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Conformational behaviors of trans-2,3-bis(methylthio)-1,4-dioxane, -dithiane and –diselenane. A hybrid-DFT study and NBO interpretations

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Abstract

The conformational behaviors of 2,3-bis(methylthio)-1,4-dioxane (**1**), 2,3-bis(methylthio)-1,4-dithiane (**2**) and 2,3-bis(methylthio)-1,4-diselenane (**3**) have been analyzed by means of hybrid-density functional theory (B3LYP/Def2-TZVPP) based method and NBO interpretation. B3LYP/Def2-TZVPP results showed that the axial conformations of compounds **1-3** are more stable than their equatorial conformations. The calculated Gibbs free energy difference (G_{eq}–G_{ax}) values (i.e. $\Delta G_{eq\text{-}ax}$) at 298.15 K and 1 atm between the axial and equatorial conformations decrease from compound **1** to compound **3**. The NBO analysis of donor-acceptor ($LP \rightarrow \sigma^*$) interactions showed that the *anomeric effects* (*AE*) decrease from compound **1** to compound **3**. On the other hand, the calculated dipole moment values between the axial and equatorial conformations [$\Delta(\mu_{eq} - \mu_{ax})$] increase from compound **1** to compound **2** but decrease from compound **2** to compound **3**. However, the variations of the calculated $\Delta(\mu_{eq} - \mu_{ax})$ values are not in the same trend observed for the corresponding *AE* and ΔG values. Therefore, the calculated $\Delta\mu$ values do not seem to be sufficient to account for the axial preferences in compounds **1-3**. These findings led to the proposal that the *AE*, due to donor→acceptor hyperconjugation effect, is more significant for the explanation of the axial conformational preferences of compounds **1-3** than the electrostatic effect.

Keywords: Anomeric effects; Stereoelectronic interactions; Molecular modeling; Ab initio; NBO; 2,3-bis(methylthio)-1,4-dithiane.

1. Introduction

The saturated heterocyclic compounds are quite widespread in nature (e.g. in alkaloids, carbohydrates, and plant growth regulators, among other compounds), the knowledge about conformational properties of heterocyclic compounds is of very general interest. The most dominant conformation-controlling factor in carbohydrate and heterocyclic compounds is known as the *anomeric effect* (*AE*) [1]. Edwards [2] was attributed the increased stability of axial polar groups at the anomeric position of pyranose rings to repulsive interaction between the ring dipole

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(generated by the unshared electrons of the endocyclic oxygen) and the nearly parallel polar bonds in the equatorial conformation [3].

The rationalization of the *anomeric effect* (*AE*) solely in terms of electrostatic interactions fails to account quantitatively for observed axial preferences [4]. The preferred geometry of many molecules can be viewed as the result of the maximization of an interaction between the best donor lone pair and the best acceptor bond [5], the stereoelectronic interactions are expected to play an important role in the conformational properties of heterocyclic compounds [6]. There is a stereoelectronic preference for conformations in which the best donor lone pair is antiperiplanar to the best acceptor bond. Praly and Lemieux have stressed that the *AE* in six membered saturated heterocyclic compounds must be considered as the difference between the sum of the *endo-AE* and *exo-AE* in the equatorial conformer and the same sum for the axial conformer [7]. Also, they have suggested that there is no *endo-AE* in the equatorial conformer, therefore, it is exclusively stabilized by *exo-AE* interactions (equation 1).

