CONFORMATIONAL EQUILIBRIA OF α-SUBSTITUTED CYCLOHEXANONES WITH DIFFERENT CHALCOGENS (O, S, Se)

by

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ABSTRACT

The conformational analysis of α-substituted cyclohexanones with different chalcogens (OH, SH, SeH, OC_6H_5, SC_6H_5, SeC_6H_5) has been studied in gas phase with semi-empirical PM3 and ab initio HF/6-31G*. The para F, Cl, Br, NO_2, NH_2, OCH_3 α-phenoxy, α-phenylthio and α-phenylseleno substituted cyclohexanones have been investigated in gas phase. The optimized structures (α-OH, SH, SeH, OCH_3, SCH_3, $SeCH_3$, OC_6H_5, SC_6H_5, SeC_6H_5) have been analyzed in polar medium (ε=37.5) using a continuum Self Consistent Reaction Field (SCRF) model. Computations have provided data on the structure, the dipole moments and the thermodynamic properties of the compounds of interest. Justification of the experimental results has been followed by predictions on similar substituents and overall generalization.

ÖZET

Farklı kalkojenlerle (OH, SH, SeH, OC_6H_5, SC_6H_5, SeC_6H_5) α'ya sübstitüye siklohekzanonların konformasyonel analizi gaz fazında yarı ampirik PM3 ve ab initio HF/6-31G* ile çalışılmıştır. Para F, Cl, Br, NO_2, NH_2, OCH_3 α-fenoksi, α-feniltiyo ve α-fenilseleno sübstitüye siklohekzanonlar gaz fazında araştırılmıştır. Optimize edilen geometriler (α-OH, OCH_3, OC_6H_5, SH, SCH_3, SC_6H_5, SeH, $SeCH_3$, SeC_6H_5) SCRF modeli kullanılarak polar ortamda (ε=37.5) analiz edilmiştir. Hesaplamalar, ilgili bileşiklerin geometrileri, dipol momentleri ve termodinamik özelliklerindeki bilgileri sağlamıştır. Deneysel sonuçlar hesapsal bulgularla kıyaslanmış ve benzer moleküllerin konformasyonel tercihleri saptanmıştır.

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LIST OF ABBREVIATIONS

AM1	Austin Model
C	Square matrix of expansion coefficients
C_{pi}	Expansion coefficient
CNDO	Complete Neglect of Differential Overlap
e	Electron
H^{el}	Electronic Hamiltonian
INDO	Intermediate Neglect of Differential Overlap
m_e	Mass of electron
m_μ	Mass of nucleus "μ"
MINDO/3	Modified INDO method
MNDO	Modified Neglect of Diatomic Overlap
NDDO	Neglect of Diatomic Differential Overlap
PM3	Parametric Method Number 3
r_i	Radius of electron "i"
r_j	Radius of electron "j"
R_μ	Radius of nuclei "μ"
R_v	Radius of nuclei "v"
SCF	Self-Consistent Field
STO	Slater-type orbitals
$\chi_p(r)$	Atomic orbitals or Basis functions
Z_μ	Charge of nucleus "μ"
ΔA_C	Cavitation energy
ΔA_E	Electrostatic interaction between the polarized solute and the reaction field
ΔA_I	Induced polarization of the solute by the reaction field
ΔA_P	Solvent polarization around the cavity
ΔA_S	Free energy of solvation
ΔA_T	Translational, rotational and vibrational partition functions of the solute

LIST OF SYMBOLS

Å	Angstrom
a_0	Radius of the spherical cavity
E	Energy
F	Fock matrix
g	Coupling tensor
G	Gibbs free energy
h	Plank's constant
H	Hamiltonian operator
HF	Hartree Fock
k	Rate constant
K	Equilibrium constant
R	Reaction (electric) field operator
S	Matrix of overlap integrals
V	Potential energy
ε	Dielectric constant
Φ	Basis functions
ρ	Hammett reaction constant
σ	Hammett substituent constant
ψ	Molecular orbital
μ	Dipole moment
∇	Laplacian operator

1. INTRODUCTION

In organic chemistry, one of the most extensively studied cyclic systems is the six-membered ring system [1-4]. The introduction of a doubly bonded oxygen into the symmetrical ring has been subjected to experimental [5-6] and theoretical [7-8] investigations during the past decade. These studies have shown that the ring flattens in comparison with cyclohexane and causes the interconversion from the axial to the equatorial positions to be more rapid. Thermodynamic calculations have shown the chair conformation to be the most stable form [1].

In the case of α-substituted cyclohexanone, axial and equatorial conformations are possible. Their relative stabilities depend on several factors, such as the structural and electronic characteristics of the substituent, the interaction between the substituent and the carbonyl group, etc. There have been numerous experimental studies aimed at determining the conformational preferences of α-substituted cyclohexanones [9-14]. The methods used to determine the axial / equatorial equilibrium constants include isomer equilibration, dipole moments, infrared, ultraviolet and proton NMR spectroscopies. The conformational preference of a monosubstituted cyclohexane is determined largely by the interaction of the substituent with the syn-axial protons. For α-substituted cyclohexanones such interactions are still important but in addition the interaction of the substituent with the carbonyl group must be taken into consideration. For a nonpolar substituent X, nonbonded interactions with the carbonyl group, are larger in the equatorial conformation.(FIGURE 1.1.)

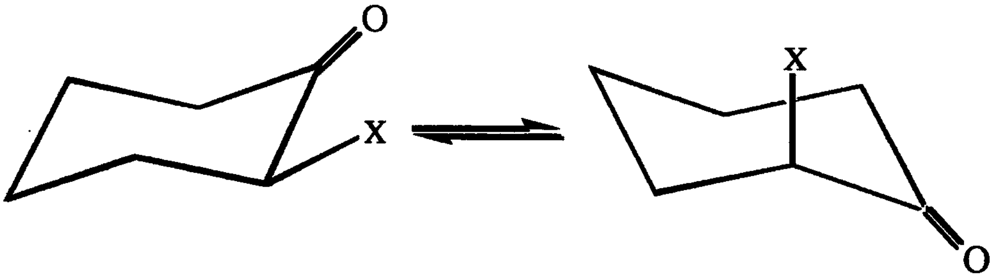

FIGURE 1.1. The conformational equilibrium of α-substituted cyclohexanone.

The dipole of an equatorial, electronegative substituent is nearly parallel to that of the carbonyl group and causes repulsive interactions, whereas that of an axial electronegative substituent is almost orthogonal to that of the carbonyl group and interacts only slightly with the carbonyl group.

The conformations of cyclohexanones bearing a halogen substituent at the α carbon have been extensively studied [15]. Experiments have shown the bromo and chloro derivatives to exist mainly in the axial conformation in nonpolar solvents with the fluoro substituent having no preference. In polar solvents, the proportion of the equatorial conformer increases, becoming dominant for the chloro and fluoro derivatives [1, 12-15]. Three main factors, steric, dipole-dipole and orbital interactions have been proposed to account for these changes in equilibrium. While the nonpolar substituents at α-carbon generally exhibit a preference for the less sterically strained equatorial conformation, the polar substituents located at this position display a wide range of diverse conformational behaviour [10, 12, 16, 17].

The conformational equilibrium in α-CN [13] and α-NO_2 [14] derivatives has shown the equatorial position to be the most favourable in CD_3Cl. This behavior has been explained by attractive electrostatic interactions between the carbonyl and the substituent, mainly because of the presence of a negative charge on the oxygen atom and a positive charge on the carbon atom or nitrogen atom of the CN or NO_2 substituent.

The conformational analysis carried out by Cantacuzene and Tordeux [18], has revealed 63 per cent of α-methoxycyclohexanone to be in the axial form in CCl_4 while 16 per cent of this conformer was present in CH_3CN.

Wladislaw et al. [19] have estimated the conformations of some α-sulphur substituted cycloalkanones from the IR spectra and found a 70 per cent axial preference for α-methylthiocyclohexanone in CCl_4.

Kazakova et al. [20] have studied the conformation of the α-methylthiocyclohexanone using electric and electrooptical methods. According to the electrooptical characteristics of the α-methylthiocyclohexanone, the general preference for the substituent was found to be in the axial gauche position.

Basso et al. [21] have measured the axial-equatorial conformational proportions for α-substituted cyclohexanones in $CHCl_3$ by the Eliel method [21] for F, Cl, Br, I, MeO, MeS, Me_2N, MeSe and Me substituents. The axial percentage was 28 per cent for α-methoxycyclohexanone, 85 per cent for α-methylthiocyclohexanone and 92 per cent for α-methylselenocyclohexanone in $CDCl_3$.

Fraser and Faibish [22], have determined the equilibrium population for both α-methylthio and α-methoxycyclohexanones in five solvents with different polarity, the percent of the axial α-methylthio conformer was found to vary from 94 per cent in cyclohexane to 59 per cent in CH_3CN, whereas that for the α-methoxy conformer was shown to vary between 57 per cent to 20 per cent.

Özbal and Zajac [23] have studied the conformational equilibrium for α-phenoxy, α-phenylthio and α-phenylselenocyclohexanones in four different solvents: the percent of the equatorial phenoxy conformer was found to vary from 54 per cent in CCl_4 to 79 per cent in CH_3CN. For the phenylthio and phenylseleno conformers, the range in percent equatorial was around 28 per cent and 27 per cent respectively in CCl_4 and 53 per cent and 51 per cent in CH_3CN.

Kazakova et al. [24] have studied α-phenylthiocyclohexanones with the same methods. The general preference for the substituent was found to be the gauche position in the axial conformer where the orientation of the ring is planar.

Later, Sebüktekin [25] has synthesized different p-substituted ($-NO_2$, -Br, -Cl, -F, -H, $-NHCOCH_3$, $-OCH_3$, $-NH_2$) α-phenylthiocyclohexanones and has analyzed them with ^1H NMR. These substituents have shown a strong preference for the axial position in CCl_4, $CHCl_3$, $CHBr_3$ and $(CH_3)_2CO$. When the substituent at the para position is of electron-withdrawing character ($-NO_2$, -Br, -Cl, -F), the general preference for the axial orientation of the α-phenylthio group is seen to shift slightly in favor of the equatorial conformation.

Cantacuzene and Tordeux [18], have investigated the different para substituted ($-NO_2$, -Br, -Cl, -H, $-OCH_3$, $-NEt_2$) α-phenoxycyclohexanones and have shown the substituent to prefer the equatorial positon.

The conformational equilibrium of some α-substituted (X= F, Cl, Br, CN, NO_2) cyclohexanones has been studied with the PM3 method in solution in our department [26]. The calculated results were in agreement with the available experimental data [9-14].

Kazakova et al. [27] have studied α-methylthio- and α-phenylthiocyclohexanones with MM2 force field calculations. For the α-methylthio substituent, the eq / ax ratio from IR-spectroscopic results [19] amounts to 0.22. The general preference for the axial position was seen to be in agreement with the experimental results. For α-phenylthio substituent, the experimental ratio [27] of the eq / ax population was the same as the calculated ratio which is 0.3 / 0.7.

In this study, we focus mainly on XC_6H_5Y substituted cyclohexanones where X= O, S, Se and Y= H, F, Cl, Br, NO_2, NH_2, OCH_3 in the gas phase. In order to understand the effect of the bulky phenyl group on the conformational equilibria, the smaller analogues of these compounds namely OH, SH, SeH substituted α-cyclohexanones have been studied. Additionally, α-OH, SH, SeH, OCH_3, SCH_3, $SeCH_3$, OC_6H_5, SC_6H_5, SeC_6H_5 substituted cyclohexanones have been investigated in polar medium (ε=37.5). Finally, we rationalize the calculated results with the available experimental results. This can be useful for the substituents not studied experimentally yet.

2. THEORY

2.1. Introduction

Computational chemistry has direct applications in all branches of chemistry. Experimental chemists have progressed well beyond the point of studying the average behaviour of reacting species described by the Arrhenius rate equation and probe the step-by-step behavior of individual atoms and molecules as they collide, from transition states and ultimately to form products. Such experiments are generally assisted by computational chemistry which helps to fill the gaps in observation and assists in the interpretation of what is observed.

Computational chemistry stimulates chemical structures and reactions by running calculations on computers. Some methods can be used to model not only stable molecules, but also short-lived, unstable intermediates and even transition states. In this way, they can give information about molecules and reactions which are impossible to obtain through observation.

Computational methods can be classified in two main classes: molecular mechanics and quantum mechanics.

Molecular mechanics constitutes an entirely different approach to the description of molecular geometry and conformation than provided by quantum chemical techniques. Instead of nuclei and electrons, molecules are thought of in terms of connected atoms and molecular geometry in terms of bond distances, bond angles and dihedral angles (internal coordinates). While these are by no means the only set of coordinates that can be used to describe molecular geometry, they are particularly attractive and convenient choice, primarily because of high degree of transferability from one molecule to another. Thus, it is possible to provide a fairly accurate guess at molecular geometry in terms of bond length, bond angles and dihedral angles, provided that the molecule has already been represented in terms of a particular valence structure.

Quantum mechanics provides a mathematical description of molecular structure in terms of atomic nuclei and the electron distribution around them. So, although many useful properties can be predicted from quantum mechanics, it should be kept in mind that fundamentally it involves computing the electron distribution in a molecule. Quantum mechanics is used to estimate the relative stabilities of molecules, to calculate the thermodynamic properties, to interpret molecular spectra, thereby allowing experimental determination of molecular properties such as bond lengths, bond angles, dipole moments, barriers to internal rotation, energy differences between conformational isomers, to investigate the properties of transition states in chemical reactions, thereby allowing estimation of rate constants.

2.2. Quantum Mechanics

Quantum mechanical calculations can be applied directly to determine various properties of molecules. All electronic structure methods seek an approximate solution of the Schrödinger equation.

$$\left(\frac{-h^2}{8\pi^2 m}\nabla^2 + V\right)\psi = E\psi \tag{2.1}$$

Here, the quantity in paranthesis on the left represents the kinetic and potential energy of an electron of mass m moving in the vicinity of a nuclear charge. E is the energy of electrons and ψ is the wavefunction, which is a function of nuclear and electronic coordinates and contains all of the information about the system. The square of the wavefunction times a small volume element gives the probability of finding the electron inside the volume element. It is straightforward to generalize the Schrödinger equation to a multinuclear, multielectron system.

$$H\Psi = E\Psi \tag{2.2}$$

Here, ψ is a many-electron wavefunction and H is the so-called Hamiltonian operator which is derived from the nuclear kinetic and potential energy terms as well as the electronic kinetic and potential energy terms. Assuming only electrostatic (Coulombic) terms in the potential, the Hamiltonian for a molecule with n electrons and N nuclei can be written as follows

$$H = -\sum_{i}^{n} \frac{1}{2} \nabla_i^2 - \sum_{\mu=1}^{N} \frac{1}{2m_\mu} \nabla_\mu^2 - \sum_{i=1}^{n} \sum_{\mu=1}^{N} \frac{Z\mu}{\left| r_i - R_\mu \right|} + \sum_{i<j}^{n} \frac{1}{\left| r_i - r_j \right|} + \sum_{\mu<\nu}^{N} \frac{Z_\mu Z_\nu}{\left| R_\mu - R_\nu \right|} \tag{2.3}$$

where from here on we have assumed atomic units, that is $m_e=1$, $h=1$, $e=1$, and $\varepsilon_o=1/4\pi$. The expressions uses summation indices (i, j) for electrons and (μ, ν) for nuclei, m_μ and Z_μ denote the mass and charge of nucleus "μ". The first term in Equation 2.3 describes the kinetic energy of electrons, the second term is the kinetic energy of nuclei, the third term is the nuclear-electron potential, the fourth term is the electron-electron potential operator and the fifth term is the nuclear-nuclear potential operator.

One way to simplify the Schrödinger equation is to separate the nuclear and electronic motions by the Born-Oppenheimer approximation. This is possible because the electrons are much lighter than nuclei and can " instantaneously " adjust their distribution as more massive nuclei change their position. Equation 2.1 becomes

$$H^{el}\psi^{el}(r,R) = E^{eff}\psi^{el}(r,R) \tag{2.4}$$

where H^{el} is the electronic Hamiltonian, ψ^{el} is the electronic wavefunction, which depends on the electronic coordinates, r, as well as the nuclear coordinates, R, and E^{eff} (R) is an effective electronic energy, which depends on the nuclear coordinates, R.

H^{el} = Kinetic energy of electrons + nuclear-electron attraction operator + electron-electron repulsion operator (2.5)

This is the Pauli exclusion principle [28], and the requirement is met by a wavefunction constructed as a determinant of the orbitals:

$$\psi = (n!)^{-1/2} \begin{bmatrix} \varphi_1(1)\varphi_2(1)\ldots\ldots\ldots\varphi_n(1) \\ \varphi_1(2)\varphi_2(2)\ldots\ldots\ldots\varphi_n(2) \\ \varphi_1(3)\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \\ \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \\ \varphi_1(n)\varphi_2(n)\ldots\ldots\varphi_n(n) \end{bmatrix} \tag{2.6}$$

where the factor $(n!)^{-1/2}$ normalizes the entire many electrons wavefunction. These wavefunctions are referred to as Slater determinants. The properties of determinants cause interchange of any two electrons, which is equivalent to interchanging two rows, to result in a change of sign of the wavefunction . Thus, the antisymmetry requirement has been met.

The Schrödinger equation is still too complicated to be solved exactly for systems of chemical interest. An approximation is the method of Linear Combination of Atomic Orbitals (LCAO) expansion, that is, the technique of expanding a (spatial) molecular orbital ψ_i (r) as a linear combination of (approximate) atomic orbitals.

$$\psi_i(r) = \sum_{p}^{N} C_{pi}\chi_p(r) \tag{2.7}$$

where C_{pi} are the expansion coefficients and $\chi_p(r)$ are the so-called atomic orbitals or basis functions.

From these approximations, the energy and the wavefunction of the molecular system is determined by reducing the Hartree-Fock Self-Consistent Field (SCF) equation:

$$FC=SCE \tag{2.8}$$

Here, C is a square matrix of expansion coefficients, F is the Fock matrix with elements consisting of kinetic energy, electron-nuclear attraction and electron-electron repulsion integrals, S is the matrix of overlap integrals between the basis functions and E is a vector of orbital energies.

2.2.1. Semiempirical Theory

The semiemprical quantum-mechanical methods developed by Dewar and co-workers [29-32] have been successful at reproducing molecular energies, replicating molecular structures and interpreting chemical reactions [33, 34]. To overcome some of the computational difficulties, approximations are made in which several of the integrals involving core orbitals are replaced by parameters. The number of two-electron integrals calculated is reduced by simply ignoring them or calculating them in an approximate fashion. Three levels of approximations have been defined by Pople and Beveridge in which certain two-electron integrals are neglected [35].

The first is known as complete neglect of differential overlap (CNDO) [36], it assumes the atomic orbitals to be spherically symmetrical when evaluating electron repulsion integrals. The directionality of p-orbitals was included only via the one-electron resonance integrals, the size of which depend on the orientations and distances of the orbitals and on a constant assigned to each type of bond.

The second is known as intermediate neglect of differential overlap (INDO) [37], it contains all terms that CNDO contains and includes all one-center two-electron integrals.

The third is known as neglect of diatomic differential overlap (NDDO) [38] in which all two-electron two-center integrals involving charge clouds arising from pairs of orbitals on an atom were retained.

In 1975, Dewar and his co-workers published the MINDO/3 method which is a modified INDO method. MINDO/3 uses a set of parameters in approximation. These parameters, along with the constants used to evaluate the resonance integrals, allow the results to be fitted as closely as possible to experimental data.

The first practical NDDO method was introduced by Dewar and Thiel in 1977 [30] called modified neglect of diatomic overlap (MNDO), the model was parametrized on experimental molecular geometries, heats of formation, dipole moments and ionization potentials. The orbital exponents and the core integral were again treated as empirical parameters to be determined in the fitting procedure.

The inability of MNDO has lead to a reexamination of the model, leading to Austin Model 1 AM1 [31]. In this model a term was added to MNDO to correct for the excessive repulsions at van der Waals distances. Toward this end, each atom was assigned a number of spherical gaussians which were intended to mimic long range correlation effects.

The third parameterization of MNDO is the Parametric Method Number 3 (PM3), AM1 being the second. In PM3, all quantities enter the Fock matrix and the total energy expression have been treated as pure parameters. The parameters were optimized using a large set of reference molecular data. This allowed 12 elements to be optimized simultaneously [32, 39, 40].

The AM1 model doesn't have any parameters for the Se compound that's why the PM3 model is used in this study which is the most precisely parametrized semiempirical model.

2.2.2. Ab initio Theory

The term ab initio, which means "from first principles" is used to describe how the Schrödinger equation is solved. In ab initio theory the Hamiltonian and the wavefunction have been defined, the effective electronic energy can be found by use of the variational method. In the variational method the "best" wavefunction is found by minimizing the effective electronic energy with respect to parameters in the wavefunctions. Using this idea, Fock and Slater simultaneously and independently developed what is known as the Hartree-Fock equations which are set of coupled integro-differential equations that can be solved only by an iterative method. To solve Hartree-Fock equations, an initial trial set of orbitals is chosen, the Fock operator is constructed

$$F_i(1)\phi_i(1) = E_i\phi_i(1) \tag{2.9}$$

Here, E_i is the orbital energy for orbital i and F_i is the Fock operator. Equation 2.9 is solved to obtain new set of orbitals, which is then used to construct a new Fock operator. This procedure is repeated until a convergence criterion is satisfied. This convergence criterion is usually based on the change in energy or change in orbitals. This procedure is referred to as the self-consistent field (SCF) method because the iterative procedure is continued until the effective electrostatic field that an electron in orbital ϕ_i sees due to the electrons in all of the other orbitals remains unchanged.

