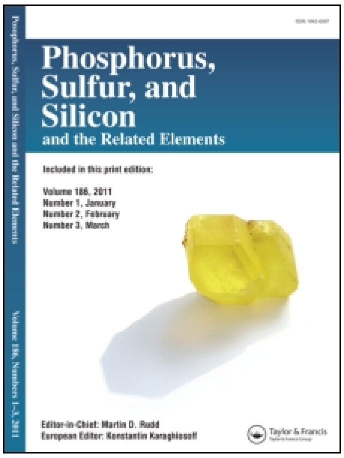

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HYBRID-DFT STUDY AND NBO ANALYSIS OF THE STEREOELECTRONIC INTERACTION EFFECTS (ASSOCIATED WITH THE ANOMERIC EFFECTS) ON THE CONFORMATIONAL PROPERTIES OF 2,3,5,6-TETRAHALO-1,4-DIOXANES AND THEIR ANALOGS CONTAINING S AND Se ATOMS

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NBO analysis and hybrid density functional theory–based method (B3LYP/6-311+G**) was used to study the anomeric effects (AE), dipole–dipole interactions, and steric repulsion effects on the conformational properties of 2,3,5,6-tetrahalo-1,4-dioxane [halo = F (1), Cl (2), Br (3)], 2,3,5,6-tetrahalo-1,4-dithiane [halo = F (4), Cl (5), Br (6)], and 2,3,5,6-etrahalo-1,4-diselenane [halo = F (7), Cl (8), Br (9)]. B3LYP/6-311+G** results revealed a strong axial preference in compounds 1–3. Gibbs free energy difference (G_{eq}–G_{ax}) values (e.g., $\Delta G_{eq\text{-}ax}$) between the axial and equatorial conformations of compound 1 to compound 3 are 8.19, 3.86, and 3.13 kcal mol^{-1}, respectively, as calculated by the B3LYP/6-311+G** level of theory. On the other hand, the NBO analysis of donor–acceptor (bond–antibond) interactions revealed that the AE for compounds 1–3 are −12.26, −16.46, and −18.11 kcal mol^{-1}, respectively. Contrary to the increase of the AE values from compound 1 to compound 3, the increase of the steric repulsions (e.g., 1,3-syn-axial repulsions) could fairly explain the decrease of the axial conformation stability in compounds 1–3 compared to their equatorial conformations. Further, the correlations between the AE, structural parameters, and conformational behavior of compounds 4–9 have been investigated.

Keywords Ab initio; anomeric effects; molecular modeling; NBO; 2,3,5,6-tetrahalo-[1,4]dioxane; 2,3,5,6-tetrahalo-[1,4]diselenane; 2,3,5,6-tetrahalo-[1,4]dithiane

INTRODUCTION

In the past several years, the conformational equilibria in alicyclic molecules have been studied using experimental and theoretical approaches. Theoretical treatments of cycloalkanes have also provided values in reasonable agreement with experimental results.[1–5]

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Contrary to the abundance of information in the cyclohexane field, there has been a paucity of data concerned with conformational properties in heterocyclic systems.[6–8] The knowledge about conformational properties of heterocyclic compounds should be of very general interest, since saturated heterocyclic compounds comprise a large segment of organic and inorganic chemistry and are quite widespread in nature, e.g., in alkaloids, carbohydrates, and plant growth regulators, among other compounds.

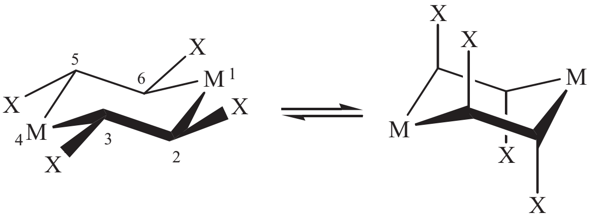
It is well known that stereoelectronic interactions could play an important role on the conformational properties of heterocyclic compounds.[9,10] There is a stereoelectronic preference for conformations in which the best donor lone pair is antiperiplanar to the best acceptor bond.[11] Praly and Lemieux have stressed that anomeric effects (AE) 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.[12] 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)].

$$\mathrm{AE} = (exo\text{-}\mathrm{AE}_{eq}) - (exo\text{-}\mathrm{AE}_{ax} + endo\text{-}\mathrm{AE}_{ax}) \tag{1}$$

According to above equation, AE can have negative or positive values that depend on the relative magnitude of the various *endo*-AE and *exo*-AE. Since there are no significant differences between the *exo*-AEs in the axial and equatorial conformations of compounds **1–9**, we modify the above AE equation as follows:

