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CONFORMATIONAL ANALYSIS OF 2,4-DIALKYL-1,3,2-DIOXABORINANES

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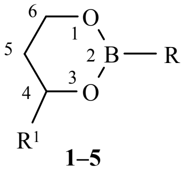
Computer modeling using the quantum-chemical empirical MM+ method and nonempirical RHF//6-31G(d), MP2//6-31G(d), and, in individual cases, RHF//3-21G methods was employed to study the potential energy surface of 2,4-dialkyl-1,3,2-dioxaborinanes. The optimal geometry and ^1H NMR spectral data gave values for ΔG^0 of the methyl and hexyl substituents at C-4 of the heterocyclic ring equal to 0.6 and 1.6 kcal/mol, respectively.

Keywords: 1,3,2-dioxaborinanes, conformer, quantum chemistry, coupling constants, conformational equilibrium, potential energy surface, conformational free energy, ^1H NMR spectroscopy.

The high conformational mobility of six-membered cyclic esters of boric acids, namely, 1,3,2-dioxaborinanes as well as the presence of an electron-deficient boron atom and electron-donor oxygen atoms in a single molecule make these compounds promising objects for conformational analysis [1-4]. In our previous work [5-9], we have shown that major minimum of the potential energy surface (PES) of 4-methyl-2-substituted 1,3,2-dioxaborinanes is the *sofa* conformer with equatorial orientation of the methyl group (*Ce*) and the maxima (or transition states, TS) correspond to 2,5-*twist* forms with pseudoequatorial and pseudoaxial orientation of the substituents (2,5-*Te* and 2,5-*Ta*) [5-9]. In the present work, conformational analysis was carried out for 2,4-dialkyl-1,3,2-dioxaborinanes **1-5** using ^1H NMR data and computer modeling of conformational isomerization by means of the empirical MM+ and nonempirical RHF//6-31G(d), MP2//6-31G(d), and, in individual cases, RHF//3-21G methods from the HyperChem package [10].



1–5

1 R = R^1 = Me; **2** R = 2-Pr, R^1 = Me; **3** R = *i*-Bu, R^1 = Me;
4 R = *i*-Bu, R^1 = C_5H_{11}; **5** R = *i*-Bu, R^1 = C_6H_{13}

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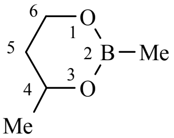
TABLE 1. MM+ Calculation for the Barriers of Inversion of Conformers *Ce* ↔*Ca* in Ester **1** (kcal/mol)



Angle	$\Delta E^{\neq}$	TS	Angle	$\Delta E^{\neq}$	TS
2-3-4-5	8.2	2,5-*T*	2-1-5-4	9.1	2,5-*T*
3-4-5-6	7.4	2,5-*T*	2-1-6-4	18.6	2,5-*T*
1-6-5-4	7.0	2,5-*T*	2-3-4-6	17.0	2,5-*T*
2-1-6-5	7.4	2,5-*T*	1-2-3-5	36.4	*C**
2-3-5-6	8.6	2,5-*T*	4-5-6-2	9.8	2,5-*T*

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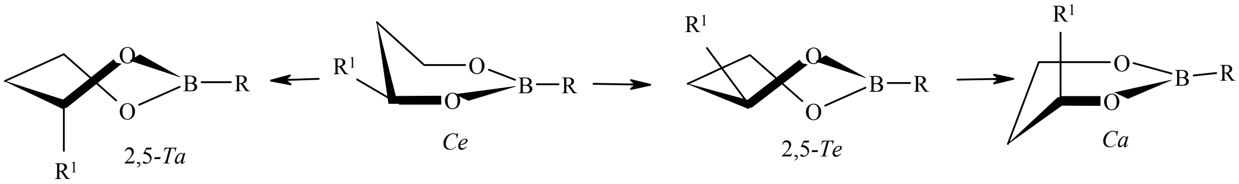
* *Sofa* conformation with planar 3-4-5-6 fragment

Conformational transitions are accompanied by a change in all the torsion angles between bonds in the ring [11]. However, the extent of this change may differ. Scanning the individual torsion angles using the MM+ method in the case of ester **1** showed that the optimal route for inversion involves variation of the 1-6-5-4 torsion angle (Table 1). On the other hand, scanning angles 1-2-3-4 and 3-4-6-1 does not lead to inversion. The maxima in all cases, except the case due to change in angle 1-2-3-5, correspond to either 2,5-*Te* or 2,5-*Ta* forms.

