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Ab initio Study and NBO Analysis of Conformational Properties of 2-Substituted Cyclohexane-1,3-diones and its Analogues Containing S and Se Atoms

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ABSTRACT

NBO analysis, hybrid density functional theory (B3LYP/6-311+G**) and ab initio molecular orbital (HF/6-311+G**) based methods were used to study the anomeric effects (*AE*), electrostatic interactions, dipole-dipole interactions and steric repulsion effects on the conformational properties of 2-methoxy- (1), 2-methylthio- (2), 2-methylseleno- (3), 2-fluoro- (4), 2-chloro- (5) and 2-bromocyclohexane-1,3-dione (6). The B3LYP/6-311+G** and HF/6-311+G** results indicates the axial preference in these compounds. The methods used show that these compounds exist predominantly in the axial chair conformation and the axial conformation stability and calculated Gibbs free energy difference (ΔG_{eq-ax}) values between the axial and equatorial conformations increase from 1 to its analogous 3 and also from 4 to its analogues 6. The NBO analysis of donor-acceptor interactions show that the *GAE* (Generalized Anomeric Effect) increases from compound 1 to compound 3 and also from compound 4 to compound 6. *GE* (Gauche Effect) does not have significant impact on the conformational behaviors of compounds that have been studied and *GAE* succeeds in accounting qualitatively for the increase of the axial preferences. On the other hand, the calculated differences between the dipole moment values of the axial and equatorial conformations, $\Delta(\mu_{eq}-\mu_{ax})$, are not in the same trend observed for the corresponding *GAE* and ΔG values. These findings led to the proposal that the calculated *GAE* values due to donor→acceptor hyperconjugation effects are more significant for the explanation of the conformational preferences of compounds that have been studied than the electrostatic interactions. Also similar results are obtained for their analogous containing S and Se atoms. The correlations between the *GAE*, *GE*, dipole-dipole interactions, donor and acceptor orbital energies and occupancies, bond orders, structural parameters and conformational behavior of compounds (1-6) and their analogous containing S and Se atoms have been investigated.

Keyword: Stereoelectronic interactions; Generalized Anomeric Effects; Ab initio; NBO; 2-Substituted cyclohexane-1,3-diones.

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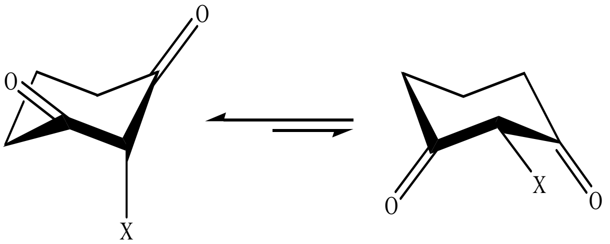
1. INTRODUCTION

The saturated heterocyclic compounds are quite widespread in nature such as carbohydrates, alkaloids and plant growth regulators, among other compounds; the knowledge about conformational properties of heterocyclic compounds is of very general interest. In 1955, Edward [1] proposed that alkoxy groups at C1 in pyranose rings are generally more stable in the axial rather than in the equatorial configuration. This proposal invokes an unfavorable disposition of the unshared electrons of the ring oxygen and the C1-O polar bond. It is appropriate to point out that this explanation may be the first reference to the importance of lone electrone-pair orientation on conformational stability [2-9]. The most dominant conformation-controlling factor in carbohydrate and heterocyclic compounds is known as the anomeric effect *(AE)* [10-12]. It should be noted that the AE is in favour 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. The rationalization of the anomeric effect *(AE)* solely in terms of electrostatic interactions fails to account quantitatively for observed axial preferences [13]. 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 [14, 15]. The stereoelectronic interactions are expected to play an important role in the conformational properties of heterocyclic compounds [16, 17]. There is a stereoelectronic preference for conformations in which the best donor lone pair is antiperiplanar to the best acceptor bond. 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 [18, 19]. Although the importance of the LP$\rightarrow\sigma^*$ electron delocalization in six membered substituted heterocycles has been investigated there is insufficient published experimental information about the stereoelctronic interactions in compound 2-X-cyclohexane-1,3-dione and also there is no published experimental or quantitative theoretical data about the donor-acceptor delocalization effects on the conformational properties of compounds 1-6 [20-29].

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 1-6 were investigated computationally using hybrid-DFT based methods and natural bond orbital (NBO) analysis (see Scheme 1 and Figure 1).