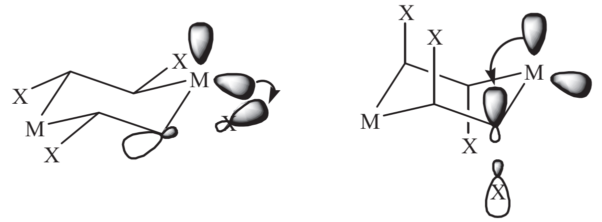
$$\mathrm{AE} = \left(\sum endo\text{-}\mathrm{AE}_{eq}\right) - \left(\sum endo\text{-}\mathrm{AE}_{ax}\right) \tag{2}$$

The precise structural parameters of various halogeno-1,4-dioxanes,[13–15] -dithianes,[16,17] and thiaoxanes[18] have shown that the C—S and C—O distances are shorter than their corresponding normal values. This fact has been explained in these systems by mixing the nonbonding electrons of M atoms (see Scheme 1) with the $\sigma^*_{\text{C-halogen}}$ antiperiplanar antibonding orbitals (e.g., LPM→ $\sigma^*_{\text{C-halogen}}$ electronic delocalizations).[14]



Scheme 1 Schematic representation of conformations of compounds **1–9**. [Numbering used for compounds **1–9** (**1**: M=O, X=F; **2**: M=O, X=Cl; **3**: M=O, X=Br; **4**: M=S, X=F; **5**: M=S, X=Cl; **6**: M=S, X=Br; **7**: M=Se, X=F; **8**: M=Se, X=Cl; and **9**: M=Se, X=Br).]

In 1959, 2,3,5,6-tetrachloro-1,4-dioxane was synthesized by Altona et al.[19] Also, the structure of 2,3,5,6-tetrachloro-1,4-dioxane was examined, and the experimental results showed that its crystalline form has all four chlorines in the axial conformation[20]; however, there are no experimental or quantitative theoretical published data about the donor–acceptor delocalization effects on the conformational properties of compounds **1–9**. In this work, the effects of the stereoelectronic interactions associated with the AE, steric



($LP_{eqM1} \rightarrow \sigma^*_{C2\text{-}Xeq}$) ($LP_{axM1} \rightarrow \sigma^*_{C2\text{-}Xax}$)

Figure 1 Schematic representation of the electronic delocalization between non-bonding and anti-bonding orbitals ($LP_{eqM1} \rightarrow \sigma^*_{C2\text{-}X}$, $LP_{eq}M \rightarrow \sigma^*_{C2\text{-}X}$) in compounds **1–9**.

repulsions, and also dipole–dipole interactions on the conformational and structural properties of compounds **1–9** were investigated computationally using a hybrid-DFT method (see Scheme 1).[21–25]

In addition, the stabilization energies (E_2) associated with $LP_{ax}M1 \rightarrow \sigma^*_{C2\text{-}X}$ and $LP_{eq}M1 \rightarrow \sigma^*_{C2\text{-}X}$ (*endo*-AEs) delocalizations (see Figures 1 and 2) and their influences on the conformational properties of compounds **1–9** were quantitatively investigated by natural bond orbital (NBO) analysis.[26,27] The LP→σ^* resonance energies are proportional

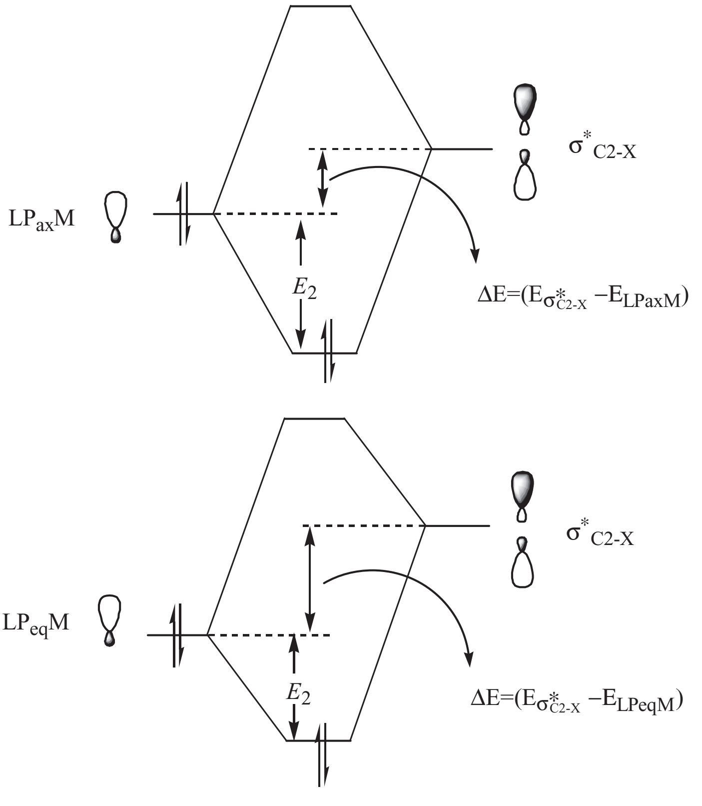


Figure 2 Schematic representation of electronic delocalizations between non-bonding and anti-bonding orbitals [$LP_{ax}M1 \rightarrow \sigma^*_{C2\text{-}Xax}$, $LP_{eq}M1 \rightarrow \sigma^*_{C2\text{-}Xeq}$ (*exo*-AEs)].

to $S^2/\Delta E$, where S is the orbital overlap and ΔE is the energy differences between the LP and σ^* orbitals:[28] stabilization or resonance energy α ($S^2/\Delta E$).