The Zefirov-Palyulin-Dashevskaya puckering parameters are an important characteristic of ring form [12]. Calculation of these parameters for the major minimum and TS of ester **1** using RHF//3-21G geometry showed that the values obtained for conformer *Ce* ($s = 0.76$, $\theta = 38.2°$, $\Psi = 2.0°$) are similar to the characteristic values of the classic *sofa* values ($\theta = 45°$, $\Psi = 0°$), while the values obtained for the 2,5-*T* conformation ($s = 0.63$, $\theta = 91.0°$, $\Psi = 28.5°$) are similar to the parameters of the classical *twist* form ($\theta = 90°$, $\Psi = 30°$).

The use of quantum-chemical methods permits us to obtain a more detailed evaluation of the differences between the *Ce* and *Ca* conformers (ΔE) as well as the height of the potential barrier ($\Delta E^{\neq}$) and the energetic nonequivalence of the 2,5-*Te* and 2,5-*Ta* forms ($\Delta\Delta E^{\neq}$).



Internal rotation of the isopropyl and isobutyl substituents about the B–C bond may affect the total energy of the conformers [13, 14]. Thus, all the calculated parameters of the conformational equilibrium studied for esters **2-5** were obtained for the B–*i*-Pr and B–*i*-Bu rotamers with minimal energy. We should also note that the conformation of the pentyl and hexyl substituents in esters **4** and **5** corresponded in all cases to a regular zigzag of the hydrocarbon chain. With all this in mind, we note that parameters ΔE and $\Delta E^{\neq}$ of esters **1-5** are virtually independent of the substituent at the boron atom. The value for $\Delta E^{\neq}$ is close to the experimental values of $\Delta G^{\neq}$ for individual 1,3,2-dioxaborinanes (7-8 kcal/mol [15], Table 2). On the other hand, as might have been expected [9], the difference between transitions states 2,5-*Te* and 2,5-*Ta* increases with increasing conformational bulk of the substituent at ring C-4 atom. The MP2//6-31G(d) calculation leads to somewhat lower values of ΔE and higher value of $\Delta E^{\neq}$.

TABLE 2. Energy Characteristics for the Inversion of Esters **1-5** (kcal/mol)

Compound	ΔE	$\Delta E^{\neq}$	$\Delta\Delta E^{\neq}$	ΔE	$\Delta E^{\neq}$	$\Delta\Delta E^{\neq}$
	RHF//6-31G(d)			MP2//6-31G(d)		
1	1.3	7.6-8.6	1.0	1.0	8.3-9.2	0.9
2	1.3	7.4-8.7	1.3	0.9	8.3-9.2	0.9
3	1.3	7.4-8.7	1.3	1.1	8.2-9.3	1.1
4	1.4	7.2-8.9	1.7	0.9	8.0-9.3	1.3
5	1.4	7.3-8.9	1.6	1.0	8.0-9.2	1.2

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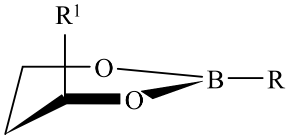
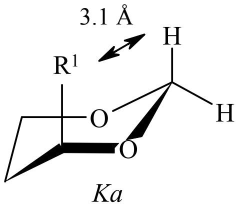
*Values for ΔE, $\Delta E^{\neq}$, and $\Delta\Delta E^{\neq}$ (designations given in the text) are given relative to the *Ce* conformer.

The ^{1}H NMR spectral values indicate that the *Ce* conformer predominates for cyclic esters **1-5** [1, 5, 6]. On the other hand, the decrease in the number of nonbonding interactions due to the planar configuration of the trigonal boron atom should lead to a greater content of the alternative conformer in comparison with monotypical substituted non-boron analogs.



Ca



Ka

In order to prove this hypothesis, we must know the conformational free energy $\Delta G°$ of the substituent at atom C-4 in 1,3,2-dioxaborinanes. In previous work [16], we showed the feasibility of determining $\Delta G°$ of substituents in different positions of the 1,3-dioxane ring using the weighted mean (from the ^{1}H NMR spectra) and standard (calculated) values of the vicinal proton coupling constants. These constants were determined using the modified Karplus equation [17]:

$$^3J_{HH} = P_1\cos^2\varphi + P_2 cos\varphi + P_3 + \sum\Delta\chi_i[P_4 + P_5\cos^2(\xi_i\varphi + P_6\,|\Delta\chi_i|)],$$

where $\Delta\chi_i$ is the difference in electronegativity between the substituents of the corresponding ethane fragment and hydrogen [18], φ is the torsion angle between the protons examined (data of the optimal geometry), ξ_i takes values ±1 depending on the orientation of the substituents at the carbon atoms of the ethane fragment, while P_1-P_6 are parameters dependent on the extent of substitution of this fragment.