[Numbering used for compounds **1-6** (**1**: X= CH_3O, **2**: X= CH_3S, **3**: X= CH_3Se, **4**: X= F, **5**: X= Cl, **6**: X= Br)

Scheme 1: *Schematic representation of conformations of compounds 1-6.*

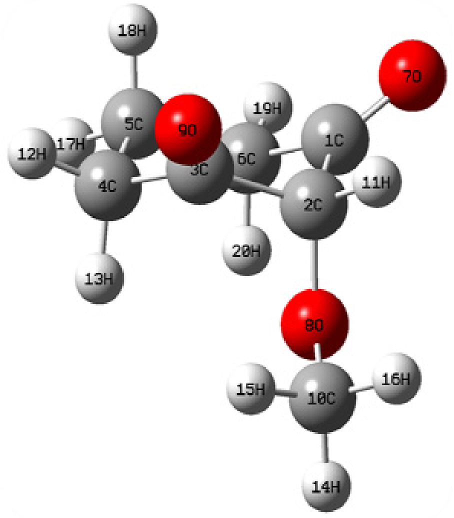


Figure 1: *The optimized equilibrium axial structure of 2-methoxycyclohexane-1,3-dione (1), and the numbering of atoms. Also, the other axial and equatorial conformations (1-6) have the same numbering.*

2. COMPUTATIONAL DETAILS

Ab initio molecular orbital calculations and Hybrid DFT were carried out using the HF/6-311+G** and B3LYP/6-311+G** levels of theory with the GAUSSIAN 03 package of programs. The energy minimization was carried out only for the axial and equatorial positions of the CH_3O- (1), CH_3S- (2), CH_3Se- (3), F- (4), Cl- (5) and Br- (6) groups on the chair conformations of cyclohexane-1,3-dione rings (Scheme 1).

The main purpose of the present work was to investigate the impacts of the *AE*, electrostatic interactions and steric repulsions on the conformational behaviors of 1-6, Energy minimum molecular geometries were located by minimizing energy with respect to all geometrical coordinates without imposing any symmetry constraints. The nature of the stationary points for compounds 1-6 has been determined by means of the number of imaginary frequencies. For minimum state structures, only real frequency values were accepted [30-32].

An NBO analysis was then performed using the B3LYP/6-311+G** level for the axial and equatorial conformations by the NBO 5.G program via the PC-GAMESS interface [33, 34]. The bonding and antibonding orbital occupancies in the axial and equatorial conformations of compounds 1-6, and also the generalized anomeric effect (*GAE*) associated with $LP_2X_8 \rightarrow \pi^*_{C1-O7}$, $LP_3X_8 \rightarrow \pi^*_{C1-O7}$, $\sigma_{C2-X8} \rightarrow \sigma^*_{C1-O7}$, $\sigma_{C2-X8} \rightarrow \pi^*_{C1-O7}$, $\pi_{C1-O7} \rightarrow \sigma^*_{C2-X8}$, $LP_2X_8 \rightarrow \pi^*_{C3-O9}$, $LP_3X_8 \rightarrow \pi^*_{C3-O9}$, $\sigma_{C2-X8} \rightarrow \sigma^*_{C3-O9}$, $\sigma_{C2-X8} \rightarrow \pi^*_{C3-O9}$, $\pi_{C3-O9} \rightarrow \sigma^*$C2-X8 electron delocalizations and also the gauche effect (*GE*) associated with $LP_2X_8 \rightarrow \sigma^*_{C1-C2}$, $LP_3X_8 \rightarrow \sigma^*_{C1-C2}$, $LP_1O_7 \rightarrow \sigma^*_{C1-C2}$, $LP_2O_7 \rightarrow \sigma^*_{C1-C2}$, $LP_2X_8 \rightarrow \sigma^*_{C2-C3}$, $LP_3X_8 \rightarrow \sigma^*_{C2-C3}$, $LP_1O_9 \rightarrow \sigma^*_{C2-C3}$, $LP_1O_9 \rightarrow \sigma^*_{C2-C3}$ electron delocalizations were calculated using NBO analysis.

The total generalized anomeric effect (*GAE*), associated with the shown electron delocalizations and also the gauche effect (*GE*) can calculate for compounds 1-6 as follows (Equation 1, 2):

$$GAE = \Sigma\,(GAE_{eq}) - \Sigma\,(GAE_{ax}) \qquad \text{(Eq. 1)}$$

$$GE = \Sigma\,(GE_{eq}) - \Sigma\,(GE_{ax}) \qquad \text{(Eq. 2)}$$

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

$$E_2 = q_i \frac{F^2(i,j)}{E_j - E_i} \qquad \text{(Eq. 3)}$$

Where q_i is the i^{th} donor orbital occupancy, E_i, E_j are off-diagonal elements (orbital energies) and $F_{(i,j)}$ off-diagonal elements, respectively associated with the NBO Fock matrix (Figure 2). There is a direct relationship between F_{ij} off-diagonal elements and orbital overlap (S). In the NBO method, the donor-acceptor electron interactions can be studied separately because this method allows separation of the energy contribution due to donor-acceptor electron interactions from those caused by steric and electrostatic interactions, therefore the NBO approach permits consideration of charge delocalization [35-40].