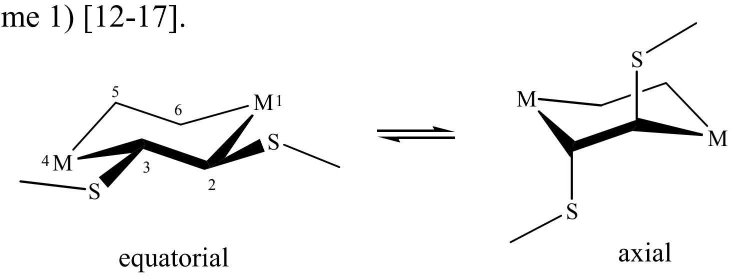
$$\textit{anomeric effect} = (\textit{exo-AE}_{\text{eq}}) - (\textit{exo-AE}_{\text{ax}} + \textit{endo-AE}_{\text{ax}}) \quad \text{(Eq. 1)}$$

According to the above equation, the *AE* can have negative or positive values depending on the relative magnitude of the *endo-AE* and *exo-AE* contributions. However, the results of this work, show that there is $LP_{eq}O_1 \rightarrow \sigma^*_{C2-S7}$ (*endo-AE*) electron delocalization in the equatorial conformation of compound **1** (see scheme 1). Therefore, we modify the above *AE* equation for the axial and equatorial conformations of compounds **1-6** as follow:

$$\textit{anomeric effect} = \sum(\textit{endo-AE}_{\text{eq}} + \textit{exo-AE}_{\text{eq}}) - \sum(\textit{endo-AE}_{\text{ax}} + \textit{exo-AE}_{\text{ax}}) \quad \text{(Eq. 2)}$$

In 1984, Pericás, Riera and Guilera determined the conformational equilibrium of compound **2** in $CDCl_3$ solution [8]. The observed 83:17 mixture of diaxial and diequatorial conformations suggests that S-C-S anomeric effect (AE) is strong enough to overcome repulsive gauche interactions [9-11].

Although the importance of the hyperconjugative interactions in compound **2** has investigated [8-11], there is no published experimental or quantitative theoretical data about the donor-acceptor delocalization effects on the conformational properties of compounds **1-3**. In this work, the impacts of the stereoelectronic interactions associated with the *AE*, electrostatic and steric interactions on the conformational and structural properties of compounds **1-3** were investigated computationally using hybrid-DFT based methods and natural bond orbital (NBO) analysis (see scheme 1) [12-17].



1: M=O, **2**: M=S, **3**: M=Se

Scheme 1 Schematic representation of conformations of compounds **1-3**.

2. Computational details

Hybrid DFT calculations were carried out using the B3LYP/Def2-TZVPP [18] levels of theory with the GAUSSIAN 03 package of programs [12]. Main purpose of the present work was to study the impacts of the stereoelectronic interaction effects, dipole-dipole interactions and steric repulsions on the conformational preferences (i.e. axial and equatorial conformations) in compounds **1-3**. The energy minimization of these compounds was carried out only for the axial and equatorial position of methylthio groups on the chair conformations of the heterocyclic 1,4-dioxane, -dithiane and -diselenane rings.

An NBO analysis was then performed for the axial and equatorial conformations of compounds **1-6** by the NBO 5.G program contained in the PC-GAMESS interface [17]. The bonding and antibonding orbital occupancies in the axial and equatorial conformations of compounds **1-3,** and also the stabilization energies associated with *endo-AEs* and *exo-AEs* were calculated using NBO analysis. The LP→σ* resonance energies are proportional to $S^2/\Delta E$ where S is the orbital overlap and ΔE is the energy differences between the LP and σ* orbitals [5, 17]:

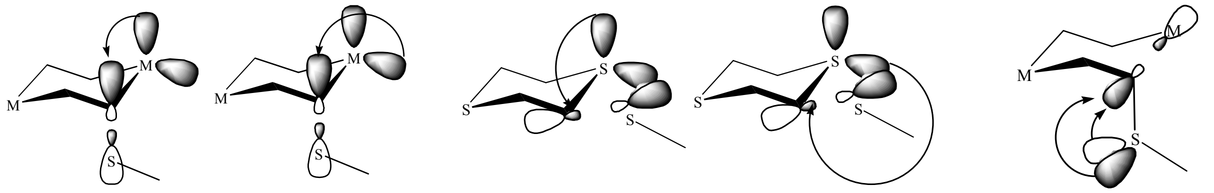
$$\textit{Stabilization or resonance energy}\ \alpha\ (S^2/\Delta E)$$

In addition, the stabilization energy (E_2) associated with $i \rightarrow j$ delocalization, is explicitly estimated by the following equation:

$$E_2 = q_i \frac{F^2(i,j)}{\varepsilon_j - \varepsilon_i}$$

where q_i is the i^th^ donor orbital occupancy, ε_i, ε_j are diagonal elements (orbital energies) and F(i,j) off-diagonal elements, respectively, associated with the NBO Fock matrix. Therefore, there is a direct relationship between F(i,j) off-diagonal elements and the orbital overlap (S).

