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Conformational behaviors of 1,7-dioxa-spiro[5,5]undecane and its dithia and diselena analogs in relation to the anomeric effect: A hybrid-DFT, ab initio MO study and NBO interpretation

Davood Nori-Shargh [a,*], Hooriye Yahyaei [b], Seiedeh Negar Mousavi [a], Mina Kianpour [a]

[a] *Department of Chemistry, Arak Branch, Islamic Azad University, Arak, Iran*
[b] *Department of Chemistry, Zanjan Branch, Islamic Azad University, Zanjan, Iran*

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ABSTRACT

NBO analysis, hybrid density functional theory (B3LYP/6-311+G**//B3LYP/6-311+G**) and ab initio molecular orbital (MP2/6-311+G**//B3LYP/6-311+G**) based methods were used to study the impacts of the *anomeric effects* (*AE*) associated with electron delocalization, total dipole differences and steric repulsion effects on the conformational properties of 1,7-dioxa-spiro[5,5]undecane (**1**), 1,7-dithia-spiro[5,5]undecane (**2**) and 1,7-diselena-spiro[5,5]undecane (**3**). Both methods showed the greater stability of conformations A (in which two heteroatoms having each an electron pair oriented antiperiplanar to the carbon–heteroatom bond) compared to their corresponding conformations B (with only one electron pair oriented antiperiplanar to the carbon–heteroatom bond) and C (without electron pair oriented antiperiplanar to the carbon–heteroatom bond). B3LYP/6-311+G** method showed that total Gibbs free energy difference ($G_C - G_A$ and $G_B - G_A$) values (i.e. ΔG_{C-A} and ΔG_{B-A}) between conformations A, B and C decrease from compound **1** to compound **3**. The NBO analysis of donor–acceptor (LP→σ*) showed that the *AE* is in favor of conformations A. The AE_{C-B}, AE_{B-A} and AE_{C-A} values calculated (i.e. AE_C–AE_B, AE_B–AE_A, AE_C–AE_A) decrease from compound **1** to compound **3**. The calculated total dipole moment values decrease from conformation A to conformation C. The calculated total dipole moment difference ($\mu_C - \mu_B$, $\mu_B - \mu_A$, $\mu_C - \mu_A$) values between conformations C, B and A increase from conformations C–B to C–A (i.e. $\Delta\mu_{C-B} < \Delta\mu_{B-A} < \Delta\mu_{C-A}$). However, the variations of the calculated $\Delta\mu_{C-B}$, $\Delta\mu_{B-A}$ and $\Delta\mu_{C-A}$ values are not in the same trend observed for the corresponding ΔG values. Therefore, the total dipole moment differences do not seem to be sufficient to account for conformation A preferences in compounds **1–3**. Although total steric exchange energy (*TSEE*) values in conformations A of compounds **1–3** are smaller than those of their corresponding conformations B and C, the calculated Δ(*TSEE*) values between conformations A, B and C cannot explain the variations of the total energy differences (e.g., ΔG_{C-A} and ΔG_{B-A}) from compound **1** to compound **3**. These findings led to the proposal that the *AE*, due to $LP_{ax}M_1 \rightarrow \sigma^*_{C2-M7}$ hyperconjugation effect, is a reasonable descriptor of the total energy differences between the various conformations of compounds **1–3** compared to the total dipole moment differences and steric effects.

1. Introduction

The saturated heterocyclic compounds comprise a large segment of organic and inorganic chemistry and are quite widespread in nature (e.g., in alkaloids, carbohydrates, plant growth regulators, etc.), the knowledge about the impacts of the stereoelectronic, steric and electrostatic interactions on the conformational properties of heterocyclic compounds is of very general interest.

Stereoelectronic effects have been recognized to influence the conformation and configuration of saturated heterocyclic compounds. The preferred geometry of the saturated heterocyclic compounds can be viewed as the result of the maximization of an interaction between the best donor lone pair and the best acceptor bond [1–3]. The most dominant conformation-controlling factor in carbohydrate compounds is known as the *anomeric effect* (*AE*) [4]. It should be noted that the *AE* is in favor of the axial conformation of a six-membered saturated ring in opposition to the steric effect which normally leads to a preference for the equatorial conformation [5–7].

Several explanations for the validity of the *AE* have been proposed in the literature [4–15]. The simplest justification is through the repulsion of dipole moments aligned in parallel between heteroatom sites in the equatorial configuration. An alternative explanation is a stabilizing hyperconjugation contribution between the unshared electron pair on the endocyclic oxygen atom in a

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[*] Corresponding author. Tel./fax: +98 21 44816110.
E-mail address: nori_ir@yahoo.com (D. Nori-Shargh).

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heterocyclic ring and the σ* orbital for the exocyclic C–M (M is an electronegative atom) bond in the axial position. These explanations, especially the latter in terms of the hyperconjugation effect, are still a subject of controversy in the recent literature [14].