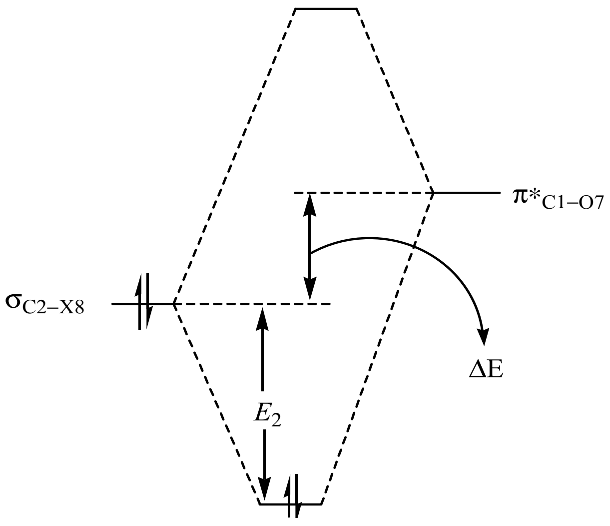


Figure 2: *Schematic representation of the correlation between the second order perturbation energies (i.e. stabilization energies E_2) and the energy gaps between donor and acceptor orbitals in the axial conformations of compounds 1-6.*

3. RESULTS AND DISCUSSION

Conformational preferences

The thermodynamic for the most stable axial and equatorial conformations of compounds 1-6 are calculated at the B3LYP/6-311+G** and HF/6-311+ G** levels of theory (Table 1). The results of all methods used showed that the differences between the Gibbs free energy difference *(ΔG_{eq-ax})* values between the axial and equatorial conformations (axial preferences) increase from compound 1 to compound 3. There is a good agreement between the calculated *(ΔG_{eq-ax})* values by using B3LYP/6-311+G** and HF/6-311+G** levels of theory (see Table 1). The results showed that the axial chair conformation of compounds 1-6 is more stable than their equatorial conformations. The B3LYP/6-311+G** results gave the Gibbs free energy difference between the axial and equatorial conformations (i.e. ΔG_{eq-ax}) of compounds 1-3 as 1.15, 3.56 and 3.92 kcal mol^{-1} while HF/6-311+G** results gave 0.33, 3.25 and 3.99 kcal mol^{-1} (see Table 1). Based on these results, there is strong axial preference for compounds 2-methylthio- (2), 2-methylseleno- (3) cyclohexane-1,3-dione. The trend is also observed for compounds 4-6.

Stabilization energies, generalized anomeric effect (GAE) and gauche effect (GE)

The NBO analysis of bonding-antibonding interactions showed that the stabilization energies associated with $\sigma_{C2-X8}\rightarrow\pi^*_{C1-O7}$ electron delocalizations for the axial conformations increases from compound 1 to compound 3 as 1.65, 6.48 and 8.67 kcal mol^{-1}, And the stabilization energy associated with $\pi_{C1-O7}\rightarrow\sigma^*_{C2-X8}$ electron delocalization increases slightly from the axial conformation of compound 1 to compound 3. Also there are no above electron delocalizations for the

Table 1: *B3LYP/6-311+G** and HF/6-311+G** calculated thermodynamic parameters [ΔH, ΔG (in kcal mol^{-1}) and ΔS (in cal mol^{-1}K^{-1})] at 25°C and 1 atm pressure for the axial and equatorial conformations of compounds 1-6.*

	B3LYP/6-311+G**//B3LYP/6-311+G**			HF/6-311+G**//HF/6-311+G**		
	ΔH^a	ΔS^a	ΔG^a	ΔH^a	ΔS^a	ΔG^a
Geometry						
1-Eq	-0.04	-1.25	0.33	0.84	-1.07	1.15
1-Ax	0.00	0.000	0.00	0.00	0.000	0.00
2-Eq	2.80	-1.523	3.25	3.16	-1.373	3.56
2-Ax	0.00	0.000	0.00	0.00	0.000	0.00
3-Eq	3.50	-1.63	3.99	3.55	-1.252	3.92
3-Ax	0.00	0.000	0.00	0.00	0.00	0.00
4-Eq	0.00	0.000	0.00	0.00	0.000	0.00
4-Ax	0.86	0.52	0.70	0.54	0.349	0.44
5-Eq	1.15	-0.426	1.28	1.97	-0.201	2.03
5-Ax	0.00	0.000	0.00	0.00	0.000	0.00
6-Eq	2.40	-0.47	2.54	3.13	-0.049	3.15
6-Ax	0.00	0.000	0.00	0.00	0.000	0.00

