleno]-1,3-dithiane with H, F, Cl, CH_3, CF_3, NO_2, OCH_3, $N(CH_3)_2$ substituents is investigated computationally with both the semiempirical PM3 method and ab initio HF/6-31G* basis set. The conformational search was done by SPARTAN 4.0 program[35], with the semi-emprical PM3 method. The global minima and second best points of PM3 optimizations have been reoptimized by GEOMOS program[36] using PM3. For all the substituents the global minimum located by SPARTAN is found to be the global minimum with GEOMOS. The optimum structures in the gas phase are then optimized in solvent with the package GEOMOS program using the ellipsodial cavity model.

The H, NO_2, CH_3, OCH_3 and $N(CH_3)_2$ 2-[(4-substituted-phenyl)seleno]-1,3-dithiane PM3 minimum energy conformers are further optimized with HF/6-31G* basis sets using GAUSSIAN 94[37] program. In cases where equatorial conformers did not give similar geometries with PM3, these conformers are frozen at the PM3 geometry and their energies and dipoles are calculated in order to make a comparison with the global minima of HF.

The thermodynamic properties of all the compounds studied are calculated with PM3 and HF/6-31G* to verify that the minimum energy conformers are real minima and compared with experimental ΔG values.

The calculated energies are compared to find out the minimum energy conformer. The bond lengths, bond angles and dihedral angles are checked to look for evidence for the anomeric effect. Thermodynamic properties (ΔH, ΔG, ΔS) for conformational equilibrium reactions are used to find out a trend between the position of the substituents (axial versus equatorial) and its nature. The ultimate aim is to compare the computational results with the experimental values and to select the computational method of interest.

The structures for the global minima located with PM3 have been optimized in polar medium (ε=3.0) using the package GEOMOS in which the cavity is ellipsoidal and the solvent is treated as a dielectric continuum.

Structures optimized with HF/6-31G* are analyzed in toluene (ε=2.4). The volume of the molecule is calculated and used as in solvent where the shape of the cavity is the Onsager's spherical cavity. Additionally, for $N(CH_3)_2$, CH_3 and OCH_3 substituents, the calculations are done with different dielectric constants such as 4.7($CHCl_3$), 8.9(CH_2Cl_2), and 20.5(acetone).

3.3 Conformational Analysis of 2-[(4-substituted-phenyl)seleno]-1,3-dithiane in Gas Phase

3.3.1 Dithiane

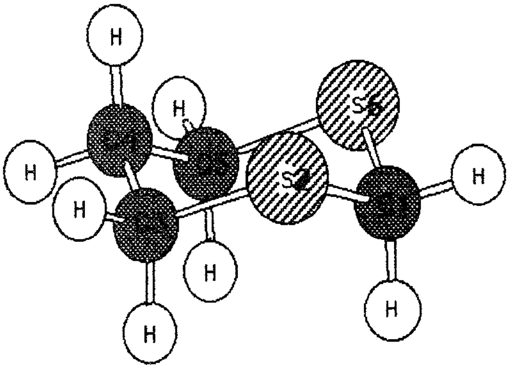


Figure 3.1 Molecular structure of dithiane

It has been reported previously that dithiane ring exists in chair form[38] (Figure 3.1). PM3 and HF/6-31G* calculations have shown that the geometry predicted by PM3 is approximately identical to the HF geometry. When the geometrical parameters of dithiane are considered (Table 3.1 and Table 3.2), it is observed that the values are close to each other except that chair geometry of dithiane is less strained with PM3 than with HF/6-31G*; e.g. S2-C3 bond is 1.822 Å in PM3 and 1.817 Å in HF calculations.

Table 3.1 The bond lengths (Å), bond angles (°), dihedral angles (°) of dithiane (PM3)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.809	S2C1H7	106.74	C3S2C1H7	169.28
C1S6	1.809	S2C1H8	109.89	C3S2C1H8	-76.12
C1H7	1.107	S6C1H7	106.74	C5S6C1H8	76.12
C1H8	1.105	S6C1H8	109.89	C5S6C1H7	-169.29
S2C3	1.822	S2C1S6	116.88		
S6C5	1.822	C3S2C1	101.99		
		C5S6C1	101.99		

Table 3.2 The bond lengths (Å), bond angles (°), dihedral angles (°) of dithiane (HF/6-31G*)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.810	S2C1H7	106.74	C3S2C1H7	177.51
C1S6	1.810	S2C1H8	109.89	C3S2C1H8	-65.70
C1H7	1.081	S6C1H7	106.74	C5S6C1H7	182.49
C1H8	1.082	S6C1H8	109.89	C5S6C1H8	65.72
S2C3	1.817	S2C1S6	116.88		
S6C5	1.817	C3S2C1	101.99		
		C5S6C1	101.99		

3.3.2 2-Selenol-1,3-dithiane

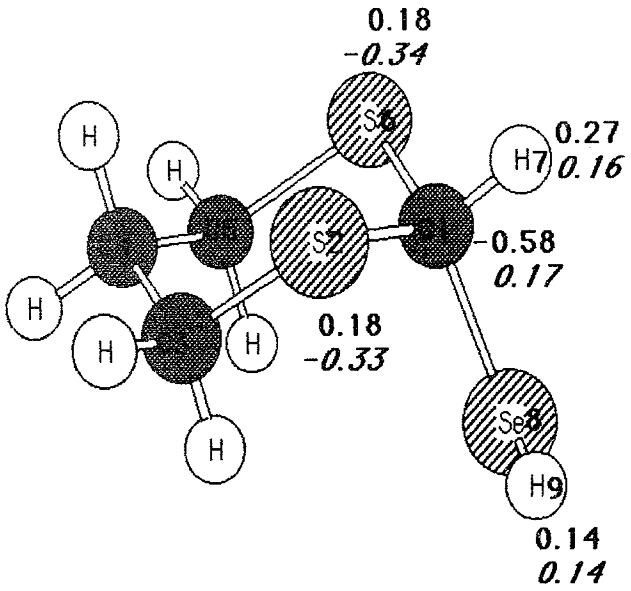

0.18
-0.34
S6
H
H
H7
0.27
0.16
S2
-0.58
0.17
H
0.18
-0.33
H
H
H
Se8
H9
0.14
0.14

Figure 3.2 Atomic charges in axial 2-selenol-1,3-dithiane (**1a**). (Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

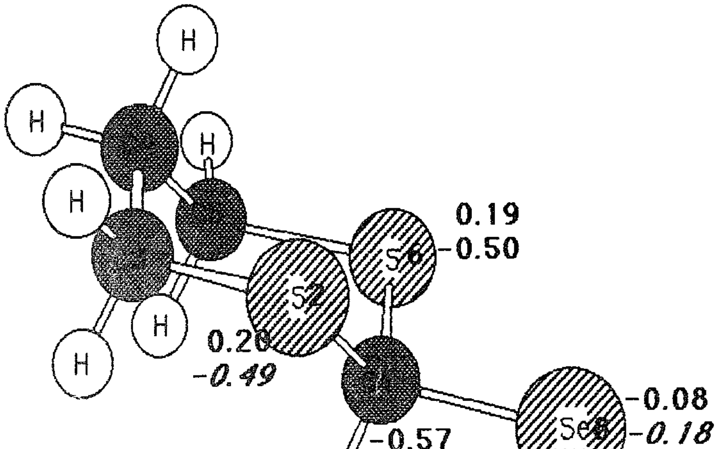

H
H
H
H
0.19
-0.50
S6
S2
H
H
0.2
-0.49
-0.08
-0.18
Se8
-0.57
0.43
H7
0.24
0.03
H9
0.14
0.13

Figure 3.3 Atomic charges in equatorial 2-selonol-1,3-dithiane (**1e**) (Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

Axial and equatorial forms of 2-selenol-1,3-dithiane are fully optimized both with PM3 and with HF/6-31G*. The axial conformer (Figure 3.2) is found to be lower in energy than the equatorial (Figure 3.3) by 3.68 kcal/mole in PM3 and by 2.69 kcal/mole in HF (Table 3.36). The axial conformers have the smaller dipole 2.72 for axial, 3.11 for equatorial in PM3 and 2.27 for axial, 3.55 for equatorial in HF.

In the axial conformer, **1a**, the C1-S6 bond lengthens and the C1-S2 bond shortens when compared with the equatorial, **1e**. Although the same trend is observed in HF calculations, the bond distance variations are more pronounced with PM3. The C1-Se bond is one of the bonds that is effected by the axial preference. It increases by 0.016 Å in PM3 (Tables 3.3 and 3.4) in the axial conformer and with HF calculation this increase is of 0.013 Å (Tables 3.5 and 3.6). Variations in bond angles are observed, too. In **1a**, the S-C1-Se angle corresponding to the shortening bond increases. This increase is more pronounced with PM3 where it is by 16°. The same kind of observation is not valid for the other S-C1-Se bond angle which is nearly kept constant in the axial and the equatorial conformers in HF calculations. In the double-bond/no-bond model, the bond adjacent to the atom which donates its electrons and its neighbor shortens, whereas bond lengthening occurs in the σ^* acceptor. The observation of S2-C1 bond shortening and C1-Se bond lengthening is consistent with this model. The widening of S-C1-Se bond angle is an indication of a transition between sp^3 (S-C-Se ≈ 109.5°) to sp^2 (S-C-Se ≈ 120°) which also verifies the double-bond/no-bond model explanation.

In the axial form of the molecule there are two endo anomeric interactions between $n_S \text{-->} \sigma^*_{C1-Se}$ regardless of the orientation of Se since the lone pairs of sulfur are antiperiplanar to the C1-Se bond. The exo anomeric effect is observed in the local minimum of the axial conformer, where the H7-C1-Se-H9 dihedral is -75.38° (Table 3.3) in PM3 and 73.5° (Table 3.5) in HF. On the other hand if H7 and H9 were eclipsed, the lone pairs of selenium would be below the dithiane ring and this would be the cause of unfavorable electrostatic interactions between selenium's and sulfurs' lone pairs. and would be sterically unfavored. The ΔH_f of this structure is 5.66 kcal/mole and dipole is 1.54 D. If H7 and H9 were anti to each other in **1a**, there would be two additional anomeric effects of exocyclic type, however the short distance between H9 with syn-axial hydrogens would cause unfavorable electrostatic effect and an increased energy. For the global minimum energy conformer, **1a**, there are two endo and one exo anomeric interactions. Endo interactions, as stated before are from $n_{S} \dashrightarrow \sigma^{*}_{C1-Se}$ and exo is acting from n_{Se} to σ^{*}_{C1-S6}. The lengthening in C2-S6 bond in the axial conformer by PM3 suggests that the exo is more dominant than the endo anomeric effect in the S6-C1-Se fragment.

In the equatorial minimum energy conformer, the H7-C1-Se-H9 dihedral is zero by PM3 and -31.48° by HF indicating that H7 and H9 are eclipsed (Tables 3.4 and 3.6 respectively). If H7 and H9 were anti to each other, (ΔH_f=7.44 kcal/mole and μ=3.28 D) the conformation would be more polar and unfavored energetically. The lone pairs on Se would than be parallel to the lone pairs of S and this would increase the dipole of the conformer. If H7-C1-Se-H9 dihedral were in between 180° and 0°, then repulsions would be taking place between sulfur's and selenium's lone pairs.

In both HF and PM3 results, Se has more negative charge, suggesting that electrons are migrating towards Se, an indication of delocalization verifying the double-bond/no-bond model explanation which seems to be acting on this molecule.

Table 3.3 The bond lengths (Å), bond angles (°), dihedral angles (°) of axial 2-selenol-1,3-dithiane (PM3).

BOND DISTANCES		BOND ANGLES		DIHEDRALS	
C1S2	1.792	S2C1Se8	90.60	S2C1Se8H9	172.73
C1S6	1.767	S6C1Se8	112.52	S6C1Se8H9	48.04
C1Se8	1.938	S2C1H7	109.64	H7C1Se8H9	-75.58
Se8H9	1.476	S6C1H7	108.78	C5S6C1H7	-176.17
C1H7	1.109	S2C1S6	121.44	C3S2C1H7	172.54
S2C3	1.830	C3S2C1	102.14	C5S6C1Se8	57.93
S6C5	1.823	C5S6C1	100.73	C3S2C1Se8	-72.78
		C1Se8H9	104.66		
		H7C1Se8	112.92		

Table 3.4. The bond length (Å), bond angle (°), dihedral angles (°) of equatorial 2-selenol-1,3-dithiane (PM3).