The first molecular orbital calculations made use of Slater-type orbitals (STO's) which are closely related to the exact solutions of the hydrogen atom. These are essentially polynomials in cartesian coordinates (x, y, z) followed by an exponential in r. While they are very simple functions, they proved to be very difficult to work with, and were soon replaced by closely-related Gaussian functions. Like STO's, Gaussian orbitals comprise a polynomial in the cartesian coordinates but replace the exponential in r by an exponential in r^2.

There are numerous different gaussian basis sets with which SCF calculations can be carried out [41]. The most widely used are those developed by Pople and co-workers [42, 43]. The simplest and lowest basis set is called STO-3G. This means that the Slater-type orbitals are represented by threee gaussian functions. The next level of basis sets developed by Pople is referred to as the split-valence basis sets and have designations such as 3-21G, 4-31G, 6-31G where the first number represents the number of gaussians used to represent the core orbitals. The valence orbitals are represented by two functions that are composed of the number of gaussians given by the second set of two numbers in the basis set designation. For greater flexibility the split-valence basis set can be augmented with polarization functions. In polarization basis sets, which are the next level of improvement in basis set, d orbitals are added to all nonhydrogenic atoms. The common polarization basis sets is 6-31G* where d functions are added to heavy atoms, is used in this study.

2.2.3. Self-Consistent Reaction Field

The interactions between the solute and the solvent molecules are responsible for variations of the models which allow a simulation in quantum-chemical computations. The solute is a distribution of charges separated from a continuum having the macroscopic dielectric properties of the solvent by a spherical surface which defines the molecular cavity. In this cavity, the averaged electric potential is non-zero. It is different from one point to another giving rise to a non-uniform electric field which is called "reaction field". The first effect of this field is to disturb the charge distribution of each solvent molecule creating an induced electric moment and to generate an angular correlation between the solvent and solute molecules.

Rivail [44] separated the solvation process of a molecule in a series of steps:
a) Creation of the cavity in the solvent (Free energy variation ΔA_C is sometimes called "cavitation energy").
b) The solvent polarization around the cavity ΔA_P.
c) The reaction field induced the polarization of the solute ΔA_L.
d) The electrostatic interaction between the polarized solute and the reaction field ΔA_E.
e) Contribution of the dispersion and repulsion forces between the solute and the neighboring solvent molecules ΔA_D.
f) The translational, rotational and vibrational partition functions of the solute takes the form ΔA_T.

The free energy of interaction of the solute with the surroundings takes the form:

$$\Delta A_S = \Delta A_C + \Delta A_P + \Delta A_L + \Delta A_E + \Delta A_D + \Delta A_T \qquad (2.10)$$

where ΔA_S is the free energy of solvation.

In these models, the solute is placed in a cavity (spherical or ellipsodial) immersed in a continious medium characterized by a dielecteric constant, ε. The electric field of the solute molecule polarizes the surrounding media, and this new field reacts back on the solute molecular system. In the quantum mechanical approach, the solvent effect is taken as an additional term H_1, in the hamiltonian of the isolated molecule (solute), H_0, obtained from the system energy :

$$E= E_0-0.5R<\psi|\mu|\psi> \tag{2.11}$$

where μ is the electric dipole moment operator and ψ is the molecular wave function. The reaction (electric) field operator, R, is proportional to the solute dipole moment, μ:

$$R= g\mu \tag{2.12}$$

The coupling tensor, g, is the Onsager factor which gives the strength of the reaction filed and depends upon the dielectric constant of medium, ε and in the simplest case, upon the radius of the spherical cavity, a_0.

$$g= 2(\varepsilon-1) / (2\varepsilon+1)\ a_0^3 \tag{2.13}$$

For the case of a self-consistent field wave function, the effects of the reaction field can be incorporated as an additional term in the Fock matrix:

$$F_\lambda= F^0_{\lambda\sigma} - g\mu<\Phi_\lambda|\mu|\Phi_\sigma> \tag{2.14}$$

where Φ_λ and Φ_σ are basis functions. After adding the solvent polarization, the energy of the system is:

$$E= <\psi|H_0|\psi> - 0.5\mu R \tag{2.15}$$

In this study, the ellipsodial cavity was used in the solvation process.

2.3. Hammett Relationships

Hammett equation is commonly used to relate chemical and physical properties to the molecular structure [45]. Depending on the meta or para position on the benzene ring, Hammett has proposed the following empirical relationship;

$$\log(k/k_o) = \sigma\rho \qquad (2.16)$$

where k_o is the rate constant for the meta or para substituent, the parameter ρ is the slope of the correlation line and measures the sensitivity of the particular reaction rate constant (or equilibrium constant) to substituent changes and σ is the substituent constant which is a measure of the electron-withdrawing or electron-donating ability of that substituent compared with hydrogen.

The Hammett equation can also be applied to equilibria in which equilibrium constants (K) are used in place of rate constants.

$$\log(K/K_o) = \sigma\rho \qquad (2.17)$$

The Hammett equation is an example of a linear free energy relationship. The free energy changes are proportional to log K:

$$\log K - \log K_o = \sigma\rho \qquad (2.18)$$

$$\log K = \sigma\rho + \log K_o \qquad (2.19)$$

$$\Delta G = -2.3RT\log K \qquad (2.20)$$

$$\frac{-\Delta G}{2.3RT} = \log K \qquad (2.21)$$

TABLE 2.1. Value of Electronic Substituent Constants [45].

NO_2	0.77
Br	0.22
Cl	0.22
F	0.22
H	0.00
OCH_3	-0.28
NH_2	-0.63

The substituents that are electron-withdrawing have positive σ values, while those that are electron-donating have negative σ values. The larger the absolute value of σ , the larger the electronic effect. Since all substituent effects are obtained by reference to H, the σ value of H is precisely 0. So in establishing the set of σ values, Hammett generated an empirical measure of electronic substituent effects.

3. RESULTS AND DISCUSSION

3.1. Methodology

In this study, the conformational equilibrium of all the compounds of interest (α–OH, SH, SeH, OCH_3, SCH_3, $SeCH_3$, OC_6H_5, SC_6H_5, SeC_6H_5) was investigated computationally with the semiempirical PM3 method and with the HF/6-31G* basis set. Based on the conformational analysis of 2-Se-1,3-dithianes [46], PM3 was found to be the most suitable semiempirical method for sulphur and selenium containing compounds. The gas phase geometries were optimized using the MOPAC 6.0 [47] package in the gas phase. The conformers corresponding to local minima were fully optimized with the HF/6-31G* level of theory using the Gaussian 94 program [48].

The para substituted F, Cl, Br, NH_2, NO_2, OCH_3 α-phenoxy, α-phenylthio, α-phenylseleno substituted cyclohexanones were optimized with PM3 using MOPAC 6.0 [47] program in the gas phase.

Frequencies of all the studied compounds were calculated in order to confirm the nature of the stationary points. The thermodynamic properties (ΔH°, ΔG°, ΔS°) for the conformational equilibrium reactions were calculated with PM3 and HF/6-31G* and used to determine a trend between the position of the substituent (ax / eq) and its nature. They are compared with the experimental ΔG° values.

The optimized structures (α–OH, SH, SeH, OCH_3, SCH_3, $SeCH_3$, OC_6H_5, SC_6H_5, SeC_6H_5) were analyzed in polar medium (ε=37.5) using a continuum Self Consistent Reaction Field (SCRF) model [49] where the solvent is represented by an infinite dielectric and polarizable continuum in which a cavity is created. The solute is placed into this cavity and its charge distribution polarizes the continuum which in turn creates an electric field inside the cavity. An ellipsoidal cavity shape that leads to efficient geometry optimization algorithms has been used [50]. Computations have been carried using the PM3 method in the Geomos package [51].

3.2 Conformational Analysis of α-(OH, SH, SeH, OCH_3, SCH_3, $SeCH_3$, OC_6H_5, SC_6H_5, SeC_6H_5) Substituted Cyclohexanones in Gas Phase

3.2.1 Cyclohexanone

It is known from theoretical and experimental studies [4] that the chair conformation of the cyclohexanone is the most stable form (FIGURE 3.1.). When the bond lengths, the bond angles and the dihedrals are considered (TABLE 3.1.), it is observed that the values are close to each other with PM3 and HF/6-31G* calculations.

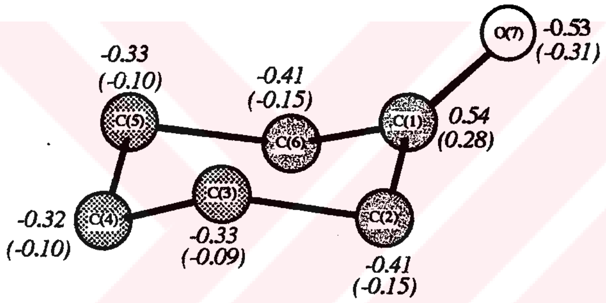

FIGURE 3.1. The optimized structure of cyclohexanone (HF/6-31G*). Mulliken charges on the atoms of interest are given in italics for HF/6-31G* and in parantheses for PM3.

TABLE 3.1. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of cyclohexanone.

	PM3	HF
C1-C2	1.514	1.517
C2-C3	1.520	1.537
C1-C6	1.514	1.517
C2-H8	1.108	1.083
C2-H9	1.108	1.090
O7-C1-C2	122.3	122.3
O7-C1-C6	122.3	122.3
C3-C2-C1	110.9	111.7
Dipole	3.45	1.78

3.2.2 α-OH, SH, SeH Substituted Cyclohexanones

The geometry and energetics of α-OH, SH, SeH substituted cyclohexanones are investigated both with PM3 and HF/6-31G* methods.

With HF/6-31G*, the substituents in the axial position prefer the + gauche (+ denotes the clockwise direction) orientation with respect to the ring. In this position the dipole is minimum, the substituent points outwards the ring (FIGURES 3.2., 3.3., 3.4.) and the lone pairs on the heteroatom are antiperiplanar with the C1-C2 and C2-H bonds. In all of these compounds the C1-C2 bond is longer than the C1-C6 bond (TABLES 3.2., 3.3., 3.4.). This observation can be explained by the so called anomeric effect [52] where the donation of electrons by the heteroatom shortens the X-C2 bond and lengthens the C1-C2 bond. Comparison of the C1-C2 bond lengths through the X= OH, SH, SeH series reveals the fact that the anomeric effect decreases as the size of the atom increases. The O7-C1-C2 angles in the compounds of interest are smaller than in cyclohexanone, long range interactions between O7 and H18 may be the cause of this behaviour. Also note that for both conformers, the C2-X-H18 angle decreases, as the size of the substituent increases. This trend is expected since hybridization decreases as the size of the atom increases and the C2-X-H18 angle approaches 90° (TABLES 3.2., 3.3., 3.4.).

The substituents in the equatorial position do not all show identical relative positions with respect to the ring (TABLES 3.2., 3.3., 3.4.). The -OH group is almost eclipsed to the ring and one can notice the long range H bonding (2.086 Å) between the carbonyl oxygen and the hydroxyl hydrogen. The same interaction, although weaker (2.430 Å) is also present in SH substituted cyclohexanone. As the size of the heteroatom increases long range interactions loose their priority and the substituent tends to adopt the sterically less hindered position inspite of its high dipole moment. The lengthening of the C2-H9 and C2-C3 bonds in the SeH substituted compound are evidences for the anomeric effect present in the SeH-eq. When the substituent is in the equatorial position, the O7-C1-C2 angle is slightly larger than the one in cyclohexanone because of the repulsions between the substituent and the carbonyl oxygen (TABLE 3.4.).

With PM3, in the axial position, the substituent (OH, SH) prefers the - (- denotes the anticlockwise direction) gauche position towards the ring, although this orientation is neither favored by the dipole nor by steric preferences of the substituent. It may be that long range stabilizing interactions between the (+) charge on the carbonyl carbon and one of the lone pairs, the + charge on the H on C3 with the other lone pair are the dominant stabilizing factors for this conformer. SeH on the other hand behaves similarly as in HF/ 6-31G*.

When the substituents are in the equatorial position, the eclipsed position with the carbonyl oxygen is preferred. Long range stabilizing interactions between O7 and H18 (2.56Å for O, 2.74Å for S) are reproduced by PM3. SeH adopts the - gauche conformation: the charge on Se with this method is smaller than with HF/ 6-31G*, thus repulsions between Se and O7 are minimized, furthermore this structure has minimum dipole.

The trend observed for the O7-C1-C2 and C2-X-C18 angles is similiar to one observed with HF/6-31G*.

For all of these compounds, the axial conformers have smaller dipole moments than the equatorial conformers. On the other hand, in the equatorial conformers a stabilizing interaction is present between H18 and O7 because of the quasi eclipsed position of the substituent.

With HF/6-31G*, the OH substituent prefers largely the equatorial orientation rather than the axial orientation. The preference shifts to the axial position as the size of the substituent increases. This behavior is confirmed by the difference in Gibbs free energies as well (TABLE 3.6.). Notice the almost equal ax / eq distribution for SH. The charge on H18 is larger in OH-eq (0.47) than in SH-eq (0.13), where long range stabilizing interactions are weak and there is no net preference for the equatorial position. For SeH, such stabilizing interactions are not present anyway because of the opposite orientation of the substituent to the carbonyl oxygen and the equilibrium shifts towards the axial conformer with minimum dipole moment. The results with PM3 mimic the trend with HF (TABLE 3.5.).

The change in entropy between the axial and equatorial conformers for these compounds is very small indicating an almost equal amount of disorder for these compounds. Both methods give the same trend.

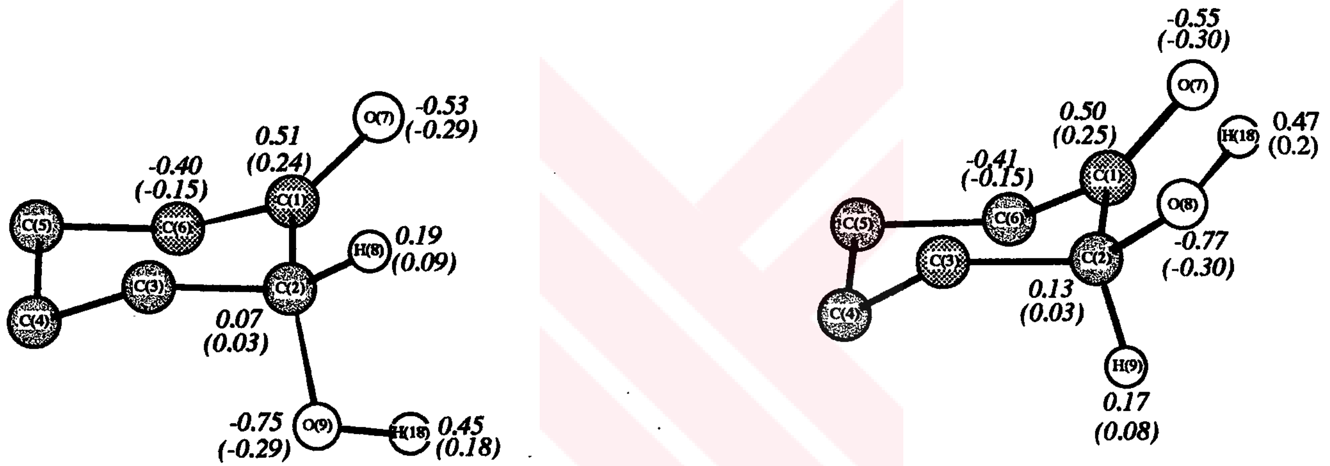

FIGURE 3.2. Structures for optimized axial and equatorial conformers (PM3) for α-OH substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics for HF/6-31G* and in parantheses for PM3.

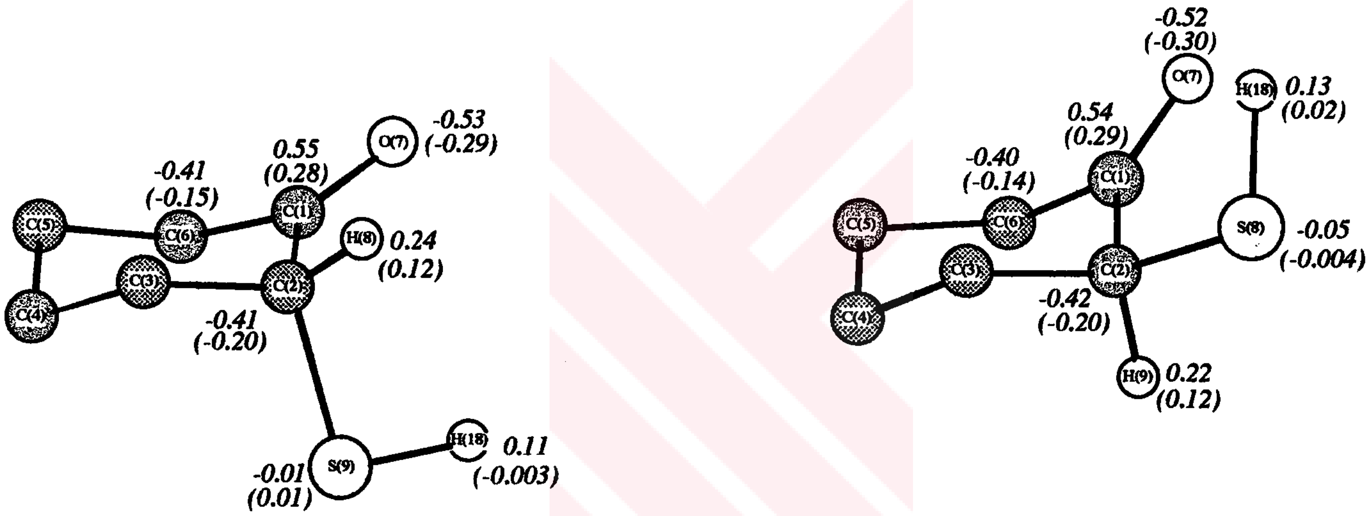

FIGURE 3.3. Structures for optimized axial and equatorial conformers (HF/6-31G*) for α-SH substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics for HF/6-31G* and in parantheses for PM3.

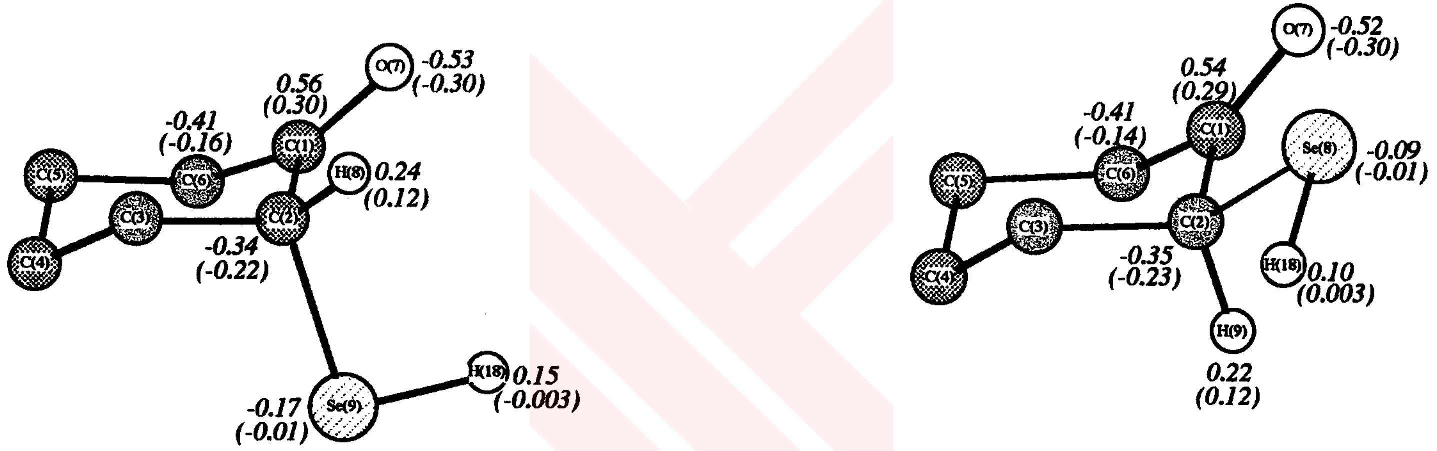

FIGURE 3.4. Structures for optimized axial and equatorial conformers (HF/6-31G*) for α-SeH substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics for HF/6-31G* and in parantheses for PM3.

TABLE 3.2. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-OH substituted cyclohexanone.

	OH-ax	OH-eq	OH-ax	OH-eq
	PM3	PM3	HF	HF
C1-C2	1.541	1.533	1.528	1.521
C2-C3	1.535	1.538	1.526	1.531
C2-O	1.406	1.402	1.410	1.388
C1-C6	1.513	1.513	1.513	1.511
C2-H	1.114	1.114	1.085	1.092
O7-H18	3.658	2.560	3.218	2.086
O7-C1-C2	121.5	123.0	121.3	120.4
C1-C2-O	111.3	114.6	108.8	111.1
C2-O-H18	107.6	107.9	109.5	108.0
C1-C2-O-H18	-67.0	49.0	70.7	351.4
Dipole	3.45	3.00	1.78	3.42

TABLE 3.3. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SH substituted cyclohexanone.

