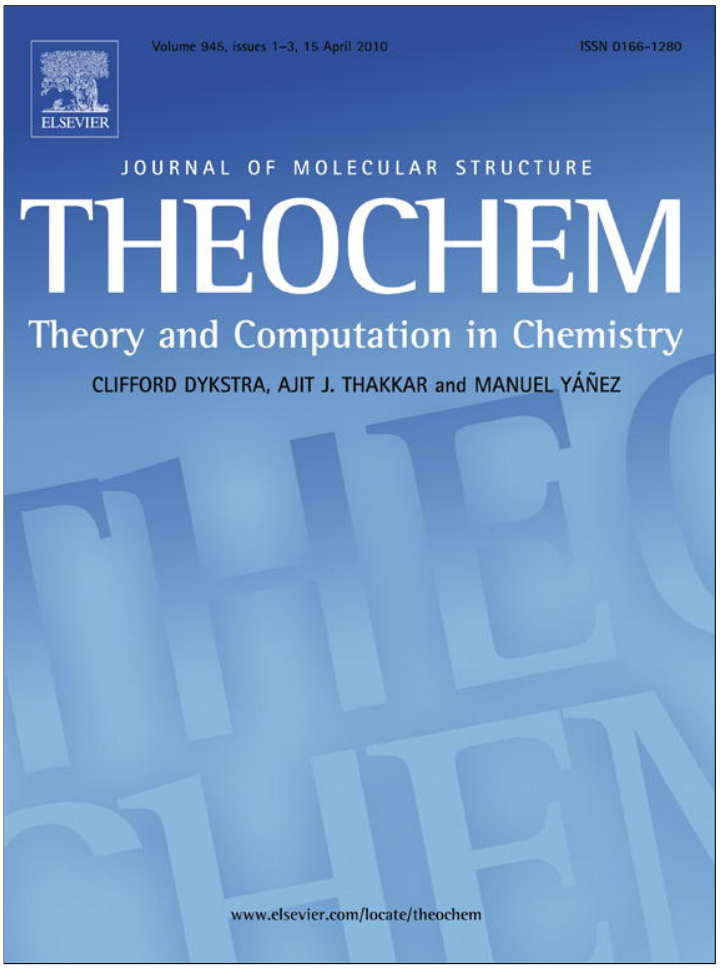

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Quantum mechanical study of substituted phenoxathiin: A study of the structure of fluorinated phenoxathiins

Iman A. Gad El-karim *

Department of Chemistry, Faculty of Science, Benha University, Egypt

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ABSTRACT

The effect induced by introducing electron captor substituent, namely, fluorine in the arene rings of phenoxathiin on the structure of the phenoxathiin nucleus have been studied using the *ab initio* method at the B3LYP/(6-31+G)+d basis set level. The study predicts and analyses the configuration of several not yet synthesized fluorinated-phenoxathiin derivatives. Thus, the magnitude of change in the puckering angle Φ_c of phenoxathiin was found to be dependent on the position of the fluorine atom with respect to the oxygen atom of the central heterocyclic ring. Substitution at the 1-position, *meta* to the oxygen did induce flattening of the nucleus i.e. increased Φ_c, while substitutions at the 2- and 4- positions, *para* and *ortho* to the oxygen, respectively, induced further puckering on the nucleus i.e. decreased Φ_c. Successive substitution at these positions enhanced these effects. Thus, 1,9-difluorophenoxathiin was found to be the most flattened, while 2,3,4,6,7,8-hexafluorophenoxathiin was found to be the most puckered fluorinated phenoxathiins. The predicted inversion barrier for all the studied compounds was very small; it did not exceed 1.67 kcal/mol for the most puckered isomer. Consequently, we anticipated these compounds to enjoy an easy *butterfly* interconversion.

1. Introduction

Phenoxathiin is a hetero tricyclic compound having a folded molecular geometry. It belongs to the chalcanthrene family that is known to be puckered (Fig. 1) and to undergo '*butterfly* interconversion' motion [1–3]. Some of the phenoxathiin derivatives are pharmacologically active [4]. Early investigators concluded that the differences in pharmacological activity among various phenoxathiin derivatives are attributable to the dihedral angle between the non-central rings and/or to the change in substituent's location [4]. The X-ray structure of phenoxathiin 1 was studied by Hosoya and Gerkin et al. [5]. The puckering value reported by Hosoya, 138.25° (denoted here by Φ_c) corresponds to the fold angle between the best planes through the carbocyclic rings. Gerkin reported a value of 147.7° corresponding to Φ_c and a value of 142.3° that corresponds to Φ_h, which is the dihedral angle between the two planar halves of the heterocyclic ring (more precisely the two least-squares best-fit planes that include the two halves O, S, C11, C12 and O, S, C14, C13). Recently, we reported a detailed *ab initio* study at the B3LYP/(6-31+G)+d level on phenoxathiin and azaphenoxathiins [6]. Our predicted values of Φ_c and Φ_h for phenoxathiin were 149.8° and 144.1°, respectively, which are in a good agreement with Gerkin's values. In addition, it was concluded that, inclusion of electronegative nitrogen atoms into the arene rings of phenoxathiin has a significant effect on the planarity of the molecule. The magnitude of such effect is dependent not only on the number of N atoms introduced but also on the orientation of the N atom relative to the S atom. Thus, successive inclusion of N atom into the arene rings induced substantial flattening on the phenoxathiin nucleus; to the extent that 1,4,6,9-tetraazaphenoxathiin is completely flat.