The stabilization energies (E_2) associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C\text{-}S7}$, $LP_{aeq}M_1 \rightarrow \sigma^*_{C\text{-}S7}$ (*endo-AE*), $LP_1S_7 \rightarrow \sigma^*_{C\text{-}M1}$ and $LP_2S_7 \rightarrow \sigma^*_{C\text{-}M1}$ (*exo-AE*) electron delocalizations (see Fig. 1) and their influences on the conformational properties of compounds **1-3** were quantitatively investigated by the NBO analysis [17]. Our recent works showed that the NBO analysis is a sufficient approach to investigate the effect of the stereoelctronic interactions on the stability, reactivity and dynamic behaviors of chemical compounds [19-25].



($LP_{ax}M_1 \rightarrow \sigma^*_{C2\text{-}S7ax}$) ($LP_{eq}M_1 \rightarrow \sigma^*_{C2\text{-}S7ax}$) ($LP_{ax}M_1 \rightarrow \sigma^*_{C2\text{-}S7eq}$) ($LP_{eq}M_1 \rightarrow \sigma^*_{C2\text{-}S7eq}$) ($LP\ S_7 \rightarrow \sigma^*_{C2\text{-}M1}$)

Fig. 1. Schematic representation of the electron delocalization between non-bonding and anti-bonding orbitals in compounds **1-3**.

3. Results and discussion

3.1. Conformation preference

The Gibbs free energy, enthalpy and entropy differences (i.e. ΔG, ΔH and ΔS) for the axial and equatorial conformations of compounds **1-3**, as calculated at the B3LYP/Def2-TZVPP level of theory are given in Table 1. The calculated Gibbs free energy difference (G_{eq}–G_{ax}) values between the axial and equatorial conformations (i.e. $\Delta G_{eq\text{-}ax}$) of compounds **1-3** are 1.61, 0.96 and 0.01 kcal mol^{-1} as calculated by the B3LYP/Def2-TZVPP level of theory, respectively.

Surprisingly, the B3LYP/Def2-TZVPP results revealed that there is no significant difference between the energies (i.e. $\Delta G_{eq\text{-}ax}$) of the axial and equatorial conformations of compound **3**. The numerical difference is not outside the limit of accuracy of the methods. The experimental observation that the crystal form shows only the axial form is not in contradiction to this, but rather is an indication of the importance of crystal forces in favoring the axial conformation.

Table 1
B3LYP/Def2-TZVPPcalculated thermodynamic functions [enthalpies, Gibbs free energies (in hartree) and entropies (in cal mol^{-1}K^{-1})], for the axial and equatorial conformations of the boat forms of compounds **1-3**.

Geometries	H (Hartree)	S (cal mol^{-1}K^{-1})	G (Hartree)	ΔH ^{a} (Hartree)	ΔS ^{a} (calmol^{-1}K^{-1})	ΔG ^{a} (Hartree)
1-Eq	-1182.688325	108.967	-1182.740098	0.002876 (1.80)^{b}	0.651	0.002567 (1.61)^{b}
1-Ax	-1182.691201	108.316	-1182.742665	0.000000 (0.00)^{b}	0.000	0.000000 (0.00)^{b}
2-Eq	-1828.644875	116.020	-1828.700000	0.002854 (1.79)^{b}	2.785	0.001531 (0.96)^{b}
2-Ax	-1828.647729	113.235	-1828.701531	0.000000 (0.00)^{b}	0.0000	0.000000 (0.00)^{b}
3-Eq	-5835.378229	123.229	-5835.436779	0.001713 (1.07)^{b}	0.000	0.000000 (0.00)^{b}
3-Ax	-5835.379942	119.601	-5835.436768	0.000000 (0.00)^{b}	-3.628	0.000011 (0.01)^{b}

^{a} Relative to the most stable form. ^{b} Numbers in parenthesis are in kcal mol^{-1}.

