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CONFORMATIONAL ENERGY OF THE METHYL GROUP AT THE $C_{(5)}$ ATOM IN 1,3,2-OXAZABORINANES

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The method of ^3H and ^{13}C NMR spectroscopy was utilized to determine the conformational energy of the methyl group at the $C_{(5)}$ atom in molecules of 2,3,5-substituted 1,3,2-oxazaborinanes. The resulting value of ΔG^0 (1 kcal/mole) is half the value of 1,3,2-dioxaborinanes and is close to the analogous value in tetrahydro-1,3-oxazines (1.2 kcal/mole). The differences observed are associated with features of the p−π-electronic interactions in the heteroatomic fragment of the organoboron ring.

It is known that the conformational properties of cyclic esters of boric acids are determined to a significant degree by electronic interactions in the heteroatomic fragment. In consequence of this, molecules of most substituted 1,3,2-dioxaborinanes, not being subject to inversion in the NMR time scale, remain in the preferred conformation of the hemiplanar form or sofa [1-5]. The substitution of one of the oxygen heteroatoms by nitrogen does not introduce principal differences: the molecules of 2,3,5-substituted 1,3,2-oxazaborinanes are also characterized by the sofa with the preferred equatorial orientation of the substituent at the $C_{(5)}$ atom [6]. Its advantageousness is also confirmed by quantum-chemical calculations [7]. It was already previously noted that the influence of the heteroatomic fragment of the 1,3,2-dioxaborinane ring leads to an increase in the conformational energy of the alkyl substituent at $C_{(5)}$ by comparison with 1,3-dioxanes [1, 4]. For the 5-methyl-1,3,2-dioxaborinanes, the corresponding value of ΔG^0 comprises from 2.5 kcal/mole (the data of configurational isomerization [8]) to 2.0 kcal/mole (the data of ^1H NMR [5]) by comparison wit the 0.8-1.0 kcal/mole for 1,3-dioxanes [9]. Interest is presented by the evaluation of the unknown value of ΔG^0 for the methyl group at $C_{(5)}$ in molecules of 2,3,5-substituted 1,3,2-oxazaborinanes [compound (I)-(IV)]. The given compounds are not stereoisomeric and, moreover, the method of configurational isomerization of organoboron heterocycles requires drastic conditions [10] and is not suitable for thermally unstable nitrogen-containing derivatives. Therefore, the present work utilized the approach associated with the application of weighted-mean and standard SSCCs according to the equation [11]:

$$^3J_{AX} + {}^3J_{BX} = N\,(J_{aa} + J_{ae}) + (1 - N)\,\cdot\,(J_{ea} + J_{ee}),$$

where N is the fraction of the equatorial conformer, $^3J_{AX}$ and $^3J_{BX}$ are observed (weighted-mean) SSCCS in the investigated molecule (data of the work [6] were utilized), and J_{aa}, J_{ae}, J_{ea}, and J_{ee} are standard SSCCs. For the last were utilized constants from the spectra of the conformationally uniform *cis*- and *trans*-2-isobutyl-4,5-dimethyl-1,3,2-oxazaborinanes [compound (V)] [12]. Parameters of the conformational equilibrium of the compounds (II) and (IV) were evaluated simultaneously with that from the data of the ^{13}C NMR using the chemical shifts of the carbon atom of the methyl group at $C_{(5)}$ [6] and the standard values of δ_A and δ_E. For the last were utilized the chemical shifts of carbon-13 for the methyl group at $C_{(5)}$ in the spectra of *cis*- and *trans*-2-isobutyl-5,6-dimethyl-1,3,2-oxazaborinanes (VI) [12]. The equilibrium constant was determined from the equation [13]:

$$K=\frac{\delta_A-\delta}{\delta-\delta_E}.$$

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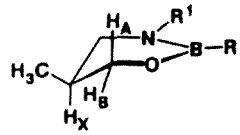
TABLE 1. Parameters of the Conformational Equilibrium of 2,3,5-Substituted 1,3,2-Oxazaborinanes According to the ^1H NMR Data

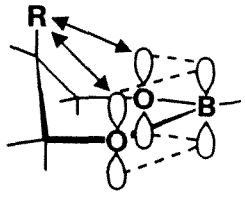


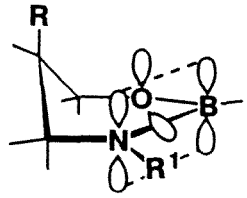
Compound	R	R^1	J, Hz						N	K	$-\Delta G_0$, kcal/mole
			$^3J_{AX}$	$^3J_{BX}$	J_{aa}	J_{ae}	J_{ea}	J_{ee}			
I	C_2H_5	$CH_2C_6H_5$	10,5	4,6	11,2	4,6	7,6	3,5	0,85	5,7	1,0
II	C_3H_7	$CH_2C_6H_5$									
III	C_2H_5	C_6H_{11}	10,2	4,2					0,70	2,3	0,5
IV	C_3H_7	C_6H_{11}									

TABLE 2. Parameters of the Conformational Equilibrium of 2,3,5-Substituted 1,3,2-Oxazaborinanes According to the ^{13}C NMR Data

Compound	δ, ppm			K	$-\Delta G^0$, kcal/mole
	δ	δ_A	δ_E		
II	14,6	12,5	15,0	5,3	1,0
IV	14,7			7,3	1,2

The data obtained, presented in Tables 1 and 2, indicate the marked lowering of the ΔG^0 in molecules of 2,3,5-substituted 1,3,2-oxazaborinanes by comparison with 1,3,2-dioxaborinanes. By all appearances, this is caused by changes in the character of the steric interaction of the axial 5-CH_3 group with the heteroatomic fragment.