Our present interest is to study the effect that substituents to the arene rings can induce on the structure and the puckering angle of the phenoxathiin nucleus.

A thorough study of substituent's effect requires a methodological approach. Firstly, to detect the most effective location – on the arene ring – for a certain substituent to affect the puckering angle Φ_c; secondly, to study the effect induced by successive substitution; thirdly, to determine the type of substituents that can induce further flattening (i.e. $+\Delta\Phi_c$ effect) and that can induce further puckering (i.e. $-\Delta\Phi_c$ effect)[1] on the nucleus. Finally, to study the effect of combining substituents of opposite electronic effect. The present study covers these points. Studies that classify substituents according to their $\pm\Delta\Phi_c$ effect and combining different substituents of opposite impact are to follow.

* Tel./fax: +20 13 3225494.
E-mail address: i.elkarim@gmail.com

[1] Through out this study, $+\Delta\Phi_c$ and $-\Delta\Phi_c$ are used to determine the degree of further flattening or further puckering induced on the phenoxathiin nucleus by a certain substituent.

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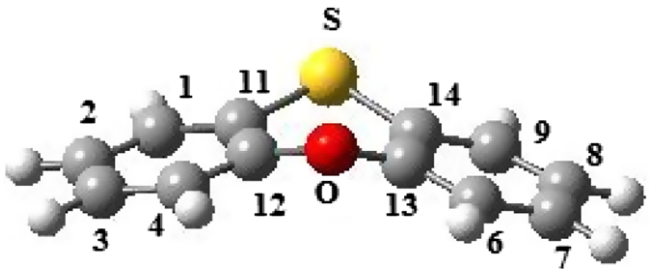

Fig. 1. Molecular structure of phenoxathiin 1 computed by *ab initio* method at the B3LYP/ 6-31+G(D) level.

2. Computational method

The optimized molecular structures for all molecules presented in this study were obtained by full optimization of all structural parameters without symmetry constraints using Gaussian 98 [7] at the closed shell B3LYP/(6-31+G)+d level. Molecular structures of the corresponding planer molecules were obtained by full optimization of all structural parameters except for the C1C11SC14 dihedral angle, which was constrained to the value of 180°.

3. Results and discussion

Previous studies showed that the inclusion of electronegative nitrogen atoms into the arene rings of phenoxathiin have a significant effect on the planarity of the molecule. Fluorine, being small in size and the most electronegative atom, is a good candidate to study the effect of introducing electronegative substituents to the arene rings. Thus, any effect it can induce will be merely attributed to electronic rather than to space factors. The numbering system employed in this study is presented in Fig. 1. In the mono fluorophenoxathiin series 2–5, the degree of puckering induced by the introduction of the fluorine atom is dependent on its position (Table 1). Interestingly, while a $+\Delta\Phi_c$ effect of the value 1.74° is encountered with the 1-fluoro-isomer 2, a $-\Delta\Phi_c$ effect of the value 0.22° and 0.46° is encountered with the 2-fluoro 3 and 4-fluoro 5 isomers, respectively. On the other hand, introducing the fluorine atom in position-3 did not influence the nucleus. The concomitant effect induced by the fluorine atom can be rationalized by analyzing the effect of the fluorine atom on the structure of the arene ring holding it. Fig. 2a describes the bond lengths and the endocyclic bond angles with respect to the fluorine atom in the fluorinated arene ring.

Examination of Table 1 reveals that, replacement of the arene hydrogen atom with the electronegative fluorine atom induces an increase of a few degrees of the endocyclic bond angle (α) opposite to the fluorine atom; a decrease of the two adjacent endocyclic angles (β); a slight increase of the endocyclic angles (γ) and a marginal decrease in the endocyclic angle (δ) para to the fluorine atom. In addition, the bond length *a* of the substituted ring shows definite, albeit small, variations from those in phenoxathiin 1. The lack of X-ray crystallographic data for fluorinated phenoxathiin did not allow fair comparison of our results with experimental findings. However, similar effect has long been recognized and reported for substituted benzene. The regular hexagonal geometry of the carbon skeleton of the benzene ring is known to be slightly deformed when a hydrogen atom is substituted with an electron-withdrawing functional group [8]. Such deformation lowers the ring symmetry from perfect D_{6h} to C_{2v}, and concerns mainly the half of the ring nearest the substituents, i.e. the *a* bonds and the α and β angles [9]. Domenicano et al. [9] had rationalized the encountered changes in terms of hybridization effects at the C atom bonded to the substituent; and, in terms of Valence-Shell Electron Pair Repulsions VSEPR theory [10]. They concluded that, whilst α is predominantly controlled by the σ-electron-withdrawing or -releasing properties of the substituent, δ is sensitive to the perturbations occurring in the π-electron system of the ring. Recently, a comparative study of anthracene and its carbonyl deriva-

Table 1
Calculated structural parameters at 6-31+G(d) /B3LYP for 1 and mono-fluorinated phenoxathiins 2–5.

