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CONFORMATIONAL COMPOSITION OF STEREOISOMERS OF 2-ALKYL-5-ISOPROPYL-4-METHYL-1,3,2-DIOXABORINANES

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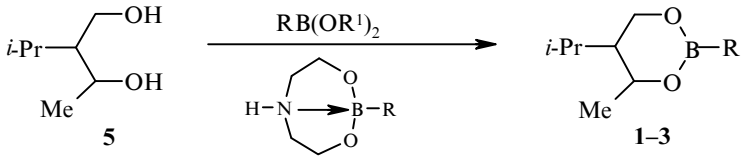
^{1}H and ^{13}C NMR spectroscopy was used to assign the configuration of a mixture of stereoisomers of 2-alkyl-5-isopropyl-4-methyl-1,3,2-dioxaborinanes with different ratios of the cis and trans forms. These forms differ in the configuration of $C_{(4)}$ in the ring. The results of MM+ and AM1 calculations for the optimal geometry indicate high conformational flexibility of both isomers, which exist in an equilibrium mixture of sofa and half-chair conformers.

Keywords: 1,3,2-dioxaborinanes, conformational analysis.

The conformational behavior of cyclic esters of boric acids is largely a function of the electron exchange at the B–O bonds such that the sofa conformer, which provides for maximum interaction of the *p*-electron pairs of the oxygen atoms and the vacant orbital of boron, is most stable for 2-, 5-, and 2,5-substituted 1,3,2-dioxaborinanes [1-6]. However, in the case of asymmetrically substituted derivatives such as 4-alkyl or 4,5-dimethyl analogs [7-9], distortion of this form is possible and a family of half-chairs appears. In the present work, we continued a study of the stereochemistry of six-membered cyclic borate esters with several chiral centers in the carbon part of the ring and studied the conformational composition of the stereoisomers of 2-alkyl-5-isopropyl-4-methyl-1,3,2-dioxaborinanes **1-3** in comparison with model 2,5-diisopropyl-1,3,2-dioxaborinanes (**4**) with an equatorial substituent at $C_{(5)}$ by ^{1}H and ^{13}C NMR spectroscopy in conjunction with data from optimal geometry calculations by means of the empirical MM+ [1] and semiempirical AM1 approximations [11, 12] provided in the HyperChem 5.02 program package [13].



5 **1–3**

1 R = Me, **2** R = *i*-Pr, **3** R = *i*-Bu

Dioxaborinanes **1-4** were obtained by transesterification of acyclic esters of the corresponding alkylboric acids or (N–B)-perhydro-2-alkyl-1,3-dioxa-6-aza-2-boracines by 2-isopropyl-1,3-butanediol (**5**) or 2-isopropyl-1,3-propanediol [1, 14].

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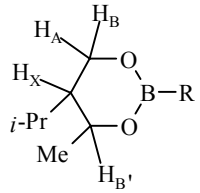
TABLE 1. ^{1}H NMR Spectra of 2-Alkyl-5-isopropyl-4-methyl- and 2,5-Diisopropyl-1,3,2-dioxaborinanes **1-4**



Compound*	Chemical shifts, δ, ppm							CCSS, *J*, Hz			
	H_A	H_B	$\Delta\delta_{AB}$	$H_{B'}$	H_X	$C_{(4)}$–CH_3	$C_{(5)}$–$(CH_3)_2$	$^3J_{AX}$	$^3J_{BX}$	$^3J_{B'X}$	$^4J_{BX}$
cis-**1**	3.62	3.88	0.26	4.13	1.31	1.10	0.84; 0.83	11.3	5.1	5.2	1.2
trans-**1**	3.70	3.86	0.16	3.90		1.20	0.91; 0.78	8.5	4.2	10.7	—
cis-**2**	3.64	3.89	0.25	4.14	1.31	1.10	0.84; 0.83	11.1	5.0	5.1	1.2
trans-**2**	3.72	3.86	0.17	3.92		1.20	0.92; 0.80	8.6	4.1	10.6	—
cis-**3**	3.69	3.94	0.25	4.17	1.31	1.11	0.86; 0.85	11.5	5.0	5.1	1.2
trans-**3**	3.75	3.92	0.17	3.97		1.21	0.93; 0.81	8.6	4.1	10.7	
4	3.43	3.83	0.40	—	1.30	—	0.75	10.0	4.5	—	—

* The signal for the protons of the isopropyl substituent at the boron atom in **2** and **4** appear as an anomalous singlet. The reasons for this effect were examined in our previous work [1, 18, 19].