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 [15]. Accordingly, based on the numbering used (see Scheme 1), we have calculated the *AE* for conformations A, B and C of compounds **1–3** as follow:

$$AE_{\mathrm{C-B}} = \sum(endo\text{-}AE + exo\text{-}AE)_{\mathrm{C}} - \sum(endo\text{-}AE + exo\text{-}AE)_{\mathrm{B}} \qquad (1)$$

$$AE_{\mathrm{B-A}} = \sum(endo\text{-}AE + exo\text{-}AE)_{\mathrm{B}} - \sum(endo\text{-}AE + exo\text{-}AE)_{\mathrm{A}} \qquad (2)$$

$$AE_{\mathrm{C-A}} = \sum(endo\text{-}AE + exo\text{-}AE)_{\mathrm{C}} - \sum(endo\text{-}AE + exo\text{-}AE)_{\mathrm{A}} \qquad (3)$$

In 1980, Deslongchamps and co-workers prepared 1,7-dioxa- and 1-oxa-7-thiaspiro[5,5]undecanes and related compounds by the acid cyclization of the appropriate ketone dithiol or hydroxyl ketone thiol precursors [16,17]. Also, they determined the configuration and conformation of products obtained by ^{13}C NMR analysis [18]. They explained the experimental results by taking into account the anomeric and *exo*-anomeric effects and the usual steric interactions [16–18].

Although the importance of the hyperconjugative interactions in six membered sulfur-containing heterocycles [19–25] and the corresponding spiro-systems has investigated [16–18], 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 contributions of the total dipole moments, steric effects and the *AE* associated with the electron delocalization on the conformational and structural properties of compounds **1–3** were investigated computationally using hybrid density functional theory (B3LYP/6-311+G**//B3LYP/6-311+G**), ab initio molecular orbital (MP2/6-311+G**//B3LYP/6-311+G**) based methods and natural bond orbital (NBO) interpretation (see Scheme 1) [26–31].

2. Computational details

Hybrid DFT and ab initio molecular orbital calculations were carried out, respectively, using the B3LYP/6-311+G**MP2/6-311+G**//B3LYP/6-311+G** levels of theory with the GAUSSIAN 03 package of programs [26]. The main purpose of the present work was to study the impacts of the stereoelectronic interaction effects, electrostatic interactions and total steric exchange energies (*TSEE*) on the conformational behaviors of compounds **1–3**.

In order to estimate quantitatively the magnitude of the plausible donor–acceptor hyperconjugative interactions in the various conformations (A, B and C) of compounds **1–3**, we conducted NBO analyses for these compounds. In the NBO analysis 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.

An NBO analysis was then performed for the various conformations (i.e. A, B and C) of compounds **1–3** by the NBO 5.G program contained in the PC-GAMESS interface [31]. 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 stabilization energies associated with LP → σ* electron delocalizations are proportional to $S^2/\Delta E$ where *S* is the orbital overlap and Δ*E* is the energy differences between the LP and σ* orbitals [1,32]:

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

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

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

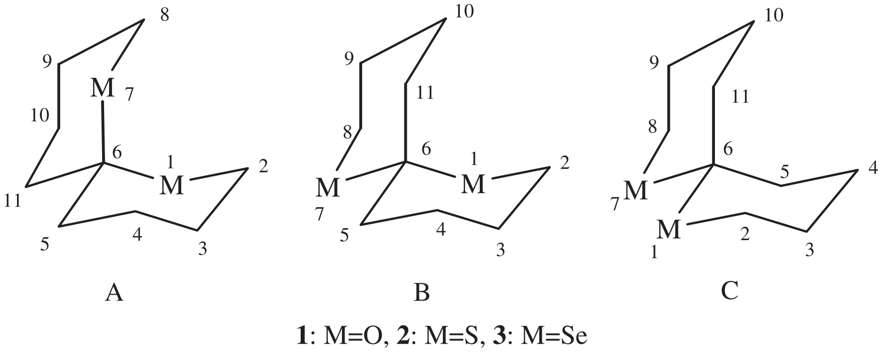
where q_i is the *i*th donor orbital occupancy, ε_i, ε_j are diagonal elements (orbital energies) and $F(i,j)$ off-diagonal elements, respectively, associated with the NBO Fock matrix. Therefore, there is a direct relationship between $F(i,j)$ off-diagonal elements and the orbital overlap (*S*).

The stabilization energies (E_2) associated with $\mathrm{LP_{ax}M_1} \to \sigma^*_{\mathrm{C6-M7}}$ (*endo-AE*) and $\mathrm{LP_{ax}M_7} \to \sigma^*_{\mathrm{C6-M1}}$ (*exo-AE*) electron delocalizations (see Figs. 1 and 2), total steric exchange energies (*TSEE*) and their influences on the conformational properties of compounds **1–3** were quantitatively investigated by the NBO analysis [31]. It has to be noted that the NBO analysis is a sufficient approach to investigate the stereoelctronic interactions on the reactivity and dynamic behaviors of chemical compounds [33].

3. Results and discussion

3.1. Conformation preference

Zero-point (*ZPE*) and total electronic (E_{el}) energies ($E_{\mathrm{o}} = E_{\mathrm{el}} + ZPE$) for conformations A, B and C of compounds **1–3**, as calculated by the density functional theory B3LYP/6-311+G**