Parameter[a]	Parent 1	1-Fluoro- 2	2-Fluoro- 3	3-Fluoro- 4	4-Fluoro- 5
C1–C2	1.396	1.388 (a)	1.396 (a)	1.397 (b)	1.396 (c)
C2–C3	1.398	1.397 (b)	1.397 (a)	1.389 (a)	1.398 (b)
C3–C4	1.396	1.396 (c)	1.388 (b)	1.389 (a)	1.388 (a)
C4–C12	1.39	1.395 (c)	1.397 (c)	1.395 (b)	1.397 (a)
C1–C11	1.40	1.396 (a)	1.400 (b)	1.399 (c)	1.400 (c)
C11–C12	1.40	1.402 (b)	1.400 (c)	1.400 (c)	1.400 (b)
S–C11	1.782	1.778	1.782	1.783	1.782
O–C12	1.384	1.380	1.375	1.379	1.375
C–S–C	98.44	97.99	98.38	98.32	98.55
C–O–C	119.1	119.56	118.92	119.11	118.54
C11–C1–C2	120.37 [γ][b]	123.11 (α) [γ]	118.74 (β) [γ]	120.94 (γ) [γ]	120.13 (δ) [γ]
C1–C2–C3	119.92 [δ]	118.25 (β) [δ]	122.61 (α) [δ]	118.12 (β) [δ]	120.37 (γ) [δ]
C2–C3–C4	120.06 [γ']	120.53 (γ) [γ']	118.28 (β') [γ']	122.71 (α) [γ']	118.78 (β) [γ']
C3–C4–C12	119.75 [β']	119.67 (δ) [β']	120.24 (γ) [β']	118.16 (β') [β']	121.95 (α) [β']
C4–C12–C11	120.69 [α]	121.21 (γ') [α]	120.62 (δ) [α]	120.96 (γ') [α]	118.75 (β') [α]
C12–C11–C1	119.17 [β]	117.22 (β') [β]	119.49 (γ') [β]	119.08 (δ) [β]	119.99 (γ') [β]
S–C11–C12	120.17	121.77	120.22	120.15	119.29
S–C11–C1	120.60	120.97	120.25	120.74	120.57
S–C14–C9	120.60	119.81	120.46	120.18	120.59
O–C12–C 4	117.01	116.95	117.12	116.62	117.81
O–C13–C 6	117.02	116.74	117.14	116.88	117.00
O–C12–C11	122.28	121.81	122.23	122.40	123.41
Φ_c	149.8	151.54	149.58	149.84	149.34
$\Delta\Phi_c$		+1.74	−0.22	+0.04	−0.46
Φ_h	144.1	146.40	143.86	144.04	143.78
ΔE[c]	1.26	0.764	1.276	1.256	1.286

[a] Bond lengths are expressed in Å, bond angles and dihedral angles are in °.
[b] Symbols in parentheses describe the orientation of the bond lengths and bond angles with respect to the fluorine atom. Those in square brackets are for O atom.
[c] Values are expressed in kcal/mol.

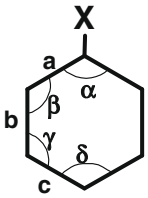

Fig. 2. (a) X = F; (b) X = O.

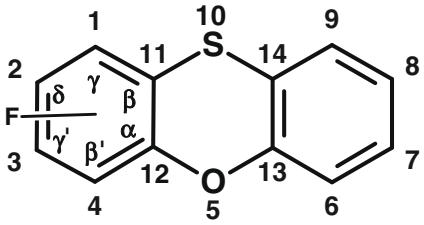

Fig. 3. Symbols describing the endocyclic bond angles with respect to the oxygen atom in the fluorinated arene ring.

tives reported the effect of substituents on the geometry of the anthracene [11]. In fact, these effects are clearly manifested in the geometry of phenoxathiin itself as compared with that of the carbocyclic isomer, 9,10-dihydroanthracene 6. Thus, compared to 6, X-ray diffraction data indicated that the oxygen atom in 1 induces an increase of 1.32°, 0.31° on the C11C12C4 [α][2], C4C3C2 [γ] and a decrease of 0.63°, 0.8°, and 0.1°, on the C12C11C1 [β], C12C4C3 [β'] and C1C2C3 [δ] endocyclic angles, respectively [3,12] (Figs. 1, 2b). This is attributed to the tendency of the electronegative oxygen atom to withdraw the electron density from the arene rings.

Concerning the mono-fluorophenoxathiins 2–5, the deformation of the arene ring geometry is a hybrid of the opposing factors resulting from the influence of the fluorine and the oxygen atoms. Both atoms are electronegative withdrawing atoms and π-electron releasing at the same time. These properties are expected to have different impact on a certain endocyclic angle, depending on the relative orientation of the two atoms.

Mainly, the highly electronegative fluorine atom withdraws the electron density from the ring. This can most effectively be accomplished through an increase in the *p* character of the carbon σ-bonding orbital directed towards the fluorine atom. This implies a decrease in the *p* character of the other two-*sp2* hybrid orbitals of the carbon atom, and leads, therefore, to an increase in their *s* character. As a result, the endocyclic angle (α) increases and the length of the adjacent C–C bonds *a* decreases. This effect is expected to enforce a decrease of the endocyclic angles (β) to preserve the planarity of the arene ring. Meanwhile, the *p*–π interaction between the *2p*-electrons of the F atom and the π-system of the arene ring dominates a certain amount of π-bonding in the C–F bond with a subsequent shortening of this bond. This is accompanied by an increase in the *p* character of the other two-*sp2* hybrid orbitals of the carbon atom. As a result the endocyclic angle (α) is closed up, whilst the lengths of the *a* bonds and the endocyclic (β) are increased. In addition, the *p*–π interaction induces partial negative charges on the *ortho*- and *para*-carbons with respect to the F atom. Consequently, these carbons are slightly pushed away from the center of the ring with the concomitant decrease of (β) and (δ) angles and increase of the (γ) angles. Generally, combination of all these factors in compounds 2–5 induces an increase in the (α, γ and γ') bond angles, and a decrease in the (β, β' and δ) bond angles. The encountered increase in (α) and decrease in (β and β') endocyclic bond angles indicates the predominance of the electron withdrawing effect of the F atom over the effect of the *p*–π interaction. The extent by which a certain parameter decreases or increases in compounds 2–5, depends on the orientation of that parameter with respect to the oxygen atom.