	SH-ax	SH-eq	SH-ax	SH-eq
	PM3	PM3	HF	HF
C1-C2	1.526	1.524	1.525	1.527
C2-C3	1.525	1.529	1.537	1.543
C2-S	1.831	1.828	1.837	1.820
C1-C6	1.514	1.515	1.515	1.516
C2-H	1.119	1.118	1.080	1.086
O7-H18	4.080	2.740	3.184	2.434
O7-C1-C2	121.5	124.0	120.4	123.7
C1-C2-S	112.5	118.4	109.6	113.9
C2-S-H18	100.9	101.3	97.1	97.5
C1-C2-S-H18	-69.6	38.1	62.7	32.6
Dipole	3.61	3.22	2.45	3.89

TABLE 3.4. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SeH substituted cyclohexanone.

	SeH-ax	SeH-eq	SeH-ax	SeH-eq
	PM3	PM3	HF	HF
C1-C2	1.507	1.504	1.520	1.521
C2-C3	1.507	1.511	1.536	1.538
C2-Se	1.958	1.948	1.973	1.956
C1-C6	1.512	1.512	1.515	1.515
C2-H	1.106	1.108	1.079	1.085
O7-H18	3.877	2.680	3.342	4.237
O7-C1-C2	121.6	121.3	120.8	122.6
C1-C2-Se	101.3	111.5	109.0	107.6
C2-Se-H18	99.6	101.1	95.2	94.1
C1-C2-Se-H18	100.8	-52.0	65.5	175.2
Dipole	2.07	3.28	2.64	4.66

TABLE 3.5. Energetics (kcal/mol) for the conformational equilibrium for α-XH substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3
	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3\ b}$	ΔG^c
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=1)
-OH	-99.46	-100.50	1.04	0.18	0.99
-SH	-47.47	-47.27	-0.20	-0.46	-0.06
-SeH	-56.55	-52.11	-4.44	-1.34	-4.04

[a] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K.

TABLE 3.6. Energetics (kcal/mol) for the conformational equilibrium for α-XH substituted cyclohexanones (HF/6-31G*).

	HF	HF	HF	HF
	ΔH^a	$\Delta S/10^{-3\ b}$	ΔG^c	ΔE^d
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)
-OH	3.68	0.59	3.51	3.58
-SH	-0.05	-1.07	0.26	-0.23
-SeH	-1.76	0.20	-1.82	-1.95

[a] ΔH= (Sum of electronic and thermal energy)$_{ax}$ - (Sum of electronic and thermal energy)$_{eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta H - T\Delta S$ at 298K.
[d] $\Delta E = E_{ax} - E_{eq}$.

3.2.3 α-OCH_3, SCH_3, $SeCH_3$ Substituted Cyclohexanones

The geometry and energetics of α-OCH_3, SCH_3, $SeCH_3$ substituted cyclohexanones are investigated with PM3 method.

In the axial conformers, OCH_3 and SCH_3 substituents prefer the - gauche position towards the ring (FIGURES 3.5., 3.6.) as in their smaller analogues. On the other hand, $SeCH_3$ behaves differently, it prefers the + gauche orientation with respect to the ring where the dipole is minimum and the substituent points outwards the ring (FIGURE 3.7.). In all of these compounds, the C1-C2 bond is longer than C1-C6 (TABLES 3.7., 3.8., 3.9.) confirming the presence of the anomeric effect in these compounds. As the size of the heteroatom increases, the anomeric effect decreases.

In the equatorial conformers, the substituents, OCH_3 and SCH_3, prefer the + gauche orientation where the dipole is minimum. $SeCH_3$ adopts the sterically less hindered position inspite of its high dipole moment.

The hydrogens of methoxy, methylthio and methylseleno groups are staggered to the carbon atom of the cyclohexanone so that the interaction is minimized.

The substituents except for OCH_3 prefer largely the axial position rather than the equatorial one. OCH_3 has a greater preference for the equatorial position where the dipole of the equatorial conformer is smaller than the axial conformer. SCH_3 substituent has a great stability in the axial conformer because the lone pair of sulphur are antiperiplanar to C1-C2 bond. $SeCH_3$ substituent display a great preference for the axial conformer where the dipole is minimum. These behaviors are confirmed by the difference in Gibbs free energies as well (TABLE 3.10.).

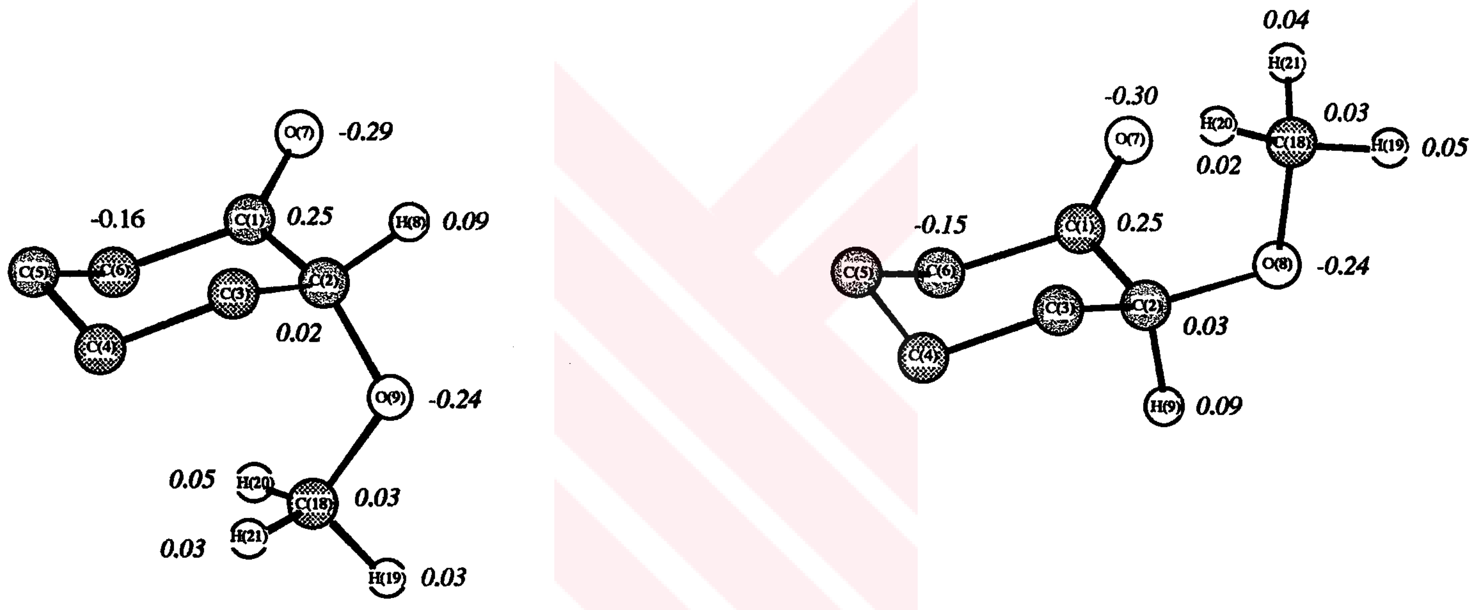

FIGURE 3.5. Structures for optimized axial and equatorial conformers (PM3) for α-OCH_3 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

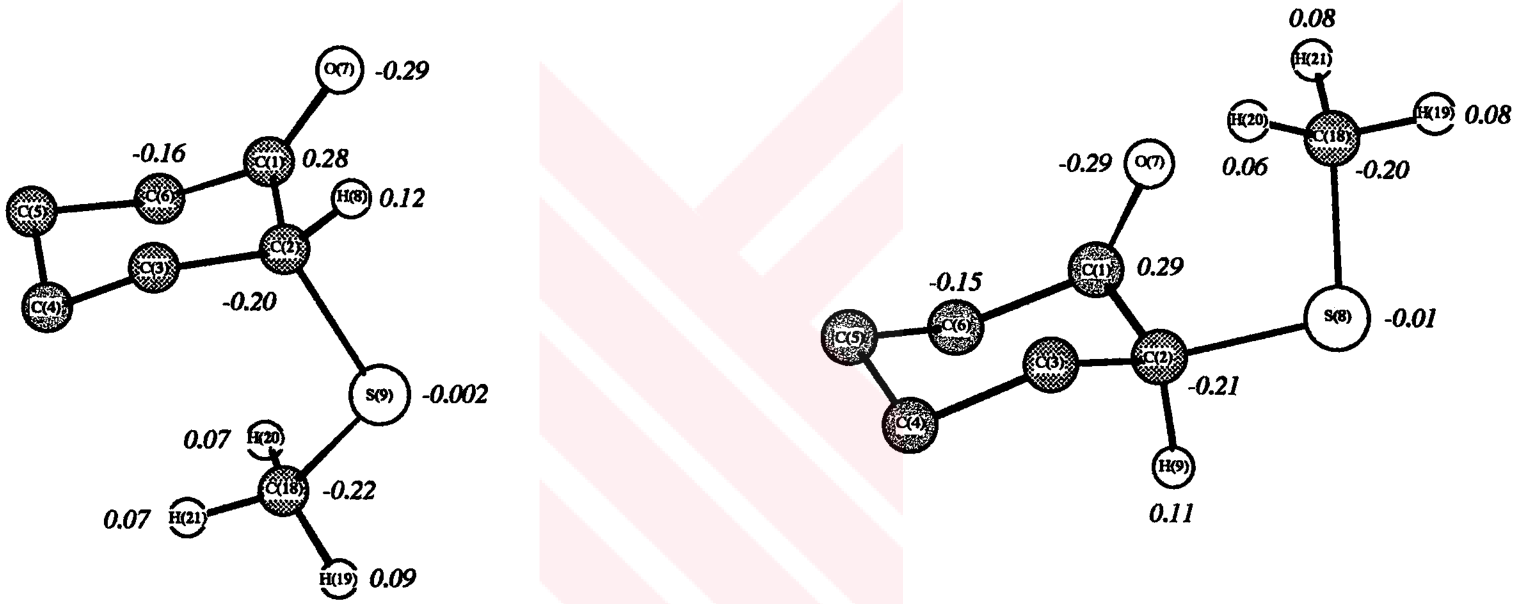

FIGURE 3.6. Structures for optimized axial and equatorial conformers (PM3) for α-SCH_3 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

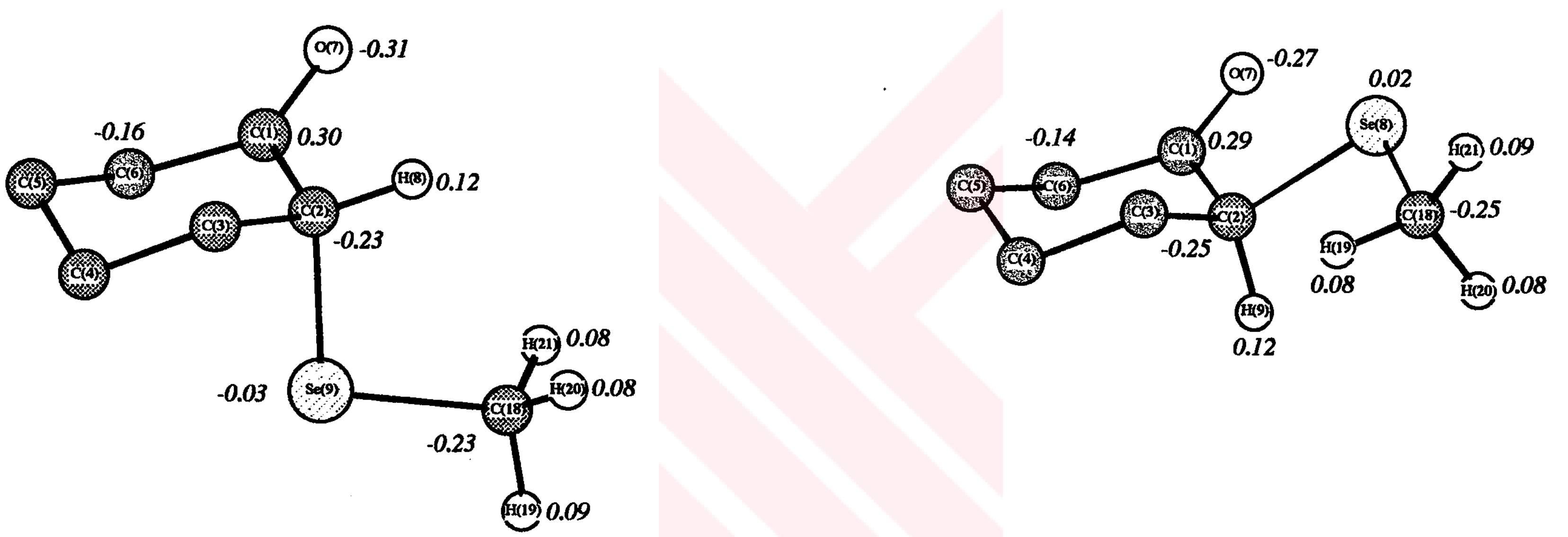

FIGURE 3.7. Structures for optimized axial and equatorial conformers (PM3) for α-$SeCH_3$ substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

TABLE 3.7. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-OCH_3 substituted cyclohexanone.

	OCH_3-ax	**OCH_3-eq**
	PM3	PM3
C1-C2	1.540	1.533
C2-C3	1.533	1.536
C2-O	1.419	1.417
C2-H	1.117	1.115
C1-C6	1.511	1.516
C18-H19	1.091	1.092
C18-H20	1.101	1.100
C18-H21	1.101	1.095
O7-C1-C2	121.0	124.0
C1-C2-O	113.0	115.3
C2-O-C18	117.8	116.0
C1-C2-O-C18	-65.0	69.1
C2-O-C18-H19	179.8	161.5
C2-O-C18-H20	61.0	42.6
C2-O-C18-H21	-61.3	-80.5
Dipole	3.37	3.08

TABLE 3.8. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SCH_3 substituted cyclohexanone.

	SCH_3-ax	**SCH_3-eq**
	PM3	PM3
C1-C2	1.525	1.525
C2-C3	1.526	1.529
C2-S	1.837	1.830
C2-H	1.120	1.120
C1-C6	1.514	1.518
C18-H19	1.095	1.097
C18-H20	1.101	1.096
C18-H21	1.101	1.096
O7-C1-C2	121.5	124.7
C1-C2-S	113.3	118.9
C2-S-C18	106.4	106.0
C1-C2-S-C18	-64.6	59.9
C2-S-C18-H19	179.8	174.7
C2-S-C18-H20	60.4	56.0
C2-S-C18-H21	-60.7	-66.7
Dipole	3.80	3.07

TABLE 3.9. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-$SeCH_3$ substituted cyclohexanone.

	$SeCH_3$-ax	**$SeCH_3$-eq**
	PM3	PM3
C1-C2	1.506	1.505
C2-C3	1.507	1.507
C2-Se	1.959	1.954
C2-H	1.107	1.109
C1-C6	1.513	1.512
C18-H19	1.092	1.096
C18-H20	1.090	1.089
C18-H21	1.090	1.091
O7-C1-C2	121.7	120.9
C1-C2-Se	101.6	103.9
C2-Se-C18	101.9	98.7
C1-C2-Se-C18	102.2	175.5
C2-Se-C18-H19	172.8	-31.5
C2-Se-C18-H20	53.7	89.7
C2-Se-C18-H21	-68.2	-150.8
Dipole	1.83	4.30

TABLE 3.10. Energetics (kcal/mol) for the conformational equilibrium for α-XCH_3 substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3
	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3\,b}$	ΔG^c
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=1)
$-OCH_3$	-93.33	-93.04	-0.02	-3.25	0.94
$-SCH_3$	-53.64	-51.66	-1.98	-4.97	-0.50
$-SeCH_3$	-77.26	-72.42	-4.84	3.11	-5.76

[a] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K.

3.2.4 α-OC_6H_5, SC_6H_5, SeC_6H_5 Substituted Cyclohexanones

When the substituent is in the axial position in HF/6-31G*, all the three compounds (X= OC_6H_5, SC_6H_5, SeC_6H_5) adopt the + gauche orientation with respect to the ring (FIGURES 3.8., 3.9., 3.10.). Comparison with the smaller analogues (X= OH, SH, SeH) shows that the C1-C2-X-C18 angle in these compounds is slightly larger than in their small counterparts (TABLES 3.11., 3.12., 3.13.). Steric hinderance with the cyclohexanone ring may explain this behavior.

In the equatorial position, long range stabilizing interactions between the substituent and the carbonyl group are weaker than in the small compounds because H is not attached directly to the heteroatom. The less hindered - gauche positon is prefered by the substituent. In this case, the nonbonded electron pairs on O and S are antiperiplanar with the C1-C2 bond. Donation of electrons from these nonbonded pairs on S and O towards the carbonyl oxygen illustrates the anomeric effect. A slight decrease in the C2-O(S)bond length and an increase in the C2-H9 is observed. The lengthening of the C1-C2 bond is also a manifestation of this effect. SeC_6H_5 on the other hand behaves differently and is anti to the C1-C2 bond, as in the SeH case, and minimizes steric repulsions.

A perpendicular orientation of the phenyl ring with respect to the C2-X bond is to be anticipated, since steric interactions between the hydrogens on the phenyl ring and the geminal hydrogen are to be minimized. Actually this dihedral angle, namely C2-X-C18-C19, is around 90° for all the substituents except for OC_6H_5 (Notice that + 90° or - 90° correspond to the same conformer). The almost coplanar orientation of the OC_6H_5 group with the C2-X bond has been rationalized by considering the length of the C2-X bond. C2-O being shorter than C2-S and C2-Se, stabilizing interactions between the carbonyl oxygen and the H's on the phenyl ring may take place. An average H9-H24 distance is 2.7Å when the ring is perpendicular to the C2-X bond; this distance is of 2.3Å when the phenyl ring is parallel to the C2-X bond. The steric repulsion between H9 and H24 explains the prefered perpendicular orientation of the phenyl ring.

With PM3, the angle C1-C2-X-C18 for each substituent is almost identical to the one with HF/6-31G*, except for OC_6H_5-ax and SC_6H_5-eq. In OC_6H_5-ax the C2-O bond is relatively short, and the C1-C2-X-C18 angle is 152°, the substituent points outwards, minimization of steric interactions holds its priority with PM3. For the equatorial position, the C1-C2-X-C18 angle shifts from −90° to 180° depending on the substituent. When the heteroatom is O the substituent is close to the carbonyl group stabilizing interactions are more effective than steric interactions. For S, the (+) charge on the phenyl H's is smaller than for the OC_6H_5 case, stabilizing interactions are minimized and the substituent prefers the less hindered position (+ gauche). SeC_6H_5 adopts the least crowded position (anti to the carbonyl group) inspite of the high dipole of this position.

As seen from TABLES 3.11., 3.12., 3.13., the phenyl ring prefers to be coplanar with the C2-X bond in all of these compounds. When the phenyl ring is parallel to the C2-X bond, the phenyl group and the carbonyl oxygen are parallel with each other, stabilization by delocalization of electrons is gained inspite of steric interactions.

With HF/6-31G*, these substituents exhibit the same trend as their smaller counterparts e.g. the population of the axial conformer increases as the size of the substituent increases. For O and S, in the - gauche orientation the distances between the O7 and the H on the C23 (~ 2.6Å) may suggest long range atteractive interactions. Furthermore the anomeric effect present in these compounds stabilizes somewhat the equatorial position. These interactions are not present in SeC_6H_5-eq conformer and the axial position is preferred.

With PM3, the substituents have a greater preference for the axial conformer where the dipole is minimum. This fact is confirmed by the difference in Gibbs free energies (TABLES 3.14., 3.15.).

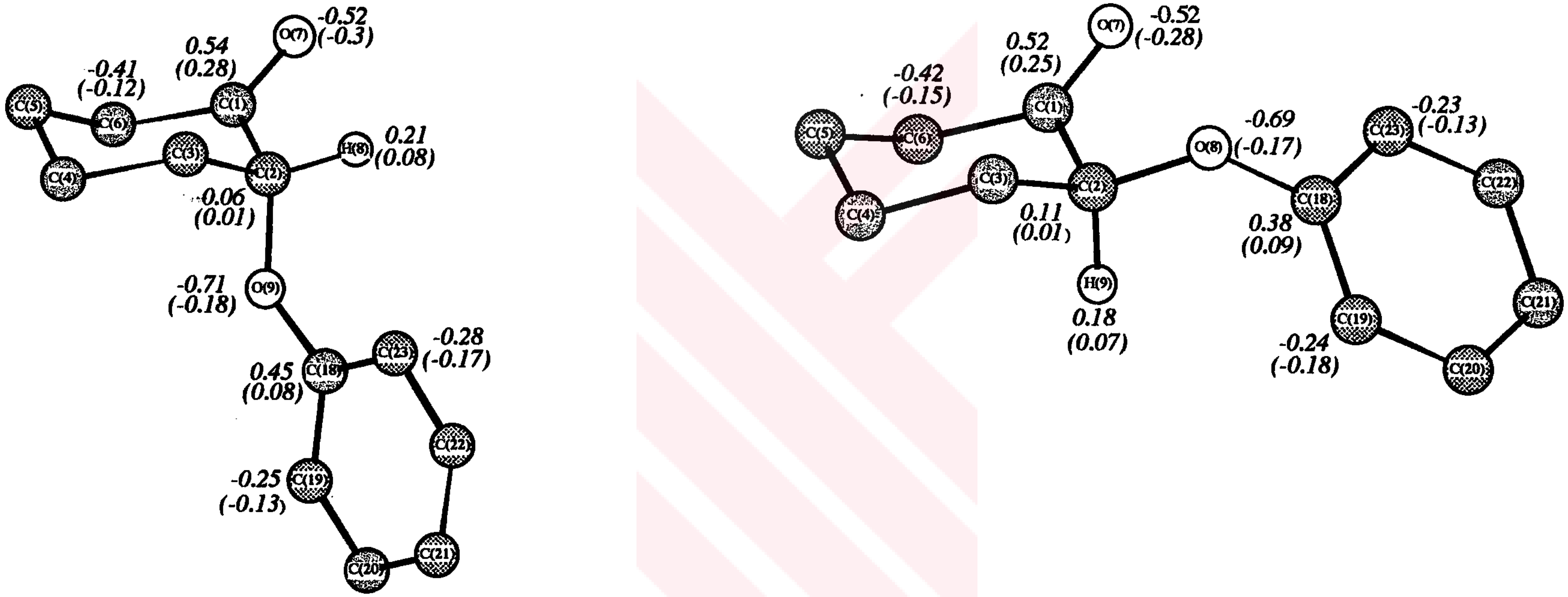

FIGURE 3.8. Structures for the optimized axial and equatorial conformers (HF/6-31G*) for α-OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics for HF/6-31G* and in parantheses PM3.