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

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

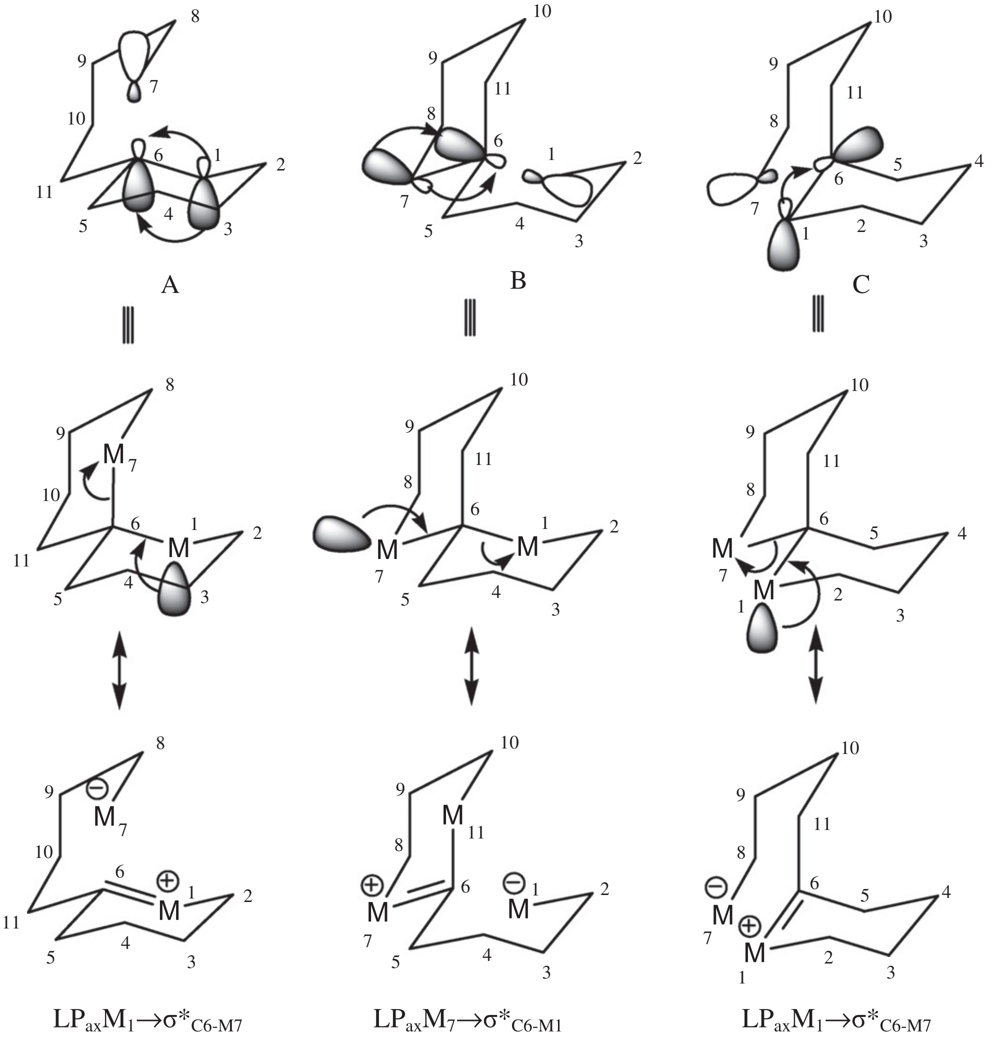


Fig. 1. Schematic representation of the electron delocalization between non-bonding and anti-bonding orbitals in conformations A, B and C of compounds **1–3**.

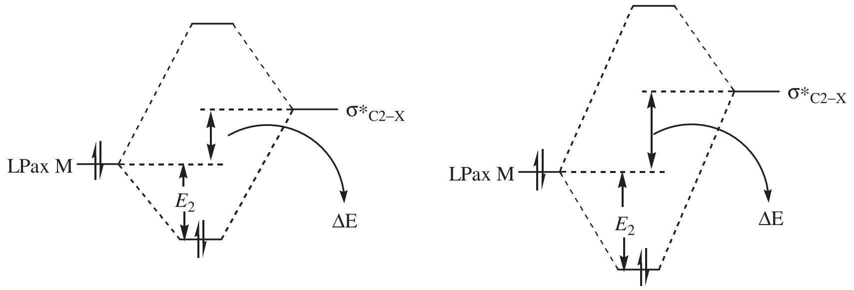


Fig. 2. Schematic representation of the correlation between the second order perturbation energies (i.e. stabilization energies E_2) and the energy gaps between donor and acceptor orbitals in conformations A and B of compounds **1–3**.

level of theory are given in Table 1. For single-point energy calculations, ab initio molecular orbital (MP2/6-311+G**//B3LYP/6-311+G**) method was used (see Table 1). Table 2 shows the value of the thermodynamic functions H, S, G and the ΔG, ΔS and ΔH parameters. The calculated ΔS values are relatively small, so that the calculated ΔH and ΔG parameters are close to the ΔE_o values. The absolute values of the thermodynamic properties certainly cannot be calculated at the accuracy level shown in this table; the correction for anharmonicity in a C–H bond may alone be on the order of 0.2 kcal mol^{-1} (the value in the C–H radical). However, the quantities of interest here are the relative values of the thermodynamic functions for different conformations of the same molecule. We expect that the errors in such differences will be very small and that even the corresponding errors between the different closely related compounds will be minimal. The smooth variation among the calculated values supports this expectation [34].

According to the B3LYP/6-311+G** (with fully geometry optimization) and MP2/6-311+G**//B3LYP/6-311+G** (single point) calculations, the conformation stability increases on going from conformations C to B and B to A. Gibbs free energy difference

Table 1
B3LYP/6-311+G**//B3LYP/6-311+G** and MP2/6-311+G**//B3LYP/6-311+G** calculated electronic energies E_{el}, zero-point energies *ZPE* (from B3LYP/6-311+G** level), E_o ($E_o = E_{el} + ZPE$) and relative energies ΔE_o (in hartree), for the various conformations (i.e. A, B and C) of compounds **1–3**.