^{a} Relative to the ground state

equatorial conformations of compounds 1-3 (Table 2). The calculated *GAE* associated with $LP_2X_8 \rightarrow \pi^*_{C1-O7}$, $LP_3X_8 \rightarrow \pi^*_{C1-O7}$, $\sigma_{C2-X8} \rightarrow \sigma^*_{C1-O7}$, $\sigma_{C2-X8} \rightarrow \pi^*_{C1-O7}$, $\pi_{C1-O7} \rightarrow \sigma^*_{C2-X8}$, $LP_2X_8 \rightarrow \pi^*_{C3-O9}$, $LP_3X_8 \rightarrow \pi^*_{C3-O9}$, $\sigma_{C2-X8} \rightarrow \sigma^*_{C3-O9}$, $\sigma_{C2-X8} \rightarrow \pi^*_{C3-O9}$, $\pi_{C3-O9} \rightarrow \sigma^*_{C2-X8}$ electron delocalizations for compounds 1-3 are -11.54, -20.79 and -23.12 kcal mol^{-1}, respectively for compounds 4-6 are -11.70, -18.15 and -20.61 kcal mol^{-1} (see Table 2). Based on the results obtained, the *GAE* increase from compound 1 to 3 and also from compound 4 to 6. This results show that the generalized anomeric effect (*GAE*) and the calculated (ΔG_{eq-ax}) are in a good accordance to explain the increase of the axial preferences of compounds 1-6. The calculated *GE* values associated with $LP_1X_8 \rightarrow \sigma^*_{C1-C2}$, $LP_2X_8 \rightarrow \sigma^*_{C1-C2}$, $LP_3X_8 \rightarrow \sigma^*_{C1-C2}$, $LP_1O_7 \rightarrow \sigma^*_{C1-C2}$, $LP_2O_7 \rightarrow \sigma^*_{C1-C2}$, $LP_1X_8 \rightarrow \sigma^*_{C2-C3}$, $LP_2X_8 \rightarrow \sigma^*_{C2-C3}$, $LP_3X_8 \rightarrow \sigma^*_{C2-C3}$, $LP_1O_9 \rightarrow \sigma^*_{C2-C3}$, $LP_2O_9 \rightarrow \sigma^*_{C2-C3}$ and $LP_3O_9 \rightarrow \sigma^*_{C2-C3}$ electron delocalizations for compounds 1-3 are 8.12, 7.33 and 6.12 kcal mol^{-1} and for compounds 4-6 are 8.16, 9.91 and 9.14 kcal mol^{-1} respectively. Based on the results obtained, *GE* cannot explain the larger equatorial preference of compound 4 and it seems that

Table 2: *NBO calculated resonance (stabilization) energies (E_2), generalized anomeric effect (GAE), off-diagonal elements (F_{ij}), orbital energy differences (ΔE), orbital occupancies and bond orders (Wiberg bond indexes, WBI) for the equatorial and axial conformations of compounds 1-6.*