BOND DISTANCES		BOND ANGLES		DIHEDRALS	
C1S2	1.783	S2C1Se8	96.16	S2C1Se8H9	120.20
C1S6	1.783	S6C1Se8	96.17	S6C1Se8H9	-120.30
C1Se8	1.922	S2C1H7	113.78	H7C1Se8H9	0.05
Se8H9	1.480	S6C1H7	113.78	C5S6C1H7	76.12
C1H7	1.103	S2C1S6	118.37	C3S2C1H7	-76.12
S2C3	1.825	C3S2C1	102.94	C5S6C1Se8	-169.29
S6C5	1.825	C5S6C1	102.94	C3S2C1Se8	169.28
		C1Se8H9	101.12		
		H7C1Se8	115.99		

Table 3.5. The bond lengths (Å), bond angles (°), dihedral angles (°) of axial 2-selenol-1,3-dithiane (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.808	S2C1Se8	114.10	S2C1Se8H9	-43.47
C1S6	1.813	S6C1Se8	108.97	S6C1Se8H9	187.20
C1Se8	1.972	S2C1H7	106.00	H7C1Se8H9	73.50
Se8H9	1.468	S6C1H7	105.53	C5S6C1H7	186.65
C1H7	1.078	S2C1S6	114.48	C3S2C1H7	174.39
S2C3	1.815	C3S2C1	99.23		
S6C5	1.820	C5S6C1	100.57		
		C1Se8H9	95.88		
		H7C1Se8	107.10		

Table 3.6. The bond lengths (Å), bond angles (°), dihedral angles (°) of equatorial 2-selenol-1,3-dithiane (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.811	S2C1Se8	108.30	S2C1Se8H9	87.05
C1S6	1.814	S6C1Se8	107.19	S6C1Se8H9	-148.25
C1Se8	1.959	S2C1H7	110.06	H7C1Se8H9	-31.48
Se8H9	1.467	S6C1H7	109.04	C5S6C1H7	67.81
C1H7	1.079	S2C1S6	115.05	C3S2C1H7	-66.31
S2C3	1.818	C3S2C1	100.33		
S6C5	1.819	C5S6C1	100.09		
		C1Se8H9	94.32		
		H7C1Se8	106.86		

3.3 3 2-(phenylseleno)-1,3-dithiane

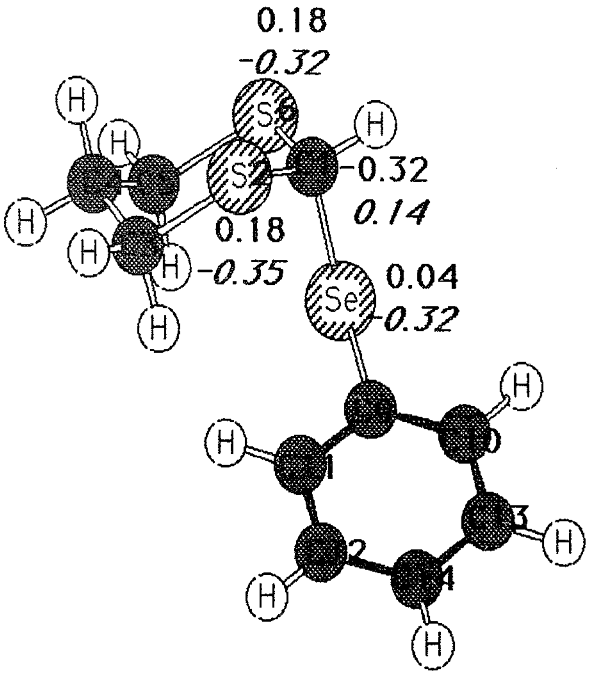

0.18
-0.32
S6
S2
-0.32
0.14
0.18
-0.35
Se
0.04
-0.32
H
10
11
13
12
14

Figure 3.4 Atomic charges in axial 2-(phenyl-seleno)-1,3-dithiane (**2a**)
(Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

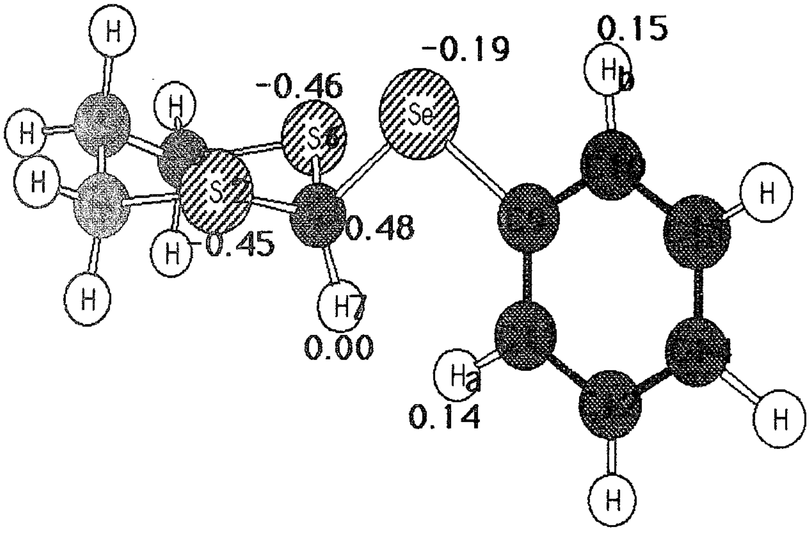

-0.19
0.15
Hb
-0.46
Se
S6
S2
-0.45
0.48
H7
0.00
Ha
0.14
H

Figure 3.5 Atomic charges in equatorial 2-(phenyl-seleno)-1,3-dithiane (**2e'**) (PM3)

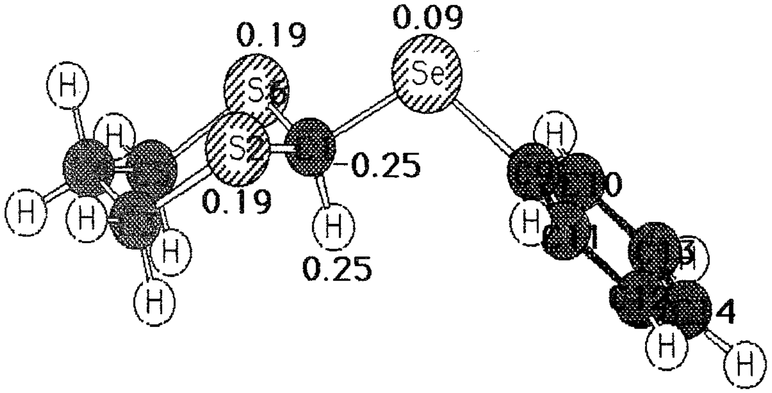


Figure 3.6 Atomic charges in equatorial 2-(phenylseleno)-1,3-dithiane (**2e**) (HF/6-31G*)

The axial conformer of 2-(phenyl-seleno)-1,3-dithiane is calculated to be more stable than the equatorial conformer with both ab initio and semi empiric methods. The energy difference is 3.46 kcal/mole with PM3 and 0.79 kcal/mole with HF/6-31G* (Table 3.40a and 3.40b). Compound **2a** is less polar (1.89 D) than **2e** (3.73 D) (Table 3.40a and 3.40b).

In HF and PM3, the C1-S2 and C1-S6 bond distances are equal to each other in the equatorial conformer but the ones predicted by HF are longer than PM3 (Tables 3.8 and 3.10). In **2a** those bond distances are no longer equal in PM3: C1-S2 shortens and C1-S6 bond lengthens but those variations are not significant with HF. The C1-Se bond is one of the bonds that is effected by the axial preference of the arylseleno moiety. This bond lengthens by 0.028 Å in PM3 (Table 3.7) and by 0.014 Å in HF (Table 3.9). The bond lengths calculated by HF are longer than PM3.

In the equatorial case, with both methods, S2-C1-Se and S6-C1-Se bond angles are equal to each other whereas this symmetry is disturbed in the axial case. The value of the angle corresponding to the short C1-S bond is the one that increases. The widening of the S-C1-Se angle is more pronounced with PM3. This is an indication of partial sp^2 character gained by C1 as a result of double-bond/no-bond delocalization.

The orientation of the phenyl group with respect to dithiane is the same with HF and PM3 for **2a**. The axial conformer has two endo anomeric interactions operating from n_S to σ^*_{C1-Se} regardless of the orientation of the phenyl ring because one of the lone pairs of S is antiperiplanar to C1-Se bond.

If the H7-C1-Se-C9 dihedral were 0° then there would be two endo anomeric interactions from n_S to σ^*_{C1-Se}, however in this geometry two of the lone pairs of Se would be below the dithiane ring and H7 would have unfavorable interactions with the p orbitals of phenyl. If the H7-C1-Se-C9 dihedral were around 120°, meaning that C9 is eclipsed with S2, the geometry would be unfavorable because the phenyl would be very close to dithiane ring, nearly below it, causing unfavorable interactions between the p orbitals on the phenyl and the dithiane ring. The anti form of H7 and C9 is certainly unfavored since the phenyl group would be positioned under the dithiane ring and this would be sterically and electrostaticly an unfavored geometry.

Actually the global minimum located by PM3 and HF is when the H7-C1-Se-C9 dihedral is 80°. At this position, there are two endo anomeric interactions between S2-C1, Se-C9 and S6-C1, Se-C9 segments and an exo anomeric interaction between Se-C2, S2-C3 segments. The exocyclic stabilization is between the C1-S6 bond that is antiperiplanar to one of the lone pairs of Se. These three interactions may be playing a dominant role in the stabilization of this geometry more than in any other orientation.

The phenyl ring is oriented perpendicular to the C1-Se bond in **2a**. If it were coplanar with the C1-Se bond, then the dipole moment would be lower but it would not be favored since H7 and Ha distances would be very close to each other.

In **2e**, HF locates the phenyl ring perpendicular to the H7-C1 bond (Figure 3.6) whereas it is coplanar with C1-Se in PM3 (Figure 3.5). The coplanar arrangement of the phenyl ring in the equatorial conformer is favored by its small dipole in comparison to the conformation where it is perpendicular to H7-C1. In **2e'** (Figure 3.5), the p orbitals on phenyl are not in the same direction with the axial lone pairs of S so the dipole moment is decreased. The coplanar arrangement causes a 1.783 Å distance between H7 and Ha and they are sterically repulsive. However the charges on H7 and Ha are 0.00 and 0.14 respectively and the repulsive forces caused by such small charges is low. PM3 thus has minimized steric hinderence of H7 and Ha and this may be the reason for having conformer **2e'** with the smaller dipole located at the minimum of potential energy surface.

The preference of the coplanar arrangement in **2e'** by PM3 may be enhanced by a Se···H-C interaction. The distance between Se and Ha is 2.81 Å in **2e'** shorter than the distance stated by Tomado[39] for a significant Se···H-C electrostatic, long range interaction. The charges of Se and and H are opposite in sign in PM3 so a Se···H-C long range interaction may be likely to occur but in HF this interaction may be reduced since Se and H7 have same charges.

For HF calculations, in the equatorial minimum energy conformer the phenyl ring is perpendicular to the C1-H7 bond. Even when **2e'** geometry is given as the starting geometry for HF calculations, the perpendicular arrangement of the phenyl ring is preferred. We have tried to freeze the C1-Se-C9-C10 dihedral to 0°, where the ring would be coplanar with H7-C1. With HF/6-31G*, the energy was higher than in the perpendicular arrangement but as in PM3, the dipole of the coplanar orientation was lower than in the perpendicular case. The frozen molecule orients such that the H7-C1-Se-C9 dihedral is -34.6° to minimize steric hinderence caused by the coplanar arrangement. We deduce that in this molecule PM3 calculations try to minimize dipolar interactions more than HF and steric factors become more important in HF.

In **2e** and **2e'**, the H7-C1-Se-C9 dihedral is zero, resulting in an eclipsed orientation. If this segment had an anti structure, the phenyl ring would be over the dithiane ring and this would be sterically and electrostaticly unfavored. The phenyl ring would be very close to dithiane, if the dihedral were between 0° and 180° and a repulsion between sulfur' lone pairs and phenyl ring's p orbitals would occur. Although the eclipsed conformer causes an increase in dipole moment, it seems that the destabilizing factors operating with other possible geometries stated above are more dominant than the high dipole moment of the eclipsed geometry.

Consideration of charges indicates that Se is more negative in its axial conformers than in its equatorial conformer, indicating that electron migration is occurring towards Se in the **2a**. This is consistent with the double-bond/no-bond model explanation of the anomeric effect as verified by bond length and bond angle variations.

Table 3.7. The bond lengths (Å), bond angles(°),dihedral angles (°) of axial 2-(phenylseleno)-1,3-dithiane (PM3).

BOND DISTANCES		BOND ANGLES		DIHEDRALS	
C1S2	1.763	S2C1Se8	116.28	S2C1Se8C9	-167.99
C1S6	1.797	S6C1Se8	88.15	S6C1Se8C9	-44.35
C1Se8	1.956	S2C1H7	110.16	H7C1Se8C9	81.02
Se8C9	1.878	S6C1H7	108.66	C1Se8C9C10	83.78
C1H7	1.108	S2C1S6	120.72		
S2C3	1.823	C3S2C1	100.75		
S6C5	1.832	C5S6C1	102.08		
		C1Se8C9	110.63		
		H7C1Se8	111.56		

Table 3.8. The bond lengths (Å), bond angles(°) and dihedral angles (°) of equatorial 2-(phenylseleno)-1,3-dithiane (PM3).

BOND DISTANCES		BOND ANGLES		DIHEDRALS	
C1S2	1.782	S2C1Se8	97.22	S2C1Se8C9	120.03
C1S6	1.782	S6C1Se8	97.29	S6C1Se8C9	-119.62
C1Se8	1.928	S2C1H7	113.95	H7C1Se8C9	0.23
Se8C9	1.889	S6C1H7	113.96	C1Se8C9C10	179.69
C1H7	1.112	S2C1S6	118.77		
S2C3	1.824	C3S2C1	102.90		
S6C5	1.824	C5S6C1	102.89		
		C1Se8C9	104.16		
		H7C1Se8	112.77		

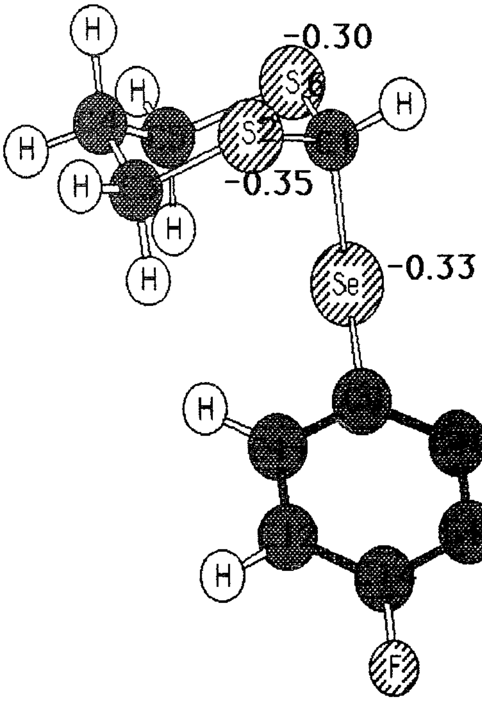
Table 3.9. The bond lengths (Å), bond angles(°) and dihedral angles (°) of axial 2-(phenylseleno)-1,3-dithiane (HF/6-31G*)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.810	S2C1Se8	114.29	S2C1Se8C9	-65.99
C1S6	1.813	S6C1Se8	109.51	S6C1Se8C9	164.76
C1Se8	1.974	S2C1H7	105.93	H7C1Se8C9	50.86
Se8C9	1.911	S6C1H7	105.58	C1Se8C9C10	-84.02
C1H7	1.079	S2C1S6	113.97		
S2C3	1.814	C3S2C1	99.73		
S6C5	1.820	C5S6C1	100.66		
		C1Se8C9	99.44		
		H7C1Se8	106.87		