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

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

where q_i is the ith donor orbital occupancy, ε_i and ε_j are diagonal elements (orbital energies), and $F(i,j)$ are 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 successful application of density functional theory (DFT)–based methods has broadened the applicability of the computational methods and now represents an interesting approach for determining activation barrier and molecular energies.[22–25] On the other hand, the B3LYP method combines Becke's three-parameter exchange function with Lee et al.'s correlation function.[22,23] Our recent works have shown that NBO analysis is a sufficient approach to investigate the stereoelectronic interactions on the reactivity and dynamic behaviors of chemical compounds.[29–32]

Computational Details

Ab initio calculations were carried out using the hybrid-density functional theory (B3LYP/6-311+G**)–based method with the GAUSSIAN 98 package of programs.[21] Since the main purpose of the present work was to estimate the energy difference between the axial and equatorial conformations of compounds **1–9**, the energy minimization of compounds **1–9** was carried out only for the axial and equatorial position of halogen atoms on a chair conformation of the heterocyclic rings. Energy minimum molecular geometries were located by minimizing energy, with respect to all geometrical coordinates without imposing any symmetrical constraints. The nature of the stationary points for compounds **1–9** has been fixed by means of the number of imaginary frequencies. For minimum state structures, only real frequency values were accepted.[33,34] The vibrational frequencies of ground states were calculated by FREQ subroutine.

NBO analysis was then performed using the B3LYP/6-311+G** level for the axial and equatorial conformations of compounds **1–9** by the NBO 3.1 program[26,27] included in the GAUSSIAN 98 package of programs.

The bonding and antibonding orbital occupancies in the axial and equatorial conformations of compounds **1**–**9**, and also the stabilization energies associated with $LP_{eq}M1 \rightarrow \sigma^*_{C2\text{-}Xeq}$, $LP_{eq}M1 \rightarrow \sigma^*_{C2\text{-}Xax}$, $LP_{ax}M1 \rightarrow \sigma^*_{C2\text{-}Xax}$, and $LP_{ax}M1 \rightarrow \sigma^*_{C3\text{-}Xeq}$ (*endo*-AEs) delocalizations were calculated using NBO analysis. The stabilizing orbital interactions are inversely proportional to the energy difference between the interacting orbitals; therefore, the strongest stabilizing interactions will take place between the most effective donors and the most effective acceptors (see Figure 2). It must be noted that in the NBO analysis,[26,27] the electronic wavefunctions are interpreted in terms of a set of occupied Lewis and a set of unoccupied non-Lewis localized orbitals. The delocalization effects (or donor–acceptor charge transfers) can be estimated from the presence of off-diagonal elements of the Fock matrix in the NBO basis. The NBO program searches for an optimal natural Lewis structure, which has the maximum occupancy of its occupied NBOs, and in general agrees with the pattern of bonds and lone pairs of the standard structural Lewis formula. Therefore, the new orbitals are more stable than pure Lewis orbitals, stabilizing the wave function and giving a set of molecular orbitals equivalent to canonical molecular orbitals.

The thermodynamic functions (all corrected for the zero-point energy), i.e., E_0, enthalpy H (sum of the electronic and the thermal enthalpy), Gibbs free energy G (sum of the electronic and thermal free energy), and entropy S, were calculated according to the following relation: $E = E_0 + E_{\mathrm{vib}} + E_{\mathrm{rot}} + E_{\mathrm{trans}}$, $H = E + RT$, $G = H—TS$, as defined in the output of the frequency calculation in the GAUSSIAN 98 manual. Finally, using the corresponding calculated thermodynamic data for ground and transition states, ΔG, ΔH, and ΔS were also determined.

RESULTS AND DISCUSSION

Gibbs free energy, enthalpy, and entropy for the axial and equatorial conformations of compounds **1–9**, as calculated by the density functional theory B3LYP/6-311+G** level of theory, are given in Table I. B3LYP/6-311+G** results revealed that the Gibbs–free-energy-difference (G_{eq}–G_{ax}) values ($\Delta G_{\text{eq-ax}}$) between the axial and equatorial conformations of compound **1** to compound **3** are 8.19, 3.86, and 3.13 kcal mol^{-1}, respectively (see Table I); therefore, there are strong axial preferences for compounds **1–3**.