Likewise, the electronegative oxygen is expected to increase the endocyclic bond angles C4C12C11, C2C1C11 and C2C3C4 [α, γ and γ'], respectively (Fig. 3); and to decrease the C1C11C12, C3C4C12 and C1C2C3 [β, β' and δ], respectively. On the other hand, the π-electron releasing nature of the O atom is expected to induce a decrease in the [α] and an increase in the [β and β'] endocyclic bond angles. Interestingly, the trend followed by the O atom is found to be greatly affected by the position of the F atom (cf. Table 2, Fig. 3). For the 1-fluoro 2 and 3-fluoro- 4 phenoxathiins, where the F atom is in a *meta* position with respect to the O atom, the electron withdrawing nature of the O atom is more predominant, leading to an increase in the [α, γ and γ'] and a decrease in [β, β' and δ] endocyclic bond angles. However, for the 2-fluoro- 3 and 4-fluoro- 5 phenoxathiins, where the F atom is in the *para* and *ortho* positions with respect to the O atom, respectively, the sp^3–π interaction between the sp^3 O electrons and the π-system of the arene ring is maximized by the pulling effect of the F atom. Consequently, a decrease in the [α, γ and γ'], and an increase in the [β, β' and δ] endocyclic bond angles is encountered in 3 and 5, thus, indicating the predominancy of the π-electron releasing nature of the O atom.

Taking into account the effect induced by the F atom on the degree of puckering of phenoxathiin, we found out that this effect is greatly dependent on the changes induced by the combined action of both the F and O atoms on the C1C11C12 [β] endocyclic bond angle. In fact, [β] is considered to be the key angle that governs the geometry of the phenoxathiin nucleus. Thus, the induced decrease in the C1C11C12 bond angle [β] is accompanied by an increase in the SC11C12 and/or SC11C1 bond angles and by subsequent flatting of the phenoxathiin nucleus, and vice versa (cf. Tables 1 and 2). Changes in the SC11C1 bond angle depend on the extent of change encountered with the SC11C12 bond angle. Thus, in 2 the C1C11C12 bond angle being β with respect to the O as well as to the F atom, it shows the highest change (−1.95°) in the series. This is accompanied with increase by 1.6° and 0.37° in the SC11C12 and SC11C1 bond angles that induces a $+\Delta\Phi_c$ effect of the value 1.74°. On the other hand, for 3 and 5, the increase in the [β] bond angle (+0.32° and +0.82°) is compensated for by a decrease in the SC11C1 (−0.35°) and SC11C12 (−0.88°) bond angles, respectively. Thus, fostering further puckering i.e. a $-\Delta\Phi_c$ effect of the value 0.22° and 0.46° on the phenoxathiin nucleus of 3 and 5, respectively. In the 3-fluorophenoxathiin 4, although the introduction of the F atom has affected the [α, β', γ, γ' and δ] endocyclic bond angles, it has negligible effect on the [β] bond angle, consequently, it did not induce noticeable change on the puckering angle. Generally, we can simply conclude that, introducing a F atom in the 1-position, i.e. *meta* to the O, induces a decrease in the C1C11C12

Table 2
Changes in the endocyclic bond angles (in °) with respect to the O atom and the puckering angle of 2–5 (in °) as compared to 1.

	2	3	4	5
α	+0.52	−0.07	+0.27	−1.94
β	−1.95	+0.32	−0.09	+0.82
β'	−0.08	+0.47	−1.59	+2.20
γ	+2.74	−1.78	+0.57	−0.24
γ'	+0.47	−1.63	+2.65	−1.28
δ	−1.67	+2.69	−1.80	+0.42
$\Delta\Phi_c$	+1.74	−0.22	+0.04	−0.46

[2] Parentheses are used to indicate the orientation of a certain bond angle with respect to the F atom, and square brackets are used to indicate the orientation with respect to the O atom.

[β] bond angle accompanied by SC11C12 bond opening leading to the flattening of the phenoxathiin nucleus. While, introduction of F atom in position 2- or 4-, *para* or *ortho* to the O atom causes an increase in the C1C11C12 [β] bond angle that leads to SC11C12 bond close-up and puckering of the phenoxathiin nucleus. However, the 4-F atom induces more puckering than the 2-F does. It should also be noted that, the magnitude of Φ_c is reflected on the inversion barrier ΔE of the molecule. Thus, a $+\Delta\Phi_c$ effect is accompanied by a decrease in the inversion barrier, and vise versa (cf. Table 1).