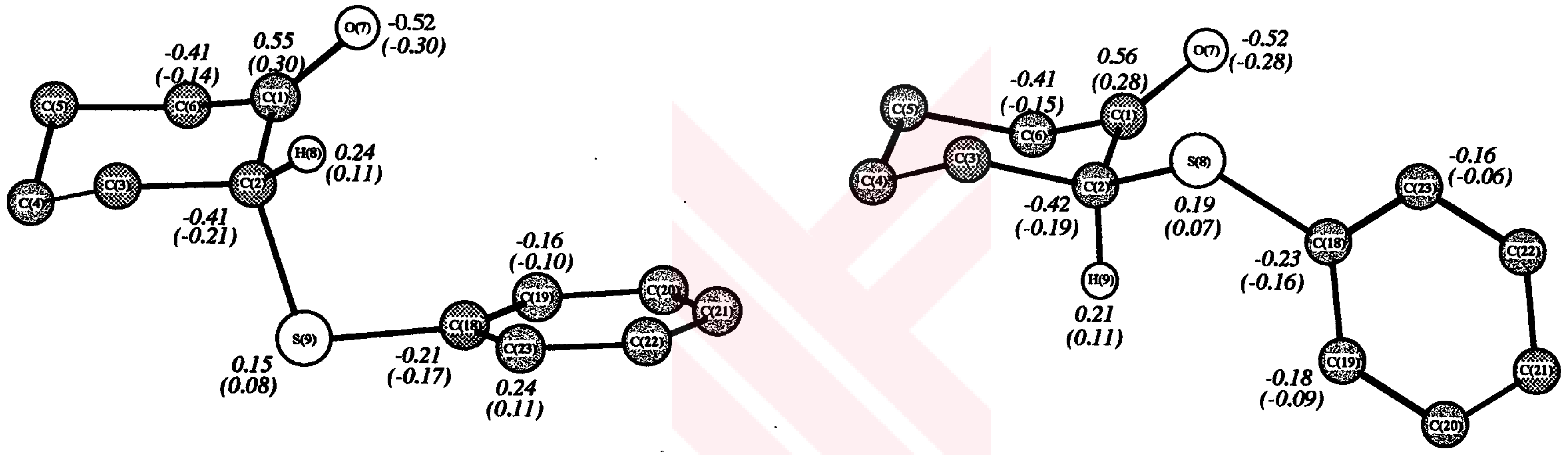

FIGURE 3.9. Structures for the optimized axial and equatorial conformers (HF/6-31G*) for α-SC_6H_5 substituted cyclohexanone. Mulliken chareges on the atoms of interest are given in italics for HF/6-31G* and in parantheses PM3.

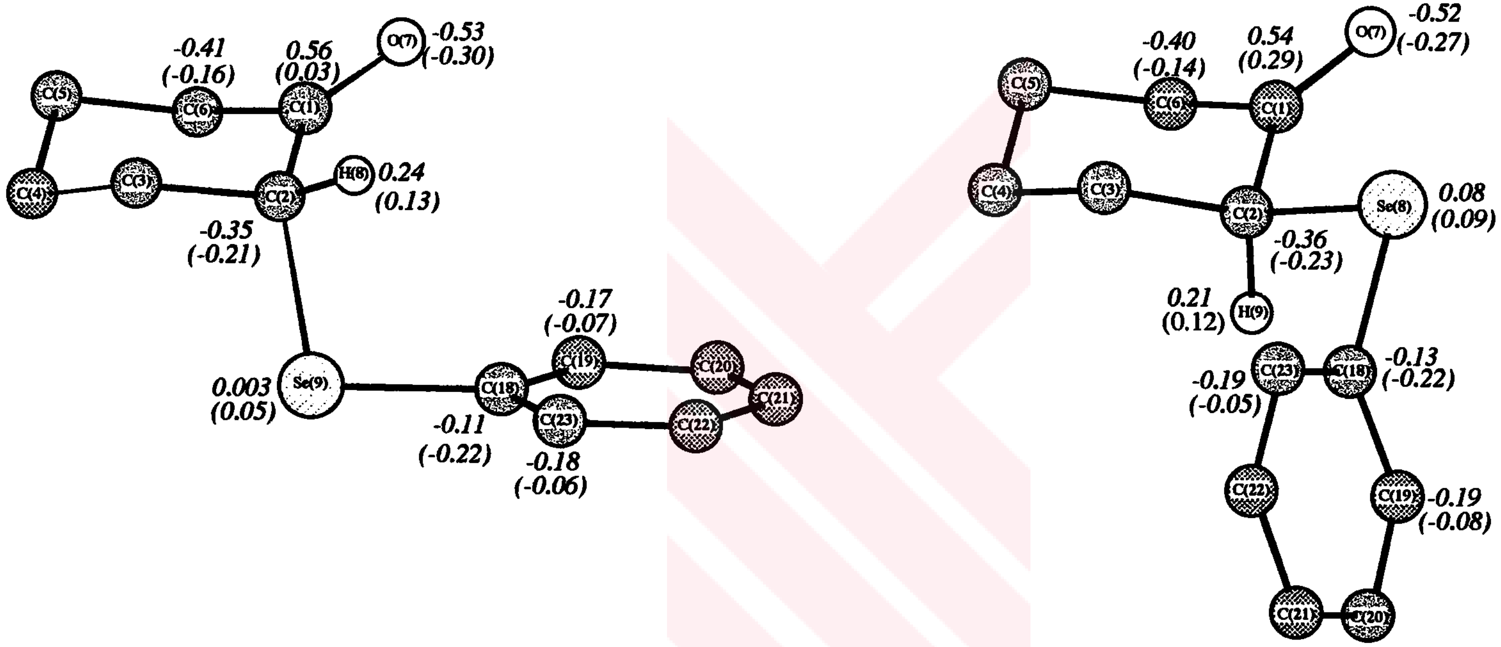

FIGURE 3.10. Structures for the optimized axial and equatorial conformers (HF/6-31G*) for α-SeC_6H_5 substituted cyclohexanone. Mulliken chareges on the atoms of interest are given in italics for HF/6-31G* and in parantheses PM3.

TABLE 3.11. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	OC_6H_5-eq	OC_6H_5-ax	OC_6H_5-eq
	PM3	PM3	HF	HF
C1-C2	1.541	1.534	1.526	1.526
C2-C3	1.533	1.535	1.532	1.531
C2-O	1.430	1.426	1.411	1.397
C2-H	1.123	1.123	1.080	1.088
C1-C6	1.510	1.516	1.511	1.516
O-C18	1.381	1.381	1.355	1.368
O7-C1-C2	120.7	123.8	121.0	123.1
C1-C2-O	105.3	112.1	105.2	112.5
C2-O-C18	117.0	117.4	121.9	118.2
C1-C2-O-H18	152.1	-93.0	81.1	-89.2
C2-O-C18-C19	162.2	-20.0	-11.6	-80.5
Dipole	2.60	3.14	3.20	3.69

TABLE 3.12. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	SC_6H_5-eq	SC_6H_5-ax	SC_6H_5-eq
	PM3	PM3	HF	HF
C1-C2	1.526	1.525	1.523	1.528
C2-C3	1.525	1.528	1.538	1.542
C2-S	1.845	1.832	1.841	1.820
C2-H	1.122	1.121	1.080	1.086
C1-C6	1.512	1.518	1.516	1.518
S-C18	1.764	1.764	1.786	1.787
O7-C1-C2	121.1	124.7	121.0	124.1
C1-C2-S	110.4	119.3	110.4	115.1
C2-S-C18	105.5	109.8	102.1	102.6
C1-C2-S-H18	101.6	56.3	76.3	-75.4
C2-S-C18-C19	6.0	32.2	-92.8	-91.6
Dipole	1.68	2.60	1.38	3.68

TABLE 3.13. Selected bond lengths(Å), bond angles(°), dihedralangles(°) and dipole moments(D) of α-SeC$_6$H$_5$ substituted cyclohexanone.

	SeC$_6$H$_5$-ax	SeC$_6$H$_5$-eq	SeC$_6$H$_5$-ax	SeC$_6$H$_5$-eq
	PM3	PM3	HF	HF
C1-C2	1.507	1.508	1.517	1.520
C2-C3	1.506	1.507	1.535	1.537
C2-Se	1.964	1.960	1.975	1.959
C2-H	1.113	1.108	1.079	1.084
C1-C6	1.512	1.511	1.516	1.516
Se-C18	1.881	1.885	1.912	1.916
O7-C1-C2	121.9	121.2	121.4	123.1
C1-C2-Se	100.9	102.2	108.7	109.4
C2-Se-C18	103.7	104.8	99.0	98.0
C1-C2-Se-H18	112.1	-169.1	81.6	-167.8
C2-Se-C18-C19	3.0	-18.0	-93.7	82.1
Dipole	2.02	3.91	1.57	4.87

TABLE 3.14. Energetics (kcal/mol) for the conformational equilibrium for α-XC_6H_5 substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3
	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3\,b}$	ΔG^c
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=1)
$-OC_6H_5$	-58.82	-58.58	-0.24	0.13	-0.27
$-SC_6H_5$	-18.24	-16.60	-1.64	2.11	-2.27
$-SeC_6H_5$	-48.76	-43.60	-5.16	-0.25	-5.08

[a] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K.

TABLE 3.15. Energetics (kcal/mol) for the conformational equilibrium for α-XC_6H_5 substituted cyclohexanones (HF/6-31G*).

	HF	HF	HF	HF
	ΔH^a	$\Delta S/10^{-3\,b}$	ΔG^c	ΔE^d
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)
$-OC_6H_5$	-0.98	-1.26	-0.60	-1.28
$-SC_6H_5$	0.16	1.79	-0.37	0.09
$-SeC_6H_5$	-2.26	0.44	-2.38	-2.41

[a] ΔH= (Sum of electronic and thermal energy)$_{ax}$ - (Sum of electronic and thermal energy)$_{eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta H - T\Delta S$ at 298K.

[d] $\Delta E = E_{ax} - E_{eq}$.

3.2.5 α-(p-F, Cl, Br, NO_2, NH_2, OCH_3) OC_6H_5, SC_6H_5, SeC_6H_5 Substituted Cyclohexanones

Substitution of F, Cl, Br, NO_2, NH_2, OCH_3 on the para position of the phenyl groups will be discussed with the PM3 method (FIGURES 3.11. - 3.28.).

When the para substitutents are added to the phenyl ring, they do not alter the geometry of the unsubstituted compounds (TABLES 3.16. - 3.33.). In the axial position of these compounds the C1-C2 bond is again longer than the C1-C6 bond. This shows us that the anomeric effect is also present in these compounds. The C-F bond is somewhat longer in OC_6H_5 compounds (1.344Å) than in SC_6H_5 (1.342Å) and SeC_6H_5 (1.343Å) substituted compounds. The same observation is true for the C-Cl bond (1.686Å in OC_6H_5, 1.683Å in SC_6H_5, 1.685Å in SeC_6H_5). This behaviour may be due to the electron withdrawing character of the heteroatom. O is more electronegative than S and Se, thus electron withdrawal by resonance weakens the bond of the para substituted halogen. It is interesting to notice the C-N bond length variation in the $XC_6H_5NO_2$ compounds. The C-N bond length is 1.492Å in OC_6H_5, 1.496Å in SC_6H_5 and 1.498Å in SeC_6H_5. This trend is opposite to the one observed for the halogen because of the contribution of the π electrons of the NO_2 group to the C-N bond. Electron withdrawal by the heteroatom activates the π electrons of the NO_2 group and π electrons are donated to the C-N bond which becomes shorter for the more electronegative atom namely O. The NO_2 group is coplanar with the phenyl ring and this position favors electron donation by resonance. The NH_2 group behaves similarly to F and Cl. The C-N bond is longer in OC_6H_5 (1.432Å) than in SC_6H_5 (1.427Å) and SeC_6H_5 (1.427Å). The amino group is not coplanar with the phenyl ring (30° out of plane) and the lone pairs on the amino group are not available for resonance with the phenyl group. Notice also that the geometrical parameters for axial / equatorial conformers do not differ from each other. The relative position of the substituent with respect to the ring (the value of the C1-C2-X-C18 and C2-X-C18-C19 angles) is similar to the one in the unsubstituted compounds.

The carbon atom of the methoxy group, C29 is coplanar with the phenyl ring and this may cause oxygen's lone pairs to have larger overlap with π orbital of the phenyl group. The hydrogens of methoxy are oriented in a way to minimize steric interactions with the phenyl hydrogens.

For α-OC_6H_5Y substituted cyclohexanones, halogens and electron donor groups direct the equilibrium to the axial position (TABLE 3.34.). A representative of the electron withdrawing groups, NO_2, shifts the equilibrium towards the equatorial position. Experimental results have shown a transition from the equatorial to the axial position as the character of the substituent changes from electron withdrawing to electron donor. Experimentally NO_2 has the largest (+) change in free energy, the same is true according to our calculations.

For α-SC_6H_5Y substituted cyclohexanones, there is a decreasing preference for the axial orientation as the character of the substituent varies from electron donor to electron withdrawing (TABLE 3.35.). Our calculations reproduce the experimental trend detected by Sebüktekin [25].

For α-SeC_6H_5Y substituted cyclohexanones, the preference for the axial position decreases as the character of the substituent varies from electron donor to electron withdrawing (TABLE 3.36.).

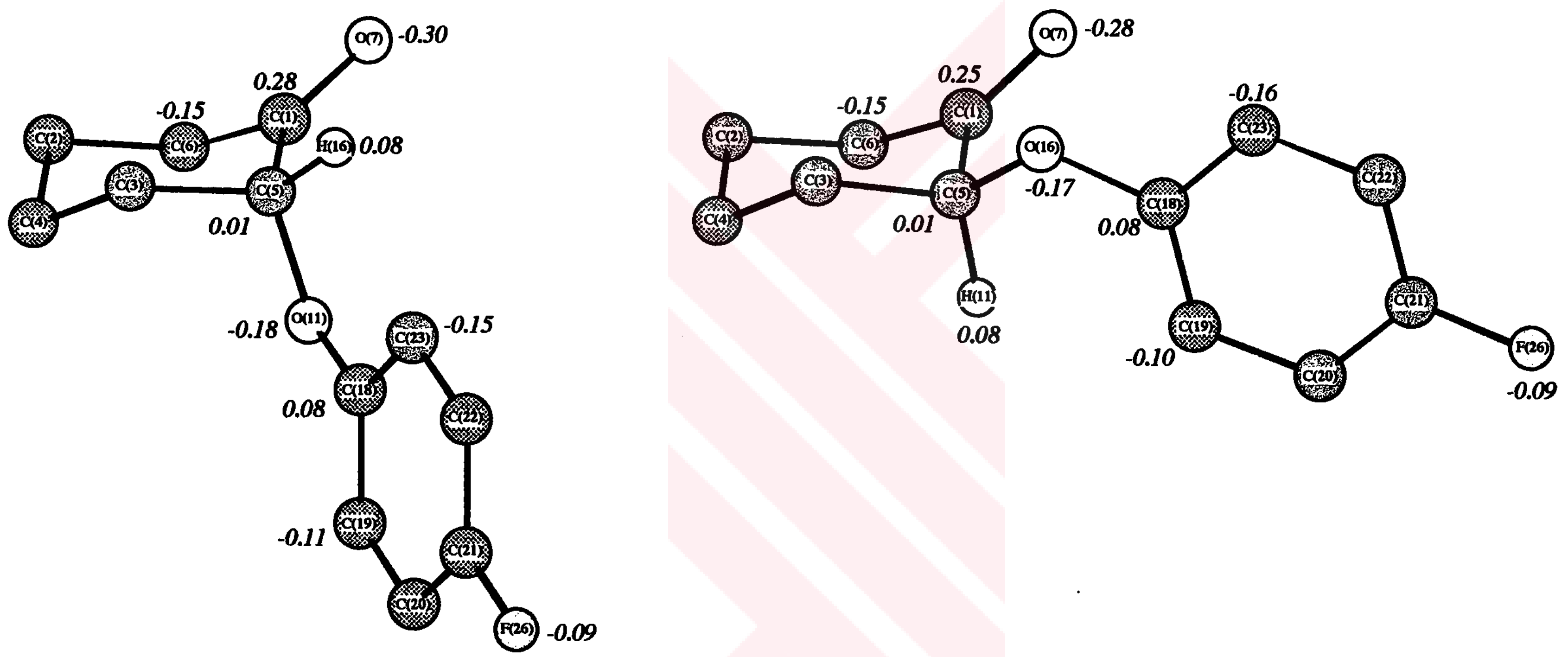

FIGURE 3.11. Structures for optimized axial and equatorial conformers (PM3) for α-(p-F)OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

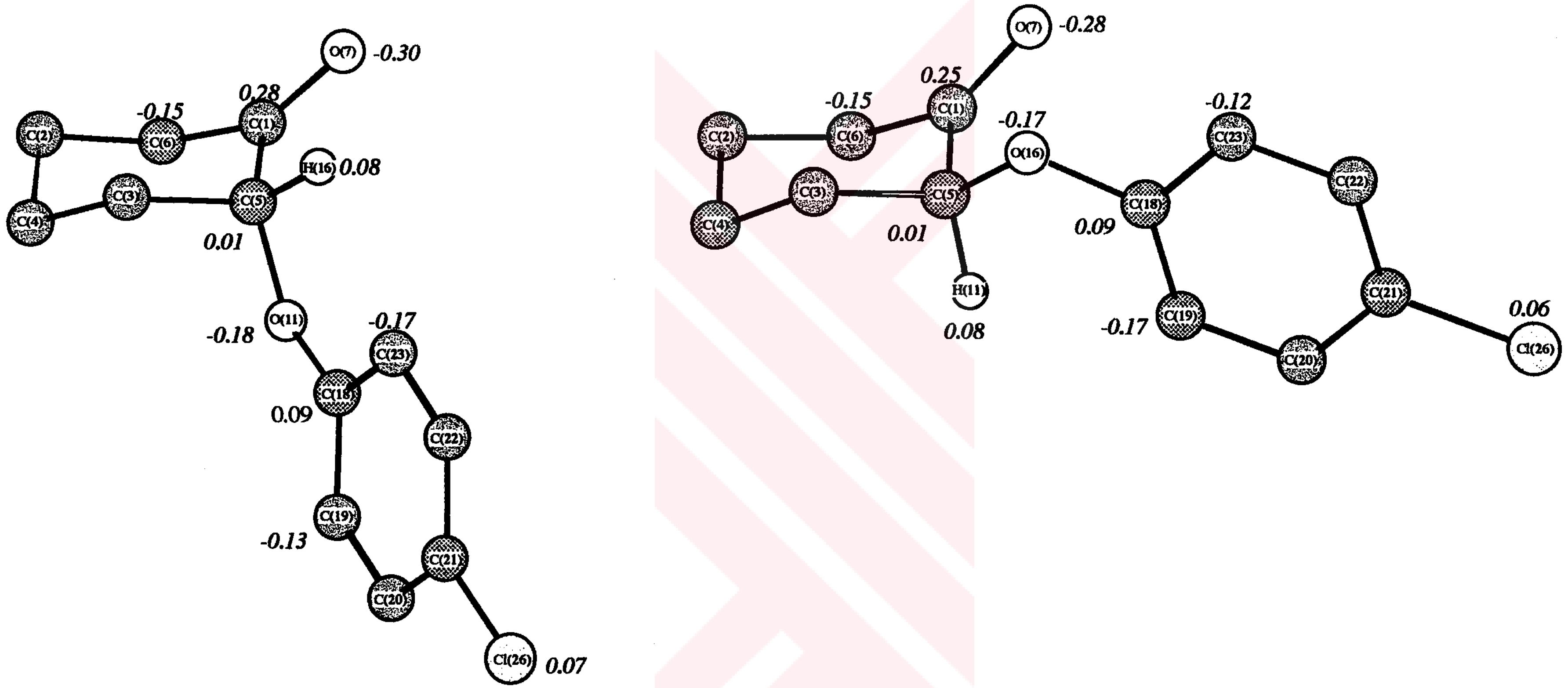

FIGURE 3.12. Structures for optimized axial and equatorial conformers (PM3) for α-(p-Cl)OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