Method	B3LYP/6-311+G**//B3LYP/6-311+G**				MP2/6-311+G**//B3LYP/6-311+G**		
Geometry	*ZPE*	E_{el}	E_o	ΔE_o[a]	E_{el}	E_o	ΔE_o[a]
1-C	0.242976	−503.173205	−502.930229	0.013005 (8.16)[b]	−501.7066942	−501.4637182	0.0137651 (8.64)[b]
1-B	0.243178	−503.180529	−502.937351	0.005883 (3.69)[b]	−501.7141732	−501.4709952	0.0064881 (4.07)[b]
1-A	0.243164	−503.186398	−502.943234	0.000000 (0.00)[b]	−501.7206473	−501.4774833	0.000000 (0.00)[b]
2-C	0.236589	−1149.129563	−1148.892974	0.006747 (4.23)[b]	−1146.9116146	−1146.6750256	0.0076404 (4.79)[b]
2-B	0.236574	−1149.132841	−1148.896267	0.003454 (2.17)[b]	−1146.9152292	−1146.6786552	0.0040108 (2.52)[b]
2-A	0.236602	−1149.136323	−1148.899721	0.000000 (0.00)[b]	−1146.919268	−1146.682666	0.000000 (0.00)[b]
3-C	0.233715	−5155.793529	−5155.559814	0.004599 (2.89)[b]	−5151.4099609	−5151.1762459	0.0050201 (3.15)[b]
3-B	0.234012	−5155.795887	−5155.561875	0.002534 (1.59)[b]	−5151.4121737	−5151.1781617	0.0031043 (1.95)[b]
3-A	0.234062	−5155.798471	−5155.564409	0.000000 (0.00)[b]	−5151.415328	−5151.181266	0.000000 (0.00)[b]

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

Table 2
B3LYP/6-311+G** calculated thermodynamic functions [enthalpies, Gibbs free energies (in hartree) and entropies (in cal mol^{-1} K^{-1})], for the various conformations (i.e. A, B and C) of compounds **1–3**.

Geometries	*H*	*S*	*G*	ΔH[a]	ΔS[a]	ΔG[a]
1-C	−502.919600	94.577	−502.964537	0.01299 (8.15)[b]	−0.069	0.013023 (8.17)[b]
1-B	−502.926765	94.361	−502.971599	0.005825 (3.65)[b]	−0.285	0.005961 (3.74)[b]
1-A	−502.932590	94.646	−502.977560	0.000000 (0.00)[b]	0.000	0.000000 (0.00)[b]
2-C	−1148.881059	101.274	−1148.929177	0.016788 (4.26)[b]	0.501	0.006551 (4.11)[b]
2-B	−1148.884374	101.040	−1148.932382	0.003473 (2.18)b	0.267	0.003346 (2.01)[b]
2-A	−1148.887847 1148.935728	100.773	−1148.935728	0.000000 (0.00)[b]	0.000	0.000000 (0.00)[b]
3-C	−5155.546905	108.838	−5155.598618	0.004769 (2.99)[b]	1.635	0.003992 (2.51)[b]
3-B	−5155.549101	107.696	−5155.600271	0.002573 (1.61)[b]	0.493	0.002339 (1.47)[b]
3-A	−5155.551674	107.203	−5155.602610	0.000000 (0.00)[b]	0.000	0.000000 (0.00)[b]

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

($G_C - G_A$ and $G_B - G_A$) values between conformations A, B and C (i.e. ΔG_{C-A} and ΔG_{B-A}) of compound **1** are 8.17 and 3.74 kcal mol^{-1}, respectively, as calculated at the B3LYP/6-311+G** level of theory. Also, ΔG_{C-A} and ΔG_{B-A} values between conformations A, B and C of compound **2** are 4.11 and 2.01 kcal mol^{-1}, respectively. The ΔG_{C-A} and ΔG_{B-A} values between conformations A, B and C of compound **3** are 2.51 and 1.47 kcal mol^{-1}, respectively. B3LYP/6-311+G** method showed that the calculated ΔG_{C-A} and ΔG_{B-A} values decrease from compound **1** to compound **3** (see Table 2).

3.2. Anomeric effect (AE) associated with electron delocalization

The various conformations of compounds **1–3** benefits from some donor–acceptor interactions. It has to be noted that conformations A of compounds **1–3** maximize the number of antiperiplanar relationship between nonbonded electron pairs ($LP_{ax}M$) and carbon–heteroatom bonds (see Fig. 1). The NBO analysis of donor–acceptor (bond–antibond) interactions showed that the stabilization energies associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C2-M7}$ electron delocalizations (*endo-AE*) for conformations A of compounds **1–3** are 12.85, 7.97 and 6.22 kcal mol^{-1}, respectively. Also, the stabilization energies associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C2-M7}$ electron delocalizations (*endo-AE*) for conformations B of compounds **1–3** are 13.01, 6.45 and 4.82 kcal mol^{-1}, respectively. There is a little stabilization energy associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C2-M7}$ electron delocalization (*endo-AE*) for conformation C of compound **1** (0.59 kcal mol^{-1}) and there is no this kind of electron delocalization for compounds **2** and **3** (see Table 3).

It should be noted that (because of the symmetry) the calculated *endo-AE* and *exo-AE* (i.e. $LP_{ax}M_7 \rightarrow \sigma^*_{C2-M1}$ electron delocalization) for conformations A of compounds **1–3** are the same. There are little *endo-AE*s for conformations C and B of compound **1**

Table 3

NBO calculated stabilization energies (E_2, in kcal mol^{-1}), generalized anomeric effect (*GAE*, in kcal mol^{-1}), off-diagonal elements (F_{ij}, in a.u.), orbital energies (in a.u.) and orbital occupancies and bond orders (Wiberg bond index, *WBI*) and total steric exchange energies (*TSEE*, in kcal mol^{-1}) based on the calculated geometries using B3LYP/6-311+G** level of theory, for the various conformations (i.e. A, B and C) of compounds **1–3**.