Compound	1		2		3		4		5		6	
Geometry	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax
E_2												
$LP_2X_8 \rightarrow \pi^*_{C1-O7}$	-	-	-	3.25	-	2.97	-	-	-	-	-	-
$LP_3X_8 \rightarrow \pi^*_{C1-O7}$	-	-	-	-	-	-	-	0.98	-	1.49	-	1.49
$\sigma_{C2-X8} \rightarrow \sigma^*_{C1-O7}$	-	0.90	-	-	0.73	-	-	0.85	-	0.60	-	-
$\sigma_{C2-X8} \rightarrow \pi^*_{C1-O7}$	-	1.65	-	6.48	-	8.67	-	1.28	-	3.75	-	5.28
$\pi_{C1-O7} \rightarrow \sigma^*_{C2-X8}$	-	2.44	-	2.45	-	2.52	-	2.74	-	3.25	-	3.53
$LP_2X_8 \rightarrow \pi^*_{C3-O9}$	-	1.67	-	-	-	-	-	-	-	-	-	-
$LP_3X_8 \rightarrow \pi^*_{C3-O9}$	-	-	-	-	-	-	-	0.98	-	1.50	-	1.49
$\sigma_{C2-X8} \rightarrow \sigma^* C_{3-O9}$	-	0.78	-	0.59	0.52	-	-	0.85	-	0.59	-	-
$\sigma_{C2-X8} \rightarrow \pi^*_{C3-O9}$	-	1.49	-	5.60	-	7.60	-	1.28	-	3. 75	-	5.29
$\pi_{C3-O9} \rightarrow \sigma^*_{C2-X8}$	-	2.59	-	2.46	-	2.61	-	2.74	-	3.25	-	3.53
Σ	0	11.54	0	20.79	1.25	24.37	0	11.70	0	18.15	0	20.61
GAE **(kcal mol^{-1})**	**-11.54**		**-20.79**		**-23.12**		**-11.70**		**-18.15**		**-20.61**	
$LP_1X_8 \rightarrow \sigma^*_{C1-C2}$	1.83	1.44	-	-	-	-	-	-	-	-	-	-
$LP_2X_8 \rightarrow \sigma^*_{C1-C2}$	0.82	-	-	3.80	-	2.65	1.87	3.89	1.38	1.04	1.09	0.76
$LP_3X_8 \rightarrow \sigma^*_{C1-C2}$	-	-	-	-	-	-	5.75	1.54	4.17	2.43	3.21	1.77
$LP_1O_7 \rightarrow \sigma^*_{C1-C2}$	1.47	1.60	1.74	1.69	1.94	1.78	1.24	1.33	1.52	1.53	1.69	1.64
$LP_2O_7 \rightarrow \sigma^*_{C1-C2}$	25.11	22.49	23.55	21.33	22.27	20.70	25.62	23.64	25.89	23.01	25.36	22.55
$LP_1X_8 \rightarrow \sigma^*_{C2-C3}$	0.65	-	0.80	-	0.63	-	-	-	-	-	-	-
$LP_2X_8 \rightarrow \sigma^*_{C2-C3}$	9.79	7.33	5.85	-	4.28	-	1.87	3.89	1.38	1.03	1.09	0.76
$LP_3X_8 \rightarrow \sigma^*_{C2-C3}$	-	-	-	-	-	-	5.75	1.54	4.18	2.44	3.21	1.77
$LP_1O_9 \rightarrow \sigma^*_{C2-C3}$	1.5 1	1.60	1.68	1.69	1.77	1.77	1.24	1.33	1.52	1.53	1.69	1.64
$LP_2O_9 \rightarrow \sigma^*_{C2-C3}$	24.01	22.61	24.18	21.90	23.45	21.32	25.62	23.64	25.89	23.01	25.30	22.55
Σ	65.19	57.07	57.8	50.47	54.34	48.22	68.96	60.8	65.93	56.01	62.58	53.44
GE **(kcal mol^{-1})**	**8.12**		**7.33**		**6.12**		**8.16**		**9.91**		**9.14**	
GAE + GE	**-3.42**		**-13.46**		**-17.0**		**- 3.54**		**-8.24**		**-11.47**	

GAE is dominant factor on conformational preference of compounds 1-6. The summations of the *GAE* and *GE* also increases from compound 1 to compound 3 and from compound 4 to compound 6 which reasonably explain the most impact of *GAE* on the increase of the axial preference of compounds 1-6 (see Table 2).

Orbital occupancies, Orbital energies and off-diagonal elements

The NBO results showed that the greatest variations of the stabilization energies of the axial conformations of compounds 1-6 observed for their corresponding $\sigma_{C2\text{-}X8} \rightarrow \pi^*_{C1\text{-}O7}$ electron delocalizations. The $\sigma_{C2\text{-}X8}$ bonding orbital occupancies in the axial conformations of compounds 1-3 are 1.980, 1.933 and 1.910 respectively. Also, the $\pi^*_{C1\text{-}O7}$ antibonding orbital occupancies in the axial conformations of compounds 1-3 are 0.073, 0.111 and 0.121 respectively.

Similar to the trend observed for compounds 1-3, the $\sigma_{C2\text{-}X8}$ bonding orbital occupancies in the axial conformations decreased from compound 4 to

