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Theoretical investigation of *para*-substituted phenyl selenobenzoates

Ali Jameel Hameed*

Department of Chemistry, College of Science, University of Basrah, Basrah 42010, Iraq

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Abstract

The structural and electronic properties of eight *para-* substituted phenyl selenobenzoates have been investigated theoretically by performing semi-empirical molecular orbital theory at the level of PM3 of theory. The substituents include: $C(O)OCH_2CH_3$, $C(O)CH_3$, F, Cl, CH_3, OCH_3 and $N(CH_3)_2$. The optimized structures, relative binding energies, atomic charges, position of HOMO and LUMO and the electrostatic potential of the molecules are obtained.

Keywords: Selenoesters; Semi-empirical PM3 method

1. Introduction

There has been a continued interest in organic and inorganic selenium chemistry. Many important biological and pharmacological functions for selenium and its compounds have been demonstrated. Organo-selenium compounds have been tested as antibacterial, antiviral, antifungal, antiparasitic, antiinflammatory and antihistamine agents [1]. Selenium is recognized as being an essential component of the active site of a number of enzymes, where it is present as the amino acids selenocyteine and selenomethionine [2–5]. Dietary selenium deficiency has been linked to such disease as cancer, heart disease, arthritis and AIDS [6]. Organo-selenium compounds have also been found capable of inhibiting and/or retarding tumorigenesis in a variety of in experiments animal models [7,8]. A series of organo-selenium compounds, Se-methylselenocysteine (MSC), *p*-methoxybenzeneselenol (MBS), benzylselenocyanate (BSC) and 4-phenylenebis-(methylene)selenocyanate (*p*-XSC), has been used as chemopreventive agents for some of human cancer [9–11]. Organo-selenium compounds have been relatively little explored because of their low stability and their extremely unpleasant odor. Theoretical investigation may be useful for the evaluation of biological selenium compounds.

In this study, I have investigated the structural and electronic properties of *para*-substituted phenyl selenobenzoates by performing semi-empirical molecular orbital theory at the level of PM3 calculations because of their biological importance.

2. Method of calculation

The semi-empirical method are done on Hyperchem program version 6.0 [12] running on a Windows XP workstation with a Pentium IV PC. Geometry optimization of the *para*-substituted phenyl selenobenzoates were done by performing the semi-empirical molecular orbital theory at the level PM3 [13] using the restricted Hartree–Fock (RHF) procedure [14]. The Polak–Ribier algorithm was used for the optimization [15]. The convergence is set to 0.001 kcal mol^{-1}.

3. Result and discussion

The optimized structures of *para*-substituted phenyl selenobenzoates (1–8) are shown in Fig. 1. The figure shows the molecules in the sticks model (a) and ball and stick model (b). The PM3 geometry optimizations yield planar structures for the phSeCOph moiety in the molecules 1–6 and a non-planar structures in molecules 7 and 8. Some of

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* Tel.: +96 47801046701; fax: +96 440412904.
E-mail address: alijamail2003@yahoo.com

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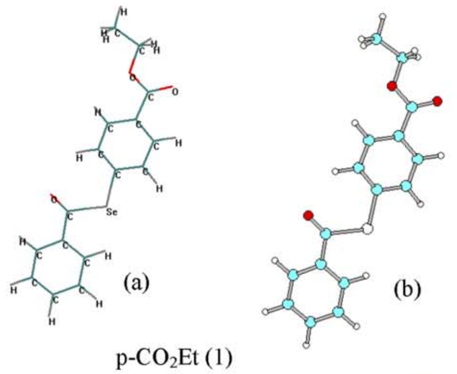
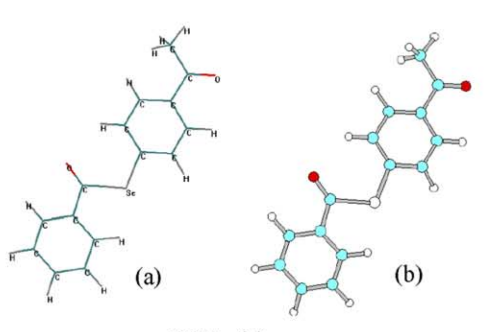
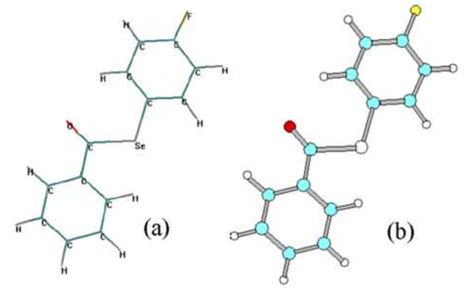