E_2 (kcal mol^{-1})	**1**			**2**			**3**		
	C	B	A	C	B	A	C	B	A
$LP_{ax}M_1 \rightarrow \sigma^*_{C6-M7}$	0.59	0.55	12.85	–	–	7.97	–	–	6.22
$LP_{ax}M_7 \rightarrow \sigma^*_{C6-M1}$	0.59	13.01	12.85	–	6.45	7.97	–	4.82	6.22
$\sum$	1.18	13.56	25.7	–	6.45	15.94	–	4.82	12.44
AE_{C-B}		−12.38			−6.45			−4.82	
AE_{B-A}			−12.14			−9.49			−7.62
AE_{C-A}		−24.52		−15.94			−12.44		
F_{ij}									
$LP_{ax}M_1 \rightarrow \sigma^*_{C6-M7}$	0.017	0.077	0.078	–	0.043	0.048	–	0.034	0.039
$LP_{ax}M_7 \rightarrow \sigma^*_{C6-M1}$	0.020	0.016	0.078	–	–	0.048	–	–	0.039
μ (Debye)	2.8887	1.9097	0.0180	3.4640	2.4215	0.4260	3.3366	2.3431	0.5392
$\Delta\mu_{C-B}$		0.9790			1.0425			0.9935	
$\Delta\mu_{B-A}$			1.8917			1.9955			1.8039
$\Delta\mu_{C-A}$		2.8707			3.038			2.7974	
TSEE	630.73	623.02	617.75	657.00	650.48	638.59	653.44	646.80	641.65
$\Delta(TSEE)_{C-B}$		7.71			6.52			6.64	
$\Delta(TSEE)_{B-A}$			5.27			11.89			5.15
$\Delta(TSEE)_{C-A}$	12.98				18.41			11.79	

(0.59 and 0.55 kcal mol^{-1}, respectively) and there is no this kind of electron delocalization for conformations C of compounds **2** and **3**.

Based on Eqs. (1)–(3), the calculated AE_{C-B}, AE_{B-A} and AE_{C-A} values decrease from compound **1** to compound **3** (see Table 3). Since the calculated total Gibbs free energy differences (i.e. ΔG_{C-B}, ΔG_{B-A} and ΔG_{C-A}) decrease from compound **1** to compound **3**, the rationalization of the conformational preference solely in terms of the *AE* succeeds to account for conformation A preferences in compounds **1–3**.

It should be remembered that the calculated *AE* value associated with electron delocalization (see Table 3) is not the energy difference between the various conformations rather has the effective impact on the conformational preferences of compounds **1–3**. Beside of *AE*, the steric repulsions and dipole–dipole interactions have impact on the conformational behavior of compounds **1–3**. Therefore, the resulted energy difference between the conformations attributes to the sum of the impacts resulting from *AE*, steric effects and dipole–dipole interactions (see Section 4).

3.3. Orbital energies and off-diagonal elements

The stabilization energies associated with donor–acceptor electron delocalizations are proportional directly to the orbital overlap integral $(S)^2$ and inversely to the energy differences between the donor and acceptor orbitals ($1/\Delta E$). Therefore, the stabilization should increase as the acceptor orbital energy decreases and the donor orbital energy increases.

The energy differences between donor (E_{LPaxM1}) and acceptor ($E\sigma^*_{C2-M1}$) orbitals [i.e. $\Delta(E\sigma^*_{C2-M7} - E_{LPaxM1})$] for the most stable conformations of compounds **1–3** (conformations A) are 0.58574, 0.36482 and 0.30169, respectively, as calculated by the NBO analysis. Effectively, the energy differences between donor (E_{LPaxM1}) and acceptor ($E\sigma^*_{C2-M7}$) orbitals [i.e. $\Delta(E\sigma^*_{C2-M7} - E_{LPaxM1})$] decrease from conformation A of compound **1** to compound **3** (see Tables 3 and 4). It seems the strong acceptor antibonding orbital of conformation A of compound **3** ($E\sigma^*_{C2-M7}$: 0.07834 a.u.), compared to those in compounds **2** and **1** (0.13274 and 0.29464 a.u., respectively) gives rise to strong *endo-AE*, but the decrease of the *orbital overlap integral* (*S*) [i.e. off-diagonal elements (F_{ij})] values could reduce the *AE* (see Table 3). NBO calculated F_{ij} values for the $LP_{ax}M1 \rightarrow E\sigma^*_{C2-M7}$ electron delocalizations in conformations A of compounds **1–3** are 0.078, 0.048 and 0.039, respectively. The decrease of F_{ij} values could be justified by the increase of the M atom radius from compound **1** to compound **3**. Since the second order perturbation energy (E_2) is related to the F_{ij}, $1/\Delta(E_{acceptor} - E_{donor})$, it seems that in conformations A of compounds **1–3** the F_{ij} values could affect and control the order of the stabilization energies associated with $LP_{ax}M_1 \rightarrow \sigma^*_{C2-M7}$ electron delocalizations.

3.4. Dipole moments

In the gas phase it is generally found that the conformation with the larger dipole moment has the larger electrostatic energy and the conformation with the larger dipole moment has an increased overall energy [35]. Therefore, there is a preference for the conformation with the smallest resultant dipole moment.