Next, we carried out an investigation of the potential cumulating effect arising from the inclusion of a second fluorine atom. Our interest is to identify which combination of two fluorine atoms can induce the highest $-+\Delta\Phi_c$ effect and which can induce the highest $-\Delta\Phi_c$ effect. Based on results obtained for 2–5, the investigated difluoro – isomers included those anticipated to induce such effects. Table 3 presents the relevant data for the studied difluorophenoxathiins 7–18. Generally, compounds 7–13 – where the F atom in position-1 (*meta* to O) is combined with another F atom – show a noticeable reduction in the C1C11C12 bond angle, which is in β position with respect to the O as well as the 1-F atoms. This is accompanied by an increase in the SC11C12 bond angle, and a subsequent $+\Delta\Phi_c$ effect. However, except for 13, the predicted combined effect of the two F atoms for 7–13 is less than the effect encountered with only one F atom in the 1-position, i.e. for 2. Obviously, regardless of its position, the effect introduced by the second F atom opposes that introduced by the 1-F atom. Thus, for 1,2-difluorophenoxathiin 7, while the 1-F oriented *meta* to the oxygen calls for a decrease in C1C11C12 [β] bond angle, the 2-F oriented *para* to the oxygen calls for an increase in C1C11C12 [β] bond angle, consequently, the two effects partly cancel each other. This results in a decrease in the [β] bond angle by 1.22° and a $+\Delta\Phi_c$ effect of 1.06°, while values predicted for 2 are 1.95° and 1.74°, respectively. It should be noted that, in 1,8-difluorophenoxathiin 8, the two F atoms are also oriented *meta* and *para* to the O atom, however, in different rings. The 8-F in this case is affecting an increase in the C9C14C13 [β] bond angle by 0.23°, while the 1-F is affecting a decrease in C1C11C12 [β] by 1.89°. The resulted $+\Delta\Phi_c$ effect is 1.58°, and is higher than that predicted for 7.

Having the two F atoms in the same arene ring, oriented *meta* to O is expected to show high impact on the same endocyclic bond angles. In 1,3-difluorophenoxathiin 9 the two F atoms manifest the expected influence on the endocyclic angles in a parallel manner. Thus, e.g. C11C1C2 bond angle, being (α) to 1-F, (γ) to 3-F and [γ] to O atoms, is increased by 3.1°. Similarly, the C1C2C3 bond angle, being (β) to 1-F and 3-F, and [δ] to O atoms, is decreased by 3.21°. These are the highest changes encountered in the difluoro-series. Concerning the C1C11C12 [β] bond angle which is the key angle that determines the geometry of the phenoxathiin, it is oriented β to 1-F and O atoms, and δ to 3-F atom. Consequently, it is decreased by 2.06°, resulting in $+\Delta\Phi_c$ effect of 1.39°, which is the highest flattening effect that can be induced by difluoro-substitution on the same arene ring. Placing the second F atom *meta* to the O in the other arene ring as in 1,7-difluorophenoxathiin 10 induces similar $+\Delta\Phi_c$ effect of 1.42°.

1,4-Difluorophenoxathiin 11 represents an interesting example in which each fluorine atom affects freely the half holding it. The 1-F atom induces the anticipated increase in C2C1C11 (α) bond angle and decrease in C1C2C3 (β) and C1C11C12 (β') bond angles. Likewise, the 4-F induces an increase in C3C4C12 (α) bond angle and a decrease in C2C3C4 (β) and C4C12C11 (β') bond angles. The predicted decrease in both C1C11C12 (β' to 1-F) [β to O] and C4C12C11 (β' to 4-F) [α to O] bond angles is unique in this series and is compensated for by the increase in the adjacent bond angles SC11C12, SC11C1 and OC12C11, OC12C4, respectively. The overall effect of these changes on the puckering angle of phenoxathiin is in favour of $+\Delta\Phi_c$ effect of the value 1.36°. In 1,6-difluorophenoxathiin 12 the 6-F *ortho* to O, induces the expected decrease on the C6C13C14 [α] and increase on the C9C14C13 [β] bond angles. Thus, while the 1-F affects further flattening on one side of the phenoxathiin nucleus, the 6-F affects further puckering on the other side of the nucleus. Consequently, the induced $+\Delta\Phi_c$ effect on 12 is 1.28°, while that for 2 is 1.74°.

Table 3
Calculated structural parameters at 6-31+G(d) /B3LYP of 1 and di-fluorinated phenoxathiins 7–18.