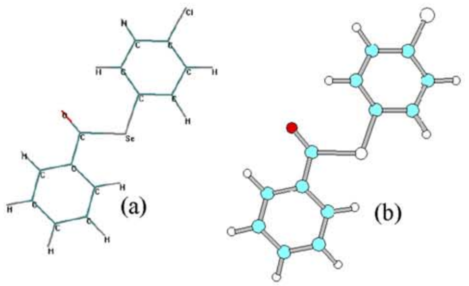
p-CO_2Et (1)



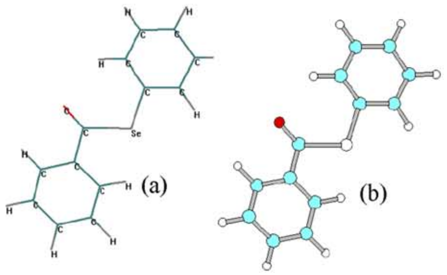
p-COMe (2)



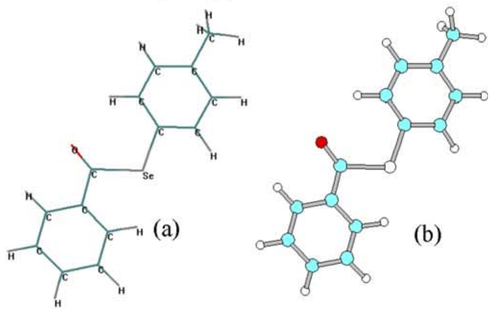
p-F (3)



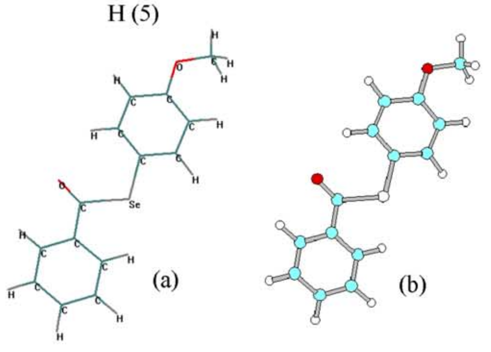
p-Cl (4)



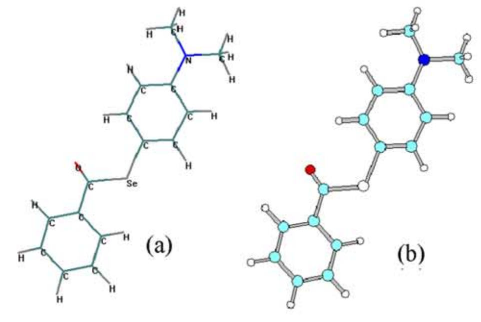
H (5)



P-Me (6)



p-OMe (7)



p-N(Me)$_2$(8)

Fig. 1. The optimized structure of *para*-substituted phenyl selenobenzoates. (a) sticks model (b) ball and sticks model.

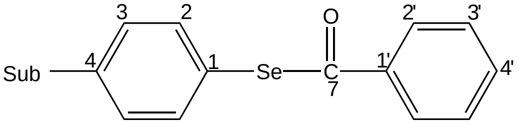
molecular information about the molecules studied are given in Table 1.