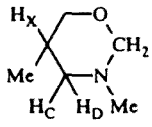


In the molecules of the oxygen analogs, there is marked hindrance to the axial substituent in the conformation of the sofa due to the interaction with the p-orbitals of the oxygen atoms, which are close to the sp^2 in their configuration [1, 3, 4]. For the 1,3,2-oxazaborinanes, which are primarily asymmetric in the heteroatomic fragment, the more available n-electron pair of the sp^2-hybridized nitrogen dominates in the p–p-electron exchange with the vacant orbital of boron; this leads to an increase in the s-character of the n-electron pairs of oxygen and to a change in their steric orientation. In consequence of this, the degree of freedom of the axial group at the $C_{(5)}$ atom increases. The significant discrepancy in the evaluation of the ΔG^0 for the compounds (III) and (IV) by the two methods utilized is most likely determined by inaccuracy in the choice of the standard compounds [(V) and (VI)], the molecules of which lack perturbations to the values both of the SSCC and the $\delta_{^{13}C}$ caused by a bulky substituent (cyclohexyl) at the nitrogen atom. The shielding of the nucleus of the last is known to depend on the γ-influence of heteroatoms, in particular the orientation of their n-electron pairs [14]. Therefore, the reliable value of ΔG^0 for the methyl group at $C_{(5)}$ at 293 K comprises 1.0 kcal/mole.

The information obtained confirms the specified influence of electronic interactions in the heteroatomic part of the ring of six-membered organoboron heterocycles on the conformational characteristics of their molecules.

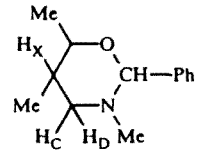
It is logical to compare the value of the ΔG^0 for the 15-CH_3 group of 1,3,2-oxazaborinanes with the analogous value for analogs not containing boron — tetrahydro-1,3-oxazines. No published value for it is known. However, it can be determined from ^1H NMR spectral data. The utilization of the values of $\delta_{^{13}C}$ in the given case is rendered difficult due to the complexity in the selection of the corresponding standard values of δ_A and δ_E. Moreover, inversion of the chemical shift of the carbon nucleus of the methyl group at $C_{(5)}$ is observed in the ^{13}C NMR spectra of tetrahydro-1,3-oxazines [15].

The molecule selected was 3,5-dimethyltetrahydro-1,3-oxazine (VII), and the and reference compounds selected were *cis*- and *trans*-isomers of 2-phenyl-3,5,6-trimethyltetrahydro-1,3-oxazine (VIII); the corresponding SSCCs are presented in the works [16-18].



$^3J_{CX}$ = 10,0 Hz;
$^3J_{DX}$ = 3,0 Hz

VII



trans-:
$^3J_{CX}$ = 11,0 Hz;
$^3J_{DX}$ = 4,0 Hz

cis-:
$^3J_{CX}$ = 3,1 Hz;
$^3J_{DX}$ = 2,2 Hz

VIII

It is known that molecules of the compound (VII) stay in the chair conformation with the mainly equatorial methyl group at $C_{(5)}$, and the configuration of the conformationally uniform *cis*- and *trans*-isomers of the compound (VIII), the molecules of which are also characterized by the chain conformation, differs in the orientation of the substituent at the $C_{(5)}$ atom [17, 18]. The selection of alternative reference compounds — 3,4,5-trimethyltetrahydro-1,3-oxazines — is not possible due to the conformational heterogeneity of the *cis*-isomers [19]. It follows by calculation from the equation presented above [11] that N = 0.885, K = 7.7, and $\Delta G^0 = -1.2$ kcal/mole. Therefore, notwithstanding differences in the character of the preferred conformation (chair, sofa), the ΔG^0 of the 5-CH_3 group in molecules of 1,3,2-oxazaborinanes shows practically no difference from that observed for tetrahydro-1,3-oxazines and other saturated heterocycles (1,3-dioxanes, 1,3-oxathiazines), but is noticeably lower than the analogous value in the series of conformationally similar 1,3,2-dioxaborinanes.

EXPERIMENTAL

Substituted 1,3,2-oxazaborinanes are described in the work [20]. The ^1H and ^{13}C NMR spectra were measured on the AM-250 instrument (250 MHz for protons and 62.89 MHz for the ^{13}C nuclei) in the solution of $CDCl_3$ with the natural content of the isotope ^{13}C relative to TMS as the internal standard. The conformational assignments of the compounds (I)-(IV) were performed in the work [6].

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