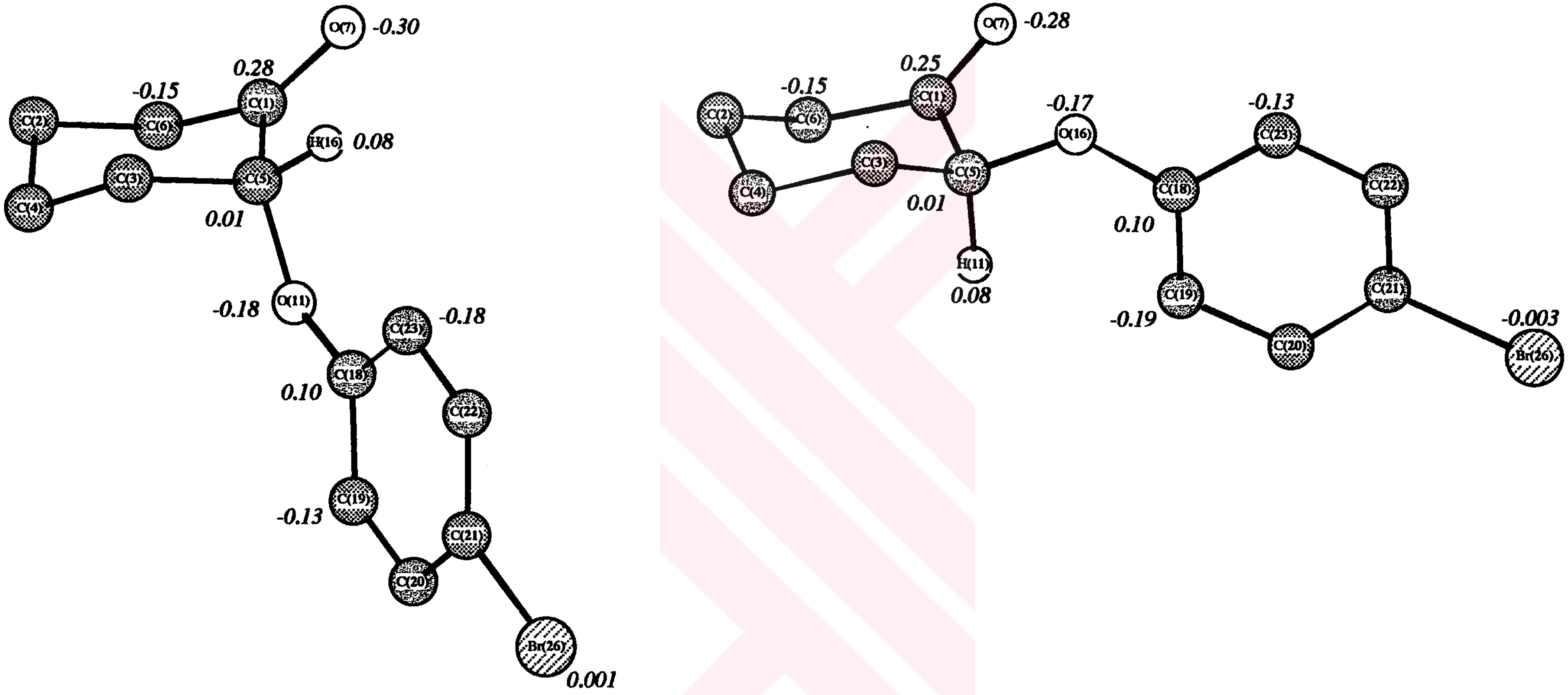

FIGURE 3.13. Structures for optimized axial and equatorial conformers (PM3) for α-(p-Br)OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

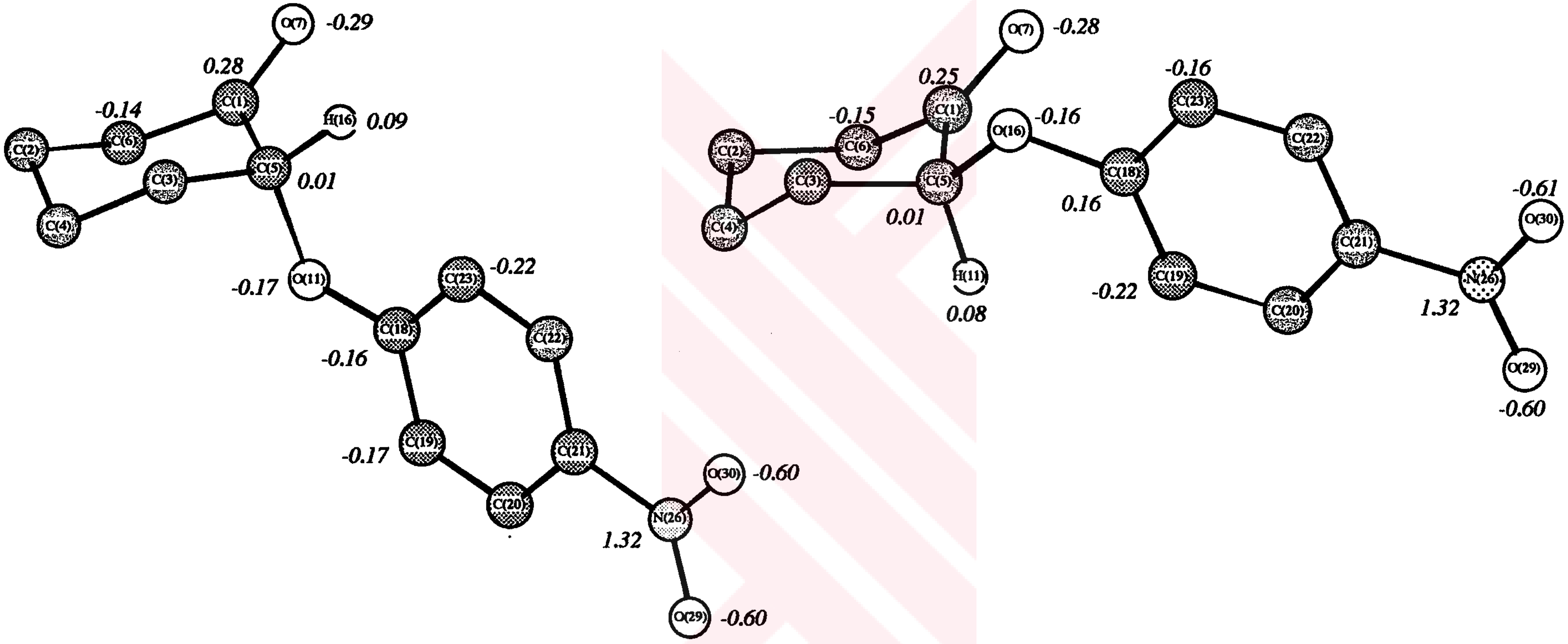

FIGURE 3.14. Structures for optimized axial and equatorial conformers (PM3) for α-(p-NO_2)OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

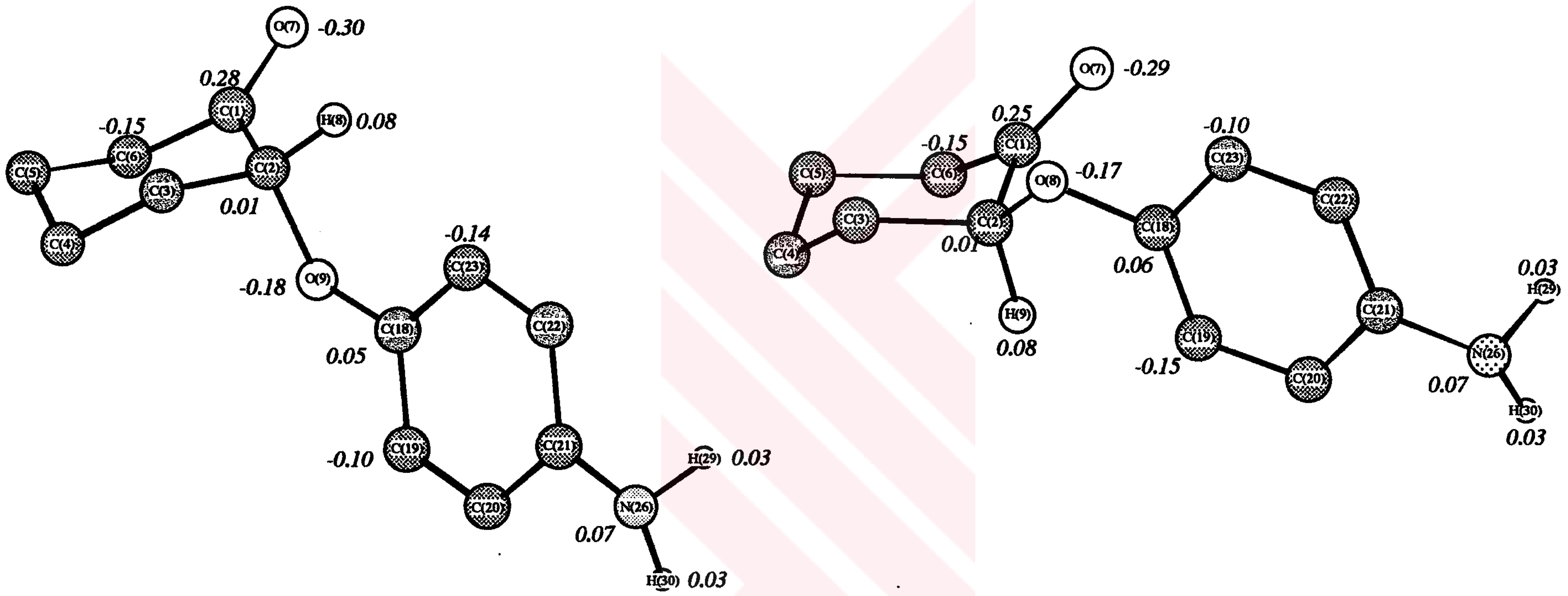

FIGURE 3.15. Structures for optimized axial and equatorial conformers (PM3) for α-(p-NH_2)OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

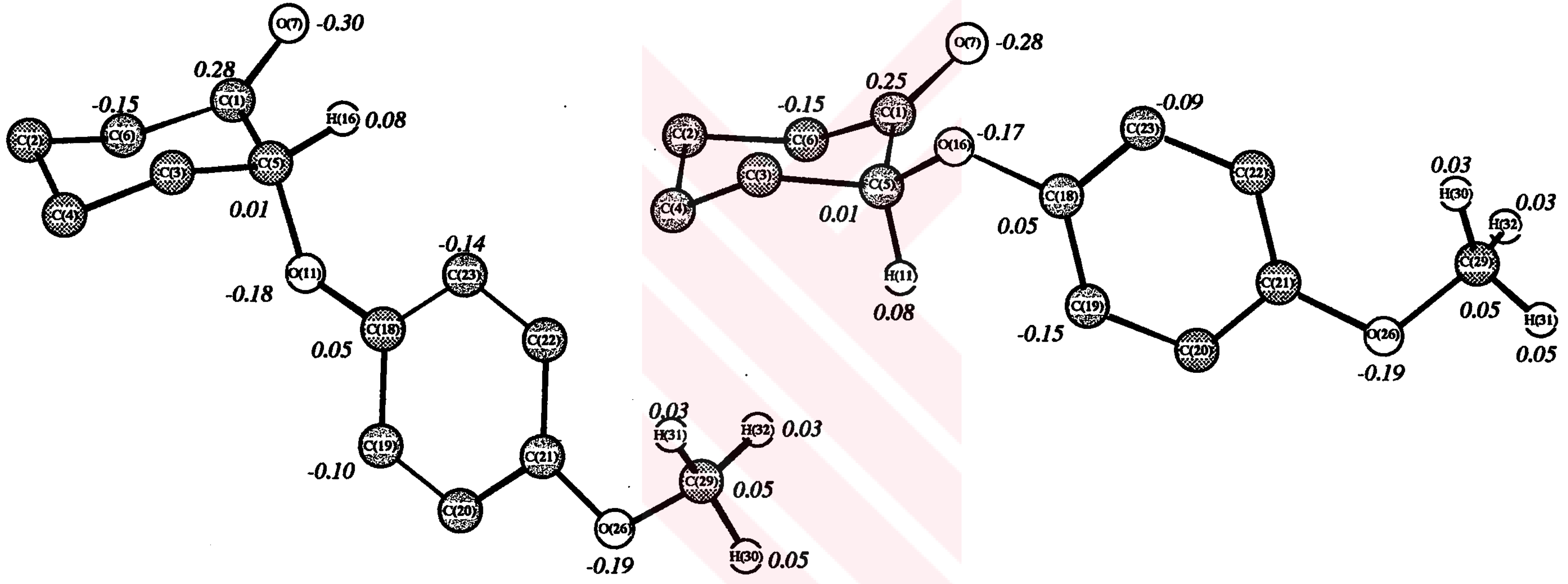

FIGURE 3.16. Structures for optimized axial and equatorial conformers (PM3) for α-(p-OCH_3)OC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

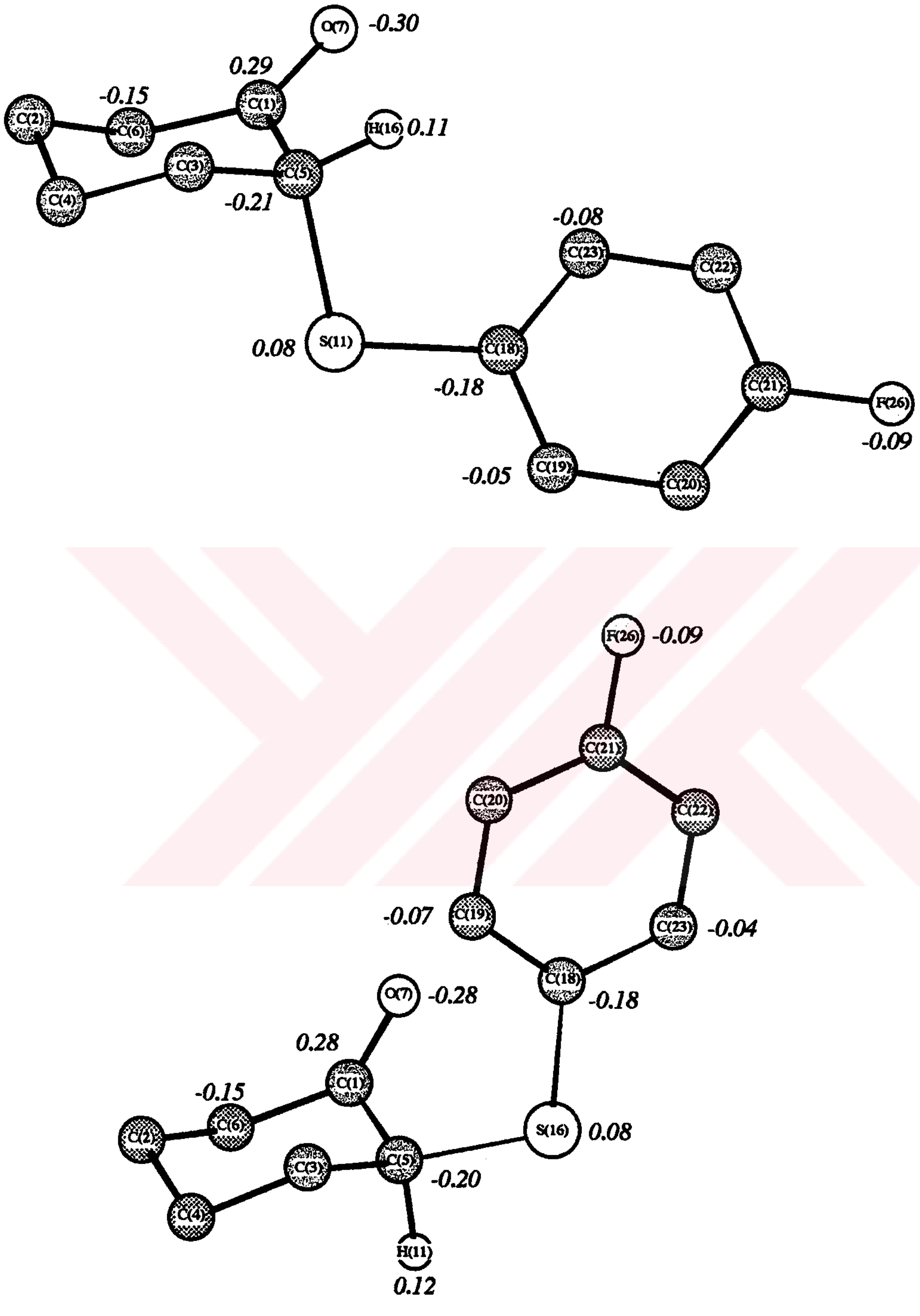

FIGURE 3.17. Structures for optimized axial and equatorial conformers (PM3) for α-(p-F)SC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

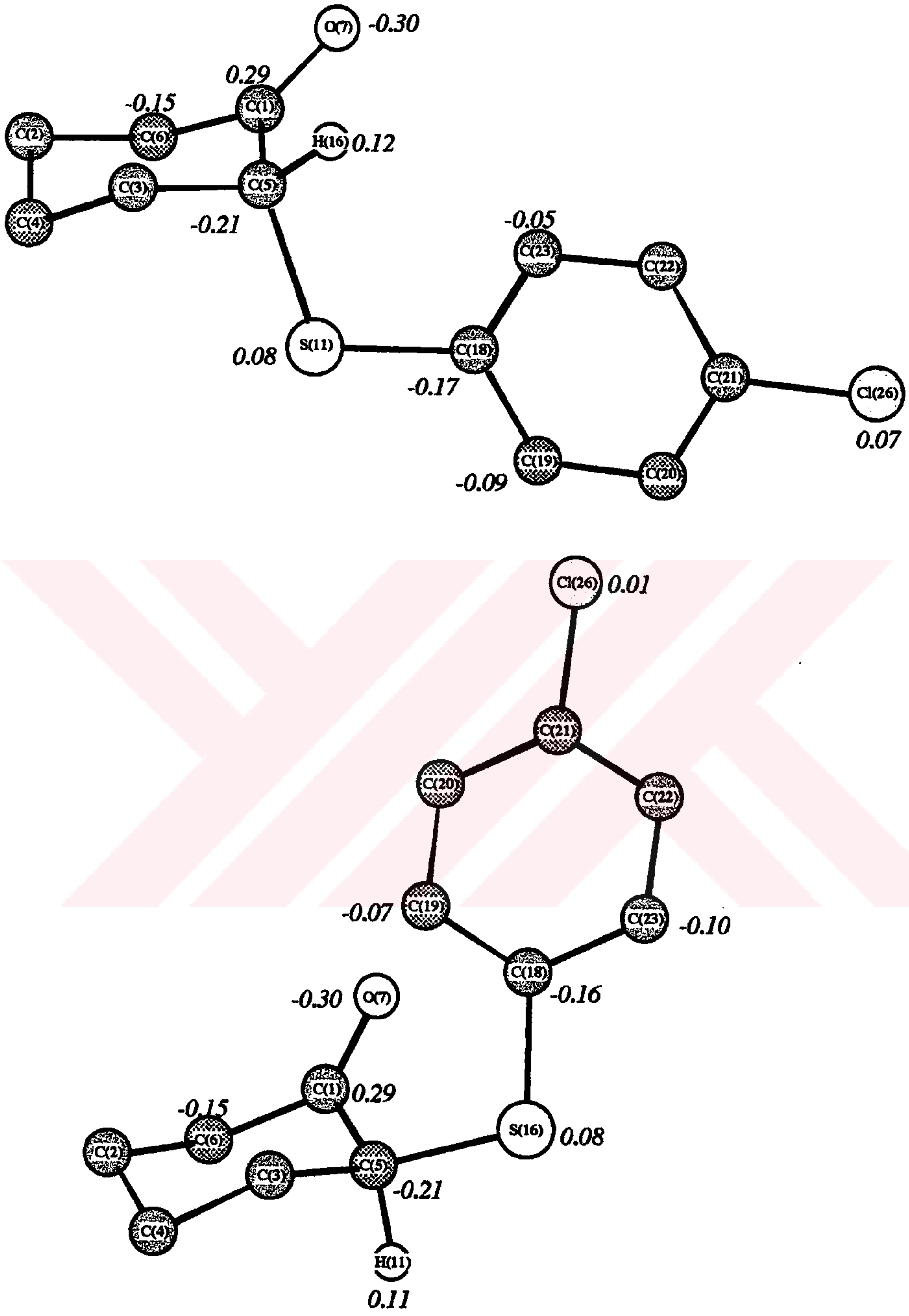

FIGURE 3.18. Structures for optimized axial and equatorial conformers (PM3) for α-(p-Cl)SC$_6$H$_5$ substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