The calculated atomic charges are given in Table 2. The calculated atomic charges of selenium and carbon atoms are in agreement with the assignments of selenium-77 and carbon-13 chemical shift reported by Mullen et al. [16]. The selenium atom has a slight positive charge varying from $+0.003$ to $+0.010$, whereas it has a slight negative charge of amount -0.004 with the *para*-N(Me)$_2$ substituent. The benzoyl moiety substituted at the selenium atom cause these slight charges. The selenium atom indicates low sensitivity in charge change with substituent effect because of being bound to an electron-withdrawing group. The carbon atoms C-1, C-2, C-3 and C-4 of the *para*-substituted phenyl ring have negative excess charge with magnitudes varying from -0.005 to -0.291. The C-4 atom only in *para*-F

Table 1
Some of the molecular information about the molecules studied

Substance	Formula form	No. of electrons	No. of double occupied levels	No. of total orbitals	Molecular point group
CO_2Et	$C_{16}H_{14}O_3Se$	102	51	94	CS
COMe	$C_{15}H_{12}O_2Se$	90	45	84	C1
F	$C_{13}H_9FOSe$	80	40	73	C1
Cl	$C_{13}H_9ClOSe$	80	40	73	C1
H	$C_{13}H_{10}OSe$	74	37	70	CS
Me	$C_{14}H_{12}OSe$	80	40	76	CS
OMe	$C_{14}H_{12}O_2Se$	86	43	80	CS
NMe_2	$C_{15}H_{15}NOSe$	92	46	87	C1

Table 2
Calculated excess charges (in units of electron charge) on the atoms of *para*-substituted phenyl selenobenzoates molecules



Sub.	Se	C-1	C-2	C-3	C-4	C-1′	C-2′	C-3′	C-4′	C-7	O
CO_2Et	0.010	−0.197	−0.086	−0.044	−0.121	−0.170	−0.036	−0.116	−0.059	0.295	−0.242
COMe	0.010	−0.200	−0.083	−0.066	−0.156	−0.170	−0.037	−0.117	−0.059	0.294	−0.244
F	0.008	−0.241	−0.039	−0.134	0.074	−0.169	−0.037	−0.117	−0.060	0.295	−0.243
Cl	0.006	−0.227	−0.053	−0.104	−0.116	−0.169	−0.037	−0.117	−0.060	0.294	−0.243
H	0.003	−0.222	−0.065	−0.102	−0.091	−0.168	−0.038	−0.117	−0.061	0.291	−0.245
Me	0.003	−0.229	−0.060	−0.107	−0.063	−0.168	−0.038	−0.117	−0.062	0.291	−0.245
OMe	0.004	−0.262	−0.030	−0.144	0.100	−0.168	−0.038	−0.117	−0.062	0.292	−0.245
NMe_2	−0.004	−0.291	−0.005	−0.170	−0.013	−0.166	−0.043	−0.111	−0.070	0.290	−0.224

and *para*-OMe has positive charge of amount +0.074 and +0.100, respectively. These carbon atoms indicate sensitivity in charge change with substituents effect. The carbon atoms C-1′, C-2′, C-3′ and C-4′ of the unsubstituted phenyl ring have negative excess charge varying from −0.036 to −0.170. The charges of these carbon atoms are unaffected with the substituent effect as every carbon atom almost has the same amount of charge for all substituents. The carbon atom C-7 which makes double bond to an oxygen atom has positive excess charge, with magnitudes varying from +0.291 to +0.295. An oxygen atom has negative excess charge, with magnitude varying from −0.224 to −0.245.