According to the NBO results, the axial conformations of compounds **1–9** benefit from some donor–acceptor interactions. Based on the optimized ground state geometries at the B3LYP/6-311+G** level of theory, the NBO analysis of donor–acceptor (bond–antibond) interactions showed that the $\mathrm{LP_{ax}M1}\rightarrow\sigma^*_{\text{C2-X}}$ (*endo*-AE) stabilization energies for the axial conformations of compounds **1–3** are 17.32, 17.65, and 19.78 kcal mol^{-1}, respectively (see Table II). Also, the $\mathrm{LP_{eq}M1}\rightarrow\sigma^*_{\text{C2-X}}$ (*endo*-AE) stabilization energies for the equatorial conformations of compounds **1–3** are 5.06, 1.19, and 1.67 kcal mol^{-1}, respectively. It should be noted that there are no $\mathrm{LP_{ax}M1}\rightarrow\sigma^*_{\text{C2-Xeq}}$ and $\mathrm{LP_{eq}M1}\rightarrow\sigma^*_{\text{C2-Xax}}$ electronic delocalizations for the axial and equatorial conformations of compounds **1–3**. Interestingly, there is $\mathrm{LP_{ax}M1}\rightarrow\sigma^*_{\text{C3-Xeq}}$ (*endo*-AE) electronic delocalization for the equatorial conformations of compounds **1–3**, and the corresponding stabilization energies are 1.19, 1.44, and 1.50 kcal mol^{-1}, respectively (see Table II). Altogether, the AE associated with $\mathrm{LPM1}\rightarrow\sigma^*_{\text{C2-X}}$ (*endo*-AEs) electronic delocalizations for compounds **1**–**3** are −11.07, −15.02, and −16.61 kcal mol^{-1}, respectively. Based on these results, the AE values increased from compound **1** to compound **3**, but calculated $\Delta G_{\text{eq-ax}}$ values decreased from compound **1** to compound **3** (see Tables I and II). It seems that the primary reason for the decrease of the stability of the axial conformation from compound **1** to compound **3** could be the increase of the nonbonding 1,3-syn-axial repulsions between the halogen atoms of 1,4-dioxane rings from compound **1** to compound **3**.

Interestingly, contrary to the observed trend for the conformational preference for compounds **1–3**, the equatorial conformations of compounds **5** and **6** are more stable than their axial forms by 0.36 and 1.53 kcal mol^{-1}, respectively; however, the axial conformation of compound **4** is more stable than its equatorial conformation by 6.77 kcal mol^{-1}, as calculated by the B3LYP/6-311+G** level of theory (see Table I). However, the $\mathrm{LP_{ax}M1}\rightarrow\sigma^*_{\text{C2-Xax}}$ (*endo*-AE) stabilization energies for the axial conformations of compounds **4–6** are 12.38, 12.11, and 14.44 kcal mol^{-1}, respectively (see Table II).

Table I B3LYP/6-311+G** calculated thermodynamic functions [enthalpies, Gibbs free energies (in Hartree), and entropies (in cal mol^{-1}K^{-1})], for the axial and equatorial conformations of compounds **1–9**

Geometries	H (Hartree)	S (cal mol^{-1} K^{-1})	G (Hartree)	ΔH^a (Hartree)	ΔS^a (calmol^{-1} K^{-1})	ΔS^a (calmol^{-1} K^{-1})	ΔG^a (Hartree)
1-Eq	−704.735757	91.022	−704.779005	0.013212 (8.29)^b	0.323	0.323	0.013058 (8.19)^b
1-Ax	−704.748969	90.699	−704.792063	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
2-Eq	−2146.139321	101.171	−2146.187391	0.005979 (3.75)^b	−0.37	−0.37	0.006154 (3.86)^b
2-Ax	−2146.145300	101.541	−2146.193545	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
3-Eq	−10601.819441	112.652	−10601.872966	0.00802 (5.03)^b	6.371	6.371	0.004993 (3.13)^b
3-Ax	−10601.827461	106.281	−10601.877959	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
4-Eq	−1350.671511	98.507	−1350.718315	0.011092 (6.96)^b	0.624	0.624	0.010795 (6.77)^b
4-Ax	−1350.682603	97.883	−1350.729110	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
5-Eq	−2792.096857	107.935	−2792.148140	0.000162 (0.10)^b	1.532	1.532	0.000000 (0.00)^b
5-Ax	−2792.097019	106.403	−2792.147574	0.000000 (0.00)^b	0.000000	0.000000	0.000566 (0.36)^b
6-Eq	−11247.783929	119.343	−11247.840632	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
6-Ax	−11247.782229	117.794	−11247.838197	0.0017 (1.07)^b	−1.549	−1.549	0.002435 (1.53)^b
7-Eq	−5357.337818	105.786	−5357.388080	0.004839 (3.04)^b	1.178	1.178	0.004279 (2.69)^b
7-Ax	−5357.342657	104.608	−5357.392359	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
8-Eq	−6798.766320	115.003	−6798.820962	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
8-Ax	−6798.760031	112.674	−6798.813566	0.006289 (3.95)^b	−2.329	−2.329	0.007396 (4.64)^b
9-Eq	−15254.454500	126.342	−15254.514529	0.000000 (0.00)^b	0.000000	0.000000	0.000000 (0.00)^b
9-Ax	−15254.445078	124.291	−15254.504133	0.009422 (5.91)^b	−2.051	−2.051	0.010396 (6.52)^b