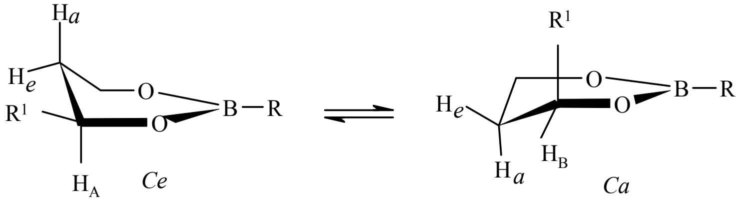
The content of the most stable conformer in the binary mixture (N) and value of $\Delta G°$ were determined using the following well-known equations [19]:

$$^3J_{AX} + {}^3J_{BX} = N\,(J_{Aa} + J_{Ab}) + (1-N)\,(J_{Ba} + J_{Bb});$$

$$\Delta G° = -RT \ln N/1-N \;(T = 298\text{ K})$$

The data obtained for esters **3** and **5** using the refined ^{1}H NMR spectral parameters measured in this work support the conclusion of high conformational flexibility of 1,3,2-dioxaborinane molecules (Table 3). In particular, $\Delta G°$ of the CH_3 group (0.6 kcal/mol) is four times lower than the value observed for

TABLE 3. Evaluation of $\Delta G°$ of Substituents at Atom C-4 in 1,3,2-Dioxaborinanes **3** and **5**



Com-pond	Torsian angles, deg*				J, Hz*^{2}				N	(–$\Delta G°$), kcal/mol
	φ_{Aa}	φ_{Ae}	φ_{Ba}	φ_{Be}	J_{Aa}	J_{Ae}	J_{Ba}	J_{Be}		
3	174.2	56.0	45.0	72.6	11.7	2.6	6.1	1.5	0.73	0.6
5	173.4	54.9	45.1	72.4	11.7	2.8	6.1	1.5	0.94	1.6

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*According to the optimal geometry data obtained in an RHF//6-31G(d) calculation.

*^{2} Experimental coupling constants: for **3** – $^3J_{AX} = 9.3$, $^3J_{BX} = 3.2$, for **5** – $^3J_{AX} = 11.0$, $^3J_{BX} = 3.1$.

4-methyl-1,3-dioxanes (2.7-2.9 kcal/mol [20]). We should note that this result differs from the data of Rossi and Pihlaja [2], who used the ^{1}H and ^{13}C NMR spectral data for 2-hydroxy-4-methyl-1,3,2-dioxaborinane to conclude that there is greater occupancy of the equatorial form of the borate (not less than 89-93%). The value of $\Delta G°$ of the C_6H_{13} group at atom C-4 in the 1,3,2-dioxaborinane ring (1.6 kcal/mol) is also lower than the analogous parameter in 4-methyl-1,3-dioxane (there are no data for 4-hexyl-1,3-dioxane in the literature). On other hand, we know that the difference in solvation energies of the conformers by the solvent affects the conformational equilibrium parameters and the geometry of the conformers themselves [21]. Thus, a more correct solution of the problem discussed involves theoretical conformational analysis of the compound in the presence of molecules of the specific solvent by means of constructing a corresponding continual or discrete model.

Found patterns indicate a higher conformational lability of molecules of 4-alkyl-1.3.2-dioxaborinanes compared to the same type substituted 1,3-dioxanes, due to decrease of number of unrelated (unbonded) interactions in the heteroatomic part of the ring because of the flat configuration of the trigonal boron atom.

EXPERIMENTAL

The ^{1}H NMR spectra of compounds **3** and **5** were taken on a Bruker AM-250 spectrometer at 250 MHz for 10% solutions of the compounds studied in $CDCl_3$ and C_6D_6 with TMS as the internal standard. A procedure for suppressing the hexyl group methylene protons was employed for a correct determination of coupling constants $^3J_{AX}$ and $^3J_{BX}$ of compound **5**. The inversion pathway and ($\Delta E^{\neq}$) values were found by scanning the individual torsion angles (in an MM+ calculation) and using a transition state search procedure (in an *ab initio* calculation) in the framework of the HyperChem package algorithm [10].. The assignment of the stationary points on the potential energy surface to maxima was confirmed by the finding of a single negative frequency in the corresponding Hesse matrix. The applicability of the calculation methods to analysis of the structural and energy characteristics of cyclic borates was discussed in our previous work [22, 23]. The electronegativities given by Huggins [18] were used in deriving the theoretical coupling constants. The following values for P_1-P_6

for the trisubstituted ethane fragment were adopted during the calculations [17]: $P_1 = 13.22$, $P_2 = -0.99$, $P_3 = 0$, $P_4 = 0.87$, $P_5 = -2.46$, $P_6 = 19.9°$. Esters **2** and **3** were described in our previous work [24], while **4** and **5** were described in our later work [5].

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