The calculated binding energies and heats of formation values of the molecules studied are given in Table 3. Binding energy is the energy required to either separate an electron from an atom or to separate the protons and neutrons of an atomic nucleus. For these calculations, we obtained the smallest value of calculated binding energy for CO_2Et substituent. The Cl substituent has the largest calculated binding energy. When we compute for the relative energy with respect to the unsubstituted molecule, we obtained the values 926.19, 546.54, 10.40, −16.42, 284.53, 372.87 and 720.95 kcal mol^{-1} for the *para*-substituted of CO_2Et, COMe, F, Cl, Me, OMe and NMe_2, respectively. On the other hand the heat of formation of *para*-substituted molecules are exothermic, while it is

Table 3
Binding energy, and heats of formation (in kcal/mol) for the *para*-substituted phenyl selenobenzoates molecules

Substance	Binding energy	Heat of formation
CO_2Et	−3779.18	−82.53
COMe	−3399.53	−37.54
F	−2863.39	−40.16
Cl	−2836.57	−3.23
H	−2852.99	+3.46
Me	−3137.52	−5.98
OMe	−3225.86	−34.76
NMe_2	−3573.94	−2.20

Table 4
The MO energy of the lowest, highest, HOMO, LUMO, levels, ΔE (in eV) and the dipole moment, μ (in Debyes) for the *para*-substituted phenyl selenobenzoates molecules

Substance	Lowest level	Highest level	HOMO	LUMO	ΔE	μ_t
CO_2Et	−40.846	7.225	−9.142	−1.315	7.827	3.772
COMe	−40.749	6.992	−9.113	−1.304	7.809	4.333
F	−40.733	6.103	−9.013	−1.272	7.741	3.724
Cl	−55.390	6.139	−8.880	−1.238	7.642	2.992
H	−40.632	6.222	−8.913	−1.139	7.774	1.897
Me	−40.615	6.244	−8.791	−1.112	7.679	1.569
OMe	−40.619	6.380	−8.638	−1.107	7.531	2.168
NMe_2	−40.543	6.326	−8.401	−1.026	7.375	1.133

endothermic for unsubstituted molecule, where it has the value of about $+3.46\ \mathrm{kcal\ mol^{-1}}$ (Table 3).

The highest occupied and the lowest unoccupied molecular orbital (HOMO and LUMO, respectively) energies and the energy band gap (LUMO–HOMO energy difference, ΔE) with the lowest and highest level energy values are given in Table 4. The energy band gaps are largely responsible for the chemical and spectroscopic properties of the molecules [17]. Substitution at the *para* position of phenyl selenobenzoate with donor or acceptor substituents affects the HOMO and LUMO energies. Strong acceptor substituents (CO_2Et, COMe) lead to