Table 3.10. The bond lengths (Å), bond angles(°) and dihedral angles (°) of equatorial 2-(phenylseleno)-1,3-dithiane (HF/6-31G*)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.812	S2C1Se8	107.59	S2C1Se8C9	-117.76
C1S6	1.812	S6C1Se8	107.56	S6C1Se8C9	117.70
C1Se8	1.960	S2C1H7	109.77	H7C1Se8C9	0.00
Se8C9	1.912	S6C1H7	109.77	C1Se8C9C10	90.66
C1H7	1.078	S2C1S6	115.12		
S2C3	1.818	C3S2C1	100.67		
S6C5	1.818	C5S6C1	100.68		
		C1Se8C9	98.12		
		H7C1Se8	106.66		

3.3.4. 2-[(4-fluorophenyl)seleno]-1,3-dithiane and 2-[(4-chlorophenyl)seleno]-1,3-dithiane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S6
H
S2
H
H
H
-0.35
H
H
Se
-0.33
H
H
H
H
F

Figure 3.7 Atomic charges of axial 2-[(4-fluorophenyl)seleno]-1,3-dithiane (3a) (PM3)

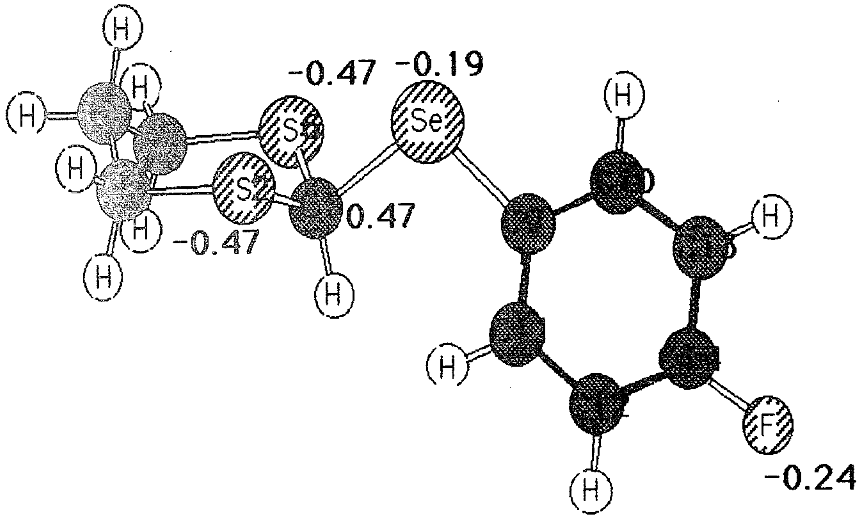
H
H
H
-0.47
-0.19
S6
Se
H
H
S2
0.47
H
H
-0.47
H
H
H
F
H
-0.24

Figure 3.8 Atomic charges of equatorial 2-[(4-fluorophenyl)seleno]-1,3-dithiane (3e) (PM3)

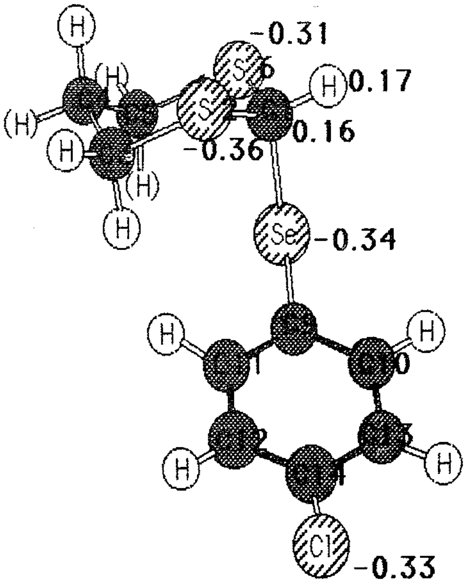
-0.31
0.17
0.16
-0.36
Se
-0.34
C10
C13
C14
Cl
-0.33

Figure 3.9 Atomic charges of axial 2-[(4-chlorophenyl)seleno]-1,3-dithiane (4a) (PM3)

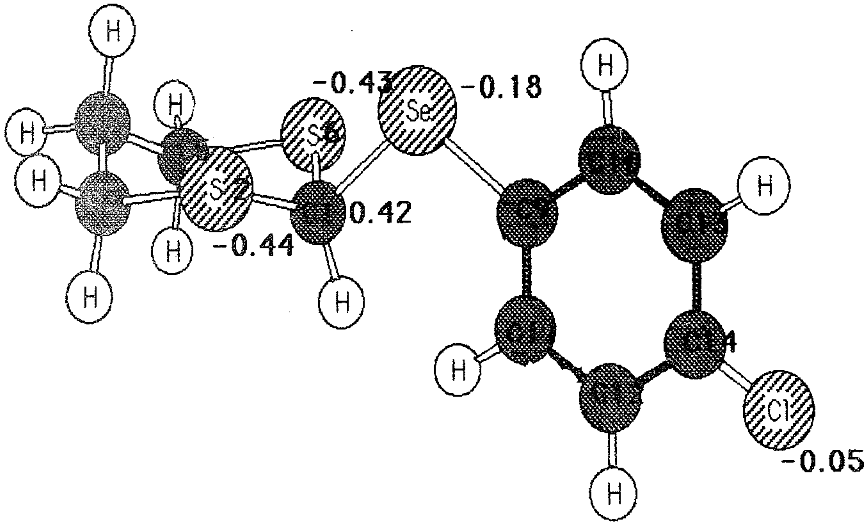
-0.43
Se
-0.18
S6
S2
0.42
-0.44
C14
Cl
-0.05

Figure 3.10 Atomic charges of equatorial 2-[(4-chlorophenyl)seleno]-1,3-dithiane (4e) (PM3)

Since the geometries corresponding to the global minima and the nature of substituents are the same for F and Cl substituted 2-(phenylseleno)-1,3-dithiane, they will be discussed together with PM3. The axial conformers of F and Cl substituted 2-(phenylseleno)-1,3-dithianes are found to be more stable than the equatorial ones by 3.78 kcal/mole and 3.62 kcal/mole (Table 3.37 and Table 3.38) respectively. The axial conformers have also the smaller dipole moment in both cases, 2.83.D in **3a** versus 3.47 in **3e** for F and 2.66 D in **4a** versus 3.08 D in **4e** in Cl(Table3.37 and Table 3.38).

In **3e** and **4e**, the C_1-S bond lengths are equal but this equivalence is disturbed in **3a** and **4a**. In the axial conformers, **3a** and **4a,** the C1-S2 bond length shortens from 1.781 Å to 1.762 Å and C1-S6 bond lengthens from 1.781 Å to 1.796 Å. This bond length variation may be interpreted as a consequence of double-bond/no-bond model which proposes C1-S2 to shorten and C1-Se bond to lengthen due to delocalization of electrons from n_S to σ^*_{C1-Se}. Lengthening of C1-S6 bonds may be attributed to exo anomeric effect, which may be acting from n_{Se} to σ^* of C1-S6 bond as in **2a**. The bond angles S2-C1-Se and S6-C1-Se are equal to each other in the equatorial conformer, but in **3a** and **4a** the S2-C1-Se angle increases by 19°. The increase in the S2-C1-Se angle is meaningful since the S2-C1 bond has double bond character and the angle has partial sp^2 character.

In **3a** and **4a** the H7-C1-Se-C9 dihedral is around 80° and the phenyl ring is perpendicular to the C1-Se bond. This orientation allows two endo and one exo anomeric interactions as discussed in **2a** (section 3.3.3).

In the equatorial minimum energy conformers, **3e** and **4e**, the phenyl ring is coplanar to H7-C1 as in the unsubstituted case. The orientation of the Se-C9 bond in the equatorial minimum energy geometry is again eclipsed with the C1-H7 bond (Figure 3.8 and 3.10). Details about the other unfavorable positions are the same as in hydrogen,discussed in section 3.3.3.

In the axial conformers, **3a** and **4a**, the negative charge on Se is higher than in the equatorial in Cl and F substituted molecules and this may be interpreted as electron delocalization from S to Se.

Table 3.11. Bond distances (Å), bond angles (°) and dihedral angles (°) of axial 2-[(4-fluorophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.762	S2C1Se8	116.36	S2C1Se8C9	-44.26
C1S6	1.796	S6C1Se8	87.80	S6C1Se8C9	-168.02
C1Se8	1.957	S2C1H7	108.65	H7C1Se8C9	81.13
Se8C9	1.877	S6C1H7	110.18	C1Se8C9C10	-101.30
C1H7	1.108	S2C1S6	120.97		
S2C3	1.823	C3S2C1	100.86		
S6C5	1.832	C5S6C1	102.16		
		C1Se8C9	110.71		
		H7C1Se8	111.53		

Table 3.12. Bond distances (Å), bond angles (°) and dihedrals angles (°) of equatorial 2-[(4-fluorophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.782	S2C1Se8	97.02	S2C1Se8C9	-119.96
C1S6	1.781	S6C1Se8	97.09	S6C1Se8C9	119.74
C1Se8	1.929	S2C1H7	114.04	H7C1Se8C9	-0.12
Se8C9	1.887	S6C1H7	114.02	C1Se8C9C10	179.99
C1H7	1.111	S2C1S6	118.81		
S2C3	1.824	C3S2C1	102.98		
S6C5	1.824	C5S6C1	102.96		
		C1Se8C9	104.29		
		H7C1Se8	112.90		

Table 3.13. Bond distances (Å), bond angles (°) and dihedral angles (°) of axial 2-[(4-chlorophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.762	S2C1Se8	116.35	S2C1Se8C9	-44.25
C1S6	1.797	S6C1Se8	87.89	S6C1Se8C9	-167.98
C1Se8	1.957	S2C1H7	108.65	H7C1Se8C9	81.14
Se8C9	1.878	S6C1H7	110.18	C1Se8C9C10	-101.24
C1H7	1.108	S2C1S6	120.91		
S2C3	1.823	C3S2C1	100.83		
S6C5	1.832	C5S6C1	102.13		
		C1Se8C9	110.70		
		H7C1Se8	111.52		

Table 3.14. Bond distances (Å), bond angles (°) and dihedral angles (°) of equatorial 2-[(4-chlorophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.781	S2C1Se8	97.08	S2C1Se8C9	-119.77
C1S6	1.781	S6C1Se8	97.16	S6C1Se8C9	119.91
C1Se8	1.929	S2C1H7	114.02	H7C1Se8C9	0.08
Se8C9	1.888	S6C1H7	114.00	C1Se8C9C10	-179.84
C1H7	1.111	S2C1S6	118.80		
S2C3	1.824	C3S2C1	102.96		
S6C5	1.824	C5S6C1	102.94		
	1.685	C1Se8C9	104.24		
		H7C1Se8	112.85		

3.3.5 2-[(4-methylphenyl)seleno]-1,3-dithiane

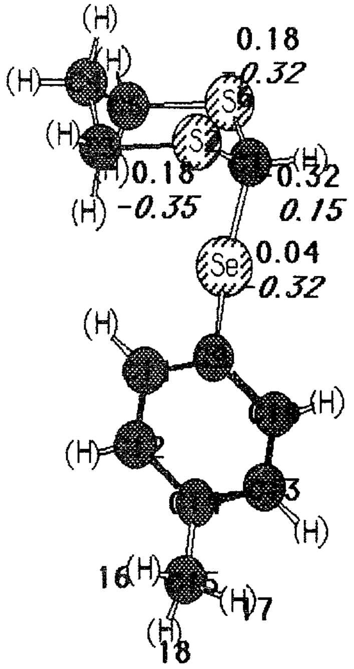
0.18
-0.32
S6
S2
0.18
-0.35
0.32
0.15
Se
0.04
-0.32
(H)
12
13
16
15
17
18

Figure 3.11 Atomic charges in axial 2-[(4-methylphenyl)seleno]-1,3-dithiane (**5a**)

Numbers in italic are from PM3, plain numbers from HF/6-31G*

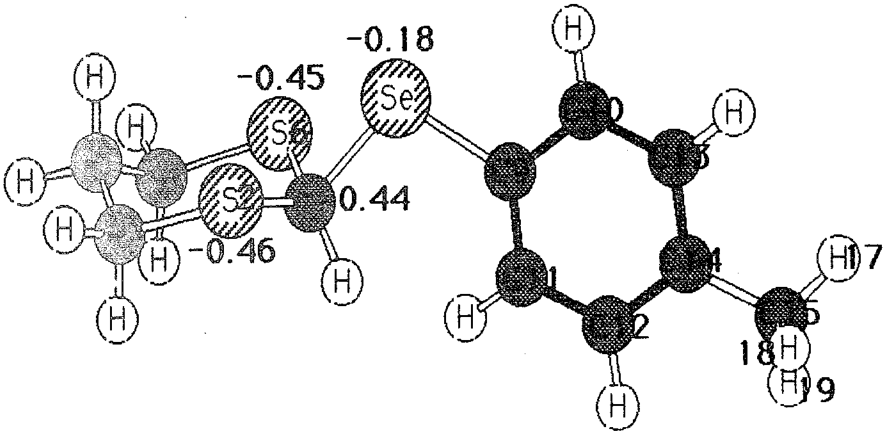
-0.18
Se
-0.45
S6
S2
0.44
-0.46
H
10
13
11
12
14
15
17
18
19

Figure 3.12 Atomic charges in equatorial 2-[(4-methylphenyl)seleno]-1,3-dithiane (**5e**) (PM3)

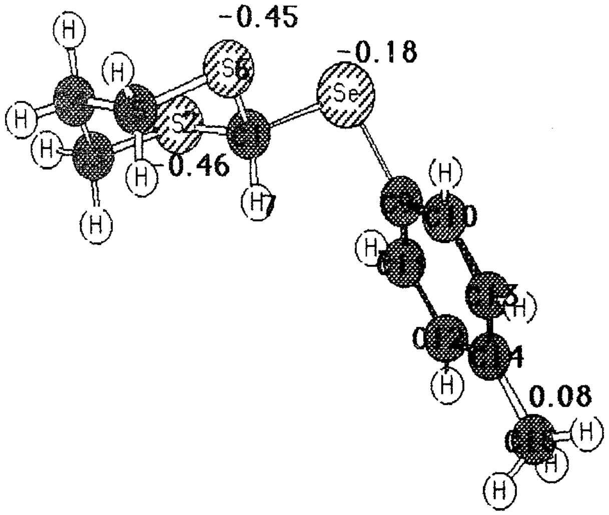

Figure 3.13 Atomic charges in 2-[(4-methylphenyl)seleno]-1,3-dithiane (**5e'**) (HF/6-31G*)

The axial form of CH_3 substituted 2-(phenyl-seleno)-1,3-dithiane is more stable than the equatorial by 3.55 kcal/mole in PM3 and 0.80 kcal/mole in HF (Table 3.41a and Table 3.41b). **5a** has lower dipole moment than the equatorial, **5e'**, with HF/6-31G* however the reverse is true with PM3.