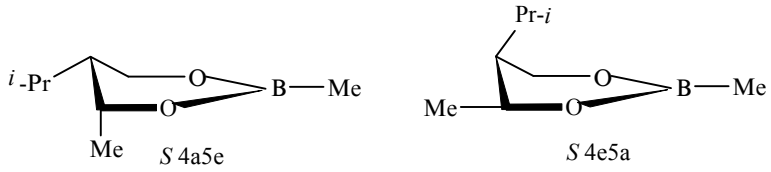
In order to increase the reliability of the configurational assignment of the isomers of **1-3** and the evaluation of the stereochemistry of their formation, we used samples of diol **5** with 70:30 (**5a**) and 39/61 ratio (**5b**) of the *erythro* and *threo* forms [17].

The parameters of the ^{1}H NMR spectra of the stereoisomer mixture of **1-3** and of model ester **4** [1, 2] are given in Table 1. The coupling constants $^3J_{AX}$ and chemical shift of H_X, which is common for the isomers of these esters, were virtually identical to the observed values in the spectrum of ester **4** and indicate an equatorial orientation of the isopropyl substituent at $C_{(5)}$ in all cases. On the other hand, the coupling constants $^3J_{B'X}$ and difference in the chemical shifts for the protons of the $C_{(4)}$–CH_3 group indicate that these isomers differ in the configuration at $C_{(4)}$. Using the vicinal coupling constants and integral intensities of the corresponding groups of signals, we note that the predominant isomers of esters **1-3** obtained from diol **5a** are *cis* derivatives and contain an axial methyl group at $C_{(4)}$. Additional evidence for this hypothesis is found in the long-range coupling constant of equatorial nuclei H_B and $H_{B'}$ (comprising a W-system, ^4J = 1.2 Hz), which is lacking for the *trans* isomers. The integral intensity data for the signals of the $C_{(4)}$–CH_3 protons indicated that the ratio of *cis* and *trans* isomers of **1-3** is 78:22 (from diol **5a**) and 34:66 (from diol **5b**). Gas-liquid chromatography indicated that these ratios were 74:26 and 36:64, respectively. Thus, in contrast to the data of our previous work [14, 20, 21], we must assume stereospecificity in the reaction leading to formation of esters **1-3**. Only the *trans* isomer of the corresponding 1,3,2-dioxaborinane is obtained from the *threo* isomer of diol **5**, while only the *cis* isomer is obtained from the *erythro* isomer of diol **5**. Similar behavior was observed in the formation of 4,5-dialkyl-1,3-dioxanes [15, 16] and also 2,4,5-substituted 1,3,2-dioxaborinanes with different substituents in the carbon part of the ring [22-24].

Other distinguishing features of the ^{1}H NMR spectra of these compounds include anisochronicity of the protons of the *gem*-dimethyl groups of the isopropyl substituent at $C_{(5)}$, which is more pronounced for the *trans* isomers ($\Delta\Delta$ 0.12-0.13 ppm) due to diastereotopy resulting from the existence of chiral centers at $C_{(4)}$ and $C_{(5)}$ and also the inequivalence of H_A and H_B arising largely from the downfield shift of the signal of H_A (Table 1), which is less in comparison with the *cis* isomers.

The configurational assignments were supported by the ^{13}C NMR data (Table 2). The major differences in the spectra of the *cis* and *trans* derivatives are related to the chemical shift of the methyl group carbon atom at $C_{(4)}$ $C_{(3)}$ and the anisochronicity of the methyl group carbon nuclei of the isopropyl moiety at $C_{(5)}$ $C_{(1)}$, which is more significant for the *trans* isomers. On the other hand, the chemical shifts of the methine carbon $C_{(2)}$ are rather similar to the value observed in the spectrum of model ester **4**, indicating identical orientation of the isopropyl group in all cases. The integral intensity data for the signals for $C_{(3)}$, $C_{(4)}$, $C_{(5)}$, and $C_{(6)}$ showed that the ratio of the *cis* and *trans* isomers corresponds to the gas-liquid chromatography and ^1H NMR spectral data.

The *cis* and *trans* isomers of 5-isopropyl-4-methyl-1,3-dioxane differ in the configuration of $C_{(5)}$ [15, 16], while the configurational features of esters **1-3**, which are similar to those found for the stereoisomers of 5-isopropyl-2,2,4-trimethyl-1,3-dioxa-2-silacyclohexane [25], are related to a change in the orientation of the substituent at $C_{(4)}$. This gives rise to a weakening of the nonbonding interactions in the silicon analog or decrease in their number in six-membered cyclic borate esters containing an atom with a planar configuration (trigonal boron, $B_{(2)}$). In such cases, the axial orientation of $C_{(4)}$–CH_3 in the *cis* isomers becomes favored to an axial isopropyl group at $C_{(5)}$. This conclusion is supported by calculation data for the relative energy of the most stable conformers of ester **1**. Sofa *S* 4a5e for the most stable conformation of the isopropyl group is much more favorable than *S* 4e5a.