Parameter[a]	1	1,2-Di-F 7	1,8-Di-F 8	1,3-Di-F 9	1,7-Di-F 10	1,4-Di-F 11	1,6-Di-F 12	1,9-Di-F 13	2,3-Di-F 14	2,4-Di-F 15	2,8-Di-F 16	4,6-Di-F 17	3,7-Di-F 18
C1–C2	1.396	1.392	1.388	1.389	1.388	1.387	1.388	1.388	1.388	1.388	1.389	1.396	1.397
C2–C3	1.398	1.388	1.397	1.389	1.397	1.397	1.397	1.397	1.393	1.390	1.389	1.397	1.389
C3–C4	1.396	1.397	1.396	1.389	1.396	1.388	1.396	1.396	1.388	1.390	1.396	1.389	1.389
C4–C12	1.394	1.394	1.395	1.395	1.394	1.398	1.394	1.395	1.395	1.397	1.394	1.397	1.394
C1–C11	1.40	1.395	1.396	1.396	1.396	1.397	1.396	1.397	1.400	1.401	1.399	1.400	1.399
C11–C12	1.40	1.403	1.402	1.403	1.401	1.401	1.401	1.401	1.401	1.400	1.400	1.399	1.401
S–C11	1.782	1.777	1.779	1.778	1.778	1.777	1.779	1.779	1.781	1.779	1.781	1.783	1.783
O–C12	1.384	1.380	1.380	1.376	1.383	1.371	1.382	1.381	1.380	1.375	1.384	1.377	1.382
C–S–C	98.44	97.90	97.91	97.85	97.83	98.10	98.09	97.55	98.22	98.51	98.30	98.65	98.16
C–O–C	119.1	119.30	119.38	119.50	119.47	119.00	118.98	120.21	118.87	118.36	118.75	118.04	119.02
C1–C11–C12 [β]	119.17	117.95	117.28	117.11	117.14	118.02	117.16	117.10	119.32	120.41	119.56	119.99	119.02
S–C11–C12	120.17	121.64	121.86	121.65	121.76	120.89	121.84	122.85	120.17	119.33	120.30	119.38	120.06
S–C11–C1	120.60	120.38	120.82	121.18	121.05	121.05	120.95	120.03	120.45	120.22	120.10	120.59	120.84
C4–C12–C11 [α]	120.69	121.09	121.20	121.62	121.38	119.33	121.43	121.27	120.86	118.68	120.59	118.92	121.09
O–C12–C11	122.28	121.75	121.70	121.86	121.75	122.97	121.62	122.15	122.37	123.42	122.14	123.21	122.38
C11–C1–C2 [γ]	120.37	121.11	123.04	123.47	123.07	122.83	123.02	123.20	119.73	118.50	118.69	120.04	120.92
C1–C2–C3 [δ]	119.92	120.56	118.27	116.71	118.31	118.74	118.32	118.23	120.43	122.90	122.59	120.42	118.17
C2–C3–C4 [γ']	120.06	119.18	120.56	122.98	120.52	119.24	120.56	120.48	120.57	117.18	118.31	118.85	122.69
C3–C4–C12 [β']	119.75	120.11	119.64	118.09	119.58	121.84	119.51	119.72	119.06	122.30	120.22	121.76	118.09
C6C13C14 [α]	120.69	120.74	120.77	120.89	121.06	120.93	118.82	121.27	120.80	120.86	120.60	118.92	121.13
C9C14C13 [β]	119.18	119.19	119.41	119.05	118.98	119.08	119.91	117.09	119.20	119.23	119.56	119.99	118.99
S–C14–C9	120.60	119.78	119.46	119.95	120.03	119.78	119.90	120.03	120.53	120.42	120.09	120.58	120.87
O–C12–C4	117.01	117.13	117.07	116.50	116.85	117.67	116.93	116.56	116.76	117.87	117.23	117.84	116.52
O–C13–C6	117.02	116.90	116.84	116.65	116.36	116.73	117.53	116.57	117.01	117.14	117.24	117.84	116.49
Φ_c	149.8	150.86	151.38	151.19	151.22	151.16	151.08	154.45	149.44	149.27	149.48	149.14	149.49
$\Delta\Phi_c$		+1.06	+1.58	+1.39	+1.42	+1.36	+1.28	+4.65	−0.36	−0.53	−0.32	−0.66	−0.31
Φ_h	144.1	145.62	146.16	145.98	145.97	146.06	146.00	149.92	143.65	143.61	143.68	143.51	143.59
ΔE[b]	1.26	0.877	0.853	0.882	0.834	0.854	0.870	0.431	1.370	1.343	1.347	1.315	1.366

[a] Bond lengths are expressed in Å, bond angles and dihedral angles are in °.
[b] Values are expressed in kcal/mol.

As for 1,9-diflorophenoxathiin 13, both F-atoms are *meta* to the O atom, each causing a decrease in the [β] bond angle in the ring holding it of the value 2.07°. This in turn calls for bond angle opening by 2.83° on both SC11C12 and SC14C13 bond angles. Consequently, a relatively high $+\Delta\Phi_c$ effect of the value +4.65° is recorded for 13. In fact, 13 has the highest Φ_c 154.45°, i.e. it is the least puckered difluorophenoxathiin in this series. This in turn is reflected on the calculated inversion barriers. Thus, ΔE for 13 is 0.43 kcal/mol, while that for 7–12 is around 0.86 kcal/mol.

Based on results from the mono-counterparts, the two fluorine atoms in 2,3-difluorophenoxathiin 14 are expected to have opposing effects on the endocyclic bond angles. In fact, the expected effects on the [α] and [β] bond angles cancel each other, resulting in an overall increase in both angles (Table 3). Therefore, the molecule suffers further puckering with $-\Delta\Phi_c$ effect of the value −0.36°.

The fact that the introduction of F atom on the 2- or 4-position induces further puckering on the phenoxathiin nucleus, promoted the study of the difluoro isomers 15–17 (Table 3). The induced puckering – in these compounds – is found to adhere to the aforementioned observation that the 4-F (*ortho* to the O) induces more puckering than the 2-F (*para* to O). Thus, the two F atoms in the 2,4-difluoro isomer 15 enhance each other's effect on the endocyclic angles, causing a noticeable bond angle opening in the C1C11C12 [β] by 1.24°. In 2,8-difluoro 16, each F atom induces [β] bond angle opening by 0.39° in the ring holding it. Consequently, the 2,4-difluoro isomer 15 induces more puckering than the 2,8-difluoro 16 does. In addition, 4,6-difluorophenoxathiin 17, where both F atoms are *ortho* to the O atom, is the most puckered isomer in the difluoro series. The calculated $-\Delta\Phi_c$ effect for 15, 16 and 17 is 0.53°, 0.32° and 0.66°, respectively. The calculated ΔE for 15, 16 and 17 is 1.34, 1.35 and 1.32 kcal/mol, respectively.