The C1-S2 and C1-S6 bonds in the the equatorial conformer, are equal but in **5a**, the C1-S6 bond is longer and the C1-S2 bond is shorter than the same bonds in the equatorial. With HF these bond changes are not as significant as in PM3. C1-Se bond length also changes from equatorial to axial. C1-Se bond length increases by 0.028 Å with PM3 and 0.014 Å with HF in **5a**. The S-C1-Se bond angle also changes in **5a**. The S-C1-Se angle corresponding to shortening of the S-C bond gets wider than in the equatorial conformer. The changes in terms of geometrical parameters are consistent with double-bond/no-model.

The geometry of the axial conformer allows two endo and one exo anomeric effect as in **2a**. In **5a**, the geometry is similar to the geometries of other substituents. Two endocyclic and one exocyclic anomeric effect may act in **5a** as confirmed by bond length and angle changes.

In equatorial case, the geometries of HF and PM3 are different from each other in terms of orientation of phenyl ring. With PM3, **5e,** the ring is coplanar with H7-C1 whereas it is perpendicular to H7-C1 in HF (Figure 3.12). The same steric and electrostatic factors influencing the orientation of phenyl ring in **2e** operate with the CH_3 substituent, as well.

The hydrogens of the CH_3 substituent group are staggered with the carbon atom of the phenyl so that their interaction is minimized.

Table 3.15. The bond lengths (Å), bond angles (°), dihedral angles (°) of CH_3 substituted axial2-(phenylseleno)-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.763	S2C1Se8	116.23	S2C1Se8C9	-44.24
C1S6	1.797	S6C1Se8	88.22	S6C1Se8C9	-167.87
C1Se8	1.956	S2C1H7	108.67	H7C1Se8C9	81.12
Se8C9	1.877	S6C1H7	110.16	C1Se8C9C10	-99.90
C1H7	1.108	S2C1S6	120.67	C12C14C15H16	-29.42
S2C3	1.823	C3S2C1	100.73	C12C14C15H17	-150.24
S6C5	1.832	C5S6C1	102.07	C12C14C15H18	90.19
		C1Se8C9	110.58		
		H7C1Se8	111.58		

Table 3.16. The bond lengths (Å), bond angles (°), dihedral angles (°) of equatorial CH_3 substituted 2-(phenylseleno)-1,3-dithiane (PM3)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.781	S2C1Se8	97.27	S2C1Se8C9	119.97
C1S6	1.781	S6C1Se8	97.30	S6C1Se8C9	-119.68
C1Se8	1.928	S2C1H7	113.94	H7C1Se8C9	0.16
Se8C9	1.888	S6C1H7	113.95	C1Se8C9C10	179.57
C1H7	1.115	S2C1S6	118.76	C12C14C15H16	147.96
S2C3	1.825	C3S2C1	102.88	C12C14C15H17	-92.49
S6C5	1.824	C5S6C1	102.88	C12C14C15H18	27.19
	1.486	C1Se8C9	104.13		
		H7C1Se8	112.75		

Table 3.17. The bond lengths (Å), bond angles (°), dihedral angles (°) of CH_3 substituted axial 2-(phenylseleno)-1,3-dithiane (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.810	S2C1Se8	114.29	S2C1Se8C9	-66.07
C1S6	1.814	S6C1Se8	109.57	S6C1Se8C9	164.68
C1Se8	1.974	S2C1H7	105.93	H7C1Se8C9	50.76
Se8C9	1.909	S6C1H7	105.93	C1Se8C9C10	-84.39
C1H7	1.079	S2C1S6	113.93	C13C14C15H16	30.37
S2C3	1.814	C3S2C1	99.72	C13C14C15H17	151.01
S6C5	1.819	C5S6C1	100.67	C13C14C15H18	-89.80
		C1Se8C9	99.53		
		H7C1Se8	106.85		

Table 3.18. The bond lengths (Å), bond angles (°), dihedral angles (°) of CH_3 substituted equatorial 2-(phenylseleno)-1,3-dithiane (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.812	S2C1Se8	107.60	S2C1Se8C9	-117.73
C1S6	1.812	S6C1Se8	107.60	S6C1Se8C9	117.69
C1Se8	1.960	S2C1H7	109.77	H7C1Se8C9	0.00
Se8C9	1.910	S6C1H7	109.77	C1Se8C9C10	90.83
C1H7	1.078	S2C1S6	115.10	C12C14C15H16	-31.94
S2C3	1.818	C3S2C1	100.70	C12C14C15H17	87.71
S6C5	1.818	C5S6C1	100.70	C12C14C15H18	-152.58
		C1Se8C9	98.24		
		H7C1Se8	106.63		

3.3.6 2-[(4-trifluoromethylphenyl)seleno]-1,3-dithiane

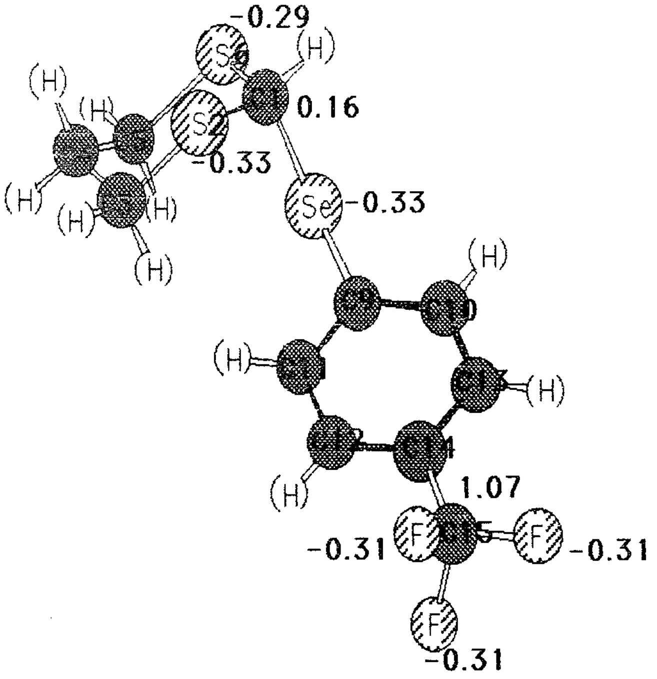
-0.29
S6
(H)
C1
0.16
S2
-0.33
Se
-0.33
C9
C10
C11
C13
C12
C14
1.07
-0.31
F
C15
F
-0.31
F
-0.31

Figure 3.14. Atomic charges of axial 2-[(4-trifluoromethyl-phenyl)seleno]-1,3-dithiane (**6a**) (PM3).

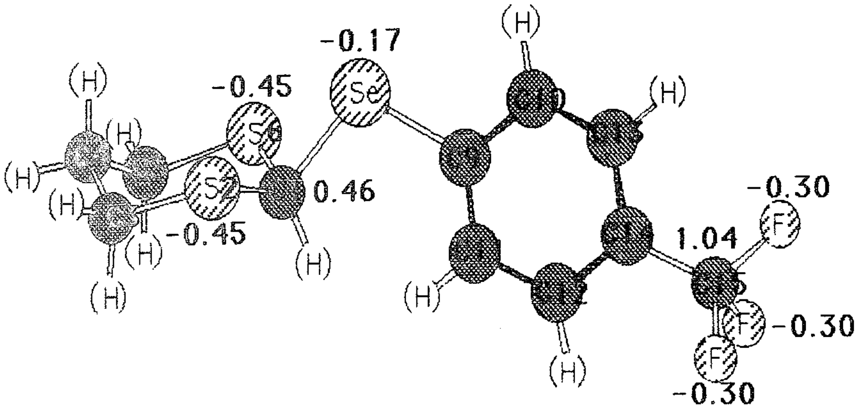
-0.17
Se
(H)
-0.45
S6
C10
C13
(H)
S2
0.46
C9
-0.30
F
-0.45
C14
1.04
C15
F
-0.30
C12
F
-0.30

Figure 3.15. Atomic charges of equatorial 2-[(4-trifluoromethyl-phenyl)seleno]-1,3-dithiane (**6e**) (PM3).

PM3 calculations for CF_3 substituted 2-(phenylseleno)-1,3-dithiane has shown to have significant anomeric effects for this molecule. The axial form, **6a** is 3.39 kcal/mole more stable than **6e** (Table 3.39).

In the equatorial conformer, the C1-S2 and C1-S6 bond lengths are equal to each other whereas this behavior is not observed in the axial conformer. C1-S2 shortens by 0.02 Å and C1-S6 Å bond lengthens by 0.015 Å in **6a**. The increase in the bond length of C1-Se 0.029 Å is an expected result as is the C-S bond length variation and as in **2a** discussed in section 3.3.3, may be explained by the double-bond/no-bond model.

The S-C1-Se bond angles show the same trend as in the other substituents. In **6a**, a widening of 20° is observed for the S2-C1-Se angle.

In **6a**, the 81° of the H7-C1-Se-C9 dihedral provides the suitable geometry for two endo and one exo anomeric interaction to occur from n_S to σ^*_{C1-Se} and from n_{Se} to σ^*_{C1-S6} respectively as explained in case of **2a**, (section 3.3.3). The perpendicular orientation of the phenyl ring in **6a** eliminates the steric repulsion of H7 and Hb as discussed in **2a**.

In the **6e**, the phenyl ring is coplanar with the C1-H7 bond although there is a distance of 1.787 Å between H7 and Hb. This position is favored in terms of the dipole moment since p orbitals of the phenyl ring are perpendicular to axial lone pairs of the sulfurs'. There may be a long range interaction as in H case favoring the coplanar arrangement. The steric interaction between H7 and Hb is not significant because of their small charges (-0.02 and 0.15) respectively and this in turn reduces the steric interference caused by the coplanar arrangement.

As explained earlier for H, compound **6e** has the H7-C1-Se-C9 dihedral equal to 0° which is favored by the destabilizing factors operating with other values of the dihedral. Although there may be unfavorable interactions between sulfurs' and selenium's lone pairs and an increased dipole moment, it is favored over other geometries where other destabilizing interactions are present as in **2a**.

The charge on Se is more negative in the axial than in the equatorial conformers indicating a migration of electrons towards Se.

Table 3.19. Bond distances (Å), bond angles (°) and dihedral angles (°) in axial 2-[(4-trifluoromethyl-phenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		BOND ANGLES		DIHEDRALS	
C1S2	1.761	S2C1Se8	116.60	S2C1Se8C9	-43.75
C1S6	1.796	S6C1Se8	87.35	S6C1Se8C9	-167.67
C1Se8	1.958	S2C1H7	116.60	H7C1Se8C9	81.67
Se8C9	1.882	S6C1H7	110.19	C1Se8C9C10	-103.22
C1H7	1.109	S2C1S6	121.27	C12C14C15F16	2.13
S2C3	1.822	C3S2C1	100.99	C12C14C15F17	-122.68
S6C5	1.832	C5S6C1	102.22	C12C14C15F18	-118.39
		C1Se8C9	110.97		
		H7C1Se8	111.38		

Table 3.20. Bond distances (Å), bond angles (°) and dihedral angles (°) in equatorial 2-[(4-trifluoromethyl-phenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		BOND ANGLES		DIHEDRALS	
C1S2	1.781	S2C1Se8	96.88	S2C1Se8C9	119.90
C1S6	1.781	S6C1Se8	96.84	S6C1Se8C9	-119.80
C1Se8	1.929	S2C1H7	114.10	H7C1Se8C9	0.06
Se8C9	1.887	S6C1H7	114.12	C1Se8C9C10	179.65
C1H7	1.111	S2C1S6	118.89	C12C14C15F16	-178.94
S2C3	1.824	C3S2C1	103.07	C12C14C15F17	-58.40
S6C5	1.824	C5S6C1	103.08	C12C14C15F18	60.53
		C1Se8C9	104.34		
		H7C1Se8	112.95		

3.3.7 2-[(4-nitrophenyl)seleno]-1,3-dithiane

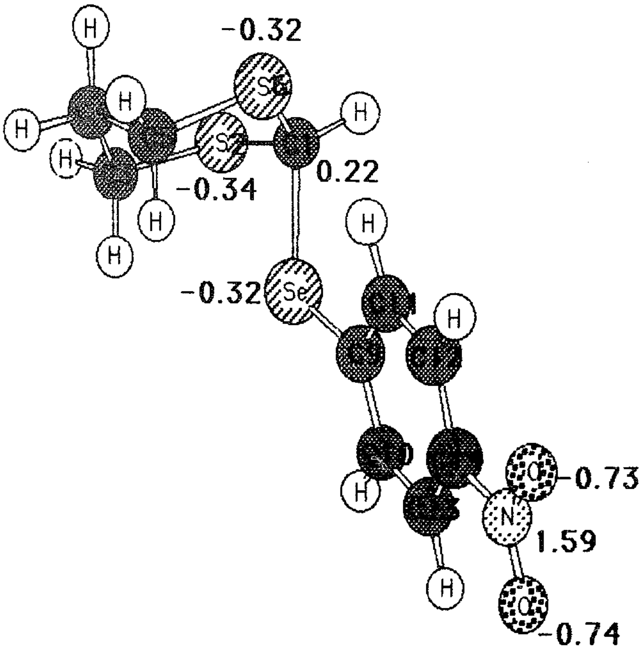
-0.32
S6
H
S2
0.22
-0.34
-0.32
Se
O
-0.73
N
1.59
O
-0.74