S 4a5e
ΔE = 0 (MM+, AM1)

S 4e5a
ΔE = 1.5 kcal/mol (MM+)
2.9 kcal/mol (AM1)

Such structural features are also reflected in the conformational properties of substituted 1,3,2-dioxaborinanes. MM+ and AM1 calculations were carried out for the relative energy of the stereoisomers of ester **1** and model **4** with complete geometrical optimization relative to the rotational angle about the $C_{(5)}$–CH(*i*-Pr) bond (the H_X–C–C–H_Y torsion angle φ) to evaluate the conformational composition of the *cis* and *trans* isomers of esters **1-3.** The AM1 results are shown in Fig. 1, while the MM+ energy curves are similar. These results show that an equilibrium is observed during rotation of the equatorial isopropyl substituent between the sofa conformer and a family of half-chairs (HC 1 and HC 2) with different extents of distortion of the corresponding fragments.

TABLE 2. ^{13}C NMR Spectra of **1, 3,** and **4**

Compound	Chemical shifts, δ, ppm					
	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$
cis-**1**	20.37; 20.66	26.89	16.45	61.13	46.25	68.03
trans-**1**	21.02; 21.50	26.30	17.54	60.84	47.51	69.65
cis-**3**	20.24; 20.61	26.87	16.55	60.97	46.23	67.73
trans-**3**	20.97; 21.54	26.19	17.62	60.53	47.52	68.33
4	19.96	26.93	—	64.57	42.49	64.57

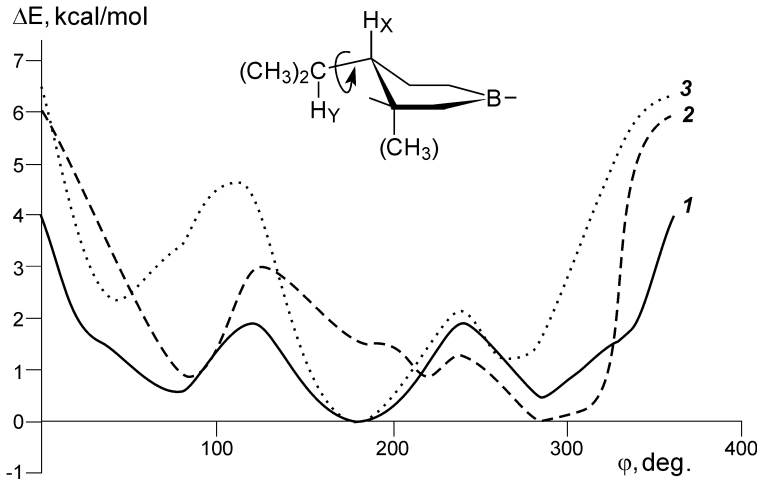
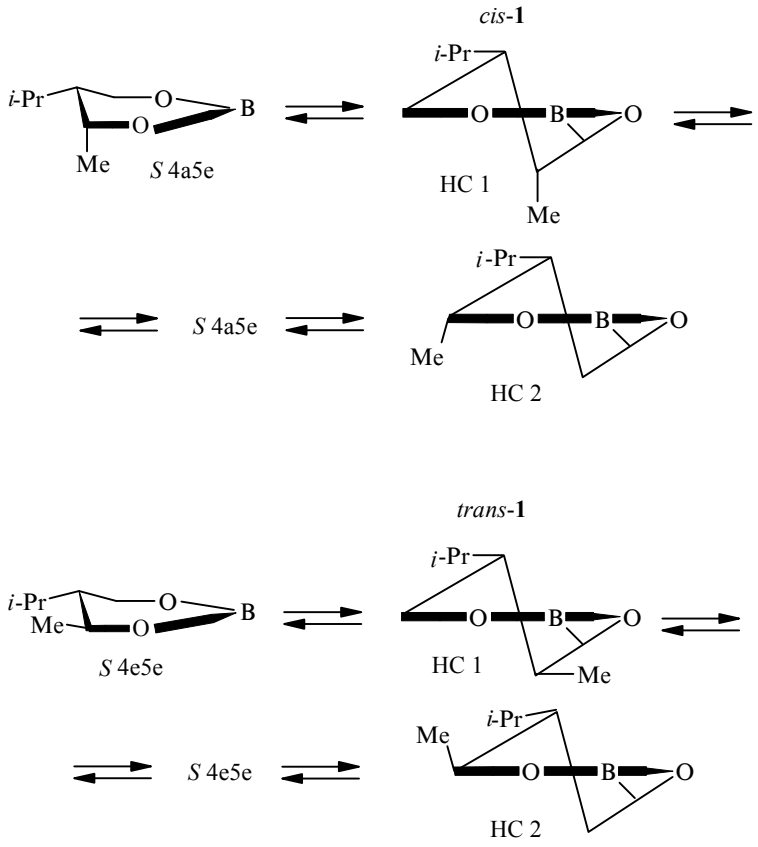
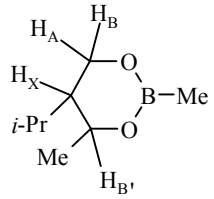