***Table 2** continued*

Off-diagonal elements F_{ij} (a.u.)												
$LP_2X_8 \rightarrow \pi^*_{C1\text{-}O7}$	-	-	-	0.026	-	0.025	-	-	-	-	-	-
$LP_3X_8 \rightarrow \pi^*_{C1\text{-}O7}$	-	-	-	-	-	-	-	0.018	-	0.020	-	0.020
$\sigma_{C2\text{-}X8} \rightarrow \sigma^*_{C1\text{-}O7}$	-	0.032	-	-	0.026	-	-	0.032	-	0.025	-	-
$\sigma_{C2\text{-}X8} \rightarrow \pi^*_{C1\text{-}O7}$	-	0.034	-	0.056	-	0.061	-	0.031	-	0.045	-	0.051
$\pi_{C1\text{-}O7} \rightarrow \sigma^*_{C2\text{-}X8}$	-	0.036	-	0.032	-	0.030	-	0.036	-	0.036	-	0.035
***ΔE* (a.u.)**												
$\Delta(E\pi^*_{C1\text{-}O7}\text{-}E\sigma_{C2\text{-}X8})$	0.875	0.836	0.609	0.585	0.553	0.530	0.990	0.938	0.692	0.663	0.621	0.596
$\Delta(E\sigma^*_{C2\text{-}X8}\text{-}E\pi_{C1\text{-}O7})$	0.720	0.670	0.561	0.516	0.497	0.456	0.645	0.601	0.533	0.488	0.468	0.435
$\Delta(E\pi^*_{C3\text{-}O9}\text{-}E\sigma_{C2\text{-}X8})$	0.870	0.831	0.608	0.588	0.553	0.532	0.990	0.938	0.692	0.663	0.621	0.596
$\Delta(E\sigma^*_{C2\text{-}X8}\text{-}E\pi_{C3\text{-}O9})$	0.725	0.673	0.563	0.518	0.497	0.457	0.645	0.601	0.533	0.488	0.468	0.435
Orbital occupancies												
$\sigma_{C2\text{-}X8}$	1.991	1.980	1.978	1.933	1.975	1.910	1.995	1.987	1.988	1.964	1.984	1.947
$\pi_{C1\text{-}O7}$	1.984	1.980	1.984	1.981	1.984	1.980	1.984	1.979	1.984	1.977	1.984	1.976
$\pi^*_{C1\text{-}O7}$	0.088	0.073	0.090	0.111	0.092	0.121	0.090	0.077	0.087	0.084	0.086	0.091
$\sigma^*_{C2\text{-}X8}$	0.017	0.024	0.026	0.028	0.031	0.031	0.017	0.026	0.024	0.029	0.030	0.033
$\pi_{C3\text{-}O9}$	1.984	1.980	1.984	1.981	1.984	1.980	1.984	1.979	1.984	1.977	1.984	1.976
$\pi^*_{C3\text{-}O9}$	0.092	0.080	0.090	0.090	0.090	0.100	0.090	0.077	0.087	0.084	0.086	0.091
Dipole moments												
μ(Debye)	4.936	3.754	5.109	2.978	4.877	2.969	6.043	3.768	5.763	3.859	5.607	3.821
$\Delta(\mu_{eq}\text{-}\mu_{ax})$	1.182		2.132		1.907		2.275		1.904		1.780	
bond order (WBI)												
C1-O7	1.841	1.845	1.845	1.836	1.843	1.825	1.862	1.856	1.865	1.896	1.864	1.837
C1-C2	0.936	0.939	0.943	0.972	0.955	0.989	0.939	0.941	0.440	0.955	0.949	0.969
C2-X8	0.959	0.906	1.001	0.941	0.957	0.892	0.880	0.821	1.034	0.970	1.013	0.950
ΔWBI ($C1\text{-}O7_{eq}$ - $C1\text{-}O7_{ax}$)	-0.004		0.009		0.018		0.005		0.019		0.027	
ΔWBI ($C1\text{-}C2_{ax}$ -$C1\text{-}C2_{eq}$)	0.003		0.028		0.034		0.002		0.015		0.020	

compound 6 and also the π^*_{C1-O7} antibonding orbital occupancies increased (see Table 2). Based on the NBO analysis, the energy difference between donor ($E\sigma_{C2-X8}$) and acceptor ($E\pi^*_{C1-O7}$) orbitals [i.e. ($E\pi^*_{C1-O7}$-$E\sigma_{C2-X8}$)] for the axial conformations decrease from compound 1 to compound 3. This results can be explained by the increase of the $\sigma_{C2-X8} \rightarrow \pi^*_{C1-O7}$ electron delocalizations from the axial conformations of compound 1 to 3 and compound 4 to 6. In addition, there is direct relationship between the orbital overlap (S) matrix

Table 3: *B3LYP/6-311+G** calculated structural parameters for the equatorial and axial conformations of compounds 1-6.*