Figure 3.16 Atomic charges in axial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (7a') (PM3)

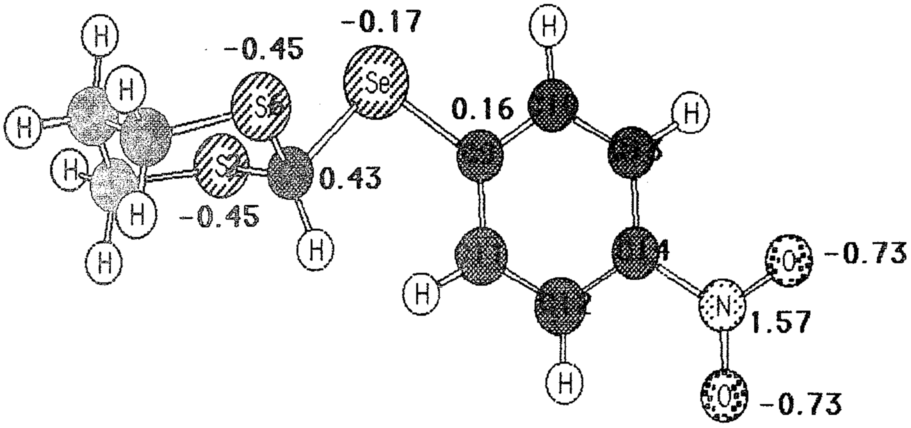
-0.17
-0.45
Se
S6
0.16
S2
0.43
-0.45
H
O
-0.73
N
1.57
O
-0.73

Figure 3.17 Atomic charges in equatorial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (7e') (PM3)

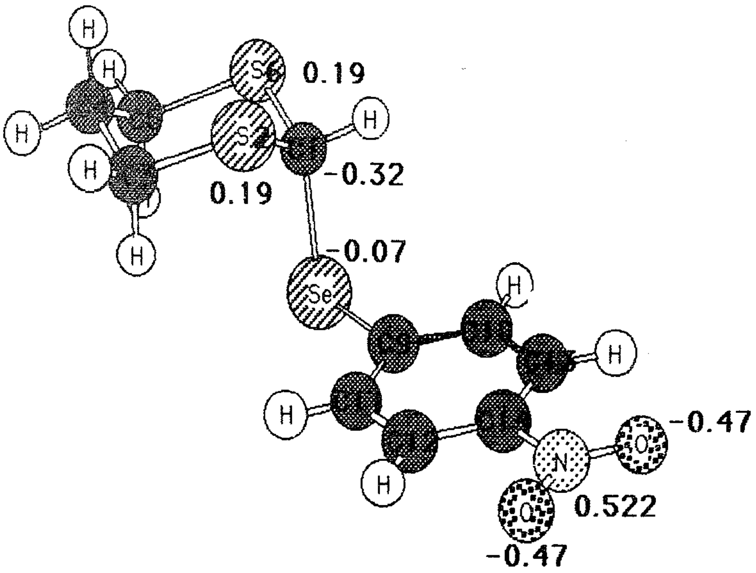
S6 0.19
0.19
-0.32
-0.07
Se
-0.47
N
O
0.522
-0.47

Figure 3.18 Atomic charges in axial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (7a) (HF/6-31G*)

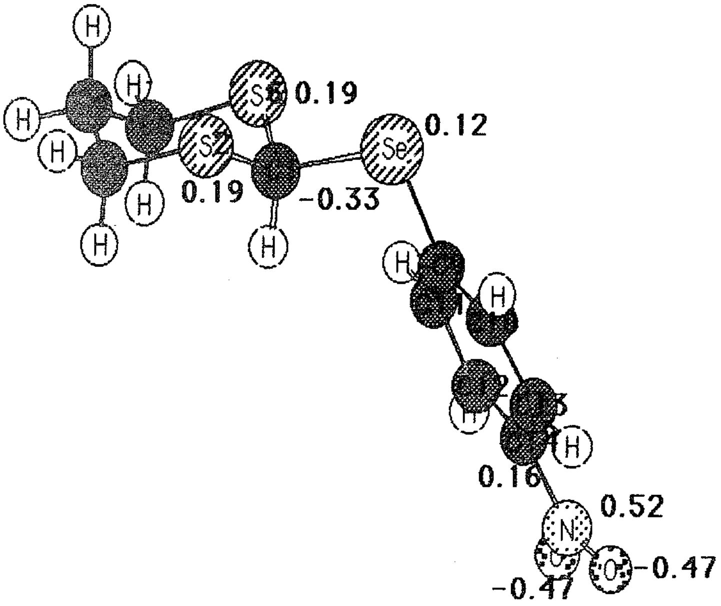
S6 0.19
0.12
Se
0.19
-0.33
0.16
N
0.52
-0.47
-0.47

Figure 3.19. Atomic charges in equatorial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (7e) (HF/6-31G*)

The minimum energy axial conformer of NO_2 substituted 2-(phenylseleno)-1,3-dithiane is 3.29 kcal/mole more stable than the equatorial with PM3 and this value is 1.06 kcal/mole with HF/6-31G* (Table 3.42a and Table 3.42b). Contrary to other substituents, the dipole moment is higher in axial conformer with both methods.

When the bond distances of C1-S2 and C1-S6 bonds are compared in the equatorial conformers, it is observed that the C1-S distances are equal to each other in PM3 and in HF. In axial conformer the C1-S2 distance shortens by 0.018 Å and the the C1-S6 bond lengthens by 0.014 Å with PM3 (Table 3.21 and 3.22). With exact calculations there is a very small amount of shortening in the C1-S2 bond and the C1-S6 bond is nearly constant in the axial and the equatorial conformers. The C1-Se bond is also affected by the axial preference of the molecule and an increase of 0.027 Å with PM3 and 0.015 Å with HF/6-31G* is observed. The angle corresponding to the shortening of the C1-S bond gets wider in the axial conformer with both methods.

The geometry of minimum energy axial conformer, as previously stated for hydrogen, has two endo and one exo anomeric interactions, explained in terms of double-bond/no-bond model. The bond lengths and bond angle variations stated above verify this explanation.

In the axial conformer, PM3 calculations locate the phenyl ring coplanar with C1-Se bond whereas in HF, it is perpendicular to the C1-Se bond. NO_2 is a strong electron-withdrawing group so it may be that there is a delocalization between the electrons of the NO_2, the π electrons of phenyl and the lone pairs of Se. When Se and the phenyl ring are coplanar, the overlap between the lone pairs on Se and π electrons of the phenyl ring can be delocalized. When NO_2 lies in their plane, delocalization is expected to increase

With PM3, in equatorial conformer, the phenyl ring is again coplanar with the H7-C1 bond as in axial case and it is perpendicular according to HF/6-31G*. Additionally, there may be the same kind of stabilization acting on the molecule as in axial PM3 geometry. NO_2's lone pairs may be contributing in a delocalization of lone pairs of Se and p orbitals of phenyl ring which is easier when phenyl is oriented coplanar H7-C1.

NO_2 substituent is in the same plane with the phenyl group which allows stabilizing interactions between the phenyl group and lone pairs of NO_2.

As discussed so far for the other molecules, the negative charge on Se in the axial position confirms the presence of anomeric effect.

Table 3.21. The bond lengths (Å), bond angles (°) and dihedral angles (°) of axial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.763	S2C1Se8	116.51	S2C1Se8C9	-52.48
C1S6	1.795	S6C1Se8	87.59	S6C1Se8C9	-177.00
C1Se8	1.957	S2C1H7	108.42	H7C1Se8C9	72.48
Se8C9	1.885	S6C1H7	109.98	C1Se8C9C10	-163.36
C1H7	1.109	S2C1S6	121.70	C13C14N15016	-1.59
S2C3	1.822	C3S2C1	101.46	C13C14N15017	-178.55
S6C5	1.831	C5S6C1	102.57		
		C1Se8C9	112.83		
		H7C1Se8	111.26		

Table 3.22 The bond lengths (Å), bond angles (°) and dihedral angles (°) of equatorial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.781	S2C1Se8	96.69	S2C1Se8C9	119.64
C1S6	1.781	S6C1Se8	96.65	S6C1Se8C9	-120.08
C1Se8	1.930	S2C1H7	114.18	H7C1Se8C9	-0.23
Se8C9	1.886	S6C1H7	114.18	C1Se8C9C10	0.29
C1H7	1.111	S2C1S6	118.95	C13C14N15016	1.58
S2C3	1.824	C3S2C1	103.16	C13C14N15017	-178.47
S6C5	1.824	C5S6C1	103.16		
		C1Se8C9	104.42		
		H7C1Se8	113.03		

Table 3.23. The bond lengths (Å), bond angles (°) and dihedral angles (°) of axial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.808	S2C1Se8	114.27	S2C1Se8C9	-63.84
C1S6	1.812	S6C1Se8	109.03	S6C1Se8C9	166.79
C1Se8	1.976	S2C1H7	106.03	H7C1Se8C9	53.17
Se8C9	1.914	S6C1H7	105.51	C1Se8C9C10	-82.35
C1H7	1.079	S2C1S6	114.37	C13C14N15016	0.65
S2C3	1.815	C3S2C1	99.89	C13C14N15017	180.65
S6C5	1.820	C5S6C1	100.83		
		C1Se8C9	99.24		
		H7C1Se8	106.95		

Table 3.24. The bond lengths (Å), bond angles (°) and dihedral angles (°) of equatorial 2-[(4-nitrophenyl)seleno]-1,3-dithiane (HF/6-31G*).

BOND DISTANCE		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.812	S2C1Se8	107.33	S2C1Se8C9	117.75
C1S6	1.812	S6C1Se8	107.33	S6C1Se8C9	-117.73
C1Se8	1.961	S2C1H7	109.80	H7C1Se8C9	0.00
Se8C9	1.914	S6C1H7	109.80	C1Se8C9C10	90.63
C1H7	1.079	S2C1S6	115.32	C13C14N15016	-0.16
S2C3	1.819	C3S2C1	100.57	C13C14N15017	180.07
S6C5	1.819	C5S6C1	100.57		
		C1Se8C9	97.66		
		H7C1Se8	106.88		

3.3.8 2-[(4-methoxyphenyl)seleno]-1,3-dithiane

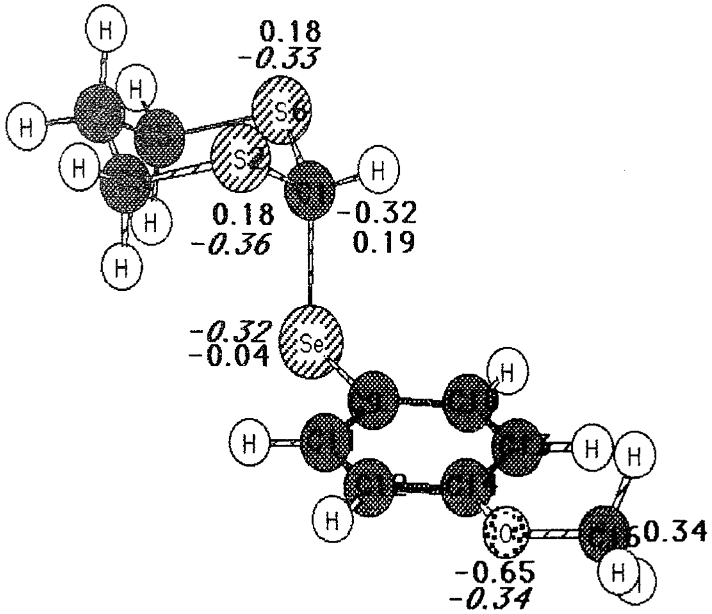
0.18
-0.33
S6
S2
0.18
-0.36
-0.32
0.19
-0.32
-0.04
Se
O
0.34
-0.65
-0.34

Figure 3.20 Atomic charges of axial 2-[(4-methoxyphenyl)seleno]-1,3-dithiane (**8a**)
(Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

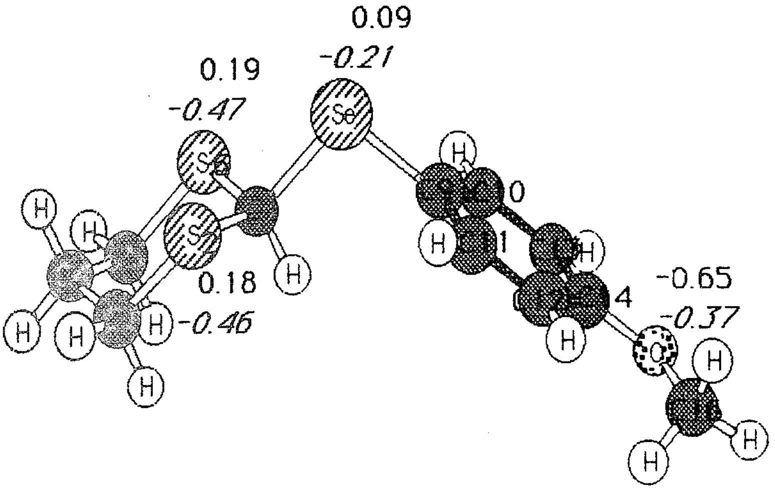
0.09
-0.21
0.19
-0.47
Se
S6
S2
0.18
-0.46
-0.65
-0.37
O

Figure 3.21 Atomic charges of equatorial 2 -[(4-methoxyphenyl)seleno]-1,3-dithiane (**8e**)
(Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

The axial conformer of OCH_3 substituted 2-(phenyl-seleno)-1,3-dithiane is 3.66 kcal/mole more stable than equatorial with PM3 and with HF/6-31G* this stabilization is 0.78 kcal/mole. The axial conformer, **8a**, has lower dipole moment than **8e** in PM3 and HF/6-31G* calculations (Table 3.43a and Table 3.43b).