Fig. 1. Change in the total energy of esters **1** and **4** upon rotation of the isopropyl substituent about the $C_{(5)}$–$CHMe_2$ bond: *1*) ester **4**, *2*) *trans*-**1**, *3*) *cis*-**1**.



The change in the total energy (ΔE) of *cis*-**1** upon rotation of the *i*-Pr group by 360° is 6.4 (AM1) and 7.1 kcal/mol (MM+). The corresponding values for *trans*-**1** are 6.0 and 8.6 kcal/mol. The value of ΔE, strictly speaking, should not be seen as the rotational barrier of the isopropyl group since the conformation of the ring itself is altered in such a case. It is readily seen that the ranges for change in ΔE upon conformational

TABLE 3. Limits of Change in the Calculated Vicinal Coupling Constants in the Conformational Equilibrium of Stereoisomers of Ester **1**



Configu-ration	Torsion angle τ, deg. (AM1)			SSCC, *J* Hz		
	τ_{AX}	τ_{BX}	$\tau_{B'X}$	$^3J_{AX}$	$^3J_{BX}$	$^3J_{B'X}$
цис-**1**	180-172.9	57.7-50.8	58.3-48.7	11.4-1.2	4.8-3.8	4.8-3.6
транс-**1**	178.7-65.9	57.0-44.0	179.1-142.9	11.4-10.8	5.7-3.9	10.8-7.6

transformations of the *cis* and *trans* isomers are virtually identical. The sofa with φ 180° for *cis*-**1** and 287° for *trans*-**1** corresponds to the equilibrium conformer (major minimum) in both cases. Two local minima and maxima also exist for each isomer. These points as well as the ascending and descending branches of the curves correspond to a continuously varying set of different modifications of the half-chair or distorted sofa. The symmetrical curve for change in the energy of model ester **4** also contains a global minimum corresponding to the sofa (φ 180°), while the other points are occupied by representatives of the half-chair family.

The calculation results show conformational nonuniformity of the *cis* and *trans* isomers of 2-alkyl-5-isopropyl-4-methyl-1,3,2-dioxaborinanes and model ester **4**. We attempted to evaluate the limits of variation of the vicinal coupling constants in these conformational transformations of the compounds studied in the case of ester **1** using a modification of the Karplus equation [26] and electronegativity data [27] as well as the torsion angles τ between the corresponding protons (AM1 optimized geometry data). The results shown in Table 3 show, that despite some difficulties with the parameters of the equation used and lack of correction for the medium effect (all the calculations were carried out for an isolated molecule in vacuum), the experimental coupling constants given in Table 1 are either within the error limits of the calculated values or close to these limits. This result indicates high conformational flexibility of esters **1-3**, permitting the existence of a considerable number of geometrically nonidentical forms near the minimum similar to other six-membered cyclic systems [28-30].

These data augment our knowledge of the stereochemistry of asymmetrically substituted 1,3,2-dioxaborinanes and should help us predict the conformational composition of such molecules with several chiral centers.

EXPERIMENTAL

The gas-liquid chromatographic analysis was carried out on a Tsvet-126 chromatograph using a flame ionization detector and 3000×4-mm columns packed with 5% OV-17 on Chromaton N-Super and 5% DC-550 on Chromaton N-AW-HMDS. Argon served as the gas carrier. The ^{1}H NMR spectra were taken on a Bruker AM-300 spectrometer at 300 MHz for 10% solutions in $CDCl_3$ relative to TMS as the internal standard. The Fourier-transform ^{13}C NMR spectra were taken on the same spectrometer with natural content of ^{13}C isotope at 75 MHz.

5-Isopropyl-2,4-dimethyl-1,3,2-dioxaborinane (1). Equimolar amounts (0.01 mol) of diisopropyl methylborate and 2-isopropyl-1,4-butanediol in benzene (100 ml) was heated at reflux for 2 h. The solvent was removed and the residue fractionated at atmospheric pressure. Yield of **1** 54%; bp 178-180°C.

Esters **2-4** were described in our previous work [14, 31]. Samples of 2-isopropyl-1,3-butanediol (**5**) with different content of *erythro* and *threo* isomers were obtained according to Bogatsky et al. [15-17].

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