Liu [36] [making use of the energy decomposition within the framework of density functional theory (DFT)] [37] systematically have looked into the validity of the anomeric effect from an energetic viewpoint. They have pointed out that the energy decomposition analyses shows three energy components (exchange–correlation, classical electrostatic, and density functional steric) are directly proportional to the total energy difference between the axial and equatorial isomers. They also found that the total dipole moment changes, is a reasonable descriptor of the total energy difference, however, these correlations are not strong enough. It seems using any of the hyperconjugation and electrostatic interactions alone is not adequately convincing to explain the general validity of the *AE*. Also, they stressed another explanation in terms of exchange–correlation and electrostatic interactions.

In this work, we have examined the contribution of the electrostatic interactions (by the calculation of the total dipole moment values) [36,37] on the total energy differences between the conformations A, B and C of compounds **1–3**. Table 3 presents the calculated dipole moments for the axial and equatorial conformations of compounds **1–3**. B3LYP/6-311+G** results showed that the dipole moment values decrease from conformations C to A of compounds **1–3** (see Table 3). Using the dipole moments obtained, a "Δ" parameter could be found as $\Delta\mu_{C-B}$, $\Delta\mu_{B-A}$ and $\Delta\mu_{C-A}$. In compounds **1–3**, the corresponding $\Delta\mu_{C-A}$ values are greater than the $\Delta\mu_{B-A}$ values and also the calculated $\Delta\mu_{B-A}$ values are greater than the $\Delta\mu_{C-B}$ values (i.e. $\Delta\mu_{C-B} < \Delta\mu_{B-A} < \Delta\mu_{C-A}$). However the variations of the calculated $\Delta\mu_{C-B}$, $\Delta\mu_{B-A}$ and $\Delta\mu_{C-A}$ values from compound **1** to compound **3** are not in the same trend observed for the corresponding ΔG_{C-B}, ΔG_{B-A} and ΔG_{C-A} values (i.e. the total

Table 4
NBO calculated donor and acceptor orbital energies, based on the geometries calculated using B3LYP/6-311+G** level of theory, for the various conformations (i.e. A, B and C) of compounds **1–3**.

	$LP_{(ax)O1}$	$LP_{(ax)O7}$	σ^*_{C6-O7}	σ^*_{C6-O1}	$\Delta(E\sigma^*_{C6-O7} - LP_{(ax)O1})$	$\Delta(E\sigma^*_{C6-O1} - LP_{(ax)O7})$
1-C	−0.28843	−0.28843	0.30269	0.30269	0.59112	0.59112
1-B	−0.28966	−0.28865	0.28172	0.31841	0.57138	0.60706
1-A	−0.29110	−0.29110	0.29464	0.29464	0.58574	0.58574
2-C	−0.22680	−0.22680	0.13609	0.13610	0.36289	0.3629
2-B	−0.23042	−0.22525	0.13201	0.14233	0.36243	0.36758
2-A	−0.23208	−0.23208	0.13274	0.13274	0.36482	0.36482
3-C	−0.21734	−0.21734	0.08253	0.08253	0.29987	0.29987
3-B	−0.22096	−0.21466	0.08056	0.08523	0.30152	0.29989
3-A	−0.22335	−0.22335	0.07834	0.07834	0.30169	0.30169

Table 5
B3LYP/6-311+G** calculated bond lengths for the various conformations (i.e. A, B and C) of compounds **1–3**.

Compound	**1**			**2**			**3**		
State	C	B	A	C	B	A	C	B	A
Bond lengths (Å°)									
r_{1-2}	1.427	1.427	1.434	1.840	1.840	1.834	1.988	1.987	1.978
r_{2-3}	1.526	1.526	1.525	1.527	1.528	1.527	1.525	1.526	1.526
r_{3-4}	1.532	1.533	1.534	1.533	1.535	1.534	1.534	1.535	1.535
r_{4-5}	1.536	1.535	1.534	1.539	1.539	1.536	1.541	1.541	1.537
r_{5-6}	1.543	1.532	1.534	1.543	1.542	1.541	1.539	1.539	1.537
r_{6-7}	1.424	1.410	1.428	1.863	1.850	1.863	2.009	2.001	2.013
r_{7-8}	1.427	1.437	1.434	1.840	1.838	1.834	1.988	1.983	1.978
r_{8-9}	1.526	1.525	1.525	1.527	1.526	1.527	1.525	1.524	1.526
r_{9-10}	1.532	1.533	1.534	1.533	1.533	1.534	1.534	1.533	1.535
r_{10-11}	1.536	1.534	1.534	1.539	1.535	1.536	1.541	1.536	1.537
r_{11-6}	1.543	1.543	1.534	1.543	1.542	1.541	1.539	1.537	1.537
r_{1-6}	1.424	1.441	1.428	1.863	1.867	1.863	2.009	2.013	2.013
$\Delta[r_{1-6} - r_{6-7}]$	–	0.031	–	–	0.017	–	–	0.012	–

energy differences). The calculated $\Delta\mu$ values are sufficient to account for conformation A preferences in compounds **1–3** but fail to account for the decrease of the calculated ΔG_{C-A} values from compound **1** to compound **3**. Therefore, the electrostatic interactions are not solely responsible for the total energy differences between the conformations A, B and C of compounds **1–3** and it seems the *AE* associated with the electron delocalization is a reasonable descriptor of the total energy differences between the various conformations of compounds **1–3**.