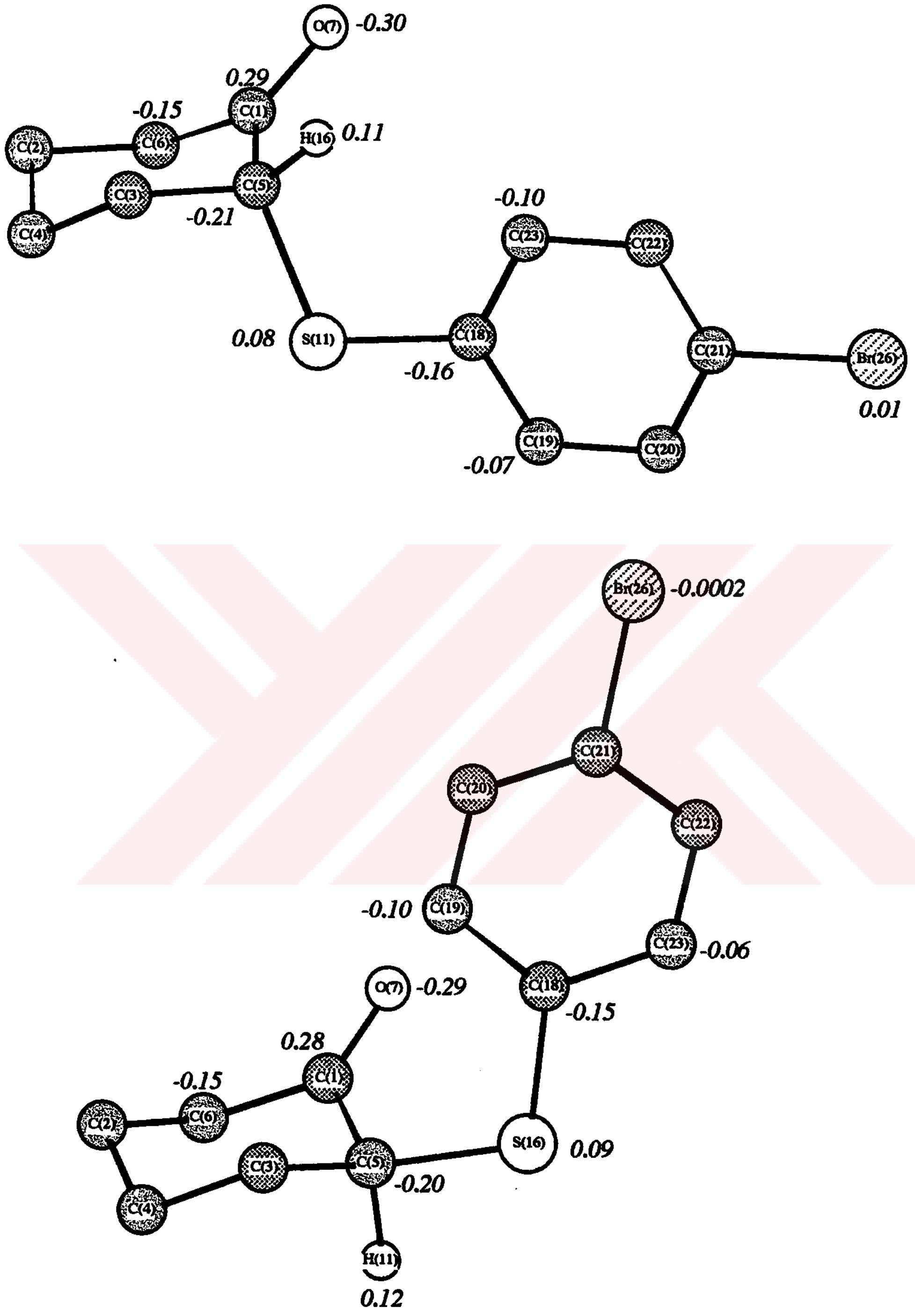

FIGURE 3.19. Structures for optimized axial and equatorial conformers (PM3) for α-(p-Br)SC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

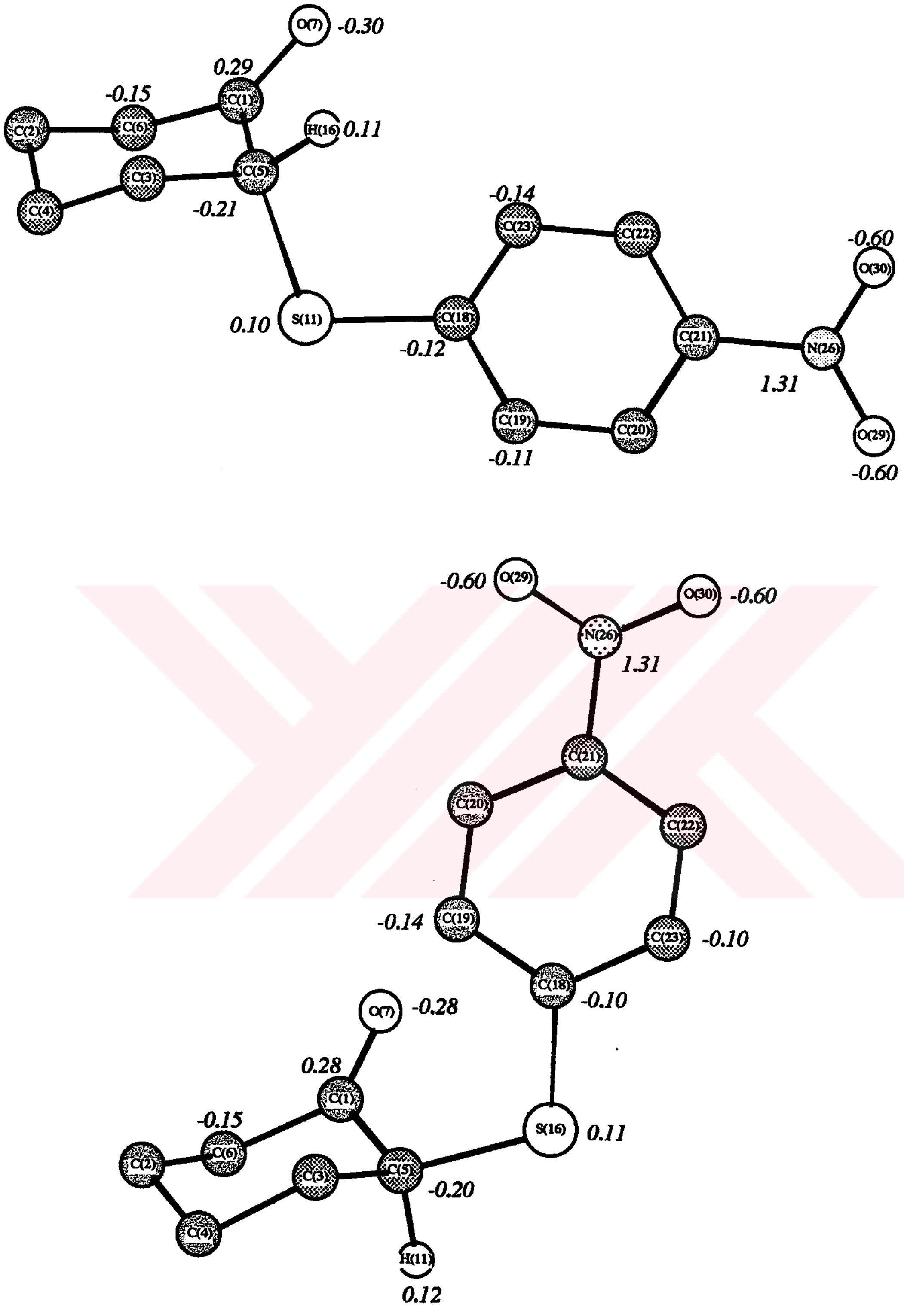

FIGURE 3.20. Structures for optimized axial and equatorial conformers (PM3) for α-(p-NO_2)SC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

FIGURE 3.21. Structures for optimized axial and equatorial conformers (PM3) for α-(p-NH_2)SC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

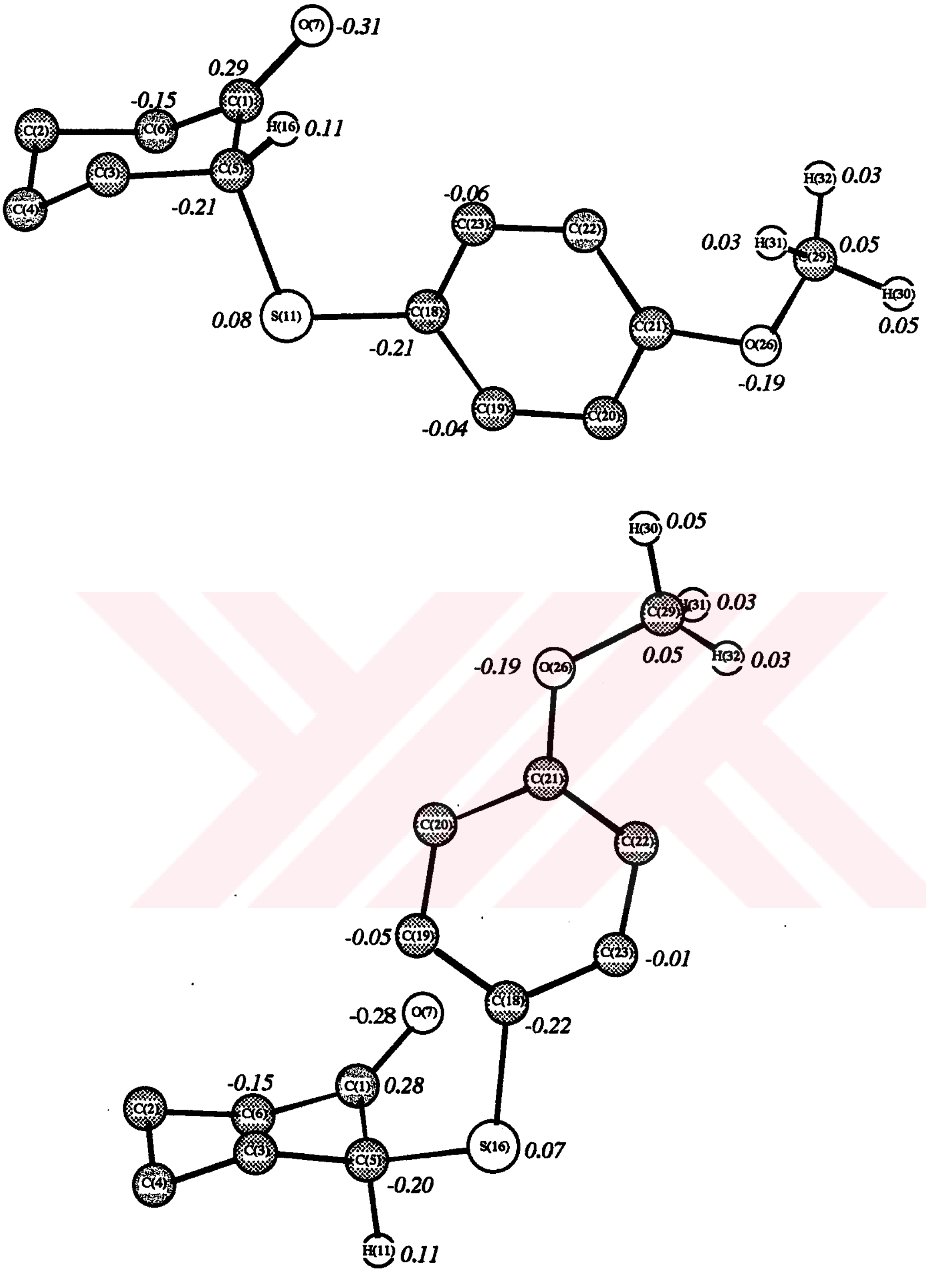

FIGURE 3.22. Structures for optimized axial and equatorial conformers (PM3) for α-(p-OCH_3)SC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

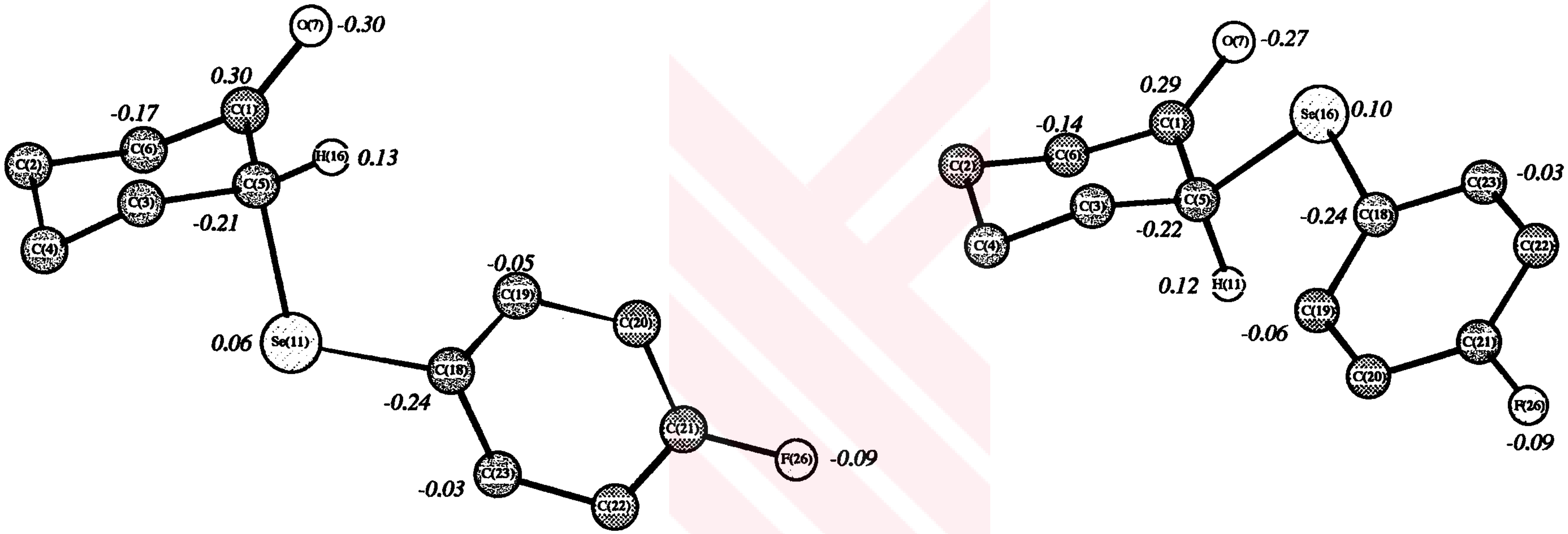

FIGURE 3.23. Structures for optimized axial and equatorial conformers (PM3) for α-(p-F)SeC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

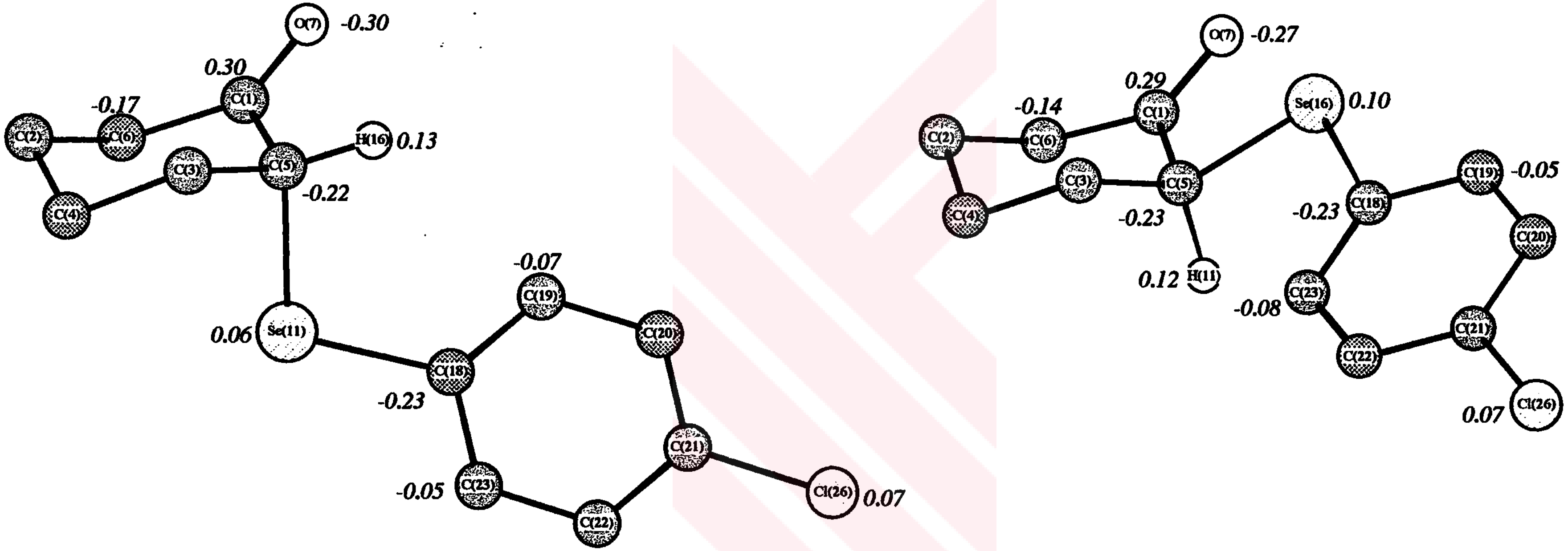

FIGURE 3.24. Structures for optimized axial and equatorial conformers (PM3) for α-(p-Cl)SeC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

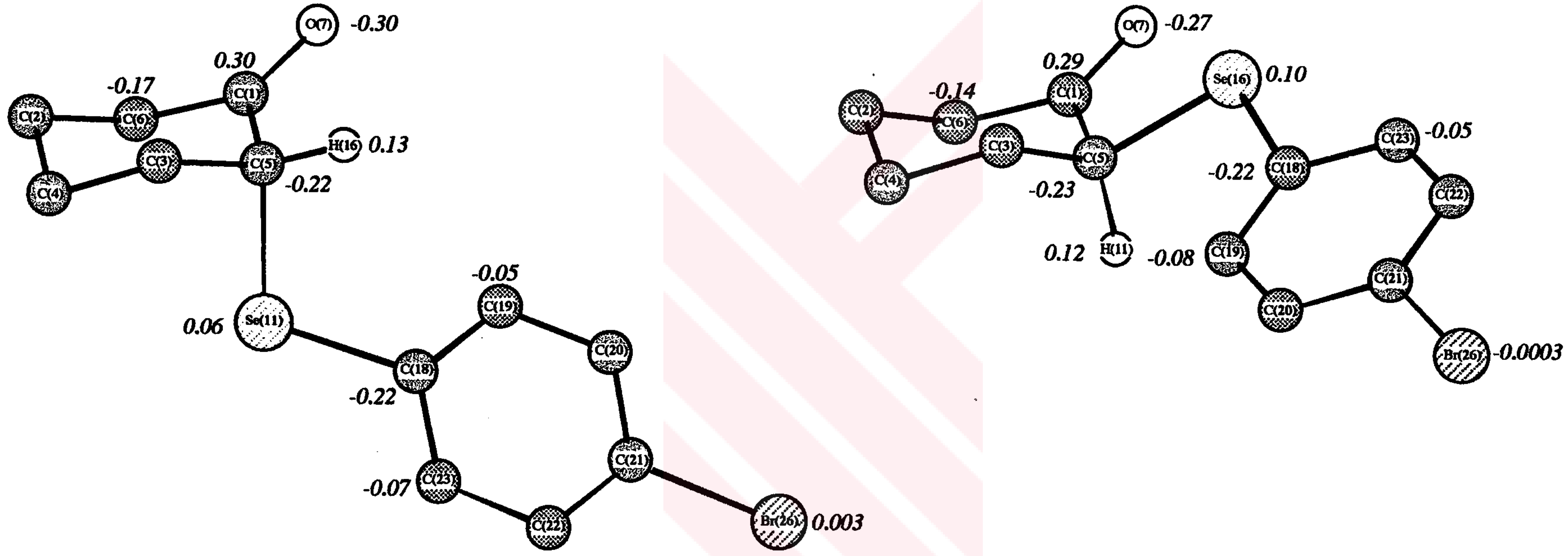

FIGURE 3.25. Structures for optimized axial and equatorial conformers (PM3) for α-(p-Br)SeC$_6$H$_5$ substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

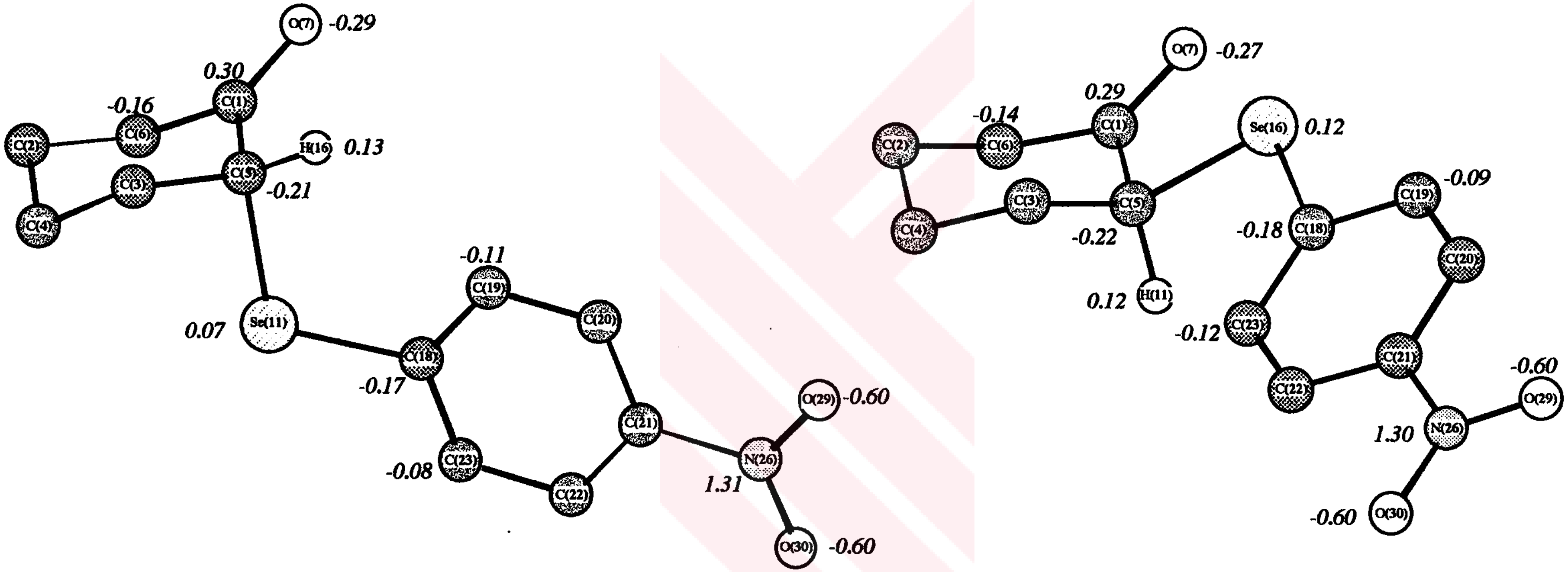

FIGURE 3.26. Structures for optimized axial and equatorial conformers (PM3) for α-(p-NO_2)SeC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