3.2. Stabilization energies

The NBO analysis shows that the axial and equatorial conformations of compounds **1-3** benefit strongly from donor-acceptor electronic delocalizations. Based on the optimized ground state geometries using the B3LYP/Def2-TZVPP method, the NBO analysis of donor-acceptor (bond-antibond) interactions showed that the stabilization energies associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$ electron delocalizations (*endo-AE*) for the axial conformations of compounds **1-3** are 26.58, 14.38 and 9.8 kcal mol^{-1}, respectively. There are no $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$ electron delocalizations for the equatorial conformations of compound **1-3**. In addition, the stabilization energy associated with the $LP_{eq}M_1 \rightarrow \sigma^*_{C2-S7}$ electron delocalization (*endo-AE*) for the equatorial conformation of compound **1** is 1.80 kcal mol^{-1} while there is not this kind of electron delocalizations for the equatorial conformations of compounds **2** and **3**.

The NBO results revealed that the stabilization energies associated with LP_2 $S7 \rightarrow \sigma^*_{C2-M1}$ (*exo-AE*) in the axial conformations of compounds **1-3** are 17.30, 16.92 and 20.48 kcal mol^{-1}, respectively. Also, the stabilization energies associated with LP_2 $S7 \rightarrow \sigma^*_{C2-M1}$ (*exo-AE*) in the equatorial conformations of compounds **1-3** are 16.66, 12.38 and 14.6 kcal mol^{-1}, respectively. Based on the results obtained, the calculated *exo-AEs* decrease from the axial and equatorial conformations of compound **1** to compound **2** but increase from compound **2** to compound **3**.

Based on Eq. 2, the *AE* associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$, $LP_{eq}M_1 \rightarrow \sigma^*_{C2-S7}$, $LP_1S_7 \rightarrow \sigma^*_{C2-M1}$ and $LP_2S7 \rightarrow \sigma^*_{C2-M1}$ electron delocalization, (*exo-* and *endo-AE*) for compounds **1-3** are -28.18, -22.82 and -19.12 kcal mol^{-1}, respectively. Based on the results obtained, the *AE* decrease from compound **1** to compound **3**. Since the calculated $\Delta G_{ax\text{-}eq}$ decreases from compound **1** to compound **3**, the rationalization of the conformational preference solely in terms of the *AE* succeeds to account for compounds **1-3**.

3.3. Orbital occupancies

The NBO results showed that the LP$_{ax}$M1 nonbonding orbital occupancies in the axial conformations of compounds **1-3** are 1.89524, 1.90133 and 1.91504, respectively (see Table 3). In addition, the NBO results revealed that the σ^*_{C2-S7} antibonding orbital occupancies in the axial conformations of compounds **1-3** are 0.07747, 0.06616 and 0.05633, respectively. This trend can be justified by the decrease of the LP$_{ax}$M$_1$→σ^*_{C2-S7} electron delocalization (*exo-AE*) from the axial and equatorial conformations of compound **1** to compound **3**.

3.4. Orbital energies and off-diagonal elements

It should be noted that the LP→σ* resonance energies are proportional to $S^2/\Delta E$ where S is the orbital overlap and ΔE is the energy differences between the LP nonbonding and σ* anti-bonding orbitals. Therefore, the stereoelectronic orbital interactions are anticipated to be more effective for the *anti* rather than the *syn* or *gauche* arrangement between the donor (LP) and acceptor (σ*) orbitals, and the stabilization should increase as the anti-bonding orbital σ* energy decreases and the non-bonding orbital LP energy increases.