C1-S2 and C1-S6 bond lengths are equal in the equatorial conformer in HF/6-31G* and PM3 . In the axial conformer the C1-S6 bond shortens by 0.019 Å and the C1-S2 bond lengthens by 0.016 Å in PM3. In HF/6-31G* the shortening and lengthenings are not as significant as in PM3. The C1-Se bond distances increased by 0.026 Å from equatorial to axial conformer in PM3 whereas this increase is by only 0.014 Å in HF. Increase in C1-Se and C1-S bond lengths is consistent with the double-bond/no-bond model as in H case.

In the minimum energy axial conformer, the endo anomeric effect with migration of electrons from n_S to σ^*_{C1-Se} are present. The C1-Se bond shorthens and C1-S6 lengthens as a result of exo anomeric effect. In the axial conformer, C1-S6 and C1-Se bonds elongate showing that in C1-S6 the exo anomeric effect and in the C1-Se bond the endo anomeric effect are more dominant. The phenyl ring is perpendicular to C1-Se bond as observed with other substituents. All other geometries of the axial conformer are either sterically or electrostatically unfavored, as discussed in **2a** (section 3.3.3).

In the equatorial case, the HF/6-31G* and PM3 calculations locate the phenyl ring perpendicular to H7-C1 bond contrary to PM3 results of H, F, Cl, CF_3, CH_3, NO_2 substituents. Electrons of the methoxy group may be moving towards Se, causing the Se-C9 bond to get shorter than in other substituents in the equatorial position. In this geometry if the phenyl ring were coplanar with H7-C1 bond, then the distance between H7 and the hydrogen of C10 would be 1.678 Å, causing repulsive interaction.

The carbon atom of the methoxy group, C16 is coplanar with the phenyl group both with HF/6-31G* and PM3 and this may cause oxygen's lone pairs to have larger overlap with the p orbital of the phenyl group. The hydrogens of methoxy group position themselves so as to minimize steric interactions with phenyl hydrogens.

The more negative charge on Se in axial conformer is another verification of electron migration towards Se.

Table 3.25. Bond lengths (Å), bond angles (°), and dihedral angles (°) of axial 2-[(4-methoxyphenyl)seleno-1,3-dithane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.797	S2C1Se8	116.20	S2C1Se8C9	-44.33
C1S6	1.763	S6C1Se8	88.23	S6C1Se8C9	-167.94
C1Se8	1.956	S2C1H7	108.68	H7C1Se8C9	81.04
Se8C9	1.873	S6C1H7	110.16	C1Se8C9C10	-99.47
C1H7	1.108	S2C1S6	120.67	C13C14015C16	0.55
S2C3	1.832	C3S2C1	100.73	C14015C16H17	61.85
S6C5	1.823	C5S6C1	102.08	C14015C16H18	-62.32
		C1Se8C9	110.53	C14015C16H19	179.77
		H7C1Se8	111.60		

Table 3.26. Bond lengths (Å), bond angles (°), and dihedral angles (°) of equatorial 2-[(4-methoxyphenyl)seleno-1,3-dithane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.782	S2C1Se8	96.48	S2C1Se8C9	119.60
C1S6	1.782	S6C1Se8	95.99	S6C1Se8C9	-121.02
C1Se8	1.930	S2C1H7	114.02	H7C1Se8C9	-0.85
Se8C9	1.877	S6C1H7	114.03	C1Se8C9C10	85.85
C1H7	1.103	S2C1S6	118.23	C12C14015C16	-1.01
S2C3	1.825	C3S2C1	102.71	C14015C16H17	-61.60
S6C5	1.825	C5S6C1	102.75	C14015C16H18	-179.54
		C1Se8C9	104.37	C14015C16H19	62.58
		H7C1Se8	113.30		

Table 3.27 Bond lengths (Å), bond angles (°), and dihedral angles (°) axial 2-[(4-methoxyphenyl)seleno-1,3-dithane (HF/6-31G*)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.810	S2C1Se8	114.32	S2C1Se8C9	-65.73
C1S6	1.814	S6C1Se8	109.57	S6C1Se8C9	164.99
C1Se8	1.974	S2C1H7	105.91	H7C1Se8C9	51.07
Se8C9	1.905	S6C1H7	105.59	C1Se8C9C10	-85.76
C1H7	1.079	S2C1S6	113.93	C13C14015C16	0.41
S2C3	1.814	C3S2C1	99.72	C14015C16H17	60.99
S6C5	1.820	C5S6C1	100.66	C14015C16H18	-61.49
		C1Se8C9	99.75	C14015C16H19	179.75
		H7C1Se8	106.82		

Table 3.28. Bond lengths (Å), bond angles (°), and dihedral angles (°) of equatorial 2-[(4-methoxyphenyl)seleno-1,3-dithane (HF/6-31G*)

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.812	S2C1Se8	107.63	S2C1Se8C9	115.47
C1S6	1.812	S6C1Se8	107.62	S6C1Se8C9	-119.95
C1Se8	1.960	S2C1H7	109.79	H7C1Se8C9	-2.26
Se8C9	1.906	S6C1H7	109.76	C1Se8C9C10	-91.90
C1H7	1.078	S2C1S6	115.08	C12C14015C16	-0.47
S2C3	1.818	C3S2C1	100.73	C14015C16H17	-61.00
S6C5	1.818	C5S6C1	100.70	C14015C16H18	-179.75
		C1Se8C9	98.50	C14015C16H19	61.00
		H7C1Se8	106.58		

3.3.9. 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane

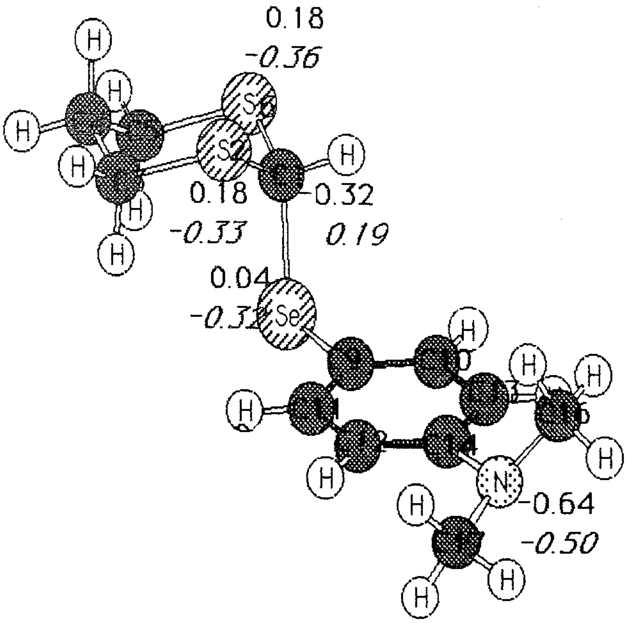
0.18
-0.36
S6
S2
0.18
-0.33
-0.32
0.19
0.04
-0.32
Se
N
-0.64
-0.50
H

Figure 3.22 Atomic charges of axial 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (**9a**)
(Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

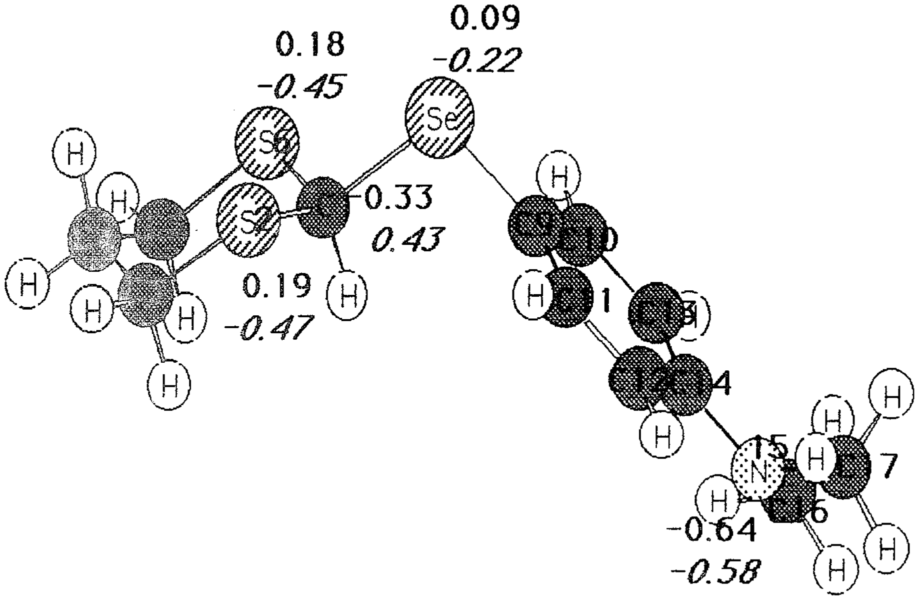
0.09
-0.22
0.18
-0.45
Se
S6
S2
-0.33
0.43
0.19
-0.47
C9
C10
C11
C13
C12
C14
N
15
C16
17
-0.64
-0.58
H

Figure 3.23 Atomic charges of equatorial 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (**9e**)
(Numbers in italics are from PM3, plain numbers are from HF/6-31G*)

The axial $N(CH_3)_2$ substituted 2-(phenyl-seleno)-1,3-dithiane (Figure 3.22) is calculated to be more stable than the equatorial by 3.49 kcal/mole in PM3 and by 0.80 kcal/mole in HF/6-31G* (Table 3.44a and Table 3.44b). The dipole moment of **9a** is higher than **9e** in PM3 but in HF the reverse is observed (Table 3.44a and Table 3.44b).

In **9a**, C1-S6 bond gets shorter than in **9e** by 0.018 Å in PM3 but in HF this result is not as pronounced as in PM3 (Table 3.29 and Table 3.31). C1-S6 bond in PM3 lengthens by 0.015 Å in **9a**. With HF this lengthening is not as pronounced as with PM3. The C1-Se bond distance also increases in **9a** in comparison to **9e** both with PM3 and with HF. This lengthening shows that the endo anomeric effect is more dominant in the C1-Se bond than the exo. As in other compounds, the S-C-Se angle corresponding to the shortening S-C bond increases in parallel to the results of double-bond/no-bond model of anomeric effect

In the geometry of global minima, **9a**, the H7-C1-Se-C9 dihedral is around 80° as observed with other substituents. This geometry causes two endocyclic and one exocyclic anomeric interactions to occur between n_S to σ^*_{C1-Se} and n_{Se} to σ^*_{C1-S}, respectively. The bond length and bond angle changes in the axial compound confirms the exo and endo anomeric effect explanations for this molecule.

In PM3 geometry of equatorial conformer, **9e**, the phenyl ring is perpendicular to the C1-Se bond although the coplanar arrangement of the phenyl ring was located as stationary point with all the substituents except OCH_3 and $N(CH_3)_2$. The nature of these two substituents suggests that an electron migration towards Se may be taking place. This effect is observed in the Se-C9 bond length. In methoxy and $N(CH_3)_2$ substituted molecule, the Se-C9 bond length is shorter than in other substituents. As discussed in the case of OCH_3, in section 3.3.8, the coplanar orientation causes a shorter distance between H7 and the hydrogen of C10. So this repulsion between hydrogens may be the cause for the preference of perpendicular arrangement with PM3.

In PM3, in **9a** and in **9e** the C13-C14-N15-C16 and C12-C14-N15-C17 dihedrals are 24 and -24 respectively. In this orientation the lone pairs of N are in the same plane with the p orbitals of phenyl but the hydrogens of amine are very close to phenyl ring's hydrogens (1.78 Å). In HF, the close distance of amine hydrogens with phenyl hydrogens is prevented by varying the stated dihedrals to -12° and -56°, respectively. In this geometry the lone pair of nitrogen is not in its best position to have maximum overlap but

HF prefers to minimize repulsions of hydrogens in favor of losing optimum geometry for conjugation

The more negative charge on Se in **9a** and the bond length changes in axial conformer confirms the double-bond/no-bond explanation of anomeric effect as in other substituents.

Table 3.29 The bond lengths (Å), bond angles (°) and dihedral angles (°) of axial 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.797	S2C1Se8	88.41	S2C1Se8C9	168.08
C1S6	1.764	S6C1Se8	116.15	S6C1Se8C9	44.55
C1Se8	1.955	S2C1H7	110.17	H7C1Se8C9	-80.82
Se8C9	1.872	S6C1H7	108.69	C1Se8C9C10	-84.63
C1H7	1.108	S2C1S6	120.53	C13C14N15C16	24.82
S2C3	1.832	C3S2C1	102.04	C13C14N15C17	160.80
S6C5	1.823	C5S6C1	100.68	C14N15C16H18	78.86
		C1Se8C9	110.48	C14N15C16H19	-42.38
		H7C1Se8	111.64	C14N15C16H20	-160.84
				C14N15C17H21	-79.03
				C14N15C17H22	160.68
				C14N15C17H23	42.22

Table 3.30 The bond lengths (Å), bond angles (°) and dihedral angles (°) of equatorial 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (PM3).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.782	S2C1Se8	96.29	S2C1Se8C9	120.34
C1S6	1.782	S6C1Se8	96.31	S6C1Se8C9	-120.28
C1Se8	1.930	S2C1H7	114.01	H7C1Se8C9	0.04
Se8C9	1.876	S6C1H7	114.01	C1Se8C9C10	91.98
C1H7	1.103	S2C1S6	118.21	C12C14N15C16	-160.81
S2C3	1.825	C3S2C1	102.69	C12C14N15C17	-24.43
S6C5	1.825	C5S6C1	102.69	C14N15C16H18	79.31
		C1Se8C9	104.32	C14N15C16H19	-160.42
		H7C1Se8	115.24	C14N15C16H20	-41.94
				C14N15C17H21	-79.28
				C14N15C17H22	160.44
				C14N15C17H23	41.97

Table 3.31. The bond lengths (Å), bond angles (°) and dihedral angles (°) of axial 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane. (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.811	S2C1Se8	114.27	S2C1Se8C9	-66.15
C1S6	1.814	S6C1Se8	109.66	S6C1Se8C9	164.62
C1Se8	1.974	S2C1H7	105.91	H7C1Se8C9	50.65
Se8C9	1.905	S6C1H7	105.58	C1Se8C9C10	-84.78
C1H7	1.079	S2C1S6	113.88	C13C14N15C16	57.01
S2C3	1.814	C3S2C1	99.70	C13C14N15C17	-166.62
S6C5	1.819	C5S6C1	100.64	C14N15C16H18	75.37
		C1Se8C9	99.64	C14N15C16H19	-45.92
		H7C1Se8	106.86	C14N15C16H20	-164.68
				C14N15C17H21	-72.2
				C14N15C17H22	49.92
				C14N15C17H23	167.91

Table 3.32. The bond lengths (Å), bond angles (°) and dihedral angles (°) of 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (HF/6-31G*).