Compound	**1**		**2**		**3**		**4**		**5**		**6**	
State	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax	Eq	Ax
Bond lengths (Å)												
r_{1-2}	1.548	1.539	1.542	1.529	1.536	1.521	1.542	1.539	1.548	1.538	1.547	1.534
r_{2-3}	1.551	1.546	1.548	1.532	1.543	1.524	1.542	1.539	1.548	1.538	1.547	1.534
r_{3-4}	1.519	1.517	1.522	1.515	1.523	1.517	1.519	1.515	1.521	1.515	1.522	1.516
r_{4-5}	1.540	1.544	1.539	1.541	1.538	1.540	1.541	1.547	1.539	1.524	1.538	1.541
r_{5-6}	1.539	1.545	1.539	1.538	1.539	1.538	1.541	1.547	1.539	1.524	1.538	1.541
r_{6-1}	1.521	1.514	1.520	1.519	1.519	1.520	1.519	1.515	1.521	1.515	1.522	1.516
r_{1-O}	1.203	1.207	1.205	1.212	1.207	1.213	1.202	1.206	1.201	1.207	1.201	1.207
r_{2-X}	1.385	1.426	1.823	1.862	1.976	2.019	1.365	1.409	1.778	1.827	1.944	1.993
Δ[$r_{1-O(ax)}$-$r_{1-O(eq)}$]	0.004		0.007		0.006		0.004		0.006		0.006	
Δ[$r_{1-2(eq)}$-$r_{1-2(ax)}$]	0.009		0.013		0.015		0.003		0.01		0.013	
Bond angles (°)												
θ_{1-2-3}	109.4	108.6	109.3	113.9	110.4	115.2	110.5	108.1	110.4	112.1	110.8	113.4
θ_{2-3-4}	114.8	113.9	114.1	115.8	114.2	116.1	113.8	113.2	113.4	115.5	113.3	115.9
θ_{3-4-5}	110.7	110.6	111.0	110.6	111.3	110.9	110.8	109.8	111.1	110.9	111.2	111.0
θ_{4-5-6}	111.8	112.8	111.9	112.1	111.9	111.9	112.1	113.2	111.9	112.6	111.9	112.4
θ_{5-6-1}	111.3	109.7	111.0	112.1	111.0	112.2	110.8	109.8	111.1	110.8	111.2	111.0
θ_{6-1-2}	114.3	113.9	114.7	116.6	115.1	116.9	113.8	113.2	113.4	115.4	113.3	115.9
θ_{O-1-2}	122.0	121.3	122.0	120.2	120.8	120.2	121.6	121.3	122.9	120.1	123.3	119.9
θ_{X-2-1}	114.5	110.0	116.5	108.3	116.8	108.1	111.6	107.7	113.2	108.4	113.4	108.1
Δ[$\theta_{X-2-1(eq)}$-$\theta_{X-2-1(ax)}$]	4.5		8.5		8.7		3.9		4.8		5.3	
Torsion angles (°)												
$\phi_{1-2-3-4}$	51.1	54.0	51.8	41.7	49.7	38.4	51.5	57.5	51.9	45.8	51.5	42.3
$\phi_{2-3-4-5}$	-54.0	-53.6	-54.3	-50.8	-53.0	-48.9	-53.6	-55.7	-53.9	-50.4	-53.7	-48.8
$\phi_{3-4-5-6}$	54.5	53.0	54.3	56.4	54.5	56.5	54.7	52.8	54.8	54.5	54.9	55.1
$\phi_{4-5-6-1}$	-54.6	-53.9	-53.8	-53.6	-53.9	-53.8	-54.7	-52.8	-54.8	-54.7	-54.9	-55.1
$\phi_{5-6-1-2}$	53.6	56.2	53.6	44.8	52.6	43.3	53.6	55.7	53.9	50.7	53.7	48.8
$\phi_{6-1-2-3}$	-50.5	-55.6	-51.6	-38.5	-49.8	-35.4	-51.6	-57.5	-51.9	-46.0	-51.5	-42.3
$\phi_{O-1-2-3}$	128.8	120.9	127.1	142.6	129.0	145.0	127.2	118.2	127.3	131.0	127.8	134.7
$\phi_{X-2-3-4}$	175.5	-62.1	178.0	-77.8	176.0	-80.7	176.3	-58.5	179.9	-73.8	-179.7	-77.5
Δ[$\phi_{6-1-2-3(ax)}$-$\phi_{6-1-2-3(eq)}$]	-5.1		13.1		14.4		-5.9		5.9		9.2	

and the off-diagonal elements (F_{ij}), therefore the increase of the off-diagonal elements F_{ij} values could increase the $\sigma_{C2\text{-}X8}\rightarrow\pi^*_{C1\text{-}O7}$ electron delocalizations. NBO calculated F_{ij} values for $\sigma_{C2\text{-}X8}\rightarrow\pi^*_{C1\text{-}O7}$ electron delocalizations in the axial conformations of compounds 1-3 are 0.034, 0.056 and 0.061, respectively and also in the axial conformations of compounds 4-6 are 0.031, 0.045 and 0.051, respectively (see Table 2).

Dipole moments

The dipole moments are effective on the stability of the various conformations of chemical compounds. In the gaseous phase it is generally found that the conformation with the larger dipole moment has the larger electrostatic energy, leading to an increased overall energy [50]. The B3LYP/6-311+G** results showed that the dipole moments for the axial conformations of compounds 1-6 are smaller than those in the equatorial conformations (see Table 2). There is an opposite trend for the variations of $\Delta(\mu_{eq}\text{-}\mu_{ax})$ and *GAE* values. Based on the results obtained, the *GAE* increases from compound 1 to compound 3 but $\Delta(\mu_{eq}\text{-}\mu_{ax})$ increases from compound 1 to compound 2 and decreases from compound 2 to compound 3. Accordingly, the rationalization of the conformation preference solely in terms of dipole-dipole interactions fails in accounting qualitatively for the increase of the axial preferences from compound 1 to compound 3 and also compounds 4-6 and it seems *GAE* is dominant factor on conformational preference of compounds 1-6 (see Table 1, 2).