3,7-Difluorophenoxathiin 18 is a special case. Although the 3-F atom (*meta* to the O) in 4 resulted in a negligible flattening ($+\Delta\Phi_c$ effect of 0.04°) on the phenoxathiin nucleus, the inclusion of the second F atom at the same position in the other arene ring resulted in further puckering on the phenoxathiin nucleus, $-\Delta\Phi_c$ effect of 0.31°. To explain, the induced decrease in the C1C11C12 [β] and C9C14C13 [β] bond angles is accompanied by a decrease in the SC11C12 and SC14C13 bond angles, in contrast to all previous observations. The decrease in both C1C11C12 and SC11C12 bond angles at one side of the S atom, and in C9C14C13 and SC14C13 bond angles at the other side results in this puckering.

In the foregoing combinations, flattening of the phenoxathiin nucleus is only achieved by introducing the F atom in the 1- and 9-positions, with the 1,9-difluoro- isomer 13 showing the highest $+\Delta\Phi_c$ effect 4.65°. Consequently, further substitution of H atoms by F atoms at any position in 13 is expected to decrease the flattening effect induced by the 1- and 9-fluorine atoms. Indeed, this is the case. Introduction of two extra F atoms in 1,2,8,9-tetrafluoro- 19, 1,3,7,9-tetrafluoro- 20 and 1,4,6,9-tetrafluoro- 21 phenoxathiins is accompanied by $+\Delta\Phi_c$ effect of the value 2.60°, 3.36° and 4.02°, respectively, which is less than that for 13 (Table 4). Interestingly, since all F atoms in 20 are *meta* to the O atom, changes in the endocyclic bond angles follows the same pattern as for the difluoro phenoxathiins 9 and 13. In addition, the C1C2C3 bond angle, being (β) to the 1-F and 3-F atoms, and [δ] to the O atom shows high bond angle close up of the value 3.17°. In 21 and as was the case with the difluoro-isomer 11, each of the four F atoms affects freely the half holding it and to the same extend on both sides of the central heterocyclic ring.

Likewise, successive substitution of hydrogen atoms by F atoms on both arene rings at orientations susceptible to induce further puckering followed the expected pattern. Examination of the data in Tables 3 and 4 shows that the introduction of the two extra fluorine atoms on the second ring of 2,3-difluoro- 14 and 2,4-difluoro- 15 phenoxathiins to get 2,3,7,8-tetrafluoro- 22 and

Table 4
Calculated structural parameters at 6-31+G(d) /B3LYP for 1 and poly-fluorinated phenoxathiins 19–26.

Parameter[a]	1	1,2,8,9-Tetra-F 19	1,3,7,9-Tetra-F 20	1,4,6,9-Tetra-F 21	2,3,7,8-Tetra-F 22	2,4,6,8-Tetra-F 23	2,3,4,6,7,8-Hexa-F 24	1,2,3,4-Tetra-F 25	Octa-F 26
C1–C2	1.396	1.392	1.389	1.387	1.388	1.389	1.388	1.392	1.393
C2–C3	1.398	1.387	1.389	1.397	1.393	1.390	1.393	1.393	1.393
C3–C4	1.396	1.397	1.389	1.388	1.388	1.390	1.394	1.394	1.394
C4–C12	1.394	1.393	1.394	1.397	1.395	1.397	1.397	1.396	1.396
C1–C11	1.40	1.396	1.396	1.397	1.400	1.400	1.399	1.395	1.395
C11–C12	1.40	1.402	1.401	1.400	1.400	1.399	1.398	1.402	1.400
S–C11	1.782	1.779	1.780	1.780	1.782	1.782	1.783	1.777	1.781
O–C12	1.384	1.381	1.379	1.374	1.383	1.378	1.377	1.370	1.375
C–S–C	98.44	97.32	97.24	97.75	97.95	98.57	98.21	97.83	97.22
C–O–C	119.1	119.57	119.96	119.14	118.56	117.65	117.49	118.57	118.13
C1–C11–C12 [β]	119.17	117.91	116.98	117.90	119.34	120.49	120.21	118.68	118.62
S–C11–C12	120.17	122.57	122.58	122.08	120.16	119.47	119.33	120.57	121.40
S–C11–C1	120.60	119.50	120.39	119.99	120.43	120.01	120.41	120.72	119.95
C4–C12–C11 [α]	120.69	121.14	121.80	119.55	120.97	118.84	119.60	119.98	120.32
O–C12–C11	122.28	121.86	122.10	123.17	122.23	123.11	123.07	122.81	122.62
O–C12–C4	117.01	116.97	116.09	117.26	116.78	118.01	117.30	117.18	117.04
C11–C1–C2 [γ]	120.37	121.13	123.50	122.85	119.66	118.36	119.30	121.54	121.43
C1–C2–C3 [δ]	119.92	120.53	116.75	118.74	120.46	122.92	121.18	119.38	119.45
C2–C3–C4 [γ']	120.06	119.18	122.92	119.29	120.58	117.31	119.20	119.86	119.91
C3–C4–C12 [β']	119.75	120.10	118.05	121.67	118.96	122.06	120.48	120.54	120.27
C9C14C13 [β]	119.18	117.92	116.98	117.90	119.34	120.49	120.21	119.11	118.62
S–C14C13	120.17	122.57	122.59	122.09	120.17	119.47	119.34	120.88	121.41
S–C14–C9	120.60	119.49	120.39	119.98	120.43	120.01	120.40	119.96	119.94
C6C13C14 [α]	120.69	121.14	121.80	119.55	120.97	118.84	119.60	121.08	120.32
O–C13C14	122.27	121.85	122.09	123.16	122.22	123.10	123.06	122.00	122.61
O–C13–C6	117.02	116.98	116.09	117.27	116.79	118.02	117.31	116.90	117.05
Φ_c	149.8	152.40	153.16	153.82	148.76	148.78	147.95	149.46	149.64
$\Delta\Phi_c$		+2.60	+3.36	+4.02	−1.04	−1.02	−1.85	−0.34	−0.16
Φ_h	144.1	147.65	148.37	149.39	142.91	143.09	142.13	144.29	144.95
ΔE[b]	1.26	0.623	0.537	0.480	1.501	1.438	1.670	1.146	0.909