BOND DISTANCES		**BOND ANGLES**		**DIHEDRALS**	
C1S2	1.812	S2C1Se8	107.64	S2C1Se8C9	118.62
C1S6	1.812	S6C1Se8	107.64	S6C1Se8C9	-116.80
C1Se8	1.961	S2C1H7	109.78	H7C1Se8C9	0.91
Se8C9	1.906	S6C1H7	109.78	C1Se8C9C10	91.01
C1H7	1.078	S2C1S6	115.06	C13C14N15C16	-12.66
S2C3	1.818	C3S2C1	100.71	C12C14N15C17	-56.56
S6C5	1.818	C5S6C1	100.72	C14N15C16H18	-75.24
		C1Se8C9	98.50	C14N15C16H19	45.92
		H7C1Se8	106.55	C14N15C16H20	164.70
				C14N15C17H21	72.28
				C14N15C17H22	-48.84
				C14N15C17H23	-166.82

3.4 Solvent Effect

As pointed out earlier, when a polar group is substituted at position 2 of 1,3-dithiane ring, if it is in the axial position, its dipole is opposite to the one created by the lone pairs on S. However, when the substituent is in the equatorial position , the dipoles of the substituent and the dithiane ring are additive. Thus, as expected, the equatorial conformers have higher dipole moments than the axial conformers except for NO_2 and $N(CH_3)_2$ because of the relative position of the substituent with respect to the phenyl ring. CH_3 substituted molecule has almost the same dipole moment in both conformations.

Table 3.33, displays the solvation energies calculated by taking differences in heats of formation in gaseous phase and polar medium as well as dipole moments with PM3. The negative sign of these values indicates that the heats of formation in solution are lower than the ones in vacuum; their magnitudes indicate the extent to which each compound is stabilized in polar medium. It is observed that the higher the dipole moment, the more the conformer is stabilized in polar medium, thus greater is the solvation energy. NO_2 is the most polar of the substituents and its stabilization energy is the highest. However, NO_2, CF_3 and OCH_3 substituted compounds do not satisfy the expected trend, it may be that quadrupole and octupole moments play also a role in their stabilization

In Table 3.34, the solvation energies for $N(CH_3)_2$, OCH_3 and CH_3 of 2-[(4-substituted-phenyl)seleno]-1,3-dithiane with HF/6-31G* single point calculations are listed in different dielectric constants. R is an indication of the radius of the spherical cavity. Solvation energy increases as the polarity of the medium increases and the more polar equatorial compounds are stabilized more in solution.

Table 3.33 The thermodynamic data of 2-(phenylseleno)-1,3-dithiane with PM3, in solvent

	$\Delta H_{fs}-\Delta H_{fg}$ (ax) (kcal/mole)	$\Delta H_{fs}-\Delta H_{fg}$ (eq) (kcal/mole)	μ_{ax} ε=3.0 (D)	μ_{eq} ε=3.0 (D)
NO_2	-6.73	- 8.18	8.25	7.98
CF_3	-3.91	-3.61	4.29	5.32
Cl	-3.04	-3.12	3.02	3.57
F	-3.27	-3.54	3.20	4.03
H	-2.86	-3.17	3.14	3.26
CH_3	-3.12	-3.13	3.30	3.21
OCH_3	-3.50	-3.00	2.29	3.59
$N(CH_3)_2$	-3.39	-2.90	4.02	2.97

Table 3.34 Thermodynamic data of $N(CH_3)_2$, OCH_3 and CH_3 substituted 2-(phenylseleno)-1,3-dithiane in solvent (HF/6-31G*)

	ΔE_{solv} (ax)	ΔE_{solv} (eq)	μ_{ax} (D)	μ_{eq} (D)	R_{ax} (Å)	R_{eq} (Å)
$N(CH_3)_2$					5.45	5.01
ε=2.4	-0.16	-0.50	2.88	4.46		
ε=4.7	-0.25	-0.77	3.01	4.70		
ε=8.9	-0.30	-0.94	3.09	4.85		
ε=20.5	-0.34	-1.06	3.15	4.96		
OCH_3					5.44	5.13
ε=2.4	-0.03	-0.49	1.41	4.56		
ε=4.7	-0.06	-0.76	1.48	4.74		
ε=8.9	-0.07	-0.91	1.52	4.84		
ε=20.5	-0.08	-1.03	1.56	4.92		
CH_3					5.47	4.87
ε=2.4	-0.13	-0.46	2.26	4.28		
ε=4.7	-0.20	-0.70	2.38	4.44		
ε=8.9	-0.25	-0.84	2.45	4.54		
ε=20.5	-0.28	-0.95	2.50	4.61		

$\Delta E_{solv}=E_{solvent}-E_{gas}$ (in kcal/mole)
R=radius of the molecule

3.5 Comparative Study of the Substituents

The PM3 and HF/6-31G* results of the conformational equilibrium of 2-[(4-substituted)pheny)]seleno-1,3-dithiane in the gas phase and in solvent are presented in Table 3.36-3.44(a,b).

ΔG^* values in PM3 are calculated by equation 3.1 at 298° K, with the data from Table 3.36-3.39.

$$\Delta G^* = (\Delta H_{fax} - \Delta H_{feq}) - T(S_{ax} - S_{eq}) \qquad (3.1)$$

$\Delta(\Delta H_f)$, defined as $\Delta H_{fax}-\Delta H_{feq}$, and ΔG^* values for the conformational equilibium reaction (axial ⇔ equatorial) have shown that the axial conformer is preferred over the equatorial one for all the substituents as in the experimental data presented by Pinto[18]. $\Delta(\Delta H_f)$ values do not show quantitative agreement since they are much larger than the experimental results, qualitative agreement for every substituent in terms of axial preference is quite satisfactory. ΔG^* seems to mimic the experimental results much better in gas phase, with $N(CH_3)_2$ susbstituents having the smallest axial preference and NO_2 the largest. CF_3 and F substituents do not fit within the expected trend. Variations of ΔG^* with temperature (300° K versus 143° K) have been investigated experimentally for all the substituents and it has been observed that differences between the results of two different temperatures are minor[18].

In solution, experimental results have shown an anomalous behavior. As the dielectric constant of the medium increases, the equatorial dominance is expected to increase and the axial-equatorial difference would be expected to decrease. The stabilization of the less polar conformer, as in OCH_3 case, is explained by Pinto in two different ways. He states that, rather than the more polar conformer, the conformer which has more polar double-bond/no-bond model will be stabilized more in polar solvents. His second explanation is based upon the expectations that the population of the conformer that has the smaller volume should increase (axial conformer) in the more polar solvent owing to high internal pressure exerted by the solvent. In the cavity model used in this study only electostatic interactions are considered, thus with this model the more polar conformer is expected to be stabilized more with this model the more polar conformer is expected to be stabilized more in polar medium. Regarding the dipoles, in most cases, the equatorial conformer is the more polar conformer in solvent and is stabilized more. (except CH_3, $N(CH_3)_2$ and OCH_3). For $N(CH_3)_2$ and CH_3 the axial conformer turns out to be the more polar compound and that conformer is stabilized more in polar medium(Table 3.33 and Table 3.34).

We were unable to calculate ΔS in solution thus ΔG values could not be compared. The conformational energy based upon $\Delta(\Delta H_f)$ only give a qualitative overview on the problem. Another discrepancy with the solvent effect calculations is the unrealistic definition of ellipsoidal cavity shape which may decrease the reliability of results.

Ab initio, HF/6-31G* calculations performed on five substituents (H, $N(CH_3)_2$, NO_2, CH_3, OCH_3) have given satisfactory results when compared to experimental ones (Table3.35).

Among the various ways of calculating conformational free energies one can state:

a) Taking the difference between total energies of the axial and the equatorial conformers, ΔE^a

b) Taking the difference between the sum of electronic and thermal energies of the axial and the equatorial conformers, ΔE^b

c) Taking the difference between the sum of electronic and thermal enthalpies of the axial and the equatorial conformers, ΔH^c

d) Taking the difference between the sum of electronic and free energies of axial and equatorial conformers, ΔG^d.

In the gas phase, differences between the sums of electronic and thermal enthalpies seem to agree almost quantitatively with the experimental results. Again with HF/6-31G*, NO_2 is the substituent that has highest axial preference and $N(CH_3)_2$ is the one that has the lowest axial preference as in the experimental data.

ΔG^d where entropy is included underestimates the axial preference although it reproduces the experimental trend. This may be because of the inadequacy of ab initio methods in calculating entropies. It is known that frequencies are not exactly evaluated by ab initio methods[40] and need to be scaled. The inadequacy in calculating entropies may be stemming from unscaled frequencies.

Since geometry optimization could not be carried out in solution, the only feasible comparison is the one based on the difference in total energies in solution in HF/6-31G*(Table 3.35b). As expected, the more polar equatorial conformer is stabilized more and the preference for axial decreases as dielectric constant of solvent increases. This is verified for every compound examined (Table 3.35b). Experimental data does not satisfy this trend in all cases (Table 3.35b) because of the specific solute-solvent interactions. Calculations are unable reproduce these interactions.

Table 3.35a Comparison of thermodynamic parameters with the experimental conformational free energies (eq<-->ax) with PM3 and HF/6-31G*.

	PM3 $\Delta(\Delta H_f)$ (ε=1)	PM3 $\Delta(\Delta H_f)$ (ε=3.0)	PM3 $\Delta G^{\#}$ (ε=1)	HF ΔE^b (ε=1)	HF ΔG^* (ε=1)	HF ΔE^a (ε=2.4)	ΔG_{exp} (ε=3.0)
$N(CH_3)_2$	-3.49	-3.99	-1.24	-0.68	0.02	-0.46	-0.47
OCH_3	-3.66	-4.16	-1.43	-0.66	0.03	-0.32	-0.59
CH_3	-3.54	-3.54	-2.07	-0.69	0.03	-0.48	-0.53
H	-3.46	-3.15	-2.02	-0.68	0.02	0.52	-0.57
F	-3.78	-3.53	-2.31	-		-	-0.64
Cl	-3.62	-3.54	-2.17	-		-	-0.69
CF_3	-3.39	-3.70	-2.02	-		-	-0.74
NO_2	-3.84	-2.41	-3.03	-0.96	-0.19	-1.42	-0.90

$\Delta(\Delta H_f) = \Delta H_{fax} - H_{feq}$

$\Delta G^{\#} = \Delta(\Delta H_f) - T\Delta S$ at T=298° K with PM3

ΔE^b = (Sum of electronic+thermal energy)$_{ax}$ - (Sum of electronic+thermal energy)$_{eq}$

$\Delta G^* = \Delta(\Delta H_f) - T\Delta S$ at T=298° K with HF/6-31G*

ΔE^a= (Total energy)$_{ax}$ - (Total energy)$_{eq}$

ΔG_{exp}= Experimental free energy difference at T=270° K

Table 3.35b Comparison of conformational free energy differences (HF/6-31G* , kcal/mole) with the experimental values given in parenthesis

	toluene (ε=2.4)	CH_2Cl_2 (ε=8.9)	acetone (ε=20.5)
$N(CH_3)_2$	-0.46 (-0.64)	-0.16 (-0.48)	-0.07 (-0.66)
OCH_3	-0.48 (-0.82)	-0.21 (-0.61)	-0.14 (-0.75)
CH_3	-0.32 (-0.86)	0.07 (-0.65)	0.17 (-0.80)

Table 3.36. Energy and dipole moment data of 2-selenol-1,3-dithiane.

	E(**1a**)	E(**1e**)	μ_{ax}	μ_{eq}
PM3	2.672#	6.350#	2.272	3.107
HF/6-31G*	-3348.7202626@	-3348.7159756@	2.265	3.548

Heat of formation in kcal/mole

@ Total energy in hartree

Table 3.37 The thermodynamic data of 2-[(4-chlorophenyl)seleno]-1,3-dithiane (PM3)

PM3	ΔH_{fax}	ΔH_{feq}	$\Delta(\Delta H_f)$	ΣH_{ax}	ΣH_{eq}	$\Delta(\Sigma H)$
Gas	4.374	7.993	-3.619	123.612	123.787	-0.175
Solvent	1.339	4.874	-3.535			

PM3	S_{ax}	S_{eq}	ΔS	ΔG*	ΔG**	μ_{ax}	μ_{eq}
Gas	124.061	128.929	-4.868	-2.168	1.276	2.66	3.08
Solvent						3.02	3.57

Table 3.38 The thermodynamic data of 2-[(4-fluorophenyl)seleno]-1,3-dithiane (PM3)

PM3	ΔH_{fax}	ΔH_{feq}	$\Delta(\Delta H_f)$	ΣH_{ax}	ΣH_{eq}	$\Delta(\Sigma H)$
Gas	-32.656	-28.857	-3.799	124.861	125.031	-0.17
Solvent	-35.921	-32.396	-3.525			

PM3	S_{ax}	S_{eq}	ΔS	ΔG^*	ΔG^{**}	μ_{ax}	μ_{eq}
Gas	121.078	126.068	-4.99	-2.311	1.318	2.83	3.47
Solvent						3.20	4.03

Table 3.39 The thermodynamic data of 2-[(4-trifluoromethylphenyl)-seleno]-1,3-dithiane (PM3).