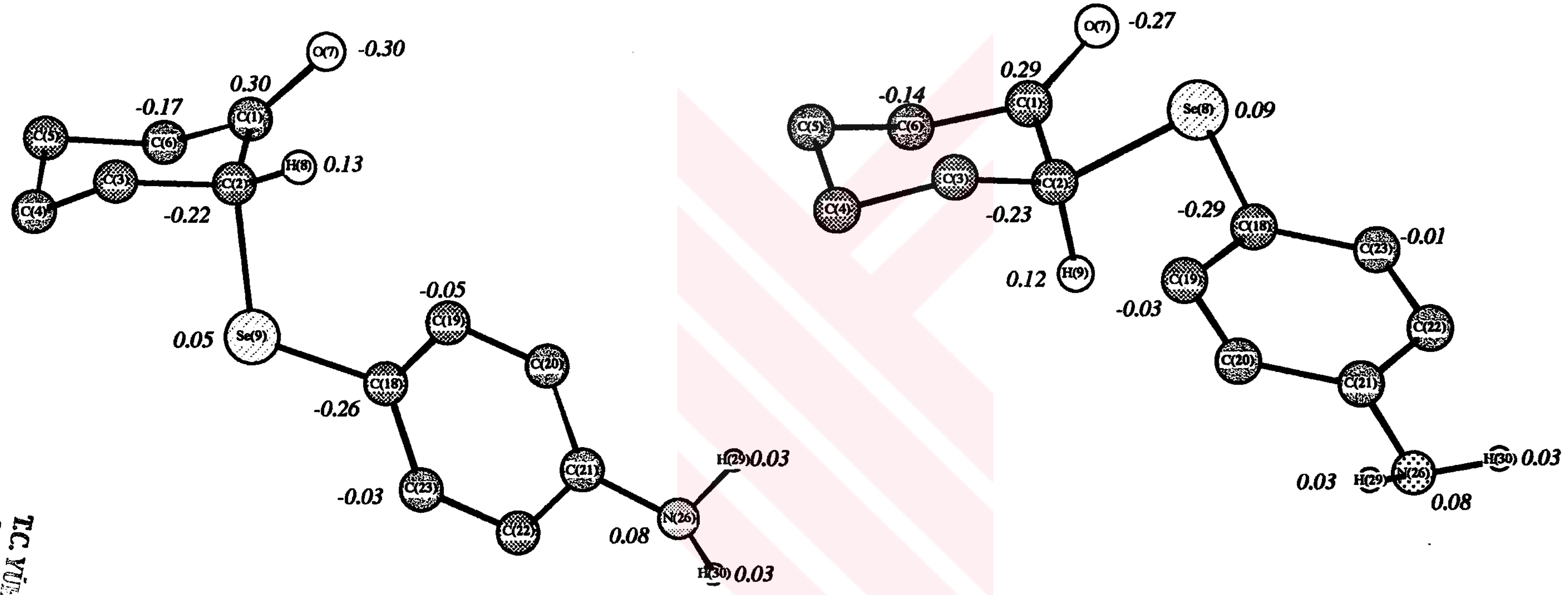

FIGURE 3.27. Structures for optimized axial and equatorial conformers (PM3) for α-(p-NH_2)SeC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

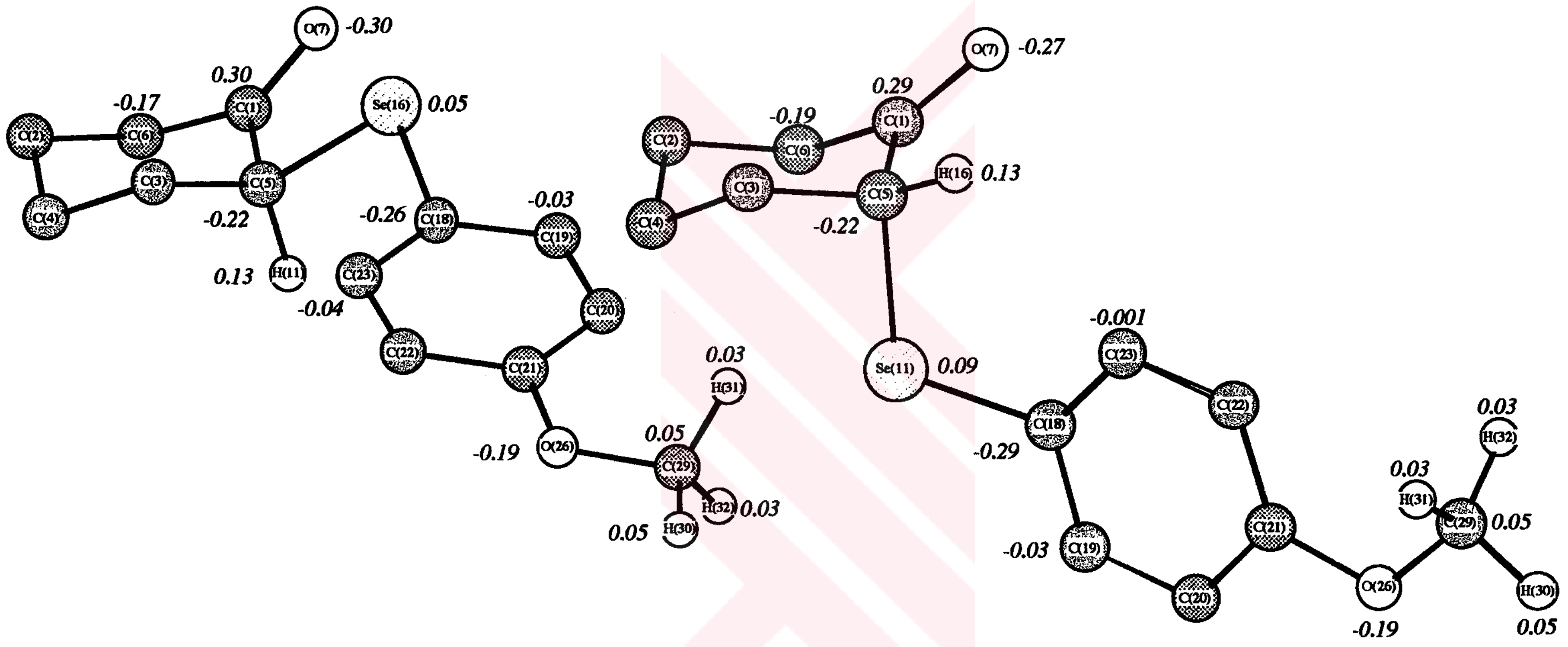

FIGURE 3.28. Structures for optimized axial and equatorial conformers (PM3) for α-(p-OCH_3)SEC_6H_5 substituted cyclohexanone. Mulliken charges on the atoms of interest are given in italics.

TABLE 3.16. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-F)OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	**OC_6H_5-eq**
	PM3	PM3
C1-C5	1.541	1.534
C3-C5	1.533	1.535
C5-O	1.431	1.426
C5-H	1.123	1.123
C1-C6	1.509	1.516
O-C18	1.381	1.381
C21-F	1.344	1.344
O7-C1-C5	120.6	123.7
C1-C5-O	105.2	112.2
C5-O-C18	117.0	117.3
C1-C5-O-C18	152.5	-92.0
C5-O-C18-C19	161.3	-22.9
Dipole	2.83	4.08

TABLE 3.17. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-Cl)OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	**OC_6H_5-eq**
	PM3	PM3
C1-C5	1.541	1.534
C3-C5	1.533	1.535
C5-O	1.431	1.427
C5-H	1.123	1.123
C1-C6	1.509	1.515
O-C18	1.380	1.380
C21-Cl	1.686	1.686
O7-C1-C5	120.6	123.7
C1-C5-O	105.3	112.1
C5-O-C18	117.1	117.5
C1-C5-O-C18	151.8	-93.1
C5-O-C18-C19	163.4	-20.6
Dipole	2.61	3.67

TABLE 3.18. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-Br)OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	OC_6H_5-eq
	PM3	PM3
C1-C5	1.542	1.534
C3-C5	1.534	1.535
C5-O	1.431	1.428
C5-H	1.124	1.123
C1-C6	1.510	1.517
O-C18	1.380	1.378
C21-Br	1.867	1.868
O7-C1-C5	120.4	123.3
C1-C5-O	105.3	111.7
C5-O-C18	117.9	118.1
C1-C5-O-H18	145.9	-94.4
C5-O-C18-C19	172.9	-12.2
Dipole	2.67	3.88

TABLE 3.19. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-NO_2)OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	OC_6H_5-eq
	PM3	PM3
C1-C5	1.542	1.535
C3-C5	1.532	1.535
C5-O	1.433	1.430
C5-H	1.123	1.123
C1-C6	1.509	1.515
O-C18	1.370	1.370
C21-N26	1.492	1.491
N26-O29	1.215	1.216
N26-O30	1.215	1.215
O7-C1-C5	120.4	123.3
C1-C5-O	105.3	111.7
C5-O-C18	117.9	118.1
C1-C5-O-H18	145.9	-94.4
C5-O-C18-C19	172.9	-12.2
C20-C21-N26-O29	0.8	0.5
C20-C21-N26-O30	-179.0	-179.4
Dipole	6.20	7.50

TABLE 3.20. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-NH_2)OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	OC_6H_5-eq
	PM3	PM3
C1-C2	1.541	1.534
C2-C3	1.534	1.536
C2-O	1.431	1.426
C2-H	1.124	1.124
C1-C6	1.510	1.517
O-C18	1.385	1.384
C21-N26	1.432	1.433
N26-H29	0.996	0.996
N26-H30	0.996	0.996
O7-C1-C2	120.7	123.9
C1-C2-O	105.3	112.3
C2-O-C18	116.2	117.0
C1-C2-O-H18	154.5	-91.7
C2-O-C18-C19	154.5	-25.1
C20-C21-N26-H29	154.4	154.8
C20-C21-N26-H30	29.9	30.6
Dipole	1.93	2.71

TABLE 3.21. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-OCH_3)OC_6H_5 substituted cyclohexanone.

	OC_6H_5-ax	OC_6H_5-eq
	PM3	PM3
C1-C5	1.541	1.534
C3-C5	1.534	1.535
C5-O	1.431	1.426
C5-H	1.124	1.123
C1-C6	1.510	1.516
O-C18	1.385	1.384
C21-O26	1.383	1.385
C29-H30	1.093	1.100
C29-H31	1.096	1.092
C29-H32	1.096	1.095
O7-C1-C5	120.7	123.9
C1-C5-O	105.3	112.3
C5-O-C18	116.3	116.9
C1-C5-O-C18	154.0	-91.4
C5-O-C18-C19	154.4	-28.0
C20-C21-O26-C29	177.6	160.2
C21-O26-C29-H30	-178.8	45.2
C21-O26-C29-H31	63.4	164.6
C21-O26-C29-H32	-60.8	-77.5
Dipole	2.47	2.06

TABLE 3.22. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-F)SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	SC_6H_5-eq
	PM3	PM3
C1-C5	1.526	1.525
C3-C5	1.525	1.528
C5-S	1.845	1.833
C5-H	1.122	1.121
C1-C6	1.512	1.518
S-C18	1.764	1.763
C21-F	1.342	1.342
07-C1-C5	120.8	124.6
C1-C5-S	110.5	119.3
C5-S-C18	105.4	109.9
C1-C5-S-C18	100.0	55.9
C5-S-C18-C19	-173.3	36.3
Dipole	2.88	3.94

TABLE 3.23. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-Cl)SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	SC_6H_5-eq
	PM3	PM3
C1-C5	1.526	1.525
C3-C5	1.525	1.528
C5-S	1.845	1.833
C5-H	1.122	1.121
C1-C6	1.512	1.518
S-C18	1.763	1.763
C21-Cl	1.683	1.684
07-C1-C5	120.9	124.6
C1-C5-S	110.4	119.3
C5-S-C18	105.5	109.9
C1-C5-S-C18	101.4	57.3
C5-S-C18-C19	-174.8	30.6
Dipole	2.29	3.52

TABLE 3.24. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-Br)SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	SC_6H_5-eq
	PM3	PM3
C1-C5	1.527	1.526
C3-C5	1.525	1.528
C5-S	1.846	1.832
C5-H	1.123	1.121
C1-C6	1.512	1.518
S-C18	1.765	1.764
C21-Br	1.867	1.867
O7-C1-C5	120.9	124.6
C1-C5-S	110.4	119.3
C5-S-C18	105.5	110.0
C1-C5-S-C18	101.4	58.0
C5-S-C18-C19	-175.3	27.3
Dipole	2.50	3.74

TABLE 3.25. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-NO_2)SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	SC_6H_5-eq
	PM3	PM3
C1-C5	1.528	1.526
C3-C5	1.524	1.528
C5-S	1.845	1.831
C5-H	1.122	1.121
C1-C6	1.511	1.517
S-C18	1.757	1.755
C21-N26	1.496	1.495
N26-O29	1.215	1.215
N26-O30	1.215	1.215
O7-C1-C5	120.6	124.4
C1-C5-S	110.3	119.1
C5-S-C18	105.5	110.2
C1-C5-S-C18	101.1	62.0
C5-S-C18-C19	-177.2	15.0
C21-C22-N26-O29	2.5	1.6
C21-C22-N26-O30	-177.2	-179.0
Dipole	6.81	7.70

TABLE 3.26. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-NH_2)SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	**SC_6H_5-eq**
	PM3	PM3
C1-C5	1.526	1.524
C3-C5	1.525	1.528
C5-S	1.845	1.834
C5-H	1.122	1.121
C1-C6	1.512	1.518
S-C18	1.764	1.763
C21-N26	1.427	1.426
N26-H29	0.996	0.996
N26-H30	0.996	0.996
O7-C1-C5	120.9	124.7
C1-C5-S	110.6	119.3
C5-S-C18	105.2	108.7
C1-C5-S-C18	98.8	55.2
C5-S-C18-C19	-168.8	45.9
C21-C22-N26-H29	29.7	-29.7
C21-C22-N26-H30	155.2	-155.3
Dipole	0.26	3.00

TABLE 3.27. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-OCH_3)SC_6H_5 substituted cyclohexanone.

	SC_6H_5-ax	**SC_6H_5-eq**
	PM3	PM3
C1-C5	1.526	1.525
C3-C5	1.525	1.528
C5-S	1.845	1.835
C5-H	1.122	1.120
C1-C6	1.512	1.519
S-C18	1.765	1.765
C21-O26	1.379	1.379
C29-H30	1.093	1.093
C29-H31	1.096	1.096
C29-H32	1.096	1.096
O7-C1-C5	120.9	124.7
C1-C5-S	110.7	119.2
C5-S-C18	105.2	108.4
C1-C5-S-C18	98.3	55.5
C5-S-C18-C19	-168.6	48.9
C20-C21-O26-C29	178.8	-178.6
C21-C26-C29-H30	-179.4	179.3
C21-C26-C29-H31	62.7	61.4
C21-C26-C29-H32	-61.5	-62.8
Dipole	1.78	1.74

TABLE 3.28. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-F)SeC_6H_5 substituted cyclohexanone.

	SeC_6H_5-ax	SeC_6H_5-eq
	PM3	PM3
C1-C5	1.507	1.509
C3-C5	1.506	1.507
C5-Se	1.964	1.961
C5-H	1.113	1.108
C1-C6	1.512	1.511
Se-C18	1.881	1.885
C21-F	1.343	1.343
O7-C1-C5	121.8	121.1
C1-C5-Se	100.9	101.9
C5-Se-C18	103.7	105.0
C1-C5-Se-C18	111.3	-169.4
C5-Se-C18-C19	4.2	-19.5
Dipole	2.94	3.98

TABLE 3.29. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-Cl)SeC_6H_5 substituted cyclohexanone.

	SeC_6H_5-ax	SeC_6H_5-eq
	PM3	PM3
C1-C5	1.507	1.509
C3-C5	1.506	1.507
C5-Se	1.964	1.961
C5-H	1.114	1.108
C1-C6	1.513	1.511
Se-C18	1.880	1.885
C21-Cl	1.685	1.685
O7-C1-C5	121.8	121.1
C1-C5-Se	100.9	102.0
C5-Se-C18	103.7	105.0
C1-C5-Se-C18	111.1	-170.1
C5-Se-C18-C19	4.2	163.7
Dipole	2.44	3.87

TABLE 3.30. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-Br)SeC_6H_5 substituted cyclohexanone.

	SeC_6H_5-ax	SeC_6H_5-eq
	PM3	PM3
C1-C5	1.508	1.509
C3-C5	1.506	1.507
C5-Se	1.965	1.961
C5-H	1.114	1.108
C1-C6	1.513	1.511
Se-C18	1.882	1.886
C21-Br	1.868	1.868
O7-C1-C5	121.8	121.0
C1-C5-Se	100.9	101.9
C5-Se-C18	103.8	105.0
C1-C5-Se-C18	111.9	-170.1
C5-Se-C18-C19	3.5	165.1
Dipole	2.61	3.91

TABLE 3.31. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-NO_2)SeC_6H_5 substituted cyclohexanone.

	SeC_6H_5-ax	SeC_6H_5-eq
	PM3	PM3
C1-C5	1.508	1.510
C3-C5	1.506	1.507
C5-Se	1.966	1.964
C5-H	1.114	1.108
C1-C6	1.513	1.510
Se-C18	1.879	1.883
C21-N26	1.498	1.497
N26-O29	1.215	1.215
N26-O30	1.215	1.216
O7-C1-C5	121.7	120.6
C1-C5-Se	100.8	101.2
C2-Se-C18	103.7	105.1
C1-C5-Se-C18	111.4	-174.2
C5-Se-C18-C19	3.2	170.7
C20-C21-N26-O29	2.4	0.2
C20-C21-N26-O30	-177.7	-179.8
Dipole	6.59	6.55

TABLE 3.32. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-NH_2)SeC_6H_5 substituted cyclohexanone.

	SeC_6H_5-ax	**SeC_6H_5-eq**
	PM3	PM3
C1-C5	1.507	1.508
C3-C5	1.506	1.507
C5-Se	1.964	1.960
C5-H	1.114	1.108
C1-C6	1.513	1.512
Se-C18	1.880	1.881
C21-N26	1.427	1.426
N26-H29	0.996	0.996
N26-H30	0.996	0.996
07-C1-C5	121.9	121.4
C1-C5-Se	101.0	102.9
C5-Se-C18	103.7	103.1
C1-C5-Se-C18	111.4	-166.0
C5-Se-C18-C19	4.7	-55.7
C20-C21-N26-H29	-29.5	-29.8
C20-C21-N26-H30	-155.1	-155.7
Dipole	0.90	3.81

TABLE 3.33. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-(p-OCH_3)SeC_6H_5 substituted cyclohexanone.

	SeC_6H_5-ax	**SeC_6H_5-eq**
	PM3	PM3
C1-C5	1.507	1.508
C3-C5	1.506	1.507
C5-Se	1.964	1.960
C5-H	1.114	1.108
C1-C6	1.513	1.512
Se-C18	1.880	1.882
C21-026	1.379	1.379
C29-H30	1.093	1.096
C29-H31	1.096	1.096
C29-H32	1.096	1.096
07-C1-C5	121.9	121.4
C1-C5-Se	101.0	102.9
C5-Se-C18	103.7	103.1
C1-C5-Se-C18	111.2	-165.9
C5-Se-C18-C19	-176.1	132.9
C20-C21-026-C29	178.9	1.0
C21-026-C29-H30	-179.5	179.5
C20-C21-C29-H31	62.6	61.6
C20-C21-C29-H32	-61.6	-62.6
Dipole	2.01	3.38

TABLE 3.34. Energetics (kcal/mol) for the conformational equilibrium for α-OC_6H_5Y substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3		
	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3\,b}$	ΔG^c	ΔG^d	ΔG^d
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=2.2)	(ε=37.5)
$-OC_6H_5$	-58.82	-58.58	-0.24	0.13	-0.27	0.10	0.79
$-OC_6H_5F$	-102.75	-101.96	-0.11	0.69	-0.32	0.08	1.04
$-OC_6H_5Cl$	-65.46	-65.31	-0.16	0.43	-0.27	0.22	1.04
$-OC_6H_5Br$	-51.14	-51.01	-0.13	0.09	-0.16	0.22	1.04
$-OC_6H_5NO_2$	-68.51	-68.70	0.19	0.60	0.01	0.93	1.04
$-OC_6H_5NH_2$	-60.65	-60.33	-0.32	0.07	-0.34	---------	1.04
$-OC_6H_5OCH_3$	-96.26	-96.05	-0.21	0.63	-0.21	-0.10	1.04

[a] $\Delta(\Delta H_f)= \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S= S_{ax} - S_{eq}$. [c] $\Delta G= \Delta(\Delta H_f) - T\Delta S$ at 298K. [d] Reference 25, $\Delta G= G_{ax} - G_{eq}$.