3.5. Structural parameters

Representative structural parameters for the axial and equatorial conformations of compounds **1–3**, as calculated at the B3LYP/6-311+G** level of theory, are shown in Table 5. Although it is not expected, in principal, to obtain exactly the experimental values because of the differences in definition of bond length values, 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.

Importantly, the structures of the various conformations of compounds **1–3** give evidence that in conformations B of compounds **1–3**, the C_6–M_7 bond lengths are significantly contracted compared to that in conformations A and C (see Table 5). In addition, the $\phi_{M7-6-M1-2}$ dihedral angles of conformations A are smaller than those in conformations B and C. These facts can be explained by the large $LP_{ax}M_7 \rightarrow \sigma^*_{C6-M1}$ electron delocalizations (*exo-AE*) in conformations B by increasing π bond character of the C_6–M_7 bonds.

Using the structural parameters obtained, "Δ" parameters could be found as $\Delta[r_{6\text{-}M7} - r_{M1\text{-}6}]$. There is a direct correlation between the $LP_{ax}M_7 \rightarrow \sigma^*_{C6-M1}$ electron delocalizations (*exo-AE*) and $\Delta[r_{6\text{-}M7} - r_{M1\text{-}6}]$ parameters for conformations B of compounds **1–3** (see Tables 3 and 5). These results indicate that with the decrease of the $LP_{ax}M_7 \rightarrow \sigma^*_{C6-M1}$ electron delocalizations (*exo-AE*) from conformations C of compound **1** to compound **3**, the corresponding $\Delta[r_{6\text{-}M7} - r_{M1\text{-}6}]$ values decrease. Consequently, the calculated $\Delta[r_{6\text{-}M7} - r_{M1\text{-}6}]$ parameter could be proposed as a criterion for the evaluation of the *exo-AE* values in conformations B of compounds **1–3**.

4. 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**–**3**. Effectively, B3LYP/6-311+G** results revealed that the calculated ΔG_{C-B}, ΔG_{B-A} and ΔG_{C-A} values decrease from compound **1** to compound **3**. Similar trend is observed for the calculated AE_{C-B}, AE_{B-A} and AE_{C-A} values. Accordingly, the correlation between the *AE* and the calculated ΔG_{C-B}, ΔG_{B-A} and ΔG_{C-A} values is strong enough. Consequently, the rationalization of the conformational preference solely in terms of the *AE* succeeds to account for conformation A preference of compounds **1–3**.

Importantly, the variations of the calculated $\Delta\mu_{C-B}$, $\Delta\mu_{B-A}$ and $\Delta\mu_{C-A}$ values from compound **1** to compound **3** are not in the same trend observed for the corresponding ΔG_{C-B}, ΔG_{B-A} and ΔG_{C-A} values. Therefore, a reasonably correlation between the dipole moment differences and total energy differences was not found.

The contracted C_6–M_7 bond lengths in conformation B compared to that in conformations A and C can be explained by the large $LP_{ax}M_7 \rightarrow \sigma^*_{C6-M1}$ electron delocalizations (*exo-AE*) in conformations B by increasing π bond character of the C_6–M_7 bonds. Importantly, the calculated $\Delta[r_{6\text{-}M7} - r_{M1\text{-}6}]$ parameter could be proposed as a criterion for the evaluation of the *exo-AE* values in conformations B of compounds **1–3**.

References

[1] N.D. Epiotis, R.L. Yates, R.J. Larson, C.R. Kirmayer, F. Bernardi, Directional effects of .sigma. conjugation on geometrical isomerism, J. Am. Chem. Soc. 99 (1977) 8379–8388.

[2] E.L. Eliel, S.H. Wilen, Stereochemistry of Organic Compounds, Wiley, New York, 1994.

[3] E. Juaristi, G. Cuevas, The Anomeric Effect, CRC Press Inc., Florida, 1995.

[4] R.U. Lemieux, S. Koto, The conformational properties of glycosidic linkages, Tetrahedron 30 (1974) 1933–1944.

[5] C. Altona, Ph.D. Thesis, University of Leiden, 1964.

[6] C. Romers, C. Altona, H.R. Buys, E. Havinga, in: E.L. Eliel, N.L. Allinger (Eds.), Topics in Stereochemistry, Vol. 4, Wiley-Interscience, New York, NY, 1968, p. 39.

[7] S. David, O. Eisentein, W.J. Here, L. Salem, R. Hoffman, Superjacent orbital control. An interpretation of the anomeric effect, J. Am. Chem. Soc. 95 (1973) 3806–3807.

[8] A.J. Kirby, Anomeric Effect and Related Stereoelectronic Effects, Oxygen Springer-Verlag, Berlin, 1983.

[9] P. Deslongchamps, Stereoelectronic Effects in Organic Chemistry, Elsevier, New York, 1983.

[10] C.J. Cramer, Anomeric and reverse anomeric effects in the gas phase and aqueous solution, J. Org. Chem. 57 (1992) 7034–7043.

[11] C.L. Perrin, K.B. Armstrong, M.A. Fabian, The origin of the anomeric effect: conformational analysis of 2-methoxy-1,3-dimethylhexahydropyrimidine, J. Am. Chem. Soc. 116 (1994) 715–722.

[12] E. Juaristi, G. Cuevas, Recent studies on the anomeric effect, Tetrahedron 48 (1992) 5019–5087.

[13] A. Vila, R.A. Mosquera, Atoms in molecules interpretation of the anomeric effect in the O–C–O unit, J. Comput. Chem. 28 (2007) 1516–1530.