PM3	ΔH_{fax}	ΔH_{feq}	$\Delta(\Delta H_f)$	ΣH_{ax}	ΣH_{eq}	$\Delta(\Sigma H)$
Gas	-146.604	-143.210	-3.394	135.349	135.533	-0.184
Solvent	-150.508	-146.815	-3.693			

PM3	S_{ax}	S_{eq}	ΔS	ΔG^*	ΔG^{**}	μ_{ax}	μ_{eq}
Gas	139.132	143.740	-4.608	-2.020	1.119	3.86	4.91
Solvent						4.29	5.32

Table 3.40a The thermodynamic data of 2-(phenylseleno)-1,3-dithiane (PM3).

PM3	$\Delta H_f(ax)$	$\Delta H_f(eq)$	$\Delta(\Delta H_f)$	$\Sigma H(ax)$	$\Sigma H(eq)$	$\Delta(\Sigma H)$	Sax	Seq	ΔS	ΔG^*	ΔG^{**}	μ_{ax}	μ_{eq}
Gas	11.098	14.557	-3.459	128.610	128.780	-0.170	116.841	121.664	-4.823	-2.021	1.268	2.75	2.77
Solvent #	8.240	11.391	-3.153									3.14	3.26

$\Delta G^* = (\Delta H_{fax} - \Delta H_{feq}) - T\,\Delta S$ $\Delta G^{**} = (\Sigma H_{ax} - \Sigma H_{eq}) - T\,\Delta S$

# dielectric constant is 3.0

Table 3.40b The thermodynamic data of 2-(phenylseleno)-1,3-dithiane (HF/6-31G*).

HF/ 6-31G*	μ_{ax}	μ_{eq}	E_{Tax}	E_{Teq}	Electronic + thermal energy ax	Electronic + thermal energy eq	Electronic + thermal enthalpy ax	Electronic + thermal enthalpy eq
Gas	1.89	3.73	-3578.271085	-3578.269821	-3578.047211	-3578.046124	-3578.046267	-3578.045180
Solvent&	2.08	3.98	-3578.271270	-3578.270441				

HF/ 6-31G*	Electronic + free energy ax	Electronic + free energy eq	ΔE^a	ΔE^b	ΔH^c	ΔG^d
Gas	-3578.100339	-3578.100372	-0.793	-0.682	-0.682	0.021
Solvent&			-0.520			

a = $E_{Tax} - E_{Teq}$ b = (Electronic + thermal energy)$_{ax}$ - (Electronic + thermal energy)$_{eq}$

c = (Electronic+thermal enthalpy)$_{ax}$ - (Electronic + thermal enthalpy)$_{eq}$ d = (Electronic +free energy)ax (Electronic +free energy)$_{eq}$

& = dielectric constant is 2.4

Table3.41a The thermodynamic data 2-[(4-methylphenyl)seleno]-1,3-dithiane (PM3).

PM3	ΔHf_{ax}	ΔHf_{eq}	$\Delta(\Delta Hf)$	ΣH_{ax}	ΣH_{eq}	$\Delta(\Sigma H)$	S_{ax}	S_{eq}	ΔS	ΔG^*	ΔG^{**}	μ_{ax}	μ_{eq}
Gas	1.574	5.118	-3.544	147.247	147.422	-0.175	127.019	131.950	-4.931	-2.074	1.294	2.89	2.75
Solvent [#]	-1.554	1.987	-3.541									3.30	3.21

$\Delta G^* = (\Delta H_{fax} - \Delta H_{feq}) - T\,\Delta S$ $\Delta G^{**} = (\Sigma H_{ax} - \Sigma H_{eq}) - T\,\Delta S$

[#] = dielectric constant is 3.0

Table3.41b The thermodynamic data of 2-[(4-methylphenyl)seleno]-1,3-dithiane (HF/6-31G*).

HF/ 6-31G*	μ_{ax}	μ_{eq}	ET_{ax}	ET_{eq}	Electronic + thermal energy ax	Electronic + thermal energy eq	Electronic + thermal enthalpy ax	Electronic + thermal enthalpy eq
Gas	2.05	3.97	-3617.308726	-3617.307445	-3617.054746	-3617.053643	-3617.053802	-3617.052699
Solvent&	2.26	4.28	-3617.308932	-3617.308172				

HF/ 6-31G*	Electronic + free energy ax	Electronic + free energy eq	ΔE^a	ΔE^b	ΔH^c	ΔG^d
Gas	-3617.110115	-3617.110159	-0.804	-0.692	-0.692	0.028
Solvent&			-0.477			

a = $ET_{ax} - ET_{eq}$ b = $(\text{Electronic + thermal energy})_{ax}$ - $(\text{Electronic + thermal energy})_{eq}$

c = $(\text{Electronic+thermal enthalpy})_{ax}$ - $(\text{Electronic + thermal enthalpy})_{eq}$ d = (Electronic + free energy)ax - $(\text{Electronic + free energy})_{eq}$

&= dielectric constant is 2.4

Table3.42a The thermodynamic data of 2-[(4-nitrophenyl)seleno]-1,3-dithiane (PM3).

PM3	ΔHf(ax)	ΔHf(eq)	Δ(ΔHf)	ΣHax	ΣHeq	Δ(ΣH)	Sax	Seq	ΔS	ΔG*	ΔG**	μax	μeq
Gas	3.152	6.439	-3.287	132.327	132.797	-0.470	136.979	137.85	-0.871	-3.027	-0.210	7.20	7.00
Solvent #	-3.586	-1.180	-2.406									8.25	7.98

$\Delta G^{*} = (\Delta H_{f ax} - \Delta H_{f eq}) - T\Delta S$ $\Delta G^{**} = (\Sigma H_{ax} - \Sigma H_{eq}) - T\Delta S$

# dielectric constant is 3.0

Table3.42b The thermodynamic data of 2-[(4-nitrophenyl)seleno]-1,3-dithiane (HF/6-31G*).

HF/ 6-31G*	μax	μeq	ETax	ETeq	Electronic + thermal energy ax	Electronic + thermal energy eq	Electronic + thermal enthalpy ax	Electronic + thermal enthalpy eq
Gas	5.49	4.85	-3781.740881	-3781.739187	-3781.510829	-3781.509306	-3781.509885	-3781.508361
Solvent&	6.34	5.42	-3781.742479	-3781.740210				

HF/ 6-31G*	Electronic + free energy ax	Electronic + free energy eq	ΔE^{a}	ΔE^{b}	ΔH^{c}	ΔG^{d}
Gas	-3781.570590	-3781.570287	-1.063	0.956	-0.956	-0.190
Solvent&			-1.424			

a = $E_{Tax} - E_{Teq}$ b = $(\text{Electronic + thermal energy})_{ax} - (\text{Electronic + thermal energy})_{eq}$

c = $(\text{Electronic+thermal enthalpy})_{ax} - (\text{Electronic + thermal enthalpy})_{eq}$ d = (Electronic + free energy)ax - $(\text{Electronic + free energy})_{eq}$

&= dielectric constant is 2.4

Table 3.43a The thermodynamic data of 2-[(4-methoxyphenyl)seleno]-1,3-dithiane (PM3).

PM3	$\Delta H_f(ax)$	$\Delta H_f(eq)$	$\Delta(\Delta H_f)$	$\Sigma H(ax)$	$\Sigma H(eq)$	$\Delta(\Sigma H)$	S_{ax}	S_{eq}	ΔS	ΔG^*	ΔG^{**}	μ_{ax}	μ_{eq}
Gas	-27.615	-23.952	-3.663	150.373	150.296	0.077	130.699	138.204	-7.505	-1.426	2.315	1.97	3.01
Solvent #	-31.105	-26.948	-4.157									2.29	3.59

$\Delta G^* = (\Delta H_{fax} - \Delta H_{feq}) - T\,\Delta S$ $\Delta G^{**} = (\Sigma H_{ax} - \Sigma H_{eq}) - T\,\Delta S$

# dielectric constant is 3.0

Table3.43b The thermodynamic data of 2-[(4-methoxyphenyl)seleno]-1,3-dithiane (HF/6-31G*).

HF/ 6-31G*	μ_{ax}	μ_{eq}	E_{Tax}	E_{Teq}	Electronic + thermal energy ax	Electronic + thermal energy eq	Electronic + thermal enthalpy ax	Electronic + thermal enthalpy eq
Gas	1.28	4.22	-3692.152536	-3692.151294	-3691.890783	-3691.889732	-3691.889839	-3691.888787
Solvent&	1.41	4.56	-3692.152590	-3692.152080				

HF/ 6-31G*	Electronic + free energy ax	Electronic + free energy eq	ΔE^a	ΔE^b	ΔH^c	ΔG^d
Gas	-3691.949670	-3691.949717	-0.780	-0.6560	-0.660	0.030
Solvent&			-0.320			

a = $E_{Tax} - E_{Teq}$ b = $(\text{Electronic + thermal energy})_{ax} - (\text{Electronic + thermal energy})_{eq}$

c = $(\text{Electronic+thermal enthalpy})_{ax} - (\text{Electronic + thermal enthalpy})_{eq}$ d = $(\text{Electronic +free energy})ax - (\text{Electronic +free energy})_{eq}$

& = dielectric constant is 2.4

Table3.44a The thermodynamic data of 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (PM3).

PM3	$\Delta H_f(ax)$	$\Delta H_f(eq)$	$\Delta(\Delta H_f)$	ΣH_{ax}	ΣH_{eq}	$\Delta(\Sigma H)$	S_{ax}	S_{eq}	ΔS	ΔG^*	ΔG^{**}	μ_{ax}	μ_{eq}
Gas	6.969	10.459	-3.490	176.415	176.497	0.082	137.648	145.208	-7.560	-1.236	2.336	3.32	2.46
Solvent #	3.576	7.563	-3.987									4.02	2.97

$\Delta G^* = (\Delta H_{fax} - \Delta H_{feq}) - T\,\Delta S$ $\Delta G^{**} = (\Sigma H_{ax} - \Sigma H_{eq}) - T\,\Delta S$

# dielectric constant is 3.0

Table3.44b The thermodynamic data of 2-[(4-dimethylaminophenyl)seleno]-1,3-dithiane (HF/6-31G*).

HF/ 6-31G*	μ_{ax}	μ_{eq}	E_{Tax}	E_{Teq}	Electronic + thermal energy ax	Electronic + thermal energy eq	Electronic + thermal enthalpy ax	Electronic + thermal enthalpy eq
Gas	2.64	4.04	-3711.350373	-3711.349104	-3711.043854	-3711.042768	-3711.042910	-3711.041824
Solvent&	2.88	4.46	-3711.350624	-3711.349893				

HF/ 6-31G*	Electronic + free energy ax	Electronic + free energy eq	ΔE^a	ΔE^b	ΔH^c	ΔG^d
Gas	-3711.106230	-3711.106256	-0.797	-0.682	-0.682	0.016
Solvent&			-0.459			

a = $E_{Tax} - E_{Teq}$ b = (Electronic + thermal energy)$_{ax}$ - (Electronic + thermal energy)$_{eq}$

c = (Electronic+thermal enthalpy)$_{ax}$ - (Electronic + thermal enthalpy)$_{eq}$ d = (Electronic + free energy)ax - (Electronic + free energy)$_{eq}$

&= dielectric constant is 2.4

4. CONCLUSION

The calculations in general have shown the axial preference of 2-(p-substituted-phenyl)seleno-1,3-dithane. Semi empirical calculations as well as HF/6-31G* can be used to predict the qualitative trend in conformational equilibrium. Quantitative agreement between experiment and theory was obtained by the difference in sum of total energies and thermal energies between the axial and the equatorial conformers with HF.6-31G*. Using differences in entropies between the axial and equatorial conformers in semi empirical calculations improves the result. Entropies with ab initio give poor results which may be because of the unscaled frequencies. Dipole moments for equatorial conformers are generally higher than the ones for the axial conformers and the anomeric effect is expected to decrease as the polarity of the medium increases.

In general, with both methods one of the C1-S bonds shortens and C1-Se bonds lengthens in the axial conformers, indicating the presence of the endo anomeric effect in all of the compounds studied. NO_2 with the highest electron withdrawal potential assists the endo anomeric effect and $N(CH_3)_2$ with the highest electron donation capability opposes the endo anomeric effect. Thus, the highest axial preference is observed for NO_2 and the lowest one for $N(CH_3)_2$.

Another general feature for the species studied is the widening of one of the S-C1-Se angles in the axial conformers.

Phenyl ring is oriented coplanar to H7-C1 bond in equatorial conformers in PM3 calculations and perpendicular in axial. In PM3 and HF/6-31G*, the phenyl ring is positioned perpendicular to Se-C9 bond in most of the cases.

In the axial conformers, the presence of exo anomeric effect was another factor stabilizing these conformers. Exo anomeric effect was not observed in the local minimum for the equatorial conformers. The position of the phenyl group with respect to the H7-C1 bond was a matter of interest. In the global minima for the axial conformers, the phenyl ring was seen to be perpendicular to H7-C1 bond. In the global minima for the equatorial conformers the position of the phenyl groups was a matter of contraversy between PM3 and HF/6-31G* : long range interactions between the negative Se and the positive hydogens on the phenyl group stabilize the coplanar position of the phenyl group with H7-C1. On the other hand, with HF/6-31G*, the charge on selenium is positive and the least crowded perpendicular position of the phenyl group with respect H7-C1 is preferred. More sophisticated basis sets may be used for a small fragment to represent 2-[(4-substituted-phenyl)seleno]-1,3-dithiane compounds in order to test the charge on selenium. So, for calculations carried out by Schleyer[23] have confirmed the positive charge on selenium, thus sustaining our HF/6-31G* results.

A suggestion for further studies in this area lies in proposing to scale the frequencies and recalculate the entropy before including it in the free energy calculations.

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