TABLE 3.35. Energetics (kcal/mol) for the conformational equilibrium for α-SC_6H_5Y substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3			
	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3\,b}$	ΔG^c	ΔG^d	ΔG^d	ΔG^d
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=2.2)	(ε=4.8)	(ε=20.7)
$-SC_6H_5$	-18.24	-16.60	-1.64	2.11	-2.27	-0.55	-0.33	-0.03
$-SC_6H_5F$	-61.56	-60.15	-1.41	1.88	-1.97	-1.20	-0.76	-0.20
$-SC_6H_5Cl$	-24.80	-23.28	-1.52	1.88	-2.08	-1.00	-0.66	-0.20
$-SC_6H_5Br$	-10.27	-8.78	-1.49	1.91	-2.06	-0.99	-0.66	-0.20
$-SC_6H_5NO_2$	-26.65	-25.57	-1.08	2.42	-1.81	-0.56	-0.37	-0.00
$-SC_6H_5NH_2$	-20.65	-19.13	-1.52	2.67	-2.31	---------	-0.93	---------
$-SC_6H_5OCH_3$	-56.29	-54.87	-1.42	2.88	-2.28	---------	---------	---------

[a] $\Delta(\Delta H_f)= \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S= S_{ax} - S_{eq}$. [c] $\Delta G= \Delta(\Delta H_f) - T\Delta S$ at 298K. [d] Reference 25, $\Delta G= G_{ax} - G_{eq}$.

TABLE 3.36. Energetics (kcal/mol) for the conformational equilibrium for α-SeC_6H_5Y substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3
	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3\ b}$	ΔG^c
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=1)	(ε=1)
$-SeC_6H_5$	-48.76	-43.60	-5.16	-0.25	-5.08
$-SeC_6H_5F$	-92.19	-87.17	-5.02	-0.21	-4.96
$-SeC_6H_5Cl$	-55.34	-50.28	-5.06	-0.11	-5.02
$-SeC_6H_5Br$	-40.88	-35.85	-5.03	0.11	-5.06
$-SeC_6H_5NO_2$	-56.85	-52.15	-4.71	0.42	-4.83
$-SeC_6H_5NH_2$	-51.25	-46.21	-5.04	0.07	-5.06
$-SeC_6H_5OCH_3$	-86.95	-81.97	-4.97	0.04	-4.98

[a] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K.

3.3 Conformational Analysis of α-(OH, SH, SeH, OCH_3, SCH_3, $SeCH_3$, OC_6H_5, SC_6H_5, SeC_6H_5) Substituted Cyclohexanones in Solution

3.3.1 α-OH, SH, SeH Substituted Cyclohexanones

In solution, the geometry and energetics of α-OH, SH, SeH substituted cyclohexanones are investigated with PM3. The more polar conformer in the gas phase is stabilized more in polar media.

For the axial position, the trend observed in solution (ε=37.5) is similar to the one in the gas phase; OH and SH prefer the - gauche orientation, SeH adopts the + gauche orientation. Also, the C1-C2 is longer than the C1-C6, like in gas phase. This again shows us that the anomeric effect is present in these compounds. As the size of the heteroatom increases the anomeric effect decreases (TABLES 3.37., 3.38., 3.39.).

The substituents in the equatorial position except for SeH prefer the + gauche orientation where the dipole is minimum. The long range interactions loose their priority in solution. SeH-eq prefers the anti orientation to the carbonyl group and adopts the least crowded position inspite of its high dipole moment.

The equatorial conformer of OH substituent is more stable than the axial one. On the other hand, the axial conformers of SH and SeH substituents are more stable than the equatorial conformers as seen from the difference in Gibbs free energies (TABLE 3.40.).

According to our calculations with PM3, the axial population of these compounds increases in solution. On the other hand, the axial preference is more dominant for SeH rather than for OH.

TABLE 3.37. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-OH substituted cyclohexanone in CH_3CN.

	OH-ax	**OH-eq**
	PM3	PM3
C1-C2	1.543	1.532
C2-C3	1.536	1.538
C2-X	1.407	1.404
C2-H	1.114	1.115
C1-C6	1.522	1.522
O7-C1-C2	121.3	123.3
C1-C2-X	111.3	114.5
C2-X-C18	107.8	107.7
C1-C2-X-C18	-68.6	60.1
Dipole	4.32	3.78

TABLE 3.38. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SH substituted cyclohexanone in CH_3CN.

	SH-ax	**SH-eq**
	PM3	PM3
C1-C2	1.527	1.523
C2-C3	1.528	1.530
C2-X	1.833	1.830
C2-H	1.120	1.120
C1-C6	1.522	1.522
O7-C1-C2	121.2	124.2
C1-C2-X	111.6	118.8
C2-X-C18	101.6	101.6
C1-C2-X-C18	-70.1	48.8
Dipole	4.62	4.01

TABLE 3.39. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SeH substituted cyclohexanone in CH_3CN.

	SeH-ax	**SeH-eq**
	PM3	PM3
C1-C2	1.506	1.506
C2-C3	1.508	1.507
C2-X	1.960	1.955
C2-H	1.106	1.110
C1-C6	1.521	1.522
O7-C1-C2	121.7	120.7
C1-C2-X	100.7	103.5
C2-X-C18	99.8	97.1
C1-C2-X-C18	106.2	174.5
Dipole	2.85	5.22

TABLE 3.40. Energetics (kcal/mol) for the conformational equilibrium for α-XH substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3	PM3
	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3}$ [b]	ΔG^c	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^d$
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=37.5)	(ε=37.5)	(ε=37.5)
-OH	1.04	0.18	0.99	-104.80	-104.78	-0.02
-SH	-0.20	-0.46	-0.06	-53.21	-51.70	-1.52
-SeH	-4.44	-1.34	-4.04	-61.56	-56.25	-5.32

[a, d] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K.

3.3.2 α-OCH_3, SCH_3, $SeCH_3$ Substituted Cyclohexanones

Calculations shows us that in polar media (ε=37.5), in the axial position, OCH_3, SCH_3 and $SeCH_3$ prefer the - gauche orientation. In all of the studied compounds, the C1-C2 is longer than the C1-C6, like in gas phase (TABLES 3.41., 3.42., 3.43.) and the anomeric effect is present in these compounds. As the size of the heteroatom increases the anomeric effect decreases.

The substituents in the equatorial position except for SCH_3 prefer the + gauche orientation where the dipole is minimum. OCH_3-eq and $SeCH_3$-eq prefer the least crowded position that's why the long range interactions loose their priority in solution (TABLES 3.41., 3.42., 3.43.).

Calculations have shown that the preference for the axial conformer increases as the size of the substituent increases. The same trend is observed experimentally in two different solvents, carbontetrachloride (ε=2.2) and acetonitrile (ε=37.5). The experimental trend in two solvents of different polarity (ε=2.2 and ε=37.5) has not been reproduced by calculations, experimentally the population of the axial conformer decreases as the polarity of the solvent increases whereas calculations indicate the reverse behaviour (TABLE 3.44.). The ellipsoidal shape of the cavity may be the cause of these discrepencies.

TABLE 3.41. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-OCH_3 substituted cyclohexanone in CH_3CN.

	OCH_3-ax	OCH_3-eq
	PM3	PM3
C1-C2	1.540	1.531
C2-C3	1.534	1.539
C2-X	1.420	1.426
C2-H	1.116	1.120
C1-C6	1.521	1.522
O7-C1-C2	120.7	124.8
C1-C2-X	113.1	109.7
C2-X-C18	118.1	114.1
C1-C2-X-C18	-63.7	-152.3
C2-X-C18-H19	178.5	113.1
C2-X-C18-H20	60.1	61.1
C2-X-C18-H21	-62.3	-62.7
Dipole	4.34	4.93

TABLE 3.42. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-SCH_3 substituted cyclohexanone in CH_3CN.

	SCH_3-ax	SCH_3-eq
	PM3	PM3
C1-C2	1.523	1.524
C2-C3	1.527	1.529
C2-X	1.840	1.833
C2-H	1.120	1.121
C1-C6	1.520	1.520
O7-C1-C2	121.3	124.7
C1-C2-X	113.2	118.8
C2-X-C18	106.7	106.1
C1-C2-X-C18	-61.7	72.1
C2-X-C18-H19	178.5	179.2
C2-X-C18-H20	59.1	60.5
C2-X-C18-H21	-62.2	-62.2
Dipole	4.93	4.09

TABLE 3.43. Selected bond lengths(Å), bond angles(°), dihedral angles(°) and dipole moments(D) of α-$SeCH_3$ substituted cyclohexanone in CH_3CN.

	$SeCH_3$-ax	**$SeCH_3$-eq**
	PM3	PM3
C1-C2	1.502	1.503
C2-C3	1.506	1.507
C2-X	1.957	1.954
C2-H	1.116	1.111
C1-C6	1.521	1.523
O7-C1-C2	121.2	120.9
C1-C2-X	108.3	105.1
C2-X-C18	108.8	99.3
C1-C2-X-C18	-57.6	175.7
C2-X-C18-H19	175.9	-30.9
C2-X-C18-H20	56.9	90.1
C2-X-C18-H21	-64.8	-150.3
Dipole	4.94	5.50

TABLE 3.44. Energetics (kcal/mol) for the conformational equilibrium for α-XCH_3 substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3	PM3		
	$\Delta(\Delta H_f)^a$	$\Delta S/10^{-3}$ ^{b}	ΔG^c	$\Delta H_{f\,ax}$	$\Delta H_{f\,eq}$	$\Delta(\Delta H_f)^d$	ΔG_{exp}^e	ΔG_{exp}^e
Substituent	(ε=1)	(ε=1)	(ε=1)	(ε=37.5)	(ε=37.5)	(ε=37.5)	(ε=2.2)	(ε=37.5)
$-OCH_3$	-0.02	-3.25	0.94	-98.50	-97.69	-0.81	0.00	1.0
$-SCH_3$	-1.98	-4.97	-0.50	-59.88	-56.17	-3.71	-1.40	-0.2
$-SeCH_3$	-4.84	3.11	-5.76	-79.53	-77.58	-1.95	----------	----------

[a, d] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K. [e] Reference 22, $\Delta G = G_{ax} - G_{eq}$.

3.3.3 α-OC_6H_5, SC_6H_5, SeC_6H_5 Substituted Cyclohexanones

From PM3 calculations, in the axial position, all the substituents point outwards the ring where the C1-C2-X-C18 angle is 152°, this can be because of the steric interactions.

In the equatorial position, OC_6H_5 prefers the anti orientation to the carbonyl group inspite of its high dipole moment. SC_6H_5 prefers the + gauche orientation where the dipole is minimum (μ_{ax}= 5.28D, μ_{eq}= 4.68D). The - gauche orientation is prefered by SeC_6H_5 where it has minimum dipole (μ_{ax}= 5.60D, μ_{eq}= 4.21D).

The positon of the phenyl ring in the axial conformer is coplanar with the C2-X bond like in gas phase. On the other hand, in the equatorial conformer the positon of the phenyl ring is almost parallel to C2-X bond which is expected since steric interactions are minimized.

The preference for the axial conformer increases as the size of the substituent increases (TABLE 3.45.). This is observed experimentally in four different solvents. Experimentally the more polar equatorial conformer is stabilized in the more polar solvent. This trend has not been reproduced with the ellipsoidal cavity.

TABLE 3.45. Energetics (kcal/mol) for the conformational equilibrium for α-XC_6H_5 substituted cyclohexanones (PM3).

	PM3	PM3	PM3	PM3	PM3	PM3				
Substituent	$\Delta(\Delta H_f)^a$ (ε=1)	$\Delta S/10^{-3\,b}$ (ε=1)	ΔG^c (ε=1)	$\Delta H_{f\,ax}$ (ε=37.5)	$\Delta H_{f\,eq}$ (ε=37.5)	$\Delta(\Delta H_f)^d$ (ε=37.5)	$\Delta G_{exp}{}^e$ (ε=2.2)	$\Delta G_{exp}{}^f$ (ε=4.8)	$\Delta G_{exp}{}^f$ (ε=20.7)	$\Delta G_{exp}{}^e$ (ε=37.5)
$-OC_6H_5$	-0.24	0.13	-0.27	-70.55	-65.31	-5.25	0.10	0.35	0.63	0.79
$-SC_6H_5$	-1.64	2.11	-2.27	-30.25	-20.22	-10.03	-0.55	-0.33	-0.03	0.07
$-SeC_6H_5$	-5.16	-0.25	-5.08	-61.17	-45.30	-15.87	-0.60	-0.43	0.02	0.02

[a, d] $\Delta(\Delta H_f) = \Delta H_{f\,ax} - \Delta H_{f\,eq}$. [b] $\Delta S = S_{ax} - S_{eq}$. [c] $\Delta G = \Delta(\Delta H_f) - T\Delta S$ at 298K. [e] Reference 22, $\Delta G = G_{ax} - G_{eq}$. [f] Reference 25.

3.4 Applications of Hammett Equation

Hammett equation has been applied to study the relationship between the equilibrium free energies and the Hammett substituent constants (σ_p) of the substituents.

We have investigated the plausible relationships between the Gibbs free energy, the change in heat of formation for the equilibrium reaction (TABLES 3.34.- 3.36.) and the σ_p parameter for α-XC_6H_5Y type of compounds (TABLE 2.1.). We have observed better relationship between the $\Delta(\Delta H_f)$ with σ_p rather than the difference in Gibbs free energy and the σ_p parameter (FIGURES 3.29., 3.30.). We have attributed this behaviour to ΔS which is poorly calculated with the harmonic oscillator approximation in PM3. The presence of Cl and Br among the substituents has decreased the regression coefficient, R; the same is true for Se.

We have thus evaluated the relationships for p-NO_2, F, OCH_3, NH_2 α-phenoxy and α-phenylthio substituted cyclohexanones. The correlation between the $\Delta(\Delta H_f)$ and σ_p parameter for p-NO_2, F, OCH_3, NH_2 α-phenoxy substituted compounds turns out to be 0.996 whereas the one for p-NO_2, F, OCH_3, NH_2 α-phenylthio substituted compounds is 0.960. Our findings confirm the fact that the parametrization in PM3 for H, F, N, C, O and S containing compounds is fairly reliable.

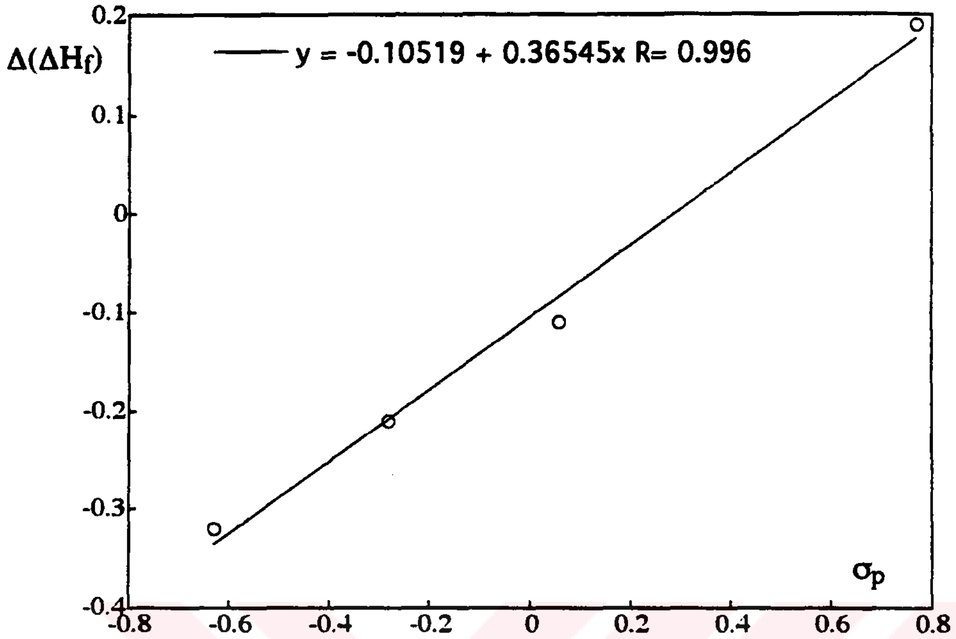

FIGURE 3.29. Correlation of Hammett substituent constants with Δ(ΔH$_f$) of α-(p-F, NO$_2$, NH$_2$, OCH$_3$)OC6H5 substituted cyclohexanones.

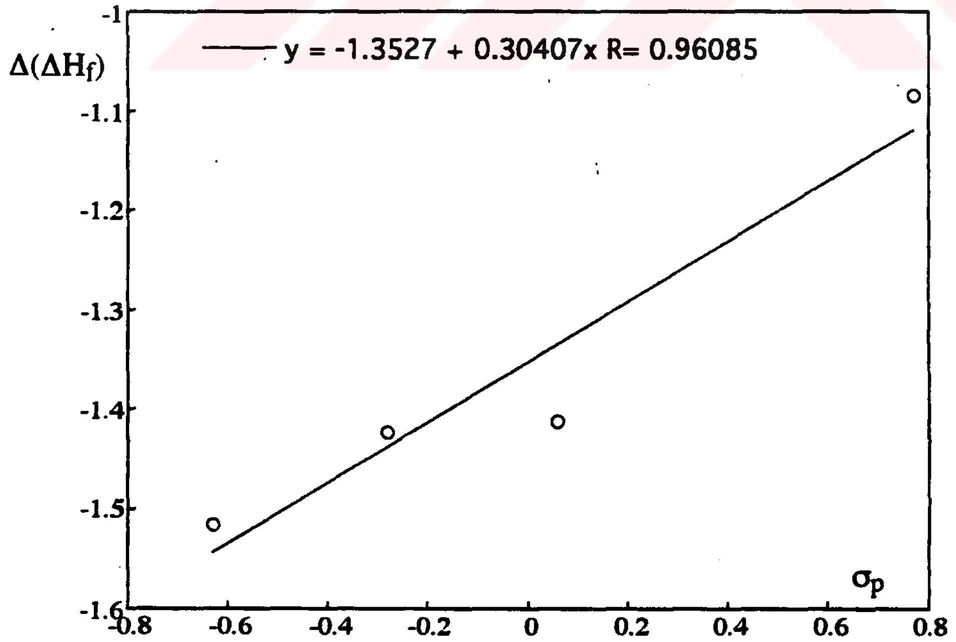

FIGURE 3.30. Correlation of Hammett substituent constants with Δ(ΔH$_f$) of α-(p-F, NO$_2$, NH$_2$, OCH$_3$)SC6H5 substituted cyclohexanones.

4. CONCLUSION

With both methods, for the XH type of substituents, the axial conformer is found to be more stable than the equatorial conformer except for OH. α-OH substituted cyclohexanone prefers the equatorial position because of the stabilizing interactions between the carbonyl oxygen and the substituent.

With PM3, the XCH_3 substituted cyclohexanones except for OCH_3 prefer largely the axial conformer rather than the equatorial conformer. OCH_3 substituent displays a greater preference for the equatorial position where the dipole is minimum.

Like in their small analogues, OC_6H_5, SC_6H_5 and SeC_6H_5 substituents prefer the axial conformer rather than the equatorial conformer with both methods where the dipole is minimum. This fact is confirmed by the difference in Gibbs free energies.

With PM3, for para F, Cl, Br, NO_2, NH_2 and OCH_3 substituted α-phenoxy, α-phenylthio and α-phenylseleno substituted cyclohexanones except for α-(p-NO_2)OC_6H_5, there is a decreasing preference for the axial orientation as the character of the substituent varies from electron donor to electron withdrawing. α-(p-NO_2)OC_6H_5 substituted cyclohexanone prefers the equatorial position because of the electronic character of the para substituent.

With HF/6-31G*, the axial conformation of the XH prefers the + gauche position where the dipole is minimum. With PM3, OH and SH substituents except for SeH prefer the - gauche orientation. This fact is explained by the long range stabilizing interactions. SeH prefers the + gauche orientation where the dipole is minimum. With PM3 and HF/6-31G* calculations, the equatorial conformation of OH is eclipsed to the ring because of the stabilizing interaction. In SH, this interaction is present, although it's weaker. With HF/6-31G*, as the size of the heteroatom increases, SeH favors the sterically less hindered position inspite of its high dipole moment but with PM3, the substituent prefers the - gauche position where it has minimum dipole.

In the axial position, the XCH_3 substituted cyclohexanones except for $SeCH_3$ prefer the - gauche orientation which is similar to OH and SH substituted ones with PM3. On the other hand, $SeCH_3$ prefers the + gauche orientation where the dipole is minimum and the substituent points outwards the ring. In the equatorial conformers, OCH_3 and SCH_3 prefer the + gauche orientation and $SeCH_3$ prefers the sterically less hindered position.

With HF/6-31G*, in the axial orientation, OC_6H_5, SC_6H_5 and SeC_6H_5 prefer the + gauche orienation with respect to the ring. This trend is observed with PM3 method except for OC_6H_5 because of the minimization of streic interactions and the substituent points outwards the ring. In the equatorial position, OC_6H_5 prefers the - gauche orientation because of the long range stabilizing interactions with PM3 and HF/6-31G*. Although the - gauche orientation is prefered by SC_6H_5 with HF/6-31G*, the + gauche orientation is preferred with PM3. SeC_6H_5 substituent adopts the least crowded position and is anti to the carbonyl group with PM3 and HF/6-31G*.

In the axial and equatorial position of all the para F, Cl, Br, NO_2, NH_2 and OCH_3 α-phenoxy, α-phenylthio and α-phenylseleno substituted cyclohexanones, the geometry of the compounds is similar to the unsubstituted compounds with PM3.

The correlation between the Hammett substituent constants and the $\Delta(\Delta H_f)$ of the p-NO_2, F, NH_2, OCH_3 α-phenoxy, α-phenylthiosubstituted cyclohexanones shows us that the parametrization in PM3 for H, F, C, N, O, S containing compounds is fairly reliable.

In solution, for the XH, XCH_3 and XC_6H_5 type of compounds, experimentally the more polar equatorial conformer is stabilized in the more polar solvent. This trend has not been reproduced with the ellipsoidal cavity in PM3.

For further studies, a better method for solvation process is suggested. Optimization of the studied compounds with ab initio methods, i.e. HF/6-31G*, using a cavity similar to the shape of the molecule may improve the results.

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