[a] Bond lengths are expressed in Å, bond angles and dihedral angles are in °.
[b] Values are expressed in kcal/mol.

2,4,6,8-tetrafluoro- 23 phenoxathiins, respectively, mainly affects the second ring and to nearly the same extend encountered with 14 and 15. The cumulating effect arising at both sides is reflected on the relatively high puckering predicted for 22 and 23, with Φ_c of the value 148.76° and 148.78°; and $-\Delta\Phi_c$ effect of 1.04° and 1.02°, respectively. Consequently, 2,3,7,8-tetrafluoro- 22 and 2,4,6,8-tetrafluoro- 23 phenoxathiins are considered to be the most puckered tetrafluorophenoxathiins. Further substitution by F atoms to include the 2-, 3- and 4-positions at both arene rings induces further puckering. The puckering angle Φ_c (147.95°) predicted for 2,3,4,6,7,8-hexafluorophenoxathiin 24 is the smallest in this study, indicating that 24 is the most puckered fluorinated phenoxathiin. The predicted $-\Delta\Phi_c$ effect is 1.85°.

Finally, we examined the cumulative effect resultant from introducing four fluorine atoms on the same arene ring, 1,2,3,4-tetrafluorophenoxatniin 25 and on both rings, octafluorophenoxathiin 26. As anticipated, the trend by which such substitutions affect the endocyclic bond angles of 25 and 26 is found to be similar, however, to a different extent (Table 4). On the other hand, the effect of these substitutions on the puckering angle Φ_c although small due to the inclusion of the 1-F atom, it is quite unique. In all the studied cases, it has been observed that as Φ_c increases, so does Φ_h. However, 25 and 26 violate this observation and these dihedral angles behave in opposite sense. Thus, although 25 and 26 show $-\Delta\Phi_c$ effect of the value 0.34° and 0.16°, both molecules show $+\Delta\Phi_h$ effect of the value 0.19° and 0.85°, respectively. This behaviour indicates that although the two best planes through the two-arene rings are folded up, the best-fit planes that include the two halves of the heterocyclic ring (O, S, C11, C12 and O, S, C14, C13) are opened. Interestingly, the accompanied inversion barrier has decreased, indicating the overall flattening of these molecules as compared to phenoxathiin 1.

It worth mentioning that, in all the studied fluorinated phenoxathiins, the predicted inversion barrier is very small, it does not exceed 1.67 kcal/mol for the most puckered isomer, that is 2,3,4,6,7,8-hexafluorophenoxathiin 24. Consequently, we anticipate these compounds to enjoy an easy *butterfly* interconversion.

4. Conclusion

In this work, we have performed a thorough study on the molecular structure of fluorinated phenoxathiin using the *ab initio* method at the B3LYP/(6-31+G)+d basis set level. Our primary interest has been to investigate the effect of successive substitution by the electron captor substituent, namely, fluorine in the arene rings of phenoxathiin on the puckering of the phenoxathiin nucleus. The encountered change in the puckering angle was found to be dependent on the position of the fluorine atom with respect to the oxygen atom of the central heterocyclic ring. This has been attributed to the competing factors arising from the σ-electron withdrawing and the π-electron releasing effects of both the F and O atoms. Substitution at the 1-position, *meta* to the oxygen has been predicted to flatten the nucleus, while substitutions at the 2- and 4- positions, *para* and *ortho* to the oxygen, respectively, were predicted to induced further puckering on the nucleus. Substitution at the 3-position, although it has shown a negligible effect at the mono-substitution level, it has enhanced the puckering at higher substitution levels. Successive substitution at these positions enhanced these effects. Thus, 1,9-difluorophenoxathiin was found to be the most flattened fluorinated phenoxathiin, while 4,6-difluorophenoxathiin and 2,3,7,8-tetrafluoro and 2,4,6,8-tetrafluorophenoxathiins were found to be the most puckered isomer in the difluoro- and tetrafluoro-series, respectively. In addition, 2,3,4,6,7,8-hexafluorophenoxathiin was found to be the most puckered fluorinated phenoxathiin. For all molecules under study, the inversion barrier is found to be quite small, thus, these compounds were anticipated to enjoy an easy *butterfly* interconversion reported for the chalcanthrene compounds.

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