[a] Relative to the ground state.

[b] Numbers in parenthesis are the corresponding thermodynamic functions values in kcal mol^{-1}.

Table II NBO-calculated stabilization energies (E_2), based on the calculated geometries using the B3LYP/6–311+G** level of theory, for LP $_{X1} \rightarrow P_{B2}$, in the axial and equatorial conformations of compounds **1–9**

	Stabilization energy (resonance energy) (kcal mol^{-1})																	
	1		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**	
donor→acceptor	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax
$LP_{eq\ M1} \rightarrow \sigma^*_{C2\text{-}Xeq}$	5.06	—	1.19	—	1.67	—	1.07	—	—	—	—	—	0.58	—	—	—	—	—
$LP_{eq\ M1} \rightarrow \sigma^*_{C2\text{-}Xax}$	—	—	—	—	—	—	—	—	—	0.88	—	1.09	—	—	—	0.89	—	1.19
$LP_{ax\ M1} \rightarrow \sigma^*_{C2\text{-}Xax}$	—	17.32	—	17.65	—	19.78	—	12.38	—	12.11	—	14.44	—	9.44	—	8.93	—	10.67
$LP_{ax\ M1} \rightarrow \sigma^*_{C2\text{-}Xeq}$	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
$LP_{ax\ M1} \rightarrow \sigma^*_{C3\text{-}Xeq}$	1.19	—	1.44	—	1.50	—	1.49	—	1.74	—	1.91	—	1.43	—	1.62	—	1.75	—
AE	−11.07		−15.02		−16.61		−9.28		−11.25		−13.62		−7.43		−8.2		−10.11	
μ (Debye)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

It should be noted that there are no $\text{LP}_{\text{eq}}\text{M1}\rightarrow\sigma^*_{\text{C2-Xeq}}$ electronic delocalizations for the axial and equatorial conformations of compounds **5** and **6**. Altogether, the AE associated with $\text{LPM1}\rightarrow\sigma^*_{\text{C2-X}}$ (*endo*-AEs) electronic delocalizations for compounds **4–6** are −9.28, −11.25, and −13.62 kcal mol^{-1}, respectively (see Table II). Similar to the observed trend for compounds **1–3**, the AE values increased from compound **4** to compound **6**, but $\Delta G_{\text{eq-ax}}$ values decreased from compound **4** to compound **6** (see Tables I and II). Therefore, there is a confrontation between the AE and steric repulsions. Although the AE increases from compound **1** to compound **3** and also from compound **4** to compound **6**, but the increase of the steric repulsions can reduce the stability of the axial isomers of compounds **1–6**. Accordingly, the increase of the nonbonding 1,3-syn-axial repulsions between the halogen atoms of 1,4-dioxane rings can decrease the stability of the axial conformations of compounds **5** and **6**.

Importantly, similar to compounds **1** and **4**, B3LYP/6-311+G** results revealed that the axial conformation of compound **7** is more stable than its equatorial conformation by about 2.69 kcal mol^{-1}. Contrary to the observed trend for the conformational preference in compound **7**, the equatorial conformations of compounds **8** and **9** are more stable than their axial conformations by about 4.64 and 6.52 kcal mol^{-1}, respectively, as calculated by the B3LYP/6-311+G** level of theory (see Table I). In this regard, the AE associated with $\text{LPM1}\rightarrow\sigma^*_{\text{C2-X}}$ (*endo*-AEs) electronic delocalizations for compounds **7–9** are −7.43, −8.20, and −10.11 kcal mol^{-1}, respectively (see Table II). Altogether, the AE values for compounds **7–9** are less than those for compounds **4–6** and compounds **1–3**. It seems that the steric repulsions in compounds **8** and **9** succeed in accounting qualitatively for the equatorial preferences in compounds **8** and **9**.