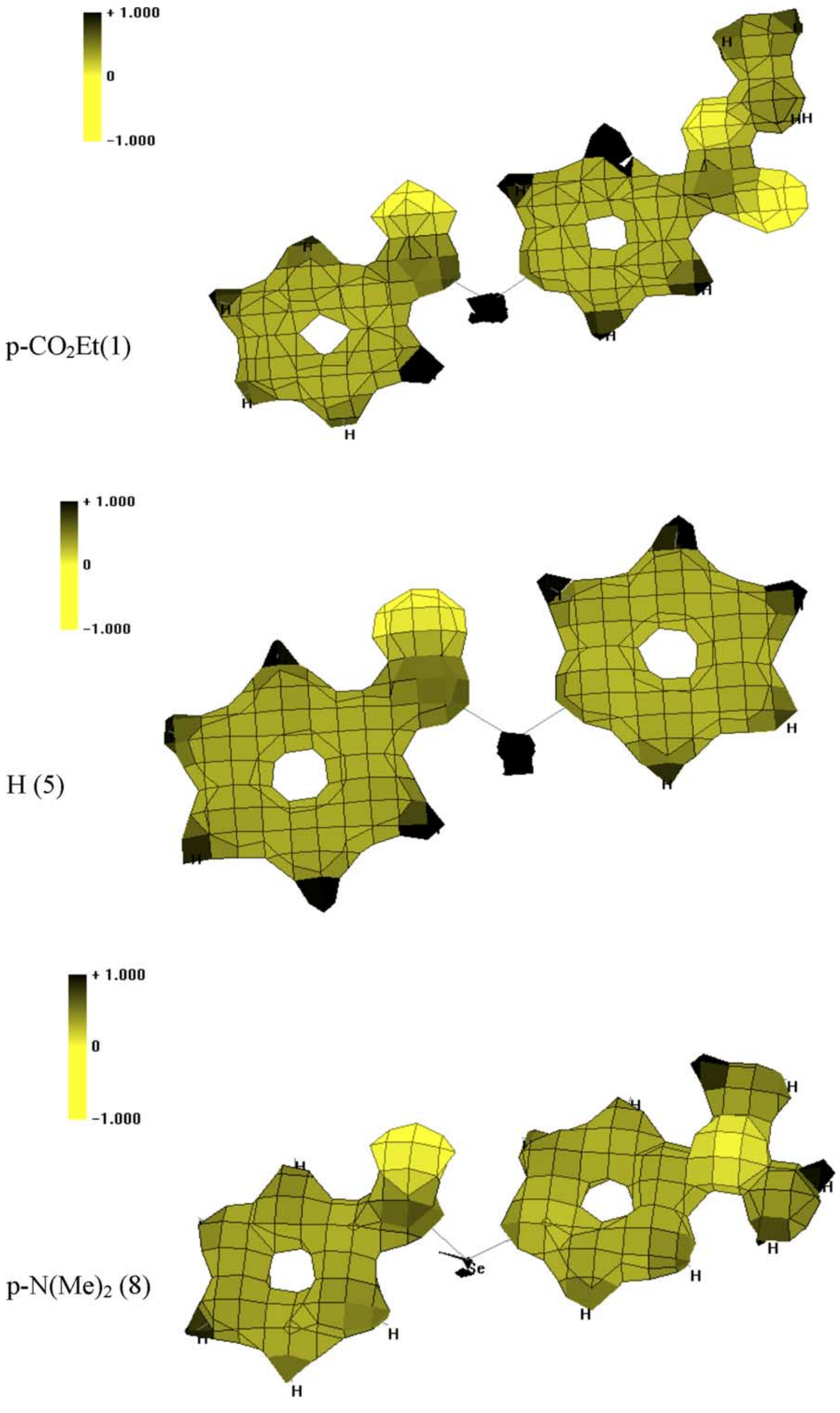


Fig. 2. Isosurface of electrostatic potential in the spatial vicinity of some *para*-substituted phenyl selenobenzoates molecules. (For interpretation of the reference to color in this legend, the reader is referred to the web version of this article.)

a slight increase in ΔE gaps, whereas the other sbstituents lead to a slight decrease in ΔE gaps. This means that in any excitation process *para*-substituted of CO_2Et and COMe molecules need more (ca. 0.053 and 0.035 eV, respectively) energy than that unsubstituted molecule, whereas the *para*-substituted of F, Cl, Me, OMe and NMe_2 molecules need less (ca. 0.033, 0.132, 0.095, 0.243 and 0.399 eV, respectively) energy than that unsubstituted molecule.

The calculated dipole moment values of the molecules considered are also given in Table 4. Molecules with acceptor substituents (1–4) have relatively larger dipole moments than that of donor substituents (6–8). This high dipole moment may make these molecules reactive and attractive for interaction with other systems, in other word the molecules with high dipole moment may be more vulnerable by oxidation reagents.

The three-dimensional mapped isosurface of the electrostatic potential of some molecules studied (1, 5 and 8) are shown in Fig. 2. This plot provides information on the reactivity of the molecules in actual reactions with electrophiles or nucleophiles. Dark (black) colors indicate positive ESP regions and light (yellow) colors indicate negative ESP regions. For all substituents, the plots show that the selenium atom has a slight positive ESP region. The C-7 atom has more positive ESP region, while The two phenyl rings gets less positive ESP regions. The oxygen atom of the carbonyl group has more negative ESP region. This suggests that oxygen atom would probably undergo protonation reaction with acidic reagents.

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