Table 2

Calculated resonance (stabilization) energies associated with donor-acceptor delocalizations, anomeric Effects and dipole moments for the axial and equatorial conformations of the chair and boat forms of compounds **1-3**, using NBO-B3LYP/Def2-TZVPPanalysis.

donor→acceptor	1		2		3	
	Eq	Ax	Eq	Ax	Eq	Ax
(LP$_{(ax)}$M1→σ^*_{C2-S7})×2	-	26.58	-	14.38	-	9.8
(LP$_{(eq)}$M1→σ^*_{C2-S7})×2	1.8	2.4	-	3.34	-	3.14
(LP$_1$S7→σ^*_{C2-M1}) ×2	1.22	1.58	1.7	2.26	1.98	2.28
(LP$_2$S7→σ^*_{C2-M1}) ×2	16.66	17.3	12.38	16.92	14.6	20.48
Σ	19.68	47.86	14.08	36.9	16.58	35.7
AE	**-28.18**		**-22.82**		**-19.12**	
F_{ij}						
(LP$_{(ax)}$M1→σ^*_{C2-S7}) ×2	-	0.138	-	0.092	-	0.076
(LP$_{(eq)}$M1→σ^*_{C2-S7}) ×2	0.046	0.052	-	0.064	-	0.064
(LP$_1$S7→σ^*_{C2-M1}) ×2	0.04	0.048	0.044	0.052	0.046	0.05
(LP$_2$S7→σ^*_{C2-M1}) ×2	0.114	0.118	0.084	0.1	0.084	0.1
μ (Debye)	2.2001	0.6165	1.7159	0.0204	1.4984	0.2409
Δμ	1.5836		1.6955		1.2575	

The energy differences between donor (E_{LPaxM1}) and acceptor ($E\sigma_{*C2\text{-}S7}$) orbitals [i.e. $\Delta(E_{\sigma^*C2\text{-}S7} - E_{LPax\ M1})$] for the axial conformations of compounds **1-3** are 0.438, 0.362 and 0.357 a.u., respectively, as calculated by NBO analysis. Based on the NBO results, the energy difference between donor (E_{LPaxS1}) and acceptor ($E\sigma_{*C2\text{-}X}$) orbitals [i.e. $\Delta(E_{\sigma^*C2\text{-}X} - E_{LPax\ S1})$] decreases from the axial conformations of compound **1** to compound **3**. It can be concluded that the strong donor nonbonding orbital of compound **3** (compared to those in compounds **1** and **2**) may give rise to strong *endo-AE* (see Table 3). It should be noted that the decrease of the *orbital overlap* (S) [off-diagonal elements (F_{ij})] values for the $LP_{ax}M_1 \rightarrow \sigma^*_{C2\text{-}S7}$ electron delocalization (endo-*AE*) from the axial conformations of compound **1** to compound **3** could reduce the *AE* (see Table 3). Importantly, there is conflict between the F_{ij}, $\Delta(E_{acceptor} - E_{donor})$ for the endo-*AE* in the axial conformations of compounds **1-3**. Since the second order perturbation energy (E_2) is related to the F_{ij}, $\Delta(E_{acceptor} - E_{donor})$, it seems that in the axial conformations of compounds **1-3** the F_{ij} could affect the order of the E_2.

Table 3
NBO calculated non-bonding and anti-bonding orbital occupancies, based on the calculated geometries using B3LYP/Def2-TZVPP level of theory, for the axial and equatorial conformations of the chair and boat forms of compounds **1-3.**