Alternatively, the NBO results showed that the $\text{LP}_{\text{ax}}\text{M}$ non-bonding orbital occupancies in the axial conformations of compounds **1–3** are 1.85671, 1.84142, and 1.82097, respectively (see Table III). In addition, the $\sigma^*_{\text{C2-Xax}}$ antibonding orbital occupancies in the

Table III Calculated bonding and antibonding orbital occupancies for the equatorial and axial conformations of compounds **1–9** by NBO analysis based on the optimized structures at the B3LYP/6–311+G** level of theory

Occupancy	LP_{eq} M1	LP_{ax} M1	$\sigma^*_{\text{C2-Xeq}}$	$\sigma^*_{\text{C2-Xax}}$	$\sigma^*_{\text{C3-Xeq}}$
1-Eq	1.94279	1.92190	0.04084	—	0.04083
1-Ax	1.96010	1.85671		0.06996	—
2-Eq	1.95504	1.91212	0.03835	—	0.03835
2-Ax	1.95324	1.84142	—	0.09128	—
3-Eq	1.95432	1.90753	0.04256	—	0.04255
3-Ax	1.95159	1.82097		0.11412	
4-Eq	1.97880	1.92830	0.04410	—	0.04411
4-Ax	1.98207	1.85567	—	0.06984	—
5-Eq	1.98324	1.91046	0.04692	—	0.04691
5-Ax	1.97538	1.84712	—	0.08566	—
6-Eq	1.98316	1.90173	0.05533	—	0.05533
6-Ax	1.97288	1.81873		0.11160	
7-Eq	1.98679	1.94079	0.04596	—	0.04599
7-Ax	1.98768	1.87902	—	0.06143	—
8-Eq	1.98931	1.92446	0.05083	—	0.05083
8-Ax	1.98266	1.87883	—	0.07269	—
9-Eq	1.98909	1.91510	0.06094	—	0.06094
9-Ax	1.98043	1.85555	—	0.09520	—

axial conformations of compounds **1–3** are 0.06996, 0.09128, and 0.11412, respectively, as calculated by the NBO analysis (see Table III). This fact could be justified by the increase of the $LP_{ax}M1 \rightarrow \sigma^*_{C2\text{-}Xax}$ (*endo*-AE) stabilization energy from the axial conformation of compound **1** to compounds **3**. Therefore, it can be concluded that the donor–acceptor interaction is an effective factor on the bonding, nonbonding, and antibonding orbital occupancies of the various conformations of compounds **1–9**.

It should be noted that the $LP \rightarrow \sigma^*$ 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^* antibonding orbitals. Also, stereoelectronic orbital interactions are anticipated to be more effective for *anti*, rather than *syn* or *gauche*, arrangement between the donor (LP) and acceptor (σ^*) orbitals, and the stabilization should increase as the antibonding orbital σ^* energy decreases and the non-bonding orbital LP energy increases.

Based on the NBO results, the energy difference between donor (E_{LPaxM1}) and acceptor ($E_{\sigma^*C2\text{-}Xax}$) orbitals [e.g., $\Delta(E_{\sigma^*C2\text{-}Xax}–E_{LPaxM1})$] for the axial conformations of compounds **1–9** decreased from: compound **1**→compound **3**, compound **4**→compound **6**, and also compound **7**→compound **9**. The energy difference between donor (E_{LPaxM1}) and acceptor ($E_{\sigma^*C2\text{-}Xax}$) orbitals [e.g., $\Delta(E_{\sigma^*C2\text{-}Xax}\text{-}E_{LPaxM1})$] for the axial conformations of compounds **1–3** are 0.55314, 0.42667, and 0.37281 eV, respectively, as calculated by NBO analysis (see Table IV). It may be concluded that the rich acceptor antibonding orbital of compound **3** ($E_{\sigma^*C2\text{-}Xax}$: −0.01461 eV), compared to those in compounds **2** and **1** (0.04400 and 0.18422, respectively), may give rise to strong *end*-AE (see Tables II and IV). The $\Delta(E_{\sigma^*C2\text{-}Xax}\text{-}E_{LPaxM1})$ values for compounds **4–6** are 0.45012, 0.33780, and 0.28373 eV, respectively. Finally, the energy difference between donor (E_{LPaxM1}) and acceptor ($E_{\sigma^*C2\text{-}Xax}$) orbitals [e.g., $\Delta(E_{\sigma^*C2\text{-}P}–E_{LPaxM})$] for the axial conformations of compounds **7–9** are 0.43747, 0.32879, and 0.27741 eV, respectively, as calculated by NBO analysis (see Table IV and Figures 1 and 2). Based on these results, the contribution of *endo*-AE in the axial conformations of **1–9** could be controlled by the energy differences between donor (E_{LPaxM1}) and acceptor ($E_{\sigma^*C2\text{-}Xax}$) orbitals.