Bond orders

The differences between the (Wiberg Bond Index) WBIs of the $C_1\text{-}O_7$ bonds in the equatorial and axial conformations, ΔWBI ($C_1\text{-}O_{7eq}\text{-}C1\text{-}O_{7ax}$) and Also, the differences between ΔWBI ($C_1\text{-}C_{2ax}\text{-}C_1\text{-}C_{2eq}$), increase from compound 1 to compound 3 and compound 4 to compound 6. The variations of the calculated $\Delta(WBI_{eq\text{-}ax})$ parameters is in accordance with the variations of the calculated *GAE* values from compound 1 to compound 3 and compound 4 to compound 6 (see Table 2). The electron delocalizations can affect the bond orders of $C_1\text{-}O_7$ and $C_1\text{-}C_2$ bonds. This results can be explained by the increase of the $\sigma_{C2\text{-}X8}\rightarrow\pi^*_{C1\text{-}O7}$ electron delocalizations from the axial conformations of compound 1 to compound 3 and compound 4 to compound 6.

Structural parameters

The structural parameters calculated can be used in order to illustrate the effects of the electron delocalizations on the structural parameters of the axial and equatorial conformations of compounds 1-6. The structural parameters for the conformations of compounds 1-6 calculated by the B3LYP/6-311+G** level of theory (see Table 3). Consideration of the structural parameters calculated of compounds 1-6 gave evidence that there is a direct correlation between the calculated generalized anomeric effect (*GAE*) and $\Delta(r_{1\text{-}Oax}\text{-}r_{1\text{-}Oeq})$, so that, with the increase of the $\Delta(r_{1\text{-}Oax}\text{-}r_{1\text{-}Oeq})$ parameter from compound 1 to compound 3 and from compound 4 to compound 6, the corresponding *GAE* values increase (see Tables 2, 3). Also, in the axial conformations of these compounds, the $r_{C1\text{-}O7}$ bond lengths is significantly longer than that of the corresponding equatorial conformations and This fact can be explicated by the greater $\sigma_{C2\text{-}X8}\rightarrow\pi^*_{C1\text{-}O7}$ electron delocalizations in the axial conformations compared to their corresponding equatorial conformations (see Table 2). The calculated $\Delta[\theta_{X\text{-}2\text{-}1(eq)}\text{-}\theta_{X\text{-}2\text{-}1(ax)}]$ and $\Delta[\phi_{6\text{-}1\text{-}2\text{-}3(eq)}\text{-}\phi_{6\text{-}1\text{-}2\text{-}3(ax)}]$ values increase from compound 1 to compound 3 and also from compound 4 to compound 6. The increase of these parameters is in agreement with the increase of the calculated *GAE*.

4. CONCLUSIONS

The above reported hybrid-DFT, ab initio molecular orbital calculations and NBO analysis provided a reasonable picture from structural, energetic, bonding and stereoelectronic points of view for the conformational behavior in compounds 1-6. Effectively, B3LYP/6-311+G** results revealed that the axial conformations of compounds 1-6 are more stable than their equatorial conformations. Similar to the increase of the anomeric effect (*AE*) values from compound 1 to compound 3 and compound 4 to compound 6, the stability of the axial chair conformations of these compounds are increased. On the other hand, the variations of the calculated $\Delta(\mu_{eq}-\mu_{ax})$ values fails in accounting for the above observation. Therefore, the electrostatic interactions are not responsible for the anomeric effect (*AE*). In addition, the NBO results showed that the variation of the calculated $\Delta(WBI_{(C2\text{-}X)eq\text{-}ax})$ parameters are in accordance with the increase of the calculated *GAE*. Interestingly, the increase of $\Delta(r_{1\text{-}Oax}-r_{1\text{-}Oeq})$, $\Delta[\theta_{X\text{-}2\text{-}1(eq)}-\theta_{X\text{-}2\text{-}1(ax)}]$ and $\Delta[\phi_{6\text{-}1\text{-}2\text{-}3(eq)}-\phi_{6\text{-}1\text{-}2\text{-}3(ax)}]$ parameters from compound 1 to compound 3 and also compound 4 to compound 6 can be explainedq by the increase of the corresponding *GAE* values. Accordingly, the calculated $\Delta(r_{1\text{-}Oax}-r_{1\text{-}Oeq})$, $\Delta[\theta_{X\text{-}2\text{-}1(eq)}-\theta_{X\text{-}2\text{-}1(ax)}]$ and $\Delta[\phi_{6\text{-}1\text{-}2\text{-}3(eq)}-\phi_{6\text{-}1\text{-}2\text{-}3(ax)}]$ parameters could be proposed as a criterion for the evaluation of the *GAE* values in compounds 1-6.

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