Occupancy	LPaxM1	LPeqM1	LP_1S_7	LP_2S_7	$\sigma^*_{C2\text{-}M1}$	$\sigma^*_{C2\text{-}S7}$
1-Eq	1.91371	1.96203	1.98391	1.90774	0.05634	0.03691
1-Ax	1.89524	1.95787	1.98553	1.91405	0.05485	0.07747
2-Eq	1.92195	1.98148	1.98324	1.90435	0.05144	0.04309
2-Ax	1.90133	1.97529	1.98258	1.91143	0.06590	0.06616
3-Eq	1.93442	1.98621	1.98262	1.89590	0.06227	0.04563
3-Ax	1.91504	1.98068	1.98133	1.90035	0.08080	0.05633
4-Eq	1.91379	1.96183	1.98504	1.91082	0.05917	0.03542
4-Ax	1.89736	1.95837	1.98588	1.91320	0.05707	0.07508
5-Eq	1.92298	1.98137	1.98409	1.91164	0.05259	0.03749
5-Ax	1.90433	1.97585	1.98221	1.91067	0.06559	0.06392
6-Eq	1.93554	1.98606	1.98351	1.90282	0.06312	0.03952
6-Ax	1.91832	1.98105	1.98072	1.89932	0.08012	0.05518

3.5. Dipole moments

There is a preference for the conformation with the smallest resultant dipole moment. Especially in the gas phase it is generally found that the conformation with the larger dipole moment has the larger electrostatic energy. Therefore, the conformation with the larger dipole moment has an increased overall energy [26]. Table 2 presents the calculated dipole moments for the axial and equatorial conformations of compounds **1-3**. The B3LYP/Def2-TZVPP results showed that the dipole moments for the equatorial conformations of compounds **1-3** are larger than those in their axial conformations. Also, the calculated dipole moments of the equatorial conformations decrease from compound **1** to **3** but for their corresponding equatorial conformations decrease from compound 1 to compound **2** and increases from compound **2** to compound **3**.

Using the dipole moments obtained, a "Δ" parameter could be found as $\Delta(\mu_{eq}\text{-}\mu_{ax})$. There is no the same trend for the variations of $\Delta(\mu_{eq}\text{-}\mu_{ax})$ and *AE*. Based on the results obtained, the *AE* increase from compound **1** to compound **3** but $\Delta(\mu_{eq}-\mu_{ax})$ increases from compound **1** to compound **2** and decreases from compound **2** to compound **3**. The variation of $\Delta(\mu_{eq}-\mu_{ax})$ values is not in accordance with the decrease of the calculated $\Delta G_{ax\text{-}eq}$ from compound **1** to compound **3**. It seems the variation of the *AE* reasonably explain the conformational behaviors of compounds **1-3**.

3.6. Structural parameters

Representative structural parameters for the axial and equatorial conformations of compounds **1-3**, as calculated at the B3LYP/Def2-TZVPP level of theory, are shown in Table 4. Although it is not expected, in principal, to obtain exactly the experimental values because of the differences in definition of bond length values [27], it is possible to carry out theoretical calculations, from which many properties and structures can be obtained with an accuracy that is competitive with experiments [27-31].

Importantly, consideration of the structures of compounds **1-3** gave evidence that in the axial conformations of these compounds, the $\sigma_{M1\text{-}C2}$ and $\sigma_{M4\text{-}C3}$ bond lengths are significantly contracted compared to those in their equatorial conformations. The B3LYP/Def2-TZVPP results showed that the $\sigma_{M1\text{-}C2}$ bond lengths in the axial conformations of compounds **1-3** are 1.411, 1.831 and 1.996 Å, respectively, while the corresponding values in the equatorial conformations are 1.426, 1.842 and 2004 Å, respectively (see Table 5). The shorter $\sigma_{M1\text{-}C2}$ and $\sigma_{M4\text{-}C3}$ bond lengths in the axial conformations of compounds **1-3**, compared to those in their equatorial conformations, are the result of the $LP_{ax}M_1 \rightarrow \sigma^*_{C2\text{-}S7}$ electron delocalization (*endo-AE*). The variation of the $\sigma_{M1\text{-}C2}$ bond length in the axial conformations of compounds **1-3** is in accordance with the variation of resonance energies associated with the $LP_{ax}M_1 \rightarrow \sigma^*_{C2\text{-}S7}$ electron delocalization (see Tables 3 and 4).