[14] Y. Mo, Computational evidence that hyperconjugative interactions are not responsible for the anomeric effect, Nat. Chem. 2 (2010) 666–671.

[15] J.-P. Praly, R.U. Lemieux, Influence of solvent on the magnitude of the anomeric effect, Can. J. Chem. 65 (1987) 213–223.

[16] P. Deslongchamps, D.D. Rowan, N. Pothier, G. Sauvé, J.K. Saunders, 1,7-Dioxaspiro[5.5]undecanes. An excellent system for the study of stereoelectronic effects (anomeric and exo-anomeric effects) in acetals, Can. J. Chem. 59 (1981) 1105–1121.

[17] P. Deslongchamps, D.D. Rowan, N. Pothier, J.K. Saunders, 1,7-Dithia and 1-oxa-7-thiaspiro[5.5]undecanes. Excellent systems for the study of stereoelectronic effects (anomeric and exo-anomeric effects) in the monothio and the dithioacetal functions, Can. J. Chem. 59 (1981) 1122–1131.

[18] N. Pothier, D.D. Rowan, P. Deslongchamps, J.K. Saunders, ^{13}C chemical shift data for 1,7-dioxaspiro[5.5]undecanes and related compounds, Can. J. Chem. 59 (1981) 1132–1139.

[19] H.T. Kalff, Thesis, University of Leiden, 1964.

[20] H.T. Kalff, C. Romers, The conformation of non-aromatic ring compounds. XIV. The crystal structure of trans-2,3-dichloro-1,4-dithiane at -180 °C, Acta Cryst. 18 (1965) 164–168.

[21] E. Juaristi, G. Cuevas, A. Vela, Stereoelectronic interpretation for the anomalous ^{1}H NMR chemical shifts and one-bond C–H coupling constants (Perlin effects) in 1,3-dioxanes, 1,3-oxathianes, and 1,3-dithianes. Spectroscopic and theoretical observations, J. Am. Chem. Soc. 116 (1994) 5796–5804.

[22] I.V. Alabugin, Stereoelectronic interactions in cyclohexane, 1,3-dioxane, 1,3-oxathiane, and 1,3-dithiane: – W-effect, $\sigma_{C-X} \rightarrow \sigma_{C-H}$ interactions, anomeric effect – what is really important?, J Org. Chem. 65 (2000) 3910–3919.

[23] G. Cuevas, E. Juaristi, Manifestation of stereoelectronic effects on the calculated Carbon−Hydrogen bond lengths and one bond 1JC-H NMR coupling constants in cyclohexane, six-membered heterocycles, and cyclohexanone derivatives, J. Am. Chem. Soc. 124 (2002) 13088–13096.

[24] M.V. Roux, M. Temprado, P. Jiménez, J.Z. Dávalos, R. Notario, G. Martín-Valcárcel, L. Garrido, R. Guzmán-Mejía, E. Juaristi, Thermochemistry of 1,3-dithiacyclohexane 1-oxide (1,3-dithiane sulfoxide): calorimetric and computational study, J. Org. Chem. 69 (2004) 5454–5459.

[25] E. Kleinpeter, in: E. Juaristi (Ed.), Conformational Behavior of Six-membered Rings, VCH Publishers, Inc., New York, 1995, pp. 201–243.

[26] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, Revision B.03, Gaussian, Inc., Wallingford CT, 2004.

[27] A.D. Becke, Density-functional thermochemistry. III. The role of exact exchange, J. Chem. Phys. 98 (1993) 5648–5653.

[28] C. Lee, W. Yang, R.G. Parr, Development of the Colle–Salvetti correlation-energy formula into a functional of the electron density, Phys. Rev. B 37 (1988) 785–789.

[29] W.J. Hehre, L. Radom, P.V.R. Schleyer, J.A. Pople, Ab initio Molecular Orbital Theory, Wiley, New York, 1986.

[30] J.M. Seminario, P. Politzer (Eds.), Modern Density Functional Theory, A Tool for Chemistry, Elsevier, Amsterdam, 1995.

[31] E.D. Glendening, J.K. Badenhoop, A.E. Reed, J.E. Carpenter, J.A. Bohmann, C.M. Morales, F. Weinhold, Theoretical Chemistry Institute, University of Wisconsin, Madison, WI, 2004 (NBO Version 5.G).

[32] P. Dionne, M. St-Jacques, Mechanism of the gauche conformational effect in 3-halogenated 1,5-benzodioxepins, J. Am. Chem. Soc. 109 (1987) 2616–2623.

[33] F. Weinhold, Rebuttal to the Bickelhaupt–Baerends case for steric repulsion causing the staggered conformation of ethane, Angew. Chem. Int. Ed. 42 (2003) 4188–4194.

[34] D. Nori-Shargh, J.E. Boggs, Complete basis set, hybrid-DFT study and NBO interpretations of the conformational behavior of 1,2-dihaloethanes, Struct. Chem. 22 (2011) 253–262.

[35] K.B. Wiberg, M.A. Murcko, Rotational barriers. 1. 1,2-Dihaloethanes, J. Phys. Chem. 91 (1987) 3616–3620.

[36] Y. Huang, A.-G. Zhong, Q. Yang, S. Liu, Origin of anomeric effect: a density functional steric analysis, J. Chem. Phys. 134 (2011) 084103(1–9).

[37] S.B. Liu, Steric effect: a quantitative description from density functional theory, J. Chem. Phys. 126 (2007) 244103(1–5).