Furthermore, it is well known that 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.[34] Table II presents the calculated dipole moments for the axial and equatorial conformations of compounds **1–9**. Because of the central symmetry elements, B3LYP/6-311+G** results showed that there are no dipole moments for the axial and equatorial conformations for compounds **1–9**. Based on these results, the rationalization of the conformation preference solely in terms of dipole–dipole interactions fails to account quantitatively for the conformational preferences in compounds **1–9**.

Representative structural parameters for the axial and equatorial conformations of compounds **1–9**, as calculated by the B3LYP/6-311+G** level of theory, are shown in Table V. Although, due to the nature of the various approximations involved in these theoretical calculations, it is not expected, in principal, to obtain exactly the experimental values.[36] 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.[36–40]

Importantly, considering the precise structures of the axial conformations of compounds **1–3**, **4–6**, and **7–9** gave evidence that in the axial conformations of these compounds, the $\sigma_{O1\text{-}C2}$ bond lengths are significantly contracted. B3LYP/6-311+G** results showed that the $\sigma_{O1\text{-}C2}$ bond lengths in the axial conformations of compounds **1–3** are 1.393, 1.393,

Table IV Calculated bonding and antibonding orbital energies for the equatorial and axial conformations of compounds **1–9** using NBO analysis based on the optimized structures at the B3LYP/6–311+G** level of theory

Energy	LP_{eq} M1	LP_{ax} M1	$\sigma^*_{C2\text{-}Xeq}$	$\sigma^*_{C2\text{-}Xax}$	$\sigma^*_{C3\text{-}Xeq}$	$\Delta(E_{\sigma^*C2\text{-}Xeq}\text{-}E_{LPeq\,M1})$	$\Delta(E\sigma^*_{C2\text{-}Xax}\text{-}E_{LPax\,M1})$	$\Delta(E\sigma^*_{C2\text{-}Xeq}\text{-}E_{LPax\,M1})$	$\Delta(E\sigma^*_{C3\text{-}Xeq}\text{-}E_{LPax\,M1})$
1-Eq	−0.64254	−0.37385	0.20169	—	0.20171	0.84423	—	0.57554	0.57556
1-Ax	−0.60855	−0.36892	—	0.18422	—	—	0.55314	—	—
2-Eq	−0.62523	−0.37165	0.07469		0.07471	0.69992	—	0.44634	0.44636
2-Ax	−0.58926	−0.38267	—	0.04400	—	—	0.42667	—	—
3-Eq	−0.61809	−0.37001	0.02229	—	0.02231	0.64038	—	0.3923	0.39232
3-Ax	−0.58429	−0.38742	—	−0.01461	—	—	0.37281	—	—
4-Eq	−0.68997	−0.28877	0.17296	—	0.17294	0.86293	—	0.46173	0.46171
4-Ax	−0.66811	−0.27455	—	0.17557	—	—	0.45012	—	—
5-Eq	−0.69820	−0.28620	0.86293	—	0.05609	1.56113	—	1.14913	0.34229
5-Ax	−0.67262	−0.28607	—	0.05173	—	—	0.3378	—	—
6-Eq	−0.69680	−0.28462	0.00419	—	0.00419	0.70099	—	0.28881	0.28881
6-Ax	−0.66731	−0.29305	—	−0.00932	—	—	0.28373	—	—
7-Eq	−0.75147	−0.27401	0.17162	—	0.17158	0.92309	—	0.44563	0.44559
7-Ax	−0.73763	−0.25612	—	0.18135	—	—	0.43747	—	—
8-Eq	−0.77532	−0.27497	0.05495	—	0.05495	0.83027	—	0.32992	0.32992
8-Ax	−0.75721	−0.26877	—	0.06002	—	—	0.32879	—	—
9-Eq	−0.77784	−0.27502	0.00325	—	0.00324	0.78109	—	0.27827	0.27826
9-Ax	−0.75463	−0.27710	—	0.00031	—	—	0.27741	—	—

Table V B3LYP/6–311+G**-calculated structural parameters for the equatorial and axial conformations of compounds **1–9**

	1		**2**		**3**		**4**		**5**	
Compound State	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax
Bond lengths (Å°)										
$r_{1–2}$	1.408	1.393	1.417	1.393(1.394)[a]	1.419	1.389	1.847	1.815	1.844	1.814
$r_{2–3}$	1.531	1.532	1.532	1.533	1.528	1.526	1.518	1.530	1.520	1.533
$r_{2–7}$	1.362	1.386	1.783	1.835(1.819)[a]	1.951	2.022	1.384	1.389	1.808	1.828
Bond angles (°)										
$\theta_{1–2-3}$	108.8	113.5	107.9	113.3	107.8	113.8	111.6	116.9	111.1	116.4
$\theta_{2–1-6}$	113.8	117.6	113.4	119.7	113.4	120.3	100.7	103.2	102.0	104.1
Torsion angels (°)										
$\varphi_{1–2-3–4}$	55.6	42.3	57.1	39.2	57.1	37.4	68.2	57.1	67.2	56.8
$\varphi_{2–3-4–5}$	−58.6	−44.1	−60.6	−41.9	−60.6	−39.7	−61.4	−50.3	−61.5	−50.6