Using the structural parameters obtained, a “Δ” parameter could be found as $\Delta[r_{1\text{-}2(Eq)}\text{-}\ r_{1\text{-}2(Ax)}]$. There is a direct correlation between the calculated *AE* and $\Delta[r_{1\text{-}2(Eq)}\text{-}\ r_{1\text{-}2(Ax)}]$ (see Tables 3, 4). These results indicate that with the decrease of $\Delta[r_{1\text{-}2(Eq)}\text{-}\ r_{1\text{-}2(Ax)}]$ parameter from compound **1** to compound **3**, the corresponding *AE* values decrease. Consequently, the calculated $\Delta[r_{1\text{-}2(Eq)}\text{-}\ r_{1\text{-}2(Ax)}]$ parameters could be proposed as a criterion for the evaluation of the *AE* values in compounds **1-3**.

In addition, the B3LYP/Def2-TZVPP results showed that the $\sigma_{C2\text{-}S7}$ bond lengths in the axial conformations of compounds **1-3** are 1.847, 1.839 and 1.826, while the corresponding values for their equatorial conformations are 1.812, 1.831 and 1.829 Å, respectively. These results indicate that with the decrease of $\Delta[r_{2\text{-}S7(Ax)}\text{-}\ r_{2\text{-}S7(eq)}]$ parameter from compound **1** to compound **3**, the corresponding *AE* values decrease. Consequently, the calculated $\Delta[r_{1\text{-}2(Eq)}\text{-}\ r_{1\text{-}2(Ax)}]$ parameters could be proposed as a criterion for the evaluation of the *AE* values in compounds **1-3**. This observation is consistent with the decrease of the $LP_{ax}M_1 \rightarrow \sigma^*_{C2\text{-}S7}$ (*endo*-AE) electronic delocalization from the axial conformations of compound **1** to compound **3**.

Table 4
NBO-B3LYP/Def2-TZVPP calculated non-bonding and anti-bonding orbital energies, based on the calculated geometries using B3LYP/Def2-TZVPP level of theory, for the axial and equatorial conformations of the chair and boat forms of compounds **1-3.**

	$LPaxM_1$	$LPeqM_1$	LP_1S7	LP_2S7	σ^*_{C2-S7}	σ^*_{C2-M1}	$\Delta[E(\sigma^*_{C2-S7})-E(LPeqM1)]$	$\Delta[E(\sigma^*_{C2-S7})-E(LP_{ax}M_1)]$	$\Delta([(\sigma^*_{C2-M1})-E(LP_2S_7)]$
1-Eq	-0.31003	-0.60202	-0.60154	-0.23277	0.14616	0.25010	0.74818	0.45619	0.48287
1-Ax	-0.31494	-0.58652	-0.60794	-0.23567	0.12270	0.26617	0.70922	0.43764	0.50184
2-Eq	-0.24221	-0.61200	-0.60690	-0.23814	0.12672	0.11778	0.73872	0.36893	0.35592
2-Ax	-0.23944	-0.61112	-0.60697	-0.24013	0.122248	0.12426	0.733368	0.361688	0.36439
3-Eq	-0.23230	-0.67656	-0.60623	-0.23834	0.12951	0.05882	0.80607	0.36181	0.29716
3-Ax	-0.22491	-0.68039	-0.60514	-0.24204	0.13183	0.06309	0.81222	0.35674	0.31

Table 5
B3LYP/Def2-TZVPPcalculated structural parameters for the axial and equatorial conformations of the chair and boat forms of compounds **1-3**.