	6		**7**		**8**		**9**	
Compound State	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax
Bond lengths (Å°)								
$r_{1–2}$	1.844	1.805	1.996	1.969	1.995	1.967	1.994	1.960
$r_{2–3}$	1.514	1.527	1.512	1.526	1.511	1.530	1.505	1.524
$r_{2–7}$	1.979	2.014	1.387	1.386	1.814	1.819	1.986	2.001
Bond angles (°)								
$\theta_{1–2-3}$	111.2	117.0	111.7	117.1	111.4	116.5	111.4	117.1
$\theta_{2–1-6}$	102.5	104.8	100.0	101.1	101.3	101.7	101.3	102.5
Torsion angels (°)								
$\varphi_{1–2-3–4}$	67.0	54.5	69.0	59.7	67.8	59.9	67.7	57.6
$\varphi_{2–3-4–5}$	−61.4	−48.6	−61.7	−51.5	−61.5	−52.3	−61.4	−50.3

[a] See Refs. 14 and 20.

and 1.389Å, respectively (see Table V). Interestingly, there is an excellent agreement between the calculated C2-Clax bond length (by B3LYP/6–31G* level of theory) in the axial conformation of compound **2** and the reported experimental data (see Ref.[14] and Table V).

Similarly, the $\sigma_{\text{S1-C2}}$ bond lengths in the axial conformations of compounds **4–6** are 1.815, 1.814, and 1.805Å, respectively, as calculated by the B3LYP/6-311+G** level of theory. Along this line, B3LYP/6-311+G** results showed the $\sigma_{\text{Se1-C2}}$ bond lengths in the axial conformations of compounds **7–9** are 1.969, 1.967, and 1.960 Å, respectively. This observation is consistent with the increase of the $\text{LP}_{\text{ax}}\text{M1}\rightarrow\sigma^*_{\text{C2-Xax}}$ (*endo*-AE) electronic delocalization, which produces the contracting of $\sigma_{\text{M1-C2}}$ bonds (see Tables II and V).

CONCLUSION

The above reported hybrid-DFT calculations and NBO analysis provided a reasonable picture from structural, energetic, bonding, and stereoelectronic points of view for the conformational behavior in compounds **1**–**9**. Effectively, B3LYP/6-311+G** results revealed that the axial conformations of compounds **1**, **2**, **3**, **4**, and **7** are more stable than their equatorial conformations. Contrary to the increase of the AE for compounds **1–3**, **4–6**, and **7–9**, the stability of the axial chair conformations of these compounds are decreased from compound **1** to compound **3**, compound **4** to compound **6**, and also from compound **7** to compound **9** by increasing of the steric repulsions associated with 1,3-syn-axial interactions between the halogen atoms. Interestingly, the equatorial conformations of compounds **5**, **6**, **8**, and **9** are more stable than their axial conformations. This fact demonstrates that the steric repulsions succeeded in accounting quantitatively for the equatorial preference in compounds **5**, **6**, **8**, and **9**.

In addition, NBO results revealed that the following:

- AE associated with the electronic delocalizations [$\text{LP}_{\text{ax}}\text{M1}\rightarrow\sigma^*_{\text{C2-X}}$ and $\text{LP}_{\text{eq}}\text{M1}\rightarrow\sigma^*_{\text{C2-X}}$ (*endo*-AEs)] increased from compounds: **1**→**3**, **4**→**6**, and **7**→**9**.
- The $\text{LP}_{\text{ax}}\text{M1}$ nonbonding orbital occupancies in the axial conformations decreased from compounds **1**→**3**, **4**→**6**, and **7**→**9**.
- The contribution of *endo*-AE in the axial conformations of **1–9** could be controlled by the energy differences between donor (E_{LPaxM1}) and acceptor ($\text{E}_{\sigma^*\text{C2-Xax}}$) orbitals.

Also, the $\sigma_{\text{M1-C2}}$ bond lengths in the axial conformations decreased from compound **1** to compound **3**. Similarly, this observation is repeated for compounds **4–6** and compounds **7–9**. It can be concluded that the conformational behavior of compounds compounds **5**, **6**, **8**, and **9** are not controlled only by AE associated with LP→σ^* delocalizations; therefore, it seems that the steric repulsions could influence the conformational preference in these compounds.

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