Compound	1		2		3	
State	Eq	Ax	Eq	Ax	Eq	Ax
Bond lengths (Å)						
r_{1-2}	1.426	1.411	1.842	1.831	2.004	1.996
r_{2-3}	1.536	1.539	1.533	1.536	1.525	1.530
r_{3-4}	1.426	1.411	1.842	1.831	2.004	1.996
r_{4-5}	1.427	1.431	1.825	1.823	1.978	1.974
r_{5-6}	1.516	1.514	1.521	1.523	1.515	1.518
r_{6-1}	1.427	1.431	1.825	1.823	1.978	1.974
r_{2-S}	1.812	1.847	1.831	1.839	1.829	1.826
r_{S-CH3}	1.817	1.817	1.817	1.814	1.817	1.814
$\Delta[r_{2-S(Ax)}- r_{2-S(eq)}]$	0.035		0.008		-0.003	
$\Delta[r_{1-2(Eq)}- r_{1-2(Ax)}]$	0.015		0.011		0.008	
Bond angles (°)						
θ_{1-2-3}	109.1	111.9	110.6	113.4	110.6	113.2
θ_{2-3-4}	109.1	111.9	110.6	113.4	110.6	113.2
θ_{3-4-5}	112.2	113.7	101.6	100.2	100.7	97.8
θ_{4-5-6}	109.7	110.1	112.7	113.6	112.9	113.9
θ_{5-6-1}	109.7	110.1	112.7	113.6	112.9	113.9
θ_{6-1-2}	112.2	113.7	101.6	100.2	100.6	97.8
θ_{S-2-1}	109.1	113.6	107.3	114.7	106.8	114.4
Torsion angels (°)						
$\phi_{1-2-3-4}$	57.1	48.3	69.1	65.8	70.0	69.2
$\phi_{2-3-4-5}$	-58.5	-51.6	-62.0	-58.4	-62.4	-60.0
$\phi_{3-4-5-6}$	58.4	56.1	59.6	58.9	59.9	60.0
$\phi_{4-5-6-1}$	-56.5	-56.5	-64.8	-67.0	-66.0	-69.7
$\phi_{5-6-1-2}$	58.4	56.1	59.6	58.9	60.0	60.0
$\phi_{6-1-2-3}$	-58.5	-51.6	-62.0	-58.4	-62.5	-60.0
$\phi_{S-2-1-6}$	179.5	72.1	175.5	68.5	174.9	67.6
$\phi_{S-C2-C3-S}$	-61.8	155.6	-51.5	166.7	-51.6	169.8

4. Conclusions

The hybrid-DFT calculations reported above and NBO analysis provided a reasonable picture from energetic, structural, bonding and stereoelectronic points of view for the conformational preference in compounds **1-3**. Effectively, the B3LYP/Def2-TZVPP results showed that the calculated ΔG_{eq-ax} decreases from compound **1** to compound **3**. The results revealed that there is axial preference for compounds **1** and **2** but there is no energetic difference between the axial and equatorial conformations of compound 3. In addition, NBO results revealed that:

- the *AE* decrease from compound **1** to compound **3**.
- the strong donor nonbonding orbital of compound **3**, compared to those in compounds **1** and **2** may gives rise to strong *endo- AE* but the decrease of Fij value of the $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$ affects the order of the corresponding stabilization energy.

- the rationalization of the conformation preference solely in terms of the *AE* succeeds to account quantitatively for the conformation preferences in compounds **1-3**.
- the electrostatic interactions can not explain the conformational behaviors of compounds **1-3**.

Also, in the axial conformations of compounds **1-3**, the σ_{M1-C2} and σ_{M4-C3} bond lengths are significantly contracted compared to those in their equatorial conformations. The shorter σ_{M1-C2} and σ_{M4-C3} bond lengths in the axial conformations of compounds **1-3** compared to those in their equatorial conformations can be the result of the $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$ electron delocalization (*endo-AE*). Also, the variation of the σ_{M1-C2} bond length in the axial conformations of compounds **1-3** is in accordance with the variation of resonance energies associated with the $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$ electronic delocalization. The decrease of the $LP_{ax}M_1 \rightarrow \sigma^*_{C2-S7}$ electron delocalization can decrease the bond order of the σ_{M1-C2} bond. This fact can justify the contracted σ_{M1-C2} bond lengths in the axial conformations of compounds **1-3**. The longer σ_{M1-C2} bond length in the equatorial conformations of compounds **1-3** can be justified by the *exo-AE*.

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